N-Nitroso-*N*,*O*-dialkylhydroxylamines: preparation, structure, and mechanism of the hydronium ion catalysed solvolytic nitrous oxide extrusion reaction

J. Ishwara Bhat,[a]† William Clegg,[b] Howard Maskill,*[a] Mark R. J. Elsegood,[b] Iain D. Menneer[a] and Peter C. Miatt[a]

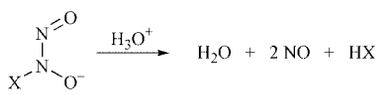
[a] *Chemistry Department, University of Newcastle, Newcastle upon Tyne, UK NE1 7RU*
[b] *X-Ray Crystallography Unit, Chemistry Department, University of Newcastle, Newcastle upon Tyne, UK NE1 7RU*

Received (in Cambridge, UK) 1st March 2000, Accepted 18th April 2000
Published on the Web 15th June 2000

Eleven *N*-nitroso-*N*,*O*-dialkylhydroxylamines, RN(NO)OR′, have been prepared and the mechanisms of their hydronium ion catalysed solvolyses in aqueous solution which liberate nitrous oxide have been investigated. All reactions are first-order in substrate and first-order in hydronium ion, and the second-order rate constants at 25 °C vary over a range of less than 140 in spite of considerable variation in substrate structure (R ranges from methyl to 4-methoxybenzyl to 2-adamantyl, for example) and changes in solvent composition (water with up to 50% methanol or 66% acetonitrile). Enthalpies and entropies of activation are qualitatively similar throughout the range ($\Delta H^{\ddagger}$ = 72–93 kJ mol^{-1} and $\Delta S^{\ddagger} = -19$ to -57 J K^{-1} mol^{-1}) which, with the product analyses, are accommodated by a mechanism involving pre-equilibrium protonation of the substrates followed by rate-limiting dissociation to give RN_2O^+ and HOR′. The oxodiazonium ion intermediate, RN_2O^+, then dissociates further to give the carbenium ion intermediate, R^+, or suffers direct nucleophilic displacement of N_2O by solvent (the external nucleophile) or by R′OH (the internal nucleophile liberated in the initial fragmentation). The carbenium ion, R^+ (if formed), suffers nucleophilic capture either by solvent or by R′OH. When acetonitrile is the co-solvent (rather than methanol) for the *N*-(2-adamantyl) substrate **3g**, the product of the Ritter reaction, 2-acetamidoadamantane, is detected. These nitrous oxide liberating reactions are compared with the nitric oxide liberating reactions of related *N*-nitrosohydroxylamines, and the origin of the difference between them is identified. The *N*(1)-nitroso group in the *N*,*O*-dibenzyl compound **3c** is shown by X-ray crystallography to be essentially coplanar with the C and O atoms also bonded to N(1).

Introduction

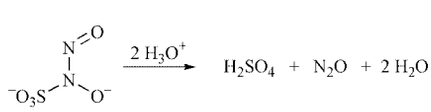
The chemistry of *N*-nitrosohydroxylamines had not received much attention prior to the discoveries that (i) nitric oxide is released under mildly acidic conditions from compounds **1**, Fig. 1, as shown in eqn. (1),[1] and (ii) nitric oxide has diverse and



(1)

1a, b

dramatic physiological effects.[2] It was known much earlier that the closely related compound **2** gives nitrous oxide under acidic conditions, eqn. (2), and a mechanistic investigation of this



(2)

2

reaction was reported some years ago.[3] The basis of the difference between the two gas extrusion reactions from such similar substrates, however, appears not to have been investigated. Indeed, although the report of the study of compounds **1** which give nitric oxide according to eqn. (1) included the observation that compound **2** behaves differently by giving nitrous oxide under the same reaction conditions, the authors did not comment further. Since one reaction liberates a compound with benign effects, and compounds which undergo this reaction are possibly useful therapeutic agents, whereas the other proceeds through potentially mutagenic reactive electrophilic alkylating agents, the molecular basis of the difference between the alternative reactions of *N*-nitrosohydroxylamines needs to be understood.

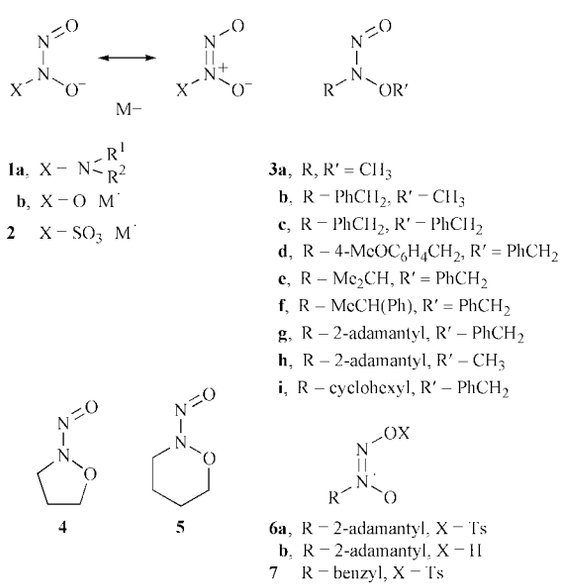


Fig. 1

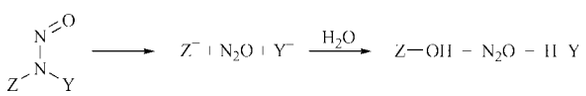
Reactions of compounds **1** by eqn. (1) occur when X is a nucleofuge although acidic conditions are required to facilitate

† Commonwealth Universities Research Fellow; *present address*: Chemistry Department, Mangalore University, Mangalore, India.

DOI: 10.1039/b001688h

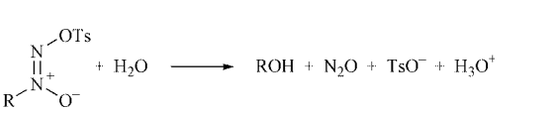
its departure when X = NR^1R^2 or O^-. The electrofuge in this reaction is the dimer of nitric oxide which undergoes concerted or step-wise homolysis to give two molecules of nitric oxide. In the decomposition of compound **2** under the same acidic conditions to give nitrous oxide by eqn. (2), sulfur trioxide is the notional electrofuge although either concerted or subsequent hydration converts it to sulfuric acid. The nucleofuge in the *O*-protonated substrate in eqn. (2) is hyponitrite (presumably *cis*) which, upon further (concerted or step-wise) protonation and fragmentation, gives nitrous oxide and water.

The significant difference between the reactions of eqn. (1) which give nitric oxide and that of eqn. (2) which gives nitrous oxide, therefore, is that X in compounds **1** is a nucleofuge whereas, in compound **2**, SO_3 is an electrofuge, *i.e. the electron flows in compounds* ***1*** *and* ***2*** *with respect to loss of the* N_2O_2 *moiety in the reactions of eqns. (1) and (2) are in opposite directions*. A generic version of eqn. (2) is given in eqn. (3) with

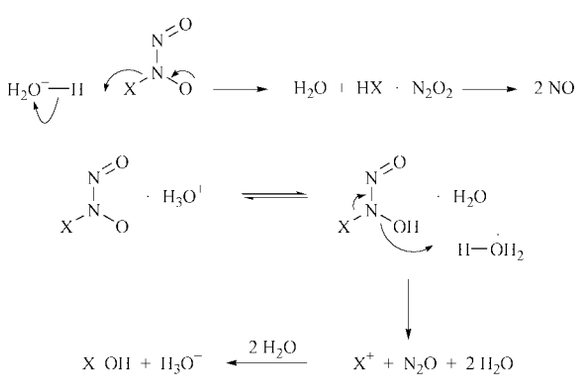


(3)

electrofuge Z^+ and nucleofuge Y^-. Reactions of this type in which a complex potential nucleofuge departs to give a stable gas molecule (N_2O in the present case) and a simpler nucleofuge, Y^-, are relatively uncommon although we previously discovered a closely related example, the solvolysis of alkyl azoxytosylates, eqn. (4), in which the fragmentation is concerted and uncatalysed.[4,5] Further examples include the nitrous acid induced deamination of primary alkylamines and modifications such as the decompositions of nitroso-amides and 1-alkyl-3-aryltriazenes,[6] and acid catalysed decompositions of nitramines.[7] The alternative NO and N_2O liberating reactions with their opposite electron flows are illustrated in Scheme 1.



(4)



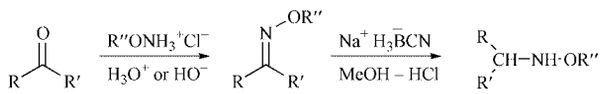
Scheme 1

We have made compounds **3**–**5** and have already reported that some of them undergo fragmentation to yield nitrous oxide under acidic conditions.[8] The electrofuge in these reactions is a potential carbenium ion (eqn. (3), Z = alkyl) which may be by-passed in an enforced concerted process, and the fragmentations involve specific acid catalysis, *i.e.* Y (= alkoxy) in eqn. (3) requires protonation to allow departure as a nucleofuge. We now report preparations of compounds **3**–**5**, some structural results, and details of our mechanistic investigations on their specific acid catalysed hydrolyses.

Methods and results

Preparations

N,*O*-Dimethylhydroxylamine is commercially available and all other *N*-alkyl-*O*-alkylhydroxylamines in our study except the precursors to **4** and **5** were made by the route shown in Scheme 2; precursors to **4** and **5** were made by established strategies,



R = aryl or alkyl R′ = H or alkyl R″ = H, Me, or $PhCH_2$

Scheme 2

and all steps involved known procedures with or without simple modifications. Nitrosation of all hydroxylamines was carried out using aqueous sodium nitrite under acidic conditions in the usual way. ***In the absence of information to the contrary, all nitrosohydroxylamines were assumed to be potent carcinogens and handled accordingly.*** Potential solvolytic products (alcohols, ethers, ketones, and amides) were prepared and characterised if not commercially available, and methods are sufficiently described in the Experimental section.

Kinetics

Decompositions of all *N*-nitroso-*N*,*O*-dialkylhydroxylamines (S) that we have investigated in dilute aqueous acidic solution followed clean *pseudo* first-order rate laws ($[H_3O^+] \gg [S]_o$). The *pseudo* first-order rate constants, k_{obs}, were independent of the initial concentration of substrate and increased with increasing hydronium ion concentrations, correlations being linear up to modest acidities at constant ionic strength; second-order rate constants, k_H, were obtained in the usual manner from the gradients of such plots, the intercepts being close to zero. Thus

$$-\frac{d[S]}{dt} = k_{obs}[S]$$

with

$$k_{obs} = k_o + k_H[H_3O^+]$$

and k_o is vanishingly small for most compounds at normal temperatures.

From second-order rate constants at different temperatures, the value at 25.0 °C (if unavailable experimentally) and activation parameters were computed using the Eyring equation in the normal way;[9] these results are shown in Table 1. At non-constant ionic strength, especially at higher acidities, upward curvature was observed in plots of k_{obs} against $[H_3O^+]$, *e.g.* Fig. 2, an effect we ascribe to our neglect of activity coefficient considerations.

To investigate the effect of changes in the reaction medium, *N*-nitroso-*N*,*O*-dibenzylhydroxylamine (**3c**) was reacted in

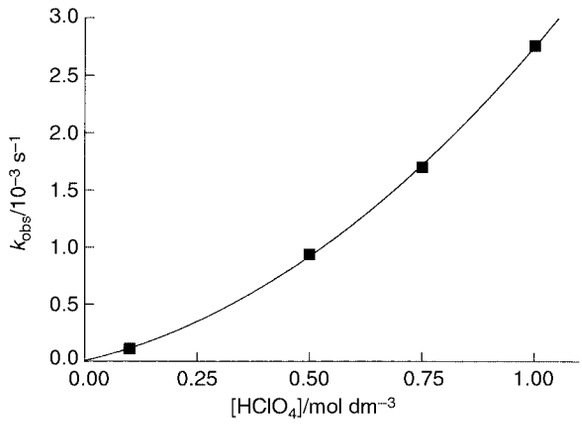


Fig. 2 Decomposition of *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine (**3g**) in aqueous perchloric acid at 25.0 °C with no added sodium perchlorate.

