Stereoisomerism of Molecular Multipropellers. 1. Static Stereochemistry of Bis- and Tris-triaryl Systems

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The static stereoisomerism of bis- and tris-triaryl systems has been analyzed by a systematic stereochemical analysis, and the resulting theoretical predictions have been experimentally confirmed by using reversed-phase HPLC and ESR and ^{1}H NMR spectroscopies with a family of seven distinct polychlorinated aromatic multipropellers. To analyze the static stereochemistry of these molecules, we have developed a specific procedure that uses a symmetry-adapted symbolic notation, allowing the theoretical prediction of both the number and symmetry of the isomers of the investigated molecules. Due to the steric hindrance introduced by the presence of bulky chlorine substituents, (all) conformational isomers can be characterized experimentally by several independent techniques confirming the theoretical stereochemical predictions. The different propeller moieties that constitute the molecule appear to be nearly independent of each other. Consequently, most of the observed isomers show comparable populations in solution at room temperature.

Introduction

The stereoisomerism of di- and triaryl systems,[1] developed by the seminal work of Mislow and co-workers in the early 1970's, has been one of the central topics of modern stereochemistry, and its study has boosted the development of novel concepts in this field.[2] Particularly, the static and dynamic stereochemistry of di- and triarylmethanes[3,4,] and many other structurally related molecules have been thoroughly investigated.[5] These studies have lead to the development of a solid theoretical framework based on group theory that have been successful in the analysis of basic stereochemical problems; such as the investigation of the number and symmetry of conformational isomers and the analysis of their interconversion paths.[2,6]

Within this context, this work presents a complete stereochemical analysis of two families of extended triaryl systems, **1** and **2**, that is based on previous mathematical methods developed for the isomer enumeration and isomerization pathway analysis worked out and applied by a variety of researchers to related systems.[2−6] Compounds **1** and **2** are constituted by two and three overlapping polychlorinated triphenylmethane or triphenylmethyl moieties, respectively (Chart 1). Each triaryl moiety of **1** and **2** is forced by the bulky chlorine atoms that substitute all the aromatic ortho positions, crowding the surroundings of the carbon atoms central to each moiety and subsequently forcing the noncoplanarity of adjacent rings. Consequently, each triaryl moiety of **1** and **2** adopts a propeller-like arrangement, and they can be taken as model structures for what may be generically called "molecular multipropellers". Compounds **1** and **2** have a superficial resemblance to substituted hexaarylbenzenes, studied by Gust et al.,[5g] because of the presence of six aromatic rings around the central benzene. The complex stereoisomerism and stereoisomerization behavior of substituted hexaarylbenzenes were elegantly analyzed by these authors using group-theoretical methods

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(1) The terms *di-* and *triaryl systems* used throughout describe molecules containing moieties such as Ar^1Ar^2ZXY (or Ar^1Ar^2ZY) and $Ar^1Ar^2Ar^3ZX$ (or $Ar^1Ar^2Ar^3Z$), respectively, where Z is the central atom of the referred moiety, having either sp^2 (Z) or sp^3 (ZX) hybridization.

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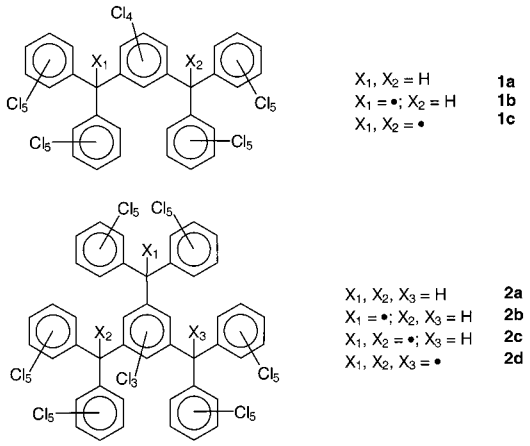
Chart 1



where isomers are treated in terms of permutations of ligands in sites on a rigid skeleton.[5g] However, the analysis of stereoisomerism of compounds **1** and **2** using the same theoretical methodology, although possible, becomes extremely cumbersome because they are much more stereochemically complex due to their lower symmetry, and therefore, they may potentially display very complex and subtle isomerization phenomena.

The synthesis, chemical characterization, and most important, physical properties of polychlorinated compounds **1** and **2** have been reported elsewhere.[7,8] In these previous works, the chlorocarbons **1a** and **2a** were used as chemical precursors for the synthesis of the target high-spin molecules **1c** and **2d**, which are still two of the most persistent purely organic open-shell species reported to date in which strong ferromagnetic interactions between their unpaired electrons has been achieved.[9−11] In the course of these studies, the understanding of the role played by stereoisomerism in extended propeller-like molecules proved essential for the correct interpretation of their spectroscopic and physicochemical properties.[7,8] This prompted us, first, to develop a general method for the prediction and description of the static and dynamic stereochemistry of molecular multipropellers and, second, to look for experimental evidence for the accuracy of this theoretical analysis. Particularly, this paper presents a thorough discussion of the static stereochemistry of seven molecules belonging to families **1** and **2**, leaving the presentation and discussion of the conformational dynamics of the above-mentioned compounds for a subsequent paper.

Results and Discussion

Basic Stereochemical Considerations Concerning "Molecular Multipropellers". The stereochemistry of molecules **1** and **2** was first analyzed using the classical method for single triaryl systems reported by Mislow and co-workers.[2,3] Since all external rings of each triaryl moiety of **1** and **2** have local C_2 symmetries, in simple systems constituted *exclusively* of a central atom with a sp^2 hybridization, such as **1c** and **2d**, the helicity is the only structural feature relevant to the stereochemistry; i.e., the unique stereogenic element.

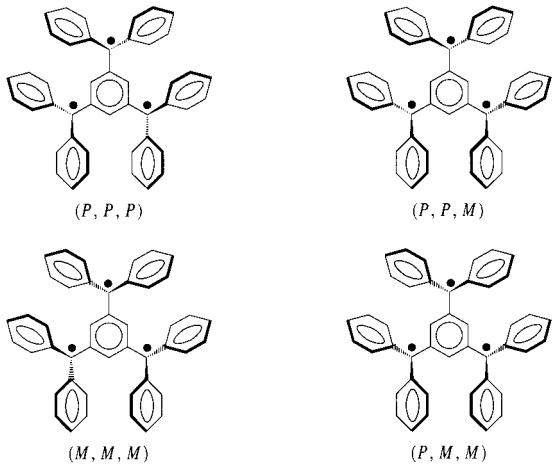


Figure 1. Stereoisomers of molecule **2d**. Chlorine atoms in all aromatic positions have been omitted for the sake of simplicity.

For such simple triaryl systems, it is relatively easy to predict and count the number of stereoisomers. Thus, taking the quartet molecule **2d** as an example (Figure 1), it is straightforward to predict the existence of four stereoisomers (two pairs of enantiomers)—namely, (*P*, *P*, *P*), (*P*, *P*, *M*), (*P*, *M*, *M*), and (*M*, *M*, *M*)—arising from the combination of two helical configurations[12] (*plus* and *minus*, denoted by *P*/*M*) for each triaryl moiety. Note that, once having specified these four configurations, other equally valid descriptions arising from other combinations of stereogenic elements, such as (*M*, *P*, *P*) and (*P*, *M*, *P*), are superfluous, since they are strictly equivalent to (*P*, *P*, *M*) by virtue of the molecular 3-fold symmetry. Therefore, they must be discarded in order to have a proper counting of the number of stereoisomers of **2d**. In accordance with Mislow's classification of topic and structural relationships,[13,14] static structures, such as those mentioned above, which are redundant from the stereochemical point of view, will be referred to as *homomers*.

