

Enantiopure and Racemic Chiral Nitronyl Nitroxide Free Radicals: Synthesis and Characterization

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A synthetic route to a series of homochiral (and achiral) nitronyl nitroxides derived from *rac*-(and *meso*)-3,4-dimethyl-3,4-dinitrohexane is described. The two forms of this precursor, *meso* and *rac*, were identified unambiguously and reduced to the corresponding *meso*- and *rac*-diamines. The *rac*-diamine was condensed with an enantiopure aldehyde specifically designed to give a diastereomeric mixture of imidazolidines easily separated by flash chromatography. Both enantiopure diamines were then obtained by acidic hydrolysis of these imidazolidines. The absolute configurations of the diamino precursors were determined by X-ray crystallography of single crystals of a manganese(II) complex [(*R,R,R*)-5E·Mn(hfac)₂] of a nitroxide containing a third chiral center of known configuration. A series of homochiral nitronyl nitroxides was then prepared from the enantiopure diamino pre-

cursors by condensation with aldehydes, followed by oxidation. Their structural properties were compared to those of their achiral *meso* counterparts and it was found that the puckering of the five-membered ring is dependent on the chirality of the imidazolyl unit. The radicals show marked optical activity, as explored by polarimetry and circular dichroism spectroscopy. These paramagnetic building blocks of known absolute configuration include chiral centers adjacent to the oxyl groups, and since they exhibit C₂ symmetry they are well suited for coordination chemistry studies because stereochemical complexity is minimized. They have been specifically designed for further developments of the metal-radical approach to molecular magnetic materials. (© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2005)

Introduction

During the two last decades there has been intense interest in molecular structures exhibiting magnetic properties.^[1] Different arrangements of spin carriers have been achieved by several strategies, among which the purely organic and the metal-organic approaches based on nitroxide free radicals have proven particularly rewarding.^[2] Indeed, use of these organic spin carriers has resulted in fascinating molecular species exhibiting unprecedented magnetic properties: purely organic ferromagnets,^[3] ferrimagnetically ordered metal-nitroxide extended species,^[2,4] molecular spin-transition copper(II) nitroxide clusters,^[5] and high-spin molecules related to single-molecule magnets.^[6]

Among all the characterized nitroxide free radicals, nitronyl and imino nitroxides (Scheme 1) deserve special mention. According to Ullman's pioneering work,^[7] and recent

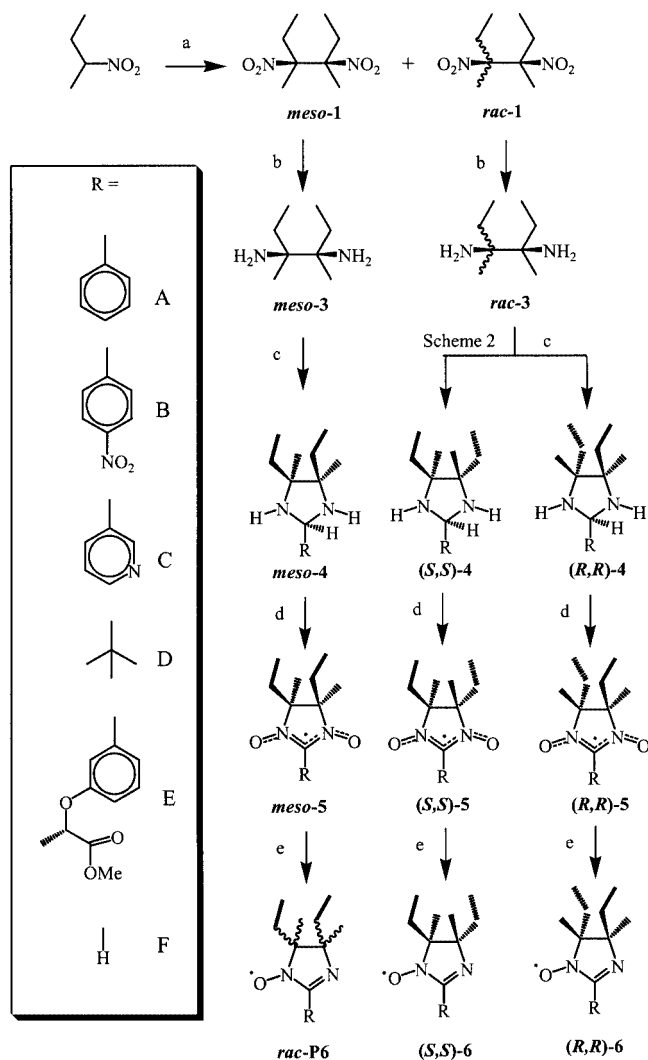
synthetic developments,^[8] any aldehyde may give rise to a nitronyl nitroxide, and hundreds of these nitroxides differing in substitution at position 2 of the imidazolyl ring have been prepared (Scheme 1). Such ease of structural variation (in combination with high stability) is mainly responsible for their popularity as spin carriers. Most of the spin density, for example, is localized on the two oxyl (or oxyl and imino) groups, but its distribution depends upon the overall chemical structure and may involve numerous other parts of the molecule.^[9] Magnetic engineering of purely organic species therefore benefits from the fact that delocalization may increase the possibilities of magnetic coupling through numerous pathways and consequently the chance of bulk ordering. In the designing of nitroxide-containing metal complexes, nitronyl and imino nitroxides bring the advantages both of their bridging character and of the potential to introduce coordination sites in chelating positions relative to the oxyl groups, which result in high-dimensional molecular structures.^[10]

Current trends in magneto-chemistry are giving importance to chiral molecular structures, and organic spin carriers such as nitroxides are well suited as potential precursors of such structures. Expected applications of chiral nitronyl nitroxides in magneto-chemistry might be illustrated as follows.

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Scheme 1. Synthetic strategy for chiral, C_2 , nitronyl nitroxides; a) LiOMe/I_2 , b) Sn/HCl , c) $\text{RCHO}/\text{Et}_2\text{O}$, d) $m\text{CPBA}/\text{Et}_2\text{O}$, $\text{NaNO}_2/\text{HCl}/\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$, e) $\text{NaNO}_2/\text{H}_2\text{O}$, HCl

(i) In purely organic nitroxide-based magnetic materials, the nature and magnitude of the intermolecular interactions are obviously dependent on crystal packing. Enantiopure nitroxides would afford materials crystallizing in chiral space groups and would give opportunities to characterize new exchange pathways.

(ii) The few copper(II) complexes to exhibit molecular spin transition behavior have centro-symmetric cyclic structures.^[5] Hopefully, chiral nitroxides could afford helical infinite arrays possessing different transition temperatures and large hysteresis.

(iii) Chirality governs the dimensionality of polymetallic complexes that could be built from bis(chelating) ligands.^[11] In the recently reported two-dimensional manganese(II) complexes of bis(chelating) nitronyl nitroxides,^[10] use of enantiopure ligands would probably produce a three-dimensional structure displaying a different ordering temperature.

(iv) All nitroxide-containing materials would be obtained in forms suitable for optical investigations such as magneto-chiral dichroism studies.^[12]

In nitroxide free radicals, most of the interesting properties (structural, magnetic, optical) originate from the unusual open-shell electronic structure of the nitroxyl group.^[13] If one is interested in the effect of chirality on these properties, one should try to introduce a chiral center as close as possible to the oxyl group carrying most of the unpaired spin. In the design of metal-organic molecular magnetic materials, for example, introduction of chiral centers close to the coordination sites offers more chance of influencing the configuration of the bound metal center. Although chiral nitroxides are described in several reports,^[14] only a few are devoted to nitronyl nitroxides and their metal complexes, and most describe nitronyl nitroxides containing chiral centers very remote from the oxyl sites.^[15] A couple of nitronyl nitroxides suitably substituted α to the nitroxyl group in the 4-(or 5-)position have been described, but their coordination properties have not been reported.^[16] It may be anticipated they should be complicated, owing to the presence of two different coordination sites.