Table 1 Second-order rate constants at 25.0 °C[a] and activation parameters[b] for the hydronium ion catalysed hydrolysis of *N*-nitroso-*N*,*O*-dialkylhydroxylamines

	Co-solvent (*I*)[c]	$10^5 k_H$/dm^3 mol^{-1} s^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}
3a	3.3% CH_3CN (1.0)	1.89	93	−24
3b	0.7% MeOH (2.5)	2.82	88	−38
3c	1.25% MeOH (2.5)	8.97	79	−57
3d	1.25% MeOH (2.5)	134	78	−41
3d	3.3% CH_3CN (2.0)	87.3	77	−47
3e	3.3% CH_3CN (1.0)	40.9	85	−24
3f	33% CH_3CN (1.0)	19.0	88	−19
3g	33% CH_3CN (1.0)	260	72	−53
3h	3.3% CH_3CN (1.0)	18.6	81	−25
3i	3.3% CH_3CN (1.0)	85.4	85	−19
4	1.9% MeOH (2.5)	181	72	−55
5	1.1% MeOH (1.0)	5.83	90	−23

[a] Calculated in some cases from results at other temperatures; estimated errors: ±10%. [b] Approximate temperature ranges employed were as follows. **3a**: 25–65 °C; **3b**, **3c**, **3e**, and **5**: 25–55 °C; **3d**, **3h**, **3i**, and **4**: 15–45 °C; **3f**: 25–60 °C; **3g**: 20–50 °C; estimated errors in $\Delta H^{\ddagger}$, ±5 kJ mol^{-1}, and in $\Delta S^{\ddagger}$, ±10 J K^{-1} mol^{-1}. [c] *I* = ionic strength/mol dm^{-3} using $NaClO_4$.

Table 2 Effect of composition of aqueous acetonitrile upon the *pseudo* first-order rate constants, k_{obs}, for acid-induced decomposition of *N*-nitroso-*N*-(1-phenylethyl)-*O*-benzylhydroxylamine (**3f**) and *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine (**3g**), $[H_3O^+] = 0.5$ mol dm^{-3}, ionic strength ($NaClO_4$) = 1.0 mol dm^{-3}

3f[a]		**3g**[b]	
%CH_3CN	$10^4 k_{obs}$/s^{-1}	%CH_3CN	$10^4 k_{obs}$/s^{-1}
3.33	16.7	10	12.2
10.0	10.1	20	18.2
33.3	5.86	33.3	15.1
50.0	4.73	66.6	13.7

[a] 40 °C, $10^4[\mathbf{3f}]_o = 4.0$ mol dm^{-3}. [b] 25 °C, $10^4[\mathbf{3g}]_o = 3.33$ mol dm^{-3}.

aqueous perchloric acid containing proportions of methanol increasing from 2.5 to 49.5% by volume (a minimum proportion was required for solubility).[8] Additionally, compound **3d** was reacted in aqueous perchloric acid containing a small proportion of acetonitrile in place of methanol (Table 1), and compounds **3f** and **3g** were investigated in aqueous perchloric acid containing various proportions of acetonitrile, Table 2. In all cases, increasing concentrations of the organic co-solvent led to modest decreases in the rate constants.

The kinetic effects of various solutes were also investigated. When it was thought that these reactions might be denitrosations, sulfamic acid was used as a trap for any nitrosating agents which may have been liberated (to prevent possible reverse reaction).[10] No effect at all was observed for **3b**, **3c**, and **5**.[8] The effect at constant acidity of increasing concentrations of the weakly nucleophilic sodium perchlorate was investigated for **5**,[8] **3b**, **3d**, **3f**, and **3g**, and of lithium perchlorate for **3g**; similarly, the effect of the more nucleophilic chloride for **3b**[8] and **5** was investigated, Table 3. There were small effects in all cases, but very much smaller than the effect of increasing concentrations of hydronium ion.

Product analysis

Preliminary mass spectrometric analysis confirmed that the gas evolved in the acid-induced solvolyses of **3c** was not nitric oxide but had MW = 44. Subsequent scrutiny of the rotational spectrum of a sample of the gas isolated from the closely related azoxytosylate **6a** and diazenium oxide **6b** established its identity as nitrous oxide.[11] We have now shown that the FTIR spectrum of the gas from the decomposition of *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine (**3g**) is identical with that of an authentic sample of nitrous oxide, and the spectroscopic parameters obtained are in excellent agreement with literature values.[12]

Authentic samples of alcohols ROH and R′OH related to substrates RN(NO)OR′ were available and shown by comparison of the ^{1}H and ^{13}C NMR spectra, and GLC retention times, to be formed in all acid-induced hydrolyses. In the cases of **3b**, **3c**, **3d**, and **3g**, ethers ROR′ were also shown to be formed in appreciable yields (typically, *ca.* 20%). Additionally, $PhCH_2OMe$ and 4-$MeOC_6H_4CH_2OMe$ were detected from the reaction of $PhCH_2N(NO)OCH_2Ph$ (**3c**) and 4-$MeOC_6H_4CH_2N(NO)OCH_2Ph$ (**3d**), respectively, in aqueous methanol. Although 1-phenylethyl benzyl ether was detected from the reaction of **3f**, it was formed in only low yield (<5%).

2-Acetamidoadamantane was detected from the reaction of 2-AdN(NO)OCH_2Ph (**3g**) in aqueous acetonitrile as a significant product (*ca.* 20%). Although acetamides were sought from reactions of substrates **3f** and **3i** in aqueous acidic acetonitrile, neither was detected by ^{1}H NMR and conventional GLC (<1%); however, capillary GC-MS did show the presence of a very low yield of amide from **3i**. Finally, low yields of benzaldehyde were detected by GLC from $PhCH_2N(NO)OCH_3$ (**3b**) and $PhCH_2N(NO)OCH_2Ph$ (**3c**). Correspondingly, a low yield of acetophenone was detected by ^{1}H NMR and GLC from **3f**. However, we were unable to detect adamantan-2-one or cyclohexanone from reactions of **3g** and **3i**, respectively (authentic samples were available and detectable by GLC). As indicated in the Experimental section, it was possible to estimate relative yields of solvolysis products of some reactions from integrated ^{1}H NMR spectra and by GLC.

N,*O*-Dibenzylhydroxylamine was shown not to be a product from *N*-nitroso-*N*,*O*-dibenzylhydroxylamine (**3c**), and to be quite stable to the solvolysis conditions. No *N*-nitroso-*N*-(2-adamantyl)-*O*-methylhydroxylamine (**3h**) was detected by ^{1}H NMR after work-up from acid-induced methanolysis of *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine (**3g**) for approximately one half-life at 25 °C.

X-Ray crystallography

The molecular structure of compound **3c**, determined by X-ray crystallography, is shown in Fig. 3. The *N*-nitroso group is essentially coplanar with the atoms C(8) and O(1) bonded to N(1) as is commonly observed in a wide range of *N*-nitroso compounds; 74 such compounds were found in the Cambridge Structural Database,[13] and X–N–N–O torsion angles for these differ from 0 or 180° by no more than 10° except in a small number of cases. The geometry of the N–N=O group in **3c** is well within the range observed in the database, and is close to that for the only previously reported *N*-nitrosohydroxylamine for which N–N = 1.311 Å, N=O = 1.234 Å, and N–N=O = 116.3°.[14]

Table 3 Effect of salts upon the *pseudo* first-order rate constants, k_{obs}, for acid-induced decomposition of *N*-nitroso-*N*,*O*-dialkylhydroxylamines **3b**, **3d**, **3f**, **3g**, and **5**, $[HClO_4] = 0.5$ mol dm^{-3}, 33.3% CH_3CN

Compound	Salt	$10^4 k_{obs}$/s^{-1} ([salt]/mol dm^{-3})				
3b[a] 25 °C	$NaClO_4$	12.8 (0)	15.9 (0.5)	19.2 (1.0)	23.3 (1.5)	
3d 25 °C	$NaClO_4$	7.62 (0)	8.12 (0.25)	12.1 (0.50)	12.6 (0.75)	15.0 (1.0)
3f 40 °C	$NaClO_4$	3.51 (0)	3.92 (0.10)	4.70 (0.25)	5.86 (0.50)	8.97 (1.0)
3g[b] 40 °C	$NaClO_4$	5.78 (0)	8.97 (0.40)	10.8 (0.65)	12.5 (0.90)	
3g[b] 40 °C	$LiClO_4$	6.75 (0)	10.6 (0.40)	13.0 (0.65)	15.9 (0.90)	
3g 25 °C	$NaClO_4$	9.27 (0.50)	11.4 (0.75)	15.1 (1.0)	18.7 (1.5)	25.5 (2.0)
5[c] 25 °C	NaCl	1.44 (0)	1.31 (1.0)	1.24 (1.75)	1.15 (2.50)	

[a] $[HClO_4] = 1.0$ mol dm^{-3}; 0.7% MeOH, 0% CH_3CN. [b] $[HClO_4] = 0.1$ mol dm^{-3}; 35% CH_3CN. [c] $[HClO_4] = 2.5$ mol dm^{-3}, 1.1% MeOH, 0% CH_3CN, $[NH_2SO_3H] = 1.0 \times 10^{-3}$ mol dm^{-3}.

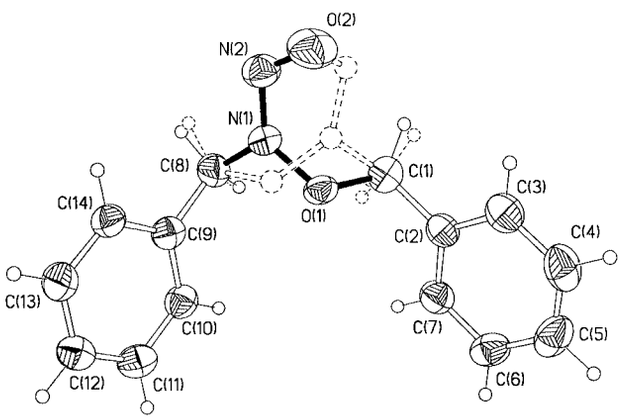
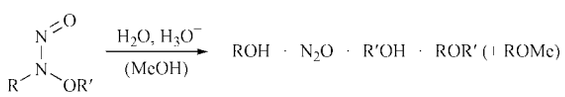


Fig. 3 Molecular structure of compound **3c** with 50% probability displacement ellipsoids. The minor disorder component is shown dashed. Key distances (Å) and angles (°): N(1)–N(2) 1.300(7), N(2)–O(2) 1.210(5), N(1)–O(1) 1.395(5), N(1)–N(2)–O(2) 117.0(4), and O(1)–N(1)–N(2)–O(2) 3.5(7).

Discussion

Early experiments established that the decompositions of *N*-nitroso-*N*,*O*-dialkylhydroxylamines under acidic conditions are not simply denitrosations to give the parent hydroxylamine, and the gas liberated has been identified as nitrous oxide by FTIR spectroscopy.[12] Identification of ROH, R′OH, and ROR′ from reactions of RN(NO)OR′ in acidic aqueous solution (plus ROMe when methanol is present as co-solvent) allows us to represent the reaction as eqn. (5). This nitrous oxide liberating



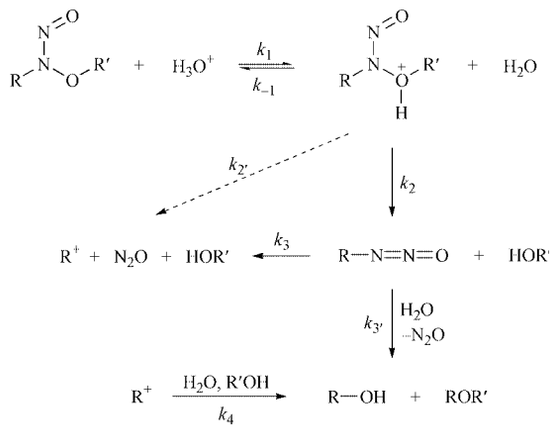
(5)

reaction is, therefore, related to the decomposition of the inorganic compound shown in eqn. (2).