As far as the less symmetrical structures of molecules **1a**,**b** and **2a**−**c** are concerned, we must take into consideration the sp^3 hybridization of some of the central carbon atoms, together with the lack of a C_2 local symmetry in any of its aromatic rings, which gives rise to a new stereogenic element—the planar chirality—in that helix.[3] Thus, in multipropeller structures, such as **1** and **2**, one might think that the simplest way to count the number of stereoisomers would be to divide each structure in two or three constitutive moieties, respectively, each adopting a propeller-like arrangement. The next step would be to calculate the total number of isomers of a given molecule as the product of the number and multiplicity of the stereogenic elements—helicity and planar chirality—contributed by each moiety; as predicted for single di- and triaryl systems by Gust et al.[15] For

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(13) Mislow, K.; Raban, M. *Top. Stereochem.* **1967**, *1*, 1−38.
(14) Mislow, K. *B. Soc. Chim. Belg.* **1977**, *86*, 595−601.
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instance, the structures of **1a**, **1b** and **1c** may be rationalized as constituted of two building blocks, one triaryl, and one diaryl moiety. Thus, according to the simple "product" approach for counting the isomers, 16, 8, and 4 different stereoisomers would be predicted for these molecules, respectively. We will show below that, except for **1b**, the number of isomers estimated in such a way exceeds the real one (see Table 3), because some of the structures generated are not true stereoisomers, but *homomers*. The failure of this simple approach arises from the fact that some wrong hypotheses are implicitly assumed as valid.[16] As the number or stereogenic elements increases and the three-dimensional structure of molecular multipropellers becomes more complicated, checking for the rotational equivalencies shown by homomeric structures becomes increasingly cumbersome and difficult to solve intuitively. It is thus essential to have an alternative methodology that enables redundant combinations to be discarded in a simple and systematic fashion.

A Symmetry-Adapted Symbolic Notation for Molecular Multipropellers. The purpose of this section is to outline a systematic and simple methodology, which will make use of a symmetry-adapted symbolic notation, capable of counting the stereoisomers of **1** and **2** in an accurate and efficient way while, at the same time, providing their respective molecular symmetries. A similar conceptual approach was developed by Willem and co-workers for the stereochemical analysis of the isomers of tetrakis(*o*-tolyl)cyclopentadienone.[5d] Here, the scope of this approach has been widened to incorporate the multipropeller molecules.

For most molecular systems, including **1** and **2**, a hypothetical planar molecular model that is constitutionally identical to the real one but nonetheless devoid of any stereogenic elements—such as the *structural formulas* usually employed by chemists to describe constitutional isomers—may be generated. In this context, a suitable *structural formula* for molecules of series **1** would be an ideally planar, unlabeled structural formula having a C_{2v} symmetry, such as **3**, whereas that for series **2** should have a D_{3h} symmetry, such as **4** (Figure 2). It is clear from *structural formulas* **3** and **4** that all moieties of the molecules under study are symmetry related from the constitutional point of view. These planar *structural formulas* can be converted into the real, three-dimensional model structures by means of a desymmetrization process. For instance, helicity can be "turned on" in *any* moiety, or else, *any* planar central atom can be rendered tetrahedral by placing a fourth substituent in the real molecule. Since the groups of atoms that constitute the different moieties are homotopically related in the original structures, the effect of a given structural change leading to a loss of general symmetry will be the same for all moieties. Thus, as many different, but rotationally equivalent, i.e. homomeric, static representations of the molecule having a certain stereogenic element can be generated as indicated by the order of the axis lost upon desymmetrization. Bearing this simple rule in mind, it follows that it is possible to check for the equivalence of two given static representations[17] of any molecule of series **1** and **2** in a simple way by first generating all possible static representations, followed by systematically rotating each representation around *all* the symmetry axes of their corresponding undesymmetrized planar *structural formulas* **3** and **4**, shown in Figure 2. In doing so, we ensure that all possible degeneracies are explored, regardless of the degree of desymmetrization achieved in the generation of the real structure.

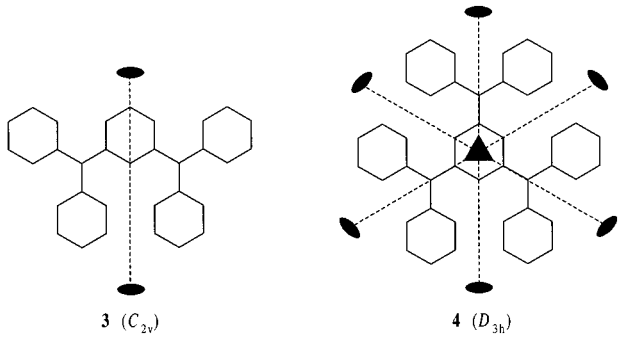


Figure 2. Planar *structural formulas* and rotation axes used in the analysis of the static stereochemistry of molecules pertaining to series **1** (left) and **2** (right).

To avoid the use of explicit three-dimensional structures that might be extremely complex, we have developed a procedure that uses a specific symbolic notation for this purpose. This symbolic notation conforms to the following requisites: (a) it purports all the three-dimensional information relevant to the stereochemical analysis and (b) it is symmetry-adapted.[18] In other words, the application of properly defined rotation and enantiomerization operations upon the notation transforms the combination of symbols unambiguously and in such a way that it truly reflects the effects of the same operations when applied on static, three-dimensional representations of molecules **1** and **2**.

To achieve the maximal simplicity in this symbolic notation, each structure will be factorized in as few relevant structural descriptors as possible, each one related to a given stereogenic element. Each descriptor is denoted by a letter, indicating the type of stereogenic element, accompanied by a "+" or "−" sign, which indicates the particular arrangement adopted by the stereogenic element. Finally, a symbolic name is assigned to each static representation by a particular set of the above-mentioned descriptors, taking into account that, in their assembly, both the signs attached to structural descriptors and the order in which these descriptors appear are determined according to a set of preestablished arbitrary rules.

(16) In the simple "product" approach, the following hypotheses are assumed: (a) the stereogenic elements of both substructures are completely independent of each other; (b) the connection of both substructures does not generate any additional stereogenic elements; and (c) no further degeneracies arise from the connection of both substructures. So far, the first hypothesis is reasonable, since both helicity and planar chirality are circumscribed to each substructure. As far as the second hypothesis is concerned, we must assume that structures are compact and rigid enough so as not to present secondary structures. The third and last hypothesis is by far the most problematic, since it is not always valid. Indeed, in molecules **1a** and **1c**, as well as in **2a**, and **2d**, the external diaryl moieties are constitutionally (and, in certain cases, stereochemically) identical to each other. It is thus possible, as already exemplified by molecule **2d**, that these two or three moieties remain homotopically related and therefore are equivalent upon free rotation of the structure. For these molecules, therefore, the number of stereoisomers should be, and is indeed, lower that predicted by the "product" approach of the number of stereoisomers of their constituting moieties.

(17) From now on, a "*static representation*" will be any motionless structure generated solely by permutation of ligands or stereogenic elements, *as seen by an external observer*. In this respect, static representations are equivalent to the so-called *ordered molecules* described by Willem et al., ref 6d,e.

(18) Mislow, K.; Siegel, J. *J. Am. Chem. Soc.* **1984**, *106*, 3319−3328.

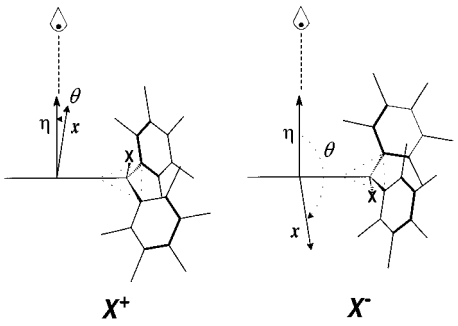


Figure 3. Rule adopted for describing the orientation of an X substituent on the central carbon atom with respect to an external observer of di- or triaryl systems having sp^3 hybridization. The reference vector ($\vec{\eta}$) is defined as normal to the reference plane—the inner ring of the molecule—and pointing toward the eye of the observer. The local vector ($\vec{x}$) for each sp^3 center is defined as that which originates in the central carbon atom and ends up in the X substituent—a hydrogen atom for all the structures investigated here—directly attached to it.

