Reactions of 3-phenyloxetane and 7-oxabicyclo[2.2.1]heptane with dinitrogen pentoxide in dichloromethane

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3-Phenyloxetane reacts initially almost entirely by *ortho* and *para* aromatic nitration. This is followed by oxetane ring-opening to give the corresponding 2-arylpropane-1,3-diol dinitrates. The oxetane ring-opening reactions, and the reaction of 7-oxabicyclo[2.2.1]heptane to give exclusively *trans*-cyclohexane-1,4-diol dinitrate, are approximately second order in dinitrogen pentoxide and have highly negative entropies of activation.

Introduction

Oxiranes[1] and 3-substituted oxetanes[2] react with dinitrogen pentoxide in dichloromethane to give the corresponding dinitrates in good yield. These and related reactions are of considerable interest as new synthetic routes for energetic materials.[3] We have sought to investigate the mechanism of these and related reactions.[4–7] We report here on the reaction of 3-phenyloxetane, **1** and of a strained five-membered cyclic ether, 7-oxabicyclo[2.2.1]heptane, **9**, with dinitrogen pentoxide.

In our study of the reaction of **1** with nitric acid in dichloromethane,[7] we found the reaction to be a mixture of aromatic nitration (to give **3** and **5**) followed by oxetane ring-opening, and oxetane ring-opening (to give **2**) followed by aromatic nitration. Both routes led to the same pair of products, **4** and **6**. Aromatic nitration kinetics exhibited a higher order in nitric acid than oxetane ring-opening, and the former route was thus preferred at the higher concentrations of nitric acid. With N_2O_5, initial aromatic nitration is overwhelmingly preferred, and subsequent oxetane ring-opening is relatively slow, as discussed below.

The reaction of 7-oxabicyclo[2.2.1]heptane, **9**, a strained five-membered ring cyclic ether, was of interest in extending the range of cyclic ethers which can be ring-opened in this way, the more so because unstrained cyclic five- and six-membered cyclic ethers give only low yields of the corresponding dinitrates.[8] There is the added advantage that stereochemical information can be gained from the possibility of *cis* and *trans* isomer formation in the expected cyclohexane-1,4-diol dinitrate product **10**. (Only the *trans* isomer is depicted.) The stereochemical advantages have been utilised previously in the reaction of **9** with dimethyl boron bromide[9] which gives exclusively the *trans* product, inversion of configuration indicating an S_N2 process. In contrast in aqueous hydrogen bromide after a much longer reaction time a mixture of *cis* and *trans* products is formed.[10]

Results

Aromatic nitration of **1** by dinitrogen pentoxide is too rapid to follow kinetically. At −60 °C using a solution of 0.5 mol dm^{-3} dinitrogen pentoxide in dichloromethane, nitration was complete within 5 min and the substrate had been converted quantitatively to 3-(2-nitrophenyl)oxetane, **3**, (10%) and 3-(4-nitrophenyl)oxetane, **5**, (90%). In contrast to the reaction of the same substrate with nitric acid,[7] there is no detectable competing oxetane-ring opening to give **2** in this initial reaction. Both the initial products, **3** and **5**, subsequently undergo oxetane-ring opening to give **4** and **6** respectively. The reaction **3**→**4** is too quick for accurate determination of the rate constant, but it appears to be 25–50 times quicker at 0 °C than **5**→**6**. Rate constants for the reaction **5**→**6**, and approximate rate constants for **3**→**4**, deduced by computer fitting[11] of data as in Fig. 1 are in Table 1. The much faster reaction of **3**→**4** compared with **5**→**6** is as found previously in our investigation of the reaction of **1** with nitric acid.[7] (As previously,[7] **3** has not been isolated. Its structure is inferred from the NMR spectrum and the fact that further reaction gives rise to **4**.)

The reaction **5**→**6** is approximately second order in N_2O_5.