The reactions are all first-order in substrate and in hydronium ion, and results shown in Table 1 represent a relatively narrow range in reactivity—a factor of only 140 for the second-order rate constants of the most and least reactive of the 11 compounds **3**–**5**. Moreover, the activation parameters are qualitatively similar indicating that all compounds react by the same general mechanism. The composite mechanism shown in Scheme 3 with a pre-equilibrium protonation of the substrate followed by an unspecified rate-limiting step *not* involving proton transfer accommodates the observed specific acid catalysis rate law and the product analyses.

The rate-limiting step for simple secondary alkyl compounds 3e, 3g–3i

We have already established that the α-deuterium secondary kinetic isotope effect for hydrolysis of **3g** is unity[11] compared with *ca.* 1.17 for **6a**[4] which proves that the C–N bond remains



Scheme 3

entirely intact in the activated complex from **3g**. For this compound, therefore, neither $k_{2'}$ nor k_3 can be rate-limiting, and $k_{3'}$ is ruled out by the impossibility of a bimolecular reaction at the 2-position of the adamantyl system. For **3g**, therefore, k_2 must be rate-limiting, and the oxodiazonium ion then dissociates by the k_3 route into N_2O and the 2-adamantyl cation which is captured by solvent or by benzyl alcohol (the internal nucleophile). An appreciable yield of 2-adamantyl benzyl ether from reaction in aqueous acetonitrile requires that neither intermediate (the oxodiazonium ion or the 2-adamantyl cation) lives long enough for the internal nucleophile to diffuse away. This step-wise reaction is different from the otherwise similar concerted fragmentation of 2-adamantyl azoxytosylate **6a** in eqn. (4).[4] A corollary is that the k_2 step of **3g** must be irreversible. When **3g** was solvolysed for just one half-life in methanol, no **3h** was detected and NMR spectra indicated that 1% of **3h** with **3g** would have been seen. Since **3h** is appreciably less reactive than **3g**, see Table 1, any **3h** formed would not have reacted further to any significant extent under the reaction conditions. Thus, the first-formed oxodiazonium ion intermediate from **3g** is not trapped at the electrophilic nitrogen by the abundant and nucleophilic solvent molecules (CH_3OH) and hence will not be trapped by the single internal nucleophile ($PhCH_2OH$) even though this does trap the subsequently formed carbenium ion to give 2-adamantyl benzyl ether. The k_2 step from **3g**, therefore, is indeed irreversible. We propose that the other simple secondary alkyl systems **3e**, **3h**, and **3i** also react with the k_2 step rate-limiting though direct evidence is so far unavailable.

The rate-limiting step for simple primary alkyl compounds 3a, 4, and 5

In view of the non-existence of methyl and simple primary carbenium ions in aqueous solution, $k_{2'}$, k_3, and k_4 routes may be dismissed for substrates **3a**, **4**, and **5** which we propose react *via* the k_2 and $k_{3'}$ channel. If the former is rate-limiting, we expect the entropy of activation to be unexceptionally modestly

negative corresponding to a second-order reaction,[9] and the kinetics parameters to be generally similar to those for **3e** and **3g–i** as is found. If the latter were rate-limiting, *i.e.* with the k_2 step being reversible, an extra solvent molecule becomes involved in the formation of the activated complex and an entropy of activation more negative than those for **3e** and **3g–i** would have been observed, but is not. We conclude that cleavage of the protonated substrate, the k_2 step, is rate-limiting for the three compounds **3a**, **4**, and **5**.

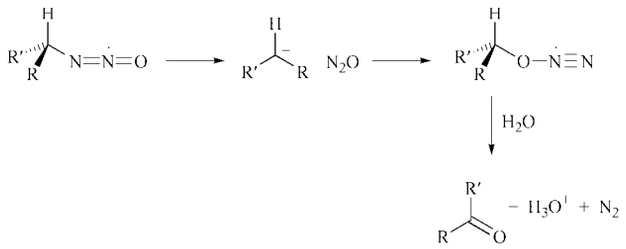
The rate-limiting step for benzylic compounds 3b–3d, and 3f

Given the similarity of the activation parameters for all our compounds, we further deduce that reaction of the protonated substrate is also rate-limiting for compounds **3b–d** and **3f**, *i.e.* either k_2, k_3, or $k_{2'}$. For these compounds, k_3 or $k_{2'}$ are less likely than k_2 as rate-limiting steps since rate-limiting fragmentation, even of a species formed in a prior bimolecular step, would not be expected to have such negative entropies of activation as we observe. The route *via* steps with elementary rate constants k_2 and k_3, and that *via* the single step with rate constant $k_{2'}$ correspond to alternative step-wise and concerted fragmentations of the protonated substrates to give a carbenium ion intermediate, and both are credible options for these substrates. The initial product of the k_2 step in the step-wise fragmentation, an oxodiazonium ion $(R–N=N=O)^+$, has previously been considered as a potential intermediate in the solvolysis of alkyl azoxyarenesulfonates,[15] and has been investigated theoretically.[16] Besides losing nitrous oxide to give the carbenium ion R^+ (elementary rate constant k_3), $(R–N=N=O)^+$ could also suffer direct bimolecular nucleophilic attack (elementary rate constant $k_{3'}$). If fragmentation of benzylic substrates **3c** and **3d** were concerted ($k_{2'}$ route), there would be a build-up of positive charge at the benzylic carbon in the transition state and an appreciable rate ratio for **3c** and **3d** may be anticipated (>300 assuming a ρ^+ value of about −3.3 using substituted benzyl azoxyarenesulfonates as a model).[17] Since the actual rate ratio for **3c** and **3d** is <20, we deduce that these benzylic substrates and, by similar arguments, **3b** and **3f** cannot involve the rate-limiting concerted $k_{2'}$ fragmentation route; they too react *via* the step-wise route with the k_2 step rate-limiting.

The remaining issue for compounds **3b–d**, and possibly **3e–f** and **3i**, is whether the oxodiazonium ion $(R–N=N^+=O)$ fragments by the k_3 and k_4 steps *via* carbenium ions, or whether it suffers direct nucleophilic attack by the $k_{3'}$ path after the rate-limiting step. There is product analysis evidence below at least for **3b** and **3c**. However, since the substitution product derived from the internal nucleophile (ROR′ from RN(NO)OR′) is invariably detected, the product-determining intermediate, regardless of whether it is R^+ or $(RN_2O)^+$, must be very short-lived, *i.e.* it is trapped by R′OH before R′OH has time to diffuse away.

Detection of carbonyl compounds from solvolysis of *N*-benzyl substrates 3b and 3c and the *N*-(1-phenylethyl) substrate 3f

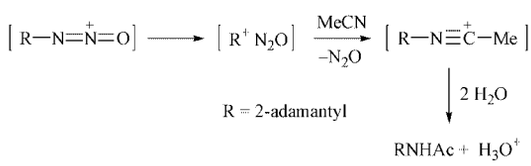
We reported earlier that benzaldehyde is formed in low yield from the solvolysis of benzyl azoxytosylate (**7**). We proposed that it arises by elimination of an α-C-H and dinitrogen from the complex cation ($PhCH_2–O–N_2^+$) formed by capture of the benzyl carbenium ion by nitrous oxide following concerted fragmentation of the substrate.[15] An analogous partial mechanism is shown in Scheme 4 for the formation of benzaldehyde from **3b** and **3c**. In the present reactions, however, the immediate precursor of the benzaldehyde is generated by isomerisation *via* an ion–molecule pair of the oxodiazonium ion ($PhCH_2–N=N^+=O$) formed in the k_2 step of Scheme 3, a process already known to be exothermic.[16] This formation of benzaldehyde shows that the oxodiazonium ion formed in the k_2 step from **3b** and **3c** undergoes a step-wise reaction at least to some degree *via* the benzyl cation. Correspondingly, a low yield of acetophenone was detected in the reaction of **3f** and, by analogy, a low yield of *p*-methoxybenzaldehyde is predicted from **3d**. Our failure to detect adamantan-2-one or cyclohexanone from reactions of **3g** and **3i** suggests that internal return with bonding of the carbenium ion to the oxygen of nitrous oxide does not occur from these substrates.



Scheme 4

The Ritter reaction from 3g in aqueous acetonitrile

In addition to the expected alcohols and the ether, 2-acetamidoadamantane was detected in appreciable yield from *N*-(2-adamantyl)-*N*-nitroso-*O*-benzylhydroxylamine in aqueous acetonitrile. The most credible explanation is that the 2-adamantyl carbenium ion is trapped by acetonitrile in a version of the Ritter reaction,[18] Scheme 5. Acetamidocyclohexane was detected but only in very low yield (<1%) from the corresponding reaction of **3i**.



Scheme 5

Experimental

Unless otherwise stated, starting materials were of reagent grade or better and used as supplied; solvents were either redistilled or of HPLC grade. ^1H and ^{13}C NMR spectra were recorded on Bruker 200 or 500 MHz spectrometers; the NMR solvent was deuteriochloroform unless otherwise stated, all chemical shifts (in ppm) are downfield from the signal (^1H or ^{13}C) of TMS, and coupling constants (J) are given in Hz. Mass spectrometry was carried out on a Kratos M580RF instrument operating in electron impact mode (70 eV). The FTIR spectrum of nitrous oxide (see below) was recorded on an ATI Mattson Genesis series spectrometer controlled by Galaxy software on a Gateway 2000 P5 75 computer.

Preparations

***N*-Nitroso-*N*,*O*-dimethylhydroxylamine (3a).** An ice-cold aqueous solution of sodium nitrite (2.12 g, 30.7 mmol) was added drop-wise to a stirred ice-cold solution of *N*,*O*-dimethylhydroxylamine hydrochloride (Lancaster, 1.48 g, 15.2 mmol) in hydrochloric acid (6 mol dm^{-3}, 5.1 cm^3) then left for 2 h. The aqueous mixture was extracted with dichloromethane (3 × 15 cm^3), and the combined organic phase was dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residual oil was distilled (bp 60–65 °C, 20 Torr; lit.,[19] 59–60 °C, 30 Torr) to yield a mobile yellow–green oil (929 mg, 10.3 mmol, 68%; δ_H: 3.77 (s), 3.75 (s); δ_C: 38.64, 61.71).

***N*-Hydroxyurethane.**[20] Ethyl chloroformate (1.75 cm^3, 14.3 mmol) was added drop-wise over *ca.* 1 h to a stirred ice-cold suspension of anhydrous potassium carbonate (1.97 g, 14.3 mmol) and hydroxylammonium chloride (1.18 g, 17.2 mmol) in tetrahydrofuran (10 cm^3). The reaction mixture was then stirred at room temperature for two days before the supernatant liquid

was decanted from the solid potassium chloride by-product, and the latter washed with diethyl ether (3 × 5 cm^3). The solvent was evaporated from the combined organic phase under reduced pressure to leave the crude product as an oil (1.44 g, 13.7 mmol, 96%; δ_H: 1.28 (t, J = 7.1, 3H, –CH_2–CH_3), 4.21 (q, J = 7.1, 2H, –CH_2–CH_3), 7.55 and 7.65 (br, 1H, v. br, 1H, HONH–CO–); δ_C: 14.26, 62.26, 159.63).

