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Preparation of Nitramine-Nitrates by Ring-Opening Nitration of Azetidines by Dinitrogen Pentoxide (N_2O_5)[1]

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Abstract: Eleven azetidines, bearing various types of substituents on the ring nitrogen, were treated with N_2O_5 in chlorinated solvents at sub-ambient temperature and in certain cases formed 1,3-nitramine-nitrate products by a novel ring-opening nitration reaction analogous to that established for aziridines. Yields of the nitramine-nitrates, where ring-opening took place, were generally moderate to high (41-88%), but azetidines bearing N-acyl substituents (acetyl, butyryl or carbamyl) instead underwent nitrolysis of the exocyclic substituent to form N-nitroazetidine. Also, azetidines bearing strongly electron-withdrawing groups such as picryl were inert to attack by N_2O_5. The different reactivity of azetidines compared with aziridines is rationalised in terms of the reduced ring strain of the four-membered ring compounds.

INTRODUCTION

The reactions of three- and four-membered saturated oxygen heterocycles (epoxides and oxetanes) with dinitrogen pentoxide (N_2O_5) in chlorinated hydrocarbons, yielding dinitrate ester products by ring-opening nitration, have already been described[3-5], as have the corresponding reactions of three-membered saturated nitrogen heterocycles (aziridines), which give 1,2-nitramine-nitrates in many cases[6,7]. The products from many of these reactions find application in propellant and explosive technology[8,9]. The purpose of the present paper is to describe the reactions of N_2O_5 with four-membered saturated nitrogen heterocycles, namely azetidines[10].

By analogy with the aziridines, azetidines (**I**) might be expected to form 1,3-nitramine-nitrates (**II**) upon treatment with N_2O_5 (see Scheme 1, route **A**). This indeed has been found to be the case with certain compounds of this class[6], notably those bearing N-alkyl or ethoxycarbonyl substituents (see below), but, as occurred in the aziridine series, albeit there to a more limited extent, the behaviour of the heterocycles is strongly influenced by the nature of the ring nitrogen substituent; in many cases a competing, deacylative, reaction pathway (route **B**) supervenes which gives rise to the nitrolysis product, N-nitroazetidine (**III**). Such behaviour is typified by the parent compound, azetidine (trimethyleneimine), where the exclusive formation of **III** has already been reported[11]. Because of this sensitivity of the reaction to the ring nitrogen substituent, the subsequent discussion is subdivided according to the nature of the substituent carried on the azetidine nitrogen, namely alkyl, aryl, or acyl. Each is now dealt with in turn.

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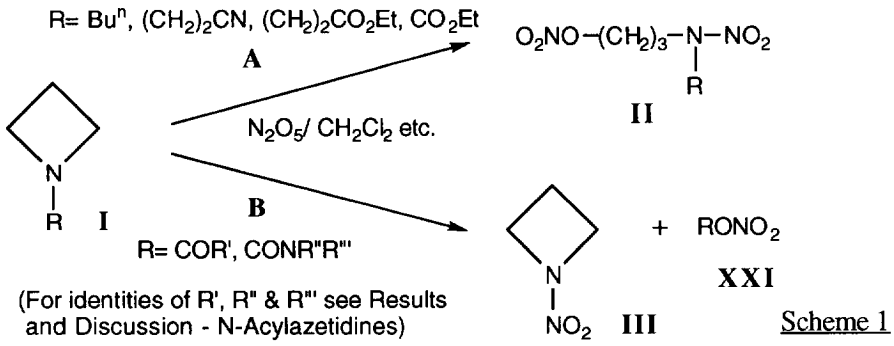
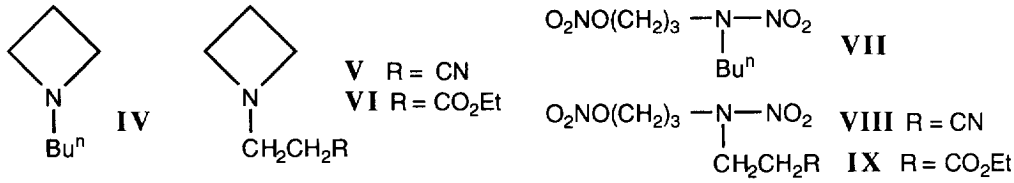


