# TOPICS IN

# STEREOCHEMISTRY

EDITOR

**SCOTT E. DENMARK**
*Department of Chemistry*
*University of Illinois, Urbana-Champaign*
*Urbana, Illinois*

**VOLUME 23**

WILEY-INTERSCIENCE

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# ADVISORY BOARD

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*To the memory of*
*Andre Collet*

# INTRODUCTION TO THE SERIES

Since its first appearance in 1967, the *Topics in Stereochemistry* series has stood as the standard-bearer for advances in the broad field of stereochemistry. The visionaries founders of the series anticipated, with remarkable foresight, the extraordinary growth and impact that stereochemistry has had all reaches of the chemical enterprise. Fortunately, there is no cease of interest in the importance of stereochemistry as the discipline of chemistry evolves and its borders expand and diffuse into the related fields of biology, medicine, physics, materials science, chemical engineering, and environmental science.

The field of stereochemistry serves as a unifying theme for the expanded definition and diversification of chemistry. The consequences of molecular and macromolecular shape and topology are central to issues of chemical reactivity, physical properties, and biological function. With that view, the importance of stereochemistry had never been greater, and it is hoped that this series will provide a forum for documentation of significant advances in all of these subdisciplines of chemistry.

The *Topics in Stereochemistry* series has set itself apart by maintaining a remarkable balance of chapters that are both definitive, standing the test of time, and current, addressing the impact of stereochemistry at the most exciting frontiers. As a student and researcher, I have often turned to chapters in *Topics in Stereochemistry* for the foundations and the state of the art in new areas of interest. It is my hope that the series continue to enjoy that level of confidence in the chemistry community and that it retain, in this second incarnation, the esteem that the founders have worked to hard to establish.

I am fortunate in having been able to enlist the help and guidance of an international board of editorial advisors who have provided great assistance by suggesting chapter topics and suitable authors for articles both here and in future volumes. While I am grateful for the assistance of this editorial advisory board, it is the editor and the authors who are solely responsible for any shortcomings of *Topics in Stereochemistry*.

S. E. Denmark

# FOREWORD

Following the publication of *Stereochemistry of Carbon Compounds* (Eliel, 1962) and *Conformational Analysis* (Eliel, Allinger, Angyal, and Morrison, 1965) N. L. Allinger and I decided in 1966 to launch a *Topics in Stereochemistry* series to keep readers informed of current and new developments in this area. The subject of stereochemistry had been in the doldrums in the first half of the twentieth century and was then just experiencing a renaissance, thanks, in no small measure, to the pioneering work of Vladimir Prelog and Derek H. R. Barton (both of whom sadly passed away earlier this year). John Wiley & Sons agreed to publish the series, which over 27 years grew into 21 volumes. Samuel H. Wilen joined the editorial team in 1982 and Lou Allinger retired as co-editor in 1986. The series was clearly buoyed by the explosive growth of stereochemistry in the 1970s and 1980s, which it may have helped along at least in a small way. In some instances the series anticipated important developments and brought them to the readers' attention at an early stage. Among the more influential articles should be mentioned an early one on determination of enantiomeric purity by nonpolarimetric means (1967), a comprehensive chapter on resolution and resolving agents (1971), a 1978 article on asymmetric synthesis, chapters on the use of carbon-13 NMR in stereochemistry (1974, 1986), an article on the stereochemistry of hydride reductions (1979), and a chapter on enzymatic resolution (1989) — one of several articles on biochemical aspects of stereochemistry. The stereochemistry of inorganic compounds was also treated in several chapters, culminating in a whole volume on this topic edited by Gregory Geoffroy in 1981.

Stereochemistry continues to be a highly viable and prolific subject. Nevertheless, in 1993 the editors reluctantly decided to retire after publication of Volume 21, in part because for some time prior they had been fully occupied with the publication of *Stereochemistry of Organic Compounds* (Wiley, 1994). Sadly, my close friend, able co-author and co-editor, and valued colleague Sam Wilen died soon thereafter. In as much as the explosive development in stereochemistry is continuing, I am delighted that Scott Denmark, who is eminently qualified for the task, has taken over editorship of the series.

I wish the new editor continued success in this "relaunch."