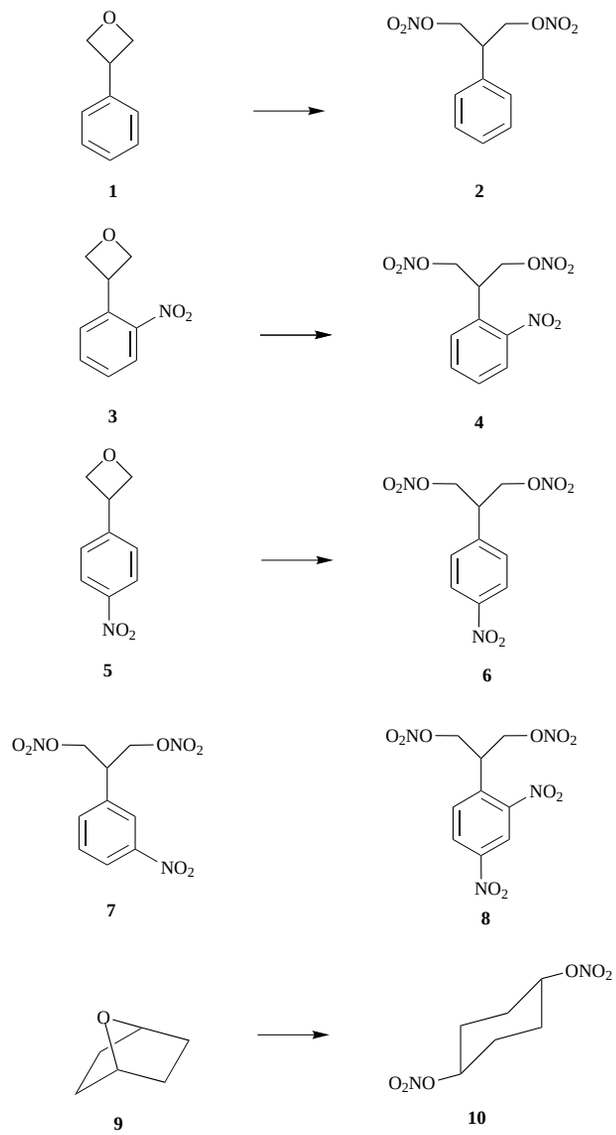


Table 1 Rate constants k for the reactions **3**→**4** and **5**→**6** deduced from the yields of **3** + **5**, **4** and **6** in samples quenched at time intervals following reaction of **1** (0.04 mol dm^{-3}) with dinitrogen pentoxide in dichloromethane

		$k/10^{-4}$ s^{-1}	
T/°C	$[N_2O_5]$/mol dm^{-3}	**3**→**4**[a]	**5**→**6**[b]
−60	0.50	4	0.0054[c]
−60	1.0	6	*d*
−21	1.0	12	0.134
0	0.50	4	0.157
0	0.75	14	0.351
0	1.0	35	0.76
0	1.8	*d*	1.66

[a] ±50%. [b] ±5% unless otherwise indicated. [c] Based on two points only, ±50%. [d] Not determined.