RESULTS AND DISCUSSION

N-Alkylazetidines

Three N-alkylazetidines were studied:- N-(n-butyl)azetidine (**IV**), N-(2-cyanoethyl)azetidine (**V**) and ethyl 3-azetidinylpropionate (**VI**). In each case, treatment with N_2O_5 resulted in moderate to good (41-79%) yields of the corresponding 1,3-nitramine-nitrates (**VII, VIII & IX**; see Table). Each product showed strong bands in the i.r. due to nitramine (1513-1521 cm^{-1}) and nitrate ester (1632 cm^{-1}) asymmetric stretching, and the corresponding symmetric bands around 1280 cm^{-1} were also present. Chemical shifts of the methylene protons adjacent to nitramine were in the range δ 3.7-4.2 ppm, and those adjacent to nitrate ester were at δ 4.53-4.62 ppm, values which correlated well with those reported for the corresponding 1,2-nitramine-nitrates (δ 3.5-4.5 and δ 4.7-4.8 ppm resp.)[7]. In addition, CI mass spectrometric analysis of compound **VIII** was in agreement with the assigned structure[12].



Thus nitramine-nitrates are formed from N-alkylazetidines, in the limited number of cases studied, in acceptable to good yield; i.e. only route **A** (Scheme 1) appears to operate with this class of substituent. Such behaviour will be seen to contrast with that found with other substituents (see below). A limitation of this reaction as a preparative route to 1,3-nitramine-nitrates is, of course, the availability of the azetidine precursors (see experimental section for their synthesis) - the syntheses often depend on functionalising the ring nitrogen of the parent compound, azetidine, which is a scarce pharmaceutical intermediate. Nevertheless, in certain cases (eg **IV** and **VI**), alternative cyclisative routes are also available, although they are more cumbersome experimentally[13].

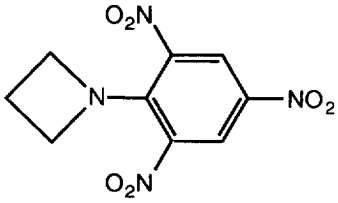
N-Arylazetidines

Two compounds in this category were examined: N-picrylazetidine (**X**) and 2,4,6-tris-(1-azetidinyl)-1,3,5-triazine (**XI**), but in neither case was a useful nitramine-nitrate synthesis realised. With **X**, quite simply no reaction was found to occur, even after 24 hr at *ca* 5°C. Such behaviour contrasts with the aziridine counterpart,

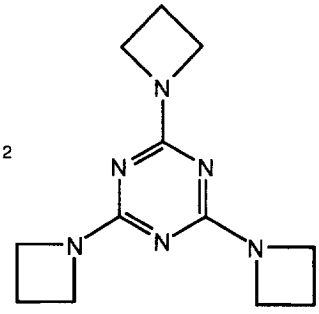
Table: Reactions of Azetidines with N_2O_5

Entry	Azetidine	Mol N_2O_5: Substrate	Solvent	Temp. ℃	Product		Notes
					Compound	Yield (%)	
1	**IV**	1.1:1	CH_2Cl_2	-5±5	**VII**	41	Nitramine-nitrate. Oil
2	**V**	1.1:1	CH_2Cl_2	-5±5	**VIII**	79	Ditto
3	**VI**	1.1:1	CH_2Cl_2	-5±5	**IX**	65	Ditto
4	**X**	1.1:1	CH_2Cl_2	0 to +5	-	0	No reaction
5	**XI**	3.3:1	CH_2Cl_2	0±2	**XII**	60	Impure nitramine-nitrate product (hplc)
6	**XIII**	1.1:1	CH_2Cl_2	-5 to 0	**XIX**	88	Nitramine-nitrate, oil. Identical to authentic sample.
7	**XIV**	1.1:1	CH_2Cl_2	-5 to 0	**III**	70	N-nitroazetidine formed
8	**XV**	1.1:1	CH_2Cl_2	-5 to 0	**III**	75	Ditto + isocyanate by-product
9	**XVI**	1.1:1	CH_2Cl_2	0±5	**III**	86	N-nitroazetidine formed
10	**XVII**	1.1:1	CH_2Cl_2	-5 to 0	**III**	90	ditto
11	**XVIII**	2.2:1	CH_2Cl_2	-5 to 0	**III**	95	ditto

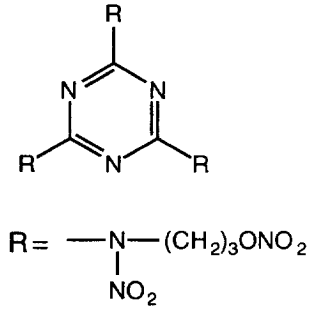
Note: Reaction times were 1.5 - 3 hr, except for entry 4 (24 hr).



