The Measurement of the One-fold Rotational Barrier of Eclipsed Bonds. A Dynamic NMR Determination of N–O or N–CH_2 Bond Rotation in *N*-Alkoxy- or *N*-Alkyl-2,2,6,6-Tetramethylpiperidines

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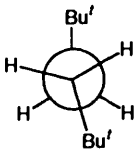
In a series of *N*-alkoxy- and *N*-alkyl-2,2,6,6-tetramethylpiperidines, the temperature dependence of NMR spectra shows that a conformational interconversion involving ring inversion, nitrogen inversion and rotation about the exocyclic bond takes place. Barriers to interconversion are reported. Except with the simplest *N*-substituents, the rate-determining step in the interconversion is rotation about the exocyclic bond at nitrogen, so the measured barriers represent the one-fold rotational barriers for that bond.

When there is only one populated minimum energy conformation for a bond during 360° of rotation or a closely grouped set of very similar conformations forming a single energy well (see Fig. 1), rotation through 360° nonetheless takes place with a frequency determined by the potential barrier. The structural features which give rise to the one-fold potential are likely to be unusual or extreme examples of the usual and to result in a barrier which is uncommonly high.

A simple example is 1,2-di-*tert*-butylethane. Molecular mechanics calculations (MM2) suggest that two equivalent near-to-*anti* conformations **1** and **2** are preferred,[1a] skewed



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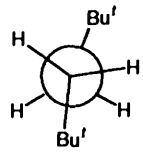

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away from the perfect *anti*-arrangement to reduce long-range interactions, and interconverting through a libration barrier small compared with kT. Conformations with the *tert*-butyl groups *gauche* to each other[1b] represent a minimum, but are almost 7 kcal mol^{-1} * less stable than **1** and **2**. Conformations **1** and **2** interconvert much less frequently by a near-to-360° rotation and the calculated value of the one-fold rotational barrier to this process (19.7 kcal mol^{-1}), which involves two *tert*-butyl groups eclipsing, is strikingly high for a simple saturated carbon–carbon bond, but the usual experimental methods of barrier measurement cannot be applied. A knowledge of low-lying vibrational energy levels and the assumption of the shape of a potential energy well cannot be exploited since there is no justifiable assumed shape of a barrier 360° wide, as the broken line in Fig. 1 implies. Likewise the dynamic NMR method requires a multi-site exchange for a given nucleus, and is excluded when a bond has only one populated site in its rotational potential and a one-fold rotation process.

We now report the stereodynamics of the title compounds **3a–e** and **4a–f**, derivatives at nitrogen of 2,2,6,6-tetramethylpiperidine, TMP, and deduce the one-fold barrier to rotation about the N–O or N–CH_2 bonds in some of these compounds. In *N*-*tert*-butoxy-TMP **3e** the barrier is measured to be at least

* 1 cal = 4.184 J.

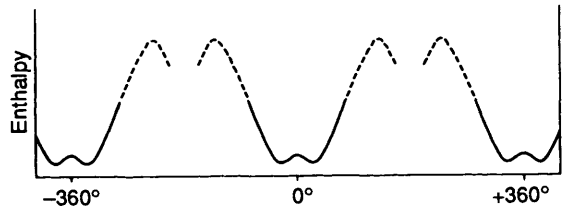
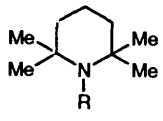


Fig. 1 Rotational potential energy diagram for a one-fold rotation. The intermediate +180° and −180° conformational minima are assumed to be so high in enthalpy that they are not significantly populated.

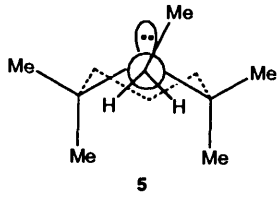


3a R = OH
3b R = OMe
3c R = OCH_2Ph
3d R = OPr^i
3e R = OBu^t

4a R = H
4b R = Me
4c R = Et
4d R = Pr
4e R = $CH_2CH(OH)Ph$
4f R = CH_2Bu^t

24.9 kcal mol^{-1}, while for the *N*-neopentyl compound **4f** it is calculated to be 15.6 kcal mol^{-1}.