From these considerations and in view of the numerous potential applications, an ideal chiral nitronyl nitroxide ligand should retain equivalence of the two coordination sites in order to minimize stereochemical problems and should also retain the functional potential of the 2-position in the imidazolyl ring, which has critical importance for the design of specific molecular structures. Asymmetry should therefore be introduced at positions 4 and 5. Accordingly, we considered the highly "symmetrical" (C_2) precursor 3,4-dimethyl-3,4-dinitrohexane, the synthesis of which had already been described.^[17] In addition to chiral species, this system also affords an achiral *meso* series, which should be very useful for testing the effect of chirality by comparison with achiral ligands with similar steric requirements. Here we describe the synthesis, enantiomeric resolution, and absolute configuration of a precursor (the diamino derivative), together with the synthesis and structural, magnetic, and optical characterization of *meso* and chiral nitroxide ligands of the type described in Scheme 1.

Results and Discussion

Syntheses

As stated above, one aim of this study was to preserve the potential of the 2-position in the imidazolyl ring for designing specific chiral nitroxide building blocks, to introduce asymmetric centers in positions 4 and 5 and thus to obtain a series of homochiral radicals. Therefore, resolution of a racemic precursor should be performed before condensation with an aldehyde (Scheme 1). Accordingly, Ullmann's synthesis involving the bis(hydroxylamino) intermediate was not used, because neither the dinitro nor the bis(hydroxylamino) compounds would be good candidates for enantiomeric separation. Indeed, diastereomeric derivatives of the former would be hard to design, and the latter would

be unlikely to survive an extensive workup in solution and chromatographic processing. In contrast, numerous diastereomeric derivatives of the highly stable diamino compounds can be prepared, giving consistency to the synthetic strategy described in Scheme 1.

Although all synthetic steps involved in the preparation of these new nitroxide free radicals are well established, the stereochemical diversity justifies a detailed report of the different compounds.

The Dinitro Compounds

Although the dinitro compounds *meso*-**1** and *rac*-**1** (and also the diamino compounds *meso*-**3** and *rac*-**3**) had been described previously,^[17] they had been poorly characterized and their stereochemistry was not firmly established. The pure *meso* and *rac* forms were isolated by chromatography on SiO₂, which we adapted for large-scale preparations.

Stereochemical characterization was performed by NMR spectroscopy and confirmed by X-ray crystallography. The prominent feature in the NMR spectra of the two isomers arises from the methylene groups, which show up as diastereotopic pairs of enantiotopic protons with anisochromy magnified by the presence of the nitro groups. Each exhibits a sextuplet pattern with chemical shift differences of 0.78 ($\delta = 2.56$ – 1.78) and 0.49 ($\delta = 2.59$ – 2.10) ppm for the *meso* and *rac* forms, respectively. Finally, full characterization

was achieved by X-ray crystallography of the *rac* form, which crystallized as a racemic compound.

The Diamino Compounds

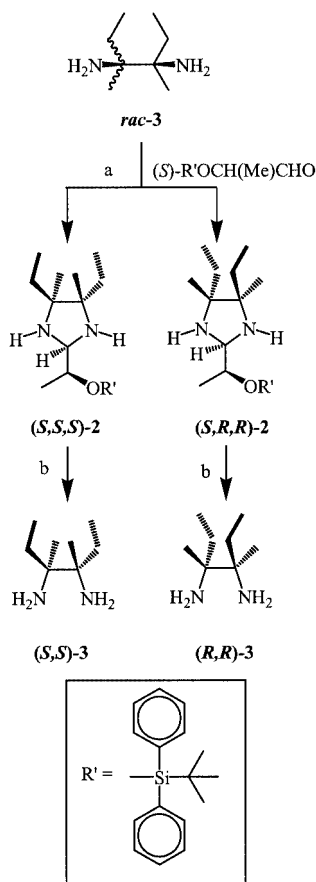
Reduction of the pure *meso* and *rac* dinitro species affords the corresponding diastereomers of the diamino compound **3**.^[17] Their stereochemistry is therefore well established, and our efforts concentrated on the resolution of the *rac* form into pure enantiomers and on the assessment of their absolute configurations.

It is notable that the hydrochloride of *rac*-**3**, of which the crystal structure was determined, exhibited spontaneous resolution, but this behavior had only marginal separation value and was not further investigated. Attempts to obtain diastereomeric salts with (+)-tartaric, (–)-mandelic, and (+)-dibenzoyltartaric acids were fruitless; although enrichment was observed after two crystallizations, it soon became apparent that the yield would be so low that the method would not have practical value for obtaining enantiopure nitroxides in quantities large enough for a study of their coordination properties.)

Accordingly, we took advantage of previous studies describing the reversible formation of imidazolidines and the availability of chiral aldehydes that should undergo condensation with *rac*-**3** to afford separable mixtures of diastereomers. Among the chiral aldehydes used for this purpose, (*S*)-(–)-*O*-(*tert*-butyldiphenylsilyl)acetaldehyde gave a 1:1 mixture of diastereomeric imidazolidines (*S,S,S*)-**2** and (*S,R,R*)-**2**, which were easily separated by flash chromatography (SiO₂, diethyl ether).^[18] Worthy of note is the fact that neither the benzyl analogue nor the commercially available (+)-myrtenal gave satisfactory results. Recovery of the free base [(*S,S,S*)-**3** or (*R,R,R*)-**3**] was performed by hydrolysis in 10% hydrochloric acid according to published procedures.^[19] The enantiomeric purities both of the diastereoisomeric imidazolidines and of the enantiopure diamines were checked by NMR spectroscopy.

Owing to the low symmetry (*C*_s) of the molecules, all groups have different features. In each imidazolidine the methyl groups located at the asymmetric centers (C4 and C5) show up as two sharp signals, the positions of which are temperature-dependent. The better peak separation is found at 30 °C in CD₃OD. When the NMR spectrum of a mixture of imidazolidines – (*S,R,R*)-**2**/(*S,S,S*)-**2** (1:3) – was recorded, integration of the signals gave an (*S,R,R*)-**2**/(*S,S,S*)-**2** ratio of 0.335. In CD₃OD, the H_α (on the imidazolidine ring) and H_β (carried by the third chiral center) protons show up as a complex pattern in the middle field region of the spectra. In [D₆]DMSO, however, they are well separated and exhibit a doublet and a quintet pattern, respectively, with equal couplings of about 5 Hz.

A similar study was performed for diamines (*S,S*)-**3** and (*R,R*)-**3**, with which diastereoisomeric derivatives were equally successfully formed in situ by addition of two equivalents of enantiopure (*S*)-mandelic acid. From these NMR studies it was concluded that the enantiomeric excesses of the imidazolidines (*S,R,R*)-**2** and (*S,S,S*)-**2** and the diamines (*S,S*)-**3** and (*R,R*)-**3** were the same as that of the enantio-



Scheme 2. Strategy for the resolution of the racemic mixture of diamines **3**; a) (*S*)-R'OCH(Me)CHO/Et₂O, b) HCl 10%

pure aldehyde used for the resolution: at least 96%. These diamines are volatile compounds, not conveniently characterizable in the pure form but only indirectly through their numerous derivatives.

Unfortunately, none of the diastereoisomeric imidazolidines was a crystalline compound, so no absolute configuration could be determined by X-ray crystallography. Moreover, attempts to prepare the corresponding nitroxide free radicals were frustrating, because extensive degradation of the O-silyl group occurs during the oxidation process. However, imidazolidines derived from methyl (*R*)-(3-phenylphenoxy)-2-propionate^[15c] were safely oxidized into the corresponding nitronyl nitroxides **5E**. Although these nitroxides were not crystalline compounds, their complexes with manganese(II) bis(hexafluoroacetylacetonate) were solid species, and single crystals of the form derived from (*R,R*)-**3** [(*R,R,R*)-**5E**·Mn(hfac)₂] were successfully grown.