In view of the structural features of molecules **1** and **2**, it seems logical to use only two kinds of structural descriptors for the two types of stereogenic elements—helicity and planar chirality—existing in these molecules and a binary index for each descriptor.[19] As far as helicity is concerned, we have adapted the usual Cahn−Ingold−Prelog nomenclature system[12]—hereafter referred to as CIP—since it distinguishes *plus* (*P*) and *minus* (*M*) configurations according to the rotation sense of the propeller. These have been translated straightforwardly into h^+ and h^-, respectively, where *h* is the helicity descriptor. As far as the configuration of chiral planes is concerned, we took a more straightforward approach than that established by CIP rules, which is very similar to that used for the analysis of tetrakis(*o*-tolyl)cyclopentadienone.[5d] Thus, we refer to the two possible *orientations* of the X substituent placed in any propeller subunit with respect to an arbitrary reference plane—the inner ring of the molecule—and the position of an external observer facing the reference plane as X^+ and X^-; as shown in Figure 3.[20,21]

Finally, a given isomer is denoted by a sequence of letters and signs, where those corresponding to the same propeller-like moiety are enclosed between brackets. The left-to-right and clockwise order in which the moieties are placed in the symbolic notation corresponds to that in which they appear to the eye of the observer, as shown in Figure 4.

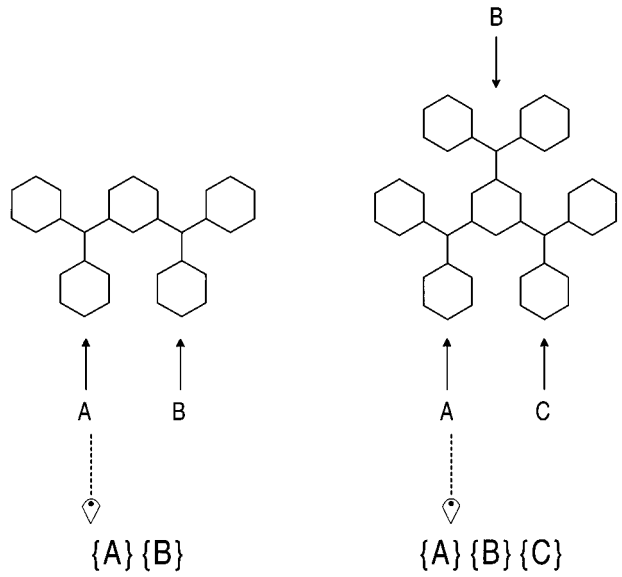


Figure 4. Rule adopted for describing the position of the two (and three) triaryl moieties with respect to an external observer.

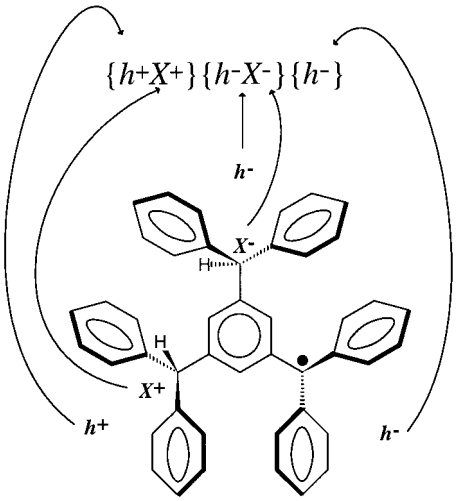


Figure 5. Example showing the relationship between the three-dimensional structure of one of the stereoisomers of **2b** and the symmetry-adapted symbolic notation developed.

Figure 5 shows an example of a static representation of one of the stereoisomers of **2b**, together with the translation of its real three-dimensional structure in terms of the symmetry-adapted symbolic notation described.

In order for the symbolic notation to be symmetry-adapted for systems **1** and **2**, it is required that it transforms appropriately upon the application of the above-mentioned symmetry operations—namely, a 2-fold in-plane rotation for **1** and three 2-fold in-plane rotations along with one 3-fold perpendicular rotation for **2**, and a reflection/enantiomerization operation for both series of molecules—to the static representations of all molecules. The determination of the "static" *transformation rules* for each symmetry operation can be carried out straightforwardly in a qualitative way as follows. First, perpendicular rotations (see Figure 6, top) do not change the orientation of X substituents with respect to the observer,

(19) The binary character ascribed to each descriptor implies that the information relevant to the stereochemical analysis can be reduced to a simple dichotomy. In our case, the dichotomy is elucidated either by the rotation sense (helicity) or by means of the orientation of X with respect a reference plane (chiral plane).

(20) A rigorous, geometrical definition of this orientation involves, first, the definition of a reference vector ($\vec{\eta}$), normal to the reference plane and pointing toward the eye of the observer. A local vector ($\vec{x}$) for each sp^3 center is then defined, as that which originates in a central atom and ends up in the X substituent—a hydrogen atom for all the structures investigated here—directly attached to it. If the angle comprised between a given local vector and the reference vector is lower than 90°, the X substituent is said to point "upwards" and is denoted by X^+, or X^- otherwise (see Figure 3). Obviously, this notation would break down if θ were exactly 90°, but no such case arises in series of compounds **1** and **2**.

(21) The obvious advantage of this arbitrary notation is that it yields the symmetry of the conformers straightforwardly once the transformation rules are established and the analysis is carried out. In our opinion, the use of "proximal/distal" notation to describe the orientation of X substituent, although more elegant, does not yield symmetry relationships so straightforwardly.

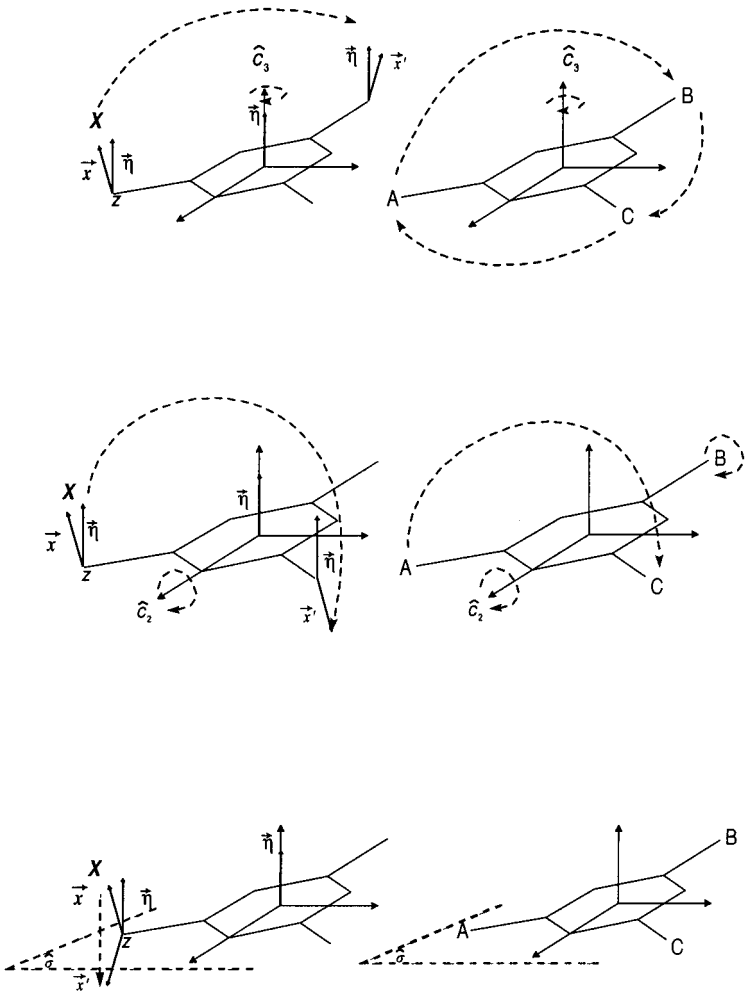


Figure 6. Determination of the changes in the orientation of X substituents (left) and the position of triaryl moieties (right) with respect to an external observer, when a three-dimensional model of a molecular propeller is subject to: (a) 3-fold rotations perpendicular to the inner aromatic ring (top), (b) 2-fold in-plane rotations (center), and (c) a reflection through the plane of the inner ring (bottom). For definitions of the reference vector ($\vec{\eta}$) and the local vector ($\vec{x}$) for each sp^3 center of the molecule, see Figure 3. The transformed vector ($\vec{x}'$) results from the application of a rotation or reflection operation to the local vector $\vec{x}$.

but exchange the positions of all triaryl moieties in a rotatory fashion. On the other hand, in-plane, binary rotations (see Figure 6, center) invert the orientations of all X substituents, while only the positions of triaryl moieties external to, i.e., not bisected by, the rotation axis are exchanged. As far as helicities are concerned, neither of the rotations change their sign, since by definition, they are true, stand-alone stereogenic elements. Last, but not least, to determine the symmetry and so to both classify stereoisomers properly and investigate the existence of meso forms, it is desirable to determine the effect of an enantiomerization operation upon a given static representation. Bearing in mind that *any* reflection plane transforms a chiral object into its mirror image and for the sake of convenience, we have chosen the molecular reference plane defined above as our enantiomerization plane (see Figure 6, bottom). Thus, only the positions of triaryl moieties with respect to the observer remain invariant, whereas *both* their respective helicities and the orientations of all X substituents are inverted. These results are summarized in Table 1, which constitute the "static" *transformation rules* for systems **1** and **2**.