We have already shown[2] that the *N*–R substituent in TMP derivatives prefers to be equatorial and that the conformation about the exocyclic N–O or N–CH_2 bond (N–Ex for short) in **3b–e** and **4c–f** is a rapid equilibrium between two nearly eclipsed conformations which, for example, in the case of **4c** can be represented as **5** and **6**. An *anti* conformation is a conformational minimum but with a small population since it involves large steric repulsions.



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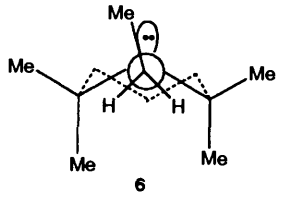

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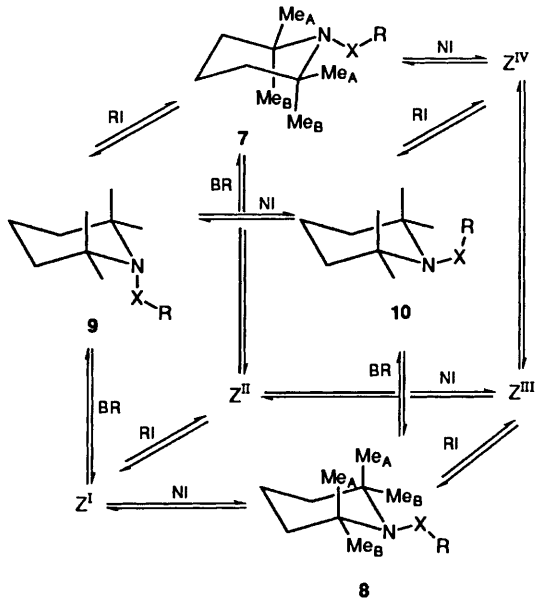
Scheme 1 shows that axial and equatorial substituents on the piperidine ring are chemically different and become equivalent on the NMR timescale only when the interconversion of



Scheme 1 Conformational diagram showing the possible stepwise interconversion pathways between conformational minima of compounds of series **3** and **4**. NI = nitrogen inversion; RI = ring inversion; BR = bond rotation. Some structures Z have been omitted for the sake of clarity.

equivalent minimum energy conformations **7** and **8** becomes rapid. Such an interconversion takes place by three successive processes of ring inversion, nitrogen inversion and N–Ex bond rotation in any order, or by some complex combination of these processes.[3] However, since all these processes have significant barriers, it is unlikely that in the rate-determining step the strain of two processes maximises simultaneously. Without excluding a small change in torsional angles or some nitrogen flattening to facilitate ring inversion and *vice versa*, a three step process, in no particular order seems to be the most likely way of interconverting **7** and **8**.

The temperature dependence of the NMR spectra of compounds **3a–e** and **4a–e**, and comparison of the barriers derived therefrom with those for simple reference compounds, along with molecular mechanics calculations, shed light on the conformational processes and on rotation about the exocyclic bond in some of the compounds studied. Allinger's MM3 program[4,5] was used for *N*-alkyl compounds **4** but is not parametrized for N–O bonds so the MMX program[6] was used for *N*-alkoxy compounds **3**. The choice of program or use of other programs should affect only minor details of calculated structures.

The alkoxy-TMP derivatives were synthesized either by conventional alkylation of 1-hydroxy-TMP (compounds **3b**, **3c**) or by treatment of TEMPO with either Grignard[7,8] or organolithium[9] reagents (compounds **3d**, **3e**). Despite the many earlier reports of the preparation of 1-alkoxy-2,2,6,6-tetramethylpiperidines,[7-16] in which doubling of signals for the methyl groups has often been noted, the origin of this doubling has not previously been discussed.

Results and Discussion

At low temperatures separate signals are seen in both proton and carbon-13 NMR for methyl groups and geminal protons on the piperidine ring in each of the compounds in sets **3** and **4**. Except in the case of **3e**, these signals broaden and coalesce as the temperature is raised, showing that the conformational process is becoming fast on the NMR timescale. Barriers to this process were calculated[17] from the NMR data and the results are as shown in Table 1. In spectra of compound **3e** separate signals still persist even at 180 °C with no sign of kinetic broadening, so the coalescence temperature is concluded to be above 200 °C. Full details of all NMR spectra are given in Table 2.

