

Stereochemistry of Phenyl α -Nitronyl Nitroxide RadicalsMaria Minguet,^[a] David B. Amabilino,^[a] Joan Cirujeda,^[a] Klaus Wurst,^[b] Ignasi Mata,^[a] Elies Molins,^[a] Juan J. Novoa,^[c] and Jaume Veciana*^[a]

Abstract: An extensive investigation of the conformations adopted by the family of phenyl α -nitronyl nitroxides has been carried out. A database containing 110 crystal structures was used in a statistical study of the solid-state geometries and conformations of these radicals. This study revealed that the favoured conformations involve a twisted distortion in the imidazolyl rings and a twist between the aromatic and heterocyclic rings in the molecules. As a consequence, these radicals show two types of preferred conformations in the solid state: the *pseudo-anti* enantiomeric pair and the *pseudo-eclipsed* pair, the

latter type being the most statistically probable. A new chiral member of this group of radicals that bears a lactate moiety, (*R*)-**1**, and its corresponding racemic compound, (*R,S*)-**1**, have been prepared in order to study the influence of chiral induction from the stereogenic centre on the torsion angle between the aromatic and heterocyclic rings of the α -nitronyl nitroxides. The X-ray crystal structures of the enantiopure and race-

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mic compounds, which both reveal chains of molecules sustained by strong O–H \cdots O hydrogen bonds between the carboxylic acid group and the ON group of the radical in the solid, as well as their magnetic properties have been determined. Remarkably, the molecules with a given stereogenic centre have a single helical sense between their component rings, even in the racemic crystal. Chiral induction from the stereogenic centre to the radical unit has also been proved by CD spectroscopy in the solid state. The results of these experiments have been rationalised by ab initio calculations of the spectra.

Introduction

The presence of chirality can have a very profound influence on the properties of a wide range of molecular materials.^[1] In this regard, the creation of chiral open-shell materials is of particular interest,^[2] since the combination of optical activity and magnetic interactions can give rise to additional magneto-optical effects.^[3] In particular, cross-effects were predicted and subsequently observed between natural and magnetically induced optical activity, so-called magneto-chiral dichroism (MChD) in absorption or emission, and magneto-chiral

birefringence (MChB) in refraction.^[4] The optical properties of chiral systems are expected to be different for light propagating parallel or antiparallel to the direction of the magnetic field. The existence of this effect may be important for the development of magneto-optical devices.^[5] Nevertheless, before such a goal can be achieved, it is necessary to understand the optical properties of the open-shell molecules at the molecular level.

With this aim in mind, we have embarked on a research programme, whose primary objective is to synthesise purely organic chiral molecules of a radical nature and to study the interplay that exists between the conformation of the chiral molecules and their optical properties.^[6] The family of phenyl α -nitronyl nitroxides^[7] is particularly appealing in this regard, owing to the wide variety of magnetic behaviour that their crystals display,^[8, 9] and their stability, which has made them popular as components in molecular magnets.^[10] Few reports concerning chiral α -nitronyl nitroxide radicals have appeared, mainly directed towards their use as spin labels,^[11, 12] and to our knowledge neither their solid-state structures nor optical and magnetic properties have been investigated. Only very recently, Kahn and co-workers reported the structure and magnetic properties of an enantiomerically pure chiral α -nitronyl nitroxide substituted with a triazole moiety in order to use this ligand to complex paramagnetic metal ions and to

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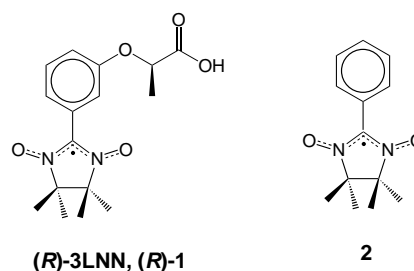
Supporting information for this article is available on the WWW under <http://www.wiley-vch.de/home/chemistry/> or directly from the author.

Abstract in Catalan: *S'ha portat a terme una investigació exhaustiva de les conformacions que pot adoptar la família dels radicals fenil α -nitronil nitroxid. S'ha desenvolupat un estudi estadístic amb una base de dades sobre les conformacions d'aquests radicals en l'estat sòlid, que posa de manifest que les conformacions més afavorides d'aquesta família de molècules implica una distorsió en l'anell imidazolinic i un angle de torsió entre els anells aromàtic i heterocíclic. Conseqüentment, aquests radicals mostren en l'estat sòlid dos tipus de conformacions: el parell enantiomeric pseudo-anti y el parell pseudo-eclipsat, essent aquest últim el més probable estadísticament. També hem preparat un nou membre quiral d'aquesta família de radicals que incorpora un grup lactat com a substituent de l'anell aromàtic, (*R*)-**1**, així com el seu corresponent compost racèmic, (*R,S*)-**1**, per tal d'estudiar la inducció quiral des del centre estereogènic en l'angle de torsió que formen els dos anells, l'aromàtic i l'heterocíclic. S'han determinat per difracció de raigs-X les estructures cristal·lines d'ambdós compostos, l'enantiopur i el racèmic, que revelen que les molècules formen cadenes, les unitats de les quals es troben formant enllaços d'hidrogen forts de tipus O–H...O entre el grup carboxílic i la unitat NO del radical en el sòlid, i també s'han determinat les seves propietats magnètiques. S'ha de destacar que les molècules que tenen un centre estereogènic determinat, mostren només un sentit en la helicitat de la torsió entre els seus dos anells, fet que s'observa també en el cristall racèmic. La inducció quiral des del centre estereogènic fins a la unitat radicalària ha estat confirmada per espectroscòpia de dicroïsm circular en l'estat sòlid. Els resultats obtinguts mitjançant aquesta tècnica han estat racionalitzats fent servir càlculs teòrics ab initio.*

Abstract in German: *Es wurde eine ausführliche Untersuchung der Konformation, die der Klasse der Phenyl α -Nitronylnitroxiden zugrunde liegt, durchgeführt. Hierzu wurde auch eine statistische Auswertung von den Konformationen dieser Radikale im festen Zustand anhand einer Datenbank-recherche herangezogen, die zeigt, dass die bevorzugte Konformation eine Verdrehung zwischen dem aromatischen und dem heterocyclischen Ring aufweist. Ein neuer, chiraler Vertreter dieser radikalischen Substanzklasse mit einer Laktat-gruppe, (*R*)-**1**, sowie dessen Racemat (*R,S*)-**1**, wurde hergestellt, um die chirale Induktion des stereogenen Zentrums auf den Torsionswinkel zwischen dem aromatischen und heterocyclischen Ring des α -Nitronylnitroxids zu untersuchen. Die magnetischen Eigenschaften, sowie die Röntgenstrukturen der enantiomeren reinen und racemischen Verbindung, die beide zeigen, dass sich im Festkörper eine Kettenstruktur der Moleküle ausbildet, die durch starke Wasserstoffbrückenbindungen zwischen der Säure- und NO-Gruppe aufrechterhalten wird, wurden bestimmt. Bemerkenswerterweise haben die Moleküle mit stereogenem Zentrum eine einzige helikale Ausrichtung ihrer Ringkomponenten, sogar im racemischen Kristall. Die chirale Induktion vom stereogenem Zentrum auf die Radikaleinheit wurde mit CD-Spektroskopie im Festkörper geprüft. Die Ergebnisse dieser Experimente wurden mit Hilfe von ab initio berechneten Spektren zugeordnet.*

control the supramolecular organisation of the resulting coordination compounds.^[13]

Our studies regarding chiral α -nitronyl nitroxides have begun with the chiral phenyl α -nitronyl nitroxide radical that bears a lactic acid moiety **3LNN** (**1**).^[6] The lactic acid moiety



was selected because it is cheap, easily incorporated synthetically, and the terminal carboxylic acid group might act as a firm structural linker to the nitroxide groups in the solid, as this feature has been previously observed in this type of radical.^[14] We are particularly interested in the effects that an asymmetric carbon atom has upon the molecular conformation and structure as well as in the material properties of these new compounds.

