# The Rotation-dominated Ring Inversion/Nitrogen Inversion/Rotation Process in *N*-Acyloxy-2,2,6,6-tetramethylpiperidines. A Dynamic NMR Study

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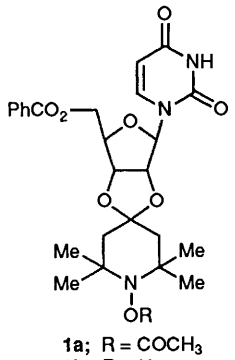
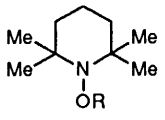
The temperature dependence of the NMR spectra of a series of *N*-acyloxy-2,2,6,6-tetramethylpiperidines is reported and discussed in terms of a conformational process which involves ring inversion, nitrogen inversion and rotation about the nitrogen–oxygen bond. Nitrogen inversion contributes *ca.* 11 kcal mol$^{-1}$ to the observed barriers, so in the compounds with higher barriers, steric interaction of the acyl and methyl groups during rotation determines the barrier height.

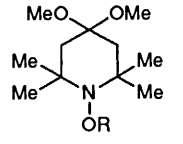
In a recent paper [1] on the synthesis and properties of spiroketals of the type **1** one of us briefly called attention to the contrasting conformational dynamics of the compounds **1a** and **1b**. In the proton and carbon-13 NMR spectra, there is a doubling of signals of groups in the substituted piperidine ring of **1a** at room temperature whereas for **1b** such a doubling only appears at temperatures below *ca.* −40 °C. While it was then noted that ring inversion of the piperidine ring is unlikely to be the source of these spectral features, the relative importance of nitrogen



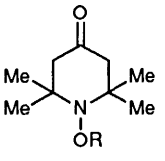
**1a**; R = $COCH_3$
**1b**; R = H



**2** R = H
**3** R = CHO
**4** R = $COCH_3$
**5** R = $COBu^t$
**6** R = $COCF_3$



**7** R = H
**8** R = $COCF_3$

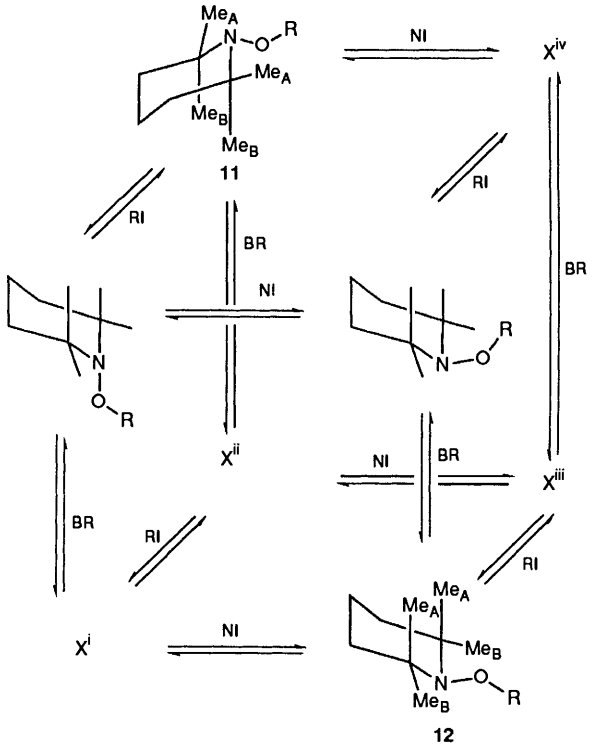


**9** R = $COCF_3$
**10** R = $COBu^t$

inversion and hindred N–O bond rotation could be settled only by more detailed investigations. The present paper reports and discusses studies of the compounds **2**–**10**.

