N-Methyl-*N*,*O*-bis(trimethylsilyl)hydroxylamine: Preparation, Properties, and Utilization

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The title compound was readily prepared from MeNHOH·HCl under alkaline conditions with silylating reagents: use of either $Me_3SiSiMe_3$ as a 'counterattack reagent' or Me_3SiCl in a classical procedure. Reaction of aldehydes or ketones with a stoicheiometric amount of the title compound gave the corresponding *N*-methyl nitrones in good to excellent yields. The reaction intermediates were hemiaminals, which decomposed to nitrones by a bimolecular push–pull mechanism. The title compound was used to protect a carbonyl group in a compound with another functionality, which was subsequently reduced *in situ*. Acidic work-up regenerated the carbonyl group. This new method of 'protection–reduction–deprotection' includes three transformations, which were carried out in one flask.

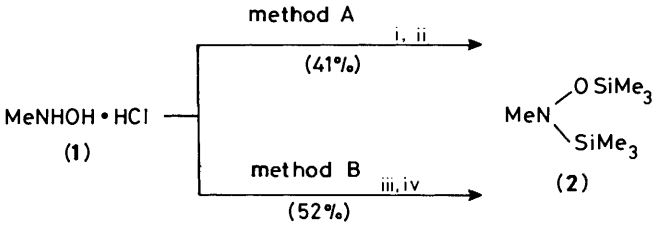
N-Methyl-*N*,*O*-bis(trimethylsilyl)hydroxylamine (**2**) is the trimethylsilylated equivalent of *N*-methylhydroxylamine. We envisioned the value of reagent (**2**) for the preparation of nitrones from aldehydes and ketones. Nitrones are versatile in organic synthesis and have been used in a variety of organic reactions, such as [3 + 2] cycloadditions.[1] Many procedures exist for the synthesis of nitrones,[2] but the conditions are often harsh and strong bases are required. In this article, we will report a new way to synthesize *N*-methylnitrones:[3] condensation of reagent (**2**) with aldehydes or ketones under aprotic conditions gave high yields of the corresponding nitrones in the anhydrous form. We will also demonstrate that under the newly developed conditions, intramolecular nitrone–alkene cycloadditions can be carried out *in situ*, without prior isolation of nitrones.

During the mechanistic study of the nitrone formation, we found that hemiaminals were the major product when an excess of reagent (**2**) was used to react with aldehydes or ketones. By taking advantage of this discovery, we were able to protect carbonyl groups with reagent (**2**). Subsequent reduction of another functionality present in the same molecule and then regeneration of the carbonyl group by hydrolysis of the hemiaminal can be performed *in situ*. In this article, we will also illustrate the chemistry of the one-flask 'protection–reduction–deprotection'.

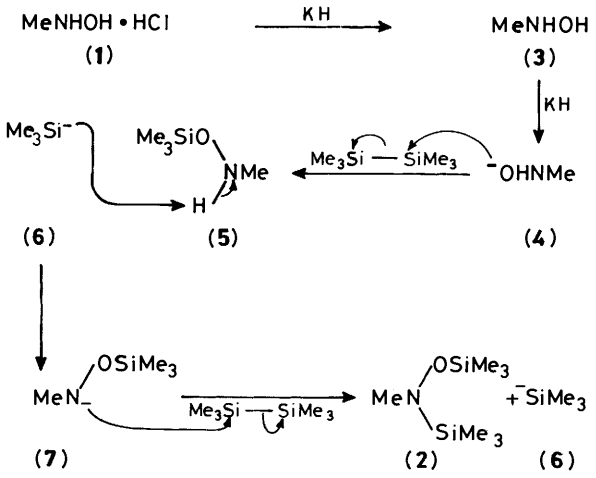
Silylated hydroxylamine (**2**) could be a widely applicable reagent based on the two functions described above. Smrekar and Wannagat reported the preparation of this reagent from anhydrous *N*-methylhydroxylamine (**3**).[4] However, to obtain (**3**) is tedious. An alternative approach to the synthesis of reagent (**2**) involves hexamethyldisilazane; unfortunately only 18% yield is obtained.[5,6] It was our intention to develop a practical and reliable method for the production of (**2**).

Results and Discussion

Preparation of N-*Methyl*-N,O-*bis(trimethylsilyl)hydroxylamine* (**2**).—Hexamethyldisilane ($Me_3SiSiMe_3$) has been applied as a 'counterattack reagent'† in functional group transformations.[7,8] We extended the 'counterattack strategy' to the preparation of hydroxylamine (**2**). Commercially available *N*-methylhydroxylamine hydrochloride (**1**) was treated with potassium hydride (KH; 2 equiv.) in anhydrous ether and hexamethylphosphoramide (HMPA; 0.5 equiv.). Then $Me_3SiSiMe_3$ (2.1 equiv.) was added at room temperature and the mixture was stirred for 3 days (Scheme 1, method A). The reaction mixture was filtered and the ether evaporated to give the desired amine (**2**) (41%) together with HMPA in 1 : 1.2 ratio.



Scheme 1. *Reagents:* i, KH/Et_2O, HMPA; ii, $Me_3SiSiMe_3$; iii, Et_3N/Et_2O; iv, Me_3SiCl



Scheme 2.

Scheme 2 shows the reaction mechanism of method A. The first equivalent of KH reacted with salt (**1**) to liberate MeNHOH (**3**). The second equivalent of KH removed the OH proton in (**3**) to give *N*-oxide (**4**), which subsequently attacked $Me_3SiSiMe_3$ to generate monosilylated hydroxylamine (**5**)[5] and $^-SiMe_3$ (**6**). This anion, acting as a base, counterattacked compound (**5**) to

† For a definition of 'counterattack reagent' see: J. R. Hwu and B. A. Gilbert, *Tetrahedron*, 1989, **45**, 1233.