The crystal structure of (*R,R,R*)-**5E**·Mn(hfac)₂^[20] (Figure 1) shows a polymeric chain structure with parameters close to those already described for the complex involving the analogous tetramethylated nitronyl nitroxide.^[15c] The metal ions are *cis*-coordinated by oxyl oxygen atoms of two radicals at distances of 2.129 (3) and 2.138 (4) Å, comparable to those observed in most manganese(II) nitroxide chain complexes reported so far.^[2b]

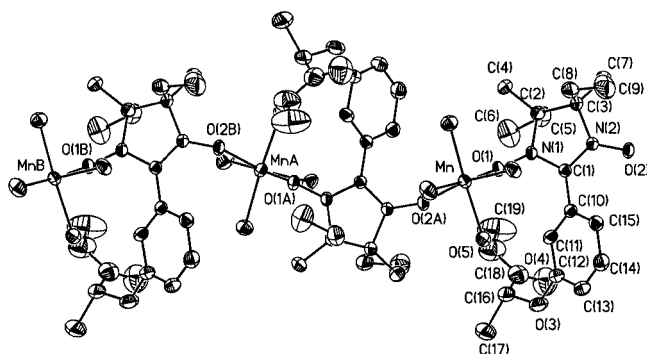


Figure 1. Part of the chain structure of complex (*R,R,R*)-**5E**·Mn(hfac)₂; only the free radical ligand and the metal coordination sphere are shown; selected parameters [Å, °]: Mn–O1 = 2.138, Mn–O2 = 2.129, O1–N1 = 1.288, O2–N2 = 1.293, Mn–O1–N1 = 126.9, Mn–O2–N2 = 130.0, O1–Mn–O2 = 89.8

From the known (*R*) configuration at the stereogenic center in the lactate substituent (carbon atom C16), the configurations at C4 and C5 are also (*R*) and the configuration at the metal center *A*. The (*S,S*) and (*R,R*) configurations were therefore assigned to the samples of the enantiopure diamines **3** derived from **2a** and **2b**, respectively.

As well as defining the absolute configurations of the synthetic precursors unambiguously, the complex (*R,R,R*)-**5E**·Mn(hfac)₂ also shows that the presence of ethyl substituents at the 4- and 5-positions in these chiral nitronyl nitroxides does not hamper their coordination capabilities. One observes that the ligand retains its bridging character, a very important property for designing extended exchange coupled species.^[21]

Nitronyl Nitroxides

The synthesis of a series of homochiral nitroxides from *meso*-, *rac*-, or enantiopure diamines is straightforward, by the procedure described elsewhere for tetramethylated analogues.^[8] Condensation of *meso*-**3**, *rac*-**3**, (*R,R*)-**3**, or (*S,S*)-**3** with any aldehyde almost quantitatively gave the corresponding imidazolidines, which were oxidized in fair to good yields by *m*-chloroperoxybenzoic acid and NaIO₄.^[8] Although mixtures of isomeric imidazolidines differing in the configuration at the C2 carbon atom were obtained in the *meso* series, no attempts were made to characterize each isomer since oxidation of both results in a unique nitronyl nitroxide. However, imidazolidine *meso*-**4F**, derived from formaldehyde and existing as a unique isomer, was fully characterized by X-ray diffraction. Corresponding imino nitroxides were obtained as by-products in the latter oxidation process or quantitatively from the nitronyl nitroxides by a reported procedure.^[22] Note that the imino nitroxides **P6**, derived from *meso*-nitronyl nitroxides, are racemates, since these compounds present planar chirality (as indicated by the **P**) and no attempt was made to separate the enantiomers.

Table 1 reports selected properties of *meso*-, *rac*-, and enantiopure nitronyl and imino nitroxides derived from phenyl, *p*-nitrophenyl, *m*-pyridyl, and *tert*-butyl aldehydes, which were selected for comparison with tetramethylated analogues because of the following features: (i) the phenyl derivatives often show enhanced stability and are widely used as reference compounds, (ii) the tetramethylated *p*-nitrophenyl radical exists as a polymorph that is a purely organic magnet,^[3d] (iii) *m*-pyridyl derivatives are precursors of Cu^{II} molecular spin transition species,^[5] and (iv) the hindered *tert*-butyl derivative is a test for the efficiency of the synthesis.^[8]

Physical Properties

This study focuses on properties related to the presence of ethyl groups in all compounds and on chirality in the enantiopure series, both features that were expected to result in structural arrangements different from those seen in the tetramethylated analogues, in particular in chiral space groups for enantiopure compounds and in different coupling pathways in the solid state. In addition, the introduction of chirality close to the oxyl groups was expected to show up strongly in the optical properties of the enantiopure nitroxides.

Structural Studies

These new nitroxides have lower melting points than the tetramethylated analogues,^[7] probably because of the presence of the ethyl groups, which do not favor close packing in the crystals. However, all nitronyl nitroxides belonging to the more “symmetrical” *meso* series are crystalline compounds. Of the twenty-two nitroxides described in the synthetic section, eleven nitronyl nitroxides and only two imino nitroxides (the enantiomeric phenyl derivatives) were solids at room temperature; they were all isolated as single crystals

Table 1. Selected properties of nitronyl nitroxides **5** and imino nitroxides **6**

Compound	<i>meso</i>	<i>rac</i>	Enantiopure	
R	M.p. [°C]	M.p. [°C]	M.p. [°C]	$[\alpha]$ ($T = 26\text{ }^{\circ}\text{C}$, CHCl_3)
Phenyl	73 <i>meso</i> - 5A	—	71 (<i>S,S</i>)- 5A (<i>R,R</i>)- 5A	$[\alpha]_{436} = +409$ ($c = 0.51\text{ mg/mL}$) $[\alpha]_{436} = -401$ ($c = 0.49\text{ mg/mL}$)
<i>p</i> -Nitrophenyl	134	—	124 (<i>S,S</i>)- 5B (<i>R,R</i>)- 5B	$[\alpha]_{546} = +238$ ($c = 0.21\text{ mg/mL}$) $[\alpha]_{546} = -220$ ($c = 0.16\text{ mg/mL}$)
<i>m</i> -Pyridyl	<i>meso</i> - 5B 64 <i>meso</i> - 5C	oil <i>rac</i> - 5C	oil (<i>S,S</i>)- 5C (<i>R,R</i>)- 5C	$[\alpha]_{436} = +280$ ($c = 0.2\text{ mg/mL}$) $[\alpha]_{436} = -277$ ($c = 0.2\text{ mg/mL}$)
<i>tert</i> -Butyl	18–22 <i>meso</i> - 5D	—	16–20 (<i>S,S</i>)- 5D	$[\alpha]_{436} = +699$ ($c = 0.16\text{ mg/mL}$)
Phenyl	oil <i>rac</i> - P6A	—	64 (<i>S,S</i>)- 6A (<i>R,R</i>)- 6A	$[\alpha]_{436} = +101$ ($c = 0.51\text{ mg/mL}$) $[\alpha]_{436} = -99$ ($c = 0.54\text{ mg/mL}$)
<i>p</i> -Nitrophenyl	oil <i>rac</i> - P6B	oil <i>rac</i> - 6B	oil (<i>S,S</i>)- 6B	$[\alpha]_{546} = +27$ ($c = 0.202\text{ mg/mL}$)
<i>m</i> -Pyridyl	oil <i>rac</i> - P6C	— (<i>R,R</i>)- 6C	oil	
<i>tert</i> -Butyl	oil	—	oil	
<i>rac</i> - P6D	(<i>S,S</i>)- 6D	$[\alpha]_{436} = +86$ ($c = 0.16\text{ mg/mL}$)	oil	

and were studied by X-ray diffractometry. Note that the Flack parameter^[23] (inconclusive for all compounds except (*R,R,R*)-**5E**·Mn(hfac)₂) was never used for assigning the absolute configuration of the enantiopure radicals; safely, absolute configurations were derived from that of the diamino precursor **3** and the crystal data were processed accordingly.^[24] Molecular structures of (*S,S*)-**5A** and (*S,S*)-**6A** (phenyl-substituted) are displayed in Figure 2 as illustrations of the enantiopure nitronyl and imino series. Both crystallize in chiral space groups as expected: $P2_12_12_1$ for the former and $P2_1$ for the latter. The nitronyl nitroxide displays two different molecules in the asymmetric unit, as also observed for *meso*-**5B** (*p*-nitrophenyl), *meso*-**5C** (3-pyridyl), and the tetramethylated analogue;^[9a,25] in contrast there is only one molecule in the cases of nitronyl nitroxides *meso*-**5A**,^[8] (*S,S*)-**5B**, and the imino nitroxide (*S,S*)-**6A**.