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# PREFACE

The chapters in this second Volume of the second era of *Topics in Stereo-chemistry* reflect the breadth of subdisciplines for which stereochemistry is of fundamental importance. I am particularly pleased that these chapters continue the precedent set by those in Volume 22 for their scholarship, timeliness and scope.

The discovery and development of fullerenes created unprecedented opportunities in both fundamental and applied chemistry. Although the intrinsic chirality of the higher fullerene spheroids was recognized early on, the consequences of modification with chiral groups as well as substitution to create chiral structures have only been fully realized in recent years. The first chapter by Carlo Thilgen, Isabelle Gosse and François Diederich provides an insightful and thorough analysis of the origins of fullerene chirality complete with a systematic classification of structural types. Each family of chiral fullerenes is amply illustrated and discussed not only for the structural novelty but also potential applications. Now liberated from the confines of tetrahedral carbon, the fullerene molecules provide fascinating new scaffolds for chiral structures. This chapter exemplifies how the importance and consequences of chirality pervade all molecular science even as new universes of compounds are discovered.

Whereas the first chapter chronicled the leap to new and fascinating templates for chiral molecules, the second takes this progression further in the jump to chirality beyond the molecule. Chemists have long been fascinated by the field of topological stereochemistry whose members include those mysterious creatures, catenanes, rotaxanes and knots (see the cover!). To understand the stereochemical world inhabited by these intriguing species requires careful meditation and Maria-Jesús Blanco, Jean-Claude Chambron, M. Consuelo Jiménez and Jean-Pierre Sauvage provide a clear and outstanding treatment. Once tamed conceptually, however, the challenge of synthesis immediately presents itself and this chapter details both principles and practice of the use of transition metals for templated synthesis of rotaxanes.

Molecules can often surprise us in their ability to retain stereochemical information despite what appear to be stereorandomizing processes. In Chapter Three by Takeo Kawabata and Kaoru Fuji a fascinating manifestation of this phenomenon is illustrated, explained and exemplified in the chemistry of enolates derived from sterically congested ketones and α-amino acid derivatives. Although these enolates are certainly planar species, the stereochemical consequences of the ancillary substituents have, until now been unappreciated. This

thought provoking exposition invites us to formulate new systems that can display this interesting property and test the limits of competing racemization and reaction rates.

The separation of chiral compounds by crystallization is deeply rooted in the history and practice of organic chemistry. Yet, the understanding of the forces and interactions that determine the success of a given resolution is still underdeveloped and most resolutions are undertaken by empiricism. Chapter Four by Kazushi Kinbara and Kazuhikio Saigo represents the state-of-the-art in the rational design of non-natural resolving agents. From a careful analysis of the crystal packing patterns and hydrogen-bonding arrays in the X-ray crystal structures of chiral molecules with their resolving agents, these authors provide remarkable insights into the origin of discrimination and guidelines for the design of new agents.

No volume of *Topics in Stereochemistry* would be complete with out a chapter illustrating the most recent advances in the power of new methods for the stereocontrolled synthesis of chiral molecules. Nature provides us with a dazzling array of chiral molecules to challenge our mettle, but perhaps none so densely packed as carbohydrates. The natural machinery (aldolases) for the assembly of key polyol subunits has been harnessed with impressive generality and selectivity as described by Michael G. Silvestri, Grace DeSantis, Michael Mitchell and Chi-Huey Wong in Chapter Five. A large number of aldolases have been conscripted into valiant service for the synthesis of many polyhydroxylated compounds in aqueous media with out recourse to protective groups. This chapter is certain to stimulate both application of this powerful technology as well as new ideas about the design of synthetic catalysts.

It is fitting to acknowledge Darla Henderson, Senior Editor at John Wiley and Sons for her efforts in maintaining the series and for providing guidance, advice and assistance.

In the intervening four years since the appearance of Volume 22, there has both joy and sadness on the advisory board. In a wonderful recognition of the importance of stereochemistry in synthesis and catalysis, the Nobel Foundation Awarded the 2001 Nobel Prize in Chemistry to two of our board members, Ryoji Noyori and K. Barry Sharpless (along with William S. Knowles). Congratulations!