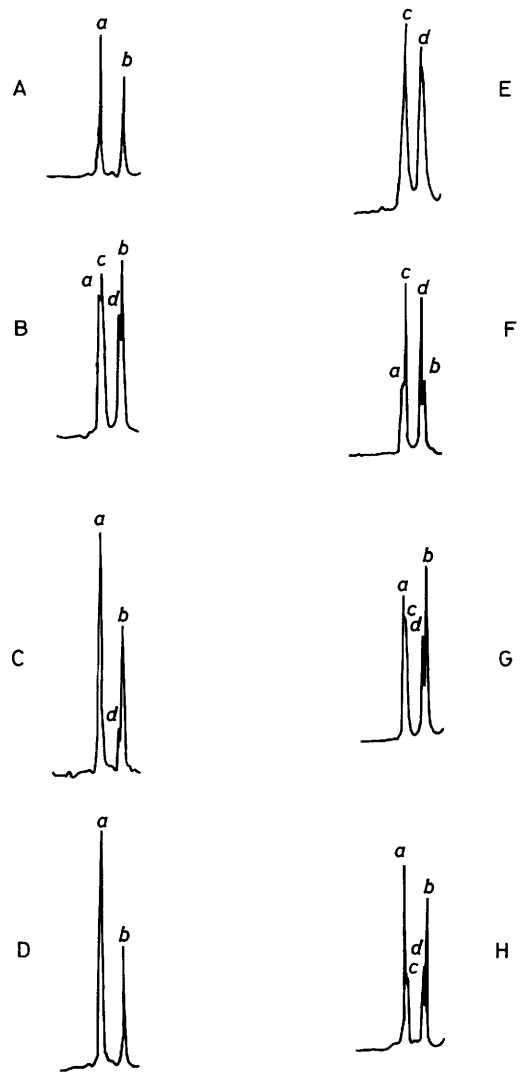


Figure 1. ^{1}H N.m.r. spectra of *N*-methyl-*N*,*O*-bis(trimethylsilyl)-hydroxylamine (**2**) in $CDCl_3$ within the region of δ 0.00—0.25 p.p.m. The δ values are: *a*, 0.14 p.p.m. ($OSiMe_3$); *b*, 0.06 ppm ($NSiMe_3$); *c*, 0.13 p.p.m. ($OSiMe_3$); *d*, 0.08 p.p.m. ($NSiMe_3$). The conditions under which spectra **A**—**H** were obtained are: **A**, (**2**) from Method A, or (**2**) from Method B + HMPA after 5 days; **B**, (**2**) from Method A + pure (**2**) after 0 h; **C**, (**2**) from Method A + pure (**2**) after 24 h; **D**, (**2**) from Method A + pure (**2**) after 72 h; **E**, pure (**2**) from Method B, or pure (**2**) from Method B + HMPA after 0 h; **F**, pure (**2**) from Method B + HMPA after 24 h; **G**, pure (**2**) from Method B + HMPA after 48 h; **H**, pure (**2**) from Method B + HMPA after 72 h

give amide (**7**). Reaction of (**7**)* with the second equivalent of $Me_3SiSiMe_3$ afforded the desired product (**2**).

The last step in Scheme 2 [*i.e.*, (**7**) ⟶ (**2**)] regenerated the anion $^-SiMe_3$ (**6**). This silyl anion could substitute for KH to convert (**3**) into (**4**) by proton abstraction. Therefore we should be able to obtain (**2**) from a mixture of (**3**) and $Me_3SiSiMe_3$ by using only a catalytic amount of KH. Indeed, we treated (**1**) with 1.3 equiv. of KH [the first equivalent neutralized HCl in (**1**)] and 2.1 equiv. of $Me_3SiSiMe_3$ to generate the desired amine (**2**), although the yield was low (< 10%).

Scheme 2 shows a special feature of the silylating reagent $Me_3SiSiMe_3$. One equivalent of this reagent was attacked by (**4**) to give monosilylated intermediate (**5**) and $^-SiMe_3$ (**6**). Then $^-SiMe_3$ counterattacked the stable intermediate (**5**). Therefore $Me_3SiSiMe_3$ was regarded as a counterattack reagent in the conversion of (**3**) into (**2**).

We found that the use of HMPA as the co-solvent was crucial for the disilylation of (**3**) with $Me_3SiSiMe_3$ to give (**2**). Method A in Scheme 1 did not produce (**2**) when HMPA was replaced by 1,3-dimethylimidazolidin-2-one, which was employed to substitute for HMPA in a related reaction.[9] We also found that a longer reaction time or use of a larger amount of HMPA did not increase the yield.

Although method A provided a simple route to (**2**), we were not able to separate (**2**) from HMPA by distillation. Chromatographic techniques were also not suitable because of the susceptibility of (**2**) towards hydrolysis. Consequently, we developed a second, practical procedure to produce amine (**2**).

Method B in Scheme 1 illustrates a classical means for the silylation of the proton-containing salt (**1**) by use of Me_3SiCl as the silylating reagent and Et_3N as the base. A slurry of MeNHOH·HCl (**1**) in anhydrous ether was treated with 3.3 equiv. of Et_3N and 2.0 equiv. of Me_3SiCl at room temperature for 3 days. Work-up of the mixture followed by vacuum distillation afforded pure (**2**) in 52% yield.† This procedure is used constantly in our laboratory to produce (**2**) in multi-gram quantities.

Properties of N-*Methyl*-N,O-*bis*(*trimethylsilyl*)*hydroxylamine* (**2**).—Compound (**2**) is a colourless liquid, which hydrolyses readily upon exposure to moisture. In contrast to MeNHOH, we were able to store reagent (**2**) without decomposition for several months in a sealed bottle at −10 to −15 °C. Zon *et al.* reported that this compound is relatively thermally stable, having $t_{\frac{1}{2}}$ = 46.5 h at 140 °C.[4]

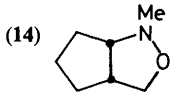
We observed that HMPA influenced the ^{1}H n.m.r. chemical shifts of (**2**) in $CDCl_3$. Method A produced (**2**) in HMPA in a molar ratio of 1:1.2. The ^{1}H n.m.r. spectrum, in the upfield region, of this mixture in $CDCl_3$ showed two peaks, at 0.14 p.p.m. (peak *a* for $OSiMe_3$) and 0.06 p.p.m. (peak *b* for $NSiMe_3$), as shown in spectrum A in Figure 1. However pure (**2**), prepared by method B, in $CDCl_3$ gave two peaks in the upfield region. They were located at 0.13 p.p.m. (peak *c* for $OSiMe_3$) and 0.08 p.p.m. (peak *d* for $NSiMe_3$), as shown in spectrum E. Gas chromatographic analysis indicated that product (**2**) obtained by both methods had the same retention time.

Addition of pure (**2**) into the sample with spectrum A provided two additional signals, *c* and *d*, as shown in spectrum B. These new signals gradually shifted to positions *a* and *b* over a 72-h period, as shown in spectra C and D. On the other hand, a spectrum obtained from the sample that was freshly prepared by addition of pure (**2**) to HMPA in $CDCl_3$ was identical with spectrum E, exhibiting only two upfield peaks, *c* and *d*. These two peaks slowly split into four signals, *a*, *b*, *c*, and *d*, as shown in spectra F, G, and H. After 5 days, the peaks *c* and *d* had disappeared and only peaks *a* and *b* remained, as shown in spectrum A. This control experiment demonstrated that disilyl-

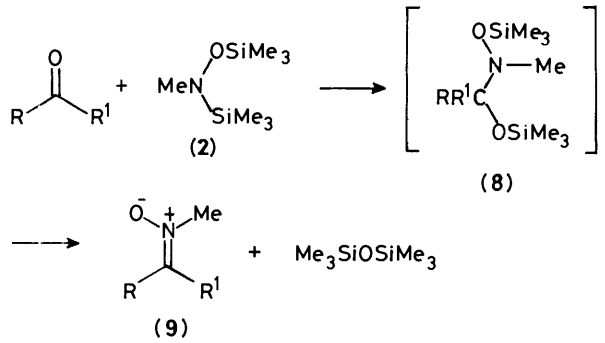
* Siloxylamide (**7**) may rearrange to the corresponding silylamine oxide $Me(Me_3Si)NO^-$, as indicated in ref. 5. Nevertheless silylation of $Me(Me_3Si)NO^-$ should also give (**2**).

† This method has been routinely used in our laboratory for the production of (**2**) in large quantities. It has been successfully carried out independently by two graduate and three undergraduate students. However, a report from Chiaki Kuroda and Garry O. Spessard stated that they were able to obtain only a trace of (**2**) using this method. The product they obtained became cloudy within 0.5 h after purification by distillation. They reported their n.m.r. data as; δ_H 0.08 (9 H, s), 0.12 (9 H, s), 2.71 (3 H, t, *J* 2—3 Hz). We have carefully checked the accuracy of this procedure and now cast a serious doubt on the correctness of their report. We cannot envisage that any compound similar to (**2**) can possess a 'single coupled' peak as they reported.