The signals of the R group and of the ring carbon atoms are temperature-independent in all compounds **3** and **4**, indicating that the 2,6- and 3,5-positions are each equivalent in the NMR at all temperatures studied. The one reasonable conformational explanation of all these NMR results is that the interconversion of **7** and **8** is slow on the NMR timescale at low temperatures, so only geminal substituents on the ring but off its mirror plane have different environments on the two sides of the equilibrium.

As Scheme 1 shows, the interconversion of **7** and **8** requires that three processes take place, ring-inversion *e.g.* **7**→**9**, nitrogen inversion *e.g.* **9**→**10**, and rotation about the N–X bond *e.g.* **10**→**8**, but these can take place in any order as the Scheme implies. The main postulate of this paper is that as the nitrogen substituent is changed, the rate-determining process in the interconversion of **7** and **8** changes. In some of the compounds studied, the rate-determining step is rotation about the exocyclic bond so that the measured barrier reflects the one-fold rotational potential.

In TMP itself **4a** the barrier is measured to be 7.7–8.0 kcal mol^{-1}. This seems to be too large for nitrogen inversion of a secondary amine, as the nitrogen inversion barrier of 6.1 kcal mol^{-1} in piperidine itself[19] illustrates. The additional substitution next to the nitrogen in TMP should lead to an even lower nitrogen inversion barrier in that compound.[21] Since N–H bond rotation does not contribute to **7**→**8** interconversion, the barrier is concluded to represent the chair to chair ring inversion step for TMP, which fits well with the known barrier of 10.1 kcal mol for piperidine[18] when compared with those of cyclohexane[22] (10.3 kcal mol^{-1}) and 1,1,3,3-tetramethylcyclohexane[20] (8.7 kcal mol^{-1}).

In the *N*–hydroxy compound **3a** the ring inversion barrier is unlikely to be much higher than in **4a**, and N–O bond rotation should be easy so the rate-determining step, involving a barrier of 11.5 kcal mol^{-1} which is markedly higher than in TMP itself, is concluded to be nitrogen inversion. This agrees with the known nitrogen inversion barriers of about 12.8 kcal mol^{-1} in acyclic *N*,*N*-dialkylhydroxylamines.[23] The barrier in **3a** is unchanged in the hydroxylic solvent deuteromethanol which does not accord with increased barriers in deuteromethanol for simpler nitrogen-inverting sytems.[24] We discuss below how this may be related to an eclipsed conformation for the N–O bond.

The interconversion process in *N*-amino-TMP **4g** has a barrier of 9.0 kcal mol^{-1}, intermediate between that of the above two compounds, which may place it near the point where ring inversion and nitrogen inversion/rotation have similar barriers. Remarkably the barrier to the **7**→**8** interconversion in the *N*-methoxy compound **3b** is much higher, 15.7–17.0 kcal mol^{-1} depending on solvent, yet there is no reason or precedent for ring inversion or nitrogen inversion to have a significantly higher barrier because of the extra *O*-methyl group. During the interconversion of **3b** however, there has to be rotation of 180° about the N–O bond in the course of which the *O*-methyl group comes close to one or other geminal dimethyl group, and we suggest that the steric confrontation involved gives rise to a high barrier determined by this rotation step.

In *N*-benzyloxy-TMP **3c** the barrier is similar in size, but the *N*-isopropoxy-compound **3d** has a noticeably lower barrier. In such a highly substituted environment a barrier reduction on increasing substitution suggests a ground state effect. Compared with **3b** two further methyl groups have to be accommodated and we suggest that this destabilizes the ground state somewhat. The transition state in the interconversion involves the methine hydrogen of the isopropyl group rotating past one of the *gem*-

Table 1 Barriers (kcal mol^{-1}) to the interconversion process **7** → **8** in compounds **3a–e** and **4a–g**