Isomer Counting for Molecules Belonging to Series 1 and 2. In structures **1** and **2,** each triaryl moiety hosts one (only helicity) or two stereogenic elements (helicity and chiral plane). Therefore, the number of distinct static representations (N) of any of these molecules is given by the following equation

$$N = 2^m \cdot 2^k \cdot P^m_{k,m-k} = 2^{m+k} \cdot \frac{m!}{k! \cdot (m-k)!} \qquad (1)$$

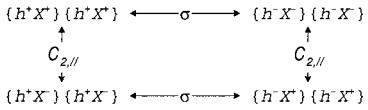
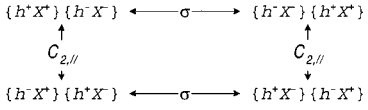
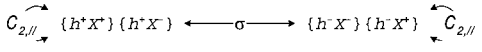
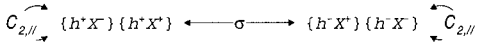
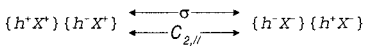
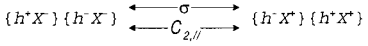
where m is the total number of triaryl moieties and k the number of those that have central atoms with sp^3 hybridization. The first factor of eq 1 accounts for the isomers generated by the existence of m helices with two (h^+ or h^-) possible configurations. In a similar fashion, the second factor takes into consideration the existence of "up" (X^+) and "down" (X^-) orientations for all the different X substituents, each located in one of the k helices supporting sp^3 central atoms. Finally, the permutational factor ($P^m_{k,m-k}$) gives the number of ways in which constitutionally different moieties can combine in the molecular skeleton. Obviously, when all moieties are constitutionally identical, i.e., when $k = m$ or $k = 0$, then $P^m_{m,0} = P^m_{0,m} = 1$; i.e., the permutation of their positions relative to an external observer does not give rise to different static representations.

We can now apply the transformation rules summarized in Table 1 to the whole set of static representa-

Table 1. "Static" Transformation Rules for Symmetry Operations Applied to Compounds 1 and 2

operation	helicity	orientation of central substituent	position of triaryl moieties
three-fold, perpendicular rotation ($\hat{C}_3$ or $C_{3,\perp}$)	no change	no change	rotatory exchange of all moieties
two-fold, in-plane rotation ($\hat{C}_2$ or $C_{2,\parallel}$)	no change	inversion	exchange of external moieties
reflection across the reference plane (σ)	inversion	inversion	no change

Table 2. Analysis of the Static Stereochemistry of Chlorocarbon 1a Employing the Symmetry-adapted Symbolic Notation

Relationships between the 16 static representations	Molecular symmetry
	C_1
	C_1
	C_2
	C_2
	C_s
	C_s

tions of a given molecule, as described by the symbolic notation presented in the previous section. This approach is exemplified by **1a**, as follows: The number of static representations of this molecule ($k = 2$, $m = 2$), as given by eq 1, is 16 (Table 2). As far as the static stereochemistry is concerned, this molecule is particularly interesting, since its conformational isomers belong to the three symmetry groups to be found for molecules **1a** and **1b**: chiral isomers (C_1), chiral isomers with a 2-fold symmetry axis (C_2), and achiral (meso) isomeric forms (C_s). Static representations belonging to conformations of a given symmetry group behave in a characteristic way, with regard to the rotation and reflection operations previously defined. Particularly, in the C_1 group, each isomer has two possible symbolic representations, and being chiral, each one has an enantiomeric counterpart. Thus, when cross-relationships are combined, the eight static representations with C_1 symmetry appear grouped in only two true enantiomeric pairs; as depicted in Table 2. In the C_2 group, no cross-relationships between different static representations are found (Table 2) by means of the 2-fold rotation, because the 2-fold rotation axis is, in fact, a true symmetry axis. As happens in the C_1 group, the chirality of the symmetry group is evidenced in the notation by the fact that reflection operations always relate different, rotationally nonequivalent, static representations; as shown in Table 2. Conversely, in the C_s group of isomers reflection operations generate rotationally equivalent static representations, which are thus achiral; as depicted in Table 2. Consequently, the total number of conformers of **1a** is 10, grouped in four pairs of enantiomers, two with C_1 and the other two with a C_2 symmetry, and two additional meso forms with C_s symmetry.[22] A similar, detailed analysis of the static representations of all the molecules belonging to series **1** and **2** may be found as Supporting Information. Overall then, the application of the methodology described in the previous section with the symbolic notation developed provides a convenient and useful way to count the specific isomers of molecular multipropellers **1** and **2**, and a straightforward means of finding the symmetry relationships within and among the isomers.

Table 3 summarizes the final results of the application of the symmetry-adapted symbolic notation and the "static" *transformation rules* to the molecules of series **1** and **2** showing the total number of stereoisomers and diastereomers as well as their symmetries. No meso forms are found for series **2**, since it possesses an odd number of helical moieties. This is not obviously the case for series **1**, where the chlorine atom in a meta position with respect to the two central carbon atoms takes the place of the biphenylmethyl substituent in series **2**. Since this Cl atom has spherical symmetry, it is possible to find a plane bisecting it that acts as a molecular mirror plane. This situation occurs in **1a** and **1c** in which this plane divides the molecule into two constitutionally identical halves, and for which meso forms are found.

As expected, the total number of isomers in series **1** increases with the number of stereogenic elements present. It should be pointed out that this rather intuitive trend breaks down in series **2** with compound **2a**, for which a dramatic reduction in the number of isomers is found with respect to **2b**; in spite that the last compound has one less stereogenic element than the former. This apparent anomaly can be qualitatively explained as follows: **2a** has three constitutionally identical moieties in contrast to **2b**, which has only two. Therefore, on the grounds of connectivity only, the chances of generating isomers are lower for **2a**. This overcompensates the fact that it is potentially more disymmetrical with regard to the number of stereogenic centers it possesses.[23]

Once the number and symmetry of the distinct stereoisomers of compounds of series **1** and **2** were theoretically determined, these results were validated by employing several different experimental techniques—chromatographic and spectroscopic—capable of observing

(22) The stereoisomers of **1a** provide a nice case of the so-called stereochemical correspondence. In fact, tetrakis(*o*-tolyl)cyclopentadienone (see ref 6d) has been previously reported to present an identical number of isomers, with the same respective symmetries, despite evident structural differences between this molecule and the two-propeller system **1a**. Thus, the former molecule has a single stereogenic element—a chiral plane—of a higher multiplicity, whereas **1a** has been factorized, according to the CIP system, into four stereogenic elements—two helices and two chiral planes—of low (binary) multiplicity.

(23) It should be noted that in the original, ideally planar structural formula **4**, that represents all the molecules pertaining to series **2**, *all* central carbon atoms are homotopic. Thus, if all of them are simultaneously homosubstituted, or replaced by the same set of stereogenic elements—such as what happen for **2a** and **2d** but never for **2b**, nor for **2c**—there would be fewer chances to break the rotational symmetry of **4**; that is, less overall symmetry is introduced. Indeed, one of the isomers of **2a** keeps much of the rotational symmetry (C_3) of the hypothetical planar model (D_{3h}).

