# Stereochemistry of Congested Cyclophanes Containing Chiral Spirobiindanol Phosphonates: Syntheses, X-Ray Structure, HPLC Enantioresolution and Clathration Properties

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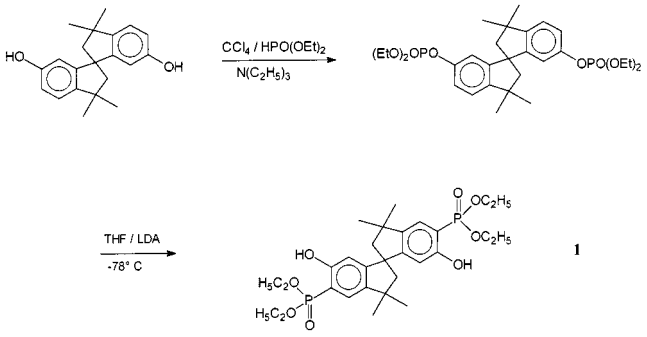
The synthesis as well as the stereochemical characterization (in solution) of sterically congested cyclophanes containing the chiral spirobiindanol phosphonate moiety is reported. The Williamson's synthetic procedure used for the preparation of our compounds proved to be very satisfactory and all cyclophanes were obtained in high yield (≥ 70%). Only the [1+1] cyclization products were found to be significatively formed in the reaction.

## Introduction

Small stereochemically-rigid cyclophanes are molecules of fundamental relevance in many aspects of macrocyclic and supramolecular chemistry, and therefore research in this fertile field is growing rapidly.[1−3] Despite the large variety of systems synthesized thus far and employed for numerous applications, specific and high interest is still devoted to the synthesis and characterization of geometrically constrained chiral macrocycles for use as specific receptors for the selective binding of neutral guests.[3−5]

There exists a need to develop three dimensional building blocks containing selected functional groups in order to introduce suitable binding sites on the cyclophane moiety. Furthermore, if the resulting structures are asymmetric or dissymetric, the system can also be used advantageously for chiral discrimination and separation of a large variety of biologically relevant molecules.

In a previous paper,[6] we adapted the synthetic strategy described by Redmore et al.[7] based on the [1,3]-sigmatropic rearrangement of bis-*ortho* metallated aryl diethyl phosphates, and reported on an easy access synthesis to the spirobiindane bisphosphonate unit (**1**) (Scheme 1). This is a new dissymetric molecule containing ancillary groups (the phosphonic ones) and which is able to act as powerful binding site for a large variety of neutral guests. Moreover, the capability of the dialkyl esters of the phosphonate group to generate, after hydrolysis, the free phosphonic acid or the corresponding mono-ester opens new frontiers for the potential applications of such water-soluble molecules as negatively charged receptors.




Scheme 1

With these ideas in mind, we decided to use monomer **1** as building block for the synthesis of different kinds of medium-sized cyclophanes. Thus, in this paper we shall report on the synthesis and stereochemical characterization (in solution) of cyclophanes **2**−**8**, together with the elucidation by X-ray diffraction methods of their preferred geometry in the solid state. Futhermore, the separation of their enantiomers by using chiral HPLC techniques, together with their clathration properties will be discussed.

## Results and Discussion

Scheme 2 gives a schematic description of the synthetic strategy employed for the preparation of our cyclophanes. The Williamson synthetic procedure used proved to be very satisfactory and all products were obtained in high yield (≥ 70%). Interestingly enough, by condensing the spirobiindane monomer (**1**) with 1,3- or 1,4-dialkylhalides, only [1 + 1] cyclization products were obtained in high yield. In contrast, when the 2,2-bis(3-diethylphosphono-4-hydroxyphenyl)propane was used as condensing agent, the main isolated product was the [2 + 2] macrocycle, accompained by small amounts of higher cyclic oligomers.[8] No doubt this different behavior is due to the geometrically constrained structure of **1**, which possesses the two hydroxyl groups in a favorable position for the [1 + 1] cyclization

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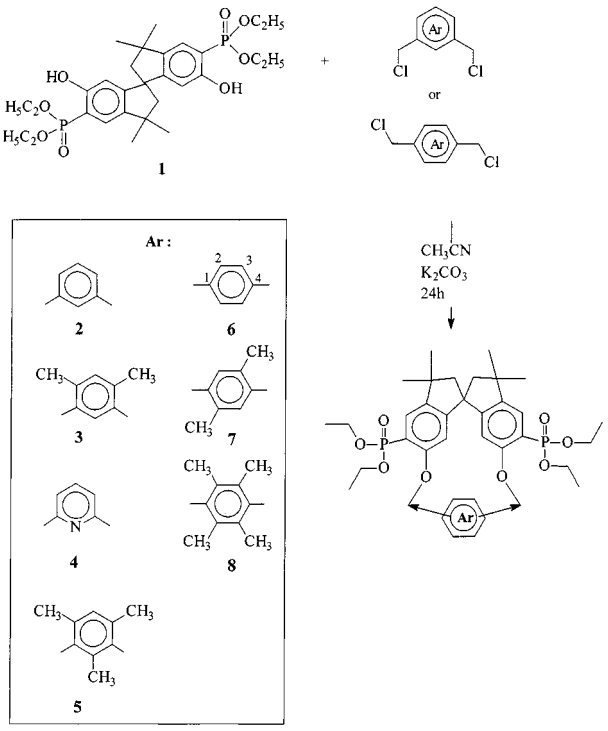
process when linkers or spacers of appropriate length are used. Decreasing the length of the spacer on going from the *para*- to the *meta*-dialkyl aryl halides does not affect the nature as well the yield of the intermolecular cyclization reaction.

Characterization in solution was performed by proton, carbon and phosphorus NMR spectroscopy. By NMR analyses, it was shown that cycles **2−4** show mobility of the aryl rings, which by π radians rotation, average the benzylic bridging protons as well as the spirobiindane phosphonic groups.




Scheme 2

Interestingly enough, the inner aromatic proton positioned between the two benzylic bridging groups is strongly upfield shifted, *ca.* 0.6 ppm, by the aromatic ring current effect of the cavity, indicating that it is pointing inside the cage.