X



XI



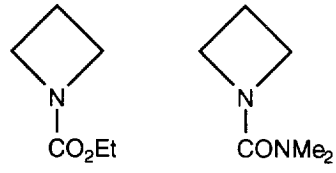
XII

where the nitramine-nitrate, N-(2,4,6-trinitrophenyl)nitraminoethanol nitrate, was isolated in 76% yield within 30 min.[7] Such a contrast in reactivity reflects the lower ring strain of **X** and consequent deactivation of the azetidine ring nitrogen to electrophilic attack.

The heteroaromatic tris-azetidine **XI**, on the other hand, underwent reaction with N_2O_5, but gave, in *ca* 60% yield, a contaminated material which appeared, from i.r. and ^1H nmr analysis, to contain some of the expected nitramine-nitrate **XII** (ν_{max} 1548 and 1633 cm^{-1} due to NO_2 asymm. for nitramine and nitrate ester resp., $\delta(CH_2)$ 4.1-4.7 ppm (cf values in previous section and for aziridine counterpart[14]: δ 4.6-4.8 ppm)). The hplc indicated two closely-eluting components in approximately equal concentrations which possessed very similar u.v. spectra; consequently, isolation would require preparative hplc, which unfortunately time did not permit. Also noteworthy was the absence of N-nitroazetidine (**III**) from the hplc trace - hence nitrolysis (route **B**) does not appear to be the competing reaction. The lack of selectivity observed in this reaction contrasts strongly with the cleanliness of reaction of the aziridine counterpart, where the nitramine-nitrate was obtained in over 90% yield[14].

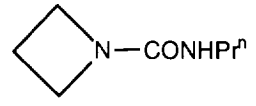
N-Acylazetidines

The remaining six azetidines studied fell into this category, and they are divided into three broad classes: a) carbamates (**XIII**), b) ureas (**XIV** & **XV**) and c) amides (**XVI**, **XVII** & **XVIII**). These are now considered in turn.

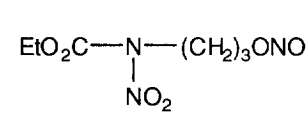


XIII

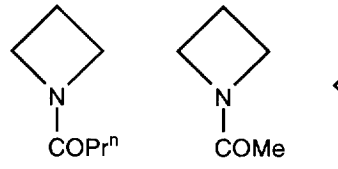
XIV



XV

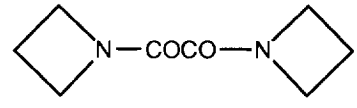


XIX

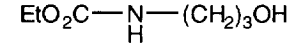


XVI

XVII



XVIII



XX

a) Carbamates. The sole example of this category of compound was interesting in that it behaved differently from the other N-acylazetidines. When **XIII** was treated with N_2O_5, ring-opening nitration took place predominantly to give the nitramine-nitrate (**XIX**) in 88% yield. The product was identical (spectra, chromatography) with an authentic sample prepared by nitration of ethyl N-(3-hydroxypropyl)carbamate (**XX**). The behaviour of carbamate **XIII** thus parallels that of the N-alkyl azetidines described above and also that of the majority of aziridines, except for those in the amide category (which also gave low yields of nitramine-nitrates[7]).

b) Ureas. Two compounds in this class were examined, a fully-substituted urea **XIV**, and one bearing one N-H function, **XV**. Both gave N-nitroazetidine (**III**) as the principal product in 70-75% yield, by a deacylative nitrolysis reaction (route **B**, Scheme 1), with no ring-opened products (nitramine-nitrates) being

evident. Small amounts of by-products were observed; in the case of **XIV** presumably an acyl nitrate (**XXI**, R = Me_2NCO), whilst with **XV** an isocyanate-containing by-product was evident from the i.r. (The mode of formation of the latter is unclear but may involve hydride abstraction from **XV** by N_2O_5[15] followed by rearrangement of the resulting ureido cation.)