Herein we report the synthesis of the enantiopure (*R*)-**1** and the racemic (*R,S*)-**1** radicals, and rationalise their conformational behaviour in the solid state (X-ray structures, IR and CD) in the context of a statistical and computational analysis of the preferred conformational arrangements of the family of substituted phenyl α -nitronyl nitroxides as a whole. In order to gain a proper understanding of the optical properties, the circular dichroism (CD) spectra of the crystals of the enantiopure radical (*R*)-**1** were determined and compared with those calculated by ab initio methods.

Results and Discussion

Conformational preferences and stereochemistry in substituted phenyl α -nitronyl nitroxides in the solid state: The expression of chirality at the molecular level in organic molecules depends not only on the presence of an asymmetric carbon atom, but also on its effects on the relative spatial arrangement of the other groups of the molecule. At the outset, in an effort to gain insight into the conformational preferences of the phenyl α -nitronyl nitroxides that incorporate a stereogenic centre, which could influence the macroscopic optical properties as well as the magnetic ones,^[15] we studied the conformations adopted by this family of radicals in general by statistical and theoretical methods.^[16] In particular, we focused on: i) the conformation of the imidazolyl ring, defined by its five endocyclic torsion angles T_i ($i = 1 - 5$), and ii) the relative arrangement of the heterocyclic and the phenyl rings, defined by the twist angle A_{PNN} between the plane of the aromatic ring and the NCN plane (Figure 1). In order to shed light on the geometrical preferences of these rings, we have analysed the crystal structures of a database that contains 110 crystal structures with 135 independent units or fragments

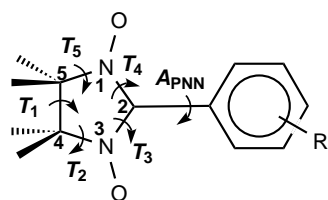


Figure 1. Definition of the torsion angles T_1 and the twist angle A_{PNN} along with the numbering scheme used for the five-membered ring.

of α -nitronyl nitroxides in a free form or co-ordinated to a metal ion.

We will first focus on the geometry and conformation of the heterocyclic fragment which is common to all α -nitronyl nitroxides. In order to establish an average geometry for this fragment, we have measured the 12 interatomic distances, 19 bond angles and 27 torsion angles for each structure in the database. The analysis of the bond lengths and angles in the rings show unimodal distributions,^[17] while all torsion angles show bimodal distributions with two maxima of opposite signs (see the Supporting Information).

The unimodal parameters are useful for the definition of a mean geometry for this family of radicals, since they do not depend on the particular conformation adopted by the imidazolyl ring and, as a consequence, they are valid for all derivatives. The parameters which describe chemically equivalent angles or distances show statistically indistinguishable distributions. This means that only the six distances and six angles that are shown in Figure 2 are representative.^[18] The

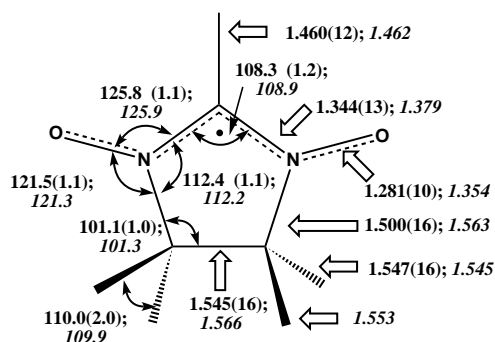


Figure 2. Mean geometry of the imidazolyl rings of α -nitronyl nitroxide radicals defined by six bond lengths and six bond angles (their standard deviations are given in parentheses). Figures in italics are the corresponding data obtained by the optimisation of the geometry of radical **2**, at the BLYP/3-21G(d) level.

interatomic distances and bond angles have also been calculated theoretically by the BLYP density functional method with the 3-21G(d) basis set for the fully optimised geometry of a reference radical, the phenyl α -nitronyl nitroxide radical (**2**) (Figure 2). With the exception of the calculated N–O and C–N bond lengths, the theoretical values are in good agreement with the mean values determined from the database.

In order to find a mean conformation of the imidazolyl ring in this family of radicals, it is convenient to inspect the parameters which show bimodal distributions. This inspection

reveals that all these parameters are mutually dependent (see the Supporting Information). Only two independent parameters are really necessary to describe unambiguously the conformation of an α -nitronyl nitroxide fragment,^[19] which can be defined using several methods.^[20] We employed that based on the *pseudo-rotation pathway*, proposed by Altona et al.,^[20c] in which the amplitude (ψ_M) and the phase angle (Φ) of the puckering in the ring are easily calculated from experimental endocyclic torsion angles (see the Experimental Section). The puckering amplitude ψ_M is the maximum torsional angle that one of the endocyclic bonds can exhibit as a result of an out-of-plane distortion of the ring, while the puckering phase angle Φ describes the location on the ring where the maximum out-of-plane distortion occurs (see the Supporting Information).

The analysis of the α -nitronyl nitroxide fragments of the database shows that the most statistically probable values for the ψ_M parameter is 24° and it has a distribution that departs strongly from normality (Figure 3). Values greater than 32°

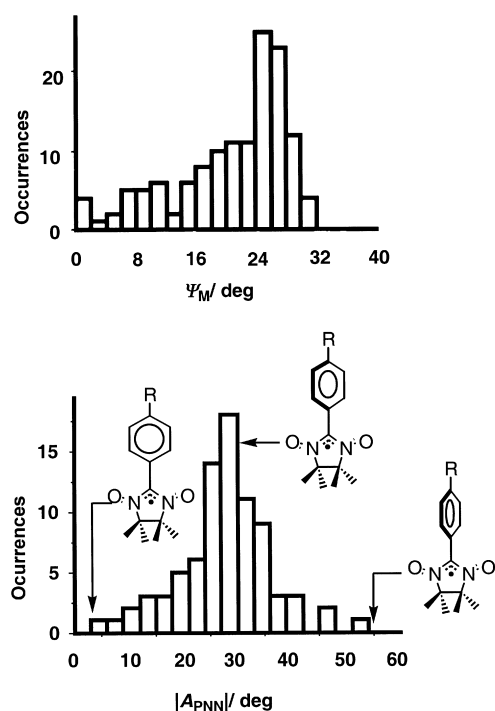


Figure 3. Top: Histogram of the absolute value of the amplitude ψ_M for the torsion of the imidazolyl rings in the solid state. Bottom: Histogram of the twist angles A_{PNN} between the two rings of the phenyl α -nitronyl nitroxides in the solid state.

are highly improbable, which indicates a significant increase in the potential energy curve as the value of this parameter increases further, with a more shallow increase towards lower angles. There is a marked preference for values between 16 and 32° ($\approx 80\%$ of the studied fragments have the puckering amplitude in this range). The asymmetry of the potential energy curve results from two opposite forces with distinct strengths that determine the final conformation: i) the conjugation of three of the five atoms of the ring which form part of the ONCNO unit, favour coplanarity, and ii) the torsional

strain and the steric repulsion of the four adjacent methyl groups favour out-of-plane distortion.

The conformational parameter Φ for the radicals of the database is centred at 0° (and 180°) with a normal distribution around this mean value that shows a very small standard deviation of 3° . This result indicates that the out-of-plane distortion of the heterocyclic rings is always located on the two C atoms with sp^3 hybridisation and is driven by their lack of conjugation with the ONCNO unit and the torsional strain and steric repulsions produced by the four methyl groups. A very similar result was previously reported for crystalline, substituted cyclopenten-2-ones and it was ascribed to the fact that three of the five C atoms of the rings are of the sp^2 type.^[20d] The mean conformation of the imidazolyl ring in this family of radicals can therefore be described completely by the following mean values: $\psi_M = 26^\circ$, $\Phi = 0^\circ$ and $\psi_M = 26^\circ$, $\Phi = 180^\circ$ for the 4T_5 and 5T_4 enantiomeric conformers, respectively (see the Supporting Information). The constant value and narrow dispersion of the Φ conformational parameter (vide supra) also make it possible to describe the mean conformation of this ring with only one parameter, the mean torsional angle T_1 and with the use of its own sign to distinguish between the two possible enantiomers; namely $T_1 = +24^\circ$ or -24° for 4T_5 and 5T_4 conformers. The optimised conformation of the reference radical **2** at the BLYP/3-21G(d) level gives a torsion angle $T_1 = \pm 19.9^\circ$ or, more properly, $\psi_M = 21.6^\circ$ and $\Phi = 0^\circ$ (180°), values similar to those found in the statistical study.