***N*-Ethoxycarbonylisoxazolidine.**[21] A small piece of sodium (*ca*. 0.06 g, 3 mmol) was stirred in *tert*-butanol (*ca*. 15 cm^3) at 65 °C overnight until it had fully reacted leaving a cloudy solution. *N*-Hydroxyurethane (0.25 g, 2.4 mmol) was then added followed by 1,3-dibromopropane (0.162 g, 0.08 cm^3, 0.8 mmol) by Pipetman, and the reaction was stirred at 65 °C for a further 6 h. When the reaction had cooled, the solvent was evaporated under reduced pressure to leave a milky oil which was dissolved in diethyl ether (*ca*. 20 cm^3) and washed with an equal volume of water. The water was separated and re-extracted with the same volume of diethyl ether. The combined organic phase was dried (Na_2SO_4), filtered, and evaporated under reduced pressure to yield a pale yellow oil (0.122 g; 100%; δ_H: 1.25 (t, J = 7.2, 3H, –CH_2–CH_3), 2.21 (quint., J = 7.2, 2H, –CH_2–CH_2–CH_2–), 3.62 (t, J = 7.4, 2H, –N–CH_2–CH_2–), 3.88 (t, J = 7.1, 2H, –CH_2–CH_2–O–), 4.17 (q, J = 7.1, 2H, –CH_2–CH_3)) which was used directly in the next step.

Isoxazolidinium chloride. A solution of *N*-ethoxycarbonylisoxazolidine (0.122 g from above) in aqueous hydrochloric acid (16%, *ca*. 2 cm^3) was heated under reflux for 2 h. The cooled reaction was diluted with water (*ca*. 15 cm^3) and extracted with diethyl ether (3 × 10 cm^3) to remove any unwanted neutral organic residues. The aqueous phase was evaporated to dryness under reduced pressure to leave crystals (64 mg, 0.59 mmol, 70%) which were washed with ice-cold ethanol to remove most of a slight orange tinge (mp 118 °C, lit.,[21] 124–125 °C; δ_H(D_2O): 2.48 (quint., J = 7.0, 2H, –CH_2–CH_2–CH_2–), 3.62 (t, J = 7.3, 2H, ≻N–CH_2–CH_2–), 4.23 (t, J = 6.8, 2H, –CH_2–CH_2–O–), 4.8 (s, solvent and ≻NH_2^+)).

***N*-Nitrosoisoxazolidine (4).**[8] An ice-cold aqueous solution of sodium nitrite was added drop-wise over *ca*. 12 min to a stirred solution of isoxazolidinium chloride (0.10 g, 0.91 mmol) in aqueous hydrochloric acid (1.82 cm^3, 1 mol dm^{-3}, 1.82 mmol) and ethanol (2.5 cm^3) at 0 °C. After approximately 1 h, the solution was tested with starch iodide paper to confirm the presence of excess nitrous acid. The reaction was extracted four times with dichloromethane then the combined organic phase was dried (Na_2SO_4), filtered, and evaporated to leave an orange oil (0.059 g, 0.58 mmol, 64%). The crude product was crystallised from petroleum ether at −78 °C under nitrogen then allowed to warm to room temperature under reduced pressure whereupon the white crystals turned into an orange oil (δ_H: 2.49 (quint., J = 7.0, 2H, –CH_2–CH_2–CH_2–), 4.33 (t, J = 6.7, 4H, –CH_2–CH_2–CH_2–); δ_C: 25.61, 35.14, 70.42).

***N*-Ethoxycarbonyltetrahydro-1,2-oxazine.**[21,22] *N*-Hydroxyurethane (1.36 g, 12.6 mmol) was added to a stirred solution of potassium *tert*-butoxide (1.42 g, 12.6 mmol) in *tert*-butanol (*ca*. 50 cm^3). 1,4-Dibromobutane (0.91 g, 0.50 cm^3, 4.21 mmol) was then added and the reaction mixture heated to 65 °C for 6 h. The *tert*-butanol was evaporated under reduced pressure from the cooled reaction mixture to leave a milky residue which was dissolved in diethyl ether. This solution was washed with a small volume of water and the separated water phase was re-extracted with diethyl ether. The organic phases were combined, dried (Na_2SO_4), filtered, and evaporated to give a pale yellow oil (0.75 g, one third of which by ^{1}H NMR was unreacted *N*-hydroxyurethane, *i.e.* an approximate yield of 74% of *N*-ethoxycarbonyltetrahydro-1,2-oxazine (δ_H: 1.26 (t, J = 7.1, 3H, –O–CH_2–CH_3), 1.72 (m, 4H, –CH_2–CH_2–CH_2–CH_2–), 3.64 (t, J = 5.2, 2H, ≻N–CH_2–CH_2–), 3.95 (t, J = 5.0, 2H, –O–CH_2–CH_2–), 4.18 (q, J = 7.1, 2H, –O–CH_2–CH_3)). The product was used directly.

Tetrahydro-1,2-oxazin-2-ium chloride. A solution of crude *N*-ethoxycarbonyltetrahydro-1,2-oxazine (2.76 g, 17.3 mmol) in aqueous hydrochloric acid (16%, 20 cm^3) was heated under reflux for 2 h. The cooled reaction was diluted with a little water and extracted with diethyl ether. The aqueous phase was evaporated to dryness under reduced pressure to leave slightly off-white crystals which were recrystallised from ice-cold redistilled propan-2-ol to give a first crop of fine white needles (0.247 g, mp 148–150 °C, lit.,[21] 141–143 °C; δ_H(D_2O): 1.88 (m, 4H, –CH_2–CH_2–CH_2–CH_2–), 3.41 (t, J = 5.6, 2H, –NH_2^+–CH_2–CH_2–), 4.20 (t, J = 5.0, 2H, –CH_2–CH_2–O–); δ_C(D_2O): 19.97, 23.12, 47.85, 73.65), a second crop of fine white needles (0.467 g), and a third crop of off-white solid (0.630 g).

***N*-Nitrosotetrahydro-1,2-oxazine (5).**[23] An ice-cold solution of aqueous sodium nitrite (1.63 mmol, 0.112 g) was added drop-wise over *ca*. 12 min to a stirred solution of tetrahydro-1,2-oxazin-2-ium chloride (0.10 g, 0.81 mmol) in aqueous hydrochloric acid (1.25 mol dm^{-3}, 0.65 cm^3, 0.81 mmol) and ethanol (5 cm^3) at 0 °C. The solution was stirred for 1 h, tested with starch–iodide paper to confirm the presence of excess nitrous acid, then extracted three times with dichloromethane. The combined organic layer was dried ($MgSO_4$), filtered, and evaporated to give an orange oil (0.060 g, 64%). The crude product was crystallised under argon from petroleum ether at −78 °C; the crystals were washed twice with petroleum ether then the flask was brought to room temperature under reduced pressure. The white crystals (0.040 g; δ_H: 1.92 (m, 4H, ≻N–CH_2–CH_2–CH_2–CH_2–O–), 4.01 (t, J = 5.0, 2H, ≻N–CH_2–CH_2–), 4.27 (t, J = 5.5, 2H, –CH_2–CH_2–O–); δ_C: 23.74, 23.93, 50.90, 74.43) melted at *ca*. 9 °C.

***N*-Methoxyphthalimide.** Anhydrous potassium carbonate (2.21 g, 16.0 mmol) was added slowly to a stirred solution of *N*-hydroxyphthalimide (4.10 g, 25.0 mmol) in dimethyl sulfoxide (37 cm^3). Methyl iodide (6.04 g, 2.65 cm^3, 42.5 mmol) was added drop-wise to the reddish brown solution at a rate such that the temperature did not exceed 30 °C. The reaction was stirred at room temperature for 24 h (the solution had turned orange after approximately 1 h) then poured into cold water and left to stand at 0–5 °C for about 30 min. The first crop of crystals (3.34 g, 18.9 mmol, 76%; δ_H: 4.08 (s, 3H, –O–CH_3), 7.81 (AB q, J = 8.6, 4H, C_6H_4≺); mp 131–132 °C, lit.,[24] 133 °C) was filtered and washed with water (3 × 10 cm^3). The washings and filtrate were combined and extracted with dichloromethane (3 × 10 cm^3). The organic phases were combined, washed with water (3 × 20 cm^3), dried (Na_2SO_4), filtered, and evaporated to leave an off-white second crop (0.360 g, 2.03 mmol, 8%).

***O*-Methylhydroxylammonium chloride.** A solution of *N*-methoxyphthalimide (18.4 g, 0.10 mol) in aqueous hydrochloric acid (6 mol dm^{-3}, 185 cm^3) was heated under reflux for 30 min then the reaction was allowed to cool and kept below 0 °C overnight. The phthalic acid precipitate was filtered and washed with cold water. The filtrate and washings were combined and extracted with dichloromethane. The aqueous phase was then evaporated under reduced pressure and the residual white crystals were dried under vacuum to a constant weight (9.16 g; δ_H(D_2O): 3.81 (s, 3H, –OCH_3), 4.78 (s, 3.5H, –NH_3^+ plus H_2O); mp 142–145 °C, lit.,[24] 150–151 °C).

Benzaldehyde *O*-benzyloxime.[25] A solution of *O*-benzylhydroxylammonium chloride (3.00 g, 18.8 mmol), freshly distilled benzaldehyde (2.19 g, 2.1 cm^3, 20.7 mmol), and sulfuric acid (1 cm^3 of 1 drop of concentrated acid in 8 cm^3 of ethanol) was heated under reflux in ethanol (30 cm^3) overnight. The cooled ethanol solution was evaporated under reduced pressure

then the residue was dissolved in diethyl ether; the solution was stirred with potassium carbonate then washed with aqueous sodium metabisulfite and with water. The diethyl ether solution was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give an orange oil (3.42 g, 16.2 mmol, 86%; δ_H: 5.24 (s, 2H, $-CH_2-O-$), 7.33–7.50 (m, 8H, Ar), 7.56–7.65 (m, 2H, Ar), 8.16 (s, 1H, –CH=N–); δ_C: 76.49, 127.17, 128.07, 128.53, 128.75, 129.93, 132.27, 137.58, 149.14).

***N*,*O*-Dibenzylhydroxylammonium chloride.** Benzaldehyde *O*-benzyloxime (0.482 g, 2.29 mmol), sodium cyanoborohydride (0.096 g, 1.5 mmol),[26] and a crystal of methyl orange were stirred in methanol (15 cm^3) under a slow flow of nitrogen. A solution of methanolic hydrogen chloride prepared from acetyl chloride (3–4 cm^3) cautiously added to methanol (20 cm^3) was slowly added drop-wise at a rate to avoid effervescence; the yellow solution turned a rose pink. When the reaction mixture had remained this colour for at least 30 min, the methanol was evaporated under reduced pressure. The pink residue was taken up in a few cm^3 of water and the pH was increased to *ca*. 9 with aqueous sodium hydroxide solution (2 mol dm^{-3}). The reaction mixture was extracted three times with dichloromethane then the organic phases were combined, dried (Na_2SO_4), filtered, and evaporated. Hydrogen chloride was bubbled through a solution of the resulting pale yellow oil in diethyl ether to give fine white crystals of the salt (0.204 g, 0.82 mmol, 36%; mp 170–171 °C, lit.,[27] 174–176 °C; δ_H(d_6-DMSO): 4.58 (s, 2H, $-NH_2^+-CH_2-$), 5.32 (s, 2H, $-CH_2-O-$), 7.5 (m, 10H, Ar), 7.72 (br m, 2H, $\geq NH_2^+$); δ_C(d_6-DMSO): 52.26, 74.83, 128.82, 128.93, 129.35, 129.52, 130.53 (quaternary), 131.06, 134.12 (quaternary); C 67.30, H 6.30, N 5.40%; $C_{14}H_{16}NOCl$ requires C 67.33, H 6.46, N 5.61%) which was easier to handle and more stable for storage than the free base.[25] The diethyl ether filtrate was evaporated to leave the impure free base (0.121 g, 0.57 mmol, 25%; δ_H: 3.95 (s, 2H, $-NH-CH_2-$), 4.56 (s, 2H, $-O-CH_2-$), 5.58 (br, 1H, $\geq$NH), 7.22 (m, 10H, Ar); δ_C: 56.61, 76.41, 127.54, 127.90, 128.46, 128.60, 129.08, 137.68, 137.96).

