N-Tritylhydroxylamines: preparations, structures, base strengths, and reactions with nitrous acid and perchloric acid

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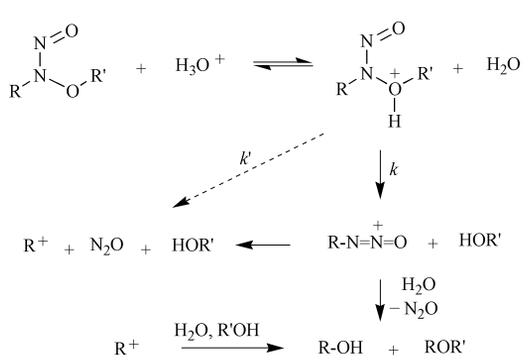
N-Trityl, *N*-(4-methoxytrityl), *N*-(4,4′-dimethoxytrityl), and *N*-(4,4′,4″-trimethoxytrityl) derivatives of hydroxylamine, *O*-methylhydroxylamine, and *O*-benzylhydroxylamine have been prepared and characterised. Additionally, *N*,*O*-ditrityl- and *N*,*O*-bis(4,4′-dimethoxytrityl)-hydroxylamines have been made, and the X-ray crystal structure of the former has been determined. The pK_a value of *O*-benzylhydroxylammonium in water (6.2) and of its *N*-trityl analogue in aqueous acetonitrile (7.5) have been measured. The *N*-tritylhydroxylamines all decompose under aqueous acidic conditions to give the corresponding trityl alcohols, and rate constants for uncatalysed and hydronium ion catalysed reactions of *N*-(4,4′-dimethoxytrityl)-*O*-methylhydroxylamine have been measured by stopped flow kinetics at 25 °C. This compound compares in reactivity with *N*-alkyl-*N*-(4,4′-dimethoxytrityl)amines rather than with 4,4′-dimethoxytritylamine. Attempted nitrosation of *N*-tritylhydroxylamine and its *O*-alkyl derivatives gave trityl alcohol, the intermediate *N*-nitroso compound being detectable but too unstable to isolate. From *N*-trityl-*O*-benzylhydroxylamine, attempted nitrosation led to the formation of triphenylmethane in addition to trityl alcohol, benzyl alcohol, and trityl benzyl ether. The mildly acidic conditions used for attempted nitrosation of methoxy-substituted *N*-tritylhydroxylamines led to deamination before addition of the nitrosating agent.

Introduction

Hydroxylamine derivatives are α-effect ambident nucleophiles;[1] they occur in nature and some synthetic analogues have potent biological activity.[2,3] The relatively recent discovery that nitric oxide has wide-ranging physiological effects,[4] and that some nitrosated hydroxylamines decompose under mild conditions with release of nitric oxide,[5] has led to renewed interest in the chemistry of hydroxylamine and its derivatives.

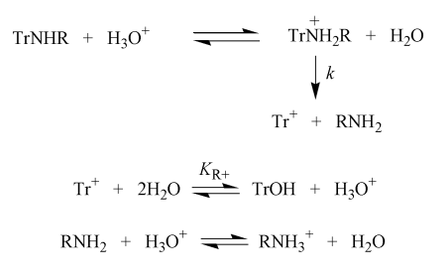
We have already reported investigations of the acid-induced solvolysis of *N*-nitroso-*N*,*O*-dialkylhydroxylamines which liberate nitrous oxide, Scheme 1.[6,7] In these reactions, acid catalysis



Scheme 1 Acid-catalysed hydrolysis of *N*-nitroso-*N*,*O*-dialkylhydroxylamines.

is required at least in part because alkoxide R′O$^-$ is not sufficiently good a nucleofuge in the initial heterolysis. Principally on the basis of an α-deuterium kinetic isotope effect of unity,[7] we proposed a step-wise mechanism involving an intermediate alkyloxodiazonium ion $(RN_2O)^+$ rather than a concerted fragmentation of the protonated substrate. Thus, the reaction involves the rate-limiting step with elementary rate constant k in Scheme 1 rather than the path with rate constant k'. We planned to nitrosate *N*-trityl-*O*-alkylhydroxylamines in order to investigate whether providing the possibility of a substantially more stable carbenium ion intermediate caused the fragmentation to become concerted, *i.e.* follow the k' route in Scheme 1 and by-pass the formation of the intermediate oxodiazonium ion. We also planned to investigate whether fragmentation, step-wise or concerted, to give a much more stable carbenium ion intermediate affects the need for acid catalysis.

In a parallel investigation of the acid-induced deamination reactions of *N*-tritylamines,[8] we discovered remarkable rate enhancements (*ca.* 10^6) caused by replacing R = H with R = alkyl or aryl, Scheme 2.[9] We also observed that *N*-trityl



Scheme 2 Acid-catalysed deamination of substituted tritylamines.

substituents have an appreciable base-strengthening effect upon arylamines $ArNH_2$ (up to *ca.* 8 pK units); this was ascribed to the steric prevention of resonance between the aryl ring

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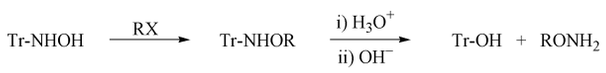
(including its substituents) and the amino group.[10] As part of an investigation into the cause of these dramatic effects upon rate and equilibrium constants, we made tritylamines substituted with hydroxy and alkoxy groups on nitrogen (R = OH and OR, Scheme 2), *i.e.* *N*-trityl- and *N*-trityl-*O*-alkyl-hydroxylamines, with a view to measuring rate constants for their deamination and pK_a values of their conjugate acids.