Compound and *N*-substituent	Solvent	T_c (°C) Coalescence temperature	Barrier to interconversion at T_c	Comments
3a OH	[$^2H_8$]THF	−42	11.5	
	CD_3OD	−43	11.5	
3b OCH_3	CCl_4	40 to 80[c]	17.0	
				$\Delta H^‡ = 18.1$
				$\Delta S^‡ = 3.3$
	C_2Cl_4	35 to 100[c]	16.6	$\Delta H^‡ = 17.1$
				$\Delta S^‡ = 1.5$
	CD_3OD	16 to 52[c]	15.7	$\Delta H^‡ = 15.8$
				$\Delta S^‡ = 0.2$
3c OCH_2Ph	$CDCl_3$	56	16.4	
	CD_3OD	44	15.8	
3d $OCH(CH_3)_2$	$CDCl_3$	13	13.9	
3e $OC(CH_3)_3$	[$^2H_6$]DMSO	> 189	> 24.9	
4a H	CHF_2Cl	−100	8.0	Ref. 17
	CD_2Cl_2	−100	7.7	This work
4b CH_3	*a*	−105	8.2	
	CD_2Cl_2	−98	8.2	
4c CH_2CH_3	CD_2Cl_2	−52	10.3	
	CD_3OD	−48	10.3	
	a	−69	10.0	
4d $CH_2CH_2CH_3$	CD_2Cl_2	−52	10.5	
4e $CH_2CH(OH)Ph$	C_2Cl_4	30–50	13.9	
	CD_3OD	0–20	12.9	
4f $CH_2C(CH_3)_3$	*b*		15.6	
4g NH_2	Me_2O	−85	9.0	

[a] $CHFCl_2/CHF_2Cl/CD_2Cl_2$ approx. 3:3:1. [b] Barrier to N–CH_2 bond rotation as calculated by molecular mechanics, see text. [c] Rate constants were measured by full line shape treatment over this temperature range to yield the thermodynamic parameters shown.

Table 2 Chemical shifts (δ) for compounds of sets **3** and **4** under conditions of slow conformational exchange

Compound and *N*-substituent	Temperature (°C)	C2, C6 signals	*gem*-dimethyl signals	C3, C5 signals	C4 signal	Nitrogen substituent
Proton NMR[a]						
3a OH	−60	—	1.039, 1.078	1.25–1.52	1.59	1.73
3b OCH_3	16	—	1.180, 1.176	1.27–1.48	1.53	
3c OCH_2Ph	18	—	1.166, 1.272	1.33–1.53	1.57	4.82, 7.28–7.38
3d $OCH(CH_3)_2$	−28	—	1.134, 1.057	1.25–1.46	1.534	1.14
3e $OC(CH_3)_3$	18	—	1.020, 1.084	1.37–1.55	1.45–1.58	1.234
4b CH_3	−128	—	1.002, 1.084	1.22–1.68	1.676	1.002, 2.245
4c CH_2CH_3	−98	—	0.836, 0.928	1.19–1.36	1.525	0.884, 2.404
4e $CH_2CH(OH)Ph$	−20	—	0.70, 0.90, 0.95, 1.00	1.30 br s	1.30 br s	2.23, 2.70, 4.35, 6.95–7.30
Carbon-13 NMR data						
3a OH	−57	60.69	19.79, 31.85	39.59	17.89	
3b OCH_3	33	59.72	20.00, 33.02	39.74	17.11	65.35
3c OCH_2Ph	18	60.00	20.30, 33.09	39.71	17.12	78.71, 127.28, 127.44, 128.21, 138.29
3d $OCH(CH_3)_2$	−29	59.45	20.17, 34.35	39.89	17.13	22.53, 75.30
3e $OC(CH_3)_3$	33	59.15	20.44, 34.82	40.90	17.22	29.51, 77.12
4b CH_3	−128	54.74	19.31, 33.21	41.22	18.38	28.45
4c CH_2CH_3	−93	54.04	19.31, 33.21	39.93	17.61	19.48, 37.78
4d $CH_2CH_2CH_3$	−70	54.8	20.7, 33.9	40.9	17.9	11.9, 17.9, 47.5
4e $CH_2CH(OH)Ph$	−30	56.5	21.1, 22.3, 33.8, 35.0	41.6	18.4	52.9, 72.1, 126.8, 128.5, 129.6, 145.9
4g NH_2	−105	59.0	18.40, 32.84	40.3	17.85	

[a] Proton NMR spectra at slow exchange were not determined for compounds **4d** and **4g**.

dimethyl groups, which is little different as a steric interaction from that during rotation of the methoxy group in **3b**. As a result the measured barrier is lower.

The very much higher barrier found on one further methyl substitution to give the *tert*-butoxy-TMP **3e** has the appearance of a transition state effect. Compared with **3b–d** a methyl group now has to pass close to one or other *gem*-dimethyl group during interconversion and this leads to a very high barrier, determined by steric crowding during the bond rotation part of the process. There are no doubt substantial but less important interactions arising from the *tert*-butyl group in the ground state.