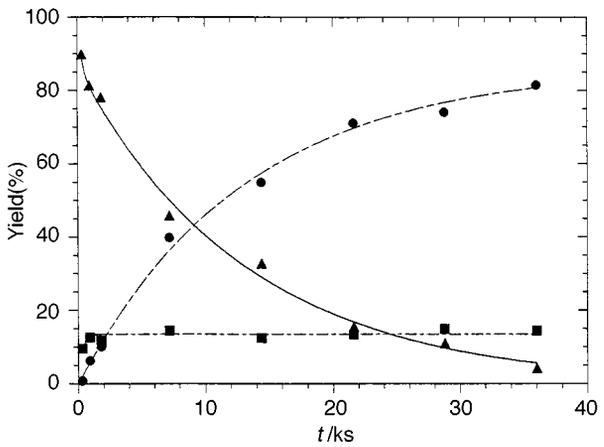


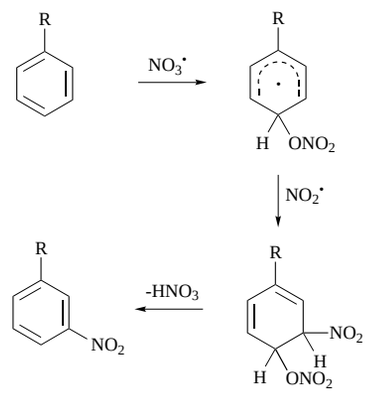
Fig. 1 Yields (% of initial **1**) of products of reaction of **1** with dinitrogen pentoxide (1 mol dm^{-3}) in dichloromethane at 0 °C, as a function of time (t/ks) Triangles (observed) and full line (calculated); **3** + **5**. Squares (observed) and dot-dash line (calculated); **4**. Circles (observed) and dashed line (calculated); **6**. Calculated[11] curves are based on the rate constants in Table 1.

Third order rate constants were calculated by dividing the first order rate constants in Table 1 by the square of the concentration of N_2O_5. From these third order rate constants over the range −60 to 0 °C, activation parameters for the reaction **5**→**6** were calculated: $\Delta H^{\ddagger} = 26$ (±4) kJ mol^{-1}, $\Delta S^{\ddagger} = -232$ (±20) J mol^{-1} K^{-1}.

A preliminary investigation was also made of the reaction of **1** with N_2O_5 at 30 °C and it was found that side reactions intruded. A significant amount (about 10%) of an additional product, possibly the *m*-nitrophenyl analogue, **7**, was detected by NMR spectroscopy. It was the major product initially but its concentration did not increase with time. This is reminiscent of some results of ozone-mediated nitrations with nitrogen dioxide, (Kyodai nitration[12]) and attributed to oxidation by the nitrate radical to give the aromatic radical cation and nitrate ion. In the early stages of the reaction these can combine and be followed by combination with NO_2 and nitric acid elimination to give the *meta* nitro product, as in Scheme 1. Later, the acid produced is thought to capture the nitrate ion and prevents further reaction by this pathway.[12] In the present work, the NO_3 and NO_2 radicals would be formed by homolytic decomposition of dinitrogen pentoxide. Traces of another reaction product, possibly the dinitro compound **8**, which also was formed initially but did not increase with time, were also detected. These reactions were not investigated further. In a separate experiment, it was demonstrated that there was no significant reaction of **1** with dinitrogen tetroxide. Compound **1** was recovered in 95% yield after 1 hour at 22 °C after treatment with N_2O_4 (1.54 mol dm^{-3} in dichloromethane).

Table 2 Rate constants k for the reaction **9**→**10** deduced from the loss of **9** in samples quenched at time intervals following reaction of **9** (7×10^{-3} mol dm^{-3}) with dinitrogen pentoxide in dichloromethane

T/°C	$[N_2O_5]$/mol dm^{-3}	$k/10^{-5}$ s^{-1}
32	0.127	33
32	0.098	14
25	0.264	71
25	0.186	60
25	0.154	24
25	0.133	13
25	0.126	24
25	0.116	10
25	0.087	5.5
25	0.063	3.3
17	0.317	65
17	0.141	16
17	0.120	15
17	0.118	10
10	0.210	41
10	0.100	6.5
10	0.084	5.1



Scheme 1

The product of nitration of **9** was exclusively the *trans*-cyclohexane-1,4-diol dinitrate **10**. This was identified by its ^{1}H NMR spectrum at −100 °C, which showed two signals in the methine region of unequal intensities corresponding to the axial–axial and equatorial–equatorial conformations. The *cis* isomer would have given two signals of equal intensity. (Comparison was made with a mixture of the *cis* and *trans* isomers prepared by nitration of a mixture of *cis* and *trans*-cyclohexane-1,4-diols.) A study of the kinetics of ring-inversion of **10** studied by variable temperature NMR spectroscopy is reported in the appendix.

The kinetics of the reaction of **9** with N_2O_5 to give **10** were investigated by GC analysis of quenched samples (see Experimental section). With N_2O_5 in excess, the reaction was quantitative and followed a pseudo-first order course; rate constants are in Table 2. These results indicate a second-order dependence on the concentration of N_2O_5. Activation parameters calculated from the derived third-order rate constants are: $\Delta H^{\ddagger} = 29$ (±6) kJ mol^{-1}; $\Delta S^{\ddagger} = -217$ (±22) J mol^{-1} K^{-1}.