On the contrary, macrocycle **5**, as well as those obtained by condensing the dihydroxy monomer **1** with 1,4-bischloromethyl aryl derivatives, *i.e.*, compounds **6−8**, are all stereochemically rigid on the NMR time scale. In particular, for **5,** restricted rotation of the 1,3-bridged mesityl ring renders the molecule asymmetric as evidenced; by the fact that all nuclei are chemically and magnetically different and this is confirmed by $^{1}H$, $^{13}C$ and $^{31}P$ NMR spectroscopy. The inner methyl group of the mesitylene ring resonates at δ = 1.59, much more up-field than the values for the other mesityl methyl protons (δ = 2.54 and 2.43). The two bridging benzylic groups are no longer homotopic, and thus their $H_a$ and $H_b$ hydrogens (as well as $H_{a'}$ and $H_{b'}$) which are diastereotopic give rise, in the $^{1}H$ NMR spectrum, to two different doublets of doublets centered at (δ = 5.20 and δ = 5.33, respectively.

Cycles **6−8** have a dissymetric structure (point group symmetry $C_2$), and for all of them kinetically restricted rotation of the 1,4-bridged aryl ring was observed, as evidenced by the presence of two sets of signals for the nuclei in positions 2 and 3.

The stereochemical pattern in our macrocycles is quite intriguing due to the presence, in the same molecule, of a $C_2$-symmetrical spirobiindane unit (which is in itself chiral) and of a xylylene bridging moiety which could impart a planar chirality. It follows, that by choosing the appropriate unit (*i.e.*, the 2,5-disubstituted 1,4-xylylene bridge) under conditions of restricted rotation of this unit, only two different distereomers are possible for macrocycle **7**. In fact, for our series, only in **7** is the xylylene bridging unit lacking a local $C_2$ axis passing through the $CH_2$ bridges. The two structures **7a** and **7b** are depicted in Figure 1. In **7a** the two homotopic methyl groups of the 1,4-substituted *p*-xylene ring are pointing out of the molecular cavity and are far from the ring shielding cone of the spirobiindane moiety; the opposite situation arises for **7b**. After workup of the reaction mixture, only one single diastereomer was isolated with a sharp melting point (m.p. 158−159°C) and which showed only one set of signals for all the diastereotopic nuclei.

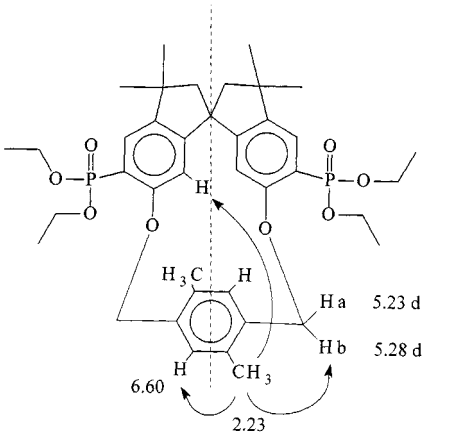
From chemical shift considerations, *i.e.*, the aryl methyl groups resonate at normal values and do not show any upfield shift due to the aromatic ring current effect, but on the contrary such an effect is seen for the aryl ring protons, and from NOE experiments, which reveals that the aryl methyl protons are spatially close to the spirobiindane hydrogens, *ortho* to the oxygen bridge, we could tentatively conclude that the isolated diastereomer has structure **7a**, which is the only one formed in our cyclization reaction (see later Figure 3).

## X-ray Structure Determination

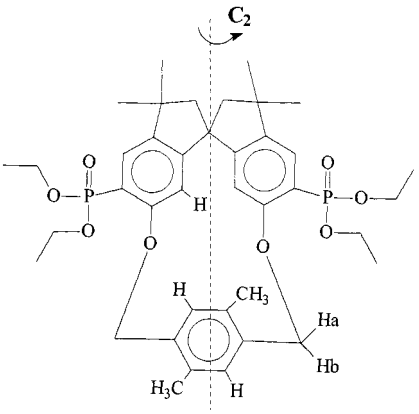
With the aim of elucidating the preferred geometry in the solid state, an X-ray structure of macrocycles **5,** complexed with two mol of cyclohexane, and **7** was thus undertaken.

The overall view of the molecular conformation of the host **5** is shown in Figure 2, which reveals that the molecule is asymmetric ($C_1$) and the inner mesityl methyl group is pointing inside the cavity under the shielding cone of the spirobiindan aromatic ring. Thus the solution geometry detected by NMR spectroscopy is consistent with that found in the solid state. The structure belongs to the triclinic system, space group $P\bar{1}$ with $Z = 2$ (Table 1). Bond lengths and angles are all in the normal range and thus values are not reported in the text, but given as supplementary materials together with atomic coordinates, equivalent isotropic displacements parameters, and with observed and calculated structure factors.

Several problems were encountered during the final stages of the refinement of **5**. The first involved two crystallographically different cyclohexane solvent molecules found to be present, along with a molecule of host **5**, in the unit cell. One cyclohexane solvent molecule was reasonably well ordered and could be refined anisotropically, with hydrogen




**7a** mp = 158-159 °C




**7b**

Figure 1. The two possible diastereomers for macrocycle **7**. Arrows indicate NOE correlations

atoms included as isotropic, riding atoms, while the other molecule was randomly oriented about its pseudo center in the lattice and could be modeled only rather poorly. These two solvent molecules were included in the final stages of the refinement. The second problem involved the usual disordering of the ethyl groups on the phosphite ends of the molecule. One ethyl group, O(4)−C(28)−C(29) was modeled with a distribution ratio of conformers of approximately 40:60, A:B. The other major disorder involved C(31), which had a very large ADP, suggesting that C(31) occupied two primary, but different positions, labeled C(31A) and C(31B) (Figure 2) with a population ratio of about 50:50.

In order to have an idea of cavity dimension in **5** we measured the following interatomic distances: C(1)−C(12) = 4.90 Å; C(1)−C(15) = 6.23 Å; O(1)−O(2) = 6.58 Å. It follows that the cavity is large, but not big enough to include small organic solvent molecules such as cyclohexane. This explains why, the two molecules of cyclohexane, enclathrated by host **5**, are present in the lattice, exterior to **5**.

Once we realized that host **5** includes cyclohexane, we examined more detail, the ability of our cyclophanes to enclathrate small organic molecules. Only macrocycle **3** was found to form inclusion complexes, once again with one mol of cyclohexane, as judged by $^1$H NMR integrations. Some other solvents (benzene, chloroform, ethyl acetate, etc.) were tested, but NMR analyses did not detected the presence of any of them as guests in **3** and **5**.