Sadly, though I must report that an esteemed Advisory Board member, Andre Collet passed away suddenly in 1999 on at the age of 54. Andre made far-reaching contributions to the understanding of resolution by crystallization methods and would have been particularly pleased by the chapter in this volume by Kinbara and Saigo. It is in his memory that Volume 23 is dedicated.

Finally, on a more positive note, I am delighted to announce that Jay S. Siegel (University of California, San Diego) will be joining *Topics in Stereochemistry* as a co-editor. Jay is a well-known and highly-respected member

of the stereochemistry community and his expertise, perspective and energy will assure the continuing success of this series.

SCOTT E. DENMARK
*Urbana, Illinois*
*26 August 2002*

# CONTENTS

# TOPICS IN STEREOCHEMISTRY

**VOLUME 23**

# Chapter 1

# Chirality in Fullerene Chemistry

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# I.  INTRODUCTION

Carbon is distinguished by its position in the periodic table and the resulting variety of covalent bonding patterns it can participate in. It may not therefore be totally by chance that it is the only element of which chiral molecular allotropes are known. A first chiral representative, $D_2$-symmetric $C_{76}$,[1,2] was isolated and characterized only a year after a new form of elemental carbon, the fullerenes, became available in macroscopic quantities.[3] In the meantime the optical antipodes of $D_2$-$C_{76}$, which does not include stereogenic centers, could be resolved[4−6] and their absolute configurations assigned.[7] According to the structural principles of fullerenes $C_n$,[8−10] the number of allowed constitutional isomers increases with increasing cage size, and so does the number of chiral representatives. For $n = 78, 80, 82$, and $84$, the ratio between theoretically possible chiral and achiral constitutional isomers equals $1:4, 2:5, 3:6$, and $10:14$, respectively.[11] A structural extreme of the fullerene concept is represented by the carbon nanotubes,[12,13] among which most members appear to be chiral. This will have significant consequences in potential technological applications as it emerges that the mechanical and electronic properties of individual tubes depend critically on the characteristics of the helical arrangement of the constituting carbon atoms.

Fullerene chirality is not limited, however, to the allotropes themselves, even if abstraction is made of the possibility to functionalize them with residues containing chiral elements. The carbon cages represent unprecedented three-dimensional building blocks allowing a great variety of spatial arrangements of chemical functions.[14−17] As opposed to the highly symmetrical arrangement of four ligands around the center of a tetrahedral structure, many less symmetrical groupings of addends around the immaterial center of a fullerene are possible. As a consequence the condition of all groups being different for a tetrahedral arrangement to be chiral is not necessary any more in the case of fullerenes. It is therefore not surprising that the abundance of fullerene derivatives synthesized during the last decade includes many chiral compounds. Furthermore macrocyclization reactions including the bridging of fullerene core atoms that do not belong to the same pentagon or hexagon on the cage surface have led to a considerable number of topologically nonplanar and even a few topologically chiral structures.[18] It is remarkable, on the other hand,

that the chirality of many molecules reported in literature has apparently passed unnoticed or was at least not addressed by the authors. Our interest in fullerene chirality originates mainly from our early work on higher fullerenes,[17] and we hope that this review will contribute to making this fascinating aspect of many fullerenes and fullerene derivatives more popular.

Regarding the plan of the chapter, we should mention that the discussion of individual molecules (generally represented in the figures by a single enantiomer) mostly follows the classification of fullerene derivatives according to different types of chirality (cf. Section II.A). For reasons of comprehension, however, we present certain chemically related compounds together even if they belong to different classes.