Table 3. Summary of the Static Stereochemical Analysis for Compounds of Series 1 and 2

molecule	no. of stereoisomers	symmetry of isomers[a]	no. of diastereomers	no. of expected ^{1}H NMR signals[b]	no. of 2- and 3-bond correlations expected in HMBC NMR spectra[b,c]	no. of expected *zfs*[d] singularities in ESR spectra[b]
1a	10	C_2 (2 pairs) C_s (2) C_1 (2 pairs)	6	8	72	
1b	8	C_1 (4 pairs)	4			
1c	3	C_1 (1 pair) C_s (1)	2			6 6
2a	12	C_3 (1 pair) C_1 (5 pairs)	6	16	143	
2b	20	C_2 (4 pairs) C_1 (6 pairs)	10			
2c	8	C_1 (4 pairs)	4			12 (6 + 6)
2d	4	D_3 (1 pair) C_2 (1 pair)	2			12 (5 + 7)

[a] Numbers between parentheses refer to the number of stereoisomers belonging to each symmetry class. [b] Number of expected signals for a mixture of all stereoisomers of the compound. [c] 2- and 3-bond correlations between ^{1}H and ^{13}C nuclei expected in the hetero multiple bond correlation spectra (see NMR Spectroscopy section). [d] *zfs* refers to the zero-field-splitting of the energy levels of high-spin states produced by the dipolar interaction between the unpaired electrons. Such dipolar interactions are responsible for the appearance of characteristic singularities (turning points and lines) in the frozen ESR spectra of these species (see ESR Spectroscopy section).

the different stereoisomers as separate species. The stereoisomers of molecular propellers and multipropellers of types **1** and **2** with high steric hindrance are generally subject to relatively slow interconversion processes, whose energy barriers range typically between 20 and 30 kcal·mol^{-1}.[24−26] Since the study of the *static* stereochemistry of these molecules requires the observation of the different stereoisomers as separate species with distinct physicochemical properties, a correct interpretation of the experimental data largely depends on the time scale of the analytical technique used, in relation to that of the interconversion processes. Standard high-performance liquid chromatography (HPLC) and nuclear magnetic resonance (NMR) and electron spin resonance (ESR) spectroscopies fulfill these conditions and as such are appropriate for our purposes. Results expected to be observed with these techniques, regarding the number and symmetries of stereoisomers, are summarized in Table 3.

Liquid Chromatography. HPLC, using achiral and chiral stationary phases, has been used in the separation of diastereoisomers[5g−i] and enantiomers[24−26] of propeller-like molecules showing restricted internal motions. In all these cases, HPLC experiments were carried out at room temperature, without the interconversion processes interfering significantly. This was due to the fact that interconversion barriers, shown to be in the mid-20 kcal·mol^{-1} region, were high enough to yield pure diastereoisomers provided that retention times were sufficiently small (minutes). As far as molecular multipropellers, such as those presented here, are concerned, previous experiments showed that the interconversion barriers barely exceeded 20 kcal·mol^{-1}, in particular for those molecules with central carbon atoms having sp^3 hybridization.[25,26] With regard to HPLC experiments, the interconversion prevented us from achieving successful separations at room temperature, requiring to run the experiments at much lower temperatures, that range from 0 to −30 °C.[7,8] Under these circumstances, separations became rather awkward because of peak broadening and the low general solubility of molecules belonging to families **1** and **2**, and thus, suitable experimental conditions had to be screened carefully.[27] Moreover, the most insoluble species turned out to be precisely the stereochemically most complex ones; namely, chlorocarbon precursors **1a** and **2a**. Despite these limitations, we managed to get satisfactory partial separations in most cases, at least for analytical detection purposes. The set of "best" chromatographic analyses obtained, one for each molecule, is depicted in Figures 7 and 8.

The number of peaks expected for an HPLC separation, using a standard reversed stationary phase, is straightforward since they must correspond to the number of diastereomers of the analyzed molecule (see Table 3) because this stationary phase is achiral. Thus, the chromatographic analyses of biradical **1c** and monoradical **1b** are fully satisfactory (Figure 7, top and center), whereas out of six chromatographic peaks expected for **1a**, only five are clearly observed in the chromatogram (Figure 7, bottom) suggesting that one of these five peaks contains two different isomers.

Similar results have been obtained for three-propeller molecules **2**. While satisfactory separations have been achieved for the diastereomeric forms of the structurally simplest systems, such as triradical **2d** and biradical **2c** (Figure 8, top and center-top), an unavoidable peak overlap causes the number of observed peaks both for monoradical **2b** and chlorocarbon **2a** to be lower than those theoretically expected (Figure 8, center-bottom and bottom).

ESR Spectroscopy and Crystal Structures. As we have previously shown,[7,8] ESR spectroscopy can be used to visualize and characterize the stereoisomers of simple triaryl-based polyradicals having $S \geq 1$ ground states, such as **1c**, **2c**, and **2d**. In this respect, advantage is taken of the fact that the *intra*molecular dipolar interaction among two or more unpaired electrons of a given high-spin molecule is directly related to its electronic spin

(24) Hayes, K. S.; Nagumo, M. Blount, J. F.; Mislow, K. *J. Am. Chem. Soc.* **1980**, *102*, 2773−2776. Okamoto, Y.; Yashima, E.; Hatada, K.; Mislow, K. *J. Org. Chem.* **1984**, *49*, 557−558.

(25) (a) Veciana, J.; Crespo, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 74−76. (b) Crespo, M.-I. Ph.D. Thesis, Institut Químic de Sarrià (Universitat Ramon Llull), Barcelona, 1991, p 306.

(26) Ventosa, N. Ph.D. Thesis, Institut Químic de Sarrià (Universitat Ramon Llull), Barcelona, 1996, p 393.

(27) Biali and co-workers reported a similar situation in which the chiral resolution of the enantiomers of decakis(dichloromethyl)biphenyl at 288 K was marred by extensive peak broadening although it was carried out successfully at 293 K; see ref 5i.

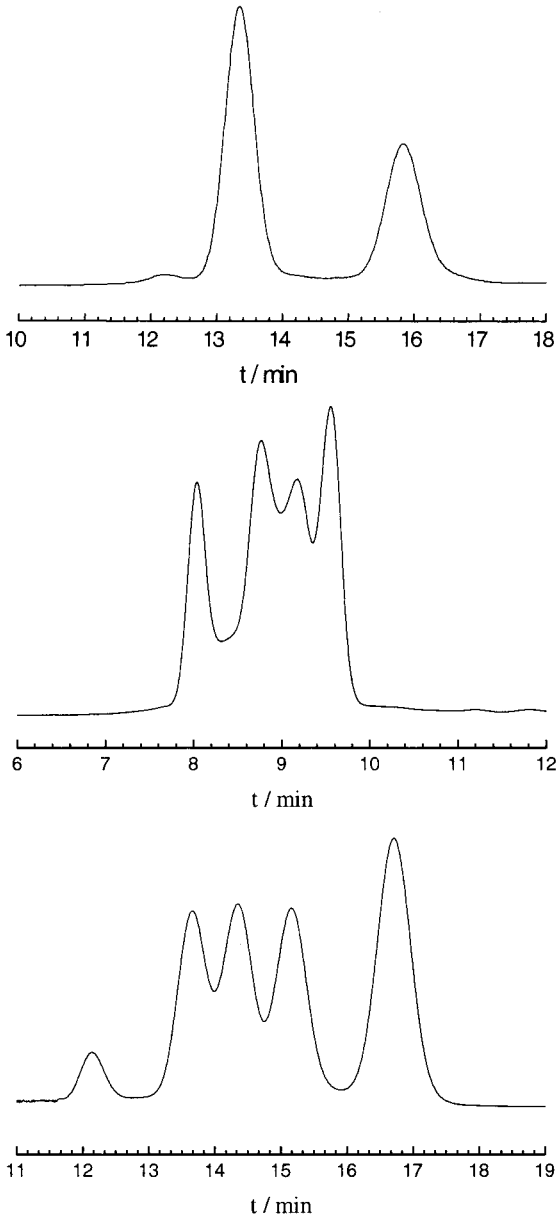


Figure 7. Separation of the diastereoisomers of molecules **1a** (bottom), **1b** (center), and **1c** (top). Experiments have been carried out using an acetonitrile/tetrahydrofuran (55:45) mixture as the mobile phase and a reversed-phase chromatographic column thermostated at 249, 276, and 257 K, respectively.