***N*-Nitroso-*N*,*O*-dibenzylhydroxylamine (3c).[28]** An ice-cold solution of sodium nitrite (0.65 g, 9.4 mmol) in a few cm^3 of water was added over *ca*. 10 min to a stirred solution of *N*,*O*-dibenzylhydroxylamine (1.0 g, 4.7 mmol) in ethanol (5 cm^3) and aqueous hydrochloric acid (1 mol dm^{-3}, 9.4 cm^3, 9.4 mmol) in an ice bath. The solution was stirred for a further 1 h by which time slightly off-white fibrous crystals had formed and were filtered off (0.965 g, 85%). The crude reaction product was recrystallised under nitrogen at −78 °C from diethyl ether–petroleum ether (1 : 1) to give white needles (mp 73–74 °C; δ_H: 4.85 (s, 2H, $-CH_2-N<$), 5.16 (s, 2H, $-CH_2-O-$), 7.19–7.42 (m, 10H, Ar); δ_C: 58.00, 77.07, 128.67, 128.86, 128.93, 129.28, 129.59, 133.05, 134.01; C 69.67, H 5.65, N 11.03%; $C_{14}H_{14}O_2N_2$ requires C 69.41, H 5.82, N 11.56%; *m*/*z*: 212 ($M^+ - NO$, 10%), 107 ($C_6H_5CH_2O$, 10), 105 ($C_6H_5CH_2N$, 48), 91 (C_7H_7, 100)). This compound was structurally characterised by X-ray crystallography (see below).

***p*-Methoxybenzaldehyde *O*-benzyloxime.** A solution of freshly distilled *p*-methoxybenzaldehyde (0.36 g, 0.32 cm^3, 2.6 mmol), *O*-benzylhydroxylammonium chloride (0.411 g, 2.57 mmol), sulfuric acid (one drop of a 1 : 1 (v/v) solution of concentrated acid and ethanol) was heated under reflux in ethanol (1–2 cm^3) for about 12 h. The reaction was worked up as described above for the unsubstituted analogue to give the crude product as a yellow oil (δ_H: 3.81 (s, 3H, $-OCH_3$), 5.17 (s, 2H, $-CH_2-$), 6.89 (d, J = 8.7, 2H, *ortho* to CH_3O), 7.29–7.43 (m, 5H, C_6H_5-), 7.51 (d, J = 8.8, 2H, *meta* to CH_3O), 8.08 (s, 1H, –N=CH–); 0.635 g, 2.6 mmol, 100%).

***N*-(*p*-Methoxybenzyl)-*O*-benzylhydroxylammonium chloride.** *p*-Methoxybenzaldehyde *O*-benzyloxime (0.567 g, 2.35 mmol) and sodium cyanoborohydride (0.177 g, 2.8 mmol) were reacted according to the procedure used for the unsubstituted dibenzyl compound,[26] and the work-up afforded a yellow oil (0.502 g, 2.06 mmol, 88%). Hydrogen chloride was bubbled through a solution of the crude product in diethyl ether (100 cm^3) for 1 h, to give a fine white precipitate which was filtered off (0.303 g, 1.08 mmol, 55%; δ_H(d_6-DMSO): 3.84 (br s, 3H, $-OCH_3$), 4.46 (br s, 2H, $\geq N-CH_2-$), 5.26 (br s, 2H, $-O-CH_2-$), 7.06 (br s, 2H, *ortho* to CH_3O), 7.62 (br s, 2H, *meta* to CH_3O), 7.48 (br s, 5H, C_6H_5-); δ_C(d_6-DMSO): 51.82, 55.67, 74.79, 114.19, 122.14, 128.96, 129.37, 129.52, 132.64, 134.15, 160.06; *m*/*z*: 243 (M^+ − HCl, 20%), 135 ($CH_3OC_6H_4CH_2N$, 23), 121 ($CH_3OC_6H_4CH_2$, 80), 107 ($C_6H_5CH_2O$, 15), 91 (C_7H_7, 100); C 64.86, H 6.16, N 5.74%; $C_{15}H_{18}O_2NCl$ requires C 64.52, H 6.45, N 5.02%).

***N*-Nitroso-*N*-(*p*-methoxybenzyl)-*O*-benzylhydroxylamine (3d).** An ice-cold aqueous solution of sodium nitrite (0.090 g) was slowly added drop-wise to a stirred cloudy solution of *N*-(*p*-methoxybenzyl)-*O*-benzylhydroxylammonium chloride (0.120 g, 0.43 mmol), aqueous hydrochloric acid (1 mol dm^{-3}, 0.9 cm^3), and a minimal amount of ethanol at 0 °C until starch iodide paper showed an excess of nitrous acid to be present. The precipitated fine white solid was filtered, washed with ice-cold water, and dried over silica gel (0.087 g, 0.32 mmol, 74%) then was recrystallised at −78 °C from (1 : 1) diethyl ether–petroleum ether (mp 69–70 °C; δ_H: 3.81 (s, 3H, $-OCH_3$), 4.81 (s, 2H, $\geq N-CH_2-$), 5.08 (s, 2H, $-O-CH_2-$), 6.89 (d, 2H, J = 8.6, *ortho* to CH_3O), 6.91–7.36 (m, 5H, C_6H_5- and 2H, *meta* to CH_3O); δ_C: 55.39, 57.49, 114.30, 124.96, 128.64, 129.23, 129.59, 130.33, 134.12, 160.03; *m*/*z*: 241 (M^+ − NOH, 20%), 151 ($M^+ - CH_3OC_6H_4CH_2$, 30), 121 ($CH_3OC_6H_4CH_2$, 60), 107 ($C_6H_5CH_2O$, 15), 91 (C_7H_7, 100); C 67.07, H 5.50, N 10.02%; $C_{15}H_{16}O_3N_2$ requires C 66.17, H 5.88, N 10.29%).

Benzaldehyde *O*-methyloxime.[29] A solution of *O*-methylhydroxylammonium chloride (1.25 g, 15.0 mmol), freshly distilled benzaldehyde (1.70 g, 1.62 cm^3, 16.0 mmol), ethanolic sulfuric acid (1 drop of a 10% (v/v) solution), and ethanol (20 cm^3) was heated under reflux overnight. The cooled reaction mixture was neutralised with calcium carbonate then the slurry was filtered; the filtrate was evaporated under reduced pressure to leave a yellow oil that was dissolved in diethyl ether. The ether solution was washed with aqueous sodium metabisulfite, with water, then was dried ($MgSO_4$), filtered, and evaporated to give a pale orange oil (δ_H: 3.96 (s, 3H, $-OCH_3$), 7.32–7.37 (m, 3H, Ar *meta* and *para* to oxime), 7.54–7.59 (m, 2H, Ar *ortho* to oxime), 8.05 (s, 1H, –CH=N–); 1.59 g, 11.8 mmol, 78%).

***N*-Benzyl-*O*-methylhydroxylammonium chloride.** Benzaldehyde *O*-methyloxime (3.91 g, 29.0 mmol) in methanol (30 cm^3) was reduced with sodium cyanoborohydride (1.20 g, 19.0 mmol), methanolic hydrogen chloride (made from 3–4 cm^3 acetyl chloride cautiously added to 20 cm^3 of methanol), and methyl orange indicator by the method described for the dibenzyl analogue.[26] Initially, the free base was isolated (3.53 g, 25.7 mmol, 87%) but was then taken up in diethyl ether and the solution was extracted with aqueous hydrochloric acid (17%). The aqueous phase was evaporated and dried under reduced pressure to leave the hydrochloride salt (2.30 g, 13.3 mmol, 46%). The product was purified by sublimation under reduced pressure (mp 160–161 °C, lit.,[30] 168–169 °C; δ_H(D_2O): 3.85 (s, 3H, $-OCH_3$), 4.44 (s, 2H, $-CH_2-N<$), 7.45 (s, 5H, C_6H_5-); δ_C(D_2O): 54.40, 63.11, 129.56, 130.67, 131.54, 132.09; C 55.35, H 7.15, N 8.05%; $C_8H_{12}ONCl$ requires C 55.34, H 6.97, N 8.07%).

***N*-Nitroso-*N*-benzyl-*O*-methylhydroxylamine (3b).** *N*-Benzyl-*O*-methylhydroxylammonium chloride (0.60 g, 3.5 mmol) was nitrosated as described for the dibenzyl analogue with aqueous hydrochloric acid (1.25 mol dm^{-3}, 7.0 mmol) and sodium nitrite

(0.483 g, 7.0 mmol) in ethanol (*ca.* 40 cm^3). The product mixture was extracted three times with diethyl ether then the combined ether phase was washed with water, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give an orange oil (0.55 g, 3.3 mmol, 94%; δ_H: 3.65 (s, 3H, $-OCH_3$), 5.28 (s, 2H, $-CH_2-N\leq$), 7.37 (s, 5H, C_6H_5-)).

Adamantanone *O*-benzyloxime. A solution of *O*-benzylhydroxylammonium chloride (0.50 g, 3.1 mmol), adamantanone (0.52 g, 3.5 mmol), sulfuric acid (1 drop of a 4% (v/v) solution in ethanol), and ethanol (10 cm^3) was heated under reflux overnight. The cooled solution was evaporated under reduced pressure and the residue dissolved in diethyl ether. The ether solution was washed with aqueous potassium carbonate then aqueous sodium metabisulfite solution, then was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to leave a slightly orange oil (0.607 g, 2.38 mmol, 77%). A portion of the product was chromatographed on silica gel, eluting with petroleum ether–ethyl acetate (20 : 1) plus 1% triethylamine, to yield a colourless oil (δ_H: 1.75–1.98 (m, 12H, adamantyl hydrogens excluding those β to oxime), 2.56 (s, 1H, β-CH *trans* to OBn), 3.57 (s, 1H, β-CH *cis* to OBn), 5.07 (s, 2H, $-O-CH_2-$), 7.24–7.38 (m, 5H, C_6H_5-); δ_C: 27.90, 29.81, 36.28, 36.57, 37.67, 39.07, 39.33, 75.01, 127.50, 127.79, 128.31, 138.60, 167.45).

***O*-Benzyl-*N*-(2-adamantyl)hydroxylammonium chloride.** The procedure described for the preparation of *N*,*O*-dibenzylhydroxylammonium chloride was followed.[25] In this case, adamantanone *O*-benzyloxime (0.209 g, 0.82 mmol) was treated with sodium cyanoborohydride (0.052 g, 0.82 mmol) in methanol (*ca.* 10 cm^3) and methyl orange indicator. Methanolic hydrogen chloride was added drop-wise until the reaction mixture was consistently pink/red. After the work-up, dry hydrogen chloride was bubbled through a solution of the crude free base in diethyl ether. The suspension was filtered to give the fine white solid hydrochloride salt (0.195 g, 0.67 mmol, 82%; mp 197–199 °C; δ_H(d_6-DMSO): 1.63–2.34 (m, 14H, adamantyl hydrogens except α-CH), 3.79 (s, 1H, α-CH), 5.43 (s, 2H, $C_6H_5-CH_2-$), 7.54 (m, 5H, C_6H_5-), 12.0–13.0 (br s, 1H, $\geq NH_2^+$); δ_C(d_6-DMSO): 26.57, 26.98, 27.55, 30.17, 36.23, 37.01, 63.59, 74.91, 128.94, 129.37, 129.62, 134.30; *m*/*z*: 257 (M^+ − HCl, 30%), 165 ($C_{10}H_{15}NO$, 40), 135 ($C_{10}H_{15}$, 60), 91 (C_7H_7, 100); C 69.40, H 7.98, N 4.34%; $C_{17}H_{24}NOCl$ requires C 69.50, H 8.23, N 4.77%).