The second conformationally significant feature in the phenyl α -nitronyl nitroxides is the twist angle A_{PNN} between the phenyl and imidazolyl rings. This factor is of great importance in determining the magnetic properties, since the distribution of the unpaired electron over the molecule might depend on the conjugation between the two rings.^[15, 16] The results of the statistical analysis^[21] show that more than 96% of the molecules exhibit absolute values of the twist angle A_{PNN} between 10° and 45° (Figure 3). The average value of the statistical distribution of $|A_{PNN}|$ is 27.5° with a standard deviation of 8.5° .^[22] Naturally, in the solid state, the absolute conformation of the α -nitronyl nitroxide radicals not only depends on the intramolecular interactions, but also on the intermolecular ones, which means that it is influenced by the chemical surroundings.^[23] There are at least three principal structural features which determine A_{PNN} : a) the optimisation of the weak hydrogen bonds established between the *ortho*-hydrogen atom of the aromatic ring and the oxygen atoms of the nitroxide groups, b) the conjugation of the ONCNO unit with the aromatic rings, and c) the optimum packing of the molecules in the solid.^[24] Factors a and b favour the planar arrangement which is the most stable form in vacuo (vide infra). Since the majority of the structures contain molecules far from this conformation, factor c apparently dominates in the solid state.

We have also tried to find a relationship between the puckering of the imidazolyl ring (described by the torsion angle T_1) and the relative conformation of the two rings (described by A_{PNN}). The chiral information inherent in them (given by the sign of both parameters) infers four possible gross conformations: $(+T_1, +A_{PNN})$, $(+T_1, -A_{PNN})$, $(-T_1,$

$-A_{PNN})$, and $(-T_1, +A_{PNN})$, where positive angles correspond to a plus (*P*) helicity and negative ones to a minus (*M*) helicity.^[25] These four conformational diastereoisomers^[26] contain two enantiomeric pairs: (*MP*, *PM*) and (*PP*, *MM*) (Figure 4). In the enantiomeric pair (*MP*, *PM*) the distortion

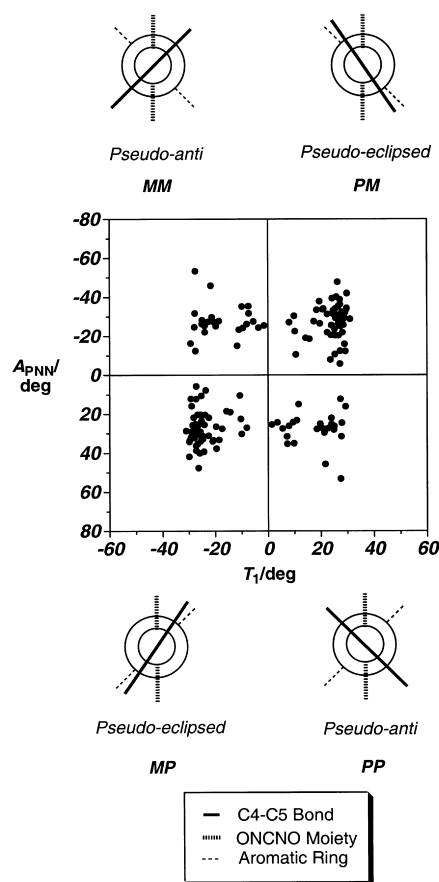


Figure 4. Scattergram of torsion angles T_1 versus twist angles A_{PNN} for substituted phenyl α -nitronyl nitroxides in the solid state and the conformational possibilities of the α -nitronyl nitroxide radicals as a function of the signs of the T_1 and A_{PNN} angles (see the Supporting Information for an alternative representation of the distribution). The structures of the four diastereomers are projected schematically down the long axis of the molecules as seen from the methyl groups of the radical part of the molecule.

of the imidazolyl ring results in a situation in which the C4–C5 bond is eclipsed with the plane formed by the aromatic group. The overall conformation is basically planar, and will be referred to as *pseudo-eclipsed*. In the enantiomers *MM* and *PP*, the identical signs of the two parameters imply a large angle between the C4–C5 bond and the plane of the aromatic ring. These conformations with the same helicity throughout the molecule will be referred to as *pseudo-anti*, and have an overall molecular shape which is more globular than those with the *pseudo-eclipsed* conformation.

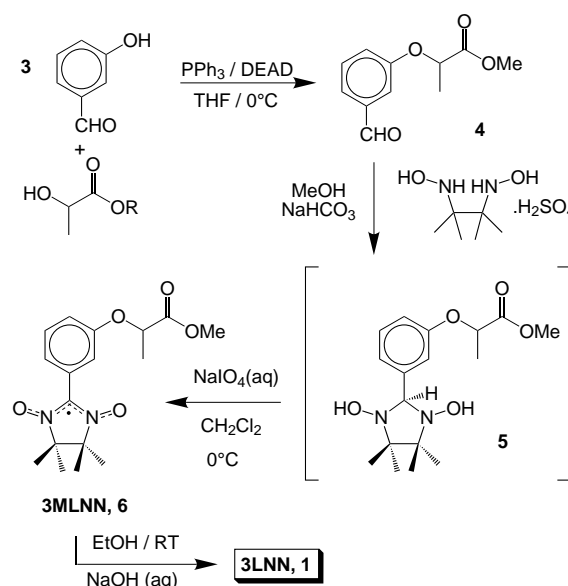
We found 57 *pseudo-eclipsed* conformations and 25 *pseudo-anti* ones (Figure 4) and, in accord with the statistic chi-square test,^[27] such frequencies of occurrence are significantly different ($\chi^2 = 12.49$) at a confidence level of 99.5%. Therefore, there is a statistically significant interdependence of the torsion angles A_{PNN} and T_1 in this family of radicals, whereby

the *pseudo-eclipsed* geometry is greatly favoured. The totally flat conformation, with $T_1 = 0^\circ$ and $A_{\text{PNN}} = 0^\circ$, is apparently disfavoured in the solid state. The calculated (BLYP/3-21G(d) level) conformation for the reference radical **2** in vacuo has the values $T_1 = \pm 19.9^\circ$ and $A_{\text{PNN}} = 0^\circ$; a situation which allows conjugation of the ONCNO moiety with the aromatic ring. The calculated energy barrier for interconversion of the enantiomers is $\approx 0.48 \text{ kcal mol}^{-1}$, while the energy difference between angles A_{PNN} of 0° and 90° (keeping T_1 constant at 19.3°) is $16.2 \text{ kcal mol}^{-1}$; more than 30 times higher than the former. Therefore, the structural factors that contribute to increase the absolute value of A_{PNN} in the solid result from the packing of the molecules. In fact, in crystals of the radical 2-phenylbenzimidazol-1-yl *N,N*-dioxide—in which the CMe_2CMe_2 group is replaced by an *ortho*-substituted benzene ring—this angle is only 10.3° , and the molecule is practically planar.^[28] The absence of a twisting force in the imidazolyl unit in this structure would seem to favour a low A_{PNN} angle which indicates that the reason for the favoured *pseudo-eclipsed* geometry is the presence of a molecule with a flat shape in the crystal. This is in agreement with the concepts expressed by Kitaigorodskii.^[24]

Finally, it is worth mentioning that the vast majority of crystals in the database contain an equal number of *MM* and *PP* (or *MP* and *PM*) enantiomers in the unit cell, since they have no asymmetric carbon atoms and crystallise in centrosymmetrical space groups.^[29] With the aim of studying the possibility of inducing a given chirality in the torsion angle between the two rings and in the distortion of the imidazolyl ring—namely to favour either *MM* or *PP* (or *MP* or *PM*)—we have synthesised the chiral radical (*R*)-**1** and its corresponding racemic compound (*R,S*)-**1**, which contain an asymmetric carbon atom close to the phenyl substituent, and have studied their solid-state structures and properties and the associated chiral induction phenomena.