distribution, which itself depends largely on its three-dimensional structure and symmetry.[28]

The three-propeller quartets **2d** and **5** (Chart 2)[29] provide particularly instructive examples in this context,

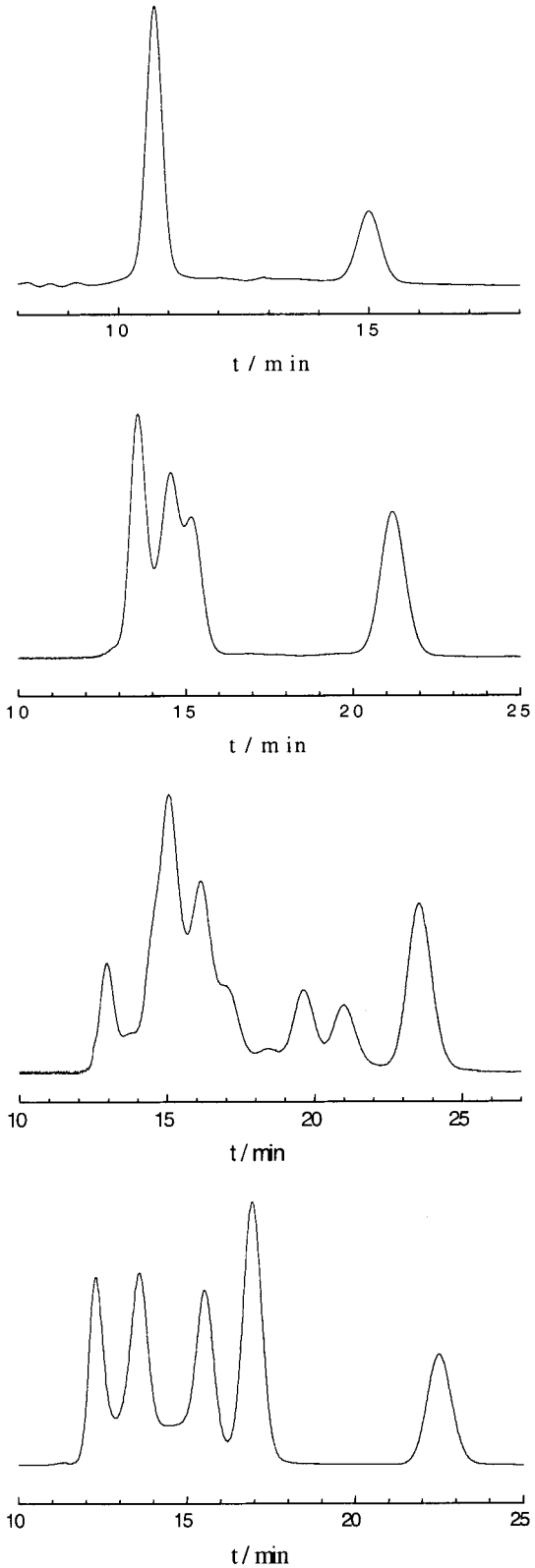


Figure 8. Separation of the diastereoisomers of molecules **2a** (bottom), **2b** (center-bottom), **2c** (center-top), and **2d** (top). Experiments have been carried out using an acetonitrile/tetrahydrofuran (50:50) mixture as the mobile phase and a reversed-phase chromatographic column thermostated at 269, 257, 256, and 248 K, respectively.

since two diastereomeric forms—one having an axial symmetry (D_3) and another presenting a nonaxial symmetry (C_2)—were predicted (Table 3) for both quartets

(28) It is widely known that the ESR spectrum of a frozen sample of a triplet species ($S = 1$) with axial symmetry shows four singularities, whereas a triplet species without axial symmetry shows six of them. Similarly, if the radical species is a quartet ($S = {}^3/_2$), the number of singularities appearing in the ESR spectrum of a frozen sample amounts to five if the species possess an axial symmetry, or seven otherwise. See: Atherton, N. M. *Principles of Electron Spin Resonance*; Ellis Horwood – PTR Prentice Hall: London, 1993. Weil, J. A.; Bolton, J. R.; Wertz, J. E. *Electron Paramagnetic Resonance: Elementary Theory and Practical Applications*; John Wiley & Sons: New York, 1994.

(29) The three-propeller quartet molecule **5**, which has hydrogens instead of chlorine atoms in all 12 meta aromatic positions, corresponds stereochemically to **2d**, since all external aromatic rings of this molecule keep their local C_2 symmetry.

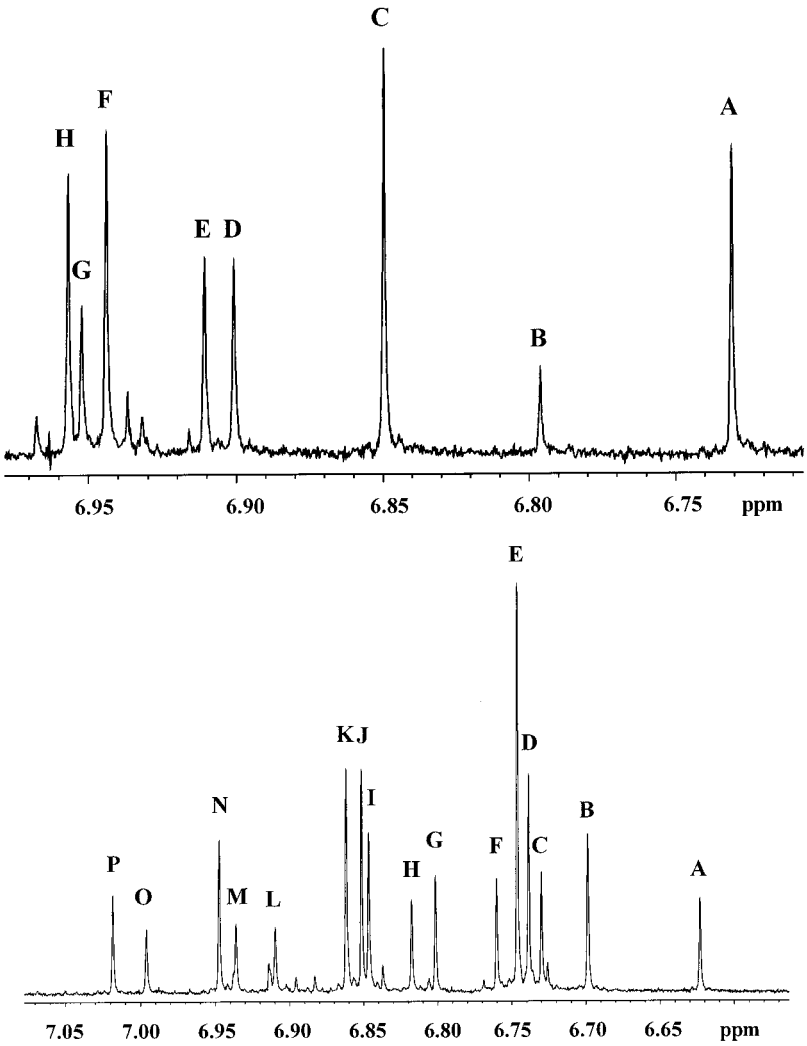
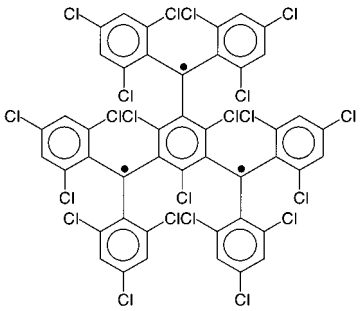


Figure 9. ^{1}H NMR spectra (in $DCCl_3$) of chlorocarbons **1a** (top) at 298 K and **2a** (bottom) at 318 K.