The reasons for the difference in behaviour of these azetidines from their aziridine counterparts (which gave nitramine-nitrates in up to 83% yield[7]) has already been commented upon[11], and it appears that the reduced ring strain energy of the azetidines influences the reaction pathway to such an extent that these acylamines behave as normal secondary aliphatic derivatives which are known to undergo such cleavage reactions[16].

c) Amides. Three compounds in this class were studied, two simple N-acyl derivatives **XVI** and **XVII** and the diazetidine **XVIII**. In each case, as with the ureas described above, N-nitroazetidine (**III**) was the sole identifiable product, obtained in somewhat higher yields of 86-95%, formed again by deacylative nitrolysis (route **B**, Scheme 1). With N-acetylazetidine (**XVII**) the product (**III**) was obtained in highest purity owing to the facility of removing the volatile acyl nitrate co-product, acetyl nitrate, and this reaction therefore constitutes a ready means of preparing **III**. The behaviour of these amides contrasts with that of their aziridine counterparts, where mixtures were generally obtained containing appreciable amounts (*ca* 15%) of nitramine-nitrates. Evidently once again the reduced propensity of the azetidine ring to undergo ring opening directs the reaction along the deacylative pathway.

Conclusions

Of the eleven azetidines studied, formation of 1,3-nitramine-nitrate products by ring-opening nitration reactions upon treatment with N_2O_5 in chlorinated solvents was a less general reaction than that utilised hitherto with epoxides, oxetanes and aziridines. Where ring-opening took place (N-alkyl- and ethoxycarbonyl-azetidines), yields of the nitramine-nitrates were generally moderate to high (41-88%). However, azetidines bearing N-acyl substituents (acetyl, butyryl, carbamyl etc.) instead underwent nitrolysis of the exocyclic substituent to form N-nitroazetidine. This behaviour contrasts with that of the corresponding aziridines, where in many cases high yields of nitramine-nitrates were obtained. Furthermore, azetidines bearing strongly electron-withdrawing groups such as picryl were inert to attack by N_2O_5, and the attempted nitration of a 1,3,5-triazinyl derivative resulted in formation of a mixture, whereas the analogous reactions in the aziridine series had yielded useful syntheses of polynitrated materials. The different reactivity of azetidines compared with aziridines is believed to result from the reduced ring strain of the four-membered ring compounds, so that such compounds in many cases behave as ordinary secondary amines.

EXPERIMENTAL

1. Materials and apparatus

All materials were used as received unless otherwise stated. Azetidine (trimethyleneimine) was supplied by Fluka Ltd (purum grade). Butyryl chloride, N-(n-propyl)isocyanate and 2,4-dinitroanisole were supplied by Aldrich Chem. Co. Ltd. 2,4,6-Trinitroanisole was prepared by nitration of 2,4-dinitroanisole as described in the literature[17] and had m.pt. 67-67.5°C (lit.[17] 67°C).

N-(n-Butyl)azetidine (**IV**) was prepared by the method of Elderfield *et al*[18] and had b.pt. 41-42°C/ 80 mbar (lit.[18] b.pt. 53-55°C/ 55 mm), ^{1}H nmr: δ ($CDCl_3$) 0.90 (t,3); 1.28 (m,4); 1.9-2.5 (m,4); 3.15 (t,4) ppm,