Preparation and study of chiral phenyl α -nitronyl nitroxide radicals: The chiral radical (*R*)-[3-(4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazolyl-1-oxy-3-oxide)phenoxy]-2-propionic acid ((*R*)-**3LNN**; (*R*)-**1**) and its corresponding racemic modification ((*R,S*)-**3LNN**; (*R,S*)-**1**), were prepared following the synthetic route described in Scheme 1. 3-Hydroxybenzaldehyde (**3**) was condensed with (*S*)-methyl or (*R,S*)-methyl lactate by means of a Mitsunobu protocol.^[30] The resulting aldehydes **4** were used to form the methyl ester derivative α -nitronyl nitroxides **3MLNN** (**6**) by condensation with 2,3-dihydroxylammonium-2,3-dimethylbutane sulfate,^[31] and subsequent oxidation of the adducts **5** with sodium periodate, following the classic procedure of Ullman.^[7] The resulting radical esters **6** were saponified with aqueous sodium hydroxide in ethanol to give the carboxylic acids **1**, as dark blue solids. Crystals suitable for X-ray diffraction were obtained by slow evaporation from dichloromethane/hexane or ethanol/toluene solutions.

The infrared spectra of crystals of (*R*)-**1** and (*R,S*)-**1** in KBr show preliminary evidence for the formation of hydrogen bonds in the solid state. The positions of the COO–H stretching bands (Table 1) are typical for associated carboxylic acids.^[32] In addition, the positions of the C=O stretching



Scheme 1. Synthesis of the chiral radical (*R*)-**1** and its corresponding racemic modification (*R,S*)-**1**.

Table 1. Selected IR frequencies for the acid-derived radicals **1** and their methyl esters **6**.

Compound	ν [cm^{-1}]		
	C=O	N–O	COO–H
(<i>R</i>)- 6	1757	1363	–
(<i>R</i>)- 1	1736	1349	2516, 2587
(<i>R,S</i>)- 6	1757	1363	–
(<i>R,S</i>)- 1	1722	1346	2530, 2608

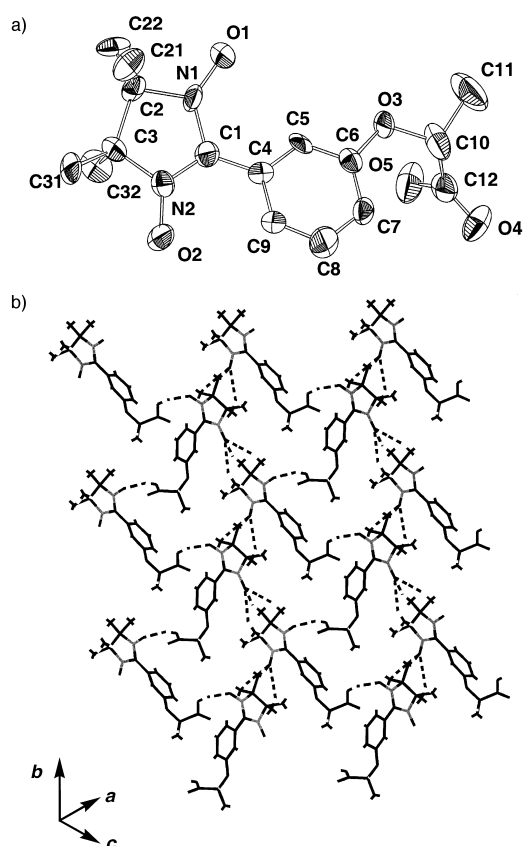
bands also indicate some kind of association, since the wavenumber is lower than the corresponding stretching for “free” carboxylic acids. On the other hand, the N–O stretching bands, which usually appear in the range 1360 – 1365 cm^{-1} , are positioned at lower wavenumbers indicating that the NO group could be the recipient of the hydrogen bond. The vibrations of the carbonyl and NO groups appear at lower wavenumbers in the case of the racemic compound, which indicates that the hydrogen bonds established between the two groups are stronger than in the enantiopure compound.

The crystal structures of (*R*)-**1** and (*R,S*)-**1** have been determined. The most important crystallographic data are given in Table 2. Their two corresponding methyl esters (*R*)-**6** and (*R,S*)-**6** have been isolated as crystalline powders; however, no single crystals suitable for X-ray diffraction have been obtained up to now.

The radical (*R*)-**1** crystallises in the monoclinic non-centrosymmetric space group $P2_1$ with one molecule in the asymmetric unit. The molecule has an extended geometry in which the carboxylic acid is directed away from the nitronyl nitroxide moiety (Figure 5a). The twist angle A_{PNN} is -25° . Therefore, in this chiral radical, the substituent induces one preferred conformation of the phenyl and heterocyclic rings. Kahn and co-workers also observed this type of phenomenon in a chiral α -nitronyl nitroxide,^[13] although in this case, the chiral group is adjacent to the atoms which link the heterocycle to the radical group, and presumably has a dominating

Table 2. Crystal structure data for radicals (*R*)-**1** and (*R,S*)-**1**.

	(<i>R</i>)- 1	(<i>R,S</i>)- 1
empirical formula	C ₁₆ H ₂₁ N ₂ O ₅	C ₁₆ H ₂₁ N ₂ O ₅
M_r	321.35	321.35
colour, habit	dark blue plates	dark blue prisms
crystal dimensions [mm]	0.4 × 0.39 × 0.02	0.65 × 0.3 × 0.15
T [K]	293(2)	218(2)
radiation	MoK α	MoK α
wavelength [Å]	0.71073	0.71073
lattice type	monoclinic	monoclinic
space group	$P2_1$	$P2_1/c$
a [Å]	6.004(1)	13.291(2)
b [Å]	12.065(1)	11.511(2)
c [Å]	11.933(1)	11.306(2)
β [°]	102.36(3)	107.29(1)
V [Å ³]	844.37(17)	1651.6(5)
Z	2	4
calculated density [g cm ⁻³]	1.264	1.292
$F(000)$	342	684
θ range [°]	3.38–23.7	2.59–20.5
unique reflections measured	1483	1923
unique reflections observed, $I > 2\sigma$	1344	1575
parameters	216	218
restraints	73	1
R indices (all data)	0.0786	0.0570
$wR2$ (all data)	0.1194	0.1133

Figure 5. a) Solid-state structure of the radical (*R*)-**1**. b) View of the crystal packing of (*R*)-**1** projected along the bc plane. Dashed lines indicate intermolecular hydrogen bonds.

steric role. At the same time, the NCCN unit of the heterocyclic ring in (*R*)-**1** exhibits a torsion angle T_1 of -18.5° ($\psi_M = 20^\circ$ and $\Phi = -2.3^\circ$). As a consequence, a *pseudo-anti* conformation with an *MM* helicity is adopted,

and the chiral transmission occurs along the length of the molecule. The most bulky group of the chiral substituent, the carboxylic acid moiety, adopts a position perpendicular to the principal plane of the molecule on the opposite side of the molecule to the NO group directed towards the same face.

