Nitrogen inversion and N–O bond rotation processes in di- and tri-substituted hydroxylamines. A dynamic NMR study

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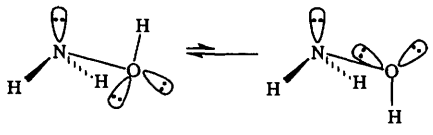
The barriers to inversion in several acyclic di- and tri-substituted hydroxylamines are determined by ^1H NMR band shape analysis. The barriers range from 49.1 to 66.8 kJ mol^{-1} and are discussed in terms of a conformational process which involves nitrogen inversion and rotation around the N–O bond. The *N*-benzyl group with an *ortho* hydroxy substituent increases the nitrogen inversion barrier by 10 kJ mol^{-1}, which indicates the requirement of breaking of the intramolecular hydrogen bond prior to inversion.

Hydroxylamines, owing to their unique conformational properties, have gained an important place in the field of conformation analysis.[1] Both theoretical calculations[2,3] and experimental discoveries[4,5] have surprised the chemists by the showing that the most stable conformation **1a**, in complete contrast to its organic counterparts (ethane, methanol, methylamine), has the lone pairs and bonds formally eclipsed and N–O bond rotation has to traverse a pathway leading to the less stable staggered conformation **1b**, with a very high barrier of *ca.* 50 kJ mol^{-1}(Scheme 1). The sp^3 hybridized nitrogen atom

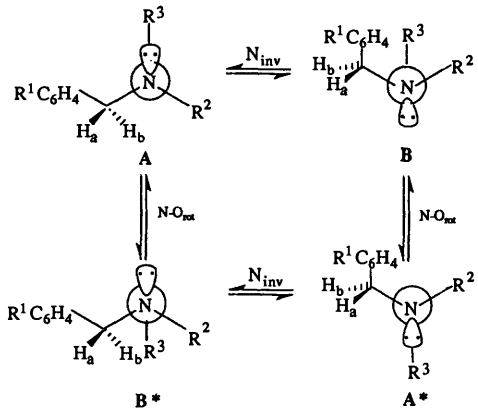


1a **1b**

Scheme 1 Stable conformers of hydroxylamine

in hydroxylamines with a pyramidal geometry is also capable of changing its conformation by inversion of its configuration *via* an sp^2 hybridized planar transition state. The s inductive effect of electronegative oxygen attached to nitrogen and p repulsive effect in the transition state, quite interestingly, raises the barrier to nitrogen inversion to a similar magnitude as in the rotational process.[6]

Inability of the chiral hydroxylamine derivative **2A** to sustain optical activity can be attributed to nitrogen inversion and N–O bond rotation[7,8] leading to the enantiomer **A*** (Scheme 2). The benzylic protons in **2** are diastereotopic in either structure but become nonequivalent when nitrogen inversion and/or bond rotation become slow on the NMR time scale.[1] Thus the NMR spectra of these compounds show temperature dependence and the methylene proton resonances at lower temperatures appear as AB quartets, which coalesce and becomes a singlet with the increase in the temperature. Whether bond rotation[9,10] or nitrogen inversion[11] or a complex composite of both is the rate determining step (in the total inversion pathway as shown in Scheme 2) still remains a matter of controversy and speculation.[12] Usually, polar solvents and steric crowding in the pyramidal ground state accelerate the nitrogen inversion process. The transition state, which has a higher dipole moment than the ground state, is stabilised by polar solvents thereby lowering the inversion barrier. On the other hand, steric crowding in the ground state raises the energy of the the ground state and hence lowers the barrier. The transition state has more space with extended CNC and ONC angles (120°) to make room for the bulky substituents.[11] However, steric deceleration and solvent independency would point



Scheme 2 Degenerate racemization of R^{1}C$_6$H$_4$N(OR^3)R^2 **2**

toward bond rotation as the rate-limiting process in the total inversion pathway.[12]