The preferred conformation of trialkylhydroxylamines has each lone pair eclipsing an alkyl group,[2,3] a tendency which is known [4] to be reinforced by repulsion from the geminal methyl groups such as in **2**–**10**. Whether N–O bond rotation or nitrogen inversion has the higher barrier has been much discussed.[2,5–9] Rotational barriers have been calculated [10–12] to be *ca.* 11–12 kcal mol$^{-1}$ but barriers determined from dynamic NMR experiments, while not much higher, have been concluded to represent nitrogen inversion as the high energy point.[2] Since the barrier becomes smaller when an *N*,*N*-dialkylhydroxylamine is acylated on the oxygen,[6,13] nitrogen inversion is once again taken to be the high point in the interconversion potential energy diagram.

In each of the compounds **2**–**10**, the process being studied is thus the interconversion of structures **11** and **12** (see Scheme 1) which is slow on the NMR timescale at the low end of the temperature range studied and fast at the high end of the range. Except that geminal groups have exchanged axial and equatorial positions, the two structures are identical and are presumed to be more stable than the intermediate structures of Scheme 1, both those drawn and those indicated by X.




**Scheme 1** Conformational diagram showing the possible stepwise interconversion pathways between stable conformations of compounds **2**–**10**. NI = nitrogen inversion, RI = ring inversion, and BR = nitrogen–oxygen bond rotation.

The interconversion is achieved by three processes, of ring inversion, nitrogen inversion and rotation about the exocyclic bond, not necessarily in that order, or by some complex composites of these individual processes. If there are three successive steps, then any one may be rate determining in a given molecule, while a substitutent, without making other processes easier may nonetheless move the crux of the interconversion to one of the other steps by making it more difficult. If complex composites of these processes obtain, then undoubtedly substituent effects will themselves be complex.

**Table 1** Barriers $\Delta G^*$ (kcal mol$^{-1}$) to the interconversion **11** to **12** for the compounds **2–10**

| Compound | Barrier | | Barrier[a] | |
|---|---|---|---|---|
| | $CDCl_3$ soln[b] | Coalescence temperature/°C | $CD_3OD$ soln | Coalescence temperature/°C |
| **2**[b] | 11.5 (11.8) | −42 | | |
| **3** | 15.6 (16.0) | 49 | 15.3 (15.8) | 47 |
| **4** | 16.0 (16.5) | 56 | 16.2 (16.6) | 67 |
| **5** | 16.2 (16.7) | 64 | | |
| **6** | 14.7 (15.1) | 32 | 14.4 (14.9) | 31 |
| **7**[b] | 11.3 (11.6) | −39 | | |
| **8** | 16.4 (16.8) | 42 | | |
| **9** | 16.3 (16.7) | 38 | | |
| **10** | 16.8 (17.3) | 45 | | |

[a] The value in parentheses assumes a transmission coefficient of 1, otherwise the coefficient is $\frac{1}{2}$. [b] For **2** and **7** the solvent was perdeuteriotetrahydrofuran.

Varying substituents may allow a better definition of the relative importance of the processes.

Jenkins and his co-workers [14] have found substantial barriers to conformational exchange in compounds **13a** somewhat similar to the present set, but with alkyl substituents on the oxygen. Ring inversion of the nearly flat five-membered ring can be excluded and they suggested that a barrier increasing with the steric size of group R indicates the importance of a rotational contribution to the barrier, while a solvent-dependent barrier can be taken to indicate the importance of nitrogen inversion.[3]

Solvent effects (usually comparing methanol and chloroform solutions) in the NMR investigations of such compounds deserve comment. There are several examples of trialkylamines where a hydroxylic solvent like methanol produces a 1–2 kcal mol$^{-1}$ increase in the barrier to a process which is convincingly said to be nitrogen inversion.[15–17] It has been argued that hydrogen bonding with methanol should stabilise the ground state and thus raise the nitrogen inversion barrier in amines.

By contrast, in both *N,N*-dialkyl- and *N,N,O*-trialkylhydroxylamines, methanol as solvent lowers the barrier to the observed process,[13,14] and this may reflect a combination of effects. In hydroxylamines, the preferred N–O bond conformation has all lone pairs eclipsed by alkyl groups, so methanol by interacting with lone pairs destabilises that eclipsed ground state and should produce a steric lowering of the barrier to all processes. On the other hand, hydrogen bonding by methanol, most likely at the oxygen of hydroxylamine, undoubtedly affects bond polarisation but how this electronic effect changes barriers to nitrogen inversion and bond rotation is not clear. Both solvent enhancement and reduction of barriers can be given some sort of rationalisation so such effects for hydroxylamines do not offer a clear indication of the process involved.