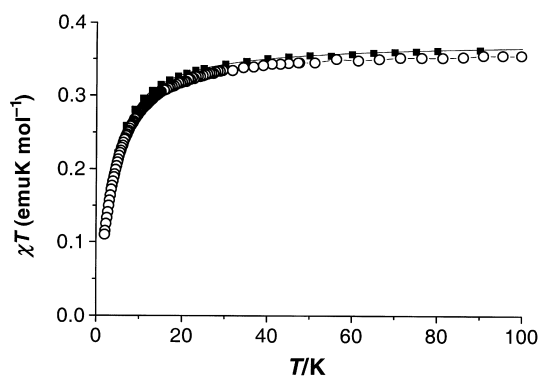
This radical forms kinked chains along the b axis (Figure 5b), in which the molecules are linked by strong hydrogen bonds (Table 3) between the carboxylic group of one mole-

Table 3. Hydrogen-bond lengths and geometries found in crystals of (*R*)-**1** and (*R,S*)-**1** radicals. For numbering see Figure 5.

Radical	H bond	[H...O] bond length [Å]	[X-H...O] angle [°]	[X-H...O] distance [Å]
<i>(R)</i> - 1	O5–H...O2	1.886	156.2	2.657
	C22–H...O1	2.766	150.3	3.632
	C31–H...O1	2.550	147.7	3.400
	C32–H...O1	2.541	150.6	3.410
<i>(R,S)</i> - 1	O5–H...O2	1.650	172.9	2.635
	C22–H...O4	2.543	163.9	3.485
	C21–H...O1	2.697	147.8	3.556
	C31–H...O1	2.482	152.4	3.372
	C8–H...O3	2.585	146.0	3.405

cule and a NO moiety of the next. Each molecule is related to the next one by a translation and a 180° rotation (a two-fold screw axis). In turn, these chains are linked to one another by [C(sp³)-H...O–N] hydrogen bonds^[33] that involve the second NO group of the molecule and three hydrogen atoms of the methyl groups in a neighbouring radical (Table 3). Polar sheets of parallel chains thus form planes, which pile up in an antiparallel manner without establishing hydrogen bonds between them.

The product of the molar magnetic susceptibility and temperature (χT) value for the (*R*)-**1** radical at room temperature is $0.376 \text{ emu K mol}^{-1}$, which is identical to that expected for uncorrelated $S = 1/2$ spins ($0.375 \text{ emu K mol}^{-1}$). When the temperature was lowered, χT decreased (Figure 6), which

Figure 6. χT versus T plot of (*R*)-**1** (○) and (*R,S*)-**1** (■) showing weak intermolecular antiferromagnetic interactions present in the crystals of both radicals. Lines correspond to the fitting of experimental data to magnetic models (see text).

indicates the dominant presence of intermolecular antiferromagnetic interactions in the crystals. This magnetic behaviour can be fitted to a one-dimensional antiferromagnetic Heisenberg $S = 1/2$ chain with a magnetic coupling constant between

spins J/k of -2.3 K, in accordance with some of the structural features. The shortest $[\text{N}-\text{O}\cdots\text{O}-\text{N}]$ distances of radicals linked by hydrogen bonds are 5.8 Å, which are too large to be magnetically important. Nevertheless, the undulating nature of the hydrogen-bonded chains results in a close contact between sheets of 4.80 Å that occurs among the $\text{N}-\text{O}$ groups, which are almost coplanar. Therefore, it seems to be this latter direct interaction between the SOMOs of radicals that are responsible for the overall antiferromagnetic behaviour. These short contacts also form chains of radicals along the b axis, although there is no direct appreciable hydrogen-bond interaction between them.

The compound (*R,S*)-**1** crystallises as a racemate in the centrosymmetric space group $P2_1/c$, and has a solid-state structure in which the molecules have an extended conformation, similar to that of the enantiopure compound. The *R* enantiomer within the racemic crystal exhibits a twist angle A_{PNN} of -24° with, therefore, the same *M* helicity in the relative arrangement of the two rings as in the crystals of the pure enantiomer (*R*)-**1**. On the contrary, the torsion angle T_1 of the *R* enantiomer in the racemic crystals is $+24^\circ$, which is opposite to that found in the enantiopure crystals and indicates that the distortion of the imidazolyl ring has a *P* helicity. As a consequence, the *R* enantiomer in the racemate crystals has a *pseudo-eclipsed PM* conformation with $\psi_{\text{M}} = 26^\circ$ and $\Phi = +6.5^\circ$. The coincidence of signs for the twist angles between the two rings for the *R* enantiomer in the enantiopure and racemic crystals ($A_{\text{PNN}} \approx -25^\circ$) may suggest that this torsion is driven mainly from the stereogenic centre—the asymmetric carbon atom. More examples are clearly necessary in order to confirm such a correlation. On the other hand, the signs of the torsion angle T_1 of the *R* enantiomer in the two studied crystals are opposite and, therefore, they seem to be related to intermolecular interactions rather than to intramolecular ones. The energy barrier for the rotation of the NCCN unit is extremely low (*vide supra*) and it could easily be overcome by any weak intermolecular interaction, for example, the hydrogen bonds between the substituent methyl groups (*vide infra*).

The packing of the racemic radical is similar to that of the enantiopure compound, in so far as chains of molecules are formed along the b axis which are maintained by hydrogen bonds between the carboxylic acid moiety of one molecule and the $\text{N}-\text{O}$ group of the next molecule (Figure 7). As revealed by the interatomic distances (Table 3), these hydrogen bonds are much stronger than in the enantiopure compound and thus lead to a more dense structure, in agreement with Wallach's rule.^[34] Owing to a slight disorder in the crystal, one of every ten of these molecules has the opposite chirality to the dominant enantiomer in this mainly homochiral chain. Compared with the enantiopure compound, an additional hydrogen bond is established between the carbonyl oxygen atom and one of the methyl groups adjacent to the $\text{N}-\text{O}$ group (see Table 3). These chains are linked to one another by weak hydrogen bonds between the "free" NO group and the methyl groups of the imidazolyl ring of a nitronyl nitroxide molecule in the neighbouring chain. Therefore, sheets of chains of homochiral molecules are formed in the ab plane. These molecular sheets pile up along

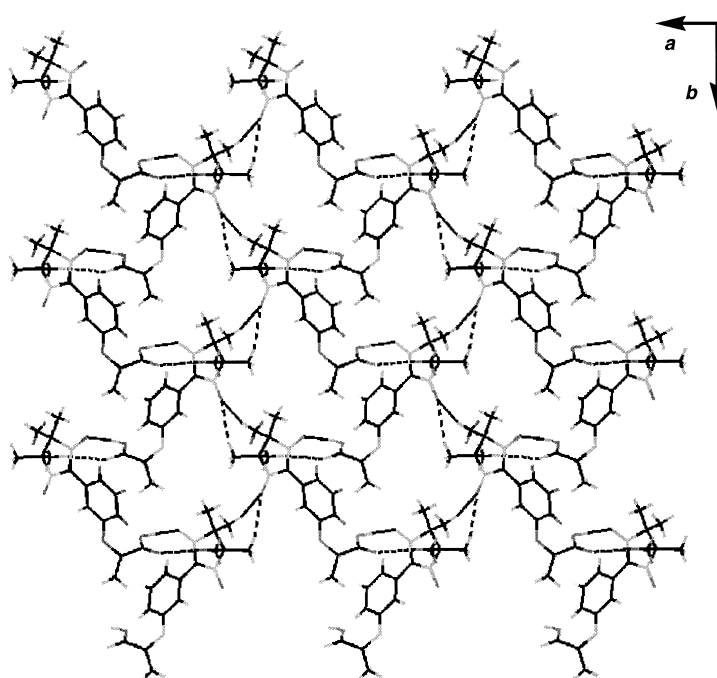


Figure 7. View of the crystal packing of (*R,S*)-**1** projected along the ab plane. Dashed lines indicate intermolecular hydrogen bonds.

the c axis with alternating chirality. There are also weak hydrogen bonds that connect the sheets between the hydrogen atom at the 5-position of the aromatic ring and the oxygen atom of the chiral group directly linked to the phenyl group. The shortest approach between SOMOs (4.901 Å) of the nitronyl nitroxide moiety take place between two molecules of different sheets related by an inversion centre and, therefore, the angle between ONCNO units is 0° to form a dimer which is magnetically relevant. Each of these dimers is surrounded by four other dimers that are orthogonally disposed with respect to the first one. The room temperature value of χT (0.359 emu K mol⁻¹) corresponds to that expected for uncorrelated spins. When the temperature was lowered to 4 K, χT decreased to 0.170 emu K mol⁻¹ (Figure 6). These qualitative features are very similar to those of the enantiopure compound and suggest that in (*R,S*)-**1**, the free radicals are predominantly antiferromagnetically coupled.^[35]

The solid-state circular dichroism (CD) spectrum of the chiral radical (*R*)-**1**, recorded as a KBr disc,^[36] (Figure 8) reveals Cotton effects centred at 470 nm (weak, negative) and 340 nm (strong, negative), which correspond approximately to electronic transitions (and combinations of them) of the component chromophores.