***N*-Nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine (3g).** By the usual method, an ice-cold aqueous solution of sodium nitrite (0.050 g, 0.7 mmol) was added over *ca.* 10 min to a stirred solution of *N*-(2-adamantyl)-*O*-benzylhydroxylammonium chloride (0.102 g, 0.35 mmol), aqueous hydrochloric acid (1 mol dm^{-3}, 0.7 cm^3, 0.7 mmol), in ethanol (*ca.* 2 cm^3) at 0 °C. A white crystalline material was isolated (0.090 g, mp 70–71 °C) of which a portion (0.035 g) was recrystallised at −78 °C from petroleum ether to give a sample (0.029 g, mp 71–72 °C; δ_H: 1.60–2.08 (m, 12H, adamantyl), 2.53 (s, 2H, β-C–H), 3.96 (s, 1H, α-C–H), 5.02 (s, 2H, $C_6H_5-CH_2-$), 7.35–7.40 (m, 5H, C_6H_5-); δ_C: 27.27, 27.34, 30.46, 31.64, 37.16, 37.46, 70.90, 76.74, 128.71, 129.23, 129.49, 134.33; *m*/*z*: 256 (M^+ − NO, 10%), 149 ($C_{10}H_{15}N$, 30), 135 ($C_{10}H_{15}$, 92), 107 ($C_6H_5CH_2O$, 85), 91 (C_7H_7, 100); C 72.24, H 7.73, N 9.20%; $C_{17}H_{22}N_2O_2$ requires C 71.30, H 7.74, N 9.78%) which was used for kinetics studies.

Acetone *O*-benzyloxime.[31] *O*-Benzylhydroxylamine hydrochloride (1.53 g, 9.56 mmol), one drop of sulfuric acid, and acetone (20 cm^3) were reacted in the same manner as in the preparation of acetophenone *O*-benzyloxime to yield a colourless clear oil (1.71 g, 8.85 mmol, 92%; δ_H: 1.86 (3H, s, CH_3 *trans* to OBn), 1.88 (3H, s, CH_3 *cis* to OBn), 5.09 (2H, s, $-CH_2-O-$), and 7.24–7.36 (5H, m, C_6H_5-); δ_C: 15.81, 21.93, 75.29, 127.63, 127.91, 128.34, 138.38, 155.25).

***O*-Benzyl-*N*-isopropylhydroxylamine.** Acetone *O*-benzyloxime (449 mg, 2.76 mmol), sodium cyanoborohydride (217 mg, 3.14 mmol), a trace of methyl orange indicator, and methanol (10 cm^3) were stirred under nitrogen.[26] A methanolic solution of hydrogen chloride prepared from acetyl chloride (4 cm^3) in methanol (20 cm^3) was added drop-wise to maintain a red colour in the reaction mixture which was then stirred for a further 20 h. The solvent was evaporated under reduced pressure and the residue made basic (aqueous NaOH) then extracted with dichloromethane (3 × 20 cm^3). The combined organic phase was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to yield a colourless oil (327 mg, 1.98 mmol, 72%; δ_H: 1.06 (6H, d, J = 6.3 $(CH_3)_2CH-$), 3.23 (1H, septet, J = 6.3, $(CH_3)_2CH-$), 4.71 (2H, s, $-O-CH_2-$), 5.08 (1H, br s, $\geq NH$), and 7.30–7.36 (5H, m, C_6H_5-); δ_C: 20.19, 51.68, 76.83, 127.79, 128.36, 128.40, 138.05).

***N*-Nitroso-*N*-isopropyl-*O*-benzylhydroxylamine (3e).** Hydrochloric acid (3.25 cm^3, 2 mol dm^{-3}, 6.50 mmol), *O*-benzyl-*N*-isopropylhydroxylamine (525 mg, 3.18 mmol), and ethanol (*ca.* 1 cm^3) were reacted in the same manner as in the preparation of *N*-nitroso-*N*-(1-phenylethyl)-*O*-benzylhydroxylamine to yield a clear yellow–green oil (512 mg, 2.64 mmol, 83%; δ_H: 1.36 (6H, d, J = 6.6, $(CH_3)_2CH-$), 4.61 (1H, septet, J = 6.7, $(CH_3)_2CH-$), 5.01 (2H, s, $-O-CH_2-$), and 7.35–7.43 (5H, m, C_6H_5); δ_C: 20.38, 57.83, 128.54, 129.23, 129.54, 134.41; *m*/*z*: 91 ($PhCH_2^+$, 100%), 164 (M^+ − NO, 5.5), and 107 ($M^+ - (CH_3)_2CHN_2O$, 2)).

Acetophenone *O*-benzyloxime. A solution of *O*-benzylhydroxylammonium chloride (1.71 g, 10.7 mmol), acetophenone (1.25 cm^3, 10.7 mmol), and a drop of sulfuric acid in ethanol (20 cm^3) was heated under reflux for 10 h. The ethanol was evaporated under reduced pressure and the residual slurry made basic (aqueous NaOH) was then extracted with dichloromethane (3 × 30 cm^3). The combined organic phase was dried ($MgSO_4$), filtered, and the solvent was evaporated under reduced pressure to yield a pale brown oil (2.26 g, 10.0 mmol, 94%; δ_H: 2.29 (3H, s, $-C(CH_3)=N-$), 5.27 (2H, s, $-O-CH_2-$), and 7.32–7.69 (10H, m, Ar); δ_C: 12.40, 76.23, 126.13, 127.77, 128.18, 128.40, 129.08, 136.69, 138.15, 155.03).

***N*-(1-Phenylethyl)-*O*-benzylhydroxylamine.**[32] Acetophenone *O*-benzyloxime (710 mg, 3.16 mmol) in methanol (10 cm^3) was reduced under nitrogen with sodium cyanoborohydride (220 mg, 4.80 mmol), methanolic HCl, and a trace of methyl orange indicator as described for the *N*-isopropyl analogue.[26] The colourless oil product (712 mg) was chromatographed (silica gel, 16 : 1 petroleum ether–ethyl acetate and 1% triethylamine) to yield the product (180 mg, 25%; δ_H: 1.36 (3H, d, J = 6.7, $-CH(CH_3)-$), 4.17 (1H, q, J = 6.6, $-CH(CH_3)-$), 4.58 and 4.66 (2H, AB q, J = 11.5, $-CH_2-O-$), 5.63 (1H, br s, $\geq NH$), and 7.22–7.39 (10H, m, Ar)).

***N*-Nitroso-*N*-(1-phenylethyl)-*O*-benzylhydroxylamine (3f).** A solution of sodium nitrite (165 mg, 2.39 mmol) was added dropwise over *ca.* 10 min to a stirred solution of hydrochloric acid (1.3 cm^3, 2 mol dm^{-3}, 2.6 mmol), *N*-(1-phenylethyl)benzyl-*O*-benzylhydroxylamine (298 mg, 1.31 mmol), and ethanol (*ca.* 1 cm^3) in an ice bath; a green oil was observed after 30 min. The reaction mixture was left for 1.5 h then extracted with dichloromethane (3 × 20 cm^3). The combined organic phase was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to yield a clear yellow–green oil (314 mg, 1.23 mmol, 94%; δ_H: 1.71 (3H, d, J = 7.0, $-CH(CH_3)-$), 4.62 and 4.83 (2H, AB q, J = 9.7, $-CH_2-O-$), 5.57 (1H, br q, J = 6.5, $-CH(CH_3)-$), and 7.12–7.30 (10H, m, Ar); δ_C: 18.72, 64.68, 77.89, 127.43, 128.58, 128.71, 128.86, 129.17, 129.57, 134.11, 137.96).

Adamantanone *O*-methyloxime.[33] *O*-Methylhydroxylammonium chloride (718 mg, 8.60 mmol), adamantan-2-one

(1.17 g, 7.81 mmol), and ethanolic sulfuric acid (1 drop of a solution of 1 drop of concentrated sulfuric acid in 20 drops of ethanol) were heated under reflux in ethanol (10 cm^3) for 6 h. The cooled solution was evaporated under reduced pressure, and the residue taken up in water then extracted with dichloromethane (3 × 20 cm^3). The combined organic phase was dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure to yield a waxy oil (1.42 g; δ_H: 1.73–1.96 (12 H, m, adamantyl), 2.50 (1H, s, β CH *trans* to MeO), 3.42 (1H, s, β CH *cis* to MeO), 3.78 (3H, s, CH_3–O–)) which was used directly.

***N*-(2-Adamantyl)-*O*-methylhydroxylamine.** Adamantanone *O*-methyloxime (421 mg, 2.35 mmol), sodium cyanoborohydride (163 mg, 2.59 mmol), a trace of methyl orange indicator, and methanol (10 cm^3) were stirred under nitrogen and treated with methanolic HCl as described for the *N*-isopropyl analogue.[26] A straw-coloured oil (330 mg, 1.82 mmol, 77%; δ_H: 1.46–2.00 (14H, m, adamantyl), 3.11 (1H, s, α-C-H), 3.55 (3H, s, CH_3–O–), 5.57 (1H, br s, >N–H); δ_C: 27.77, 27.86, 30.78, 31.56, 37.27, 37.87, 62.50, 64.04) was isolated.

***N*-Nitroso-*N*-(2-adamantyl)-*O*-methylhydroxylamine (3h).** A solution of *N*-(2-adamantyl)-*O*-methylhydroxylamine (100 mg, 0.55 mmol), hydrochloric acid (552 l, 2 mol dm^{-3}, 1.10 mmol), and ethanol (1 cm^3) was treated with sodium nitrite (76 mg, 1.10 mmol) as for the *N*-isopropyl analogue to yield a clear yellow–green oil (113 mg, 0.54 mmol, 97%; δ_H: 1.62–2.08 (12 H, m, adamantyl), 2.53 (2H, s, β-C-H), 3.84 (3H, s, CH_3–O–), 4.14 (1H, s, α-C-H); δ_C: 27.26, 27.33, 30.41, 31.68, 37.12, 37.45, 67.70, 70.03).

Cyclohexanone *O*-benzyloxime. Cyclohexanone (2.00 cm^3, 1.89 g, 19.3 mmol), sodium acetate trihydrate (4.35 g, 91.3 mmol), and *O*-benzylhydroxylamine hydrochloride (2.62 g, 16.4 mmol) were dissolved in water–methanol (20 : 10, 30 cm^3) and heated under reflux for 2.5 h. The methanol was removed from the cooled solution under reduced pressure and the residue was extracted with dichloromethane (5 × 20 cm^3). The combined organic phase was dried (Na_2SO_4), filtered, and the solvent was removed under reduced pressure to yield a pale yellow oil (4.29 g; δ_H: 1.58–1.68 (6H, m, –$(CH_2)_3$–), 2.19 (2H, t, J = 5.99, –CH_2– *trans* to OBn), 2.49 (2H, t, J = 6.11, –CH_2– *cis* to OBn), 5.04 (2H, s, –O–CH_2–), 7.24–7.37 (5H, m, C_6H_5–); δ_C: 25.54, 25.80, 25.85, 27.07, 32.23, 75.14, 127.59, 127.91, 128.31, 138.29, 161.00) which was used directly.

***N*-Cyclohexyl-*O*-benzylhydroxylamine.**[34] Cyclohexanone *O*-benzyloxime (325 mg, 1.60 mmol), sodium cyanoborohydride (112 mg, 1.78 mmol), and methyl orange were stirred under nitrogen in methanol (4 cm^3) and treated as described above. The reaction yielded a colourless oil (289 mg, 1.41 mmol, 88%; δ_H: 1.00–1.90 (10H, m, –$(CH_2)_5$–), 2.87 (1H, m, >N–CH<), 4.69 (2H, s, –O–CH_2–), 7.26–7.35 (5H, m, C_6H_5–); δ_C: 24.66, 26.15, 30.71, 59.49, 76.91, 127.78, 128.36, 128.40, 138.00).

***N*-Nitroso-*N*-cyclohexyl-*O*-benzylhydroxylamine (3i).** Aqueous sodium nitrite (82 mg, 1.20 mmol), *N*-cyclohexyl-*O*-benzylhydroxylamine (78 mg, 0.380 mmol), hydrochloric acid (2 mol dm^{-3}, 570 µl, 1.14 mmol), and ethanol (1.5 cm^3) were reacted in the usual manner to yield an apple-green oil (74 mg, 0.316 mmol, 83%; δ_H: 1.10–2.04 (10 H, m, –$(CH_2)_5$–), 4.21 (1H, m, >N–CH<), 5.06 (2H, s, –O–CH_2–), 7.26–7.38 (5H, m, C_6H_5); δ_C: 25.08, 25.15, 30.76, 65.14, 77.52, 128.66, 129.21, 129.52, 134.32).