Reactions with higher concentrations of **9**, approximately equimolar with N_2O_5, were less successful. The yield of **10** was substantially reduced and there was an unidentified product. This was not investigated further.

There was no reaction of **9** with anhydrous nitric acid under the conditions of these experiments. However reactions with N_2O_5 in the presence of nitric acid showed rate enhancement over those where nitric acid was absent. The order in N_2O_5 remained approximately two. Details are in Table 3. When ^{15}N enriched N_2O_5 was used, the ^{15}N NMR analysis during the course of the nitration at 25 °C revealed no chemically induced dynamic nuclear polarization (CIDNP) signals. There was thus no evidence for the intrusion of a radical reaction.

Table 3 Rate constants k for the reaction **9**→**10** deduced from the loss of **9** in samples quenched at time intervals following reaction of **9** (7×10^{-4} mol dm^{-3}) with dinitrogen pentoxide in dichloromethane, in the presence of HNO_3 at 25 °C

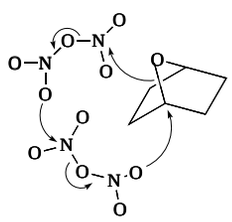
$[N_2O_5]$/mol dm^{-3}	$[HNO_3]$/mol dm^{-3}	$k/10^{-4}$ s^{-1}
0.101	0.037	2.0
0.152	0.056	4.0
0.163	0.057	5.6
0.174	0.066	5.0
0.260	0.098	15

Discussion

Aromatic nitration of **1** is too rapid for kinetic study but the isomer proportions are similar to those observed in nitric acid nitration,[7] and it seems likely that a similar, normal nitronium ion mechanism is operative. With nitric acid, the reacting substrate was identified as the oxetane hydrogen-bonded to nitric acid. With N_2O_5 it must be the free oxetane which is reacting.[7] Even so the preference for *para* nitration is again marked.

Ortho nitration leads to oxetane **3** which ring-opens to **4** much more rapidly than **5** to **6**, (indicative of intramolecular assistance of ring-opening by the *ortho*-nitro group as has been discussed before[7]) and it was possible to find conditions (0 °C, 5 min) where the products were a mixture of **4** (7%) and **5** (93%) which could readily be separated chromatographically. Thus **5** can be prepared in high yield by this method.

The ring-openings **5**→**6** and **9**→**10** proceed at similar rates. Both reactions are approximately second order in N_2O_5, and both show large negative entropies of activation. It seems likely that the two reactions proceed by a similar mechanism. We could find no evidence that the reactions are radical in character, and it seems more likely that one molecule of N_2O_5 provides an incipient nitronium ion to the ether oxygen whilst the other concertedly provides an incipient nitrate ion for backside nucleophilic attack. It is conceivable in view of the entropies of activation that in this relatively non-polar medium full charge development is avoided in a 10-membered cyclic transition state as in **11**. (Entropies of activation for third-order reactions cannot be compared directly with those for second-order reactions because the comparison is dependent on the concentration unit used. However on the molar scale as here, pre-association of any two components would be expected to have an associated entropy change of about −50 J K^{-1} mol^{-1}.[13] This accounts for only a part of the observed large negative entropies of activation.)



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These reactions share some characteristics (second order in N_2O_5, large negative activation entropies) with the oxirane ring-opening reactions of aryl oxiranes. However 4-nitrophenyloxirane is 300–400 times more reactive than 3-(4-nitrophenyl)oxetane, **5**, and aryloxirane ring-opening is accompanied by racemisation, not inversion.[4] The oxirane reaction shows substituent effects indicative of aryl-ring stabilised carbocation character in the transition state. No such possibility exists with the ring-opening reactions of **5** and **9**. It therefore seems likely that despite the similarities mentioned the transition states for the reactions **5**→**6** and **9**→**10** on the one hand and aryloxirane→arylethane-1,2-diol dinitrate on the other are substantially different.