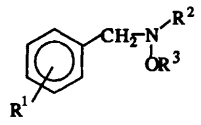
While hydrogen bonding solvents like methanol raise the nitrogen inversion barrier in trialkylamines[13–15] by 4–8 kJ mol^{-1} by stabilizing the staggered ground state conformers, protic solvents by contrast lower the barrier in acyclic dialkyl- and trialkyl-hydroxylamines[9,16,17] but increase the barrier in cyclic trialkylhydroxylamines[18] (in which the N–O bond is a part of the ring skeleton). In acyclic systems solvent interaction with lone pairs destabilizes the eclipsed ground state and hence lowers both the nitrogen inversion and bond rotation barriers. In cyclic systems, however, geometric constraints do not permit N–O bond rotation or lone pair eclipsing with bonds and the hydrogen bonding thus stabilizes the ground state. The site of hydrogen bonding (at N or O) may also vary from compound to compound and as such study of solvent effects does not really add much to the knowledge of distinguishing inversion from rotation process.[12]

In order to shed more light on the relative importance of the nitrogen inversion and N–O bond rotation, we prepared a series of acyclic hydroxylamines (Scheme 3) and herein we report a study of steric and intramolecular hydrogen-bonding effects on the barrier of nitrogen inversion and rotation processes by ^1H dynamic NMR spectroscopy.

Results and discussion

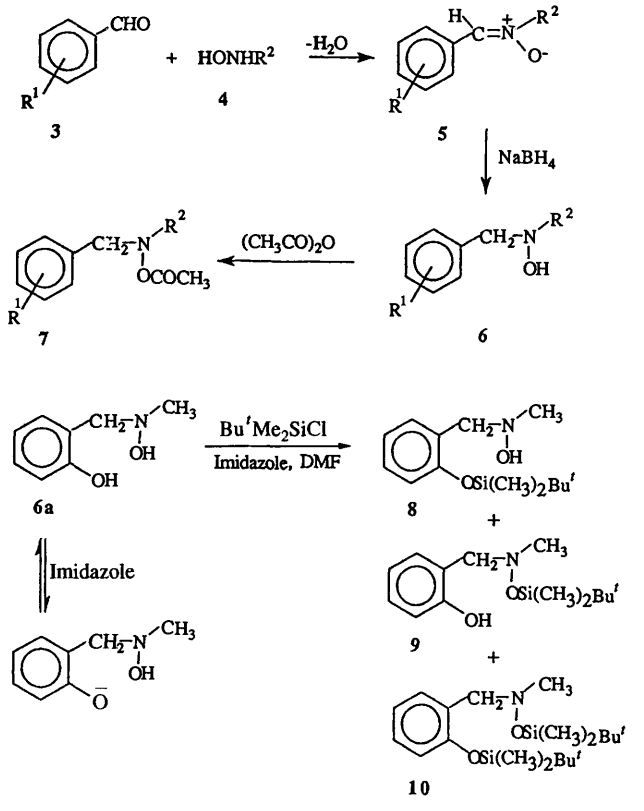
Condensation of aromatic aldehydes **3** with hydroxylamines **4** gave the nitrones **5** which on reduction with sodium borohydride afforded the hydroxylamines in good overall yield. The hydroxylamines, on treatment with 1.1 equiv. of acetic anhydride, led to the formation of monoacetyl derivatives **7**

Table 1 Compounds studied and their nitrogen inversion barriers in $CDCl_3$



Compound	R^1	R^2	R^3	$\Delta G^{\ddagger}$ (273 K)/ kJ mol^{-1}
6a	*o*-OH	CH_3	H	61.2
7a	*o*-OH	CH_3	Ac	57.8
6b	*o*-OH	Pr^i	H	59.8 (53.5[a])
7b	*o*-OH	Pr^i	Ac	60.6
6c	*o*-OH	Bu^t	H	58.8
7c	*o*-OH	Bu^t	Ac	59.2
6d	*p*-OH	Pr^i	H	52.2 (51.7[a])
7d	*p*-OH	Pr^i	Ac	51.9
6e	*o*-OMe	Pr^i	H	51.0
7e	*o*-OMe	Pr^i	Ac	49.2
6f	H	Pr^i	H	51.9
7f	H	Pr^i	Ac	49.1
8	*o*-$OSiMe_2Bu^t$	Me	H	54.9
9	*o*-OH	Me	$SiMe_2Bu^t$	66.8
10	*o*-$OSiMe_2Bu^t$	Me	$SiMe_2Bu^t$	62.8

[a] In CD_3OD.