We previously postulated that for macrocycle **7** only diastereomer **7a** was expected to be formed through a stereospecific coupling reaction; the X-ray structure of the isolated diastereomer with m.p. 158−159°C reveals that the structure is consistent with that one deduced by NMR observations in solution. In fact, inspection of Figure 3 shows that the *p*-xylyl aryl methyl groups are pointing out of the cavity and are close to the hydrogens of the spirobiindan moiety *ortho* to the oxygen bridging atom.

For **7**, the hydrogens on the methyl carbon atom, C(32), were found to be disordered from the ΔF map and were modeled as consisting of two primary orientations 60° apart, with populations of approximately 50% each. In addition, disorder was observed in several other parts of the molecule. Two of the four phosphite groups were disordered, as can be seen by the elongated ellipsoids in Figure 3 for carbon atoms C(34)/C(35) and C(36)/C(37) and even O(8). This often occurs for groups of this type, but no attempt was made to model the disorder here. Also, the ellipsoid of the methyl carbon atoms, C(26) and C(27), in one of the five-membered rings had abnormal ellipsoid. The five-membered ring C(1), C(2), C(3), C(4), C(9) is slightly puckered, as expected, but the C(1), C(23), C(22), C(21), C(24) ring is observed to be flat. Actually, this latter ring is only apparently flat, but actually is disordered with respect to two puckered conformations, one up and one down, which gives the appearance of a flat ring with subsequent elongation of the ellipsoids of carbon atoms C(23), C(26) and C(27) (Figure 4). Again, it was not felt necessary to completely model the conformational disorder in this molecule as these effects are relatively minor and are understood.

A comparison of the geometry of cycles **5** and **7** reveals that in **7**, for example, the *para* substituted phanes are quite hindered with respect to π rotation of the 1,4-substituted aryl ring, which flattens the structure and in turn reduces the cavity size of the cycle. Thus, the *meta*-substituted phanes of this series generally present a higher degree of rotational freedom and a large cavity size, as found experimentally.

## Chiral Chromatographic Separation

Considering that the spirobiindane phosphonate monomer **1** is a preorganized dissymetric molecule which exists as a pair of enantiomers, this compound can be used as a chiral template for building chiral polycondensates or inducing chirality in replicant strands. The resulting macrocycles could be of interest also for chiral recognition and chiral separations.

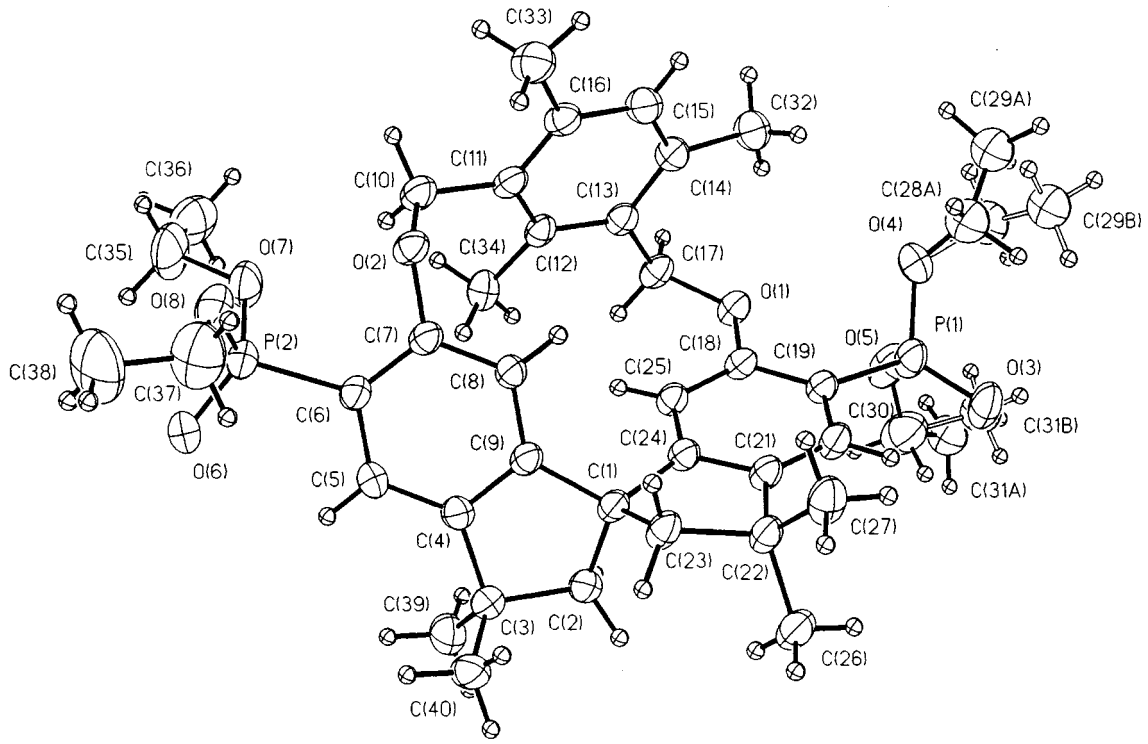



Figure 2. Molecular conformation and atomic numbering scheme of **5**

Table 1. Crystal data and summary of data collection and refinement of macrocycles **5** and **7**