We now report the synthetic aspects, base strength measurements, and an initial rate study of an investigation linking the two projects mentioned above. By an X-ray crystal structure determination, we are also able to correct an earlier literature supposition regarding the structure of ditritylhydroxylamine.[11] If it subsequently proves generally possible to alkylate substituted *N*-tritylhydroxylamines on oxygen and then remove the substituted trityl group under mildly acidic conditions in high yield (Scheme 3), the way will be open for the use of substituted



Tr = trityl or substituted trityl

Scheme 3 Trityl as a protecting group in the synthesis of *O*-alkylhydroxylamines.

trityl as a protecting group in a general flexible synthesis of *O*-alkylhydroxylamines, $RONH_2$. This will be complementary to the older method by *O*-alkylation of *N*-hydroxyphthalimide then removal of the phthalic residue under strongly basic/nucleophilic conditions,[12] and appreciably easier and safer.

Results and discussion

Preparations of tritylhydroxylamines

Baeyer and Villiger[13] described a reaction of triphenylmethanol and hydroxylamine under acidic conditions, then Mothwurf[11] reported a reaction of triphenylmethyl chloride and hydroxylamine under basic conditions, but no single pure product was isolated in either case. Subsequently, Guthmann and Stieglitz[14] synthesised *N*-trityl-*O*-methylhydroxylamine, and Ayres and Hauser[15] reported the *O*-benzyl analogue. We have found that, in general, introduction of a single trityl group onto the nitrogen of hydroxylamine and its *O*-methyl or *O*-benzyl derivatives to give TrNHOH and TrNHOR (R = Me or CH_2Ph) is straightforward using trityl chloride in pyridine as solvent. Yields are good and crystalline products well characterised.

N-(4-Methoxytrityl)hydroxylamines (MMTrNHOR) were also preparable from 4-methoxytrityl chloride, but were less easy to isolate with MMTrNHOH appreciably less stable than the *O*-methyl and *O*-benzyl analogues, and usually requiring chromatographic purification on either silica or alumina. *N*-(4,4′-Dimethoxytrityl)hydroxylamines, prepared from 4,4′-dimethoxytrityl tetrafluoroborate, were less stable to even mildly acidic conditions, but were preparable and could be chromatographed. Prepared from 4,4′,4″-trimethoxytrityl tetrafluoroborate, the *N*-(4,4′,4″-trimethoxytrityl)hydroxylamines were even less stable and decomposed on attempted chromatography on silica; they could be purified by alumina chromatography with a basic eluent or by recrystallisation.

Preparations of ditritylhydroxylamines

There is a single report by Mothwurf[11] of ditritylhydroxylamine which was presumed to be the *N*,*N*-ditrityl isomer (Tr_2NOH) on the basis of indirect evidence. However, our X-ray crystallographic results (Fig. 1) on the product from hydroxylamine and two equivalents of trityl chloride clearly show that the compound is the *N*,*O*-ditrityl isomer (TrNHOTr). It is disordered across a centre of symmetry such that the O and NH are interchangeable; the N–trityl and O–trityl bond lengths are thereby indistinguishable, with a value of 1.470(2) Å, comparable to C–N bond lengths reported in four structures of *N*,*O*-dialkylhydroxylamines in the Cambridge crystallographic data-base,[16] but longer than the corresponding C–O bond lengths. The angles C–N–O and N–O–C are 110.25(13)° and the inversion centre enforces a C–N–O–C torsion angle of exactly zero, whereas the previous four structures have torsion angles ranging from 101.5 to 149.3°. There are no hydrogen-bond interactions, the centre of the molecule being sterically shielded by the bulky substituents. It is interesting that, in contrast, the data-base contains 32 structures of *N*,*N*-dialkylhydroxylamines, so the *N*,*N*-isomers represent a large majority of known dialkylhydroxylamines. Presumably, the steric bulk of the first *N*-trityl group prevents further *N*-alkylation even though the nitrogen remains more basic than the oxygen. This property of the trityl group can be exploited in its use as a protecting group for nitrogen in the ambident hydroxylamine as over-alkylation on nitrogen can be a problem with less bulky alkyl groups.[3] We also prepared the *N*,*O*-bis(4,4′-dimethoxytrityl)hydroxylamine (DMTrNHODMTr) from hydroxylamine and 4,4′-dimethoxytrityl tetrafluoroborate; it was isolated as an oil and, although the ^{1}H-NMR spectrum confirmed its formation, it was too unstable to allow complete purification and characterisation.

Compounds prepared are shown in Fig. 2 and Table 1.

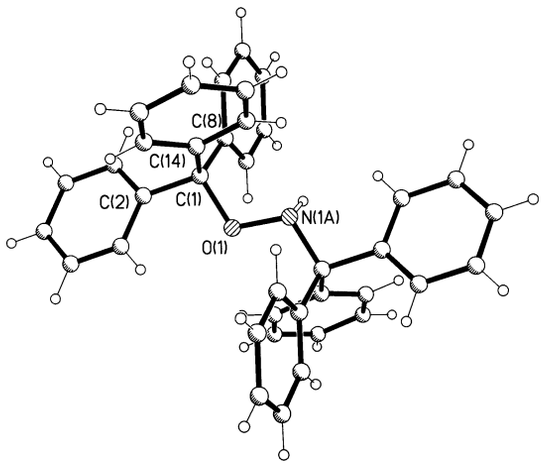
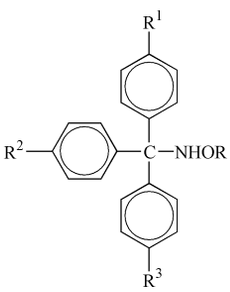


Fig. 1



(**1**) $R^1 = R^2 = R^3 = H$
(**a**) R = H
(**b**) R = Me
(**c**) R = CH_2Ph
(**d**) R = CPh_3

(**3**) R^1 = H, $R^2 = R^3$ = OMe
(**a**) R = H
(**b**) R = Me
(**c**) R = CH_2Ph
(**d**) R = DMTr

(**2**) $R^1 = R^2$ = H, R^3 = OMe
(**a**) R = H
(**b**) R = Me
(**c**) R = CH_2Ph

(**4**) $R^1 = R^2 = R^3$ = OMe
(**a**) R = H
(**b**) R = Me
(**c**) R = CH_2Ph

Fig. 2 Structures of hydroxylamines.