A better distinction between inversion and rotation may well come from the effect of sterically large substituents which should lower nitrogen inversion barriers while raising rotational barriers. An electron-withdrawing substituent such as an acyl group on the oxygen should lower both rotational barriers and nitrogen inversion barriers in so far as these arise from repulsion of oxygen and nitrogen lone pairs in the transition state, but may raise the rotation barrier in so far as the substituent has a steric effect. On these bases Fletcher and Sutherland [13] interpreted the lower barriers in *O*-acetyl-*N,N*-dialkylhydroxylamines as indications of a nitrogen inversion process.

## Results

The series of compounds **2–10** was synthesised and NMR spectra were determined at a range of temperatures for each compound. At *ca.* −50 °C in the proton NMR spectrum, geminal groups (methyl, methoxy and methylene hydrogens) on the piperidine ring give rise to two equal signals. The carbon-13 NMR signals of the methyls are likewise doublets, since at that temperature axial and equatorial groups at each position are discrete on the NMR timescale, while carbons 2 and 6 and carbons 3 and 5 remain equivalent as the oxygen substituent on the average is symmetrical about the N(1)···C(4) axis of the ring.

On raising the temperature these doubled signals broaden and coalesce to give a single set of signals and in agreement with our earlier results [1] this happens at a much lower temperature for the *N*-hydroxy compounds than for the *N*-acyloxy compounds. From the changes in the spectrum and the coalescence temperature of signals, barriers to the conformational process in each molecule were determined as shown in Table 1. The two values given for each compound are explained in the following section. Full NMR details are indicated in Table 2. For three compounds, barriers were also measured in perdeuteriated methanol as solvent, and results are included in Table 1.

The NMR spectrum of the compound **5** was further examined at several temperatures down to −156 °C but no changes which could be attributed to a second conformational type or to a second process becoming slow on the NMR timescale were observed.

## Discussion

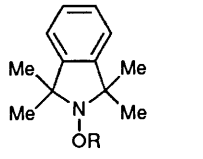
There has been much awareness over recent years [18–21] of the unusual conformational properties of *N*-substituted-2,2,6,6-tetramethylpiperidines such as **14** where the X--Y link may be a single or double bond. These properties are the result of the steric congestion due to the two tertiary alkyl substituents on the nitrogen atom, and the three bonds to nitrogen which are shorter than would be found in the equivalent cyclohexyl compound.

The steric congestion should reinforce the preference [2,3] of the alkyl groups in simple trialkylhydroxylamines to eclipse lone pairs along the N–O bond. This can be confirmed somewhat from the crystal structure [4] of the compound **13b** in which the substituent on the oxygen is within 13° of eclipsing the nitrogen lone pair, which is assumed to be located symmetrically with respect to the ring. In the present work a near to eclipsing conformation is indicated for all compounds studied by the equivalence of the 2- and 6-positions in the piperidine ring in all spectra. Exceptions with the substituent on the nitrogen atom transverse to the lone pair are found only occasionally [19d–g] when the X–Y link in **14** is a double bond with a strong conjugative interaction with the ring nitrogen.

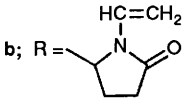
**Table 2** Proton and (carbon-13) NMR spectra of compounds **2**–**10** at slow exchange