ν_{max} (film): 1197(w) cm^{-1}. N-(2-Cyanoethyl)azetidine (**V**) was prepared by the method of Chen *et al*[19], ^1H nmr: δ ($CDCl_3$) 1.8-2.9 (m,6); 3.27 (t,4) ppm; ν_{max} (film): 2248 (CN) cm^{-1} (lit.[19] ν_{max} 2250 cm^{-1}). Ethyl 3-azetidinylpropionate (**VI**) was prepared similarly (from azetidine and ethyl acrylate) and had b.pt. 105-110°C/ 8 mm, ^1H nmr: δ ($CDCl_3$) 1.20 (t,3); 1.9-2.8 (m,6); 3.17 (t,4); 4.13 (qr,2); ν_{max} (film): 1736 (CO) cm^{-1}. N-(Ethoxycarbonyl)azetidine (**XIII**) was prepared by the method of Sheehan *et al*[20] and had b.pt. 90-95°C/ 5 mm (lit.[20] 78°/ 15 mm), ^1H nmr: δ ($CDCl_3$) 1.21(t,3); 2.20 (qn,2); 4.07 (t,4); 4.13 (qr,2) ppm. 2,4,6-Tris-(1-azetidinyl)-1,3,5-triazine (**XI**) was prepared by the method of Schaefer[21], m.pt.(from ethanol-benzene) 260°C dec. (lit.[21] 256-259°C), ^1H nmr: δ ($CDCl_3$) 2.23 (qn,6); 4.10 (t,12).

Other N-acylazetidines (except N-(n-propyl)-N',N'-(trimethylene)urea - see below) were prepared by reaction of the corresponding acyl chloride with azetidine in the presence of an auxiliary base, as exemplified by the preparation of N-butyrylazetidine (**XVI**):- a mixture of azetidine (7.63 g, 134 mmol) and N,N,N',N'-tetramethylguanidine (17.0 g, 147 mmol) in benzene (80 ml) was added dropwise over 50 min. at 10 to 15°C (ice-bath cooling) to butyryl chloride (14.3 g, 135 mmol) in the same solvent (100 ml). The mixture was stirred for 1.5 hr at room temp. and then filtered to remove N,N,N',N'-tetramethylguanidinium chloride. Evaporation under reduced pressure at below 40°C gave a pale yellow oil which was filtered through glass wool and distilled (Kugelrohr) to give *N-butyrylazetidine* (**XVI**), 13.06 g (77%), b.pt. 100-115°C/ 0.9 mm, ^1H nmr: δ ($CDCl_3$) 0.65 (m,5); 1.15-2.2 (m,4); 3.75 (t,2); 3.90 (t,2) ppm; ν_{max} (film): 1649 (CO) cm^{-1}. Similarly prepared were *N-acetylazetidine* (**XVII**) (52% after fractionation[22]), b.pt. 83.5°C/ 9 mm (lit.[23] 46°C/ 1 mm), ^1H nmr: δ ($CDCl_3$) 1.80 (s,3); 2.20 (qn,2); 4.00 (t,2); 4.12 (t,2) ppm; ν_{max} (film): 1647 (CO) cm^{-1}, and *N,N-dimethyl-N',N'-(trimethylene)urea* (**XIV**) (from azetidine and N,N-dimethylcarbamyl chloride[24]), b.pt. 100-115°C/ 0.9 mm (lit.[25] 62-63°C/ 1.33 hPa). ^1H nmr: δ ($CDCl_3$) 2.18 (qn,2); 2.80 (s,6); 3.95 (t,4) ppm; ν_{max} (film): 1640 (CO) cm^{-1}.

1,1'-Oxalyldiazetidine (**XVIII**) was prepared from azetidine and oxalyl chloride as follows: oxalyl chloride (6.35 g, 50 mmol) in benzene (10 ml) was added dropwise with stirring at 5 to 15°C (ice-salt bath cooling) to a mixture of azetidine (5.70 g, 100 mmol) and triethylamine (5.55 g, 55 mmol) in the same solvent (30 ml). The addition was complete after 1 hr (further benzene (30 ml) added to facilitate stirring), and after stirring a further 30 min. at 15°C, the mixture was filtered through celite to give a clear brown solution. Removal of solvent under reduced pressure gave 1,1'-oxalyldiazetidine (**XVIII**) as an off-white solid (6.15 g, 73%), which was recrystallised from propan-2-ol and dried in a vacuum oven, m.pt. 119-120.5°C. ^1H nmr: δ ($CDCl_3$) 2.31 (qn,4); 4.11 (t,4); 4.60 (t,4) ppm; ν_{max} (mull): 1632 (CO) cm^{-1}.