This propensity for crystallizing as different conformers in the same crystal is already documented for nitronyl nitroxides,^[26] but the presence of non-rigid ethyl groups in these series may well be another important factor diminishing the chance of having a single conformer.

The conformations of the aromatic substituted nitronyl and imino nitroxides in the solid state were analyzed according to a recent study,^[27] by use of the torsion angles T_{IM} (defined as the N1–C5–C4–N2 angle) and A_{PNN} (the mean of the torsion about the bond indicated in Figure 3) to specify the puckering of the five-membered ring and the relative orientation of the two rings respectively, and of T_1 and T_2 (where T_1 is the angle C4–C5–CH₂–CH₃ and T_2 is C5–C4–CH₂–CH₃) to describe the orientations of the ethyl groups. Note that the sign of the angle T_{IM} is *opposite* to that of the helicity shown in the imidazolyl ring, as defined by the angle between planes formed by the NCN bonds and the C4–C5 bond.^[28] The results are summarized in Table 2.

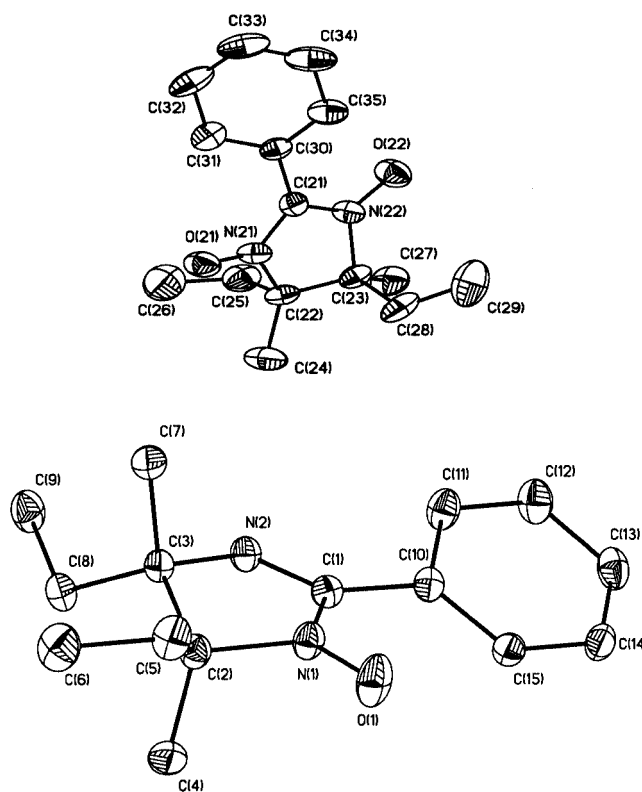


Figure 2. Molecular structure of chiral nitronyl nitroxide (*S,S*)-**5A** (only molecule A is represented) and imino nitroxide (*S,S*)-**6A**; thermal ellipsoids are drawn at the 30% probability level

The mean values of T_{IM} (25.6°) and A_{PNN} (25.6°) fall well within the statistically significant range independently of the presence of the ethyl groups. *Pseudo-eclipsed* conformations, described as (*MP*) or (*PM*)^[27,28] and corresponding to the more planar conformations, are observed in all

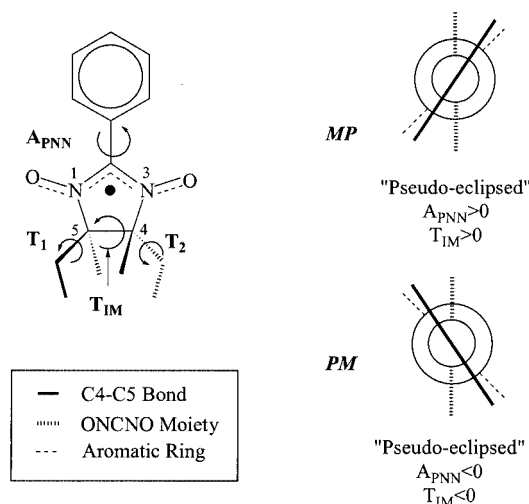


Figure 3. Definition of torsion angles used in the conformational analysis

Table 2. Selected parameters – T_{IM} , A_{PNN} [°], the puckering amplitude (Ψ_M), and the puckering phase angle (Φ) – for describing the conformations of the solid aromatic-substituted nitroxides; for the (*S,S*) series the angles have opposite sign

Compound	T_{IM}	A_{PNN}	Descriptor	T_1	T_2	Ψ_M	Φ
<i>meso</i> -5A	$\pm 27.3 \pm 31.7$	(PM) and (MP)	± 72.6	± 163.8	29.7	–5.7	
<i>meso</i> -5B							
A	$\pm 25.5 \pm 20.4$	(PM) and (MP)	± 72.6	± 69.4	27.7	–0.5	
B ^[a]	$\pm 27.7 \pm 28.0$	(PM) and (MP)	± 153.2	± 166.8	30.1	–5.7	
				± 69.9	± 73.8		
<i>meso</i> -5C							
A	$\pm 23.0 \pm 33.2$	(PM) and (MP)	± 67.5	± 72.5	22.9	–2.3	
B	$\pm 23.2 \pm 29.3$	(PM) and (MP)	± 64.3	± 72.1	25.0	5.4	
(<i>R,R</i>)-5A							
A	$+25.6 \pm 29.3$	(MP)		$+169.7 \pm 80.5$	27.6	4.1	
B	$+28.6 \pm 27.6$	(MP)		$+167.6 \pm 168.0$	30.9	0.9	
(<i>R,R</i>)-5B	$+29.3 \pm 23.4$	(MP)		$+160.5 \pm 163.3$	31.7	–0.6	
(<i>R,R</i>)-6A	$–23.1 \pm 21.0$	(PM)		$–177.3 \pm 69.9$	–	–	
Mean ^[b]	25.6	25.6		68.6	72.6		
	167.6	165.5					

[a] Disordered ethyl groups. [b] Absolute value.

compounds. While this form is predominant in the tetramethyl analogues in the solid state since it favors dense packing, it is striking that *none* of the compounds studied here shows the *pseudo-anti* arrangement. Furthermore, the puckering amplitudes (Ψ_M) – describing the maximum torsion angle that one of the endocyclic bonds can adopt as a result of out-of-plane distortion – calculated by a standard procedure from all the angles in the imidazolyl ring came within the range (although in general at the upper limit) of those seen in the tetramethyl analogues, where the average value for this parameter is 24° .^[27] Most values for the nitronyl nitroxides described here are close to 30° (Table 2), indicating larger of the ring than in the case of the tetramethyl-substituted compounds. Furthermore, the puckering phase angles (Φ) – describing the point on the ring where the maximum distortion occurs – of the chiral compounds are in general slightly displaced from 0 (the average value it

takes in the tetramethyl analogues^[26]) indicating a slightly different conformational nature.

Since the torsion angles are related to chirality,^[27] this behavior was further analyzed for the few enantiopure compounds. One can observe that T_{IM} and A_{PNN} are positive for the (*R*) enantiomers, corresponding to the (*MP*) diastereomeric conformation, while they are negative for the (*S*) series, corresponding to the (*PM*) conformation. These situations are favorable since they minimize steric interactions between the ethyl groups.