| Compound | **5**·2 $C_6H_{12}$ | **7** |
|---|---|---|
| Formula | C40H54O8P2·2 $C_6H_{12}$ | $C_{39}H_{52}O_8P_2$ |
| Formula weight | 880.99 | 710.75 |
| Crystal system | Triclinic | Monoclinic |
| Space group | *P*1 | $P2_1/n$ |
| *a* [Å] | 12.453(3) | 10.613(4) |
| *b* [Å] | 13.328(4) | 16.342(4) |
| *c* [Å] | 16.602(5) | 21.817(8) |
| *α* [°] | 89.47(3)° | 90° |
| *β* [°] | 86.64(2)° | 90.80(3)° |
| *γ* [°] | 69.68(3)° | 90° |
| V [Å$^3$] | 2579.4(13) | 3784(2) |
| *Z* | 2 | 4 |
| $\rho_{calcd.}$ [g/cm$^3$] | 1.134 | 1.248 |
| μ [mm$^{-1}$] | 0.133 | 0.165 |
| *F*(000) | 944 | 1520 |
| Crystal size [mm] | 0.51 × 0.27 × 0.26 | 0.59 × 0.45 × 0.25 |
| Diffractometer | Enranf−Nonius CAD4 | Enranf−Nonius CAD4 |
| Radiation | Mo-$K_\alpha$ | Mo-$K_\alpha$ |
| *λ* [Å] | 0.71073 | 0.71073 |
| *T* [K] | 293(2) | 293(2) |
| θ range for data collection [°] | 1.23 to 23.98 | 1.56 to 24.98 |
| Limiting indices | $-14 \le h \le 14$; $-15 \le k \le 15$; $0 \le l \le 18$ | $-14 \le h \le 14$; $-15 \le k \le 15$; $0 \le l \le 18$ |
| Reflections collected | 8387 | 14342 |
| Independent reflections | 8068 ($R_{int}$ = 0.0203) | 6645 ($R_{int}$ = 0.0607) |
| Absorption correction | None | Psi |
| Refinement method | Full-matrix least-squares on $F^2$ | Full-matrix least-squares on $F^2$ |
| Data/restrained/parameters | 8061/0/540 | 6643/0/442 |
| Goodness-of-fit on $F^2$ | 1.214 | 1.197 |
| Final *R* indices [$I>2\sigma(I)$] | $R1$ = 0.0915, w$R2$ = 0.2169 | $R1$ = 0.0915, w$R2$ = 0.0380 |
| *R* indices (all data) | $R1$ = 0.1676, w$R2$ = 0.2675 | $R1$ = 0.2299, w$R2$ = 0.0484 |
| Largest diff. Peak and hole [e Å$^{-3}$] | 0.386 and −0.626 | 0.480 and −0.344 |

The chromatographic results for compounds **1**−**8** are presented in Table 2. The separation factors, (α), range from 1.67 for compound **5** to 1.15 for compound **7**, using as eluent *n*-hexane/2-propanol at a flow rate 0.7 mL/min at ambi-

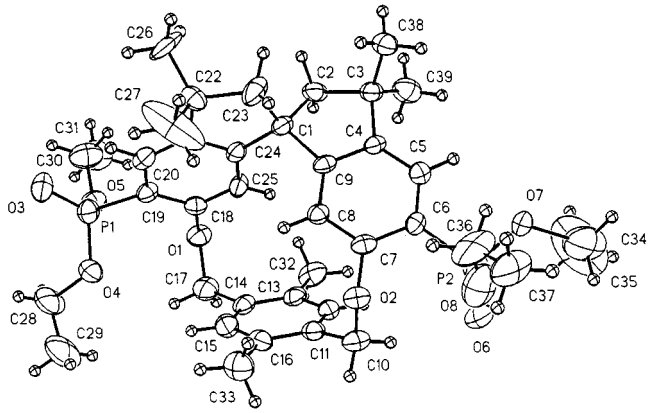



Figure 3. Molecular conformation and atomic numbering scheme of **7**

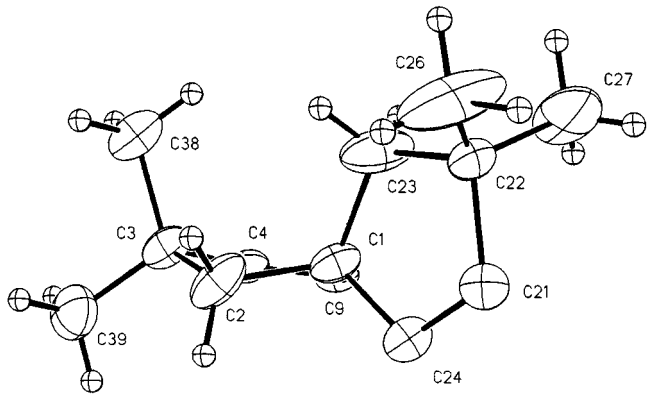



Figure 4. Puckered conformation of the five-membered spiro rings in **7**

ent temperature. However, compounds **2** and **3**, which showed internal mobility of the aryl rings on the NMR time scale, are not separated into their enantiomers. Compound **4**, although also possessing a mobile aryl ring, shows a good α value; this can be due to greater interaction of the 2,5 disubstituted pyridine ring with the 3,5-dimethylphenyl end groups of the carbamate moieties of the chiral stationary phase. Compounds **5**−**8**, which are stereochemically rigid, are well separated and an increase in the polarity of the mobile phase has a beneficial effect on their separation factor. This behavior is, however, opposite in compounds **1** and **4**, where the usual normal phase expectation is observed. The very high capacity factor of compounds **6** and **7**, using as mobile phase *n*-hexane/2-propanol 95:5 is due to their scarce solubility in it, and this fact has a marked detrimental effect on the chiral recognition process. Thus, the choice of an opportune composition of the mobile phase is crucial for obtaining a good enantioseparation in these compounds and avoiding excessively high retention times. Figure 5 shows typical chromatograms of the resolution of racemic spirobiindanes **1**, **4**, **5**, **6** and **8**, for which a resolution factor greater than 1 was obtained.

The good resolution factor (1.5) and low elution times of the enantiomeric pair for compound **5** afforded a quantitative separation of the enantiomers by repeated 50 μL injections of the racemic compound (corresponding to 0.2 mg for each injection) and collection of the eluates. The CD spectra of both eluates were measured and they were almost mirror images of each other as shown in Figure 6, indicating the enantiomeric relationship between the two eluates. Their specific rotations were also measured, [α] = −189.8 and 190.3, for the first and second eluted enantiomers, respectively.

Analogously, a similar isolation procedure was applied to the compound **1** and the CD spectra of the individual enantiomers are reported in Figure 6. The specific rotation measured gave [α] = 25.9 and −24.0 for the first and second eluted enantiomers respectively.