Chart 2



5

and later on confirmed by ESR spectroscopy.[8,30] In addition, we also reported very recently the resolution of two crystal structures of quartet **5**, providing for the first time suitable first-hand evidence of the accuracy of our predictions.[30] Thus, regardless of minor structural distortions caused by crystal packing forces, each crystal was shown to be a racemic mixture of one of the predicted diastereomeric forms with C_2 and D_3 molecular symmetries. Due to severe signal overlap, the derivation of structural information from ESR spectra becomes increasingly awkward as the number of stereoisomers increases in a given compound. Thus, it was impossible to sort out all four diastereoisomers of triplet **2c** from each other. In fact, the contributions of only three of the four expected diastereoisomers were clearly observed.[8] Compared with **2d**, the lack of axial symmetry in both diastereomeric forms of the two-propeller biradical **1c** accounts for the apparent major complexity of its ESR dipolar spectrum (Table 3).[7]

NMR Spectroscopy. ^{1}H NMR experiments were carried out only on the closed-shell, diamagnetic chlorocarbons **1a** and **2a**. In both molecules, each triaryl moiety supports a single hydrogen atom which, as mentioned in previous Sections, acts as the X substituent of the helix. This particular structural feature has proven extremely useful for our analytical purposes, since it gives the *minimum* number of proton signals ensuring that the spectroscopic identity of each moiety is conserved. In other words, because each propeller supports a single proton, this constitutes the simplest (magnetic) probe of the conformational changes taking place in each propeller. All signals corresponding to symmetry unrelated nuclei appear as singlets with characteristic chemical shifts ranging from 6.5 to 7.0 ppm. The number of resonance signals appearing in ^{1}H NMR spectra of species **1a** and **2a** in solution ($CDCl_3$) are in full agreement with our theoretical expectations, as summarized in Table 3. As seen in Figure 9, top, the separation of

(30) Sedó, J.; Ventosa, N.; Ruiz, D.; Mas, M.; Molins, E.; Rovira, C.; Veciana, J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 330−333.

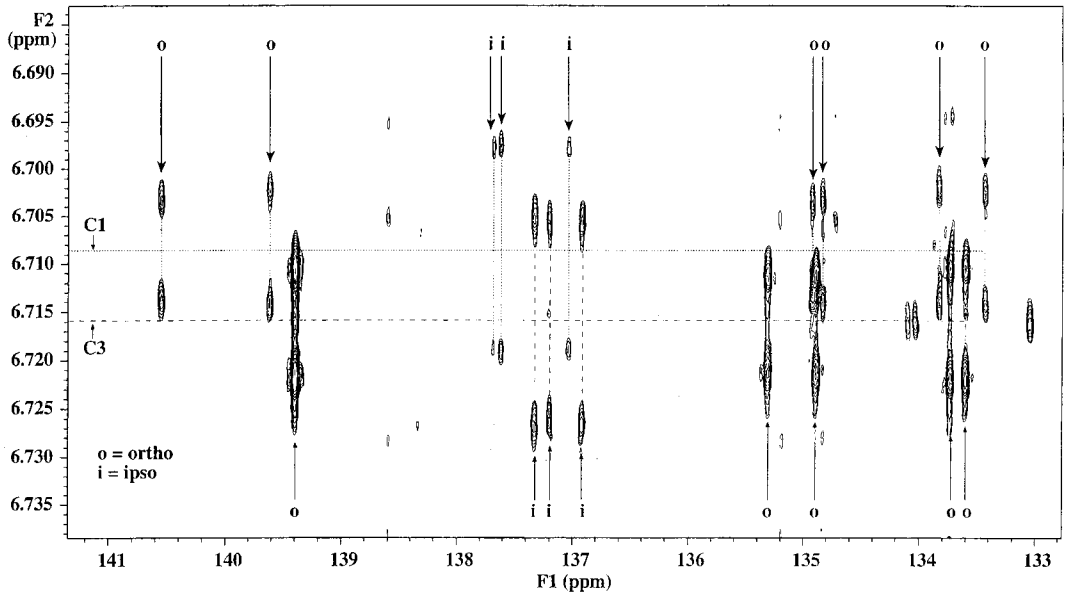


Figure 10. Expansion of the HMBC spectrum of chlorocarbon **2a.**

the eight signals of **1a** is excellent. Because all 16 signals of **2a** appear scattered in almost the same spectral range, their separation is somewhat smaller in this case (Figure 9, bottom). However, it is large enough for both molecules, so that the interpretation of both spectra is clear and unambiguous.

A different insight into the symmetry properties of the different isomers of **1a** and **2a** can be obtained from ^{13}C NMR data. However, direct observation of such signals is precluded by the low solubility, long relaxation times, and the severe spectral overlap of nonequivalent aromatic carbons of all the different isomers (124 for **1a** and 224 for **2a**). Hetero multiple bond correlation (HMBC) spectra,[31] however, provide a better way of observing with a good sensitivity the aromatic carbons that show two-bond and three-bond couplings to protons, i.e., the carbons at the ipso and ortho positions with respect to the protonated substituent. This fact reduces the maximum number of observable aromatic carbons in the isomer mixture to 70 for **1a** and 128 to **2a**. Additionally, carbon resonances are separated by the chemical shift of the coupled proton and therefore a better resolution is achieved. Thus, each proton in a low symmetry isomer, C_1, shows long-range correlations to nine different carbon atoms: three ipso and six ortho carbons. C_2 and C_s symmetry isomers of **1a** also show the same number of correlations as the symmetry elements relate the two propeller units but each of them is completely nonsymmetrical. The C_3 isomer of **2a** shows only eight correlations to its single proton signal as the two ortho positions of the inner ring are made equivalent by the symmetry axis. Aromatic carbons in the meta and para positions show no coupling to protons and are not observed. Therefore, the total number of expected $^1H-^{13}C$ correlation signals in the isomer mixture (see Table 3) is 72 for **1a** and 143 for **2a**. Experimentally 67 and 137 of such correlation signals could be resolved for **1a** and **2a**, respectively.

Figure 10 shows an expansion of the HMBC spectrum showing the long-range $^1H-^{13}C$ correlations of the isomer with a C_3 symmetry and one of the C_1 isomers of **2a**. Spectra were obtained without carbon decoupling during the acquisition, and therefore, each correlation appears as a doublet and allows an easy differentiation of ipso and ortho carbons. No further assignments were attempted. Thus, HMBC spectra provide a straightforward means of grouping signals that belong to the same diastereomeric form. Signals from low symmetry isomers of **2a** give rise to a six cross-peak pattern in the three-propeller molecules as each proton is coupled to two nonequivalent ortho carbons in the inner ring, and each of these is coupled to two nonequivalent protons (see Figure S8). For two-propeller molecules, such as **1a**, the two potentially different protons share only one common coupling partenaire.

Figure 11 shows an expansion of the HMBC spectra of compounds **1a** and **2a**. It reveals that peaks (A, F) and (D, E) in the proton spectra of chlorocarbon **1a** and (A, H, P), (B, I, N), (C, F, G), (D, J, K), and (L, M, D) in that of **2a** belong to different C_1 symmetry isomers. The remaining signals correspond to high-symmetry isomers, i.e., C_2, C_s, or C_3.

Conclusions obtained from NMR spectra allowed us to reanalyze the results acquired by HPLC.[32] Although one chromatographic peak remained unresolved for **1a** and **2a**, a tentative assignment was carried out by comparison between the integrated intensity of the ^1H NMR signals and the integrated areas of the observed chromatographic peaks. In this respect, we assumed that one of the observed chromatographic peaks comprises actually the contributions of two isomers. In view of the severe peak overlap, asymmetric Gaussian functions were used to deconvolute both chromatograms. The results of the best assignments for **1a** and **2a** are summarized in Tables S8 and S9 (see the Supporting Information), respectively. There is a good agreement between the two techniques with average discrepancies of only 0.5% between population values calculated by both techniques and also very

(31) Bax, A.; Summers, M. F. *J. Am. Chem. Soc.* **1986**, *108*, 2093−2094.