Table 1. Formation of nitrones from aldehydes or ketones with $Me_3SiN(Me)OSiMe_3$ (2)

Entry	Aldehyde or ketone[a]	Conditions (temp./time + reagent[b])	Nitrone, $RN^+O^-(Me)$ or [3 + 2] adduct	Yield[c,d] (%)
1	PhCHO	50 °C/24 h	(**10**) R = PhCH=	97 (73—99)[33,34]
2	Pr^iCHO	50 °C/22 h	(**11**) R = Pr^iCH=	80 (NA)
3	Bu^tCHO	50 °C/22 h	(**12**) R = Bu^tCH=	62 (NA)[35]
4	Me_2CO	50 °C/24 h	(**13**) R = Pr^iCH=	78 (30)[10]
5	CH_2=$CH(CH_2)_3CHO$	50 °C/20 h + 80 °C/72 h	(**14**) 	78 (40)[12]
6	p-$Me_2NC_6H_4CHO$	50 °C/28 h + Me_3SiOTf/r.t./42 h	(**15**) R = p-$Me_2NC_6H_4CH$=	93 (63)[36]
7	p-$O_2NC_6H_4CHO$	50 °C/24 h + Me_3SiOTf/r.t./24 h	(**16**) R = p-$O_2NC_6H_4CH$=	98 (75—92)[32b,34]
8	2-Furyl-CHO	50 °C/18 h + Me_3SiOTf/r.t./24 h	(**17**) R = 2-Furyl-CH=	98 (NA)[32a]

[a] All reactions were run in anhydrous benzene at concentrations of 0.25—0.39M. The ratio of aldehyde or ketone to $Me_3SiN(Me)OSiMe_3$ was 1:1 in all cases except entries 2—4. For isobutyraldehyde and acetone (entries 2 and 4), the carbonyl compounds were used as solvent. The ratio of trimethylacetaldehyde to $Me_3SiN(Me)OSiMe_3$ (entry 3) was 1.2:1. [b] Trimethylsilyl trifluoromethanesulphonate (Me_3SiOTf) (0.03—0.04 equiv.) was used as a catalyst. [c] Numbers represent isolated yields. [d] Numbers in parentheses represent yields from literature.



Scheme 3.

ated hydroxylamine (**2**) gradually co-ordinated with HMPA. Peaks *a* and *b* came from the species of (**2**) co-ordinated with HMPA: peaks *c* and *d* resulted from free (**2**).

Formation of Nitrones.—Generally nitrones are readily hydrolysed by moisture under acidic conditions.[2d] We believe that anhydrous nitrones (**9**) could be obtained by reaction of reagent (**2**) with aldehydes or ketones under aprotic conditions (Scheme 3). The resulting nitrones (**9**) could then be used directly for other reactions without drying.

We utilized reagent (**2**) to generate some nitrones that had been reported in the literature. Therefore we were able to compare the efficiency of our method with others (Table 1). The best conditions for the nitrone formation with (**2**) were investigated by use of benzaldehyde as the substrate. Treatment of benzaldehyde with a stoicheiometric amount of (**2**) in benzene at 50 °C for 24 h gave the corresponding nitrone (**10**) and hexamethyldisiloxane. The volatiles were removed under reduced pressure by rotary evaporation and a mixture of ether and hexanes was used to recrystallize the residue. We obtained white crystals of *N*-methyl-α-phenyl nitrone (**10**) in 97% yield. We also found that other aprotic solvents, such as chloroform, dichloromethane, and toluene, were suitable for *N*-methyl nitrone formation.

We obtained *N*-methyl nitrones in good to excellent yields by treating reagent (**2**) with non-hindered and hindered aliphatic aldehydes (Table 1): isobutyraldehyde and trimethylacetaldehyde gave the nitrones (**11**) and (**12**) in 80 and 62% yields, respectively. Also, acetone gave the nitrone (**13**) in 78% yield. Because of the volatility of isobutyraldehyde and acetone, these substrates were used as solvents for the reactions. The only reported synthesis of (**13**) involves a two-step process, requiring acetone and acetone dimethyl ketal as starting materials.[10] This procedure gives (**13**) in an overall yield of 30%.

Reagent (**2**) did not condense appreciably with aromatic ketones. For example, treatment of acetophenone with (**2**) gave a very small amount of the corresponding *N*-methylnitrone even after the reaction mixture was heated at 50 °C for 100 h.

We also used reagent (**2**) to prepare an isoxazolidine from an alkenyl aldehyde. Treatment of hex-5-en-1-al[11] with (**2**) at 50 °C in benzene gave the corresponding nitrone. The nitrone solution was heated at 80 °C for 3 days to afford the nitrone–alkene cycloaddition product (**14**) in 78% yield. Other conventional methods used to prepare (**14**) include mercuric oxide oxidation of *N*-methyl-*N*-hex-5-enylhydroxylamine and condensation of hex-5-en-1-al with freshly prepared *N*-methylhydroxylamine, followed by heating. These methods give the isoxazolidine (**14**) in lower yields (≤41%).[12]

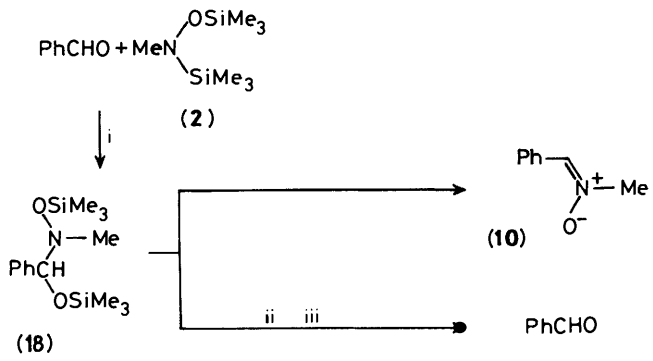
The Formation and the Decomposition of Silylated Hemiaminals.—During the study of the nitrone formation, we examined a variety of reaction conditions. One of the most important observations was that, in general, the highest yields of nitrones (**9**) were obtained when the ratio of aldehyde or ketone to reagent (**2**) was 1:1. Use of an excess of (**2**) did not increase, but rather decreased, the amount of nitrone. Meanwhile, the amount of the silylated hemiaminal intermediates (**8**) increased. Conversely, the reactions went to completion to give the nitrones (**9**) in high yields when an excess of aldehyde or ketone was used.

We found that the formation of hemiaminal intermediates (**8**) was often much faster than their decomposition to the corresponding nitrones (**9**). The hemiaminals (**8**) were easily detected by n.m.r. spectroscopy when the reaction shown in Scheme 3 was stopped before completion or an excess of (**2**) was used. The formation of related, stable hemiaminals HRC(OH)-NR′(OR″) from *N*,*O*-dialkylhydroxylamines and aldehydes was reported by Zinner *et al.*[13]

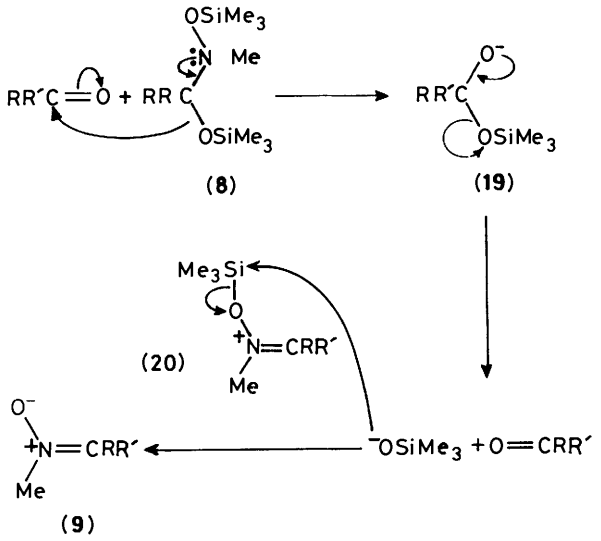
Table 2 lists the conditions for the formation of the hemiaminal (**18**) and the nitrone (**10**) from reagent (**2**) and benzaldehyde (also see Scheme 4). Using a 1:1 ratio of benzaldehyde

