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Aryl[2.2]paracyclophane-Based Chiral Regioisomeric Analogs of Salicyl Aldehyde: Novel Sources for Construction of Phenoxy-Imine Ligands

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Abstract: The efficient, high-yield approaches to two novel regioisomeric salicyl aldehyde analogs, 4-formyl-13-(2-hydroxyphenyl)-[2.2]paracyclophane and 4-formyl-12-(2-hydroxyphenyl)-[2.2]paracyclophane (***iso*-FHPhPC** and ***pseudo*-FHPhPC**, respectively), constructed on the basis of an aryl-[2.2]paracyclophane backbone are described. The key stage of the backbone formation is the Suzuki cross-coupling of paracyclophanyl halides with arylboronic acids. Efficient procedures for the resolution of the racemic hydroxy aldehydes into enantiomers via Schiff bases with enantiomers of α-phenylethyl amine were elaborated, and the absolute configurations of enantiomers were established on the basis of X-ray analysis of diastereomeric imines. Starting from these chiral hydroxy aldehydes the first representatives of bi-, tri-, and tetradentate phenoxy-imine ligands belonging to an aryl[2.2]paracyclophane family were obtained. The induction power of the ligands was tested in the Et_2Zn asymmetric addition to aldehydes.

Keywords: biaryls · cyclophanes · planar chirality · Schiff bases · Suzuki cross-coupling

1. Introduction

Salicyl aldehydes are bifunctional compounds the importance of which as building blocks in organic chemistry is very well known.[1] They are used, for instance, for the synthesis of coumarins possessing a wide spectrum of biological activity[2] or several natural products the preparation of which requires an *o*-quinone methide intermediate.[3] They are also actively employed in the synthesis of various imines (Schiff bases in general, salenes in particular). These are most popular ligands since they are easily obtainable from salicyl aldehydes by condensation with amines, amino alcohols, and diamines while the imino-products give rise to a rich coordination chemistry with a wide range of metal ions.[4] The resulting complexes are widely used in various areas, especially in supramolecular chemistry (in modeling active sites of metalated enzymes[5] and for the construction of synthetic molecular receptors[6] capable of selective recognition of enantiomers in various substrates), or as molecular loops and squares,[7] as molecular building blocks for macromolecular matrices,[8] as olefin[9] oligo- and polymerisation catalysts, and as asymmetric catalysis agents in various synthetically important organic reactions.[10,11]

The induction ability of the imine ligands used in asymmetric catalysis certainly depends on the structure of the parent salicyl aldehyde, and the ligand nature and architecture could further be optimized by introduction of various substituents (donor or acceptor groups, sterically large substituents) into either the carbonyl or imino component of the phenoxy-imine ligand. Chirality of the Schiff base ligands can be created in various ways. The achiral parent salicyl aldehyde would require chiral amino derivative as the second component. With chiral salicyl aldehydes, one may use either achiral or chiral amino components[12,13] to get an imine that contains either one or several stereogenic sites (the configurations of which may be varied in order to establish an appropriate chiral environment). Among some well-known chiral hydroxy aldehydes there are salicyl aldehyde analogs which bear elements of central (**1**),[14,15] axial (**2**),[15,16] or planar chirality (**3**, 4-hydroxy-5-formyl-[2.2]paracyclophane, FHPC)[17] (Figure 1), and the phenoxy-imine ligands based on them have been shown to be good asymmetric inductors.[12,18]

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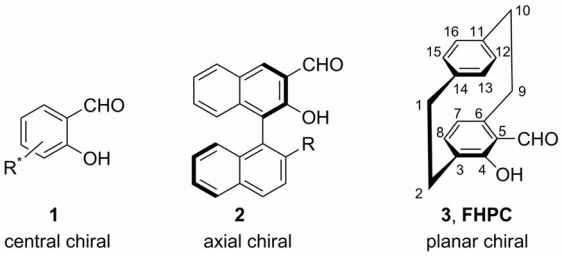


Figure 1. Hydroxy aldehydes with various types of chirality.

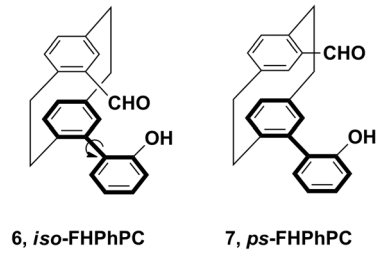


Figure 3. Salicyl aldehyde analogs of *pseudo*-biaryl type based on an aryl[2.2]paracyclophane backbone.