## II.   CONFIGURATIONAL DESCRIPTION OF CHIRAL FULLERENES AND FULLERENE DERIVATIVES WITH A CHIRAL FUNCTIONALIZATION PATTERN

### A.   Classification of Chiral Fullerenes and Chiral Fullerene Derivatives

Soon after the existence of chiral carbon spheroids and tubes had been anticipated as a result of the discovery of the structural principles of fullerenes,[8–10] the first representatives, $D_2$-symmetric $C_{76}$[1,2] and $D_3$-symmetric $C_{78}$,[19–21] were isolated and characterized. Since then a number of other chiral as well as achiral higher fullerenes could be isolated and their structures elucidated (cf. Section III). Yet, chirality in fullerene chemistry is not limited to the chiral carbon cages themselves.[17,22] In 1992 the first enantiomerically pure covalent fullerene adducts, $C_{60}$ sugar conjugates with stereogenic centers located exclusively in the addend, were prepared (cf. Section IV.C.2.c).[23] In many cases of chiral fullerene derivatives, however, the chirality is neither inherent to the parent spheroid nor related to chiral elements in the addends, but it can be attributed to the geometrical arrangement of addends[24] on the fullerene surface, a formation that we will describe by *chiral addition pattern* or more generally by *chiral functionalization pattern*.

Depending on the origin of their chirality, three classes of chiral fullerene derivatives can be distinguished (Figure 1.1):[22,25]

1. Derivatives of achiral parent fullerenes in which the functionalization creates a chiral addition pattern on the spheroid, regardless of the addends being identical or different, have an inherently chiral functionalization pattern. The derivatives of chiral parent fullerenes automatically have an inherently chiral functionalization pattern.

```
┌─────────────────────────────────┐
│  Functionalized fullerene spheroid │
└─────────────────────────────────┘
                 │
                 ▼
┌─────────────────────────────────┐  yes  ┌─────────────────────────┐
│   Replacement of all addends by  │ ────▶ │   Inherently chiral      │
│   the same achiral test-addend.  │       │   addition pattern       │
│   Is the resulting structure chiral? │   └─────────────────────────┘
└─────────────────────────────────┘
                 │ no
                 ▼
┌─────────────────────────────────┐  yes  ┌─────────────────────────┐
│ Replacement of all addends by achiral │ ──▶ │ Noninherently chiral   │
│ test-addends, non-/identities among │     │ addition pattern       │
│ initial addends being considered.  │      └─────────────────────────┘
│ Is the resulting structure chiral? │
└─────────────────────────────────┘
                 │ no
                 ▼
┌─────────────────────────────────┐  yes  ┌─────────────────────────────┐
│                                 │ ────▶ │ Achiral addition pattern,    │
│  Is the initial molecule chiral? │      │ stereogenic unit(s) reside(s) │
│                                 │       │ in addend(s) only            │
└─────────────────────────────────┘       └─────────────────────────────┘
                 │ no
                 ▼
┌─────────────────────────────────┐
│      No chiral elements,         │
│      or combination of           │
│   enantiomorphic substructures   │
└─────────────────────────────────┘
```

*Figure 1.1.*   Flow diagram for the facile classification of different types of fullerene-spheroid chirality in fullerene derivatives.

2. Derivatives of achiral parent fullerenes in which the chirality of the functionalization pattern is due only to nonidentities among addends, have a noninherently chiral functionalization pattern. The analogy of this situation to that of a center of chirality should be noted.

3. Derivatives of achiral parent fullerenes in which the addition of chiral residues does not create a chiral addition pattern on the fullerene surface. Their chiral elements are located exclusively in the addends.

As the addends of derivatives belonging to classes 1 or 2 can be achiral or chiral, a superposition of different types of chiral elements in a single molecule is possible. The type of a given functionalization pattern can easily be determined by application of a simple, formal substitution test (Figure 1.1) consisting in (1) replacing *all* addends with *the same achiral* test-addend, (2) replacing *non-/identical* original addends with *non-/identical achiral* test-addends, and (3) considering the original molecule. After each step, the resulting structure of increasing degree of complexity is checked for chirality and as soon as it is found, the type of functionalization pattern is recognized.