Table 1 Summary of tritylhydroxylamines **1**–**4**

Comp.	R^1	R^2	R^3	R^4	Mp/°C
1a[11]	H	H	H	H	132–134
1b[14]	H	H	H	Me	90–91
1c[15]	H	H	H	CH_2Ph	115–116
1d[11]	H	H	H	Trityl	199–200
2a[27]	MeO	H	H	H	113–116
2b	MeO	H	H	Me	89–91
2c	MeO	H	H	CH_2Ph	80–81
3a	MeO	MeO	H	H	136–137
3b	MeO	MeO	H	Me	86–87
3c	MeO	MeO	H	CH_2Ph	80–81
3d	MeO	MeO	H	Dimethoxytrityl	Oil
4a	MeO	MeO	MeO	H	139–140
4b	MeO	MeO	MeO	Me	125–126
4c	MeO	MeO	MeO	CH_2Ph	81–83

Table 2 pK_a values of hydroxylammonium and related ions in water, 25 °C

Ion	pK_a
NH_4^+	9.8[a]
$MeNH_3^+$	10.65[b]
$Me_2NH_2^+$	10.8[b]
Me_3NH^+	9.8[b]
NH_3OH^+	6.06[c]
$MeNH_2OH^+$	5.9[d]
Me_2NHOH^+	5.2[e]
NH_3OMe^+	4.6[e]
$MeNH_2OMe^+$	4.75[e]
Me_2NHOMe^+	3.65[e]
$NH_3OCH_2Ph^+$	6.2[f]
$TrNH_2OCH_2Ph^+$	7.5[g]

[a] Ref. 30. [b] Ref. 18. [c] Ionic strength = 1.0 mol dm^{-3}, ref. 31. [d] Ref. 32. [e] Ref. 19. [f] Ionic strength ($NaClO_4$) = 0.1 mol dm^{-3}, 5% MeCN, present work. [g] Ionic strength ($NaClO_4$) = 0.1 mol dm^{-3}, 38% MeCN, present work.

Base strengths of hydroxylamines

A routine pH titration technique was used for determining the pK_a's of alkylhydroxylammonium ions.[10,17] Acetonitrile was used as cosolvent to overcome solubility difficulties in water alone for *O*-benzylhydroxylamine and its *N*-trityl derivative (**1c**) but our previous work indicates that this is unlikely to have an appreciable effect.[10] The initial acidic pH of the solution for titration was chosen to minimise solvolytic deamination of the *N*-trityl-*O*-benzylhydroxylammonium ion.[8,9] As seen in Table 2, introducing a hydroxy group weakens the base strength of ammonia by almost 4 pK_a units, but then there are only small differences between the base strengths of hydroxylamine, *N*-methylhydroxylamine, and *N*,*N*-dimethylhydroxylamine which is unsurprising in view of the close similarity between the base strengths of ammonia, methylamine, dimethylamine, and trimethylamine.[18] The effect of alkyl groups on the oxygen is less clear cut; the *O*-benzyl compound is similar in base strength to the parent hydroxylamine whereas an *O*-methyl substituent in hydroxylamine, *N*-methylhydroxylamine, and *N*,*N*-dimethylhydroxylamine appears to be base weakening.[19] Although the result for **1c** is imprecise due to difficulties in measuring equilibrium properties of a compound which is to some degree unstable to the reaction conditions, *N*-tritylation modestly increases the base strength of *O*-benzylhydroxylamine, *i.e.* the *N*-trityl reduces the base weakening effect of the *N*-alkoxy group. However, this effect is much smaller than the effect of *N*-trityl upon the base strengths of substituted anilines.[10] In the latter, the *N*-trityl is able to negate completely the powerful base-weakening effects through resonance of aryl groups attached to nitrogen, but in hydroxylamines it has only a small effect on the inductive base-weakening effect of an OR group.

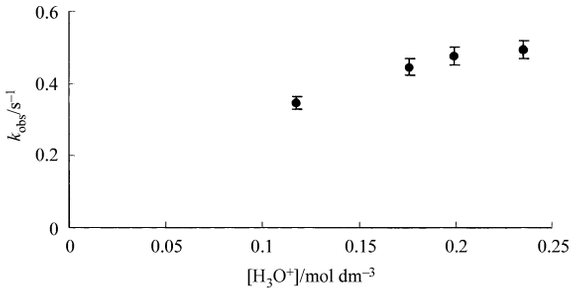


Fig. 3 Decomposition of **3b** in aqueous perchloric acid at 25 °C (the bars indicate 5% error ranges on rate constants).

Table 3 Kinetics of acid-induced deamination of *N*-(dimethoxytrityl)-amino compounds, 25 °C, ionic strength ($NaClO_4$) = 1 mol dm^{-3}

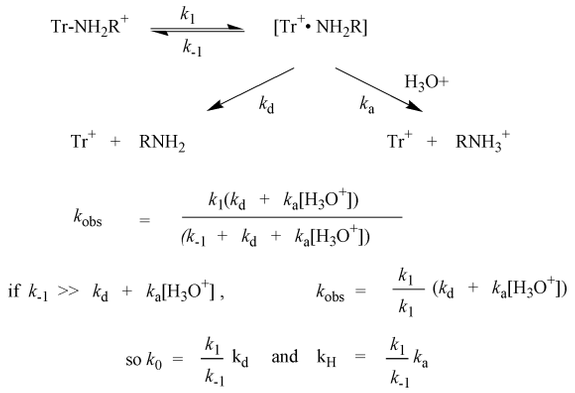
Comp.	k_o/s^{-1}	$k_H/dm^3\ mol^{-1}\ s^{-1}$	Co-solvent
DMTrNHOMe (**3b**)[a]	0.20	1.3	2% CH_3CN
$DMTrNH_2$[b]	3.1×10^{-5}	1.6×10^{-5}	2% CH_3CN
DMTrNHBn[b]	4.2	179	1% CH_3CN

[a] $[DMTrNHOMe]_0$ *ca.* 2×10^{-5} mol dm^{-3}. [b] Ref. 9.