In order to give a precise assignment to these Cotton effects associated with the electronic transitions of (*R*)-**1** in its crystal, and to determine their precise origin, we performed *ab initio* molecular orbital calculations by means of the CIS method with the crystal geometry co-ordinates of the (*R*)-**1**. The calculated CD spectrum of (*R*)-**1** (Figure 8) reproduces the experimental spectrum remarkably well after an appropriate correction.^[37] Given this excellent agreement, we can assume that intermolecular effects of the crystal field on the CD spectrum are, if any, very small and therefore the optical

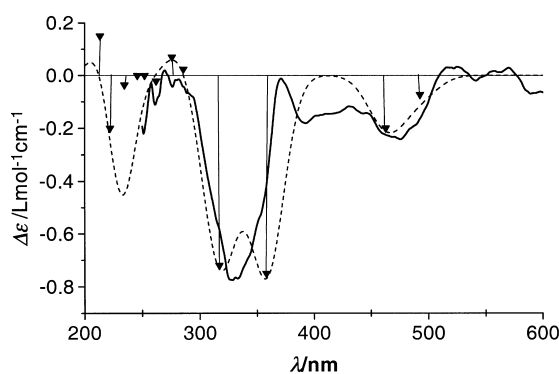


Figure 8. Solid-state CD spectrum of (*R*)-**1** recorded in KBr (continuous line), and calculated transitions (vertical arrows), at the CIS/3–21 G(d) level with the geometry of the molecule in the crystal. The simulated spectrum (dashed line) was constructed by the addition of a different Gaussian function to each calculated transition,^[37] and its maximum is scaled to the same value of the experimental spectrum.

activity results exclusively from the molecular asymmetry. The Cotton effect located at approximately 470 nm is associated with $n \rightarrow \pi^*$ transitions of the nitronyl nitroxide moiety (see the Supporting Information for calculated orbital contributions). The two Cotton effects in the calculated spectrum located at ≈ 355 and 315 nm, which are presumably jointly responsible for the negative Cotton effect in the experimental spectrum at approximately 340 nm, are associated with $\pi \rightarrow \pi^*$ transitions of the ONCNO moiety from a common ground state to excited states which have two orbital contributions (see the Supporting Information for calculated orbital contributions). In order to maximise the CD signal in these radicals, which is important for the observation of magneto-optical effects, it is important to know which asymmetric structural features—torsions—are the most optically active. To shed light on this matter, we have assessed the chiral influence of each torsion angle in the molecule on the CD spectrum. We used the experimental solid-state conformation as a starting point, and reversed the angles T_1 and A_{PNN} , keeping all bond lengths and angles equal to those in the solid so as to generate the three other possible stereoisomers for the molecule (Figure 4) and their CD spectra were then calculated. This study reveals (Figure 9) that when the torsion

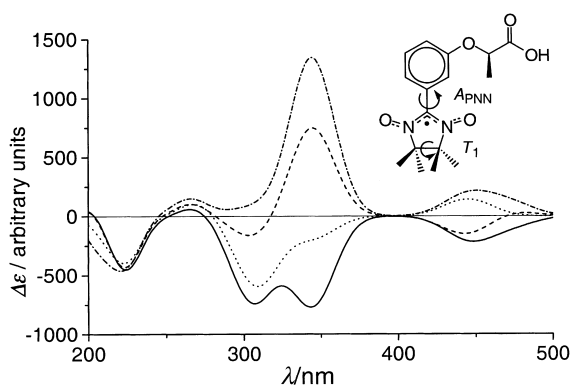


Figure 9. Calculated CD spectra (in arbitrary units) of the four possible diastereomeric conformations of (*R*)-**1** which were generated by changing the signs of the angles A_{PNN} and T_1 , obtained in its crystal structure. — $T_1 = -18^\circ$, $A_{\text{PNN}} = -25^\circ$ (*MM*); - - - $T_1 = -18^\circ$, $A_{\text{PNN}} = +25^\circ$ (*MP*); $T_1 = +18^\circ$, $A_{\text{PNN}} = -25^\circ$ (*PM*); - · - · $T_1 = +18^\circ$, $A_{\text{PNN}} = +25^\circ$ (*PP*).

angle of the NCCN group has a negative value ($T_1 < 0$), as in the case of crystalline (*R*)-**1**, the transition presents a negative Cotton effect at 470 nm. If T_1 is positive, the Cotton effect associated with this transition is positive. The twist angle A_{PNN} , between the phenyl and imidazolyl rings, does not greatly influence the sign of the Cotton effect associated with the $n \rightarrow \pi^*$ transition of the radical moiety; however, it does drastically change the one centred at approximately 340 nm, associated with the $\pi \rightarrow \pi^*$ transition. Overall, the intensity of the signals in this region is much more intense for the *pseudo-anti* conformations than for the *pseudo-eclipsed* conformations, which sustains the hypothesis that the former is “more chiral”, or, more properly, “more optically active”.

The sign of the contribution of the $\pi \rightarrow \pi^*$ transition located at ≈ 355 nm mainly reflects the sign of the angle A_{PNN} , the Cotton effect being negative when the angle is negative, and opposite when it is positive, although the intensity of the signal also greatly depends on the global conformation. The contribution located at ≈ 320 nm, on the other hand, seems to be influenced by both the natures of the two torsion angles as well as by the chiral group, since in three of the four diastereomers, the Cotton effect is negative. The Cotton effect located at ≈ 235 nm in the calculated spectrum, which is associated with the $\pi \rightarrow \pi^*$ transition of the phenyl group, remains of virtually constant negative intensity, and only appears to be influenced by the stereogenic centre in its proximity, whose conformation was not varied in these calculations. The chiral group also influences somewhat the intensity of the transitions located at 340 and 355 nm, as can be observed in Figure 9.

Finally, it is interesting to compare the CD spectra of radical (*R*)-**1** in CH_2Cl_2 solution with that in the solid state. The negative Cotton effect attributed to the ONCNO chromophore is shifted by ≈ 30 nm to higher wavelengths in solution. This fact could be explained in terms of a hydrogen bond between the COOH group and the NO moiety which hinders the charge separation involved in the $\pi \rightarrow \pi^*$ transition. The negative Cotton effect centred at 470 nm in the solid-state spectrum is not observed in solution, while a positive signal centred at 430 nm is only observed in solution.

Conclusions

Phenyl α -nitronyl nitroxides have two dominant conformations in the solid state: one in which the chiralities of the twist of the two rings and of the distortion of the imidazolyl ring are the same—the *pseudo-anti* conformation—, and another, which is more probable in solid state, in which the two chiralities are opposite—the *pseudo-eclipsed* conformation. In the new chiral nitronyl nitroxide reported here, the stereogenic centre is able to induce one preferred chiral conformation between the aromatic ring and the ONCNO unit in its non-centrosymmetric crystals as well as in the individual enantiomeric molecules of the racemic crystals. Cotton effects are observed in transitions which involve the unpaired electron, and the results of CD ab initio calculations help us to understand which conformational features are responsible for the optical activity of the radical unit at each wavelength.

Investigations of possible magneto-optical effects in this and related chiral radicals is underway.