(32) The complete assignment of all ^1H NMR resonance signals to specific locations of hydrogen atoms in the structures of all diastereomers of **1a** and **2a**, needed for the analysis of 2D-EXSY−NMR experiments, is described: Sedó, J.; Ventosa, N.; Molins, M. A.; Pons, M.; Rovira, C.; Veciana, J. *J. Org. Chem.* **2001**, *66*, 1579−1589.

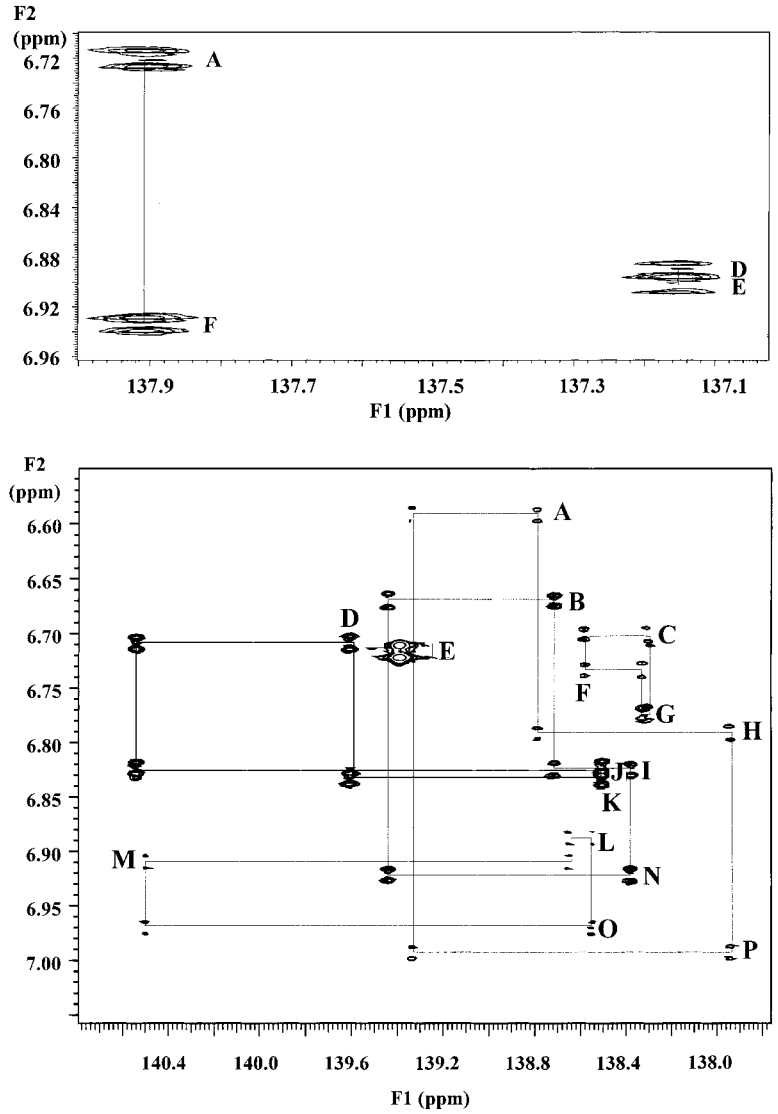


Figure 11. HMBC NMR spectra of chlorocarbons **1a** (top) and **2a** (bottom). Lines connect signals corresponding to couplings in a given stereoisomer.

good correlation factors. Overall, these satisfactory assignments confirm that, in both chromatograms, unobserved diastereoisomers appear overlapped.

Also noteworthy is the observation, both by HPLC and ^{1}H NMR techniques, of roughly similar populations for the diastereomers of **1** and **2**. Thus, the population of isomers of **1** and **2** range from 10 to 30%, except for one (or two) of the diastereomers. Consequently, this result suggests that the relative orientation of the two or three propeller-like moieties constituting such molecules is quite independent from each other and, therefore, there are no strong repulsive forces between the atoms belonging to the neighboring moieties. Thus, the population of most of the diastereoisomers seems to be mainly controlled by entropic factors.

Summary

The static stereochemistry of two structurally complex families of molecules, **1** and **2**, constituted by two and three propeller-like moieties, has been analyzed using a unified theoretical methodology based on a symmetry-adapted symbolic notation. This study has been performed despite the remarkable differences in structural complexity of the seven molecules studied; as evidenced by the distinct number (from 3 to 20) of stereoisomers and their differences in molecular symmetries (C_1, C_2, C_s, C_3, and D_3).

Three different experimental techniques (NMR, ESR, and HPLC) have been used in order to check the validity of the previous theoretical analysis performed with this methodology. As a technique of general application, standard HPLC chromatographic analyses with achiral stationary phases were carried out at low temperature for all seven molecules showing the presence of several diastereoisomers. Unfortunately, we could not achieve complete separations of all diastereoisomers for the most stereochemically complex molecules because of the low solubility of the species and an unavoidable peak overlap throughout all our experiments. ^{1}H NMR spectroscopy, in particular HMBC NMR experiments, afforded accurate results with excellent signal resolution precisely in two of these cases, allowing a complete structural assignment. This technique could not be applied to the rest of molecules because of their paramagnetic nature. As far as the paramagnetic species with high-spin ($S \geq 1$) ground states are concerned, ESR spectroscopy had

already proven very useful, with regard both to the number and to symmetry of their respective diastereomeric forms.

Overall, the experimental evidence at hand fully confirms our theoretical expectations. In this respect, our work on molecular multipropellers expedites the extension of the classical analysis of two- and three-blade single propellers to stereochemically more complex multipropeller systems.

Experimental Section

Compounds **1** and **2** were synthesized as described elsewhere[7,8] and purified by column chromatography (*n*-hexane, silica). All fractions were analyzed by HPLC chromatography in order to assess their purity and the purest ones collected for subsequent purification. To avoid the interference of impurities in the experiments presented here, up to three consecutive purification procedures were found necessary to obtain suitable samples. After these purifications, compounds were recrystallized twice from *n*-pentane or *n*-hexane in order to replace solvent residues. HPLC experiments were performed using an octadecylsilane column (0.46 × 25 cm; 5 μm particle size) with a flow rate of 1.0 mL·min^{-1} and an CH_3CN/THF mixture, as a mobile phase, on a spectrophotometer equipped with a diode array detector operating at 383 nm. The column was thermostated at different working temperatures with a homemade jacket using a thermostat with external circulation. NMR spectra were taken on a 500 MHz spectrometer using $CDCl_3$ as solvent. HMBC spectra were obtained using 4096 × 512 data points that were zero-filled in F2 and extended by linear prediction in F1 to give a 8192 × 2948 matrix. Spectral widths were 820 Hz (^{1}H) and 2515.4 Hz (^{13}C) for **2a** and 169.8 (^{1}H) and 2515.4 Hz (^{13}C) for **1a**. The total recycle time was 9 s for **2a** and 10 s for **1a**.

Acknowledgment. This work was supported by grants from DGES (PB96-0862-C02-01 and PB97-0933), CIRIT (1998SGR-0106 and 1997SGR-102), and the 3MD Network of the TMR program of the E.U. (ERBFMRXCT 980181). We thank Dr. D. A. Amabilino (ICMAB, CSIC) for correcting the manuscript and his useful comments. J.S. and N.V. also thank the MEC for fellowships.

Supporting Information Available: Results obtained from the analysis of the static stereochemistry of multipropeller molecules **1** and **2**, employing the procedure that uses the symmetry-adapted symbolic notation, are provided (Tables S1−S9 and Figures S1−S8). Three-dimensional structures of all the stereoisomers of the seven studied compounds are provided along with their equivalent static representations. Symmetry relationships between all these stereoisomers are provided in the form of graphs. Finally, the correspondence between the chromatographic peaks and the ^{1}H NMR signals for chlorocarbons **1a** and **2a** are also provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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