Thus, it clearly appears that the configuration at the carbon center drives the puckering of the imidazolyl ring and the position of the aromatic substituent according to steric preferences associated with chirality. However, it is not possible to make a firm statement about the helicity associated with A_{PNN} , since its sign seems better related with the preference of the molecule to adopt a planar *pseudo-eclipsed* conformation, as already reported for the tetramethylated achiral analogues.^[26,27]

With regard to the ethyl groups, the values of T_1 and T_2 are distributed between two sets, A (ca. 70°) and B (ca. 166°), corresponding to two preferred orientations of the terminal methyl, roughly perpendicular or parallel to the C4–C5 bond; the resulting conformation in each case matches an expected preferred *gauche* conformation and keeps the molecule as a whole approximately planar. Examination of Table 2 shows that all combinations (AA, AB, BB) are found and are probably close in energy, as shown by the presence of different conformers in the same crystal. For each possibility, the relative sign of the torsion angles is such that the terminal methyl groups are located as far apart as possible. Surprisingly, however, in some compounds one of these methyl groups points toward the five-membered ring but only when the sign of T_{IM} corresponds to the ring distortion that minimizes interactions with the closest oxyl group of the ring. Therefore, correlation between the orientation of the ethyl groups with chirality and the T_{IM} angle is only indirect.

Finally, as shown in Table 3, distances and angles in all nitroxides are within the ranges expected for nitroxide free radicals and do not need further comments.

Table 3. Selected structural [$\text{\AA}$, °] and Weiss (θ [K]) parameters

Compound	N1–O1	N2–O2	N1–C1	N2–C1	N1–C1–N2	θ
<i>meso</i> -5A	1.287(1)	1.283(1)	1.346(1)	1.344(2)	108.3(2)	–3.9(1)
<i>meso</i> -5B						+1.2(3)
A	1.282(2)	1.280(2)	1.352(3)	1.353(2)	107.7(2)	
B	1.279(2)	1.284(2)	1.350(2)	1.349(2)	108.1(2)	
<i>meso</i> -5C						–1.3(1)
A	1.279(1)	1.277(1)	1.345(2)	1.347(2)	108.8(1)	
B	1.278(1)	1.277(1)	1.354(2)	1.345(2)	108.5(1)	
(<i>R,R</i>)-5A						–2.2(2)
A	1.300(5)	1.274(5)	1.328(6)	1.335(6)	109.1(5)	
B	1.264(4)	1.278(4)	1.341(6)	1.329(5)	108.7(4)	
(<i>S,S</i>)-5B	1.280(2)	1.282(3)	1.358(3)	1.362(3)	106.9(2)	–1.8(1)
(<i>R,R</i>)-6A	1.276(2)	–	1.397(2)	1.288(2)	113.0(2)	+1.1(2)
Mean	1.280(3)	1.279(3)	1.352(4)	1.339(4)	108.8(3)	

Magnetic Properties

The magnetic behavior of the compounds described here was investigated in the solid state by magnetometry and in solution by EPR and ENDOR spectroscopy in order to obtain insight into modifications of the spin distribution associated with the presence of ethyl groups.

In the solid state, the magnetic behavior of these nitroxides is characterized by weak values of θ , which suggest weak interactions (Table 3, last Entry). This result is not surprising, since the magnitude of intermolecular interactions would be expected to suffer from the steric demand of the ethyl groups. Figure 4 displays the variation in χT with temperature for *meso*-**5B** and (*S,S*)-**5B**, *meso* and enantiopure forms of the same *p*-nitrophenyl-substituted radical, which illustrate ferro- and antiferromagnetic behavior, respectively. Attempts to correlate these features with crystal packing and close intermolecular contacts were unsuccessful. In particular, there are no close intermolecular contacts between NO₂ and oxyl groups of neighboring molecules in either compound, as observed in the methylated analogue. A recent study devoted to tetramethylated analogues^[26] concluded that no correspondence could be established between the nature of intermolecular magnetic interactions and the geometry of close contacts. In the present case, such a study was even more hopeless, owing to different cell contents and different conformations.

The few compounds exhibiting dominant intermolecular ferromagnetic interactions will be investigated at lower temperature to verify whether or not they order.

In solution (10⁻³ M in CH₂Cl₂), the EPR spectra of *meso*-**5A** and (*S,S*)-**5A** each exhibit the expected five-line pattern attributable to coupling of the unpaired electron with two equivalent ¹⁴N nuclei, whereas the hyperfine pattern of (*R,R*)-**6A** is composed of seven lines, due to the presence of two non-equivalent ¹⁴N nuclei.^[7,29] Additional hyperfine structure due to other magnetically active nuclei was not observed, either in other solvents or for radicals in which the phenyl substituent is deuterated (*vide supra*). Values of hyperfine coupling constants (*hfccs*) are listed in Table 4. The numbering scheme used for the various *hfccs* reported in Table 4 corresponds to the one used in Figure 2 for (*S,S*)-

6A. For the sake of comparison, previously reported values^[30] for a *p*-nitrophenyl nitronyl nitroxide (noted as NIT-Ph) are given in the last column of Table 4.

ENDOR spectra were recorded as described previously.^[30] For phenyl non-deuterated *meso*-**5A** and (*S,S*)-**5A**, one observes four and three pairs of lines, respectively (Figure 5a, c), each symmetrically split around the free ¹H NMR frequency, in agreement with previous studies.^[30] In all studied compounds, the ¹⁴N ENDOR resonance was observed at half the hyperfine coupling of ¹⁴N (inset in Figure 5).

With reference to the ¹H nuclei of the five-membered ring, the phenyl group was fully deuterated in radicals *meso*-**5A**, (*S,S*)-**5A**, and (*R,R*)-**6A**.^[31] The ENDOR spectra of [D₅]-*meso*-**5A**, [D₅]-(*S,S*)-**5A**, and [D₅]-(*R,R*)-**6A** show two, one, and four pairs of lines, respectively, attributable to the coupling constants on methyl and ethyl hydrogen atoms (Figure 5b, d; Table 4). In order to help in the assignment of the various ¹H signatures, DFT calculations were performed. The results for all similar groups could be accurately related to those of previous theoretical studies.^[29,32] The overall assignment was carried out consistently with the trends shown by numerical calculations and with previous results.^[30] Table 4 shows an interesting effect in the apparent larger spin density distribution over the ethyl group than over the methyl group in the corresponding tetramethylated compound. This may be due to spin polarization. The asymmetry of the spin distribution in (*R,R*)-**6A** is readily apparent and was previously determined for the non-hydrogen atoms.^[32] The spin density is not negligible up to the terminal methyl protons of the ethyl group.

Optical Properties

The UV/Vis absorption spectra of all compounds are identical to those of the tetramethylated analogues,^[7] the $n \rightarrow \pi^*$ transition of the radical moiety for the phenyl nitronyl nitroxide derivatives being centered at about 640 nm, while the $\pi \rightarrow \pi^*$ transition occurs at 365 nm. This study concentrates on properties associated with the chirality of the compounds by circular dichroism (CD).

The solution state CD spectra of the two enantiomers of the phenyl nitronyl nitroxides **5A** (Figure 6) reveal a broad Cotton effect of moderate intensity centered on 425 nm, followed by an intense exciton coupled effect at approximately 365 nm, which coincides with the absorption maximum for the $\pi \rightarrow \pi^*$ transition. There are no detectable Cotton effects in the region corresponding to the $n \rightarrow \pi^*$ transition at 640 nm. It should be pointed out that the magnitudes of the Cotton effects are much greater than those observed for the chiral radicals prepared to date in which the stereogenic center is located on the phenyl substituent at the 2-position of the imidazolyl ring, remote from the radical chromophore.^[15b,15c] In the compounds here, the stereogenic centers are very close to the chromophore and in addition cause greater conformational restrictions, both important factors in determining the magnitude of the Cotton effects. The intensity of the Cotton effects is dramatically lower in the

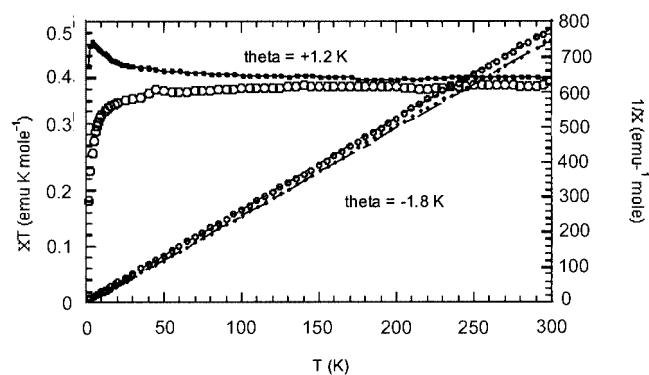


Figure 4. Solid-state magnetic behavior of the *p*-nitrophenyl-substituted nitronyl nitroxides *meso*-**5B** (solid circles) and (*S,S*)-**5B** (open circles) in the form of χT vs. T and $1/\chi$ vs. T .