Table 4 Rate constants (k/s^{-1}) for ring inversion of **10**

T/K	Minor to major conformer	Major to minor conformer
193	90	68
198	165	124
203	300	226
208	520	392
216	1000	754
223	2750	2075

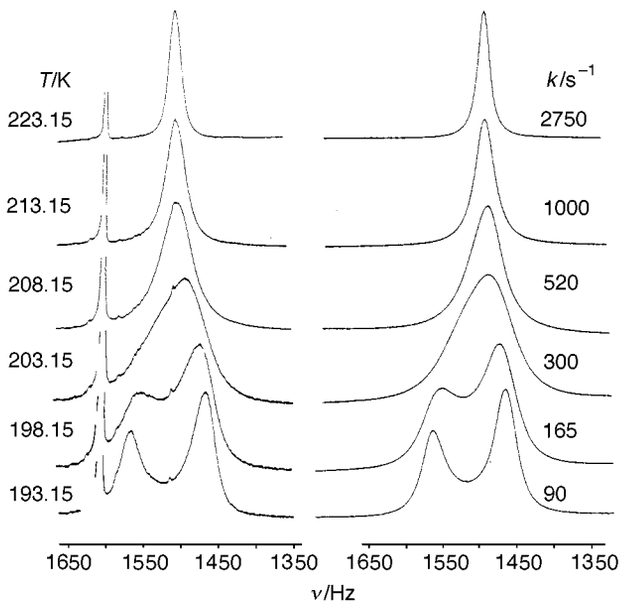

Fig. 2 Observed (l.h.s.) and computed (ref. 14, r.h.s.) ^{1}H NMR spectra in the methine region of **10**

Appendix

The kinetics of ring-inversion of *trans*-cyclohexane-1,4-diol dinitrate, **10**, were investigated by dynamic NMR. Spectra at various temperatures, and the corresponding computer fits,[14] are shown in Fig. 2. The spectrum at −100 °C (not shown) has two unequal sharp peaks in the methine region, with the major equatorial–equatorial conformation being favoured over the minor axial–axial one in the ratio 3:2. At higher temperatures these peaks broaden and coalesce. Rate constants for interconversion are in Table 4. Activation parameters deduced from these results are: minor to major conformer: $\Delta H^{\ddagger} = 39.4$ (±0.6) kJ mol^{-1}; $\Delta S^{\ddagger} = -0.3$ (±2.9) J mol^{-1} K^{-1}; major to minor conformer: $\Delta H^{\ddagger} = 39.4$ (±0.6) kJ mol^{-1}; $\Delta S^{\ddagger} = -2.6$ (±2.9) J mol^{-1} K^{-1}.

Experimental

Apparatus

All NMR spectra were recorded on either a 250 MHz Bruker, a 300 MHz Bruker or a 400 MHz Bruker spectrometer. IR spectra were recorded by a Perkin-Elmer 881 Infra-red spectrophotometer.

Materials

Dichloromethane was dried by distillation in silanised vessels from calcium hydride. Precautions were taken to exclude moisture throughout the experiments described. 7-Oxabicyclo-[2.2.1]heptane, **9**, was fractionally distilled (bp 118 °C). Dinitrogen pentoxide,[5] anhydrous nitric acid,[15] 3-phenyloxetane, **1**,[15] 2-(*o*-nitrophenyl)propane-1,3-diol dinitrate, **4**,[7] 3-(*p*-nitro-

phenyl)oxetane, **5**[15] and 2-(*p*-nitrophenyl)propane-1,3-diol dinitrate, **6**,[7] were prepared as described.

Preparation of ^{15}N-labelled N_2O_5

Anhydrous ^{15}N-labelled HNO_3 was added dropwise with stirring to P_2O_5 in a slow stream of ozonised oxygen, then passed through a tube containing P_2O_5 before collection in an NMR tube fitted with a B 10 joint and cooled in a dry-ice–acetone bath. After collection the NMR tube was subasealed, removed to the glove-box, and reweighed. A known volume of dichloromethane was added by syringe, and the solution was used immediately.