Table 2. HPLC Chiralpak AD resolution of inherently chiral spirobiindans **1**−**8**

| Compound | *A* (%)[a] | $K'_1$[b] | α | $R_s$ |
|---|---|---|---|---|
| **1** | 10 | 0.409 | 1.23 | < 0.5 |
| | 5[c] | 0.891 | 1.42 | 1.4 |
| **2** | 5 | 8.390 | NS[d] | |
| **3** | 10 | 1.770 | NS[d] | |
| | 5 | 6.700 | NS[d,e] | |
| **4** | 10 | 1.169 | 1.47 | 1.5 |
| | 5 | 5.458 | 1.58 | 2.9 |
| **5** | 10[c] | 0.742 | 1.67 | 1.5 |
| | 5 | 3.968 | 1.58 | 2.8 |
| **6** | 10 | 2.836 | 1.50 | 2.1 |
| | 5 | 9.700 | NS,[d,e] | |
| **7** | 10 | 1.928 | 1.15 | < 0.5 |
| | 5 | 10.29 | NS[f] | |
| **8** | 10 | 0.771 | 1.49 | 1.0 |
| | 5 | 4.035 | 1.32 | 1.3 |

[a] Percentage of 2-propanol in *n*-hexane at a flow rate of 0.7 mL/min, $t_0$ = 4.86 min. − [b] Capacity factor of the first eluted enantiomer. − [c] Experimental condition used for semipreparative isolation. − [d] Not separated. − [e] Flat-topped peak. − [f] Shoulder in the rising edge of the peak.

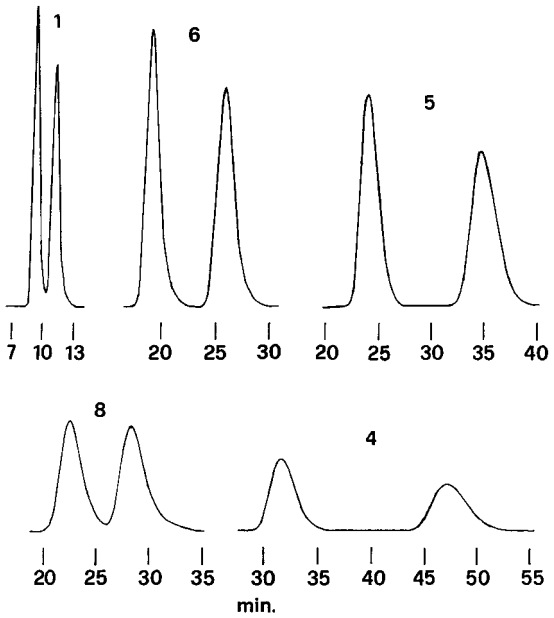



Figure 5. Chiralpak AD HPLC enantioseparation of compounds **1**, **4**−**6** and **8**. Mobile phase: *n*-hexane/2-propanol 95/5 (**1**, **4**, **5**, **8**), n-hexane/2-propanopl 9/1 (**6**), in all cases flow 0.7 mL/min.

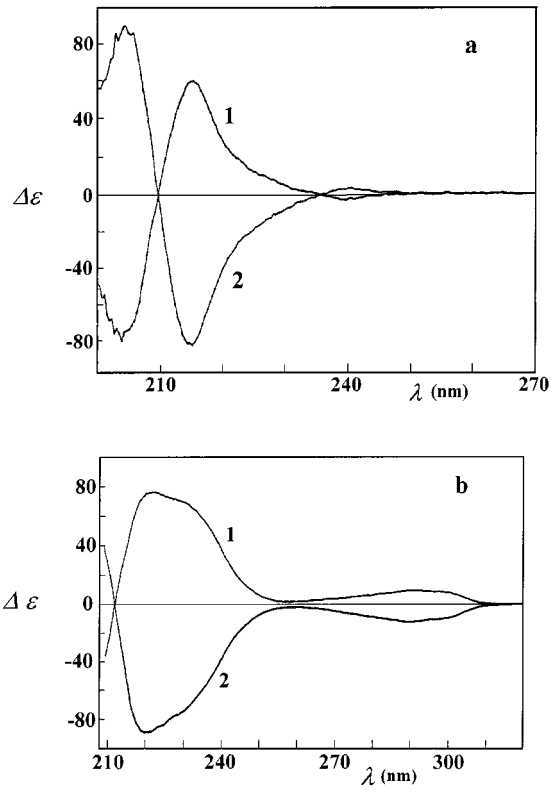



Figure 6. CD spectra (ethanol 95%) of the enantiomers of compound **1** (a) and **5** (b) obtained from the first (1) and second (2) HPLC eluted peaks.

Analytical HPLC reruns of the eluates indicated enantiomeric purity (100%) for the both peaks of compound **5** and 98% (*ee*) and 88% (*ee*) for the first and second eluted peak of compound **1**.

The CD spectrum of compound **1** showed remarkable Cotton effects (CE). In fact the CD split shows a positive CE ($\Delta\varepsilon$ +60 at 215 nm, $\Delta\varepsilon$ −78 at 205 nm) for the less retained enantiomer. A negative CE is observed for the most retained enantiomer. A similar behavior can be envisaged for compound **5**, although the CD splitting cannot be observed due to the shorter wavelengths of the CD bands. The exciton chirality method is extremely versatile for establishing the absolute configuration.[9] The sign of the shorter frequency CD band is related to the sense of handness of the interacting transition electric moments, however, the accurate direction of these moments can be established only by CNDO or INDO semiempirical calculations, so no further efforts in this direction were carried out.

Hagishita *et al.* proposed absolute configuration from the CD spectra of differently substituted bi-1,1′-spiroindanes,[10] but their spectra are very different and cannot be compared with those we obtained. Spirobisindanol esters were resolved into their enantiomers using cholesterol esterase[11][12] and, although a method of enantioseparation using a chiral stationary phase is suggested on analytical scale,[11] this experiment has not been carried out, to our knowledge. Thus, the present results represent the first direct HPLC resolution of inherently chiral spirobiindanol derivatives as well as the first CD spectra of individual enantiomers of spirobiindan bisphosphonates.