The interconversion barrier in *N*-methyl-TMP **4b** is close to that in TMP itself discussed above, and this fits well with ring inversion being the process involved. In the *N*-ethyl and *N*-propyl derivatives **4c** and **4d** the barrier is about 2 kcal mol^{-1}

greater. The results above for the *N*-alkoxy series suggest that rotation about the N–CH_2 is the rate-determining step in **4c** and **4d**. The even larger barrier in **4e** suggests that here steric interactions are even greater in the transition state.

N-Neopentyl-TMP **4f** has not been synthesized but molecular mechanics calculations[2] suggest that the barrier to rotation about the N–CH_2 bond in this compound is 15.8 kcal mol^{-1}, much higher than is likely for the barrier to the ring inversion or nitrogen inversion steps. The reliability of the calculations is shown by the calculated barrier to rotation in the *N*-ethyl compound **4c** (9.6 kcal mol^{-1}), which agrees well with the observed barrier of 10.0–10.3 kcal mol^{-1} depending on solvent.

In the methoxy-compound **3b**, the effect of a hydroxylic solvent is to reduce the interconversion barrier substantially from 17.0 to 15.7 kcal mol^{-1}. It is known[2] that the N–O bond is eclipsed in the ground state conformation. The immediate steric interactions along the N–O bond are not great, with each substituent, two on nitrogen and one on oxygen eclipsing a lone pair. A hydrogen bonding solvent like methanol interacts presumably with one or more of the available lone pairs and sterically destabilizes this eclipsing so that the rotational barrier is lower. Such a solvent effect on rotation in hydroxylamines is not unprecedented[23] and can thus be explained in terms of an eclipsed conformation. The interconversion in the methoxy-compound was examined over a range of temperatures in each solvent and the enthalpy and entropy of activation were determined as shown in Table 1. There are trends in the enthalpies and entropies of activation with solvent which emphasize that the above solvent effect is real but do not noticeably enhance the explanation offered.

It thus seems that when the R group in the *N*–XR substituent is other than hydrogen, rotation about the eclipsed N–X bond is the rate-determining step in the overall conformational interconversion. The transition state occurs when the R group has its maximum interaction with an equatorial methyl group about 120° on either side of the ground state. There is expected to be a minimum after 180° of rotation at the *anti*-conformation, and molecular mechanics calculations suggest that for **4f** such a conformation is less stable than the ground state by 5.5 kcal mol^{-1} and is little populated at room temperature. This *anti*-conformation is important, however, since either nitrogen inversion (with or without ring inversion) or bond rotation takes a molecule to such a conformation. The second half of the overall interconversion which modifies the NMR spectrum must then comprise the remaining process(es), for a repeat of the original process(es) returns the molecule to conformation **7** rather than moving on to **8** and so has no effect on the NMR spectrum. The success of this NMR method of measuring a 360° rotational barrier thus depends on there being an unstable intermediate with two different and so unequal barriers separating it from the two degenerate ground states, and on having a credible analysis of barrier sizes which suggests that bond-rotation is the rate-determining step. In such circumstances the NMR experiment allows measurement of the barrier for rotation through 180°, which for symmetry reasons is equal to the one-fold rotational barrier. It should be emphasized that once 180° rotation has taken place, it is much more likely that ring inversion plus nitrogen inversion will then follow to complete the **7**→**8** interconversion but that if a further 180° of rotation were to take place to complete the one-fold rotation the height of the overall one-fold barrier would be as reported here for the half-barrier.

We note that in the *N*-alkoxy compounds, inversion of configuration at oxygen[24] would avoid the need for a high-barrier 180°-rotation about the N–O bond. The linear N–O–C arrangement in the transition state of this process would keep the *O*-alkyl group far from the flanking geminal dimethyl groups. Some experimental investigations[24,25] suggest that the linearity barrier at oxygen is high and various calculations[25,26] agree with this, with that for dimethyl ether being 36.3 kcal mol^{-1} at the [6–31G(d)] level.[26e] Since nothing in the NMR spectra allows a distinction of rotation and inversion, and rotation barriers are not expected to be so large, it has become the practice[27–29] to use observed interconversion barriers for X–OC bonds as experimental indications of the lower limit to the oxygen inversion barrier. By comparable reasoning we conclude that the lower limit of 24.9 kcal mol^{-1} for the interconversion process in **3e** raises the lower limit for the oxygen inversion barrier in an *N*-alkoxyamine from 13 kcal mol^{-1} reported previously[28,30] to 24.9 kcal mol^{-1}.