Scheme 3

selectively (Scheme 3, Table 1). The phenolic hydroxy group was found to be unreactive towards acetic anhydride under the reaction conditions. Quite interestingly, this was found not to be the case in the reaction with 1.1 equiv. of *tert*-butyldimethylchlorosilane. Thus, the hydroxylamine **6a** afforded a mixture of mono-(**8**, **9**) and di-silylated (**10**) derivatives. The difference in the selectivity of the two hydroxy groups towards acetic anhydride and the silylating agent could be attributed to the differences in the nucleophilicity of the oxygens in phenolic OH and N–OH. While oxygen attached to the nitrogen is more nucleophilic due to the lone pair repulsion, the lone pair in the phenolic hydroxy group is appreciably delocalized. However, in the presence of imidazole, presumably, the conjugate base (obtained by abstraction of the more acidic phenolic proton) in equilibrium with the hydroxylamine **6a** can effectively compete with the N–OH to give a mixture of compounds (**8**–**10**).

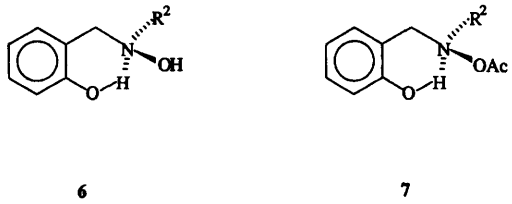
With a series of di- and tri-substituted hydroxylamines in hand we proceeded to study the inversion–rotation process by ^1H NMR spectroscopy. At ambient temperature benzylic protons in most of the compounds appeared as broad singlets, which on lowering the temperature became AB quartets. The complete band shape analysis yielded the rate constants and the free energy of activation ($\Delta G^{\ddagger}$) calculated using transition state theory [eqn. (1)]. The activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were

$$k = (k_B T/h) \exp(-\Delta G^{\ddagger}/RT) \qquad (1)$$

calculated from the plots of $\ln(k/T)$ *vs.* $1/T$. It is well known [19] that NMR bandshape fitting frequently gives mutually compensating systematic errors in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ (± 0.8 kJ mol^{-1} and ± 4 J mol^{-1} K^{-1}, respectively). However, the band shape fitting is viewed [19] as a method of getting rather accurate values (probably to within ± 0.5 kJ mol^{-1}) for $\Delta G^{\ddagger}$ in the vicinity of the coalescence temperature. The $\Delta G^{\ddagger}$ values calculated at 0 °C are reported in Table 1.

For the hydroxylamines **6d**–**f** and **7d**–**f** the barriers obtained fit best with nitrogen inversion as the rate determining step. The acetyl derivatives **7d**, **e** and **f** have lower barriers than their corresponding N–OH compounds **6d**, **e** and **f**. An acetyl ($CH_3C{=}O$) group with a strong conjugative interaction with the oxygen lone pair reduces the lone pair repulsion in the transition state for the inversion process, which thus results in the decrease in the barriers. Acetyl being bulkier than hydrogen also helps the inversion process. A dominant contribution from N–O bond rotation would have resulted in an increased barriers for the acetyl derivatives.

The compounds discussed so far have substantially lower barriers than the barriers observed for the rest of the hydroxylamines in Table 1. Sterically, the pair **6e**, **7e** is not much different from the pair **6b**, **7b**; however an increase of *ca.* 10 kJ mol^{-1} in the barrier is observed for the latter. This could be attributed to the presence of intramolecular hydrogen bonding as depicted in Scheme 4, which stabilizes the pyramidal



Scheme 4

ground state, and an additional amount of energy must be supplied to break the hydrogen bond in the inversion pathway. In the series **6a**, **6b** and **6c** changing the R^2 from methyl to isopropyl to *tert*-butyl group, a gradual decrease in the barrier reflects the dominance of inversion rather than N–O bond rotation. In the acetyl derivatives **7a**, **7b** and **7c** no clear trend is observed. Both isopropyl and *tert*-butyl derivatives **7b** and **7c** have higher barriers than their corresponding N–OH compounds **6b** and **6c** and the acetyl derivative **7a**. Repulsion between oxygen and nitrogen lone pairs in the transition state is reduced by electron withdrawing conjugating acyl substituent on the oxygen and as such this electronic effect should lower both nitrogen inversion and rotational barriers. However, steric effects raise the rotational barriers but lower the inversion barrier. In compounds **7b** and **7c** the dominant rotational contribution due to steric crowding of isopropyl/tertiary butyl and acetyl groups increases the overall barrier for the inversion pathway. The dominant rotational contribution should have