Reactions of *N*-tritylhydroxylamines

In early qualitative tests, we established that all our *N*-tritylhydroxylamines were unstable to acidic conditions, and that this instability increased with increasing methoxy substitution in the trityl group. When aqueous acetonitrile solutions of *N*-trityl-*O*-methylhydroxylamines, with and without methoxy substituents, were treated with aqueous perchloric acid at room temperature, the colour characteristic of the trityl cation was immediately observed and the corresponding alcohol was readily detected by TLC.

Our normal method for measuring rates of reaction of substituted *N*- and *O*-trityl compounds is to monitor the formation of the substituted trityl cation by UV absorption spectroscopy.[8,9,20] The concentration of the substituted trityl cation in equilibrium with the alcohol (Scheme 2) is a function of the acidity of the medium;[20,21] so, the higher the acidity, the higher the equilibrium concentration of the cation and hence the easier it is to measure its rate of formation. However, the deamination reactions are acid catalysed and, depending upon the particular compound, too high an acidity may lead to the reaction being immeasurably fast using conventional or even stopped-flow techniques. In the case of tritylamines, 4,4′-dimethoxytritylamine was the most convenient to investigate as appreciable concentrations of the dimethoxytrityl carbenium ion exist in equilibrium with the alcohol at low hydronium ion concentrations in water. Consequently, in the present context, we initiated our kinetics study with the *N*-(4,4′-dimethoxytrityl) substituted compound **3b**, this being more readily available than **3a**. In contrast to the reaction of 4,4′-dimethoxytritylamine under similar conditions, this reaction proved too fast to be measurable by conventional UV kinetics, and stopped-flow methodology was required. The pseudo first-order rate constant was measured at 25 °C at different low concentrations of perchloric acid ([substrate] $\ll [H_3O^+]$), and the results are shown in Fig. 3 and Table 3. They clearly indicate catalysed and uncatalysed reaction channels for compound **3b**, as was observed for tritylamines in general, but the rate constants obtained are much greater than those for $DMTrNH_2$ and broadly comparable with those for DMTrNHR.[8,9] The differences between DMTrNHR and DMTrNHOR, however, are interpretable on the basis of our reported mechanism for deamination of tritylammonium ions, Scheme 4.[8,9] Replacement of an alkyl on the nitrogen by an alkoxy yields an α-effect nucleofuge/nucleophile,[22] so there will be a higher proportion of internal return for the hydroxylamine, *i.e.* k_1/k_{-1} in Scheme 4 will be



Scheme 4 Mechanism for deamination of *N*-tritylammonium ions under acidic conditions.

smaller than for alkyl-substituted analogues, with correspondingly smaller overall rate constants, k_0 and k_H.

N-Nitroso-*N*-tritylhydroxylamines

Following Mothwurf,[11] Schlenk and Bergmann[23] reported a nitrosation reaction of the parent tritylhydroxylamine with amyl nitrite and hydrochloric acid in ether now seen to have been unsuccessful. In the present study, attempts to isolate *N*-nitroso-*N*-trityl-*O*-methylhydroxylamine by the usual acidified sodium nitrite method failed.[6] The *N*-trityl-*O*-methylhydroxylammonium ion appeared adequately stable under mildly acidic conditions in aqueous ethanol at 0 °C, and addition of ice-cold aqueous sodium nitrite led to a yellow coloration, presumably the *N*-nitroso compound. However, following the usual work-up, the only products identified by TLC and ^{1}H NMR were trityl alcohol (presumably by decomposition of the transient *N*-nitroso-product, Scheme 1) and unreacted starting material. Attempted nitrosation using isoamyl (3-methylbutyl) nitrite under non-aqueous conditions also failed,[24] as did attempts to nitrosate *N*-tritylhydroxylamine itself. Interestingly, triphenylmethane was identified amongst the products of attempted nitrosation of the *N*-trityl-*O*-benzyl analogue. Presumably, hydride transfer occurs between the closely proximate trityl cation and benzyl alcohol generated in the decomposition of the transient nitroso compound. As trityl is well known as a hydride abstracting agent,[25] this finding indicates that nitrosation did indeed occur but that, under the reaction conditions, the product decomposes by the heterolytic mechanism.[6,7]

Methoxy-substituted *N*-trityl-*O*-alkylhydroxylamines underwent immediate deamination upon dissolution in the acidic medium (Scheme 2) before the nitrosating agent had been added, and the only products detected were the methoxy substituted trityl alcohols in equilibrium with the methoxy-substituted trityl cations.

Experimental

Preparations

TLC was carried out with aluminium backed Kieselgel 60 F_{254} plates (Merck), 0.2 mm thickness, and column chromatography with silica gel (BDH, 40–63 μm). Unless otherwise stated, ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WP-200 instrument (200 MHz for ^{1}H) with tetramethylsilane as standard and $CDCl_3$ as solvent; coupling constants (J) are given in Hz.