As a part of our long-term project devoted to the regioselective synthesis of novel planar chiral [2.2]paracyclophane derivatives and to their application as ligands in stereoselective processes,[12,13,17,19–23] we have recently obtained two novel **FHPC** analogs, namely 4-formyl-13-hydroxy[2.2]paracyclophane **4**[19] and 4-formyl-12-hydroxy[2.2]paracyclophane **5**[20] (*iso*-FHPC and *pseudo*-FHPC, Figure 2), the functional groups of which are situated in the different aromatic rings of the conformationally rigid [2.2]paracyclophane molecule (in *pseudo-gem*-position, one above the other; and in *pseudo-ortho*-position, thus mimicking the classical salicylaldehyde itself). We have also shown that bi- and tridentate Schiff bases derived from **4** and **5** are highly enantioselective catalysts in diethylzinc addition to aldehydes and display higher chiral induction power in this reaction than do the Schiff bases derived from **3** (up to 97% *ee* of the product).[20] These results demonstrated that varying the mutual arrangement of hydroxy and formyl functional groups in the molecule of the chiral ligand (i.e., their deviation from the position they occupy in salicyl aldehyde) is a very promising project to be undertaken for the development of various aspects of [2.2]paracyclophane stereochemistry.[24]

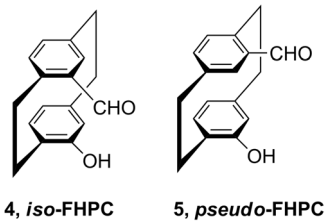


Figure 2. Planar chiral analogs of FHPC.

Recently we proposed a new backbone for chiral ligands, viz. *aryl[2.2]paracyclophane*,[21,22] which unites a conformationally flexible biphenyl fragment with the configurationally rigid [2.2]paracyclophane moiety. We have shown that the "hybrid" nature of the backbone allows the construction of a wide range of chelating ligands which may belong to essentially diverse types characterised by different mutual arrangement of their functional groups in three aromatic rings, and we have introduced their classification [biaryl, *pseudo*-biaryl (Figure 3), paracyclophanyl, and aryl types]. Key strategic approaches to the synthesis of various ligands in enantiomerically pure form were considered.[22]

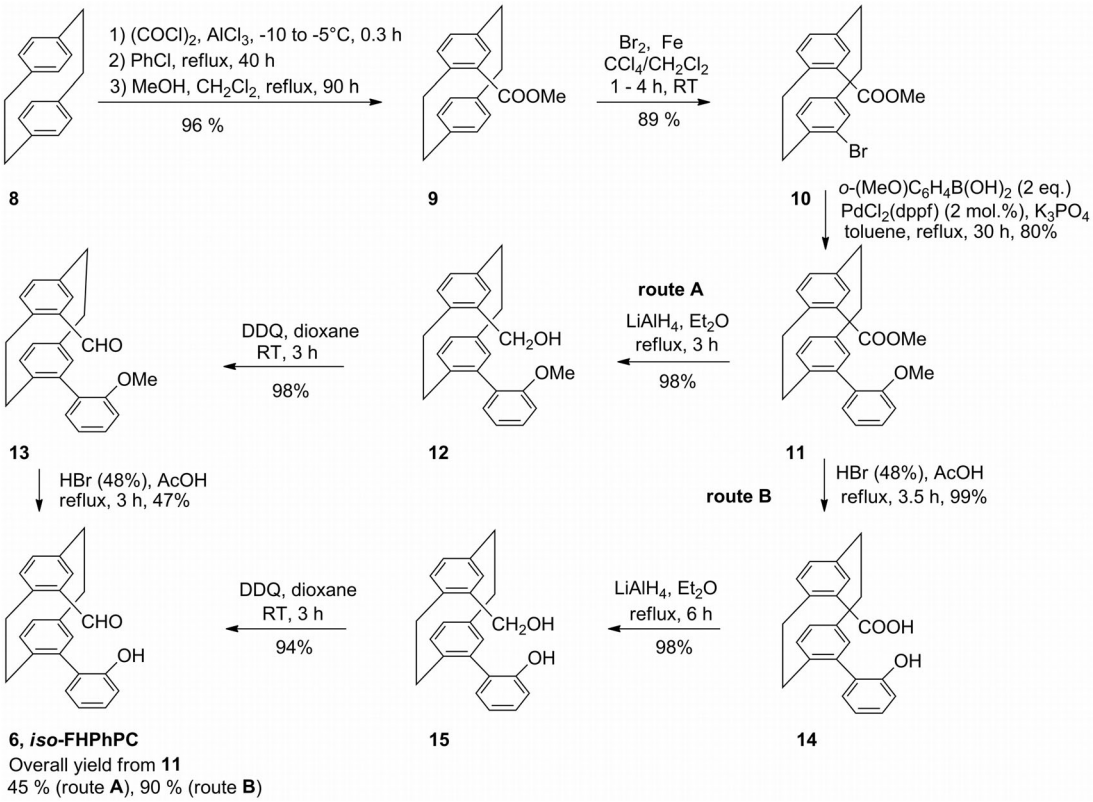
In this paper we disclose the detailed synthesis of two principally novel hydroxyaldehydes of the *pseudo*-biaryl type constructed on the base of the aryl-[2.2]paracyclophane backbone, namely ***iso*-FHPhPC 6** (4-**F**ormyl-13-(2-**H**ydroxy**Ph**enyl)-[2.2]**P**ara**C**yclophane) and ***pseudo*-FHPhPC 7** (4-**F**ormyl-12-(2-**H**ydroxy**Ph**enyl)-[2.2]**P**ara**C**yclophane) (Figure 3), and their resolution into enantiomers. In these compounds one functional group (OH) belongs to the biaryl fragment while the other group (CHO) is situated over this fragment in the second paracyclophane aromatic ring in *pseudo-gem* (in **6**) or *pseudo-ortho* position (in **7**) with respect to the aryl substituent. The spatial arrangement of these functional groups could be varied due to free rotation around the aryl[2.2]paracyclophane bond (in contrast to their rigid fixation on the [2.2]paracyclophane backbone in *iso*-FHPC and *pseudo*-FHPC), thus providing the possibility of the additional fine tuning of the chiral environment.