## B.  Principles of the Configurational Descriptor System

With the explosive development of covalent fullerene chemistry during the last decade,[14−17,26−30] an increasing number of chiral fullerene derivatives has been published[17,22] and the need for an appropriate configurational description became imperative. Two main reasons motivated us to introduce a new configurational descriptor system for chiral fullerenes and fullerene derivatives with a chiral functionalization pattern:[25] (1) Chiral higher fullerenes do not include any stereogenic centers to be specified by the CIP (*Cahn*, *Ingold*, and *Prelog*) system,[31,32] and the consideration of other chiral elements (e.g., axes or planes) does not appear to be straightforward. (2) The configuration of fullerene derivatives with a chiral functionalization pattern could in principle be described by indicating the absolute configuration — ($R$) or ($S$) — of each stereogenic center of the molecule according to the CIP procedure.[31,32] For stereogenic centers in the spheroid moiety of fullerene derivatives, however, this operation is usually lengthy and unintuitive due to the highly branched carbon framework.[33] This may require the development of very complex hierarchic digraphs[32] of the fullerene molecule, with a difference in CIP priority becoming apparent only for high generations of connected atoms if the distance between addends is large on the surface of the spheroid.[25] For multifunctionalized fullerenes, the operation would have to be repeated for all stereogenic centers that are not equivalent by symmetry and result in a multitude of configurational descriptors accompanied by the locants of the respective atoms. Furthermore, in a specific constitutional isomer of a fullerene derivative, the configuration of individual core-resident stereogenic centers cannot be inverted, in general, independently of the others,[34] and therefore it makes sense considering their ensemble as a single chiral unit.

For these reasons we have proposed a new procedure allowing the configurational description of chiral fullerene spheroids by a single descriptor, regardless of the functionalization degree.[25,35] Even chiral parent fullerenes, or heterofullerenes, and isotopically labeled fullerenes derived from achiral parent spheroids can be assigned an absolute configuration. The system is based on the fact that in a three-dimensional model, the numbering schemes proposed for fullerenes, which can be deduced from their structure,[36,37] are chiral (helical) (cf. Figure 1.2) and thus constitute an ideal reference for differentiating between enantiomeric carbon cages.[38] Whereas two isometric, mirror-symmetric numbering schemes can be applied to an achiral parent fullerene, such as $C_{60}$ (Figure 1.2), a unique one is associable with a specific enantiomer of an inherently chiral carbon spheroid[25,35−37] and, consequently, with all its derivatives (cf. Figure 1.3 and Section II.C.1).[25] Similarly, for a chiral derivative resulting from an inherently chiral addition pattern "laid over" an achiral parent fullerene, there is a unique numbering leading to the lowest
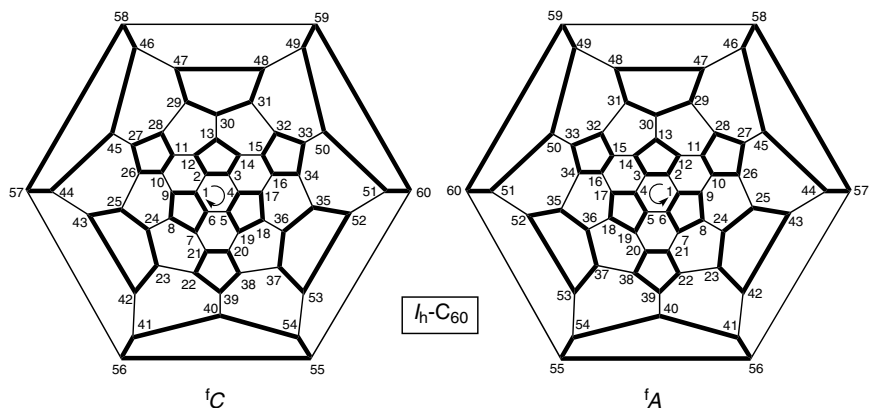
*Figure 1.2.* Schlegel diagrams of $I_h$-C$_{60}$ with enantiomeric numbering schemes according to Godly and Taylor.[36] The arrows in the central, proximal hexagon indicate the direction of the numbering commencement.
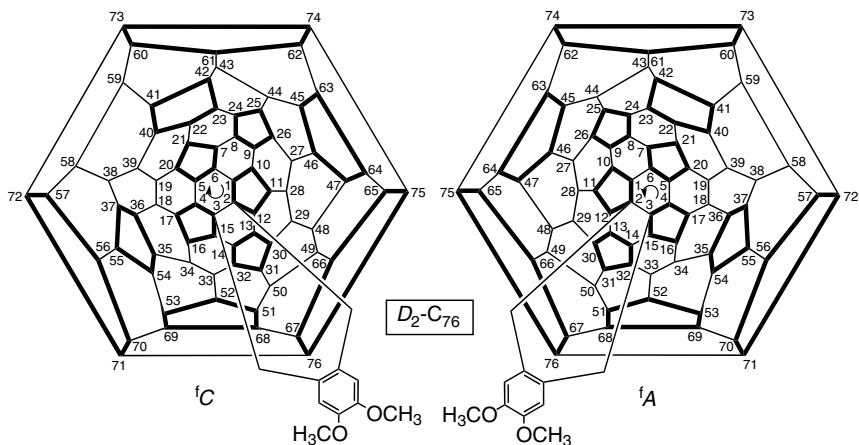