4,4′-Dimethoxytrityl tetrafluoroborate. Aqueous tetrafluoroboric acid (40%, 1.4 cm^3, 8 mmol) was added drop-wise over 30 min to a solution of 4,4′-dimethoxytrityl alcohol (1.2 g, 3.8 mmol) in acetic anhydride (5 cm^3) at such a rate that the temperature did not exceed 25 °C. The red solution was stirred for a further 2 h, then was diluted with ether (25 cm^3); the deep red precipitate was filtered at the pump and dried under vacuum (1.3 g, 89%, mp 194–196 °C, lit.,[26] 193–196 °C).

4,4′,4″-Trimethoxytrityl tetrafluoroborate. Aqueous tetrafluoroboric acid (40%, 2.2 cm^3, 13 mmol) was added drop-wise over 1 h to an ice-cold solution of 4,4′,4″-trimethoxytrityl alcohol (2.17 g, 6.2 mmol) in acetic anhydride (12 cm^3). Dilution of the red reaction mixture with ether (30 cm^3) gave plum coloured crystals which were filtered at the pump and dried under vacuum (2.98 g, 74%, mp 176–178 °C, lit.,[27] 177–178 °C).

***N*-Tritylhydroxylamine (1a).** A solution of trityl chloride (300 mg, 1.08 mmol) in pyridine (1 cm^3) was added drop-wise over 5 min to a solution of hydroxylammonium chloride (90 mg, 1.3 mmol) in pyridine (1 cm^3) and the solution was stirred at room temperature for 11 h as pyridinium chloride crystallised. Water (15 cm^3) was added and the precipitated mixture of trityl alcohol and *N*-tritylhydroxylamine was filtered at the pump then separated by column chromatography (80 : 20, petrol–ethyl acetate). The hydroxylamine was recrystallised from 9 : 1 petrol–ethyl acetate (215 mg, 72%, mp 132–134 °C, lit.,[11] 126–134 °C; δ_H: 4.60 (1H, br, NH), 7.17–7.40 (15H, m, arom)).

***N*-Trityl-*O*-methylhydroxylamine (1b).** A solution of trityl chloride (300 mg, 1.08 mmol) in pyridine (1 cm^3) was added drop-wise over 5 min to a solution of methoxylammonium chloride (108 mg, 1.3 mmol) in as little pyridine as possible (*ca.* 1 cm^3). The reaction was stirred for *ca.* 15 h as pyridinium chloride crystallised, then water (15 cm^3) was added and the mixture was extracted with dichloromethane (3 × 3 cm^3). The combined organic phase was dried (Na_2SO_4), filtered, and the solvent was evaporated under reduced pressure. The residual hydroxylamine and trityl alcohol were separated by column chromatography (80 : 20, petrol–ethyl acetate), and the hydroxylamine was recrystallised from ethyl acetate–petrol (196 mg, 63%; mp 90–91 °C, lit.,[14] 91 °C; δ_H: 3.52 (3H, s, OCH_3), 6.29 (1H, br, NH), 7.23–7.31 (15H, m, arom)).

***N*-Trityl-*O*-benzylhydroxylamine (1c).** Trityl chloride (330 mg, 1.18 mmol) and *O*-benzylhydroxylammonium chloride (160 mg, 1.00 mmol) in pyridine (3 cm^3) were stirred under nitrogen for approximately 60 h. Water was added to the reaction mixture which was then extracted with dichloromethane (3 × 5 cm^3). The combined organic extract was washed with saturated copper(II) sulfate solution (2 × 8 cm^3) then with water, dried ($MgSO_4$), filtered, and evaporated under reduced pressure to yield an off-white solid which was then chromatographed (dichloromethane, 1% triethylamine) to yield a white solid (240 mg, 0.66 mmol, 66%, mp 115–116 °C (sharp), lit.,[15] 118–119 °C; δ_H: 4.72 (2H, s, CH_2), 6.32 (1H, br, NH), 7.15–7.37 (20H, m, arom); δ_C: 73.99, 75.99, 126.91, 127.66, 127.78, 128.21, 128.33, 129.18, 137.78, 144.50).

***N*,*O*-Ditritylhydroxylamine (1d).** A solution of hydroxylammonium chloride (26 mg, 0.37 mmol) in pyridine (2 cm^3) was added to a stirred solution of trityl chloride (210 mg, 0.8 mmol) in pyridine (3 cm^3), and the reaction was stirred for 3 h. After the usual work-up, the dichloromethane phase was dried (Na_2SO_4), filtered, and the solvent was evaporated under reduced pressure. The crystalline residue was chromatographed twice (first, 80 : 20 dichloromethane–petrol, second, 90 : 10 petrol–ether); white crystals were obtained and recrystallised from ethyl acetate–petrol (65 mg, 34%, mp 199–200 °C (sharp), lit.,[11] 184 °C; δ_H: 1.54 (1H, br, NH), 7.12–7.24 (30H, m, arom); C: 88.16, H: 6.04, N: 2.70%; $C_{38}H_{31}NO$ requires C: 88.17, H: 6.04, N: 2.71%)

***N*-(4-Methoxytrityl)hydroxylamine (2a).** A solution of 4-methoxytrityl chloride (231 mg, 0.7 mmol) in pyridine (3 cm^3)

was added drop-wise to a solution of hydroxylammonium chloride (57 mg, 0.8 mmol) in pyridine (1 cm^3). The reaction was stirred overnight at room temperature during which time pyridinium chloride crystallised. After the usual work-up, two columns (first, 80 : 20 petrol–ethyl acetate, then dichloromethane) were necessary to separate 4-methoxytrityl alcohol (mp 79–80 °C) from the product (white crystals, 127 mg, 52%, mp 113–116 °C, lit.,[28] 100–110 °C; δ_H: 3.77 (3H, s, OCH_3), 6.81 (2H, d, *J* 8.9, H-3,5), 7.12–7.33 (12 H, m, arom); δ_C: 55.42, 72.38, 112.97, 126.77, 127.80, 128.86, 130.25, 136.79, 143.54, 158.26; C: 78.76, H: 6.72, N: 3.87%; $C_{20}H_{19}NO_2$ requires C: 78.40, H: 6.58, N: 4.57%).