Table 4. Experimentally acquired isotropic hyperfine coupling constants (in mT); the atom numbering corresponds to Figure 2 for (*S,S*)-**6A**; NIT-Ph stands for a previously studied *p*-nitrophenyl nitronyl nitroxide derivative^[30]

	(<i>S,S</i>)- 5A Deuterated	Non-deuterated	<i>meso</i> - 5A Deuterated	Non-deuterated	(<i>R,R</i>)- 6A Deuterated	NIT-Ph ^[30]
<i>a</i> (N1)	0.747	0.747	0.752	0.752	0.907	—
<i>a</i> (N2)	0.747	0.747	0.752	0.752	0.413	—
<i>a</i> (C4H ₃)	0.019	0.019	0.018	0.019	0.066	0.020
<i>a</i> (C5H ₂)	0.027	0.027	—	—	0.035	0.020 ^[a]
<i>a</i> (C6H ₃)	—	—	—	—	0.021	—
<i>a</i> (C7H ₃)	0.019	0.019	0.018	0.019	0.012	0.020
<i>a</i> (C8H ₂)	0.027	0.027	—	—	—	0.020 ^[a]
<i>a</i> (C9H ₃)	—	—	—	—	—	—
<i>a</i> (11-H)	—	0.050	—	0.050	—	0.052
<i>a</i> (12-H)	—	—	—	—	—	0.029 ^[b]
<i>a</i> (13-H)	—	0.044	—	0.043	—	0.047

^[a] Methyl groups instead of ethyl groups. ^[b] Very weak signals reported.

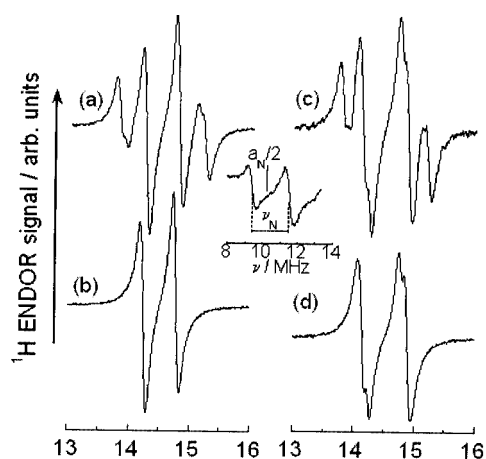


Figure 5. Liquid-phase ¹H-ENDOR spectra recorded at 285 K in paraffin oil for: (a) *meso*-**5A**, (b) *meso*-**5A** with deuterated phenyl group, (c) (*S,S*)-**5A**, (d) (*S,S*)-**5A** with deuterated phenyl group; inset: ¹⁴N-ENDOR spectrum for (*S,S*)-**5A**

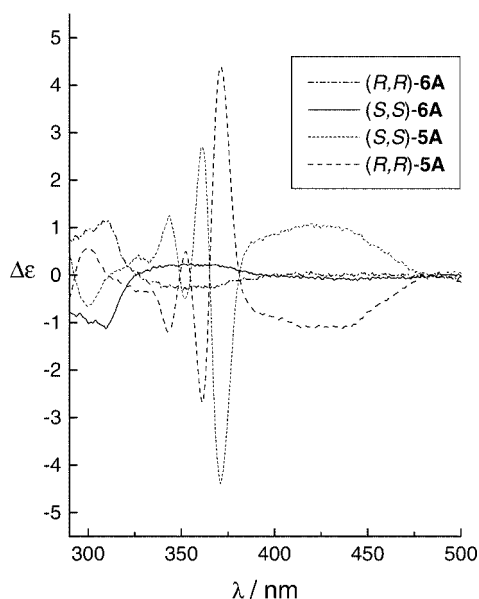


Figure 6. Solution-state CD spectra of the chiral nitronyl and imino nitroxides recorded in THF at room temperature

imino nitroxides **6A**. The absorptions are weaker and shifted with respect to their more conjugated cousins.

In the solid state (Figure 7), all the radicals show general CD spectral features similar to those seen in solution, except that for the nitronyl nitroxides the band at 450 nm appears somewhat sharper than in solution and the exciton coupled band is not observed in the solid state, an effect possibly due either to the broadness of the bands in the solid or to interaction of neighboring molecules with the chromophores. In any case, we can confirm that the overall conformation must be very similar in the two states, given the similarities in the spectra, in line with the rigid nature imposed on the imidazolyl ring by the bulky groups at the 4- and 5-positions. It is also interesting to note that the signs and positions of the Cotton effects are in general agreement with those calculated for the corresponding conformational isomers.^[27]

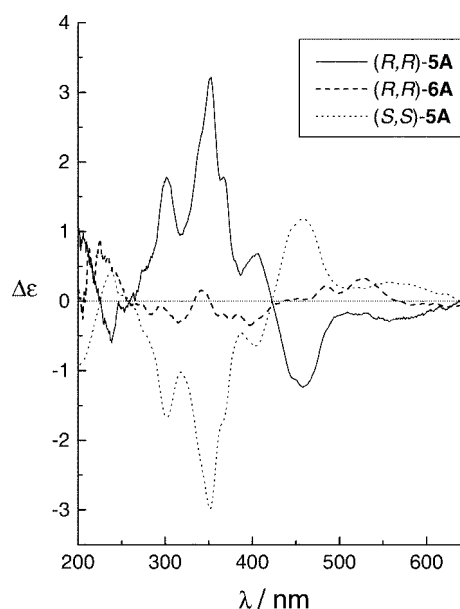


Figure 7. Solid-state CD spectra of the chiral nitronyl and imino nitroxides recorded in KBr discs at room temperature

Conclusion

The chiral, enantiopure precursors (3*S*,4*S*)-(+)- and (3*R*,4*R*)-(–)-3,4-diamino-3,4-dimethylhexane have been prepared and their absolute configurations established. Condensation with aldehydes quantitatively afforded chiral imidazolidines, which were oxidized into the corresponding enantiopure nitronyl and imino nitroxides.

The nitronyl nitroxide building blocks include identical chiral centers adjacent to the oxyl groups and since they exhibit C_2 symmetry they are well suited for coordination chemistry studies as stereochemical complexity is minimized. As an example, the complex (*R,R,R*)-**5E**·Mn(hfac)₂, which has a chain structure in which the two oxyl groups are coordinated, not only unambiguously establishes the absolute configurations of the precursors, but also demonstrates that, despite the presence of ethyl groups close to the oxyl coordination sites, these nitronyl nitroxides retain their bridging character while presenting appreciable optical activity, and are thus good candidates for the designing of chiral magnetic materials that may show interesting magneto-optical properties.

Experimental Section

Synthesis: All reagents were from Aldrich and were used as received, except for *m*-chloroperoxybenzoic acid, which was purified by washing with a phosphate buffer (pH = 7.5) and dissolved in CH₂Cl₂, and the solution was dried with Na₂SO₄. After evaporation of the solvent, the resulting solid was dispersed in *n*-pentane and dried by azeotropic removal of the last traces of water. Iodometric assay indicated 97% purity.

Magnetic Measurements: Magnetic susceptibility data were collected by use of a Quantum Design SQUID susceptometer working at a 0.5 T field strength in the 2–400 K temperature range. The SQUID outputs were corrected for the contribution of the sample holder, and the magnetic susceptibilities were corrected for the diamagnetic contribution of the constituent atoms by use of Pascal constants. EPR and ENDOR experiments were performed at room temperature with a BRUKER ESP 300E spectrometer operating at X-band, and equipped with an RF amplifier ENI 300. Samples for EPR and ENDOR measurements were prepared by dissolving radicals in CH₂Cl₂, and by then mixing 10% of this solution in paraffin oil. The resulting solution was degassed by thaw-freeze pumping cycles.