Experimental Section

Conformational analysis: A total of 136 crystal structures that contain α -nitronyl nitroxide radical fragments were used initially. The majority were retrieved from the Cambridge Crystallographic Structure Database (CSD),^[38] and the rest from our own research, directly from the literature, or supplied by other authors. The criteria employed to select the final set of structures were as follows: The structures were discarded that had a) R factors greater than 0.10, b) which were determined with very limited data, c) exhibited large thermal vibrational terms, d) some structural disorder in atoms of the five-membered ring or those directly linked to them and e) structures in which one of the five bond lengths of the imidazolyl ring was more than three times the standard deviation of the mean values. Following these criteria, the final database consisted of 110 crystal structures (60 correspond to purely organic compounds and 50 to coordination complexes) that contained 135 crystallographically independent α -nitronyl nitroxide compounds. Most of these crystal structures were centrosymmetric (94) and contained both conformational enantiomers in the unit cell. The most frequent space groups were $P2_1/n$ (No. 14), $P\bar{1}$ (No. 2), and $C2/c$ (No. 15) with 56, 19, and 10 occurrences, respectively. The determination of geometrical parameters of the fragments that belonged to the centrosymmetrical structures was performed by measuring only those of one of the two enantiomers contained in the unit cell. Since this procedure could cause a bias in the enantiomeric abundance, the database was duplicated by changing the sign of all the torsion angles in order to include both enantiomers of each radical in the database. The non-centrosymmetric crystal structures (16) were also duplicated in the same way, since the absolute configuration of the structures has not been determined and both enantiomers must be equally abundant. Moreover, no spontaneous resolution over the bulk samples was mentioned. The statistical analysis of the geometry was performed with the corresponding CSD software package,^[38] and also the SYSTAT statistical package.^[39]

Equations (1)–(4) were used for the calculation of ψ_M and Φ parameters from the experimental endocyclic torsion angles T_1 – T_5 (defined in Figure 1) of the imidazolyl rings, the following equations were used.

$$Sa = \sum_{i=1}^5 T_i \cos[144(i-1)] \quad (1)$$

$$Sb = \sum_{i=1}^5 T_i \sin[144(i-1)] \quad (2)$$

$$\tan \Phi = \frac{Sb}{Sa} \quad (3)$$

$$\psi_M = \sqrt{Sa^2 + Sb^2} \quad (4)$$

where the Sa and Sb parameters are the Cartesian coordinates equivalent to the polar coordinates ψ_M and Φ , that permit the unequivocal description of the conformation of an imidazolyl ring (see the Supporting Information).

Theoretical calculations: Molecular geometries were optimised with the BLYP density functional method and the 3-21G(d) basis set. Rationalisation of the CD spectrum was carried out by a comparison of the experimental results with the values of ab initio computations of the lowest 12 electronic transitions (the UV spectrum) and the rotational strength of each of these transitions. The UV spectrum of each conformation of interest was computed by means of the CIS method^[40] (configuration interaction including all mono-excitations from the ground state) and the 3-21 G(d) basis set, starting from the UHF doublet ground state. The rotational strength was computed by scalar multiplication of the electric and magnetic dipole moments of the electronic transition computed at the CIS/3-21 G(d) level. We have checked the accuracy of this methodology by a computation of the shape and relative positions of the experimental UV and CD spectra of substituted azulene and phthalamide^[41] molecules and the qualitative results were in very satisfactory agreement with the computed UV bands shifted towards lower energies. This conclusion is different to that reached by Pople et al.,^[40] from the evaluation of the

performance of the CIS method to reproduce the UV spectrum of closed-shell molecules and is likely to be a consequence of the open-shell nature of the ground state of the (*R*)-1 radical, which shows a small spin contamination at the UHF level.

Materials and methods: Solvents were purified according to literature methods when necessary.^[42] In particular, THF was dried over Na/benzophenone ketyl and distilled. 3-Hydroxybenzaldehyde (**3**) and diethylazodicarboxylate (DEAD, 85%) were purchased from Aldrich Chemical Company, triphenylphosphine from Merck, and (*R,S*)-methyl lactate, and (*S*)-methyl lactate from Fluka. All the reagents were used as received. Thin-layer chromatography (TLC) was performed on aluminium plates coated with Merck Silica gel 60F₂₅₄. Developed plates were air-dried and scrutinised under a UV lamp. Silica gel 60 (35–70 mesh, SDS) was used for column chromatography. Melting points were determined by differential scanning calorimetry (DSC) with a Perkin Elmer DSC 7 instrument. LDI-TOF-MS were obtained with a Kratos Kompact Maldi 2 K-probe (Kratos Analytical) that operated with pulsed extraction of the ions in the linear high-power mode. Microanalyses and electron-impact mass spectra were performed by the Servei d'Anàlisi de la Universitat Autònoma de Barcelona. ¹H and ¹³C NMR spectra were recorded on a Bruker ARX 300 spectrometer (with the deuterated solvent as a lock and tetramethylsilane as the internal reference). ESR spectra were recorded on a Bruker ESP 300E. Polarimetry was performed with a Dr. Kernchen Optik + Electronic Propol polarimeter in a 1 cm cell. Circular dichroism spectra were recorded on a JASCO-715 spectrometer and UV spectra on a VARIAN Cary 5 spectrometer. Magnetic susceptibility measurements were obtained with a Quantum Design SQUID magnetometer. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications nos. CCDC-134668 and CCDC-134797. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

(*R*)-Methyl(3-formylphenoxy)-2-propionate [(*R*)-4]: 3-Hydroxybenzaldehyde (**3**; 400 mg, 3.28 mmol), (*S*)-methyl lactate (416 μ L, 3.94 mmol) and triphenylphosphine (1.031 g, 3.94 mmol) were dissolved in dry THF (30 mL) with stirring under an atmosphere of argon. The mixture was cooled in an ice bath to 0°C and a solution of diethylazodicarboxylate (DEAD, 685 μ L, 3.94 mmol) in dry THF (5 mL) was added dropwise over a period of 30 min. The mixture was allowed to warm to room temperature and was then stirred overnight. After addition of water (10 mL), the THF was removed in vacuo, and the residue was partitioned between dichloromethane (50 mL) and water (50 mL). The aqueous phase was extracted once more with the same solvent. The combined organic phases were dried over Na₂SO₄, filtered, and stripped of solvent. The residue was subjected to column chromatography (SiO₂, hexane/CH₂Cl₂, 1:10) to give the product as a clear oil (475 mg, 67%). [α]₅₄₆ = +59.8 ($c = 0.479$ M, CH₂Cl₂); UV/Vis (CH₂Cl₂): λ_{\max} (ϵ) = 270 (9000), 310 nm (2000); CD (CH₂Cl₂): λ_{\max} ($\Delta\epsilon$) = 310 nm (+0.6); IR (neat): $\tilde{\nu}$ = 2995, 2957, 2846, 2740, 1757 (*C(O)OCH*), 1702 (*C(O)H*), 1592, 1484, 1451, 1260, 1136, 789 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 1.64 (d, $J = 6.9$ Hz, 3H; *OCHCH*), 3.77 (s, 3H; *COOCH*), 4.86 (q, $J = 6.9$ Hz, 1H; *OCHCH*), 7.19 (dxdxd, 1H (*H*₄), J (*H*₄,*H*₅) = 7.6 Hz, J (*H*₄,*H*₂) = 2.7 Hz, J (*H*₄,*H*₆) = 1.5 Hz), 7.35 (dxd, 1H (*H*₂), J (*H*₂,*H*₄) = 2.7 Hz, J (*H*₂,*H*₆) = 1.4 Hz), 7.47 (t, 1H (*H*₅), $J = 7.6$ Hz), 7.51 (dxt, 1H (*H*₆), J (*H*₆,*H*₅) = 7.6 Hz, J (*H*₄,*H*₂) = 1.5 Hz), 9.96 (s, 1H; *CHO*); ¹³C NMR (75 MHz, CDCl₃): δ = 30.9 (CH₃CH), 52.5 (OCH₃), 72.6 (CH₃CH), 113.6 (C2), 122.2 (C4), 124.1 (C6), 130.3 (C5), 137.8 (C1), 158.2 (C3), 172.1 (COO), 191.8 (CHO).