***N*-(4-Methoxytrityl)-*O*-methylhydroxylamine (2b).** Methoxylammonium chloride (96 mg, 0.8 mmol) and 4-methoxytrityl chloride (231 mg, 0.75 mmol) were reacted as described above for the unsubstituted trityl compound. The work-up produced a yellow oil which was dissolved in a few drops of ethyl acetate to which petrol was added until the solution became cloudy. The product crystallised overnight and was recrystallised from ethyl acetate–petrol to give a white solid (170 mg, 74%, mp 89–91 °C; δ_H: 3.51 (3H, s, $NOCH_3$), 3.78 (3H, s, OCH_3), 6.26 (1H, br, NH), 6.81 (2H, d, *J* 8.9, H-3,5), 7.20–7.30 (12H, m, arom); δ_C: 55.35, 72.6, 112.99, 126.80, 127.76, 128.86, 130.18, 136.87, 143.8, 158.0; C: 78.92, H: 6.66, N: 4.35%; $C_{21}H_{21}NO_2$ requires C: 78.97, H: 6.63, N: 4.39%).

***N*-(4-Methoxytrityl)-*O*-benzylhydroxylamine (2c).** The reaction was as for the unsubstituted trityl compound but starting with 4-methoxytrityl chloride (271 mg, 0.8 mmol) and *O*-benzylhydroxylammonium chloride (140 mg, 0.9 mmol). Following the usual work-up, chromatography, and recrystallisation (ether–petrol), white crystals were obtained (206 mg, 65%, mp 80–81 °C; δ_H: 3.77 (3H, s, OCH_3), 4.64 (2H, s, CH_2), 6.29 (1H, br, NH), 6.80 (2H, d, *J* 8.9, H-3,5), 7.15–7.35 (17H, m, arom); δ_C: 55.24, 73.10, 76.01, 113.02, 126.81, 127.61, 127.71, 128.20, 128.30, 129.12, 130.40, 136.95, 137.86, 144.76; C: 82.16, H: 6.08, N: 3.58%; $C_{27}H_{25}NO_2$ requires C: 82.00, H: 6.37, N: 3.54%).

***N*-(4,4′-Dimethoxytrityl)hydroxylamine (3a).** 4,4′-Dimethoxytrityl tetrafluoroborate (312 mg, 0.8 mmol) and hydroxylammonium chloride (60 mg, 0.9 mmol) were reacted as described for the monomethoxy compound, but for just 3 h, then the reaction was worked up in the usual way. The product was chromatographed twice (first, 80 : 20 petrol–ethyl acetate; second, dichloromethane) to give colourless crystals (107 mg, 40%, mp 136–137 °C; δ_H: 3.78 (6H, s, OCH_3), 6.82 (4H, d, *J* 8.9, H-3,3′,5,5″), 7.17 (4H, d, *J* 8.9, H-2,2′,6,6′), 7.25–7.26 (5H, m, arom); δ_C: 55.26, 113.69, 126.18, 127.83, 129.84, 130.00, 130.39, 136.50, 158.04; C: 74.68, H: 6.93, N: 3.89%; $C_{21}H_{21}NO_3$ requires C: 74.75, H: 6.87 N: 4.15%).

***N*-(4,4′-Dimethoxytrityl)-*O*-methylhydroxylamine (3b).** A solution of dimethoxytrityl tetrafluoroborate (312 mg, 0.8 mmol) in pyridine (1.5 cm^3) was added drop-wise to a solution of methoxylammonium chloride (75.2 mg, 0.9 mmol) in pyridine (1 cm^3) and the resultant yellow solution was stirred for 2 h, then quenched with water (20 cm^3) and extracted with dichloromethane (3 × 3 cm^3). The combined organic phase was washed with saturated aqueous copper(II) sulfate (2 × 5 cm^3), dried (Na_2SO_4), and filtered, then the solvent was evaporated under reduced pressure. Column chromatography of the residue (80 : 20, petrol–ethyl acetate) gave a pale yellow oil which crystallised from ethyl acetate–petrol overnight in the refrigerator. The product was recrystallised at −78 °C from petrol–ether (151 mg, 54%, mp 86–87 °C; δ_H: 3.50 (3H, s, $NOCH_3$), 3.77 (6H, s, OCH_3), 6.23 (1H, br, NH), 6.80 (4H, d, *J* 8.9, H-3,3′,5,5′), 7.17–7.30 (9H, m, arom); δ_C: 55.23, 61.97, 73.03, 113.05, 126.77, 127.73, 128.89, 130.19, 136.87, 144.95, 158.34; C: 75.99, H: 6.15, N: 3.88%; $C_{22}H_{23}NO_3$ requires C: 75.84, H: 6.36, N: 4.01%).

***N*-(4,4′-Dimethoxytrityl)-*O*-benzylhydroxylamine (3c).** The reaction was as described for the unsubstituted trityl compound but using 4,4′-dimethoxytrityl tetrafluoroborate (260 mg, 0.7 mmol) and *O*-benzylhydroxylammonium chloride (117 mg, 0.8 mmol) and gave white crystals (130 mg, 45%, mp (recryst. petrol–ethyl acetate) 80–81 °C; δ_H: 3.78 (6H, s, OCH_3), 4.70 (2H, s, CH_2), 6.24 (1H, br, NH), 6.80 (4H, d, *J* 8.9, H-3,3′,5,5′), 7.17–7.30 (14H, m, arom); δ_C: 55.24, 73.10, 76.04, 113.01, 126.76, 127.61, 127.70, 128.23, 128.30, 129.04, 130.33, 136.95, 137.93, 144.99, 158.33; C: 79.13, H: 6.85, N: 3.20%; $C_{28}H_{27}NO_3$ requires C: 78.85, H: 6.62, N: 3.28%).