Unlike the TMP derivatives reported here, the NMR spectrum of the corresponding 1-*tert*-butoxy-2,2,6,6-tetramethylcyclohexane would be temperature-independent for there are no interconverting conformations **7** and **8** which might produce pairs of NMR signals suitable for study, even though 360° rotation with a high barrier about the ring-to-oxygen bond no doubt does take place as often as in **3e** or **4f**. The value of the tetramethyl piperidine system **7**→**8** is that it allows the measurement of such a rotational barrier.

A few earlier reports exist[31–37] in which a comparable kind of rotational barrier can be determined by dynamic NMR in molecules where a conformational process requires both rotation and nitrogen inversion. In the last two of these reports[36,37] it was recognized that when there is a high degree of substitution, rotation has a much higher barrier than nitrogen inversion, but it was not suggested that because processes are likely to be successive[3b,3c] the barrier observed corresponds closely to the pure one-fold rotational barrier.

Experimental

General.—Routine ^1H NMR specta were recorded at 90 MHz with the probe temperature at 33 °C. Variable temperature ^1H and ^{13}C NMR spectra were recorded at 400 MHz. Temperature calibration was by ethylene glycol above ambient and by 2-chlorobutane[38] below ambient. Silica gel for flash chromatography was Merck Type 9385. *N*-Methyl-2,2,6,6-tetramethylpiperidine **4b**,[39] *N*-ethyl-2,2,6,6-tetramethylpiperidine[40] **4c** and *N*-(2-hydroxy-2-phenylethyl)-2,2,6,6-tetramethylpiperidine[41] **4e** were prepared by minor variations of published procedures.

1-*Methoxy*-2,2,6,6-*tetramethylpiperidine* (**3b**).—1-Hydroxy-2,2,6,6-tetramethylpiperidine was prepared as described previously[3] by reduction of TEMPO with sodium ascorbate. The crude material obtained from TEMPO (1 g) was dissolved in anhydrous DMF (10 cm^3) and added under N_2 to hexane-washed NaH (from 60% suspension in oil; 384 mg). The mixture was stirred for 0.5 h, then treated with methyl iodide (1 cm^3) and stirred under N_2 for 16 h. Excess NaH was destroyed by slow addition of methanol and the mixture was partitioned between diethyl ether and water. The ether was dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography (hexane–ether = 95:5 v/v). Short path distillation at 4 mm Hg (oven temperature 130 °C) gave a colourless liquid (0.45 g, 41%); IR (film) ν/cm^{-1} 1470, 1375, 1360, 1135, 1050, 1040, 975 and 715; $\delta_H(CDCl_3)$ 1.09 and 1.15 (2 × s, 12), 1.44 (br s, 6) and 3.60 (s, 3). Kurumada *et al.*[11] reported an identical NMR spectrum except that the two C-methyl groups were observed as a singlet at δ 1.12, *i.e.* midway between the two signals reported here. The spectrum was obtained at 60 MHz (T. Kurumada, personal communication), where at ambient temperature the exchange rate would result in an averaged signal.

1-*Benzyloxy*-2,2,6,6-*tetramethylpiperidine* (**3c**).—A mixture of NaH and 1-hydroxy-2,2,6,6-tetramethylpiperidine in anhydrous

DMF, prepared as above, was treated with benzyl bromide (1.71 g) and stirred under N_2 for 16 h. Triethylamine (2 cm^3) was added and the mixture stirred for 3 h, then diluted with water and extracted with ether. The ether layer was washed with water, dried (Na_2SO_4) and evaporated. The residue was subjected to flash chromatography (hexane–ether = 99:1 v/v) to give first the compound **3c** as a pale oil (0.91 g), followed by dibenzyl ether (0.33 g), identified by its ^1H NMR and IR spectra. Compound **3c** was purified by short-path distillation at 0.5 Torr (oven temperature 190 °C), yield (0.87 g, 63%); IR (film) ν/cm $^{-1}$ 1470, 1455, 1375, 1360, 1135, 1050, 1030, 730 and 695; $\delta_H(CDCl_3)$ 1.15 and 1.24 (2 × s, 12), 1.50 (br s, 6), 4.82 (s, 2) and 7.32 (br s, 5). Patel *et al.*[15] described an identical spectrum, except for the *C*-methyl groups reported as a multiplet at δ 1.2, *i.e.* midway between the two signals described here.