***p*-Methoxybenzyl methyl ether.** *p*-Methoxybenzyl chloride (0.092 g, 80 µl, 0.59 mmol) and silver(II) oxide (0.50 g, 3.5 mmol) were stirred in methanol (1–2 cm^3) at room temperature.[35] After 30 min, the reaction mixture was filtered (cotton wool) and the solvent was evaporated under reduced pressure to yield a pale straw-coloured oil (0.077 g, 93%; δ_H: 3.35 (s, 3H, –CH_2–O–CH_3), 3.78 (s, 3H, CH_3–O–Ar–), 4.38 (s, 2H, –CH_2–O–), 6.88 and 7.26 (4H, AB q, J = 8.6, Ar); δ_C: 55.28, 57.85, 74.39, 113.83, 129.42, 130.33, 159.26) which, by GLC, was principally a single compound.

***p*-Methoxybenzyl benzyl ether.** *p*-Methoxybenzyl chloride (69 mg, 60 µl, 0.44 mmol) and silver(II) oxide (0.37 g, 2.98 mmol) were stirred in benzyl alcohol (1–2 cm^3) at room temperature.[35] After 30 min, the reaction mixture was percolated through silica gel then evaporated under reduced pressure to yield a pale straw-coloured oil (78 mg, 0.34 mmol, 78%; δ_H: 3.80 (s, 3H, CH_3–O–), 4.50 (s, 2H, $MeOC_6H_4CH_2$–O–), 4.53 (2H, s, $C_6H_5CH_2$–O–), 6.90 (2H, half of AB q, J = 8.62), 7.24–7.42 (7H, m, half of AB q plus C_6H_5); δ_C: 55.33, 71.82, 113.90, 127.05, 127.61, 128.48, 129.52, 130.40, 141.06, 159.28).

2-Adamantyl benzyl ether. A mixture of sodium hydride (60% w/w dispersion in oil rinsed with petroleum ether, 426 mg, 10.7 mmol) and adamantan-2-ol (1.08 g, 7.1 mmol) in THF (several cm^3) was gently warmed under nitrogen then left for 0.5 h. Benzyl bromide (1.20 g, 6.99 mmol) was next added drop-wise then the reaction was stirred overnight. Water was added (*ca*. 3 cm^3) to the reaction mixture which was then made basic with aqueous ammonia (s.g. = 0.880). The bulk of the THF was removed by rotary evaporation and combined ethyl acetate extracts of the residue were washed with water (3 × 20 cm^3). The organic phase was dried ($MgSO_4$), filtered, and evaporated to yield a colourless mobile oil (1.38 g, 5.69 mmol, 81%; δ_H: 1.18–2.85 (14H, m, adamantyl), 3.48 (1H, s, α-C-H), 4.48 (–O–CH_2–), and 7.18–7.71 (5H, m, C_6H_5)).

2-Acetamidoadamantane. Adamantan-2-amine (226 mg, 1.49 mmol) was heated under reflux for 6 h in acetic anhydride (4 cm^3). Water (20 cm^3) was added to the cooled reaction mixture which was then heated further to decompose the excess acetic anhydride. The cooled reaction mixture deposited a cream-coloured precipitate which was filtered and recrystallised from water (209 mg, 1.08 mmol, 73%, mp 191 °C, lit.,[36] 193–195 °C; δ_H 1.54–1.84 (14H, m, adamantyl), 2.00 (3H, s, CH_3–CO), 4.03 (1H, d, C*H*–NH) and 5.82 (1H, br s, NH); δ_C 23.78, 27.12, 27.24, 31.92, 37.14, 37.55, 53.32, 169.17).

Crystal structure determination of 3c‡

Measurements were made at 160 K on a Bruker AXS SMART CCD diffractometer with Mo-Kα radiation (λ = 0.71073 Å) from a crystal of size 0.78 × 0.14 × 0.05 mm.

Crystal data. $C_{14}H_{14}N_2O_2$, M = 242.27, monoclinic, space group $P2_1$, a = 7.776(4), b = 5.832(3), c = 14.092(8) Å, β = 97.65(5)°, U = 633.4(6) $Å^3$, Z = 2, D_c = 1.27 g cm^{-3}, μ = 0.086 mm^{-1}. Intensities were measured by narrow-frame exposures (0.3° in ω) covering more than a hemisphere of reciprocal space. Because anomalous scattering effects were very small, Friedel pairs were averaged; the absolute structure cannot be established.[37] Of 2661 measured reflections, 1139 were unique ($2\theta \leq 25.26°$, R_{int} = 0.0461), and 1054 had $F^2 > 2\sigma(F^2)$. The structure was solved by direct methods and refined on F^2 values of all unique reflections.[38] A minor disorder component of refined occupancy 12.7(6)% was resolved for the central N_2O_2 unit, the terminal oxygen atom having a common site for both components, and was included in the refinement with the aid of restraints on geometry and displacement parameters. A riding model was used for isotopic H atoms, and anisotropic

‡ CCDC reference number 188/245. See http://www.rsc.org/suppdata/p2/b0/b001688h/ for crystallographic files in .cif format.

displacement parameters were refined for all other atoms. At convergence, $R = 0.0523$ (F values, $F^2 > 2\sigma$), $R_w = 0.1158$ (F^2 values, all data), goodness of fit = 1.298, final difference map within ±0.22 e Å^{-3}.

Kinetics

Perchloric acid stock solutions were made to approximately the required dilution then calibrated by titration against standard sodium hydroxide solution with phenolphthalein indicator. Ionic strengths were kept constant as appropriate using sodium perchlorate. First-order rate constants were measured by our normal UV method [39] using a Cecil 5502 double beam spectrophotometer connected to an Elonex PC-433 computer and a Grant W6 thermostatted waterbath connected to the cell block with a circulating pump. The temperature was monitored with a platinum resistance thermometer in the cell block and was constant to within 0.1 °C. Spectra and kinetics runs were recorded by remote control using solutions with initial absorbances in the range 0.8–1.0 in 1 cm quartz cells; the most suitable wavelength for kinetics was between 230 and 245 nm. Absorbance–time data were fitted to a single exponential decay equation and *pseudo* first-order rate constants were calculated by a non-linear iterative method. Standard deviations on individual *pseudo* first-order rate constants, k_{obs}, were generally less than 1% and reproducibility between runs was usually better than 5%. Second-order rate constants for the hydronium ion catalysed reactions were then calculated from plots of average *pseudo* first-order rate constants from several duplicate runs against hydronium ion concentration in the normal way.[9] Second-order rate constants, k_H, were usually measured over a temperature range of at least 30 °C (typically 4 results) then used to determine the value at 25.0 °C (if an experimental result was not available) and activation parameters for the acid catalysed reaction, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, using the Eyring equation.[9]

The acid catalysed decomposition of *N*-nitroso-*N*-(2-adamantyl)-*O*-methylhydroxylamine in MeOH at 25 °C. This was investigated because *N*-nitroso-*N*-(2-adamantyl)-*O*-methylhydroxylamine was a possible intermediate in the solvolysis of *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine in methanol. Solutions of **3h** in methanol (100 μl) and perchloric acid in water were separately injected into a UV cell containing methanol to give [substrate]$_o$ = 1.59 × 10^{-4} mol dm^{-3} and acid concentrations indicated below; neither ionic strength nor percentage water was maintained constant in these reactions.

[H_3O^+]/mol dm^{-3}	10^4 k_{obs}/s^{-1}
0.0500	0.677
0.100	1.06
0.200	1.75
0.300	2.40

$k_2 = 6.86 \times 10^{-4}$ dm^3 mol^{-1} s^{-1} at 25 °C; when [H_3O^+] = 0.178 mol dm^{-3}, $k_{obs} = 1.58 \times 10^{-4}$ s^{-1} and $t_{\frac{1}{2}} = 73$ min at 25 °C.

Product analysis

General considerations. Reactions were carried out under conditions as near as practicable to those of the kinetics reactions though on a larger scale and the substrate was more concentrated than in the kinetics experiments by a factor of about ten, *i.e.* [substrate]$_o$ *ca.* 10^{-3} mol dm^{-3}. In all cases, the substrate was reacted at the highest acid concentration used in the kinetics, typically 2.5 mol dm^{-3} perchloric acid, and left to react for at least 10 half-lives. ***Explosive organic perchlorates can be produced in methanolic perchloric acid, so great care should be taken in the work-up when using this system***. Completed reactions were made basic (NaOH) then sometimes carefully neutralised (potassium phosphate buffer, pH = 7). In early experiments when denitrosation was thought to be a possible reaction, sulfamic acid was used to trap any liberated nitrosating agent. The organic products were separated by extraction into dichloromethane or diethyl ether for analysis by GLC (3% OV17, 4 mm id × 2.4 m, 100–250 °C at 12 °C min^{-1} or 5% OV1, 4 mm id × 1.8 m, 80–240 °C at 8 °C min^{-1}) then, after isolation, by NMR. A Pye Unicam series 104 gas chromatograph fitted with a Shimadzu C-E1B integrator was used for all GLC analyses, the carrier gas in all cases being nitrogen.

Reaction of *N*-nitroso-*N*,*O*-dibenzylhydroxylamine (3c). A solution of *N*-nitroso-*N*,*O*-dibenzylhydroxylamine (0.10 g, 0.40 mmol), sulfamic acid (0.40 g, 4.1 mmol), aqueous perchloric acid (70%, *ca.* 11.9 mol dm^{-3}, 53 cm^3), water (132 cm^3), and methanol (50 cm^3) was stirred at room temperature for 24 h, then the methanol was removed under reduced pressure. The pH of the reaction mixture was increased to *ca.* 11 with aqueous sodium hydroxide solution then the mixture was extracted three times with diethyl ether. The combined organic phase was dried (Na_2SO_4), filtered, and evaporated to give a straw-coloured oil (0.048 g) which was shown by GLC and TLC to be principally two compounds. In a repeat experiment, the two products were separated by silica gel column chromatography using petroleum ether–ethyl acetate (2:1) and identified as benzyl alcohol and dibenzyl ether by comparison (GLC, ^{1}H NMR, and ^{13}C NMR) with authentic samples. The integrated ^{1}H NMR spectrum of the total reaction mixture indicated the benzyl alcohol and dibenzyl ether to be in the ratio 80:20 with *ca.* 2% of benzyl methyl ether (by comparison with an authentic sample); GLC analysis of the total reaction mixture supported this analysis and also showed a small yield (<1%) of benzaldehyde.

Possible involvement of *N*,*O*-dibenzylhydroxylamine. A solution of *N*,*O*-dibenzylhydroxylammonium chloride (0.10 g), aqueous perchloric acid (60%, *ca.* 9.14 mol dm^{-3}, 68 cm^3), water (132 cm^3), and methanol (50 cm^3) was stirred at room temperature for 24 h. The reaction was then worked up as for the *N*-nitroso derivative to give a straw-coloured oil (0.075 g) which was shown by ^{1}H and ^{13}C NMR to be recovered *N*,*O*-dibenzylhydroxylamine.

Reaction of *N*-nitroso-*N*-(*p*-methoxybenzyl)-*O*-benzylhydroxylamine (3d). A solution of *N*-nitroso-*N*-(*p*-methoxybenzyl)-*O*-benzylhydroxylamine (0.031 g, 0.11 mmol) in methanol (5–10 cm^3) was added to aqueous perchloric acid (1.0 mol dm^{-3}, 100 cm^3) and the solution was stirred as bubbles of a colourless gas collected on the stirrer bar. After *ca.* 2.5 h, the reaction mixture was worked up in the usual manner. The dichloromethane solution of products was dried (Na_2SO_4), filtered, and evaporated to give an orange oil which was analysed by GLC and NMR. Comparison with authentic samples indicated appreciable yields of benzyl alcohol, *p*-methoxybenzyl alcohol, *p*-methoxybenzyl methyl ether, and a smaller yield of benzyl *p*-methoxybenzyl ether.