## Experimental Section

**General:** All reactions were performed under an inert atmosphere of nitrogen, and the solvents were heated under reflux and freshly distilled before use. − $^1$H, $^{13}$C, and $^{31}$P NMR spectra were recorded on a Varian−Inova 500 MHz instrument operating at 500 MHz, 125 MHz and 200 MHz respectively, using $SiMe_4$ as internal reference and 85% $H_3PO_4$ as external reference. − Mass spectra were obtained using a double-focusing Kratos MS 50S instrument equipped with a standard FAB source and DS 90 data system using 3-nitrobenzyl alcohol as matrix. − Melting points were determined on a Büchi 530 melting point apparatus and are uncorrected. − The HPLC system consisted of a Varian 5060 liquid chromatograph with Valco sample loops, a Jasco Uvidec III UV spectrophotometer operating at 240 nm and a Varian CDS 401 Data System with Omniscribe Houston recorder for fraction collecting. The column (250 × 4.6 mm) used for the chromatographic chiral resolution was a Chiralpak AD (amylose tris-3,5-dimethylphenyl carbamate) coated on 10 μm silica gel, from Daicel (Tokyo). Column void time ($t_0$) was measured by injection of tri-*tert*-butylbenzene as a nonretained sample. Resolution ($R_s$) was evaluated according to $R_s = 2\,(t_2 - t_1)/(w_1 + w_2)$, i.e. the peak separation divided by the mean value of the baseline widths. Retention times ($t$) were mean values of two replicate determinations. Other HPLC chromatographic parameters were those typically employed.[13] Experiments were performed at ambient temperature − CD spectra were recorded on a Jasco 600 spectropolarimeter, and optical rotations were measured with a Jasco DIP-730 polarimeter, using a 10-cm microcell.

**Materials:** Acetonitrile was dried by distillation from calcium hydride under nitrogen. Compound **1** was prepared according to a published procedure.[6] Unless otherwise stated, commercial chemicals were used as supplied.

**Crystal Structure Determination of Macrocycles 5 and 7:** A suitable crystal of host **5**, obtained from a cyclohexane/ethyl acetate solution, or of **7**, obtained from a hexane/ethyl acetate solution, was glued to a glass fiber held in a brass pin, placed in a goniometer head on the Enraf−Nonius CAD4 diffractometer, and centered optically. Unit cell parameters and an orientation matrix for data collection were obtained by using the centering program in the CAD4 system. Details of the crystals data are given in Table 1. For each crystal, the actual scan range was calculated by scan width = scan range + 0.35 tan θ and backgrounds were measured by using the moving-crystal-moving-counter technique at the beginning and end of each scan. Two representative reflections were monitored every 2 h as a check on instrument and crystal stability. Lorentz, polarization, and decay corrections were applied. No absorption correction was necessary. The weighting scheme used during refinement was $1/\sigma^2$, based on counting statistics.

Both structures were solved by Direct Methods using SHELXS-86[14] for **5** and SHELXTL/PC[15] for **7** which revealed the positions of most of the heavier atoms. All other nonhydrogen atoms were found by successive difference Fourier syntheses. Hydrogen atoms were placed in their expected chemical positions using the HFIX comand in SHELXL-93[16] and all hydrogens were included in the final cycles of least squares with isotropic Uij′s related to the atom's ridden upon. All other nonhydrogen atoms were refined anisotropically.

Scattering factors were taken from International Tables for X-ray Crystallography.[17] All data processing of **5** was carried out on a DEC 3000 AXP computer using the Open MolEN system of programs;[18] whereas for **7**, the XCAD4[19] program was used (PC version). Structure solution, refinement and preparation of figures and tables for pubblication were carried out on PC′s using SHELXS-86,[14] SHELXL-93[16] and XP/PC.[20] Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. 117656 for **5** and no. 117657 for **7**. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: +44 (0)1223 336033; E-mail: deposit@ccdc.cam.ac.uk].

**General Synthetic Procedure:** A solution of **1** (1.0 g, 2 mmol) and 2,6- or 2,4-bis(halomethyl)aryl derivative (2 mmol) in freshly distilled $CH_3CN$ (100 mL in total) were added dropwise, at equal rates over a period of 3 h from two different dropping funnels, to a stirred suspension of anhydrous $K_2CO_3$ (1.38 g, 10 mmol) in anhydrous $CH_3CN$ (200 mL) at refluxing temperature. After the addition was completed, the reaction mixture was heated under reflux and stirred overnight, after which it was filtered and the solvent evaporated to give a powder, which was collected with hexane by filtration and washed several times with water. The product was purified by crystallization from hexane/ethyl acetate to give **2**−**8** as white prismatic crystals.

**1,1′-Spirobiindan 2:** 1.16 g, 85%. White crystals, − m.p. 181−182°C (cyclohexane/ethyl acetate). − FAB-MS; *m*/*z*: 683.2 (100) $[M + H]^+$. − $^1$H NMR ($CDCl_3$): δ = 7.58 (d, 2 H, ArH, $^3J_{HP}$ = 14.5 Hz), 7.48 (d, 2 H, ArH, $J_{ortho}$ = 8.0 Hz, $J_{meta}$ = 1.5 Hz), 7.31 (t, 1 H, ArH, $J_{ortho}$ = 8.0 Hz), 6.62 (t, 1 H, $J_{meta}$ = 1.5 Hz), 5.73 (d, 1 H, ArH, $^4J_{HP}$ = 5.5 Hz), 5.11 (s, 4 H, $ArCH_2Ar$), 4.25 (m, 8 H, $POCH_2CH_3$), 2.33 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.91 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.42 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.41 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.33 (s, 6 H, spiro-$CH_3$), 1.29 (s, 6 H, spiro-$CH_3$). − $^{13}$C NMR ($CDCl_3$): δ = 158.35 (d, $^2J_{CP}$ = 3.8 Hz), 155.13 (d, $^4J_{CP}$ = 2.3 Hz), 146.31 (d, $^3J_{CP}$ = 14.4 Hz), 139.81, 135.68, 133.00, 129.68, 129.39, 128.20 (d, $^2J_{CP}$ = 7.6 Hz), 119.25 (d, $^1J_{CP}$ = 187.4 Hz), 116.29 (d, $^3J_{CP}$ = 10.6 Hz), 73.45, 62.29 (d, $^2J_{CP}$ = 6.0 Hz), 57.80, 57.51, 43.39, 31.24, 29.76, 16.45 (m), 14.46. − $^{31}$P{H} NMR ($CDCl_3$): 18.333. − Anal. calcd. for $C_{37}H_{48}O_8P_2$ (682.73): C 65.09, H 7.09; found C 64.91, H 7.19.