Computational Methods: The DFT calculations were performed by use of Gaussian 03^[33a] by the hybrid B3LYP method with Becke's^[33b] three-parameter non-local exchange potential coupled to the non-local correlation functional of Lee et al.^[33c] The basis set used for the radical – namely, 6-31+g* – was used in order better to describe the region far from the nuclei covered by the unpaired electron in open-shell systems.

Crystal Structure Determinations: These were carried out with the aid of a Bruker SMART system (Mo- K_{α} , λ = 0.71073 Å, graphite monochromator). The data were processed by use of the SAINT^[34a] data reduction software, the structure was solved with the aid of the SHELXTL^[34b] software package, and the absolute structure of the crystal used was established as described by

Flack.^[23] CCDC-233359 (*rac*-**1**), -233360 (*rac*-**3**·HCl), -233356 (*meso*-**4F**), -152832 (*meso*-**5A**), -233357 (*meso*-**5B**), -233358 (*meso*-**5C**), -233364 (*S,S*)-**5A**], -233361 [(*R,R*)-**5B**], -233362 [(*R,R*)-**6A**], and -233363 [(*R,R,R*)-**5E**·Mn(hfac)₂] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].

Circular Dichroism Measurements: Circular dichroism spectra were recorded with a JASCO-715 spectropolarimeter, and were processed by use of the associated software. The solution spectra have background solvent spectra subtracted, while the solid-state spectra were recorded in ground KBr discs of the compounds by the method reported elsewhere.^[15b]

Mixture of *meso*- and *rac*-3,4-Dimethyl-3,4-dinitrohexane (1): The crude dinitro compound could be prepared according to a reported procedure.^[17] Alternatively, the yield was improved as follows: LiOMe (3.7 g, 0.097 mol) was dissolved in dry DMF (125 mL), and *rac*-2-nitrobutane (10 g, 0.097 mol) was added. This solution was stirred at room temperature for 15 min, and the solution was then cooled in a ice bath. A solution of iodine (12.3 g, 0.0485 mol) in DMF (100 mL) was added dropwise until the brown color had disappeared. After the system had been stirred for additional 2 h, H₂O (1.5 L) was added. A white precipitate was immediately observed and filtered. This precipitate was dissolved in diethyl ether and washed with three portions (100 mL) of sodium thiosulfate (20%) solution. After drying (Na₂SO₄) and evaporation of the solvent, one obtained 8.3 g (84%) of a mixture of the two dinitro isomers, which was used in the next step.

Separation of *meso*- and *rac*-3,4-Dimethyl-3,4-dinitrohexane (1): Quantitative large-scale (50 g) separation of the *meso* and *rac* forms was performed by HPLC on an SiO₂ (60 µm) semi-preparative column eluted with hexane/ethyl acetate (90:10). The compound eluted first was *meso*-**1** (m.p. 90–91 °C). ¹H NMR (500 MHz, 20 °C, CDCl₃): δ = 0.93–0.95 (t, 3 H, CH₃–CH₂), 1.66 (s, 3 H, CH₃), 1.76–1.80 (m, 1 H, CH₂), 2.54–2.58 (m, 1 H, CH₂) ppm. The compound eluted second was *rac*-**1** (m.p. 86–87 °C). ¹H NMR (500 MHz, 20 °C, CDCl₃): δ = 0.91–0.94 (t, 3 H, CH₃–CH₂), 1.59 (s, 3 H, CH₃), 2.12–2.07 (m, 1 H, CH₂), 2.61–2.56 (m, 1 H, CH₂) ppm.

***meso*-(or *rac*)-3,4-Diamino-3,4-dimethylhexane (3):** These were obtained by a slight modification of a reported procedure;^[17] *meso*-(or *rac*)-3,4-dimethyl-3,4-dinitrohexane (**1**, 5.1 g, 25 mmol) was suspended in concentrated hydrochloric acid (37%, 60 mL). Granular Sn (50 g) was then added in five portions at 1/2 h intervals, and the mixture was heated at reflux for 2 h. After cooling, the clear solution was extracted with diethyl ether, and the aqueous phase was made strongly basic with sodium hydroxide pellets (40 g) and centrifuged to get rid of a viscous precipitate. The aqueous solution was extracted with dichloromethane (4 × 50 mL), the solvent was distilled off, and the residual oil was dried with pentane; *meso*-(or *rac*)-3,4-diamino-3,4-dimethylhexane was obtained as a colorless liquid (2.3 g, 64%). *meso*-**3**: ¹H NMR (400 MHz, 20 °C, CDCl₃): δ = 0.991 (t, 3 H, CH₃–CH₂, J = 7.37 Hz), 1.176 (s, 3 H, CH₃), 1.567–1.622 (m, 2 H, CH₂–CH₃) ppm. *rac*-**3**: ¹H NMR (400 MHz, 20 °C, CDCl₃): δ = 0.994 (t, J = 7.37 Hz, 3 H, CH₃–CH₂), 1.094 (s, 3 H, CH₃), 1.563–1.618 (m, 2 H, CH₂) ppm.

Resolution of *rac*-3,4-Diamino-3,4-dimethylhexane (2): The racemic mixture of **3** (1 g, 6.9 mmol) was treated in diethyl ether for 20 h with enantiopure (*S*)-(–)-*O*-(*tert*-butyldiphenylsilyl)acetaldehyde

{2.2 g, 7 mmol, $[\alpha]_D = -8.5$ (21 °C, $c = 13.4$ mg/mL, ethanol)}, prepared by a reported procedure.^[18] The solution was dried with Na_2SO_4 and concentrated under vacuum, and the mixture of diastereoisomers, (*S,S,S*)-**2** and (*S,R,R*)-**2**, was separated by flash chromatography (SiO_2 , 15 μm ; $p = 2$ bar) with elution with hexane/ethyl acetate (80:20). (*S,S,S*)-**2**: 1.4 g, 93%, $[\alpha]_{436} = +5$ (25 °C, $c = 4.12$ mg/mL) and $[\alpha]_{589} = +3$ (25 °C, $c = 3.49$ mg/mL). ^1H NMR (400 MHz, 30 °C, CD_3OD): $\delta = 0.845$ (s, 3 H, CH_3), 0.889 (t, $J = 7.6$ Hz, 3 H, $\text{CH}_3\text{--CH}_2$), 0.918 (t, $J = 7.6$ Hz, 3 H, $\text{CH}_3\text{--CH}_2$), 1.019 (s, 3 H, CH_3), 1.08 (d, $J = 5$ Hz, 3 H, $\text{CH}_3\text{--CH}_\beta$), 1.077 (s, 9 H, *t*Bu), 1.28–1.42 (m, 2 H, $\text{CH}_2\text{--CH}_3$), 1.46–1.58 (m, 2 H, $\text{CH}_2\text{--CH}_3$), 3.74–3.83 [m, 2 H, $H_\beta \pm H_\alpha$ (see text)], 7.38–7.77 (m, 10 H aromatic) ppm. (*S,R,R*)-**2**: 1.35 g, 90%, $[\alpha]_{436} = -7.7$ (25 °C, $c = 3.5$ mg/mL) and $[\alpha]_{589} = -2.6$ (25 °C, $c = 3.46$ mg/mL). ^1H NMR (400 MHz, 30 °C, CD_3OD): $\delta = 0.898$ (t, 3 H, $\text{CH}_2\text{--CH}_3$), 0.924 (t, 6 H, $\text{CH}_2\text{--CH}_3$), 0.935 (s, 3 H, CH_3), 1.047 (s, 3 H, CH_3), 1.09 (d, $J = 5$ Hz, 3 H, $\text{CH}_3\text{--CH}_\beta$), 1.082 (s, 9 H, *t*Bu), 1.3–1.42 (m, 2 H, $\text{CH}_2\text{--CH}_3$), 1.48–1.58 (m, 2 H, $\text{CH}_2\text{--CH}_3$), 3.78–3.90 [m, 2 H, $H_\beta \pm H_\alpha$ (see text)], 7.38–7.77 (m, 10 H aromatic) ppm. The two fractions (1.4 and 1.35 g) were separately poured into H_2SO_4 (10%, 50 mL) and stirred at room temperature for 20 h. The solution was extracted with diethyl ether, made strongly basic with NaOH, and extracted again (4×50 mL) with CH_2Cl_2 . The two enantiomers (*S,S*)-**3** and (*R,R*)-**3** were obtained in 50–60% yields and had NMR spectra identical to that of the racemic mixture. (*S,S*)-**3**: $[\alpha]_{589} = +80$ (25 °C, $c = 0.1$ mg/mL, MeOH) and $[\alpha]_{365} = +250$ (25 °C, $c = 0.1$ mg/mL, MeOH). (*R,R*)-**3**: $[\alpha]_{589} = -78$ (25 °C, $c = 0.1$ mg/mL, MeOH) and $[\alpha]_{365} = -238$ (25 °C, $c = 0.1$ mg/mL, MeOH). Single crystals of the hydrochloride of the racemic diamine were grown by slow concentration of a THF solution and the X-ray structure was determined.

