Tetrahedron Letters,Vol.29,No.22,pp 2731-2734,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

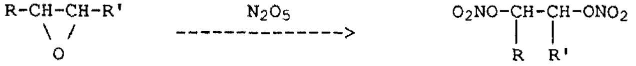
NITRATION BY OXIDES OF NITROGEN, PART 1: PREPARATION OF NITRATE ESTERS BY REACTION OF STRAINED-RING OXYGEN HETEROCYCLES WITH DINITROGEN PENTOXIDE

P Golding, R W Millar*, N C Paul and D H Richards (deceased)
Ministry of Defence, R.A.R.D.E., Powdermill Lane, Waltham Abbey, Essex EN9 1AX.

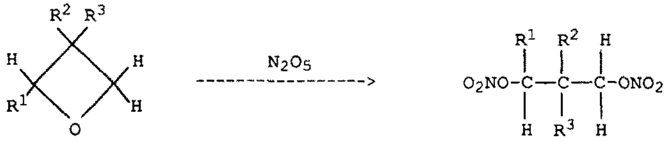
Summary: Epoxides and oxetanes react with dinitrogen pentoxide to give the corresponding dinitrates in high to near quantitative yields. The scope and limitations of the method are briefly discussed.

We describe herein a novel method for the preparation of polynitrates (nitrate esters of polyols), which are important ingredients of many explosives and propellants[1], and are also used medicinally[2] and as protecting groups in sugar chemistry[3]. Nitrate esters are usually prepared by reacting the appropriate alcohol with a nitrating agent such as pure nitric acid or nitric acid-sulphuric acid mixtures[4], although recent reports describe their preparation by the reaction of alcohols or their derivatives (eg triflates) with novel nitrating agents such as thionyl chloride nitrate[5] or tetrabutylammonium nitrate[6], or by direct attack on alkenes by electrophiles such as thallium (III) nitrate[7] or mercury (II) nitrate[8]. Other well established methods include transfer nitrations utilising the action of nitrocollidinium tetrafluoroborate[9] or acridinium nitrate[10] on alcohols, as well as attack by mercury (I) or mercury (II) nitrates on alkyl halides[11]. Many of these methods are unsuitable for large-scale application, however, since they employ excessively expensive or toxic reagents, or are not directly applicable to polynitrate synthesis.

Our method uses a non-hydroxylic starting material, a small-ring oxygen heterocycle, which is cleaved upon reaction with an oxide of nitrogen, principally dinitrogen pentoxide (N_2O_5), a material readily and cheaply preparable by ozonation of dinitrogen tetroxide[12]. Poly- (di-, tri- and tetra-) nitrates are thus generated, arising from cleavage of the ring at the C-O bond with addition of one mole of N_2O_5 and consequent relief of ring strain (eqns 1A & 1B). The reaction is carried out in a halogenated solvent at sub-ambient temperature, and the polynitrate is formed cleanly and in high to near-quantitative yield in all but two cases (Table).

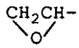


---------- 1A



---------- 1B

TABLE

Entry	Heterocycle			Mol N_2O_5: substrate	Reaction time (min.)	Temp. °C	Yield %
	A. Epoxides						
	R	R'					
1	H	H		1.1:1	5	10 to 15	96[1,16]
2	Me	H		1.1:1	5	10 to 15	96[1,17]
3	Me	Me		1.1:1	5	15 to 20	94[1]
4	Et	H		1.1:1	5	15 to 20	96[17]
5	$-(CH_2)_4-$			1.1:1	5	15 to 20	>97
6	Ph	H		1.1:1	15	-5 to 5	96
7	Ph	Ph		1.1:1	15	-5 to 5	94[18]
8	CH_2OH	H		3.0:1	240	0 to 10	73*[1,16]
9		H		3.0:1	270	0 to 10	55**[1]
	B. Oxetanes						
	R^1	R^2	R^3				
10	H	H	H	1.33:1	45	5 to 10	88[1]
11	H	$-(CH_2)_5-$		1.33:1	180	10 to 15	86
12	H	Me	Me	1.33:1	180	10 to 15	73
13	H	CH_2OH	Me	4.0:1	28 hr	0 to 10	88*[1]
14	Me	Et	Et	1.30:1	180	-10 to 0	16
15	Pr^n	Et	H	1.37:1	90	-5 to 5	21