**1,1′-Spirobiindan 3:** 1.04 g, 73%. White crystals, − m.p. 170°C (cyclohexane). − FAB-MS; *m*/*z*: 711.2 (100) $[M + H]^+$. − $^1$H NMR ($CDCl_3$): δ = 7.58 (d, 2 H, ArH, $^3J_{HP}$ = 15.0 Hz), 7.01 (s, 1 H, ArH), 6.61 (s, 1 H, ArH), 6.12 (d, 2 H, ArH, $^4J_{HP}$ = 6.0 Hz), 5.15 (d, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 13.5 Hz), 5.01 (d, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 13.5 Hz), 4.22 (m, 8 H, $POCH_2CH_3$), 2.47 (s, 6 H, $ArCH_3$), 2.39 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 12.5 Hz), 1.92 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 12.5 Hz), 1.41 (s, 12 H, cyclohexane), 1.39 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.38 (s, 6 H, spiro-$CH_3$), 1.36 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.30 (s, 6 H, spiro-$CH_3$). − $^{13}$C NMR ($CDCl_3$): δ = 159.07 (d, $^2J_{CP}$ = 3.8 Hz), 155.03 (d, $^4J_{CP}$ = 2.3 Hz), 145.93 (d, $^3J_{CP}$ = 14.4 Hz), 138.74, 134.64, 133.46, 130.65, 128.56 (d, $^2J_{CP}$ = 6.2 Hz), 118.34 (d, $^1J_{CP}$ = 189.6 Hz), 114.78 (d, $^3J_{CP}$ = 10.2 Hz), 71.53, 62.36 (d, $^2J_{CP}$ = 6.1 Hz), 61.83 (d, $^2J_{CP}$ = 5.4 Hz), 57.92, 57.54, 43.20, 31.07, 30.06, 18.81, 16.43 (m), 14.46. − $^{31}$P{H} NMR ($CDCl_3$): δ = 18.48. − Anal. calcd. for $C_{39}H_{52}O_8P_2{\cdot}C_6H_{12}$ (794.94): C 67.99, H 8.11; found C 67.86, H 8.22.

**1,1′-Spirobiindan 4:** 0.96 g, 70%. White crystals, m.p. 183−184°C (hexane/ethyl acetate). − FAB-MS; *m*/*z*: 684.2 (100) $[M + H]^+$. − $^1$H NMR ($CDCl_3$): δ = 7.65 (t, 1 H, PyH, $^3J_{HH}$ = 8.5 Hz), 7.57 (d, 2 H, PyH, $^3J_{HH}$ = 8.5 Hz) 7.56 (d, 2 H, ArH, $^3J_{HP}$ = 14.5 Hz), 5.80 (d, 2 H, ArH, $^4J_{HP}$ = 6.5 Hz), 5.26 (d, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 13.0 Hz), 5.06 (d, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 12.5 Hz), 4.25 (m, 8 H, $POCH_2CH_3$), 2.33 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.88 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.42 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.40 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.33 (s, 6 H, spiro-$CH_3$), 1.28 (s, 6 H, spiro-$CH_3$). − $^{13}$C NMR ($CDCl_3$): δ = 158.87 (d, $^2J_{CP}$ = 3.6 Hz), 156.01, 155.40 (d, $^4J_{CP}$ = 2.6 Hz), 146.65 (d, $^3J_{CP}$ = 14.7 Hz), 137.79, 128.02 (d, $^2J_{CP}$ = 7.8 Hz), 123.67, 118.88 (d, $^1J_{CP}$ = 188.6 Hz), 116.10 (d, $^3J_{CP}$ = 10.9 Hz), 74.98, 62.26 (d, $^2J_{CP}$ = 5.9 Hz), 61.96 (d, $^2J_{CP}$ = 5.9 Hz), 57.69, 57.56, 43.34, 31.11, 29.82, 16.44 (d, $^3J_{CP}$ = 16.5 Hz). − $^{31}$P{H} NMR ($CDCl_3$): δ = 18.28. − Anal. calcd. for $C_{36}H_{47}NO_8P_2$ (683.71): C 63.24, H 6.93, N 2.05; found C 62.98 H 7.02, N 2.12.

**1,1′-Spirobiindan 5:** 1.34 g, 75%. White crystals, m.p. 174−176°C (cyclohexane/ethyl acetate). − MALDI-TOF MS; *m*/*z*: 748 (100) $[M + Na]^+$, 1472 (38), 901 (68), 581 (75). − $^1$H NMR ($CDCl_3$): δ = 7.66 (d, 1 H, ArH, $^3J_{HP}$ = 14.5 Hz), 7.46 (d, 1 H, ArH, $^3J_{HP}$ = 14.5 Hz), 6.88 (s, 1 H, ArH), 5.99 (d, 1 H, ArH, $^4J_{HP}$ = 6.5 Hz), 5.63 (d, 1 H, ArH, $^4J_{HP}$ = 5.5 Hz), 5.33 (dd, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 13.5 Hz, $^2J_{HH}$ = 14.0 Hz), 5.20 (dd, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 13.5 Hz, $^2J_{HH}$ = 14.0 Hz), 4.25 (m, 8 H, $POCH_2CH_3$), 2.54 (s, 3 H, $ArCH_3$), 2.43 (s, 3 H, $ArCH_3$), 2.38 (d, 1 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 2.27 (d, 1 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.91 (d, 1 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.82 (d, 1 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.59 (s, 3 H, $ArCH_3$), 1.43 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 6.5 Hz), 1.40 (s, 24 H, cyclohexane), 1.38 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.355 (s, 3 H, spiro-$CH_3$), 1.336 (s, 3 H, spiro-$CH_3$), 1.331 (s, 3 H, spiro-$CH_3$), 1.19 (s, 3 H, spiro-$CH_3$). − $^{13}$C NMR ($CDCl_3$): δ = 159.96 (d, $^2J_{CP}$ = 3.8 Hz), 157.75 (d, $^2J_{CP}$ = 3.8 Hz), 155.46 (d, $^4J_{CP}$ = 3.0 Hz), 149.18 (d, $^3J_{CP}$ = 14.5 Hz), 143.21 (d, $^3J_{CP}$ = 14.4 Hz), 139.81, 139.05, 136.59, 131.79, 130.51, 130.23, 128.62 (d, $^2J_{CP}$ = 7.9 Hz), 128.33 (d, $^2J_{CP}$ = 7.3 Hz), 122.08 (d, $^1J_{CP}$ = 186.6 Hz), 121.17 (d, $^3J_{CP}$ = 10.6 Hz), 115.62 (d, $^1J_{CP}$ = 188.1 Hz), 108.69 (d, $^3J_{CP}$ = 10.6 Hz), 71.61, 64.96, 62.66 (d, $^2J_{CP}$ = 6.1 Hz), 58.05, 57.95, 57.34, 43.07, 43.02, 31.10, 30.87, 30.57, 30.31, 26.90, 20.71, 19.64, 16.42 (m), 14.46. − $^{31}$P{H} NMR ($CDCl_3$): δ = 19.16 and 17.98. − Anal. calcd. for $C_{40}H_{54}O_8P_2{\cdot}2C_6H_{12}$ (895.13): C 69.93, H 8.80; found C 69.75, H 8.63.