Table 2. Reaction of PhCHO with $Me_3SiN(Me)OSiMe_3$ (**2**) at 50 °C to give the hemiaminal (**18**) and the nitrone (**10**) under various conditions

Entry	PhCHO:(2)	Solvent	Time	Yield (%) (18)	Yield (%) (10)
1	1:1.0	Benzene	24 h	0	97
2	1:1.1	Benzene	16 h	21	79
3	1:2.0	Benzene	18 h	89	11
4	1:1.1	$CHCl_3$	19 h	25	70
5	1:1.1	Benzene + SiO_2	24 h	0	95



Scheme 4. *Reagents:* i, benzene; ii, reducing agent; iii, H_3O^+



Scheme 5.

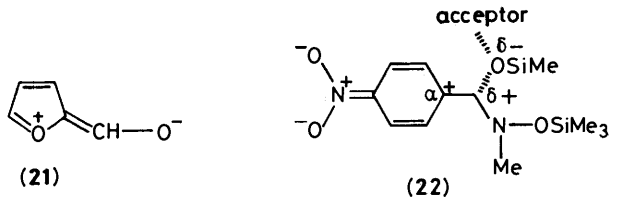
to (**2**) in benzene (entry 1), we obtained the nitrone (**10**) in 97% yield and did not detect any hemiaminal (**18**). Increasing the ratio of benzaldehyde:(**2**) to 1:1.1 (entry 2), we obtained the hemiaminal (**18**) in 21% yield and nitrone (**10**) in 79% yield. With 2.0 equiv. of reagent (**2**) (entry 3), the reaction gave the hemiaminal (**18**) as the major product (89%) along with a small amount of nitrone (**10**) (11%). Change of the solvent to chloroform did not significantly affect the product ratio (see entries 2 and 4). Also, the reaction of benzaldehyde with a slight excess of (**2**) (1.1 equiv., entry 5), followed by addition of silica gel to the reaction mixture, gave the nitrone (**10**) (95%) as the only product.

In order to search for the best conditions to decompose the hemiaminals (**8**), we heated the solution of (**18**) in deuteriated benzene. This allowed us to monitor the reaction directly by n.m.r. spectroscopy without isolation of products. After the solution was heated at 50 °C for 48 h, hemiaminal (**18**) still did not decompose to the corresponding nitrone (**10**). However, in the presence of silica gel at 50 °C for 18 h, (**18**) was converted almost quantitatively into (**10**) and $Me_3SiOSiMe_3$, as shown by n.m.r. spectroscopy. Furthermore, after we added 0.05 equiv. of benzaldehyde to the pure hemiaminal (**18**) in benzene and heated the solution at 50 °C for 40 h, 42% of the hemiaminal (**18**) was converted into the corresponding nitrone (**10**).

Bimolecular Push-Pull Mechanism.—We found that weak Lewis acids, such as silica gel,[14] were able to decompose the hemiaminal (**18**) to give the nitrone (**10**). Furthermore, benzaldehyde catalyzed the transformation of (**18**) to (**10**). To rationalize this phenomenon, we proposed a bimolecular push-pull mechanism[15] as shown in Scheme 5. The carbonyl compounds acted as a Lewis acid[16] (*i.e.*, the trimethylsiloxide acceptor), while hemiaminals (**8**) acted as the trimethylsiloxide donor. Reaction of the hemiaminals (**8**) with RR'C=O generated the hemiacetal alkoxide intermediates (**19**) and *N*-(trimethylsilyloxy)iminium species (**20**). The collapse of the hemiacetal alkoxides (**19**) gave Me_3SiO^- and regenerated catalyst RR'C=O. Then Me_3SiO^- attacked the iminium intermediates (**20**) to afford the nitrones (**9**) and $Me_3SiOSiMe_3$. Given this proposed push-pull mechanism, RR'C=O were both the starting materials and the catalysts for the nitrone formation shown in Scheme 3. Therefore, when an excess of reagent (**2**) was present, all of the starting materials RR'C=O were quickly consumed and were no longer available to act as catalysts to decompose the intermediates (**8**). Thus (**8**) built up and nitrones (**9**) were generated in a lower yield.

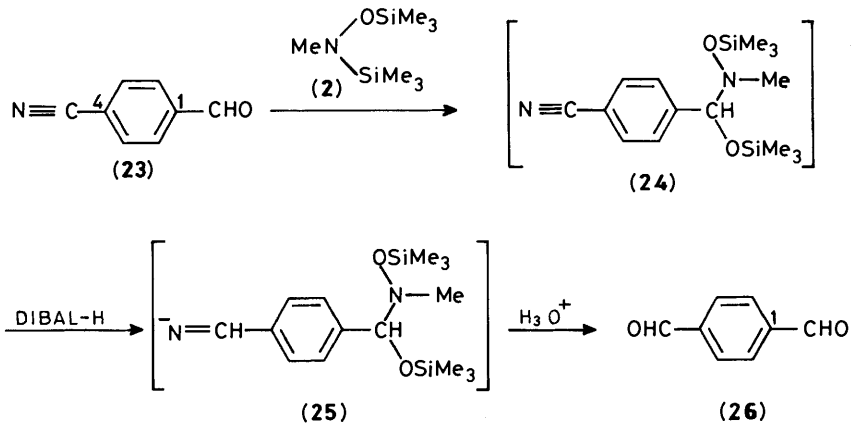
Trimethylsilyl Trifluoromethanesulphonate Catalysed Nitrone Formations.—By treating 4-(dimethylamino)benzaldehyde, 4-nitrobenzaldehyde, or 2-furaldehyde with reagent (**2**) in benzene at 50 °C, we obtained the corresponding hemiaminal as the major product. The desired nitrones were obtained in very low yields regardless of the ratio of aldehydes to reagent (**2**). For the aldehydes in which the C=O group was affected by another functionality with electron donating or withdrawing capability, the corresponding hemiaminal intermediates did not decompose at an appreciable rate. However, we found that acid catalysts were able to convert these hemiaminals into the corresponding nitrones in high yields. We treated these aldehydes with 1.0 equiv. of reagent (**2**) at 50 °C in benzene for 18–28 h. To the resulting solutions was added 0.03–0.04 equiv. of trimethylsilyl trifluoromethanesulphonate. For 4-nitrobenzaldehyde and 2-furaldehyde, the formation of the corresponding nitrones (**16**) and (**17**) was completed in 24 h. Longer reaction time was necessary to convert 4-(dimethylamino)benzaldehyde into the nitrone (**15**). The complexation of trimethylsilyl trifluoromethanesulphonate with the dimethylamino group could retard its complexation with the hemiaminal moiety in the intermediate (**8**) from 4-(dimethylamino)benzaldehyde.