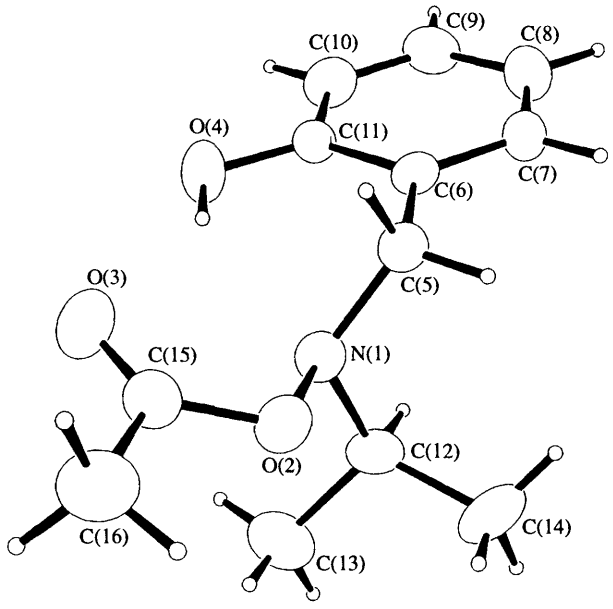


Fig. 1 X-Ray structure of **7b**

imparted greater destabilization of the transition state for the tertiary butyl derivative **6c** than for its isopropyl counterpart **6b**. However, this was found not to be the case. Steric and electronic effects give different contributions to the barriers to inversion and rotation. Comparing the energy barriers in compounds **6b**, **6e**, **6f**, **7b**, **7e** and **7f** it is evident that the breaking of the hydrogen bond contributes an additional 10 kJ mol^{-1} of energy to the barrier.

Among the compounds presented in Table 1 the monosilyl derivative **9** was found to have the highest barrier of 66.8 kJ mol^{-1}. Involvement of vacant d orbitals in silicon in bonding with the oxygen lone pair should decrease the barriers for both the inversion and rotational processes in so far as the destabilization of the transition state by lone pair repulsion is concerned. However steric encumbrance of the silyl group forces the rotational process to play a dominant role in the overall process. Among the compounds **6a**, **8-10**, the disilylated derivative **10** is the most crowded around the N–O bond, yet steric acceleration of the process is not observed. The compound **10** has an even higher barrier than that of **6a**, indicating that the additional difficulty in N–O bond rotation in the former is more significant than the difficulty in the nitrogen inversion due to hydrogen bonding in the latter. While the nitrogen inversion is the rate controlling step in the monosilyl compound **8**, the N–O bond rotation dictates the barrier in the mono- (**9**) and disilylated (**10**) derivative.

While in methanol the inversion barrier is decreased noticeably for the *ortho*-hydroxy compound **6b** by 6.3 kJ mol^{-1}, the barrier remained almost unchanged for the *para*-hydroxy derivative **6d**. This strongly suggests the involvement of intramolecular hydrogen bonding in **6b** in $CDCl_3$ but not in methanol which effectively competes with the *ortho*-hydroxy substituent for hydrogen bonding with the nitrogen lone pair.

Intramolecular hydrogen bonding can be confirmed somewhat from the crystal structure of the compound **7b**. As is evident from the ORTEP diagram (Fig. 1) the N(1)–O(4)-distance of 2.748 Å indicates the presence of intramolecular hydrogen bonding. The dihedral angles of C(5)–N(1)–O(2)–C(15) and C(12)–N(1)–O(2)–C(15) were found to be 105.97 and 129.46°, respectively. Assuming the nitrogen lone pair is symmetrically located with respect to the dialkyl substituents on nitrogen, the oxygen substituent is thus found to be within 12° of eclipsing the nitrogen lone pair. The ORTEP diagram also demonstrates the expected *cis* planar arrangement of the O–N and C=O bonds[20] [the N(1)–O(2)–C(15)–O(3) dihedral angle was found to be 4.21°].

To the best of our knowledge, this study demonstrates for the first time the effect of intramolecular hydrogen bonding (involving a phenolic hydroxy group) on the nitrogen inversion barrier in acyclic hydroxylamines. By increasing the bulk around the N–O bond, the rate controlling step of the overall inversion pathway switches from nitrogen inversion to N–O bond rotation. The X-ray structure substantiates the finding that the more stable form has the eclipsed conformation.