*Figure 1.3.* Schlegel diagrams of the enantiomers of 80,81-dimethoxy-2,3-(methano[1,2]ben-zenomethano)[76]fullerene.[50] In all cases of inherently chiral carbon cages, the same numbering scheme is used for a given enantiomer of the parent fullerene and its derivatives.

set of locants[39] for the addends. Depending on whether the path traced from C(1) via C(2) to C(3) of this numbering is clockwise (*C*) or anticlockwise (*A*), the descriptors are defined as $^fC$ and $^fA$ (f = fullerene), respectively.[25] In the case of a noninherently chiral functionalization pattern, CIP priorities are attributed to the addends (in the way they are to the ligands of a stereogenic

center), and the handedness of the numbering helix is chosen such that lowest locants are allocated to the addition sites bearing the addends of highest CIP priority. The configuration of chiral elements that are located exclusively in the addend(s) is described in the classical way by the descriptors $(R)$ and $(S)$, or $(M)$ and $(P)$.[31,32]

Being based on numbering, a great advantage of this descriptor system is its easy handling by computers.[40] As different numbering schemes have appeared in literature,[36,37] it should be pointed out that the principle of the descriptor system above is valid for any helical numbering. Of course, a correct interpretation of a given configurational descriptor requires knowledge of the used numbering system.

A final question to be addressed is that of the limits of the descriptor system with regard to the structures it can be applied to. In a stricter sense, it should be valid for all fullerenes and their derivatives having a cage framework that is unaltered with respect to the number of atoms and their coordination within the core. In practice, however, as various core-modified fullerenes have been synthesized,[41-49] it may appear convenient to apply it to all compounds that are relatively closely related to the carbon spheres and to which fullerene nomenclature can be easily applied.

## C. Examples for the Configurational Description of the Different Classes of Chiral Fullerene Spheroids

### 1. Inherently Chiral Fullerenes and Their Derivatives

In the case of inherently chiral fullerenes and their derivatives, each of the two mirror-symmetric, isometric numbering schemes fits only a single parent fullerene enantiomer. Hence it is the chirality of the latter that determines the numbering scheme to be used and therefore the descriptor $^fC$ or $^fA$ specifying the absolute configuration of these carbon spheroids and of all their derivatives, regardless of the number and arrangement of addends (cf. Section IV.A.3) (Figure 1.3).

### 2. Derivatives of Achiral Parent Fullerenes with an Inherently Chiral Functionalization Pattern

As the parent fullerene is achiral, its C-atom numbering can in principle be achieved with either one of the two mirror-symmetric numbering schemes. For a particular enantiomer of its derivatives with an inherently chiral functionalization pattern, however, a single numbering scheme only leads to the lowest set of locants for the addends (cf. Sections IV.A.1 and IV.A.2) (Figure 1.4).
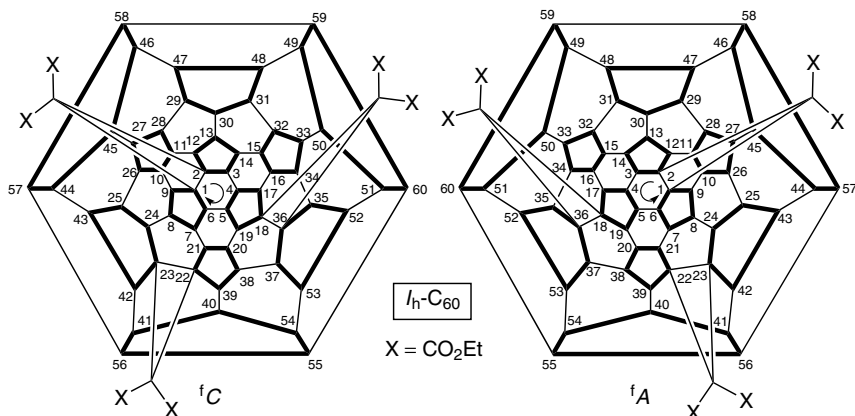
*Figure 1.4.* Schlegel diagrams of the enantiomers of hexaethyl 1,2:18,36:22,23-tris (methano)[60]fullerene-61,61,62,62,63,63-hexacarboxylate (*e,e,e* isomer).[51] Using the numbering scheme of opposite handedness would afford a higher set of locants for the addends (1,2:18,36:31,32) of each structure.