The conversion of 4-(dimethylamino)benzaldehyde, 4-nitrobenzaldehyde, and 2-furaldehyde into the corresponding nitrones required Lewis acids as catalysts. Therefore the bimolecular push-pull mechanism shown in Scheme 5 is not applicable to these reactions. We explain the discrepancy as follows. The dimethylamino group in 4-(dimethylamino)-benzaldehyde decreases the electrophilicity of the carbonyl carbon because of the resonance effect.[17] This group makes 4-(dimethylamino)benzaldehyde a poor trimethylsiloxide acceptor, although the corresponding hemiaminal should be a good trimethylsiloxide donor. The same reasoning can be applied to 2-furaldehyde because of its canonical form (**21**).[18] For 4-nitrobenzaldehyde, the nitro group makes the α-carbon an electron deficient centre[19] which is adjacent to the carbon



method for the protection-reduction-deprotection of carbonyl compounds: a carbonyl group in a bifunctional compound would first be protected in the hemiaminal form by reagent (**2**); then the other functional group in the molecule could be reduced *in situ*; finally, the carbonyl group would be regenerated during work-up under acidic conditions.

Scheme 6 shows the concept of the new protection-reduction-deprotection strategy by use of 4-cyanobenzaldehyde (**23**) as the



Scheme 6.

Table 3. Stability of hemiaminal as a protecting group in compound (**18**) towards reducing agents

Reducing agent[a]	Solvent, temp.	Yield of PhCHO (%)[b]	Ref.
$NaBH_4$	THF, r.t.	89	20
Super-Hydride	THF, r.t.	84	21
L-Selectride	THF, r.t.	93	22
K-Selectride	THF, r.t.	80	23
LS-Selectride	THF, r.t.	87	24
BH_3·THF	THF, r.t.	82	25
9-BBN	THF, r.t.	84	26
DIBAL-H	CH_2Cl_2, r.t.	86	27
Red-Al	THF, r.t.	86	28
Bu_3SnH[c]	Toluene, 95 °C	86	29

[a] The ratio of (**18**) to reducing agent was 1:4. [b] Numbers represent g.c. yields. [c] 2,2′-Azo(2-methylpropionitrile) (0.73 equiv.) was added as initiator.

bearing a partial positive charge in the transition state [see structure (**22**)]. Hence, the silylated hemiaminal of 4-nitrobenzaldehyde is a poor trimethylsiloxide donor although 4-nitrobenzaldehyde might be a good acceptor. Decomposition of the hemiaminals (**8**) to the nitrones (**9**) proceeds well only if a suitable balance exists between the acceptor and the donor. Addition of catalytic trimethylsilyl trifluoromethanesulphonate overrides the electronic effects; therefore nitrones are obtained in high yields.

One-Flask Protection-Reduction-Deprotection of Carbonyl Compounds.—We considered that the hemiaminal moiety in (**8**) might be stable towards various reducing agents.[20–29] If so, reagent (**2**) could be used to protect an aldehydic or a ketonic carbonyl group in a compound that contains another functional group to be reduced. Consequently, we developed a 'one-flask' starting material. We treated (**23**) with 1.3 equiv. of reagent (**2**) in CH_2Cl_2 to give the hemiaminal (**24**). Subsequent addition of 1.2 equiv. of DIBAL-H[27,30] to the mixture, which was then refluxed for 33 h, gave reduced species (**25**). Acidic work-up of the solution followed by chromatographic separation of the crude products afforded terephthaldehyde (**26**) in 83% yield. Therefore the hemiaminal group in (**24**) can be regarded as a masked carbonyl functionality, which was inert under the reduction conditions. Regeneration of the C-1 carbonyl group in (**26**) was readily accomplished by decomposition of the hemiaminal functionality in (**25**) under acidic conditions.

To define the scope and the limitation of the protection-reduction-deprotection method, we tested the stability of the hemiaminal functionality towards commonly used reducing agents. They included $NaBH_4$, Super Hydride (lithium triethylborohydride), L-Selectride (lithium tri-s-butylborohydride), K-Selectride (potassium tri-s-butylborohydride), LS-Selectride (lithium trisiamylborohydride), BH_3·THF, 9-BBN (9-borabicyclo[3.3.1]nonane), DIBAL-H (di-isobutylaluminium hydride), Red-Al [sodium bis(2-methoxyethoxy)aluminium hydride], and Bu_3SnH.

The conditions we used to check the stability were as harsh as or more vigorous than those employed to reduce carbonyl groups.[20–29] Thus, we treated hemiaminal (**18**) with 4.0 equivalents of a reducing agent listed in Table 3, and then added 10% aqueous sulphuric acid to the reaction mixture (Scheme 4). The intact hemiaminal should lead to the parent aldehyde upon hydrolysis. By this procedure, we recovered 80—93% of benzaldehyde (see Table 3). These results indicated that carbonyl groups can be protected as the hemiaminal form with reagent (**2**).

We also found that hemiaminal (**18**) was unstable towards strong reducing agents, such as $LiAlH_4$ and $LiAlH(OBu^t)_3$. We did not recover any benzaldehyde when using $LiAlH_4$, and obtained only in 40—50% yield when using $LiAlH(OBu^t)_3$. Hemiaminal (**18**) was also destroyed by alkylating agents: MeMgBr (<23% recovery of benzaldehyde), EtMgBr (40—50% recovery), and Bu^sLi (0% recovery). Furthermore, we found that hemiaminal (**18**) was unstable towards DIBAL-H in benzene. However, when DIBAL-H was used in CH_2Cl_2,* we recovered benzaldehyde in 86% yield.

* Dichloromethane was used as a solvent in reactions with DIBAL-H, see: D. Tanner and P. Somfai, *Tetrahedron*, 1987, **43**, 4395.

Conclusions

A new method was developed to generate *N*-methyl nitrones from aldehydes or ketones with *N*-methyl-*N*,*O*-bis(trimethylsilyl)hydroxylamine (**2**). In addition to providing good to excellent yields, this new method possesses the following advantages. (1) Reactions can be carried out efficiently in aprotic solvents, which are superior to protic solvents for intramolecular 1,3-dipolar cycloadditions.[31] (2) Subsequent 1,3-dipolar cycloadditions can be carried out *in situ*. (3) Formation of $Me_3SiOSiMe_3$ as the by-product drives the reaction to completion. This by-product (b.p. 101 °C/760 Torr), as well as the unchanged reagent [(**2**), b.p, 40—41 °C/10 Torr], is volatile and can be removed by rotary evaporation. (4) No aqueous work-up is required and all nitrones can be isolated directly in their unhydrated forms.* (5) Often only a stoicheiometric amount of the carbonyl compound is required. (6) Under most circumstances, the reaction does not require external catalysts. (7) Several solvents, such as benzene, chloroform, dichloromethane, and toluene, can be used.

N-Methyl-*N*,*O*-bis(trimethylsilyl)hydroxylamine (**2**) was prepared from MeNHOH·HCl and counterattack reagent $Me_3SiSiMe_3$ under alkaline conditions. Use of a classical method, involving MeNHOH·HCl, Et_3N, and Me_3SiCl, can produce (**2**) in a large quantity.

The carbonyl group in a compound containing another functionality can be protected as the hemiaminal form by reagent (**2**). *In situ* the other functionality was reduced. Subsequently, the carbonyl group was regenerated by hydrolysis of the hemiaminal functionality under acidic conditions. This provides a new way to carry out protection-reduction-deprotection in one flask.