| Compound | *gem*-$Me_2$ | Ring 2/6 | Ring 3/5 | Ring 4 | Substituent carbonyl | Other |
|---|---|---|---|---|---|---|
| **2** | 1.04, 1.08 | — | 1.29–1.60 | | — | 1.73 (OH) |
| **3** | 1.10, 1.18 | — | 1.37–1.68 | | — | 8.34 (*C*HO) |
| | (20.51, 31.81) | (60.06) | (39.44) | (16.78) | (168.51) | |
| **4** | 1.06, 1.15 | — | 1.39–1.70 | | — | 2.08 ($COCH_3$) |
| | (20.41, 31.91) | (59.89) | (38.88) | (16.91) | (177.88) | (19.08) ($COCH_3$) |
| **5** | 1.04, 1.17 | — | 1.52, 1.69 | 1.41, 1.62 | — | 1.28 [$C(CH_3)_3$] |
| | (20.85, 31.90) | (60.20) | (39.05) | (17.10) | (177.06) | (27.65) [$C(CH_3)_3$] |
| | | | | | | (38.96) [$C(CH_3)_3$] |
| **6** | 1.10, 1.22 | — | 1.55–1.75 | 1.37–1.48 | — | — |
| | (20.33, 31.49) | (61.24) | (38.90) | (16.61) | (158.50)[a] | (115.10)[b] ($COCF_3$) |
| **7** | 1.09, 1.17 | — | 1.43, 1.98[c] | — | — | 1.73 (OH) |
| | | | | | | 3.06, 3.10 (2 × $OCH_3$) |
| | (19.30, 33.90) | (58.20) | (44.10) | (98.90) | (—) | (47.00, 47.70) (2 × $OCH_3$) |
| **8** | 1.08, 1.29 | — | 1.81, 2.00[d] | — | — | 2.10 ($COCH_3$) |
| | | | | | | 3.16, 3.18 (2 × $OCH_3$) |
| | (20.80, 32.60) | (59.50) | (43.40) | (98.10) | (170.62) | (19.11) ($COCH_3$) |
| | | | | | | (47.32, 47.61) (2 × $OCH_3$) |
| **9** | 1.14, 1.15 | — | 2.21, 2.85[e] | — | — | 2.17 ($COCH_3$) |
| | (22.30, 31.40) | (63.20) | (53.30) | (206.76) | (170.56) | (18.85) ($COCH_3$) |
| **10** | 1.21, 1.30 | — | 2.25, 2.84[f] | — | — | |
| | (22.43, 31.40) | (63.06) | (53.19) | (206.93) | (176.94) | (27.55) [$C(CH_3)_3$] |
| | | | | | | (39.01) [$C(CH_3)_3$] |

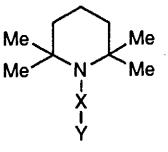
[a] $J_{CCF}$ 45 Hz. [b] $J_{CF}$ 287 Hz. [c] $J_{AB}$ 13.4 Hz. [d] $J_{AB}$ 13.4 Hz. [e] $J_{AB}$ 12.7 Hz. [f] $J_{AB}$ 13.2 Hz.



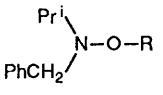

**13a**; R = alkyl




**b**; R =




**14**




**15** R = H
**16** R = $COCH_3$

The barrier to ring inversion of tetramethylpiperidine[19f] is 8.0 kcal $mol^{-1}$ and should be lower if the 4-position is disubstituted as in **7** and **8** to give a hexasubstituted six-membered ring.[22] The barrier to ring inversion of the 4-keto derivative, while unknown, is expected to be even smaller, just as the cyclohexanone and cyclohexane ring inversion barriers are 4.0 and 10.3 kcal $mol^{-1}$, respectively.[23,24] Ring inversion cannot be the important process in any of the present cases with barriers of 11–17 kcal $mol^{-1}$.

The barrier to nitrogen inversion in a dialkylhydroxylamine is illustrated[13] by the 12.8 kcal $mol^{-1}$ value for **15**. In compound **2** a somewhat lower barrier might be expected since flattening of the nitrogen to relieve the cross ring interactions of axial methyl groups in the ground state has already started the molecule along the nitrogen inversion pathway. The barrier of 11.8 kcal $mol^{-1}$ that we find for **2** fits best with nitrogen inversion as the high energy point in the **11** to **12** interconversion in that molecule. The report[6] of an exceptionally low barrier putatively much less than that found for **2** in the five-membered ring analogue *N*-hydroxy-2,2,5,5-tetramethylpyrrolidine probably reflects accidental coincidence of chemical shifts.