***N*,*O*-Bis(4,4′-dimethoxytrityl)hydroxylamine (3d).** The procedure for the unsubstituted bis(trityl)hydroxylamine was used but starting from dimethoxytrityl tetrafluoroborate; the initial product (a colourless oil, δ_H: 3.77 (12H, s, OCH_3), 5.45 (1H, s, NH), 6.78–7.27 (26H, m, arom)) turned yellow overnight and did not crystallise.

***N*-(4,4′,4″-Trimethoxytrityl)hydroxylamine (4a).** The reaction was as described for the monomethoxytritylhydroxylamine using 4,4′,4″-trimethoxytrityl tetrafluoroborate (210 mg, 0.5 mmol) and hydroxylammonium chloride (40 mg, 0.6 mmol). As the product decomposed on silica and alumina, it was isolated by crystallisation from ether–petrol in the refrigerator for 48 h as orange crystals (80 mg, 44%, mp 139–140 °C; δ_H: 1.60 (1H, br, OH), 3.87 (9H, s, OCH_3), 6.94 (6H, d, *J* 8.9, H-3,3′,3″,5,5′,5″), 7.77 (6H, d, *J* 8.9, H-2,2′,2″,6,6′,6″); δ_C: 55.21, 72.52, 113.07, 130.04, 137.12, 158.29; C: 72.01, H: 7.23, N: 3.65%; $C_{22}H_{23}NO_4$ requires C: 71.72, H: 7.11, N: 3.80%).

***N*-(4,4′,4″-Trimethoxytrityl)-*O*-methylhydroxylamine (4b).** The reaction was as described for the dimethoxytrityl compound but starting from trimethoxytrityl tetrafluoroborate (336 mg, 0.8 mmol) and methoxylammonium chloride (73 mg, 0.9 mmol). The crude product gave white crystals from petrol–ethyl acetate in the refrigerator overnight which were recrystallised from ethyl acetate–petrol (176 mg, 58%, mp 125–126 °C; δ_H: 3.50 (3H, s, $NOCH_3$), 3.78 (9H, s, OCH_3), 6.80 (6H, d, *J* 8.9, H-3,3′,3″), 7.17–7.21 (6H, m, H-2,2′,2″,6,6′,6″); δ_C: 55.23, 62.00, 72.59, 113.04, 130.11, 137.14, 158.30; C: 72.92, H: 6.38, N: 3.80%; $C_{23}H_{25}NO_4$ requires C: 72.80, H: 6.64, N: 3.69%).

***N*-(4,4′,4″-Trimethoxytrityl)-*O*-benzylhydroxylamine (4c).** The procedure described for *N*-tritylhydroxylamine was followed using trimethoxytrityl tetrafluoroborate (336 mg, 0.8 mmol) and *O*-benzylhydroxylammonium chloride, and gave white crystals (234 mg, 65%, mp 81–83 °C; δ_H: 3.78 (9H, s, OCH_3), 4.69 (2H, s, CH_2), 6.22 (1H, br, NH), 6.79 (6H, d, *J* 8.9, H-3,3′,3″,5,5′,5″), 7.19 (6H, d, *J* 8.9, H-2,2′,2″,6,6′,6″), 7.24–7.26 (5H, m, arom); δ_C: 55.25, 72.70, 113.01, 127.61, 128.30, 130.27, 137.20, 138.00, 158.31; C: 76.69, H: 6.65, N: 3.01%; $C_{29}H_{29}NO_4$ requires C: 76.46, H: 6.42, N: 3.07%).

Attempted nitrosation of *N*-tritylhydroxylamines

The following is representative.

***N*-Trityl-*O*-benzylhydroxylamine (1c).** The attempted nitrosation of **1c** using either nitrous acid[6] in aqueous ethanol or isoamyl nitrite[24] in dichloromethane–methanol failed to yield the desired product. Approximately the same combination of trityl alcohol, benzyl alcohol, trityl benzyl ether, and triphenylmethane was shown to be formed from both reactions by a combination of TLC, GLC, and NMR; there were minor

unidentified products, but starting material and trityl ethyl ether from the reaction in aqueous ethanol were shown to be absent.

X-Ray crystallography †

Crystal data for **1d**: $C_{38}H_{31}NO$, $M = 517.6$, triclinic, space group $P\bar{1}$, $a = 8.677(6)$, $b = 9.042(6)$, $c = 10.769(7)$ Å, $\alpha = 113.29(4)$, $\beta = 90.24(4)$, $\gamma = 115.20(3)°$, $V = 686.9(8)$ Å^3, $Z = 1$; $R(F, F^2 > 2\sigma) = 0.0370$, $R_w(F^2$, all data) = 0.0947 for 185 parameters and 2409 unique data. The molecule lies on an inversion centre, and so is disordered with O and N atoms effectively superimposed. The half-occupancy H atom bonded to N was located and refined subject to a bond length restraint; other H atoms were constrained with a riding model.[29]

pK_a Determinations

A pH titration method was used for both compounds,[17] and has already been described.[10] A combined glass electrode coupled to a Metrohm 716 DMS Titrino automatic titrator was used to record the pH during the titration of the conjugated acid of the hydroxylamine against standard sodium hydroxide. The reported pK_a values were optimized by fitting the experimental results to the appropriate sigmoidal equations derived from the Henderson–Hasselbach equation using a non-linear optimization algorithm.

Kinetics of deamination of *N*-(4,4′-dimethoxytrityl)-*O*-methylhydroxylamine (3b)

The rates of decomposition of the title compound under acidic conditions were investigated under the usual pseudo first-order conditions at 25 °C using stopped flow equipment kindly made available to us by Professor D. L. H. Williams at the University of Durham. The observed pseudo first-order rate constants were plotted against [$HClO_4$] to give the second-order catalytic constant from the gradient and the first-order rate constant for the uncatalysed reaction from the intercept.