Experimental

Variable temperature proton NMR spectra were recorded on a Varian XL 200 NMR spectrometer operating at 200.05 MHz in the Fourier transform mode; *J* values are given in Hz. Compounds were examined in $CDCl_3$ solutions at 0.15 mol dm^{-3} concentrations. Temperature control was achieved using the XL-200 temperature controller and calibrated using standard chemical shifts of methanol for low temperatures. The temperatures are accurate to ± 1.0 °C.

Simulations of exchange affected NMR spectra were carried out using the library program ABSHAPE[21] which calculates the band shapes for the mutually exchanging spin system of AB going to BA. The matching of simulated and experimental spectra were carried out by superposition of calculated and experimental spectra by eye.

All melting points are uncorrected. Elemental analyses were performed on a Fisons Instruments Elemental Analyser 1108. IR spectra were recorded on a Nicolet 5 DXB FTIR and are reported in wave numbers (cm^{-1}). Silica gel chromatographic separations were performed with flash silica gel (Baker Chemicals Co). 'Ether' refers to diethyl ether.

General procedure for the preparation of the hydroxylamines

To a solution of the hydroxylamine (5.0 mmol) in ethanol (10 cm^3) was added the aldehyde (5.5 mmol). The reaction mixture was stirred at 50–60 °C for 5 h and TLC experiment (silica, ether) revealed the complete formation of the nitrone. To this solution was added $NaBH_4$ (10 mmol) and the mixture was then stirred at 50 °C for 5 h. Again another 10 mmol of $NaBH_4$ was added and the reaction mixture was stirred at 20 °C for 24 h to ensure complete reduction of the nitrone (checked by TLC). After removal of the ethanol by a gentle stream of N_2 the reaction mixture was taken up in H_2O (15 cm^3) and extracted with $CHCl_3$ (3 × 25 cm^3). Removal of the solvent followed by passing through a silica column using hexane–ether (3:1) as eluent afforded the hydroxylamines in 70–85% yield. While the hydroxylamines were used as their free bases, *N*-methylhydroxylamine was introduced as its hydrochloride and the base was liberated from its salt by adding 1.1 equiv. of sodium acetate to the reaction mixture. After removal of the solvent by a gentle stream of N_2 the residual mixture was taken up in H_2O (15 cm^3) and extracted with $CHCl_3$ (3 × 25 cm^3). The organic layer was dried (Na_2SO_4), concentrated, and reduced with $NaBH_4$ in ethanol as described above. Sodium borohydride reduction of the nitrone derived from *p*-hydroxybenzaldehyde and *N*-isopropylhydroxylamine was unsuccessful. The nitrone remained unreacted and only minor amounts of the product hydroxylamine was obtained. However, catalytic hydrogenation (1 atm, PtO_2, ethanol, 3 h, 20 °C) afforded the hydroxylamine after silica gel chromatography in 65% yield.

***N*-*o*-Hydroxybenzyl-*N*-methylhydroxylamine 6a.** Colourless crystals, mp 108–109 °C (CH_2Cl_2–hexane) (Found: C, 62.74; H, 7.29; N, 9.09. $C_8H_{11}NO_2$ requires C, 62.72; H, 7.24; N, 9.15%); ν_{max}(KBr)/cm^{-1} 3256, 3060, 2995, 2873, 1598, 1465, 1378, 1357, 1273, 1248, 1109, 959, 812, 758 and 730; δ_H($CDCl_3$, 25.0 °C) 2.72 (3 H, s), 4.01 (2 H, s), 6.84–7.32 (4 H, m and 2 H, hydroxy underneath); (−50.0 °C) 2.72 (3 H, s), 3.94 (1 H, d, *J* 14.0), 4.06 (1 H, d, *J* 14.0), 6.88–7.37 (4 H, m), 8.87 (2 H, br s).