1-*Isopropoxy*-2,2,6,6-*tetramethylpiperidine* (**3d**).—A solution of TEMPO (1 g, 6.4 mmol) in anhydrous ether (20 cm^3) was cooled to 0 °C under N_2 and treated with 1.2 mol dm^{-3} isopropylmagnesium iodide in ether (4.0 cm^3, 4.8 mmol). After 5 min the solution was quenched with methanol (1 cm^3), diluted with water and extracted with diethyl ether. The ether extract was washed with water, dried (Na_2SO_4) and evaporated, and the residue was flash chromatographed (hexane) to remove polar impurities. Short-path distillation at 0.5 Torr (oven temperature 95 °C) gave a colourless liquid (0.11 g, 8.6%); IR (film) ν/cm^{-1} 1460, 1375, 1360, 1135, 1115 and 960; δ_H 1.11 (s, 12), 1.15 (d, *J* 6.2, 6), 1.45 (br s, 6) and 3.98 (septet, *J* 6.2, 1); MS accurate mass (M^+) 199.1916, calc. for $C_{12}H_{25}NO$ 199.1936.

1-tert-*Butoxy*-2,2,6,6-*tetramethylpiperidine* (**3e**).—A solution of TEMPO (1 g, 6.4 mmol) in anhydrous hexane 2 (35 cm^3) was cooled to −78 °C under N_2 and treated with 1.7 mol dm^{-3} *tert*-butyllithium in hexane (3.8 cm^3, 6.46 mmol). After 5 min, the solution was quenched with methanol (1 cm^3), warmed to r.t., diluted with ether and washed with water. The solution was dried (Na_2SO_4) and evaporated, and the residue (1.22 g) was flash chromatographed (hexane) to remove polar impurities. Short-path distillation at 0.5 Torr (oven temperature 100 °C) gave a colourless liquid (0.47 g, 34%); IR (film) ν/cm^{-1} 1470, 1450, 1375, 1360, 1170, 1135 and 940; δ_H 1.07 and 1.12 (2 × s, 12), 1.27 (s, 9), 1.46 (br s, 6). Kovtun *et al.*[8] reported an identical spectrum except that all signals are displaced by approx. 0.05 ppm.

1-*Propyl*-2,2,6,6-*tetramethylpiperidine* (**4d**).—Propionyl chloride (6.49 g, 70 mmol) was added dropwise to a solution of 2,2,6,6-tetramethylpiperidine (7.52 g, 53.4 mol) and triethylamine (8.72 g, 86.4 mmol) in chloroform (40 cm^3), keeping the temperature below 25 °C, and the mixture was then refluxed for 6 h and cooled. Water (30 cm^3) was added with stirring and after 0.5 h the organic layer was separated, washed with dilute HCl and water, dried and evaporated. The crude residue (5.3 g) was added to an ice-cold suspension of $LiAlH_4$ (1.48 g, 40 mmol) in butyl ether (42 cm^3) and ethyl ether (10 cm^3). The solvent was distilled until the temperature reached 100 °C, then refluxed for 3 h and cooled to 5 °C. Saturated NH_4Cl solution (40 cm^3) was added dropwise, the precipitate was filtered and the filtrate was extracted with 3 mol dm^{-3} HCl. The acid extracts were basified with NaOH, extracted with ether and the extract was dried and evaporated. The residue was distilled to give the amine (**4d**) as a colourless liquid (1.26 g, 12.9%); δ_H 0.78 (t, 3), 1.0 (s, 12), 1.35–1.43 (m, 6), 1.43–1.55 (m, 2), 2.3 (m, 2) (Found: C, 78.8; H, 13.5; N, 7.7. Calc. for $C_{12}H_{25}N$: C, 78.69; H, 13.66; N, 7.65%).

Acknowledgements

We are grateful to Dr. M. Mruzek for the high resolution mass spectral data. D. C. and L. L. acknowledge the financial support of MURST and CNR, Rome. The international collaboration was made possible by a NATO research grant (RG86/0200).

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Paper 3/01700A
Received 24*th March* 1993
Accepted 19*th April* 1993