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References

1 P. A. S. Smith, *The chemistry of open-chain organic nitrogen compounds*, Vol. 2, W. A. Benjamin, New York, 1966; J. S. Roberts, *Derivatives of Hydroxylamine*, in *Comprehensive Organic Chemistry*, Vol. 2, ed. I. O. Sutherland, Pergamon Press, Oxford, New York, 1979.
2 Y. Isowa, T. Takashima, M. Ohmori, H. Kurita, M. Sato and K. Mori, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 1461; E. Quiñoà and P. Crews, *Tetrahedron Lett.*, 1987, **28**, 2467; M. Strasser, P. Cooper, B. Dewald and T. Payne, *Helv. Chim. Acta*, 1988, **7**, 1156; A. R. Carroll and P. J. Scheuer, *Tetrahedron*, 1990, **46**, 6637.
3 M. A. Staszak and C. W. Doecke, *Tetrahedron Lett.*, 1994, **35**, 6021.
4 R. M. J. Palmer, A. G. Ferrige and S. Monacada, *Nature*, 1987, **327**, 524.
5 J. Saavedra and L. Keefer, *Chem. Br.*, 2000, 30.
6 H. Maskill, I. D. Menneer and D. I. Smith, *J. Chem. Soc., Chem. Commun.*, 1995, 1855; J. I. Bhat, W. Clegg, M. R. J. Elsegood, H. Maskill, I. D. Menneer and P. C. Miatt, *J. Chem. Soc., Perkin Trans. 2*, 2000, 1435.
7 J. Haider, M. N. S. Hill, I. D. Menneer, H. Maskill and J. G. Smith, *Chem. Commun.*, 1997, 1571.
8 C. Bleasdale, B. T. Golding, W. H. Lee, H. Maskill, J. Riseborough and E. Smits, *J. Chem. Soc., Chem. Commun.*, 1994, 93; J. Crugeiras and H. Maskill, *J. Chem. Soc., Perkin Trans. 2*, 1998, 1901.
9 M. C. Lopez, J. C. Martinez, I. Demirtas, H. Maskill and E. Stix, *Org. React. (N.Y.)*, 1997, **31**, 71.
10 M. Canle L., W. Clegg, I. Demirtas, M. R. J. Elsegood and H. Maskill, *J. Chem. Soc., Perkin Trans. 2*, 2000, 85.
11 A. Mothwurf, *Ber. Dtsch. Chem. Ges.*, 1904, **37**, 3150.
12 R. N. Warrener and E. N. Cain, *Angew. Chem., Int. Ed. Engl.*, 1966, **5**, 511; G. H. L. Nefkens and G. I. Tesser, *J. Am. Chem. Soc.*, 1961, **83**, 1263.
13 A. Baeyer and V. Villiger, *Ber. Dtsch. Chem. Ges.*, 1902, **35**, 3013.
14 W. S. Guthmann and J. Stieglitz, *J. Org. Chem.*, 1936, **1**, 31.
15 E. B. Ayres and C. R. Hauser, *J. Org. Chem.*, 1948, **13**, 116.
16 F. H. Allen and O. Kennard, *Chem. Des. Autom. News*, 1993, **8**, 31.
17 A. Albert and E. P. Serjeant, *Ionization Constants of Acids and Bases. A Laboratory Manual*, John Wiley and Sons, Inc., New York, 1962; E. J. King, *Acid-Base Equilibria*, Pergamon Press, New York, 1965.
18 H. Maskill, *The physical basis of organic chemistry*, Oxford University Press, Oxford, 1985, p. 176.
19 T. C. Bissot, R. W. Parry and D. H. Campbell, *J. Am. Chem. Soc.*, 1957, **79**, 796.
20 J. Crugeiras and H. Maskill, *Can. J. Chem.*, 1999, **77**, 530; J. Crugeiras and H. Maskill, *J. Chem. Soc., Perkin Trans. 2*, 2000, 441.
21 W. H. Lee and H. Maskill, *J. Chem. Soc., Perkin Trans. 2*, 1994, 1463.
22 N. S. Isaacs, *Physical organic chemistry*, Longman, London, 1987.
23 W. Schlenk and E. Bergmann, *Justus Liebigs Ann. Chem.*, 1928, **464**, 1.
24 P. S. J. Canning, K. McCrudden, H. Maskill and B. Sexton, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2735.
25 M. E. Jung, *J. Org. Chem.*, 1976, **41**, 1479; M. E. Jung and M. L. Speltz, *J. Am. Chem. Soc.*, 1976, **98**, 7882; P. Barua, N. C. Barua and R. P. Sharma, *Tetrahedron Lett.*, 1983, **24**, 5801.
26 C. Bleasdale, S. B. Ellwood and B. T. Golding, *J. Chem. Soc., Perkin Trans. 1*, 1990, 803.
27 A. P. Henderson, J. Riseborough, C. Bleasdale, W. Clegg, M. R. J. Elsegood and B. T. Golding, *J. Chem. Soc., Perkin Trans. 1*, 1997, 3407.
28 M. S. Newman and P. M. Hay, *J. Am. Chem. Soc.*, 1953, **75**, 2322.
29 G. M. Sheldrick, SHELXTL manual, version 5.1, Bruker AXS Inc., Madison, WI, USA, 1997.
30 M. N. Hughes and G. Stedman, *J. Chem. Soc.*, 1963, 2824.
31 P. Lumme, P. Lahermo and J. Tummavouri, *Acta Chem. Scand.*, 1965, **19**, 2175.
32 M. N. Hughes, T. D. B. Morgan and G. Stedman, *Chem. Commun.*, 1966, 241.