Reaction of *N*-nitroso-*N*-benzyl-*O*-methylhydroxylamine (3b). A solution of *N*-nitroso-*N*-benzyl-*O*-methylhydroxylamine (0.10 g, 0.60 mmol), perchloric acid (70%, *ca.* 11.9 mol dm^{-3}, 53 cm^3), water (192 cm^3), sulfamic acid (0.582 g, 6.0 mmol), and methanol (5 cm^3) was stirred at room temperature for 24 h; after *ca.* 30 min, small bubbles of a colourless gas had collected on the stirrer magnet. The reaction was worked-up as described for the dibenzyl analogue above with initial neutralisation by concentrated sodium hydroxide solution and adjustment to pH = 7 by buffer. The reaction mixture was extracted three times with dichloromethane then the combined organic phase was washed with water, dried (Na_2SO_4), filtered, and evaporated to leave a pale orange oil (0.072 g) which was shown by ^{1}H and ^{13}C NMR analysis to be benzyl alcohol and benzyl methyl ether; analysis of the ^{1}H spectrum indicated a ratio of 89:11. GLC analysis of

the initial crude reaction mixture also showed the presence of benzaldehyde (<5%).

Reaction of *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine (3g) in acidic aqueous acetonitrile. (i) A solution of *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine (0.044 g, 0.15 mmol) aqueous perchloric acid (70%, *ca*. 11.9 mol dm^{-3}, 16.9 cm^3), water (115 cm^3), and acetonitrile (67 cm^3) was stirred for *ca*. 1.5 h at room temperature. The reaction mixture was neutralised (buffer, pH = 7) then extracted three times with dichloromethane. The combined organic phase was dried (Na_2SO_4), filtered, and evaporated under reduced pressure to leave a waxy solid (0.033 g). Benzyl alcohol and adamantan-2-ol were shown to be present by comparison with authentic samples (^1H and ^{13}C NMR, and GLC) and in similar yields (^1H NMR integration of the α-C-H signals); GLC indicated the presence of two additional products.

(ii) A solution of **3g** (51 mg, 0.178 mmol) in acetonitrile (83 cm^3) was added to aqueous perchloric acid (166 cm^3, 0.249 mol), at approximately 25 °C and the reaction was stirred for *ca.* 100 min. It was quenched with aqueous NaOH and extracted with dichloromethane (3 × 80 cm^3); the combined organic phase was dried ($MgSO_4$) and evaporated under reduced pressure to yield a waxy white solid (31 mg). GLC (0.6 m OV17, initial temperature 100 °C for 240 s, up to 250 °C at 12 °C min^{-1} and hold), GLC-MS (WCOT, Rtx-1), and ^1H NMR showed this to be a mixture of adamantan-2-ol, benzyl alcohol, 2-adamantyl benzyl ether and 2-acetamidoadamantane in similar amounts (comparison with authentic samples).

Perchloric acid catalysed partial decomposition of *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine in methanol. Perchloric acid (70% w/w, *ca.* 11.9 mol dm^{-3}, 2.00 cm^3) was added to a stirred solution of *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine (150 mg, 0.524 mmol) in methanol (129 cm^3) at 25 °C, and the reaction was stirred for one hour (*ca.* 1 half-life at $[H_3O^+] = 0.178$ mol dm^{-3}). The reaction was quenched with NaOH (980 mg, 24.5 mmol) in water (*ca*. 7 cm^3) and the methanol was removed under reduced pressure. Water (40 ml) was added to the residue and the mixture was extracted with dichloromethane (3 × 15 cm^3). The combined organic layer was dried ($MgSO_4$), filtered, and evaporated to yield a brown oil (86 mg) which was dissolved in $CDCl_3$ and analysed by ^1H NMR (200 and 500 MHz). Signals due to residual starting material (δ_H 3.97, 5.04) were evident as also were signals due to benzyl alcohol (δ_H 4.65), 2-adamantyl methyl ether (δ_H 3.35),[40] and 2-adamantyl benzyl ether (δ_H 3.57, 4.56). There was no evidence of the presence of *N*-nitroso-*N*-(2-adamantyl)-*O*-methylhydroxylamine (a sample of which was available for spectral comparison), the upper limit being estimated at 1% of the concentration of residual starting material.

Identification of nitrous oxide by FTIR. A solution of *N*-nitroso-*N*-(2-adamantyl)-*O*-benzylhydroxylamine (**3g**) (138 mg, 0.483 mmol) in acetonitrile (2.40 cm^3) was added to a stirred solution of aqueous perchloric acid (10.2 cm^3, *ca.* 70%, *ca.* 11.9 mol dm^{-3}), acetonitrile (40 cm^3), sodium perchlorate monohydrate (17.0 g, 0.121 mol), and distilled water (68.4 cm^3) at 30 °C under a nitrogen flow, and stirring was continued for *ca.* 1 h. The gas flow was passed through a tower of potassium hydroxide pellets and through a trap at liquid nitrogen temperature. The atmosphere above the trapped material was removed by a high vacuum pump, then the trap was brought to room temperature and connected to a previously evacuated FTIR gas cell. The spectrum (ν_{max}/cm^{-1} 3493 and 3467 (ν_{1+2}), 2576 and 2549 ($2\nu_1$), 2235 and 2213 (ν_3, asym. str.), 1300 and 1278 (ν_1 sym. str.)) was identical with a previously recorded spectrum of authentic nitrous oxide and concordant with published results.[12]

Acknowledgements

We thank the EPSRC for studentships to I. D. M. and P. C. M. and for equipment funding, Stirling Winthrop for a CASE award to I. D. M., the Association of Commonwealth Universities for a Research Fellowship to J. I. B., Dr J. G. Smith for advice and assistance in recording the FTIR spectrum of N_2O, and Miss L. Sinigaglia for the preparation of compound **3d**.

References

1 J. E. Saavedra, T. M. Dunams, J. L. Flippen-Anderson and L. K. Keefer, *J. Org. Chem.*, 1992, **57**, 6134; C. M. Maragos, D. Morley, D. A. Wink, T. M. Dunams, J. E. Saavedra, A. Hoffman, A. A. Bove, L. Isaac, J. A. Hrabie and L. K. Keefer, *J. Med. Chem.*, 1991, **34**, 3242.
2 A. R. Butler, *Chem. Br.*, 1990, 419; A. R. Butler and D. L. H. Williams, *Chem. Soc. Rev.*, 1993, 233.
3 E. G. Switkes, G. A. Dash and M. N. Ackermann, *Inorg. Chem.*, 1973, **12**, 1120.
4 H. Maskill, P. Murray-Rust, J. T. Thompson and A. A. Wilson, *J. Chem. Soc., Chem. Commun.*, 1980, 788; H. Maskill, J. T. Thompson and A. A. Wilson, *J. Chem. Soc., Perkin Trans. 2*, 1984, 1693.
5 J. K. Conner and H. Maskill, *Bull. Soc. Chim. Fr.*, 1988, 342.
6 J. H. Ridd, *Q. Rev. Chem. Soc.*, 1961, **15**, 418; E. H. White, in *The Chemistry of the Amino Group*, ed. S. Patai, Interscience, New York, 1968, ch. 8.
7 R. A. Cox, *Can. J. Chem.*, 1996, **74**, 1779.
8 H. Maskill, I. D. Menneer and D. I. Smith, *J. Chem. Soc., Chem. Commun.*, 1995, 1855.
9 H. Maskill, *The Physical Basis of Organic Chemistry*, Oxford University Press, Oxford, 1985.
10 D. L. H. Williams, *Nitrosation*, Cambridge University Press, Cambridge, 1988.
11 J. Haider, M. N. S. Hill, I. D. Menneer, H. Maskill and J. G. Smith, *Chem. Commun.*, 1997, 1571.
12 G. Herzberg, *Molecular Structure and Molecular Spectra: vol. 2, Infra-red and Raman Spectra of Polyatomic Molecules*, D. Van Nostrand, New York, 1945.
13 F. H. Allen and O. Kennard, *Chem. Des. Autom. News*, 1993, **8**, 31.
14 I. Yu. Bagryanskaya, T. V. Rybalova, Y. V. Gatilov, V. K. Khlestkin and D. G. Mazhukin, *Acta Crystallogr., Sect. C*, 1998, **54**, IUC9800073.
15 H. Maskill and W. P. Jencks, *J. Chem. Soc., Chem. Commun.*, 1984, 944; H. Maskill and W. P. Jencks, *J. Am. Chem. Soc.*, 1987, **109**, 2062.
16 P. M. W. Gill, H. Maskill, D. Doppinger and L. Radom, *J. Chem. Res.* (*S*), 1987, 54.
17 I. M. Gordon and H. Maskill, *J. Chem. Soc., Chem. Commun.*, 1989, 1358.
18 J. J. Ritter and P. P. Minieri, *J. Am. Chem. Soc.*, 1948, **70**, 4045; L. I. Krimen and D. J. Cota, *Org. React.* (*N.Y.*), 1969, **17**, 213.
19 A. B. Boese, Jr., L. W. Jones and R. T. Major, *J. Am. Chem. Soc.*, 1931, **53**, 3535.
20 R. T. Major, F. Dürsch and H.-J. Hess, *J. Org. Chem.*, 1959, **24**, 431.
21 H. King, *J. Chem. Soc.*, 1942, 432.
22 F. G. Riddell and D. A. R. Williams, *Tetrahedron*, 1974, **30**, 1083.
23 O. Wichterle and J. Novák, *Collect. Czech. Chem. Commun.*, 1950, **15**, 309 (*Chem. Abstr.*, 1951, **45**, 3849g).
24 T. Fujii, C. C. Wu and S.-i. Yamada, *Chem. Pharm. Bull.*, 1967, **15**, 345.
25 G. Bashiardes, G. J. Bodwell and S. G. Davies, *J. Chem. Soc., Perkin Trans. 1*, 1993, 459.
26 R. F. Borch, M. D. Bernstein and H. D. Durst *J. Am. Chem. Soc.*, 1971, **93**, 2897.
27 B. J. Ludwig, F. Dürsch, M. Auerbach, K. Tomeczek and F. M. Berger, *J. Med. Chem.*, 1967, **10**, 556.
28 A. Baranowski, *Pol. J. Chem.*, 1991, **65**, 1993.
29 H. Goda, H. Ihara, C. Hirayama and M. Sato, *Tetrahedron Lett.*, 1994, **35**, 1565.
30 D. H. Moore, J. G. Cannon, W. M. McIsaac and B. T. Ho, *J. Med. Chem.*, 1969, **12**, 45.
31 K. E. Rodriques, A. Basha, J. B. Summers and D. W. Brooks, *Tetrahedron Lett.*, 1988, **29**, 3455.
32 F.-C. Huang, T. S. Shoupe, C. J. Lin, T. D. Y. Lee, W.-K. Chan, J. Tan, M. Schnapper, J. T. Suh, R. J. Gordon, P. A. Sonnino, C. A. Sutherland, R. G. Van Inwegen and S. M. Coutts, *J. Med. Chem.*, 1989, **32**, 1836.

33 Y. Dong and J. L. Vennerstrom, *J. Org. Chem.*, 1998, **63**, 8582.
34 M. Fujita, H. Oishi and T. Hiyama, *Chem. Lett.*, 1986, 837.
35 B. Ortiz, F. Walls, F. Yuste, H. Barrios, R. Sànchez-Obregón and L. Pinelo, *Synth. Commun.*, 1993, **23**, 749.
36 F. Vincent, R. Tardivel and P. Mison, *Tetrahedron*, 1976, **32**, 1681.
37 H. D. Flack, *Acta Crystallogr.*, *Sect. A*, 1983, **39**, 876.
38 G. M. Sheldrick, SHELXTL manual (ver. 5.1), Bruker AXS Inc., Madison, WI, USA (1997).
39 J. Crugeiras and H. Maskill, *J. Chem. Soc.*, *Perkin Trans. 2*, 1998, 1901.
40 P. J. Kropp and R. L. Adkins, *J. Am. Chem. Soc.*, 1991, **113**, 2709.