Application of regioisomeric FHPhPC **6** and **7** for the synthesis of the various phenoxy-imine ligands and demonstration of their ability to act as chiral inductors in Et_2Zn addition to aldehydes are presented as well.

2. Results and Discussion

2.1. Synthesis of *iso*-FHPhPC 6 and Its Resolution into Enantiomers

The synthetic approach to racemic *iso*-FHPhPC **6** relies on two general operations: 1) the generation of the *pseudo-gem* substitution pattern by the regioselective bromination of [2.2]paracyclophane carbonyl derivatives,[25] and 2) the formation of the aryl[2.2]paracyclophane backbone by Suzuki cross-coupling reaction followed by further transformations (Scheme 1).[21] 4-Methoxycarbonyl-[2.2]paracyclophane **9** was obtained from parent [2.2]paracyclophane **8** by a multistep procedure described in the literature.[26a] *pseudo-gem*-Regioselective bromination of **9**[26] produced 4-bromo-13-methoxycarbonyl-



Scheme 1. Preparation of *iso*-FHPhPC **6** from [2.2]paracyclophane **8**.

[2.2]paracyclophane **10**, which then was introduced into Suzuki cross-coupling with a double excess of anisylboronic acid under non-aqueous conditions in the presence of 1 to 2 mol % $Pd(dppf)Cl_2$ catalyst. We have used two solvent/base systems: THF/KF and toluene/K_3PO_4. The first one produced the aryl[2.2]paracyclophane **11** in a yield of 60 % after refluxing the mixture for 55 h, while some of the unreacted starting bromide **10** (25 %) was recovered. The toluene/K_3PO_4 system was superior: the yield of **11** was increased to 80 % while refluxing for 30 h only and the recovery rate of **10** was lower (15 %).

To convert the key aryl[2.2]paracyclophane precursor **11** to the target *iso*-FHPhPC **6**, we considered two routes, **A** and **B** (Scheme 1). Route **A** comprises the reduction of the methoxycarbonyl group in **11** by $LiAlH_4$ in diethyl ether leading to the methoxy carbinol **12** in quantitative yield. The carbinol **12**, oxidized under mild conditions (DDQ, dioxane, RT), has produced the expected methoxy aldehyde **13** in quantitative yield also. At the third stage of Route **A**, however, after elimination of the methyl group by refluxing **13** in an HBr/AcOH mixture, the desired *iso*-FHPhPC **6** was obtained in a moderate yield only (47 %), while the reaction mixture did not contain any other [2.2]paracyclophane derived compounds. Consequently, the overall yield of **6** as obtained from **11** by Route **A** was 45 % only.