### 3. *Derivatives of Achiral Parent Fullerenes with a Noninherently Chiral Functionalization Pattern*

In the case of a noninherently chiral functionalization pattern (which is always associated with an achiral parent fullerene), no distinction between enantiomers is possible on the base of the criteria above. The same lowest set of locants is obtained with both mirror-symmetric numbering schemes, which is due to a symmetrical arrangement of the addends on the fullerene spheroid. However, the overall symmetry of the molecule is lowered by structural differences in the addends.[52] For making a discrimination between the two applicable numbering pathways, a classification of addends or of heteroatoms of the core is used. It can be achieved conveniently by use of the CIP system that allows a hierarchic ordering of ligands differing in constitution or configuration, and this has proved very useful in the configurational description of stereogenic centers, axes, and planes.[31,32] For the fullerene derivatives considered in this section, substituting heteroatoms of the cage and addends are treated alike by starting the comparison among the concerned substructures according to the CIP rules at the atom located within the fullerene core and then progressively moving outward until a priority difference becomes apparent. Of the two mirror-symmetric numbering schemes leading to the lowest set of locants, that one assigning the lower locant to an addend of higher CIP priority at the first point of difference is preferred and confers its descriptor to the enantiomer in question. Typical representatives of this class are 1,4-adducts of $C_{60}$ with two different addends (cf. Section IV.B) (Figure 1.5).
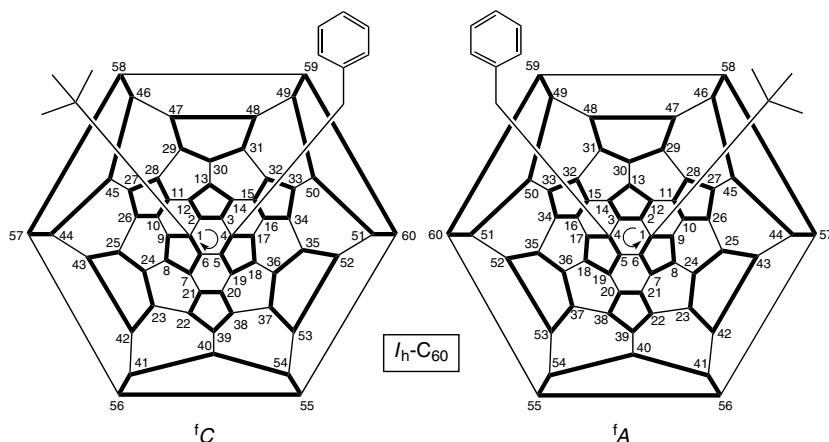
*Figure 1.5.*   Schlegel diagrams of the enantiomers of 1-(*tert*-butyl)-4-(phenylmethyl)[60]fulle-rene.[53] In each structure, the lowest locant (1) is allocated to the addend of highest CIP priority (*tert*-butyl).
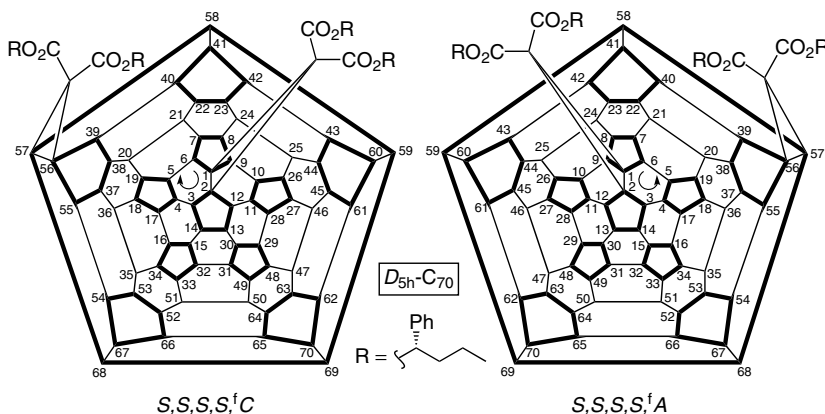