***N*-*o*-Hydroxybenzyl-*N*-isopropylhydroxylamine 6b.** Colourless crystals, mp 140–142 °C (CH_2Cl_2–ether) (Found: C, 66.48;

H, 8.41; N, 7.51. $C_{10}H_{15}NO_2$ requires C, 66.27; H, 8.34; N, 7.73%); ν_{max}(KBr)/cm^{-1} 3238, 2957, 2864, 1598, 1462, 1374, 1277, 1174, 1106, 987, 859, 752 and 726; δ_H($CDCl_3$, 25.0 °C) 1.2 (6 H, d, *J* 12.0), 1.95 (1 H, s), 3.15 (1 H, m), 4.05 (2 H, s), 6.70–7.35 (4 H, m), hydroxy protons signal not observed; (−40.0 °C) 1.24 (6 H, q, *J* 8.0), 2.12 (1 H, s), 3.17 (1 H, m), 4.02 (1 H, d, *J* 14.0), 4.23 (1 H, d, *J* 14.0), 6.82–7.38 (4 H, m), 7.48 (1 H, s).

***N*-*o*-Hydroxybenzyl-*N*-*tert*-butylhydroxylamine 6c.** Colourless crystals, mp 101–103 °C (ether) (Found: C, 68.84; H, 8.88; N, 7.35. $C_{11}H_{17}NO_2$ requires C, 67.66; H, 8.78; N, 7.18%); ν_{max}(KBr)/cm^{-1} 3349, 2985, 2967, 1592, 1494, 1481, 1403, 1387, 1361, 1252, 1211, 918, 761 and 750; δ_H($CDCl_3$, 24.2 °C) 1.26 (9 H, s), 2.54 (1 H, s), 4.1 (2 H, br s), 6.72–7.32 (4 H, m), hydroxy proton signal not observed; (−39.0 °C) 1.3 (9 H, s), 2.63 (1 H, s), 3.85 (1 H, d *J* 15), 4.42 (1 H, d, *J* 15), 6.5–7.36 (4 H, m), 10.5 (1 H, br s).

***N*-*p*-Hydroxybenzyl-*N*-isopropylhydroxylamine 6d.** Colourless crystals, mp 147–148.5 °C (ether) (Found: C, 66.42; H, 8.33; N, 7.73. $C_{10}H_{15}NO_2$ requires C, 66.27; H, 8.34; N, 7.73%); ν_{max}(KBr)/cm^{-1} 3305, 2969, 1615, 1519, 1270, 1226, 1169 and 791; δ_H($CDCl_3$, 23.2 °C) 1.17 (6 H, d, *J* 14), 3.0 (1 H, m), 3.75 (2 H, s), 6.84 (2 H, d, *J* 8), 7.29 (2 H, d, *J* 8), hydroxy proton signal not observed; (−29.7 °C) 1.15 (6 H, br s), 3.0 (1 H, m), 3.54 (1 H, d, *J* 11.5), 3.86 (1 H, d, *J* 11.5), 6.0 (2 H, br s), 6.94 (2 H, d, *J* 8), 7.15 (2 H, d, *J* 8).

***N*-*o*-Methoxybenzyl-*N*-isopropylhydroxylamine 6e.** Colourless crystals, mp 79–81 °C (ether–hexane) (Found: C, 68.84; H, 8.92; N, 7.29. $C_{11}H_{17}NO_2$ requires C, 67.66; H, 8.78; N, 7.18%); ν_{max}(KBr)/cm^{-1} 3219, 2967, 2892, 2827, 1604, 1497, 1464, 1438, 1428, 1363, 1249, 1118, 1033, 751 and 724; δ_H($CDCl_3$, 17.6 °C) 1.13 (6 H, d, *J* 6), 2.88 (1 H, m), 3.84 (2 H, s), 3.87 (3 H, s), 6.02 (1 H, s), 6.9–7.48 (4 H, m); (−49.2 °C) 0.97 (6 H, t *J* 6), 2.48 (1 H, m), 3.37 (1 H, d, *J* 14), 3.86 (3 H, s), 4.01 (1 H, d, *J* 14), 6.9–7.44 (4 H, m), 8.45 (1 H, s).

General procedure for the preparation of acetyl derivatives

Acetic anhydride (2.4 mmol) was added to a solution of the *N*-hydroxylamine (2.0 mmol) in CH_2Cl_2 (3 cm^3) at 0 °C and the mixture stirred at 0 °C for 1 h. TLC (ether–hexane) was used to ensure the completion of the reaction. The reaction mixture was taken up in 5% aq. $NaHCO_3$ (10 cm^3) and extracted with CH_2Cl_2 (3 × 20 cm^3). The organic layer was dried (Na_2SO_4), filtered and the solvent was removed by a gentle stream of N_2 at 10 °C to give the acetate which was purified either by crystallization or by passing through a short column of silica using ether–hexane as the eluant to give the acetate as colourless liquid.