Strikingly, while the nitrogen inversion barrier[13] for the *O*-acetyl derivative **16** is 12.1 kcal $mol^{-1}$, 0.7 kcal $mol^{-1}$ lower than for the parent hydroxylamine **15**, we find here that the acetyl derivatives **4** and **8** have barriers more than 4 kcal $mol^{-1}$ higher than those of the N–OH compounds **2** and **7**. The comparison of an *O*-pivaloyl group and an *O*-acetyl group *i.e.* comparing **5** and **10** with **4** and **9**, respectively, shows only a 0.5 kcal $mol^{-1}$ increase in the barrier.

For the present set of acyl compounds, any reduction in barrier compared to the parent as found for **16** *cf.* **15** (the electronic effect on nitrogen inversion outlined in the introduction), is masked in the substantially higher observed barriers which are due to a steric effect on the overall process **11**–**12** at the stage of rotation about the N–O bond. The acyl group in a near to eclipsing ground state is quite distant from the *gem*-dimethyl groups, but rotation moves them closer. No rotation about the *O*-acyl bond can remove the consequent steric interactions and a higher overall barrier is found. A rotational contribution is thus added to what is mainly a nitrogen inversion barrier. Changing the O-substituent from formyl to acetyl to pivaloyl (**3** to **4** to **5**) produces a relatively small increase in the barrier suggesting that it is the carbonyl group which undergoes the steric interaction during rotation and this fits well with the expected *cis* planar arrangement of the O–N and C=O bonds.[25]

A clear indication that the electronic effect is nonetheless present is provided by the trifluoroacetyl derivative **6** which also has an enhanced barrier but at 14.7 kcal $mol^{-1}$ it is smaller even than the acetyl derivative. The steric effect of the trifluoroacetyl group should raise the barrier at least as much as that of the acetyl group, so the lower measured barrier for **6** *cf.* **4** and (other acyl compounds) shows an electronic effect due to the electron-withdrawing propensity of the trifluoromethyl group operating on the nitrogen inversion part of the barrier and underlying the more marked steric effect.

We shall report elsewhere[26] results for the alkoxypiperidine analogues of these acyloxypiperidines which show that the rotational part of the overall process comes to dominate much more markedly with enhanced substitution, as has already been reported[18] for *N*-alkylthiopiperidines.

Two or all three of these separate processes might combine with an energy saving such as to produce a two or one stage process since, for example, rotation about congested C–N bonds is easier when the nitrogen configuration is flat (C–N–C bond angle = 120°) than when it is tetrahedral. It is easy to imagine that a process with a low barrier might be subsumed into a process with a higher barrier to give a single complex process. This seems less likely for processes which required considerable reorganization and which have comparably high barriers. More probably, some reversible component of one process facilitates the other process.

If there is an intermediate stable state in a conformational pathway after passage through the transition state from which passage back to the initial state is about as likely as passage forward to the final state then the frequency of interconversion of initial and final states (which is what dynamic NMR measures) is only half the frequency of passing through the transition state, and a barrier calculated without taking account of this by using a transmission coefficient of between 0.5–1, will be too high by up to $RT\ln 2$ kcal mol$^{-1}$. This possibility arises when the barriers to nitrogen inversion and rotation are about the same as presumably happens for some intermediate sized RO-substituent on nitrogen. The barriers for the *N*-hydroxy compounds **2** and **7** are so much smaller than all others as to suggest that a transmission coefficient of 1 is more appropriate, but both sets of barriers are shown in Table 1.

The barriers to the overall process are little altered in deuteriomethanol compared with deuteriochloroform solution which conforms to the earlier observation for *O*-acylhydroxylamines of Sutherland and Fletcher.[13]

The failure to observe a second dynamic NMR process for **5**, even at −150 °C, may seem discrepant with the postulate of two separate contributions to the overall process from nitrogen inversion and rotation. However, if all the structures intermediate between **11** and **12** are significantly less stable than these structures, only the overall process will be observed although the two steps may be more or less distinct as we have discussed. The third process, ring inversion, which must take place is assumed to occur at some convenient point such that it need not contribute noticeably to the barrier.