Experimental

General.—All reactions were carried out in oven-dried (120 °C) glassware under an atmosphere of nitrogen. Acetone, chloroform, chlorotrimethylsilane, dichloromethane, ethyl acetate, hexanes, and triethylamine were dried and distilled over CaH_2. Benzene and diethyl ether were freshly distilled from Na and benzophenone. Hexamethylphosphoramide was dried over molecular sieves 13X. Benzaldehyde and isobutyraldehyde were purchased from the Aldrich Chemical Co. and distilled prior to use. *N*-Methylhydroxylamine hydrochloride was purchased from the Aldrich Chemical Co. or ICN Biomedicals, Inc. and was dried over P_2O_5 at 56 °C under an oil pump vacuum for 5 h. Trimethylacetaldehyde, 4-(dimethylamino)benzaldehyde, 4-nitrobenzaldehyde, 2-furaldehyde, 4-cyanobenzaldehyde, $NaBH_4$, Super Hydride, L-Selectride, K-Selectride, LS-Selectride, BH_3·THF, 9-BBN, DIBAL-H, Red-Al, Bu_3SnH, $LiAlH_4$, $LiAlH(OBu^t)_3$, MeMgBr, EtMgBr, Bu^sLi, $Me_3SiSiMe_3$, KH, and trimethylsilyl trifluoromethanesulphonate were purchased from the Aldrich Chemical Co. and were used directly. Analytical t.l.c. was performed on precoated plates purchased from Analtech, Inc. (silica gel GHLF). Visualization of spots on t.l.c. plates was made by use of u.v. light and/or 2.5% phosphomolybdic acid in ethanol with heating. Mixtures of ethyl acetate and hexanes were used as eluants. I.r. spectra were measured on a Perkin-Elmer 599B or a 710B spectrophotometer. The wavenumbers reported are referenced to the polystyrene 1 601 cm^{-1} absorption. Spectra of ^1H n.m.r. were obtained on a Varian CFT-20 (80 MHz) spectrometer by use of deuteriochloroform as solvent and tetramethylsilane as an internal standard. High-resolution mass spectra were obtained with a VG analytical 70-S mass spectrometer. Elemental analyses were carried out by MicAnal Organic Microanalysis located at Tucson, Arizona. M.p.s were determined on a Büchi 510K melting point apparatus and are uncorrected. Gas chromatography analyses were performed on a Hewlett–Packard 5794A instrument equipped with a 12.5-m cross-linked methylsilicone gum capillary column (0.2-mm i.d.).

N-*Methyl*-N,O-*bis*(*trimethylsilyl*)*hydroxylamine* (**2**)[4–6]
Method A.—A dry, three-neck round-bottomed flask equipped with a magnetic stirring bar was fitted with a condenser and a powder addition funnel under an atmosphere of nitrogen. Potassium hydride (35% in mineral oil; 0.69 g, 5.99 mmol, 2.0 equiv.) was added to the flask and washed with hexanes (3 × 5 ml). Traces of hexanes were removed under reduced pressure to give KH as a white powder. Diethyl ether (15 ml) and HMPA (263 mg, 1.47 mmol, 0.5 equiv.) were added to the flask, followed by the addition of *N*-methylhydroxylamine hydrochloride (98%; 245 mg, 2.93 mmol, 1.0 equiv.) through the powder addition funnel. The suspension was stirred at room temperature for 2 h. Hexamethyldisilane (95%; 1.32 ml, 900 mg, 6.15 mmol, 2.1 equiv.) was then added and the solution was stirred at room temperature for 72 h. The reaction mixture was filtered through Celite and diethyl ether was removed under reduced pressure at 0 °C to give a yellow solution (493 mg) of (**2**) in HMPA. ^1H N.m.r. analysis indicated that (**2**) was obtained in 41% yield; $\delta_H(CDCl_3)$ 0.06 (9 H, s, $NSiMe_3$), 0.14 (9 H, s, $OSiMe_3$), 2.58 and 2.70 [NMe in (**2**) and HMPA]; g.c. (injector temperature 50 °C; column temperature 40 °C) t_R 1.19 min.

Method B. A dry 500 ml round bottom flask equipped with a large magnetic stirring bar was charged with *N*-methylhydroxylamine hydrochloride (98% pure; 9.73 g, 114 mmol, 1.0 equiv.) and diethyl ether (250 ml). The mixture was stirred vigorously under nitrogen at room temperature while Et_3N (37.75 g, 373 mmol, 3.3 equiv.) was added over 5 min. After the mixture had been stirred for 3 h, chlorotrimethylsilane (25.2 g, 232 mmol, 2.0 equiv.) was added dropwise over 15 min with rapid stirring. The slightly exothermic reaction was cooled if necessary with an ice-bath during the addition. After the addition of chlorotrimethylsilane was complete, the mixture was stirred vigorously for 3 days at room temperature.

The thick slurry was filtered to remove triethylamine hydrochloride and this salt was washed with dry diethyl ether. The filtrate was concentrated under reduced pressure at 0 °C to *ca.* 100 ml. The mixture was filtered again, concentrated to 30 ml and finally filtered by gravity through glass wool.

Distillation of the crude product by use of a Vigreux column afforded *N*-methyl-*N*,*O*-bis(trimethylsilyl)hydroxylamine (**2**) (8.68 g) as a clear colourless liquid, b.p. 40—41 °C (10 Torr). The fore-fractions, which usually contained major amounts of the desired product with minor amounts of triethylamine and hexamethyldisiloxane, were redistilled to give further (**2**) (2.67 g). In total 11.35 g of (**2**) (59.3 mmol, 52% yield) was obtained; n_D^{20} 1.4146 (lit.,[4] 1.4163); g.c. (injector temp. 50 °C; column temp. 40 °C), t_R 1.18 min; $\delta_H(CDCl_3)$ 0.08 (9 H, s, $NSiMe_3$), 0.13 (9 H, s, $OSiMe_3$), and 2.71 (3 H, s, NMe); $\nu_{max.}$(neat) 2 958, 2 909, 2 863, 1 435, 1 405 (C–N), 1 250 (SiMe), 1 195 (NSi), 1 035 (OSi), 940, 851, 840, 752 ($SiMe_3$), 699, and 666 cm^{-1} (Found: M^+, 191.1160. Calc. for $C_7H_{21}NOSi_2$: *M*, 191.1162).

N-(*Benzylidene*)*methanamine* N-*Oxide* (**10**).[33,34]—A mixture of benzaldehyde (51.8 mg, 0.49 mmol, 1.0 equiv.) and hydroxylamine (**2**) (93.4 mg, 0.49 mmol, 1.0 equiv.) in benzene (1.5 ml) was stirred at 50 °C for 24 h. Removal of the solvent followed by recrystallization of the residue from a mixture of Et_2O and hexanes afforded the nitrone (**10**) as white crystals (97%, 64.5 mg, 0.475 mmol), m.p. 82—83 °C (lit.,[33] 84—86 °C); $\delta_H(CDCl_3)$ 3.90 (3 H, s, NMe), 7.34—7.51 (4 H, m, $ArH_{o,p}$ and CH=N), and 8.15—8.30 (2 H, m, ArH_m); $\nu_{max.}(CHCl_3)$ 3 078w

* The melting points we observed are consistent with those of the known unhydrated nitrones in the literature. See ref. 32.