The acetate solution should not be warmed since heating leads to decomposition. Samples were kept in the freezer to avoid decomposition.

***O*-Acetyl-*N*-*o*-hydroxybenzyl-*N*-methylhydroxylamine 7a.** Colourless plates, mp 73–74 °C (ether–hexane) (Found: C, 62.62; H, 6.80; N, 7.19. $C_{10}H_{13}NO_3$ requires C, 61.52; H, 6.71; N, 7.18%); ν_{max}(KBr)/cm^{-1} 3302, 3060, 2883, 1742, 1585, 1491, 1371, 1243, 1197, 1081, 903 and 758; δ_H($CDCl_3$, 23.0 °C) 2.1 (3 H, s), 2.74 (3 H, s), 4.08 (2 H, br s), 6.80–7.38 (4 H, m), 9.01 (1 H, s); (−29.0 °C) 2.14 (3 H, s), 2.74 (3 H, s), 3.76 (1 H, d, *J* 12.0), 4.42 (1 H, d, *J* 12.0), 6.82–7.4 (4 H, m), 9.2 (1 H, s).

***O*-Acetyl-*N*-*o*-hydroxybenzyl-*N*-isopropylhydroxylamine 7b.** Colourless plates, mp 53.0–54.0 °C (ether–hexane) (Found: C, 65.63; H, 7.79; N, 6.20. $C_{12}H_{17}NO_3$ requires C, 64.55; H, 7.67; N, 6.28%); ν_{max}(KBr)/cm^{-1} 3275, 3069, 2976, 2939, 2883, 1749, 1487, 1370, 1247, 1207, 999 and 763; δ_H($CDCl_3$, 26.8 °C) 1.12 (6 H, d, *J* 8.0), 2.07 (3 H, s), 3.13 (1 H, m), 4.16 (2 H, s), 6.79–7.33 (4 H, m), 9.33 (1 H, s); (−20.0 °C) 1.11 (6 H, q, *J* 8.0), 2.12 (3 H, s), 3.12 (1 H, m), 4.12 (1 H, d, *J* 14.0), 4.2 (1 H, d, *J* 14.0), 6.82–7.35 (4 H, m), 9.54 (1 H, s).

***O*-Acetyl-*N*-*o*-hydroxybenzyl-*N*-*tert*-butylhydroxylamine 7c.** Colourless crystals, mp 87.5–89.5 °C (decomp) (Found: C, 66.84; H, 8.23; N, 5.80. $C_{13}H_{19}NO_3$ requires C, 65.80; H, 8.07; N, 5.90%); ν_{max}(KBr)/cm^{-1} 3342, 2974, 2930, 1737, 1604, 1505, 1456, 1370, 1327, 1264, 1249, 1225, 1207, 1179, 1105, 756 and 732; δ_H($CDCl_3$, 24.0 °C) 1.25 (9 H, s), 1.92 (3 H, s), 4.17 (2 H, br s), 6.75–7.41 (4 H, m), 9.24 (1 H, s).

***O*-Acetyl-*N*-*p*-hydroxybenzyl-*N*-isopropylhydroxylamine 7d.** Colourless crystals, mp 92–93 °C (ether–hexane) (Found: C, 65.47; H, 7.76; N, 6.28. $C_{12}H_{17}NO_3$ requires C, 64.55; H, 7.68; N, 6.27%); ν_{max}(KBr)/cm^{-1} 3346, 2956, 2942, 2895, 1752, 1614, 1519, 1366, 1248, 1232, 1177 and 811; δ_H($CDCl_3$, 22.0 °C) 1.21 (6 H, d, *J* 8.0), 1.87 (3 H, s), 3.22 (1 H, m), 3.96 (2 H, s), 6.79 (2 H, d, *J* 8), 7.28 (2 H, d, *J* 8), hydroxy proton signal not observed; (−39.1 °C) 1.24 (6 H, t, *J* 4), 1.94 (3 H, s), 3.29 (1 H, m), 3.84 (1 H, d, *J* 12), 4.11 (1 H, d, *J* 12), 6.77 (2 H, d, *J* 8), 7.27 (2 H, d, *J* 8), hydroxy proton signal not observed.