## Experimental

Analyses were carried out by Butterworth Laboratories, Teddington, Middlesex. Variable temperature NMR spectra were determined on a Varian VXR400 spectrometer. Temperature calibration was by ethylene glycol above ambient and by 2-chlorobutane[27,*] below ambient. *J*-Values are given in Hz. The high resolution mass spectrum was determined on a VG 7070H instrument. Merck 9385 silica gel was used for flash chromatography. Light petroleum was of the fraction boiling at 40–60 °C. 1-Acetoxy-4,4-dimethoxy-2,2,6,6-tetramethylpiperidine (**8**) and 1-acetoxy-2,2,6,6-tetramethyl-4-piperidone (**9**) were prepared as previously described.[1]

1-*Hydroxy*-2,2,6,6-*tetramethylpiperidine* (**2**).—As previously reported[28] this compound readily re-oxidises to 2,2,6,6-tetramethyl-1-piperidyloxy radical (TEMPO) and was therefore prepared *in situ*. TEMPO (15.6 mg, 0.1 mmol) was dissolved in [$^2H_8$]tetrahydrofuran (0.75 cm$^3$) which contained phenyl hydrazine[29] (8.1 mg, 0.075 mmol). The solution decolourised rapidly, with evolution of $N_2$, and remained stable for many hours. The use of THF as solvent avoids the coloured impurities which are formed in chloroform solution.[29]

1-*Formyloxy*-2,2,6,6-*tetramethylpiperidine* (**3**).—TEMPO (1 g, 6.4 mmol) was suspended in a solution of sodium ascorbate (2.1 g, 10.6 mmol) in water (18 cm$^3$) and shaken vigorously until completely decolourised (*ca.* 5 min). The resulting suspension was extracted with ether and the ether extracts were washed with water and brine, dried ($Na_2SO_4$) and evaporated under reduced pressure. The crude product (1-hydroxy-2,2,6,6-tetramethylpiperidine) was dissolved in dry pyridine (5.5 cm$^3$), cooled to 10 °C and treated dropwise with acetic–formic anhydride[30] (4 cm$^3$), keeping the temperature below 10 °C. The mixture was allowed to stand at room temperature for 2 h, and was then diluted with ether and washed with water, dilute HCl, $NaHCO_3$ and brine, dried and evaporated to leave a pale oil (0.7 g). Flash chromatography (EtOAc–light petroleum, 20:80) removed traces of TEMPO and other polar impurities to leave the formate **3** as a colourless liquid (0.60 g), which was purified by short-path distillation at 0.7 mmHg (Kugelrohr oven temperature 120 °C) (Found: $M^+$, 185.1429. $C_{10}H_{19}NO_2$ requires *M*, 185.1416); $\nu_{max}$(film)/cm$^{-1}$ 1745 and 1130.

1-*Acetoxy*-2,2,6,6-*tetramethylpiperidine* (**4**).—TEMPO (1 g, 6.4 mmol) was reduced with sodium ascorbate as above and the aqueous suspension was diluted with ice-cold saturated $NaHCO_3$ (30 cm$^3$). Acetic anhydride (5 cm$^3$) was added dropwise with ice-cooling and portions of solid $NaHCO_3$ were added to maintain the mixture at pH 8 until no further pH change occurred. The mixture was extracted with ether and the extract was washed with $NaHCO_3$ and brine, dried ($Na_2SO_4$) and evaporated. The residue crystallised from light petroleum (−20 °C) to give the acetate **4** as prisms (1.04 g), m.p. 63.5–65 °C (lit.,[31] 63.5–65 °C).

1-(2,2-*Dimethylpropanoyloxy*)-2,2,6,6-*tetramethylpiperidine* (**5**).—TEMPO (1 g) was reduced as for compound **2** and the crude product was immediately dissolved in dry pyridine (15 cm$^3$) and treated with pivaloyl chloride (1.53 g). After standing overnight at room temperature, the solution was diluted with water, extracted with ether and the organic extract was washed with dilute HCl, $NaHCO_3$ and brine, dried and evaporated. The residual oil was purified by short-path distillation at 0.4 mmHg (Kugelrohr oven temperature 150 °C) to give the product **5** as a colourless oil (1.2 g) which crystallised to a white solid, m.p. 44–45 °C on storage at −20 °C (Found: C, 69.7; H, 11.5; N, 5.6. $C_{14}H_{27}NO_2$ requires C, 69.7; H, 11.3; N, 5.8%); [lit.,[32] oil, $\delta_H$ 1.6 (br s, 6 H), 1.3 (s, 9 H), 1.2 (s, 3 H) and 1.1 (s, 3 H)].