N-(n-Propyl)-N',N'-(trimethylene)urea (**XV**) was prepared from azetidine and N-(n-propyl)isocyanate as follows:- a solution of azetidine (4.10 g, 72 mmol) in anhydrous ether (5 ml) was added dropwise with stirring over 30 min. to the isocyanate (5.30 g, 62 mmol) in the same solvent (20 ml); a flocculent precipitate of the product separated shortly after commencement of the addition, and further ether (40 ml) was added to assist stirring. After a further 10 min., the solid mass was filtered, washed well with ether and dried under vacuum to give *N-(n-propyl)-N',N'-(trimethylene)urea* (**XV**) as colourless fine needles (7.07 g, 81%), m.pt. 102-103°C (from acetonitrile), ^1H nmr: δ ($CDCl_3$) 0.87 (t,3); 1.45 (qn,2); 2.20 (qn,2); 3.15 (qr,2); 3.95 (t,4); 4.4 (br.s, 1) ppm; ν_{max} (mull): 1660 (CO) cm^{-1}.

N-(2,4,6-Trinitrophenyl)azetidine (**X**) was prepared from azetidine and 2,4,6-trinitroanisole as follows:- azetidine (1.2 g, 21 mmol) in methanol (4 ml) was added dropwise with stirring at room temp. over 10 min. to trinitroanisole (4.86 g, 20 mmol) in the same solvent (50 ml). An orange precipitate separated and, after stirring

a further 1.5 hr, the reaction mixture was filtered and the resulting solid dried under vacuum to give *N-(2,4,6-trinitrophenyl)azetidine* (**X**) as an orange-red solid (4.98 g, 93%), m.pt. 171-172.5°C (from 1,4-butyrolactone), ^{1}H nmr: δ (D_6-acetone) 2.5 (m,2); 4.18 (t,4); 8.88 (s,2) ppm; δ (D_6-DMSO) 2.32 (qn,2); 4.05 (t,4); 8.85 (s,2) ppm; ν_{max} (mull): 1565, 1531, 1512 (NO_2 asymm.); 1352, 1328 (NO_2 symm.) cm^{-1}.

Solvents and the remaining inorganic reagents were all supplied by BDH (reagent grade) with the following exceptions: dichloromethane was hplc grade (BDH); methanol, acetonitrile and water used in hplc separations were Fisons hplc grade (acetonitrile was "Far u.v." grade); 95% ethanol was supplied by Burroughs Ltd; $CDCl_3$ by Aldrich (99.5% isotopic purity); fuming nitric acid (95-98% assay) by BDH Ltd. N_2O_5 was prepared by ozonation of N_2O_4[26] and was storable for short periods at -40 to -80°C. Dichloromethane was dried by passage through a column of chromatographic silica gel (BDH), and $CDCl_3$ was allowed to stand over 4A molecular sieves (BDH) before use. Acetic anhydride was supplied by Fisons plc (reagent grade). All other reagents were used as received.

^{1}H nmr spectra were recorded on a Varian Associates EM 360A nmr spectrometer equipped with an EM 3630 homonuclear lock-decoupler operating at 60 MHz (except where marked thus: # - Varian XL 200 spectrometer operating at 200 MHz). Chemical shifts are reported in ppm downfield from tetramethylsilane (TMS) used as internal standard. The ^{13}C nmr spectrum was run on a Varian XL 200 spectrometer, operating at 50 MHz). Chemical shifts are reported in ppm from the TMS position. Infra-red spectral measurements were carried out using either a Nicolet 5SX Fourier transform i.r. spectrometer operating in transmittance mode and equipped with DTGS detector, or a Perkin-Elmer 157G i.r. spectrometer.

Hplc separations were performed on a Waters 600 Series gradient system linked to a Waters WISP 710 autosampler with monitoring by a Pye-Unicam PU4021 u.v. spectrophotometer operating at 210 nm unless otherwise stated. Output was to Pye-Unicam 4850 Video Chromatography Control Centre. Columns used measured 22 cm x 5 mm with Lichrosorb RP18 (7μ) packings (Merck GmbH) and were supplied pre-packed by BDH Ltd, Poole.

Melting points were determined in open capillaries on a Büchi 510 apparatus using a heating rate of 3°C/min. and are uncorrected.

CAUTION: All reactions utilising N_2O_5 were carried out in armoured cupboards.