Preparation of a mixture of *cis*- and *trans*-cyclohexane-1,4-diol dinitrate

To anhydrous nitric acid (8 g) sulfuric acid (98%, 19.3 g) was cautiously added in an ice-bath. The mixed acid was cooled to −35 °C and dry dichloromethane (20 cm^3) added. To this cold solution a mixture of *cis*- and *trans*-cyclohexane-1,4-diol (3 g, 0.026 mol) was added slowly, with stirring, over 15 min. Towards the end of the addition the solution became very viscous, and the temperature was allowed to rise to −25 °C to facilitate stirring which was continued for 1 hour. The reaction mixture was quenched with ice and the organic layer was washed with sodium hydrogen carbonate solution, separated and dried over $MgSO_4$. Removal of solvent gave a pale yellow crystals (2.9 g, 0.14 mol, 54% yield); δ_H(300 MHz, $CDCl_3$) 5.05 (2H, br s, CH) 1.95 (8H, m, CH_2 ring); δ_C(75.5 MHz, $CDCl_3$) 79.04, 78.65 (2 × CH) 25.74, 25.31 (2 × CH_2 ring); ν_{max}/cm^{-1} 1625 (asym. NO_2 str.) 1274 (sym. NO_2 str.).

Preparation of *trans*-cyclohexane-1,4-diol dinitrate, 10

To a solution of dinitrogen pentoxide (5.6 mmol) in dichloromethane (20 cm^3) at 25 °C 7-oxabicyclo[2.2.1]heptane (1.06 mmol) was added, and the mixture was kept at 25 °C for 4 hours. After this time it was quenched in water and the organic layer was separated and dried with $MgSO_4$. The solvent was removed to leave a pale yellow solid. This was dissolved in ethanol and refluxed with activated carbon, then filtered hot and recrystallised from ethanol to give white crystals (mp 124.4–125.1 °C, 99% yield); δ_H(300 MHz, $CDCl_3$) 5.08 (2H, s, CH) 2.12 (4H, m, CH_2 ring) 1.79 (4H, m, CH_2 ring). (In the ^{15}N proton decoupled spectrum there was a single sharp signal at −42.60 relative to external nitromethane. In the proton coupled spectrum this signal was a doublet with a coupling constant, $^3J_{NH}$, of 2.6 Hz.); ν_{max}/cm^{-1} 1632 (asym. NO_2 str.) 1275 (sym. NO_2 str.).

Products of reaction of 1 with N_2O_5

To each of several aliquots (1 cm^3) of a solution of N_2O_5 in dichloromethane in separate flasks were added aliquots (0.25 cm^3, 0.2 mol dm^{-3}) of a solution of **1** in dichloromethane. Each was quenched in an excess of cold aqueous sodium hydrogen carbonate solution after an appropriate time interval at the required temperature. Repeated extractions with dichloromethane, followed by drying ($MgSO_4$) and removal of solvent gave a mixture of products which was dissolved in $CDCl_3$ and analysed by ^1H NMR spectroscopy.

Typical kinetic experiment with 7-oxabicyclo[2.2.1]heptane, 9

To N_2O_5 (7.7 mmol) in a dry volumetric flask in a dry glove box, dichloromethane at 35 °C (*ca*. 20 cm^3) was added. The dichloromethane was added at this temperature to overcome the temperature loss due to the cold glass. More dichloromethane at 25 °C (*ca*. 20 cm^3) was then added followed by a solution of **9** (7 mmol dm^{-3}, 5 cm^3). This solution also contained the GC reference standard. The solution was quickly made up to 50 cm^3 with dichloromethane and then placed in a thermostatted compartment. Four aliquots (10 cm^3) were taken at time intervals and syringed into sealed flasks containing water, and shaken. Flasks were removed from the glove box and the contents extracted with dichloromethane (3 × 10 cm^3). The organic fractions were combined, dried ($MgSO_4$) and the bulk of the solvent removed by distillation using a small fractionating column, until only a small volume remained. This was analysed by GC. (Column Dextril 400 at 100 °C, N_2 flow rate 40 cm^3 min^1, response factor relative to reference standard 3-fluoronitrobenzene 0.852. Retention times of **9** and ref. standard 3.0 and 14.06 min, respectively.)

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