***O*-Acetyl-*N*-*o*-methoxybenzyl-*N*-isopropylhydroxylamine 7e.** Colourless liquid (Found: C, 65.65; H, 7.90; N, 6.03. $C_{13}H_{19}NO_3$ requires C, 65.80; H, 8.07; N, 5.90%); ν_{max}(neat)/cm^{-1} 2976, 2939, 1760, 1495, 1465, 1365, 1248, 1211 and 756; δ_H($CDCl_3$, 18.0 °C) 1.22 (6 H, d, *J* 6), 1.86 (3 H, s), 3.26 (1 H, m), 3.84 (3 H, s), 4.1 (2 H, s), 6.96–7.50 (4 H, m); (−49.0 °C) 1.28 (6 H, t, *J* 8), 1.98 (3 H, s), 3.30 (1 H, m), 3.90 (3 H, s), 3.98 (1 H, d, *J* 13.0), 4.34 (1 H, d, *J* 13.0), 6.94–7.48 (4 H, m).

General procedure for the preparation of *tert*-butyldimethylsilyl derivatives

To a solution of imidazole (408 mg, 6.0 mmol) in dry DMF (2.0 cm^3) was added *tert*-butyldimethylchlorosilane (332 mg, 2.2 mmol) at 0 °C. To this mixture was added the hydroxylamine **6a** (300 mg, 2.0 mmol) and then it was stirred at 50 °C for 2 h. The resulting reaction mixture was taken up in ether (30 cm^3) and washed with H_2O (5 × 25 cm^3). The organic layer was dried (Na_2SO_4) evaporated and the residual liquid was chromatographed using hexane–ether (95:5) as the eluent. The first compound isolated was compound **10** as a colourless liquid. Continued elution afforded a mixture of compound **9** and **10** and then the pure compound **9** as a colourless liquid. Further elution with hexane–ether (4:1) gave the compound **8** as colourless prisms.

***N*-*o*-*tert*-Butyldimethylsiloxybenzyl-*N*-methylhydroxylamine 8.** Colourless plates, mp 78–79.5 °C (Found: C, 64.00; H, 9.56; N, 5.38. $C_{14}H_{25}NO_2Si$ requires C, 62.87; H, 9.42; N, 5.24%); ν_{max}(KBr)/cm^{-1} 3219, 2957, 2855, 1802, 1493, 1280, 1266, 1115, 957, 933, 925, 837, 781 and 753; δ_H($CDCl_3$, 24.4 °C) 0.25 (6 H, s), 1.03 (9 H, s), 2.63 (3 H, s), 3.83 (2 H, s), 6.19 (1 H, br s), 6.82–7.50 (4 H, m).

***O*-*tert*-Butyldimethylsilyl-*N*-*o*-hydroxybenzyl-*N*-methylhydroxylamine 9.** Colourless liquid (Found: C, 63.14; H, 9.46; N, 5.35. $C_{14}H_{25}NO_2Si$ requires C, 62.87; H, 9.42; N, 5.24%); ν_{max}(neat)/cm^{-1} 2957, 2929, 2855, 1489, 1249, 883, 838, 782 and 754; δ_H($CDCl_3$, 24.1 °C) 0.17 (3 H, s), 0.25 (3 H, s), 0.93 (9 H, s), 2.58 (3 H, s), 3.90 (1 H, d, *J* 13), 4.29 (1 H, d *J* 13), 6.80–7.52 (4 H, m), 9.10 (1 H, s); (60.1 °C) 0.14 (6 H, s), 0.92 (9 H, s), 2.56 (3 H, s), 4.04 (2 H, s), 6.87–7.46 (4 H, m), 8.86 (1 H, s).

***O*-*tert*-Butyldimethylsilyl-*N*-*tert*-butyldimethylsiloxybenzyl-*N*-methylhydroxylamine 10.** Colourless liquid (Found: C, 64.20; H, 10.79; N, 3.78. $C_{20}H_{39}NO_2Si_2$ requires C, 62.93; H, 10.30; N, 3.67%); ν_{max}(neat)/cm^{-1} 2957, 2929, 2864, 1493, 1267, 1255, 923, 886, 837 and 780; δ_H($CDCl_3$, 45.1 °C) 0.08 (6 H, s), 0.31 (6 H, s), 0.93 (9 H, s), 1.53 (9 H, s), 2.61 (3 H, s), 3.92 (2 H, br s), 6.83–7.57 (4 H, m).

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