2. Reactions of azetidines with N_2O_5

General, and Description of Standard Method. Eleven N-substituted azetidines were submitted to reaction with N_2O_5; five were found to yield nitramine-nitrate products, a further five yielded principally N-nitroazetidine (**III**), and one failed to react. Workup methods for those reactions which did not yield nitramine-nitrates are detailed separately (see "Other Methods"). Details of quantities of reagents and conditions employed in this and the following section, where not specifically mentioned, are as indicated in Table 1.

The following compounds were treated by the standard method and yielded nitramine-nitrates:-

a) N-(2-Cyanoethyl)azetidine (**V**)

b) N-(n-Butyl)azetidine (**IV**)

c) N-(Ethoxycarbonyl)azetidine (**XIII**)

d) Ethyl 3-azetidinylpropionate (**VI**)

e) 2,4,6-Tris(1-azetidinyl)-1,3,5-triazine (**XI**).

The substrate (20 mmol) was dissolved in the appropriate solvent (10-15 ml) and added dropwise with stirring and cooling to a solution of N_2O_5 (22 mmol) in the same solvent (20-40 ml). After addition was complete (usually 10-15 min.) the mixture was stirred for a further 0.5-1 hr at the temperature of addition. Thereafter the mixture was allowed to warm to room temperature and stirred at this temperature for an additional period of 1-2 hr, or until completion of reaction was indicated (tlc, hplc or ^{1}H nmr). The reaction mixture was then drowned in ice-water (30-40 ml) and the organic layer separated. The aqueous layer was extracted with dichloromethane and the combined extracts were washed further with saturated sodium bicarbonate solution, dried over anhydrous $MgSO_4$ and evaporated under water-pump vacuum below 30°C. The product was then identified by spectroscopy and, in certain cases, examined by hplc to assess its purity.

The products were characterised as follows (yields shown in parentheses):-

a) *N-(2'-cyanoethyl)-3-(nitramino)propanol nitrate* (**VIII**) 79%, oil. ^{1}H nmr: δ ($CDCl_3$) 2.20 (qn,2); 2.90 (t,2); 4.05 (m,4); 4.62 (t,2) ppm; ν_{max} (film): 1631, 1521 (NO_2 asymm.); 1280 (NO_2 symm.) cm^{-1}. The CI mass spectrum[12] was in agreement with the assigned structure.

b) *N-(n-butyl)-3-(nitramino)propanol nitrate* (**VII**) 41%, oil. ^{1}H nmr: δ ($CDCl_3$) 0.95 (t,3); 1.52 (m,4); 2.18 (qn,2); 3.76 (t,2); 3.88 (t,2); 4.58 (t,2) ppm; ν_{max} (film): 1632, 1513 (NO_2 asymm.); 1280 (NO_2 symm.) cm^{-1}.

c) *ethyl N-(3-hydroxypropyl)nitrocarbamate nitrate* (**XIX**) 88%, oil. The ^{1}H nmr and i.r. spectra and chromatographic behaviour of this compound were identical to those of an authentic sample (see section 3).

d) *N-(2-(Ethoxycarbonyl)ethyl)-3-(nitramino)propanol nitrate* (**IX**) 65%. ^{1}H nmr: δ ($CDCl_3$) 1.28 (t,3); 2.15 (qn,2); 2.78 (t,2); 3.85-4.15 (m,4); 4.17 (qr,2); 4.53 (t,2) ppm; ν_{max} (film): 1732 (CO); 1632, 1518 (NO_2 asymm.); 1279 (NO_2 symm.) cm^{-1}.

e) *N,N',N''-Tris(3-hydroxypropyl)-N,N',N''-trinitromelamine trinitrate* (**XII**) 60%, in admixture with an unidentified material which could only be separated by hplc (see discussion). ^{1}H nmr: δ ($CDCl_3$) 2.1-2.45 (m, 6); 4.1-4.7 (m,12) ppm; ν_{max} (film): 1633 (NO_2 asymm.), 1601, 1548 (NO_2 asymm.), 1385, 1282 & 1251 (NO_2 symm.) cm^{-1}. The hplc trace (RP18 column, acetonitrile-water 60:40 eluant) indicated the absence of N-nitroazetidine (**III**).