**1,1′-Spirobiindan 6:** 1.09 g, 80%. White crystals, m.p. 110−111°C (cyclohexane/ethyl acetate). − FAB-MS; *m*/*z*: 683.1 (100) $[M + H]^+$. − $^1$H NMR ($CDCl_3$): δ = 7.52 (d, 2 H, ArH, $^3J_{HP}$ = 15.0 Hz), 7.16 (dd, 2 H, ArH, $J_{ortho}$ = 8.3 Hz, $J_{meta}$ = 1.5 Hz), 6.92 (dd, 2 H, ArH, $J_{ortho}$ = 8.3 Hz, $J_{meta}$ = 1.5 Hz), 5.55 (d, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 12.0 Hz), 5.40 (d, 2 H, ArH, $^4J_{HP}$ = 6.0 Hz), 5.08 (d, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 12.0 Hz), 4.27 (m, 8 H, $POCH_2CH_3$), 2.21 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.90 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.43 (t, 12 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.28 (s, 6 H, spiro-$CH_3$), 1.25 (s, 6 H, spiro-$CH_3$). − $^{13}$C NMR ($CDCl_3$): δ = 157.68, 155.25, 146.21 (d, $^3J_{CP}$ = 14.4 Hz), 136.17, 129.83, 127.51, 127.53 (d, $^2J_{CP}$ = 7.4 Hz), 119.71 (d, $^1J_{CP}$ = 187.4 Hz), 118.32 (m), 73.80, 62.37 (d, $^2J_{CP}$ = 6.1 Hz), 62.02 (d, $^2J_{CP}$ = 6.1 Hz), 58.26, 57.35, 43.17, 31.39, 29.99, 16.43 (m). − $^{31}$P{H} NMR ($CDCl_3$): δ = 18.53. − Anal. calcd. for $C_{37}H_{48}O_8P_2$ (682.73): C 65.09, H 7.09; found C 65.15, H 7.18.

**1,1′-Spirobiindan 7:** 1.03 g, 72%. White crystals, m.p. 158−159°C (hexane/ethyl acetate). − FAB-MS; *m*/*z*: 711.3 (100) $[M + H]^+$. − $^1$H NMR ($CDCl_3$): δ = 7.53 (d, 2 H, ArH, $^3J_{HP}$ = 14.5 Hz), 6.60 (s, 2 H, ArH), 5.32 (d, 2 H, ArH, $^4J_{HP}$ = 6.0 Hz), 5.26 (dd, 4 H, $ArCH_2Ar$, $^2J_{HH}$ = 12.5 Hz), 4.27 (m, 8 H, $POCH_2CH_3$), 2.23 (s, 6

H, $ArCH_3$), 2.20 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.5 Hz), 1.90 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.44 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.43 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.27 (s, 6 H, spiro-$CH_3$), 1.25 (s, 6 H, spiro-$CH_3$). – $^{13}C$ NMR ($CDCl_3$): δ = 158.06, 155.14, 146.79 (d, $^3J_{CP}$ = 13.6 Hz), 134.67, 134.54, 132.77, 127.53 (d, $^2J_{CP}$ = 5.25 Hz), 120.35 (d, $^1J_{CP}$ = 187.4 Hz), 119.25 (m), 72.61, 62.39 (d, $^2J_{CP}$ = 6.0 Hz), 61.96 (d, $^2J_{CP}$ = 5.3 Hz), 58.39, 57.33, 43.17, 31.29, 30.17, 17.98, 16.49 (m). – $^{31}P\{H\}$ NMR ($CDCl_3$): δ = 18.58. – Anal. calcd. for $C_{39}H_{52}O_8P_2$ (710.83): C 65.90, H 7.37; found C 65.74, H 7.83.

**1,1′-Spirobiindan 8:** 1.04 g, 70%. White crystals, m.p. 174–175°C (cyclohexane). – FAB-MS; *m/z*:739 (100) $[M + H]^+$, 579.9 (50). – $^1H$ NMR ($CDCl_3$): δ = 7.47 (d, 2 H, ArH, $^3J_{HP}$ = 14.5 Hz), 5.83 (d, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 12.5 Hz), 5.39 (d, 2 H, ArH, $^4J_{HP}$ = 6.0 Hz), 5.24 (d, 2 H, $ArCH_2Ar$, $^2J_{HH}$ = 13.0 Hz), 4.34 (m, 4 H, $POCH_2CH_3$), 4.23 (m, 4 H, $POCH_2CH_3$), 2.32 (s, 6 H, $ArCH_3$), 2.19 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.86 (s, 6 H, $ArCH_3$), 1.83 (d, 2 H, spiro-$CH_2$, $^2J_{HH}$ = 13.0 Hz), 1.43 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.42 (t, 6 H, $POCH_2CH_3$, $^3J_{HH}$ = 7.0 Hz), 1.26 (s, 6 H, spiro-$CH_3$), 1.24 (s, 6 H, spiro-$CH_3$). – $^{13}C$ NMR ($CDCl_3$): δ = 158.15, 154.48, 147.72 (d, $^3J_{CP}$ = 14.4 Hz), 135.62, 134.89, 132.90, 127.02 (d, $^2J_{CP}$ = 6.8 Hz), 121.83 (d, $^1J_{CP}$ = 187.9 Hz), 121.24 (m), 70.46, 62.54 (d, $^2J_{CP}$ = 6.1 Hz), 61.89 (d, $^2J_{CP}$ = 5.6 Hz), 58.21, 57.44, 43.01, 31.10, 30.51, 16.50 (d, $^3J_{CP}$ = 11.0 Hz), 16.06. – $^{31}P\{H\}$ NMR ($CDCl_3$): δ = 18.17. – Anal. calcd. for $C_{41}H_{56}O_8P_2 \cdot H_2O$ (756.85): C 65.07, H 7.72; found C 64.85, H 8.07.

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