(=CH), 2 989s, 1 597m (C=N), 1 451m (C=C), 1 419s, 1 328w, 1 171s (NO), 1 165m, 956m, 825w, 697w, and 668w cm^{-1}. The physical and spectroscopic data of this compound were consistent with those reported in the literature.[33,34]

Formation of N-(*benzylidene*)*methanamine* N-*oxide* (**10**) *in the presence of silica gel.* A mixture of benzaldehyde (47.7 mg, 0.45 mmol, 1.0 equiv.) and hydroxylamine (**2**) (94.6 mg, 0.49 mmol, 1.1 equiv.) in benzene (1.5 ml) was stirred at 50 °C for 24 h. Silica gel (EM Reagents silica gel 60, 0.063—0.200 mm, 26.2 mg) was added to the solution and the mixture was stirred at 50 °C for an additional 24 h. The solution was filtered and the silica gel was washed with a small amount of MeCN. Removal of the solvents followed by recrystallization of the residue from Et_2O–light petroleum afforded the nitrone (**10**) as white crystals (95%, 57.8 mg, 0.43 mmol). Its spectroscopic data are listed above.

Formation of N-(*benzylidene*)*methanamine* N-*oxide* (**10**) *by use of benzaldehyde as a catalyst.* A mixture of silylated hemiaminal (**18**) (90.4 mg, 0.304 mmol, 1.0 equiv.) and benzaldehyde (1.5 mg, 0.014 mmol, 0.05 equiv.) in benzene (1.0 ml) was stirred at 50 °C for 40 h. The solvent was removed under reduced pressure at 45 °C to give a cloudy oil (71.6 mg). ^1H n.m.r. analysis of the residue showed 59 mol% of unchanged silylated hemiaminal (**18**) and 41 mol% of the corresponding nitrone (**10**). A yield of 58 mol% hemiaminal and 42 mol% nitrone was determined based on mass balance calculations.

N-(2-*Methylpropylidene*)*methanamine* N-*Oxide* (**11**).—A mixture of isobutyraldehyde (1.5 ml) and hydroxylamine (**2**) (76.4 mg, 0.40 mmol, 1.0 equiv.) was stirred at 50 °C for 22 h. Removal of the volatile materials by rotary evaporation at 40 °C gave the pure *nitrone* (**11**) as a colourless liquid (80%, 32.2 mg, 0.32 mmol): $\delta_H(CDCl_3)$ 1.09 (6 H, d, *J* 6.9 Hz, 2 × Me), 3.17 (1 H, m, $CHMe_2$), 3.64 (3 H, s, NMe), and 6.50 (1 H, d, *J* 7.3 Hz, CH=N); $\nu_{max.}$(neat) 2 942s, 2 868s, 1 595s (C=N), 1 461s, 1 389m, 1 288m, 1 180s (N–O), 1 100m, 969m, and 914m cm^{-1} (Found: C, 59 3; H, 10.9; N, 14.0. $C_5H_{11}NO$ requires C, 59.4; H, 11.0; N, 13.9%).

N-(2,2-*Dimethylpropylidene*)*methanamine* N-*Oxide* (**12**).[35]—A mixture of trimethylacetaldehyde (111.0 mg, 1.29 mmol, 1.2 equiv.) and hydroxylamine (**2**) (205.1 mg, 1.07 mmol, 1.0 equiv.) in benzene (3.7 ml) was stirred at 50 °C for 22 h. The volatile materials were removed by rotary evaporation to give the pure nitrone (**12**) as a clear, colourless liquid (62%, 76.0 mg, 0.66 mmol); $\delta_H(CDCl_3)$ 1.27 (9 H, s, CMe_3), 3.66 (3 H, d, *J* 0.8 Hz, NMe), and 6.45 (1 H, d, *J* 0.8 Hz, CH=N); $\nu_{max.}$(neat) 2 944s, 2 907s, 2 857m, 1 591s (C=N), 1 479m, 1 410s, 1 387m, 1 365s, 1 228s, 1 157s (NO), 958m, 938m, 920s, 840m, and 732s cm^{-1}. The physical and spectroscopic data of this compound were consistent with those reported in the literature.[35]

N-(*Isopropylidene*)*methanamine* N-*Oxide* (**13**).[10]—A mixture of dry acetone (3 ml) and hydroxylamine (**2**) (72.4 mg, 0.378 mmol) was stirred at 50 °C for 24 h. The solution was concentrated by rotary evaporation at 45 °C to give a colourless liquid (39.4 mg) which contained the desired nitrone and hexamethyldisiloxane. Integration of the ^1H n.m.r. spectrum of the mixture showed the nitrone was obtained in 88% yield. Complete removal of $Me_3SiOSiMe_3$ by rotary evaporation gave the nitrone (**13**) as a colourless oil (78%, 25.7 mg, 0.295 mmol); $\delta_H(CDCl_3)$ 2.13 (6 H, br s, 2 × Me) and 3.67 (3 H, br s, NMe); $\nu_{max.}$(neat) 2 948s, 1 603m (C=N), 1 434 m, 1 376m (NC), 1 310m, 1 244m, 1 213s (NO), 1 142m, 1 052m, 914s, and 838m cm^{-1}. The physical and spectroscopic data of this compound were consistent with those reported in the literature.[10]

cis-6a-*Methylhexahydrocyclopent*[c]*isoxazole* (**14**).[12]—A mixture of hex-5-en-1-al (65.2 mg, 0.664 mmol, 1.0 equiv.) and the hydroxylamine (**2**) (126.7 mg, 0.662 mmol, 1.0 equiv.) in benzene (1.7 ml) was heated at 50 °C for 20 h and then at 80 °C for 3 days. Because of the volatility of (**14**), the product was purified in the following manner. Without removal of the solvent, the cooled solution was chromatographed directly on silica gel (50% Et_2O in pentane as eluant). Fractions containing pure product were pooled and the solvent was removed under reduced pressure (solid CO_2–acetone condenser) at −30 °C to give the title compound (**14**) (65.4 mg, 0.514 mmol) as a clear, colourless liquid (78% yield); t.l.c. R_F 0.27 (40% EtOAc in hexanes); $\delta_H(CDCl_3)$ 1.22—1.70 [7 H, m, $(CH_2)_3$ and CH], 2.63 (3 H, s, NMe), 3.04 (1 H, m, CHN), 3.40 (1 H, m, CHO), and 4.09 (1 H, m, CHO); $\nu_{max.}(CHCl_3)$ 2 956vs, 2 875s, 1 462m, 1 440m, 1 358m (NMe), 1 252m (CN), 1 057w, 1 038m, 1 012s (CO), and 953w cm^{-1}. The physical and spectroscopic data of this compound were consistent with those reported in the literature.[12]

N-[4-(N′,N′-*Dimethylamino*)*benzylidene*]*methanamine* N-*Oxide* (**15**).[36,37]—A mixture of 4-(dimethylamino)benzaldehyde (66.3 mg, 0.444 mmol, 1.0 equiv.) and hydroxylamine (**2**) (85.2 mg, 0.445 mmol, 1.0 equiv.) in benzene (1.5 ml) was stirred at 50 °C for 28 h. The solution was cooled to room temperature and treated with trimethylsilyl trifluoromethanesulphonate (3.0 mg, 0.013 mmol, 0.03 equiv.). The reaction mixture gradually became thick with a yellow precipitate. After 42 h, the mixture was diluted with light petroleum (3 ml) and stirred for 10 min. The solid was filtered off and washed with light petroleum. Recrystallization of the solid from $CHCl_3$–light petroleum afforded the nitrone (**15**) as yellow crystals (93%, 73.7 mg, 0.414 mmol), m.p. 129—130 °C (lit.,[36] 132 °C); $\delta_H(CDCl_3)$ 3.02 (6 H, s, NMe_2), 3.79 (3 H, s, NMe), 6.69 (2 H, d, *J* 9.1 Hz, ArH), 7.19 (1 H, s, CH=N), and 8.13 (2 H, d, *J* 9.1 Hz, ArH); $\nu_{max.}(CHCl_3)$ 3 089w (=C–H), 2 949m, 1 608s (C=N), 1 523m, 1 416m, 1 368s (CN), 1 156s (NO), 948m, and 837m cm^{-1}. The physical and spectroscopic data of this compound were consistent with those reported in the literature.[36,37]