Notes

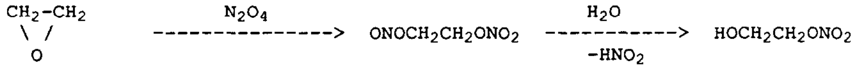
All reactions were carried out in dichloromethane; in entries 8 & 9, anhydrous aluminium chloride (1 mol) was also added as catalyst.
All yields are isolated yields.
All products were identical to authentic samples prepared by nitration of the corresponding polyols (except for entries 6 & 7, which were identified by i.r. and ^1H nmr spectroscopy).
* Trinitrate
**Tetranitrate

A typical procedure is as follows: CAUTION: Many of the products described herein are highly explosive and appropriate precautions should be taken in their handling. A dry flask of appropriate size, fitted with a thermometer and a guard tube containing anhydrous calcium chloride, was placed in a constant temperature bath and a known weight of N_2O_5 (25 to 50 ml solution in dichloromethane) was added with magnetic stirring. When the solution was at *the stated temperature (Table) sufficient dichloromethane solution of the oxygen heterocycle (ca 500mg per ml) was added over 2 to 5 mins to achieve the stated molar ratio. The mixture was then stirred for the appropriate time, agitated with saturated sodium hydrogen carbonate solution to remove any excess acidity, and the dichloromethane layer was separated, dried over anhydrous magnesium sulphate and filtered. Removal of solvent from the filtrate under reduced pressure (temperature <30°C) gave the product, generally in the form of a viscous oil.*

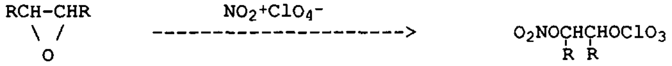
Thus the cleavage of small-ring oxygen heterocycles by N_2O_5 constitutes a general route for the introduction of nitro groups which possesses advantages over conventional nitrations, namely: i) ease of temperature control - reactions are essentially non-exothermic, ii) simple product separation - evaporation of solvent often suffices, iii) absence of waste acids for disposal and iv) high selectivity in position of attack - stilbene and styrene oxides are not attacked in the aromatic ring. With hydroxyl-containing substrates, eg glycidol and 3-methyl-3-(hydroxymethyl)oxetane, the ring cleavage proceeds in similar manner, albeit under more forcing conditions; when 2 mol N_2O_5 are used the corresponding trinitrates are formed, consistent with the reported facility of hydroxyl group nitrations by this reagent[13]. Butadiene diepoxide (entry 9) was likewise deactivated, presumably for steric reasons, and forcing conditions ($AlCl_3$ catalyst) were also required with this substrate.

Problems from side-reactions were encountered rarely: oligomer formation (by cationic ring-opening polymerisation of the heterocycle) occurred in general only if the mode of addition of the reagents was reversed, whilst oxidative degradation was only a problem with highly substituted (polyalkyl) substrates in which ring opening was hindered. Finally, it was established that ring strain in the substrate was essential for the formation of polynitrates in high yield: cyclic ethers with ring size greater than four or acyclic ethers reacted very slowly to give only traces of nitrate esters, yielding instead mainly oxidation products such as aldehydes and carboxylic acids.