*Figure 1.6.*   Schlegel diagrams of two stereoisomers of tetrakis[(*S*)-1-phenylbutyl] 1,2:56,57-bis(methano)[70]fullerene-71,71,72,72-tetracarboxylate.[35,54] The two types of stereogenic elements (inherently chiral addition pattern and stereogenic centers in the ester groups) are specified independently of each other. As can be seen from the descriptors (*S,S,S,S,*$^{\mathrm{f}}C$) and (*S,S,S,S,*$^{\mathrm{f}}A$), the depicted molecules are diastereoisomers.

## 4.  *Superposition of Chiral Elements in a Fullerene Derivative*

It should be mentioned that the addition of chiral residues to an achiral fullerene does not necessarily lead to a chiral addition pattern (cf. Section IV.C and Figure 1.1). In such a case the configuration of the chiral addend(s) only

has to be determined in the usual way by application the CIP rules.[31,32] If, on the other hand, a chiral functionalization pattern is superposed to chiral addends, the configuration of both types of chiral elements has to be indicated (Figure 1.6).

## III.   INHERENTLY CHIRAL FULLERENES

### A.   The Higher Fullerenes

Even though fullerene chirality is not limited to the inherently chiral larger carbon cages, it was the isolation and characterization of the first chiral member in the series, $D_2$-$C_{76}$,[2] that initiated the study of the handedness of many fullerenes and fullerene derivatives. Diederich, Whetten, and co-workers showed that the $^{13}$C NMR spectrum of $C_{76}$ consists of 19 lines of equal intensity, which confirmed the $D_2$-symmetric cage type fullerene structure (Figure 1.7). As a result of a computer search based on qualitative MO (molecular orbital) theory, this structure, being the only closed-shell isomer obeying the IPR (isolated pentagon rule),[55] had been predicted by Manolopoulos to be the only stable form of [76]fullerene.[8] It can be considered as a spiraling, double-helical arrangement of two identical edge-sharing strands of anellated pentagons and hexagons, tied up at the ends of the long axis of the fullerene which corresponds to one of the $C_2$-axes. This view emphasizes the helical distortion of the structure along this direction.[56]

Whereas the structural assignment by one-dimensional $^{13}$C NMR spectroscopy is unambiguous in the case of $D_2$-$C_{76}$,[2,57] Achiba and co-workers were able to determine the carbon atom connectivity by 2D $^{13}$C NMR INADEQUATE (incredible natural abundance double-quantum transfer experiment) analysis performed on an isotopically enriched sample (20% $^{13}$C).[58] In particular, they found that the observed chemical shifts correlate well with the curvature of the spheroid, the more strongly pyramidalized carbon atoms being shifted toward lower magnetic field.

The structure of $D_2$-$C_{76}$ was further supported by X-ray crystallographic data of the van der Waals compound $[(\pm)$-$D_2$-$C_{76}](S_8)_6$.[59] However, pronounced disorder in the measured crystal that contained both enantiomers of $C_{76}$ impeded a detailed analysis, and so far, more conclusive crystallographic data are available neither for the parent fullerene nor for a $C_{76}$ derivative. The resolution of the enantiomers of $D_2$-$C_{76}$,[4−6] $D_3$-$C_{78}$,[5] and $D_2$-$C_{84}$[5,60] will be described separately in Section III.C.

$C_{78}$ can theoretically occur as five possible IPR-satisfying structures among which a single one is chiral (Figure 1.7).[9,11] This constitutional isomer, $D_3$-$C_{78}$, was indeed isolated as minor component next to achiral $C_{2v}$-$C_{78}$