1-*Trifluoroacetoxy*-2,2,6,6-*tetramethylpiperidine* (**6**).—TEMPO (1 g) was reduced and the product recovered as described above. The crude product was dissolved in dry pyridine (15 cm$^3$) and treated with trifluoroacetic anhydride (2.69 g). After standing overnight at room temperature, the solution was evaporated *in vacuo* (1 mmHg) and the residue was mixed with ice. After work-up as for compound **5**, the residual red oil was purified by short-path distillation at 0.4 mmHg (Kugelrohr oven temperature 100 °C) to give a pale yellow oil (1.1 g) which crystallised on standing. Repeated short-path distillation gave the product **6** as colourless prisms, m.p. 33–35 °C (Found: C, 51.9; H, 7.1; N, 5.6. $C_{11}H_{18}F_3NO_2$ requires C, 52.2; H, 7.2; N, 5.5%); $\nu_{max}$(Nujol)/cm$^{-1}$ 1805, 1215, 1165 and 1120.

4,4-*Dimethoxy*-1-*hydroxy*-2,2,6,6-*tetramethylpiperidine* (**7**).—A solution of 1-acetoxy-4,4-dimethoxy-2,2,6,6-tetramethylpiperidine (**8**) (130 mg) in MeOH (37 cm$^3$) was treated with 1.67 mol dm$^{-3}$ KOH (6.7 cm$^3$) and kept exposed to air at room temperature for 70 h, then neutralised with glacial acetic acid (0.67 cm$^3$) and concentrated under reduced pressure. The residue was diluted with brine and extracted with EtOAc. The organic phase was washed with $NaHCO_3$ and brine, dried and evaporated and the residual pale orange oil (4,4-dimethoxy-2,2,6,6-tetramethyl-1-piperidyloxy) was redissolved in EtOAc (5 cm$^3$) and stored at 4 °C. An aliquot (1.25 cm$^3$ containing *ca.* 25 mg of 4,4-dimethoxy-TEMPO) of this solution was evaporated and the residue was redissolved in MeOH (2.5 cm$^3$), treated with 0.1 mol dm$^{-3}$ sodium ascorbate (0.5 cm$^3$) and concentrated under reduced pressure. The mixture was diluted with brine and extracted with EtOAc. The organic extract was dried and evaporated and the residue was purified by flash

* When $\delta$ is the relative shift of C-3 and C-4 of 2-chlorobutane, $T = 9296 - 975.6\,\delta + 24.98\,\delta^2$.

chromatography in EtOAc–light petroleum (35:65). The recovered material was dried thoroughly *in vacuo* to leave the hydroxy compound **7** as a colourless solid (15 mg) which was dissolved in [$^2H_8$]THF (0.75 $cm^3$) containing phenylhydrazine (8.1 mg) to maintain it in the reduced form and used directly for NMR studies.

1-(2,2-*Dimethylpropanoyloxy*)-2,2,6,6-*tetramethyl*-4-*piperidone* (**10**).—This compound was prepared from 4-oxo-TEMPO (1 g) in an analogous manner to the desoxo compound **5**. The crude product (1.25 g) was subjected to short-path distillation at 0.4 mmHg (Kugelrohr oven temperature 170 °C) to give the pure ketone **10** which solidified on standing, m.p. 56–57 °C. A portion recrystallised from light petroleum (−20 °C) gave cubes, m.p. 59–60 °C (Found: C, 65.7; H, 10.0; N, 5.3. $C_{14}H_{25}NO_3$ requires C, 65.8; H, 9.9; N, 5.5%).

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