N-(4-*Nitrobenzylidene*)*methanamine* N-*Oxide* (**16**).[32b,34,38]—A mixture of 4-nitrobenzaldehyde (2.79 g, 18.4 mmol, 1.0 equiv.) and hydroxylamine (**2**) (3.54 g, 18.5 mmol, 1.0 equiv.) in benzene (65 ml) was stirred at 50 °C for 24 h. The solution was cooled to room temperature and treated with trimethylsilyl trifluoromethanesulphonate (0.123 g, 0.55 mmol, 0.03 equiv.). The reaction mixture gradually became thick with a yellow precipitate. After 24 h, the mixture was diluted with light petroleum (65 ml) and stirred for 10 min. The solid was collected by suction filtration and then washed successively with benzene–light petroleum (1 : 1, v/v) and light petroleum. The nitrone (**16**) was obtained as an amorphous yellow solid (98%, 3.28 g, 18.2 mmol). Recrystallization from hot ethanol afforded the analytically pure nitrone (**16**), m.p. 214—215 °C (lit.,[38] 217—218 °C); $\delta_H([^2H_6]$-DMSO) 3.95 (3 H, s, NMe), 7.52 (1 H, s, CH=N), and 8.32 (4 H, m, ArH); $\nu_{max.}(CHCl_3)$ 2 996w, 1 590m (C=N), 1 521m (NO of nitro), 1 419w, 1 367s (NO of nitro), 1 175s (NO of nitrone), 959m, 869s (CN of nitro), and 843m cm^{-1} (Found: C, 53.4; H, 4.4; N, 15.5. Calc. for $C_8H_8N_2O_3$: C, 53.3; H, 4.5; N, 15.6%). The physical and spectroscopic data of this compound were consistent with those reported in the literature.[32b,34,38]

N-(2-*Furylidene*)*methanamine* N-*Oxide* (**17**).[32a]—A mixture of 2-furaldehyde (38.4 mg, 0.40 mmol, 1.0 equiv.) and hydroxylamine (**2**) (76.7 mg, 0.40 mmol, 1.0 equiv.) in benzene (1.5 ml) was stirred at 50 °C for 18 h. The solution was cooled to room temperature and treated with trimethylsilyl trifluoromethanesulphonate (3.4 mg, 0.015 mmol, 0.04 equiv.). After 24 h the solvent was removed under reduced pressure and the residue

was placed under high vacuum. The resulting solid was recrystallized from CH_2Cl_2–light petroleum to give the pure nitrone (**17**) (98%, 48.3 mg, 0.39 mmol), m.p. 89.5—90 °C (lit.,[32a] 90 °C); $\delta_H(CDCl_3)$ 3.76 (3 H, s, NMe), 6.50 (1 H, br s, CH=N), and 7.29—7.75 (3 H, m, ArH); $\nu_{max.}(CHCl_3)$ 2 984m, 1 601m (C=N), 1 486s (C=C), 1 409s, 1 402s, 1 238m, 1 209m, 1 147s (NO), 1 017m, 965m, 950s, 891m, and 832m cm^{-1}. The physical data of this compound were consistent with those reported in the literature.[32a]

N-*Methyl*-N-(α-*trimethylsilyloxybenzyl*)-O-*trimethylsilylhydroxylamine* (**18**).—A mixture of benzaldehyde (46.3 mg, 0.436 mmol, 1.0 equiv.) and hydroxylamine (**2**) (169.6 mg, 0.89 mmol, 2.0 equiv) in benzene (1.8 ml) was stirred at 50 °C for 21 h. The solvent was removed by rotary evaporation and the residue was rapidly purified on silica gel (6 mm × 11 cm column, 20% Et_2O in pentane as eluant) to give the pure silylated hemiaminal (**18**) as a clear, colourless liquid (88%, 114.7 mg, 0.385 mmol); R_F 0.77 (20% EtOAc in hexanes when developed *immediately* after spotting); $\delta_H(CDCl_3)$ 0.18 (18 H, s, 2 × $OSiMe_3$), 2.28 (3 H, s, NMe), 5.56 (1 H, s, CH), and 7.27—7.59 (5 H, m, ArH); $\nu_{max.}$(neat) 3 082w (=CH), 3 058w (=CH), 3 027w (=CH), 2 949s, 2 891m, 1 490w (C=C), 1 457m (C=C), 1 247s (SiC), 1 195m, 1 172m, 1 090s (CO), 1 055s (OSi), 890s, 839s, 751m, 730m, and 698m (=CH) cm^{-1} (Found: M^+, 297.1583. Calc. for $C_{14}H_{27}NOSi_2$: *M*, 297.1580).

Reaction of the Hemiaminal (**18**) *with Reducing Agents followed by Hydrolysis.*—A reducing agent (see Table 3; 4.0 equiv.) was added to a 10 ml, pear-shaped flask containing a solution of hemiaminal (**18**) (0.100 g, 0.336 mmol, 1.0 equiv.) in a solvent (see Table 3, 2.0 ml) at 0 °C, and the mixture was stirred under nitrogen (see Table 3 for temperatures) for 24 h. The solution was cooled to 0 °C and neutralized with 10% aqueous sulphuric acid. The mixture was poured into ether (10 ml); the ether solution was washed successively with water and brine and then dried ($MgSO_4$). Filtration and removal of solvents afforded crude benzaldehyde. The yield of benzaldehyde was determined by g.c. analysis in comparison with an authentic sample of benzaldehyde: g.c. (injector temp. 260 °C; column temp. program; initial temp. 40 °C; duration 2 min; increment rate 10 °C/min; final temp. 245 °C, duration time 10 min), t_R 4.63 min.

Terephthaldehyde (**26**).*—Hydroxylamine (**2**) (133 mg, 0.694 mmol, 1.3 equiv.) was added to a 5 ml pear-shaped flask containing a solution of 4-cyanobenzaldehyde (**23**) (69.3 mg, 0.528 mmol, 1.0 equiv.) in dichloromethane (1.7 ml) and the mixture was refluxed under nitrogen for 24 h. The solution was cooled to room temperature, treated with DIBAL-H (1.5M in toluene; 0.427 ml, 0.641 mmol, 1.2 equiv.), and then refluxed for an additional 33 h. The orange-brown solution was cooled to 0 °C and acidified with 10% aqueous sulphuric acid. The mixture was stirred for 20 min and then poured into ether. The ether solution was washed successively with water and brine, dried ($MgSO_4$), filtered, and evaporated to afford a light yellow solid (62.5 mg), m.p. 111—112 °C. Recrystallization of this from dichloromethane–hexanes gave pure (**26**) as a white solid (83%, 58.7 mg, 0.438 mmol), m.p. 114.5—115.5 °C (lit.,* m.p. 115—116 °C); $\delta_H(CDCl_3)$ 8.03 (4 H, s, ArH) and 10.13 (2 H, s, 2 × CHO); $\nu_{max.}(CHCl_3)$ 2 995 (=CH) and 1 700 (C=O) cm^{-1}.

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* This compound is commercially available from the Aldrich Chemical Co.

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