Prior to this study, only one instance of the cleavage of small-ring oxygen heterocycles by an oxide of nitrogen had been reported[14]. Here, ethylene oxide and its alkyl derivatives were reacted with N_2O_4 (eqn 2) to yield, as isolated products, 1,2-diol mononitrates, which could only be converted to polynitrates in a separate stage utilising conventional nitration media. We have established further that the intermediate nitrite-nitrate can be converted *in situ* by oxidation with ozone to the dinitrate, but conclude that direct nitration to the dinitrate as shown in eqn 1A is preferable. After the commencement of this study a report appeared describing a closely-related reaction, the cleavage of epoxides by nitronium perchlorate[15] (eqn 3) to yield covalent perchlorate derivatives. No experimental details were given, however, and because such products are of little practical value, being dangerously unstable, this route is of limited value. In contrast, our method has been shown to have wide applicability generating valuable products using cheap and readily available reagents. Additional synthetic and mechanistic aspects will be presented in future publications.



$$\underset{\diagdown O \diagup}{CH_2-CH_2} \xrightarrow{N_2O_4} ONOCH_2CH_2ONO_2 \xrightarrow[-HNO_2]{H_2O} HOCH_2CH_2ONO_2 \qquad \text{---------- 2}$$



$$\underset{\diagdown O \diagup}{RCH-CHR} \xrightarrow{NO_2{}^+ClO_4{}^-} O_2NO\underset{R}{C}H\underset{R}{C}HOClO_3 \qquad \text{---------- 3}$$

Acknowledgements

The authors wish to thank Dr A V Cunliffe and Mr R Morrell for assistance with nmr spectroscopy, and the following for assisting in the synthesis of precursor compounds: Mr D Harrison, Mrs J. Mistry, Mr S Palmer, Mr R Doctor and Mr I Brown.

References

1. T Urbanski, "Chemistry and Technology of Explosives", Vol. 2, Pergamon Press, Oxford, 1967

2. R E Kirk and D F Othmer, "Encyclopedia of Chemical Technology", 1st Edition, Vol. 3, p 221 (The Interscience Encyclopedia Inc., New York, 1949)

3. Ref. 2, Vol. 13, p 264 (1954)

4a R Boschan, R T Merrow and R W van Dolah, *Chem. Rev.*, 55, 485-510 (1955)
 b Ref. 1, p 20
 c P A S Smith "Open Chain Nitrogen Compounds", Vol. 2, 483-490, Benjamin, New York, 1966

5. G Hakimelahi, H Sharghi, H Zarrinmazeli and A Khalafi-Nezhad, *Helv.Chim. Acta,* 67(3), 906 (1984)

6. N Afza, A Malik, F Latif and W Voeltzer, *Liebig's Annalen*, 1929 (1985)

7. W J Layton, C P Brock, P A Crooks and S L Smith, *J. Org. Chem.*, 50, 5372 (1985) and references contained therein

8. A Bloodworth and P N Cooper, *Chem. Commun.,* 709 (1986)

9. S C Narang, R L Pearson and C A Cupras, *Synthesis,* 452 (1978)

10. A R Katritzky and L Marzorati, *J. Org. Chem.*, 45, 2515 (1980)

11. A McKillop and M E Ford, *Tetrahedron*, 30, 2467 (1974)

12. C C Addison and N Logan, *Dev. Inorg. Nitrogen Chem.* (Ed. C B Colburn), Vol. 2, 42 (1973)

13. J W H Oldham, *J. Chem. Soc.* 127, 2480 (1925)

14a A M Pujo and J Boileau, *Mém. Poudres*, 37, 35 (1955)
 b A M Pujo, J Boileau and C Fréjacques, *Compt. Rend.*, 239, 974 (1955)

15. N S Zefirov, A S Kozmin, N M Yureva, V V Zhdankin and V N Kirin, *Bull. Acad. Sci. USSR Div. Chem. Sci. Part 2,* 32(3), 642 (1983)

16. F Pristera, *Analyt. Chem.*, 25, 844 (1953)

17. T Urbanski and M Witanowski, *Trans. Faraday Soc.*, 59, 1039, 1510 (1963)

18a L D Hayward, M Jackson and I G Csizmadia, *Canad. J. Chem.*, 43, 1656 (1965)
 b R J Bertsch and R J Ouellette, *J. Org. Chem.*, 39, 2755 (1974)

(Received in UK 6 April 1988)