(*R,S*)-Methyl-(3-formylphenoxy)-2-propionate [(*R,S*)-4]: The product was isolated in 57% yield after reaction of 3-hydroxybenzaldehyde (**3**) with (*R,S*)-methyl lactate by the procedure described for the chiral butyl ester. This compound showed the same UV, IR and NMR spectra as the corresponding enantiopure (*R*)-4.

(*R*)-Methyl[3-(4,4,5,5-tetramethyl-4,5-dihydro-1*H*-imidazolyl-1-oxo-3-oxo-phenyl)-2-propionate [(*R*)-6]: (*R*)-Methyl(3-formylphenoxy)-2-propionate (*R*)-4; 374 mg, 1.8 mmol), and 2,3-dihydroxylammonium-2,3-dimethylbutane sulfate^[31] (439 mg, 1.8 mmol) were dissolved in dry methanol (20 mL) and the mixture was stirred at room temperature overnight. After addition of NaHCO₃ (151 mg, 1.8 mmol) in water (20 mL), the precipitate which formed was filtered off. Without further purification, this adduct was dissolved in CH₂Cl₂ (50 mL) and oxidised with a solution of

NaIO₄ (385 mg, 1.8 mmol) in water (30 mL). After stirring the two-phase mixture for 30 min at 0 °C, the organic phase was separated, and the aqueous phase was extracted with CH₂Cl₂ (2 × 20 mL). The combined organic phases were dried over Na₂SO₄, filtered, and stripped of solvent. The residue was subjected to column chromatography (SiO₂, AcOEt/CH₂Cl₂ 1:12) to yield the product as a dark blue solid (240 mg, 40%). M.p. 113 °C; UV/Vis (CH₂Cl₂): λ_{\max} (ϵ) = 269 (11 000), 365 (13 000), 589 (500), 620 nm (500); CD (CH₂Cl₂): λ_{\max} ($\Delta\epsilon$) = 260 (+0.85), 365 (−0.95), 435 nm (+0.14); IR (KBr): $\tilde{\nu}$ = 2987, 2952, 1757 (C(O)OCH₃), 1588, 1398, 1370, 1363 (NO), 1250, 1208, 1138, 1096, 1054, 804, 688, 540 cm^{−1}; LDI-TOF MS: m/z : 335.8 [M⁺], 303.8 [M − 2O]⁺; C₁₇H₂₃O₅N₂ (335.38): calcd: C 60.75, H 6.76, N 8.27; found: C 60.88, H 6.91, N 8.35; ESR (CH₂Cl₂, 10 μ M): g = 2.0066, a_N = 7.55 (2N), a_{ortho} = 0.431 (1H)/0.442 (1H), a_{meta} = 0.193 (1H), a_{para} = 0.378 (1H), a_{Me} = 0.212 (12H).

(R,S)-Methyl-[3-(4,4,5,5-tetramethyl-4,5-dihydro-1H-imidazolyl-1-oxy-3-oxido)phenoxy]-2-propionate [(R,S)-6]: The product was isolated in a 40% yield as a dark blue solid after reaction of (R,S)-methyl-(3-formylphenoxy)-2-propionate and 2,3-dihydroxylammonium-2,3-dimethylbutane sulfate by the procedure described for the chiral methyl ester (R)-6. M.p. 107 °C, UV/Vis (CH₂Cl₂) to the enantiopure compound; IR (KBr): $\tilde{\nu}$ = 2995, 2945, 1757 (C(O)OCH₃), 1581, 1447, 1391, 1363 (NO), 1286, 1237, 1138, 1096, 1054, 794, 688, 540 cm^{−1}; LDI-TOF MS: m/z : 335.8 [M⁺], 303.8 [M − 2O]⁺; ESR (CH₂Cl₂, 10 μ M): g = 2.0065, a_N = 7.57 (2N), a_{ortho} = 0.419 (1H)/0.430 (1H), a_{meta} = 0.222 (1H), a_{para} = 0.381 (1H), a_{Me} = 0.213 (12H).

(R)-[3-(4,4,5,5-Tetramethyl-4,5-dihydro-1H-imidazolyl-1-oxy-3-oxido)phenoxy]-2-propionic acid [(R)-1]: (R)-Methyl-[3-(4,4,5,5-tetramethyl-4,5-dihydro-1H-imidazolyl-1-oxy-3-oxido)phenoxy]-2-propionate (266 mg, 0.8 mmol) was dissolved in a solution containing NaOH (1 g, 25 mmol) in water (10 mL) and ethanol (10 mL) and was stirred at room temperature for 3 h. The mixture was acidified with aqueous HCl (10%) and the blue product was extracted with CH₂Cl₂ (3 × 20 mL). The combined organic phases were dried over Na₂SO₄, filtered, and stripped of solvent. The residue was purified by crystallisation from CH₂Cl₂/hexane to yield the product as a dark blue solid (240 mg, 94%). M.p. 130 °C; UV/Vis (CH₂Cl₂): λ_{\max} (ϵ) = 270 (11 000), 366 (13 000), 586 (500), 618 nm (500); CD (CH₂Cl₂): λ_{\max} ($\Delta\epsilon$) = 290 (+0.40), 365 (−0.70), 435 nm (+0.12); IR (KBr): $\tilde{\nu}$ = 2987, 2931, 2587 (C(O)OH), 2516 (C(O)OH), 1736 (C(O)OH), 1574, 1454, 1349 (NO), 1279, 1236, 1131, 1089, 1070, 794, 688, 540 cm^{−1}; LDI-TOF MS: m/z : 360.8 [M+K]⁺, 345.1 [M+Na]⁺, 329.1 [M+Li]⁺, 321.8 [M]⁺, 307.8 [M − CH₂]⁺, 291.8 [M − CH₂ − O]⁺; C₁₆H₂₁O₅N₂ (321.35): calcd: C 59.80, H 6.59, N 8.72; found: C 58.87, H 6.43, N 8.54; ESR (CH₂Cl₂, 10 μ M): g = 2.0064, a_N = 7.57 (2N), a_{ortho} = 0.448 (1H)/0.468 (1H), a_{meta} = 0.189 (1H), a_{para} = 0.392 (1H), a_{Me} = 0.208 (12H).

(R,S)-[3-(4,4,5,5-tetramethyl-4,5-dihydro-1H-imidazolyl-1-oxy-3-oxido)phenoxy]-2-propionic acid [(R,S)-1]: (R)-Methyl-[3-(4,4,5,5-tetramethyl-4,5-dihydro-1H-imidazolyl-1-oxy-3-oxido)phenoxy]-2-propionate was saponified by means of the same procedure as for (R)-1. The product was purified by crystallisation from CH₂Cl₂/hexane and isolated as a dark blue solid (240 mg, 94%). M.p. 145 °C; UV/Vis identical to the enantiopure compound; IR (KBr): $\tilde{\nu}$ = 3438, 3001, 2980, 2931, 2608 (C(O)OH), 2530 (C(O)OH), 1722 (C(O)OH), 1577, 1480, 1453, 1347 (NO), 1386, 1234, 1130, 1089, 1044, 790, 687, 539 cm^{−1}; LDI-TOF MS: m/z : 360.8 [M+K]⁺, 345.1 [M+Na]⁺, 329.7 [M+Li]⁺, 321.8 [M]⁺, 307.8 [M − CH₂]⁺; C₁₆H₂₁O₅N₂ (321.35): calcd: C 59.80, H 6.59, N 8.72; found: C 60.03, H 6.36, N 8.44; ESR (CH₂Cl₂, 10 μ M): g = 2.0065, a_N = 7.58 (2N), a_{ortho} = 0.448 (1H)/0.468 (1H), a_{meta} = 0.189 (1H), a_{para} = 0.392 (1H), a_{Me} = 0.208 (12H).

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