Other Methods. The following compounds were treated by the standard method and yielded N-nitroazetidine[11] as the principal product (together with, in some cases, other ill-defined components, likely acyl nitrates and other decomposition products):-

f) N,N-Dimethyl-N',N'-(trimethylene)urea (**XIV**)

g) N-(n-Propyl)-N',N'-(trimethylene)urea (**XV**)

h) N-Butyrylazetidine (**XVI**).

i) N-Acetylazetidine (**XVII**)

j) 1,1'-Oxalyldiazetidine (**XVIII**)

For example, with N,N-dimethyl-N',N'-(trimethylene)urea (**XIV**), an oil was obtained, ^{1}H nmr: δ ($CDCl_3$) 2.20 (qn,2); 3.42 (s,1.6); 3.45 (s, 1.6); 4.38 (t,4) ppm [N-nitroazetidine lit.[11] δ ($CDCl_3$) 2.21(quin., 2H, J = 8 Hz), 4.42(t, 4H, J = 8 Hz) ppm]; the signals at *ca* δ 3.4 ppm are presumably due to the acyl nitrate $O_2NOCON(CH_3)_2$ formed as co-product. Chromatography of the product mixture (RP18, acetonitrile-water 50:50, internal standard: diethyl phthalate) showed a prominent post-eluting peak, R_t 314 s. (cf **III**, 241 s.). In the case of N-(n-propyl)-N',N'-(trimethylene)urea (**XV**), an i.r. band at 2280 cm^{-1} was also observed, likely

due to isocyanate (see discussion). By contrast, when N-acetylazetidine (**XVII**) and 1,1'-oxalyldiazetidine (**XVIII**) were treated with N_2O_5 (1.1 and 2.2 mol resp.), the acyl nitrate by-products were volatile and, after evaporation (prolonged in the case of the product from **XVIII**), yields of N-nitroazetidine (**III**) were obtained of 92 and 95% respectively. The hplc traces of these products (RP18 column, acetonitrile-water 60:40 eluant) showed that no significant amounts of by-products were present.

The following compound was inert to reaction with N_2O_5, and was recovered unchanged from the reaction mixture:-

k) N-(2,4,6-Trinitrophenyl)azetidine (**X**). The azetidine, dissolved in anhydrous sulpholane, was added to N_2O_5 as described above; after 24 hr, workup in the usual manner afforded an orange oil which, from ^{1}H nmr and hplc, was found to contain the unchanged azetidine (47%). No N-nitroazetidine (**III**) was detected (hplc).

3. Preparation of authentic nitramine-nitrates

Ethyl N-(3-hydroxypropyl)carbamate (**XX**) was nitrated to the nitrocarbamate-nitrate (**XIX**) using acetyl nitrate as follows: Acetyl nitrate solution was prepared[27] by dropwise addition of fuming nitric acid (0.55 ml, 11.25 mmol) with vigorous stirring at a temperature not exceeding 12°C (but >5°C) to acetic anhydride (3 ml). The resulting solution was kept at 12 to 15°C for 10 min., then the carbamate[28], as a neat liquid (0.51 g, 3.5 mmol), was added dropwise over 1 min. with rapid stirring to the nitrating solution at 20±5°C (cardice-acetone cooling), and stirring was continued at 15 to 20°C for a further 20 min. The mixture was then poured into water (10 ml) and stirred for 1 hour at room temperature. The pale yellow oil which separated was transferred by pipette to a separating funnel containing ether (10 ml) and the ethereal solution was washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$ and evaporated to yield *ethyl N-(3-hydroxypropyl)-nitrocarbamate nitrate* (**XIX**) as a pale yellow oil (0.55 g, 67%). ^{1}H nmr#: δ ($CDCl_3$) 1.385 (t,3; J = 7.1 Hz); 2.164 (qn,2; J = 6.4 Hz); 4.227 (t,2; J = 6.7 Hz); 4.395 (qr,2; J = 7.1 Hz); 4.550 (t,2; J = 6.1 Hz) ppm; ^{13}C nmr#: δ ($CDCl_3$) 14.03, 26.11, 46.07, 65.11, 70.06, 150.34 ppm; ν_{max} (film): 1780, 1745 (CO); 1645, 1635, 1580 (NO_2 asymm.); 1280 (NO_2 symm.) cm^{-1}.

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