Absolute Configurations of (*S,S*)-3** and (*R,R*)-**3**:** A solution of enantiopure methyl (*R*)-(+)-(3-formylphenoxy)-2-propionate (70 mg, 0.35 mmol, $[\alpha]_D = +59.8$), (*R,R*)-**3** (50 mg, 0.35 mmol), and *p*-toluenesulfonic acid in toluene (20 mL) was heated at reflux with azeotropic removal of water for 3 h.^[35] The solvent was evaporated off under vacuum, and the resulting oil (*R,R,R*)-**4E** was dissolved in CH_2Cl_2 (15 mL). Saturated aqueous NaHCO_3 (12 mL) was then added, followed by MCPBA (137 mg) in CH_2Cl_2 (8 mL), and the mixture was stirred for 2 h. The blue organic phase was separated, dried, concentrated, and flash-chromatographed (SiO_2 , 15 μm ; Et_2O /petroleum ether, 50:50) to afford (*R,R,R*)-**5E** {73 mg, 0.2 mmol, 61%, $[\alpha]_{436} = -191$ (25 °C, 0.11 mg/mL, CHCl_3)} as a blue oil. The corresponding Mn^{II} complex, (*R,R,R*)-**5E**· $\text{Mn}(\text{hfac})_2$, was obtained by mixing this nitronyl nitroxide and Mn^{II} hexafluoroacetylacetonate (90 mg, 0.2 mmol) in heptane (10 mL) at 70 °C. Slow concentration of the solution in the dark afforded the complex (22 mg, 45%, m.p. 141 °C) as dark green crystals suitable for a X-ray diffraction study, which identified the (*S,S*) configuration for (*S,S*)-**3** and the (*R,R*) configuration for (*R,R*)-**3**.

meso-(or rac- or enantiopure)4,5-Diethyl-4,5-dimethylimidazolidines [meso-4** or rac-**4** or (*S,S*)-**4**/(*R,R*)-**4**]:** General procedure for meso-**4A**. Benzaldehyde (700 mg, 7 mmol) in diethyl ether (10 mL) was added dropwise to meso-3,4-diamino-3,4-dimethylhexane (meso-**3**, 1 g, 7 mmol) in diethyl ether (20 mL). Condensation was complete in a few minutes [except in the case of **4d** ($R = t\text{Bu}$) for which condensation was performed in boiling chloroform]. The solution was dried with Na_2SO_4 and the solvents were evaporated to provide meso-**4A** (1.67 g, 92%), meso-**4B** (86%), meso-**4C** (78%), meso-**4D** (69%), meso-**4F** (92%). For the meso series (symmetry C_s), except in the case of meso-**4F** ($R = \text{H}$), mixtures of the two possible isomers were obtained, depending on the stereochemistry at carbon

atom C2; in contrast, only single isomers were obtained in the rac and enantiopure series (symmetry C_2). The crude compounds were used for the following steps since oxidation of mixtures of isomers afforded unique free radicals. Single crystals of meso-**4F** were obtained from methanol solutions at 6 °C and the crystal structure was solved.

meso-(or rac- or enantiopure)Nitronyl Nitroxides: The compounds meso-**5** or rac-**5** or (*S,S*)-**5**/(*R,R*)-**5** were obtained as recently reported,^[8] by oxidation of meso-**4** or rac-**4** or (*S,S*)-**4**/(*R,R*)-**4** (**A–F**) with *m*-chloroperoxybenzoic acid and sodium periodate. In a typical experiment, meso-**4A** (1 g, 4.31 mmol) was dissolved in a mixture of dichloromethane (100 mL) and a saturated solution of NaHCO_3 (50 mL). The solution was cooled in an ice bath, and a solution of *m*-chloroperoxybenzoic acid (2.85 g, 2.5 equiv.) in CH_2Cl_2 (20 mL) was added dropwise, followed, after 1 h, by NaIO_4 (1.4 g, 1.5 equiv.) in water (30 mL). Stirring was continued for 1/2 h. The organic phase was dried with Na_2SO_4 and concentrated, and the residue was chromatographed (SiO_2 , diethyl ether). The imino nitroxide (rac-P**6A**, 198 mg, 19%) and the nitronyl nitroxide meso-**5A** (810 mg, 72%), meso-**5B** (75%), meso-**5C** (52%), meso-**5D** (75%), rac-**5C** (61%), (*S,S*)-**5A** (58%), (*R,R*)-**5A** (62%), (*S,S*)-**5B** (49%), (*R,R*)-**5B** (53%), (*S,S*)-**5C** (46%), (*R,R*)-**5C** (49%), and (*S,S*)-**5D** (60%) were eluted successively. Nitroxides meso-**5A–C** and (*S,S*)-**5A–B** were obtained as single crystals suitable for X-ray diffraction studies by slow concentration of hexane solutions, except for meso-**5B**, which crystallized from methanol. **Imino Nitroxides:** meso-P**6**, rac-**6**, (*S,S*)-**6**, or (*R,R*)-**6** were obtained in low yield as by-products in the syntheses of the corresponding nitronyl nitroxides or quantitatively from the nitronyl nitroxides **5** by a reported procedure.^[22] Satisfactory elemental analyses were obtained for all compounds. Table 1 lists selected physical properties of these new nitroxides.

Acknowledgments

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- ^[20] **Crystal Data.** **a) (R,R,R)-5E·Mn(hfac)₂**: C₂₉H₂₉F₁₂N₂O₉, *M* = 832.48, orthorhombic, *P*2₁2₁2₁, *a* = 11.880(4), *b* = 14.302(5), *c* = 21.278(7) Å, *V* = 3615(2) Å³, *Z* = 4, *D*_{calcd.} = 1.530 Mg/m³, λ(Mo-K_α) = 0.71073 Å, *T* = 298(2) K, 21917 reflections collected, 8648 independent reflections, full-matrix, least-squares on *F*², 546 parameters, final *R* indices [*I* > 2σ(*I*): *R*₁ = 0.043, *wR*₂ = 0.10, Flack parameter −0.003(15). **b) (S,S)-5A**: C₁₅H₂₁N₃O₂, *M* = 261.34, orthorhombic, *P*2₁2₁2₁, *a* = 9.920(2), *b* = 10.222(2), *c* = 28.391(7) Å, *V* = 2879.0(12) Å³, *Z* = 8, *D*_{calcd.} = 1.206 Mg/m³, 8561 reflections collected, 5646 independent reflections, full-matrix, least-squares on *F*², 343 parameters, final *R* indices [*I* > 2σ(*I*): *R*₁ = 0.0725, *wR*₂ = 0.1724. **c) (S,S)-6A**: C₁₅H₂₁N₃O, *M* = 245.34, monoclinic, *P*2₁, *a* = 7.1497(7), *b* = 10.0532(10), *c* = 10.1157(10) Å, β = 109.026(2)°, *V* = 687.27(12) Å³, *Z* = 2, *D*_{calcd.} = 1.185 Mg/m³, 4429 reflections collected, 2974 independent reflections, full-matrix least-squares on *F*², 247 parameters, final *R* indices [*I* > 2σ(*I*): *R*₁ = 0.0405, *wR*₂ = 0.094. CCDC-202737. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].
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