The same set of reagents and reaction conditions may be applied in a different way, however. Thus we have changed the sequence of converting the functional groups of the precursor **11** (Scheme 1, Route **B**). Demethylation of **11** was the first step in this case. The reaction was carried out in a refluxing HBr/AcOH mixture and resulted in the hydroxy carboxylic acid **14** in a yield of 98 %. Reduction of **14** with $LiAlH_4$ (Et_2O, under reflux) produced the respective carbinol **15** in quantitative yield. Oxidation of this carbinol under conditions similar to those applied in Route **A** produced the target *iso*-FHPhPC **6**. The overall yield of **6** as obtained from **11** by Route **B** came up to 90 %, thus making it more attractive for a preparative synthesis of *iso*-FHPhPC. Note also that the procedure for the synthesis of compound **6** may be simplified by using the crude intermediates **14** and **15** (no purification on silica gel or crystallisation is necessary). Nevertheless, all novel [2.2]paracyclophane derivatives shown in Scheme 1 were isolated as individual compounds and characterised by ^1H NMR spectra, mass spectra, and elemental analyses. These compounds are attractive as potential aryl[2.2]paracyclophane ligands of *pseudo*-biaryl type or their precursors, and could be obtained in enantiomerically pure form starting from enantiomers of [2.2]paracyclophane-4-carboxylic acid.[27]

The resolution of *iso*-FHPhPC into enantiomers was accomplished by a traditional approach repeatedly and

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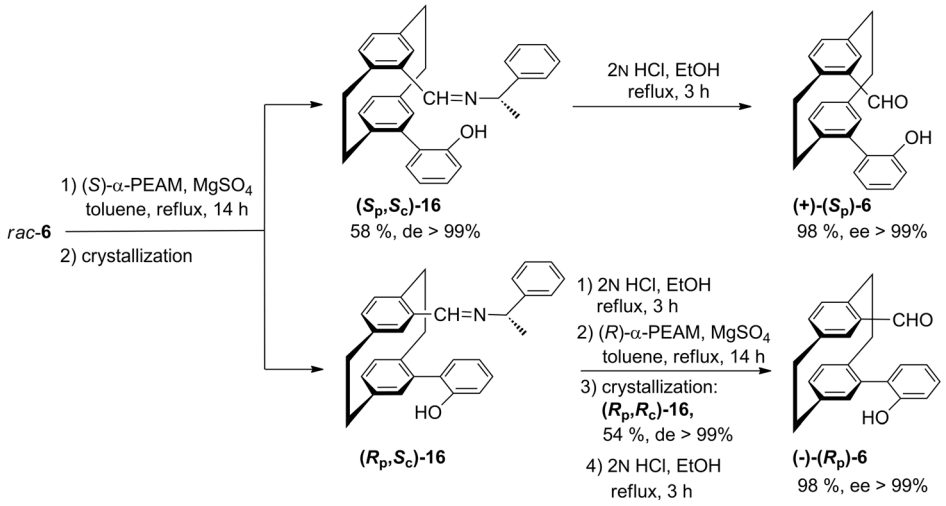


Scheme 2. Resolution of *iso*-FHPhPC **6** into enantiomers.

successfully applied by us for the resolution of [2.2]paracyclophane based salicylaldehyde, its hydroxyaldehyde analogs and hydroxyketones.[17a,b,19,20,22,23d,e] The elaborated procedure relies on the different solubility of the diastereomeric Schiff bases formed from **6** with α-phenylethylamine (α-PEAM) enantiomers. The diastereomeric mixture of (R_p,S_c)- and (S_p,S_c)-**16** was obtained in quantitative yield by condensation of racemic **6** with (*S*)-α-PEAM and it was crystallized from a toluene/hexane mixture, then from ethanol, to produce (S_p,S_c)-**16** in a yield of 58% (Scheme 2). The compound was diastereomerically pure as confirmed by ^{1}H NMR analysis. The partially resolved **6** was recovered by hydrolysis of the filtrate with aqueous HCl in ethanol and introduced into the reaction with (*R*)-α-PEAM. Crystallization of the mixture under similar conditions produced diastereomerically pure (R_p,R_c)-**16** in 54% yield. The absolute configuration of enantiomers **6** was determined by an X-ray structural analysis of the single crystal of this diastereomer (Figure 4). The individual enantiomers, (R_p)- and (S_p)-**6**, were obtained by hydrolysis of (R_p,R_c)- and (S_p,S_c)-**16** with 2 N HCl in ethanol in almost quantitative yields with enantiomeric purity >99% as verified by HPLC analysis on a Chiralpak AD-H column (retention times: (S_p)-**6** t_R = 22.2 min; (R_p)-**6** t_R = 26.4 min).

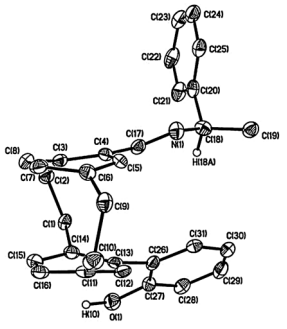


Figure 4. Molecular structure of (R_p,R_c)-**16** in the solid state.

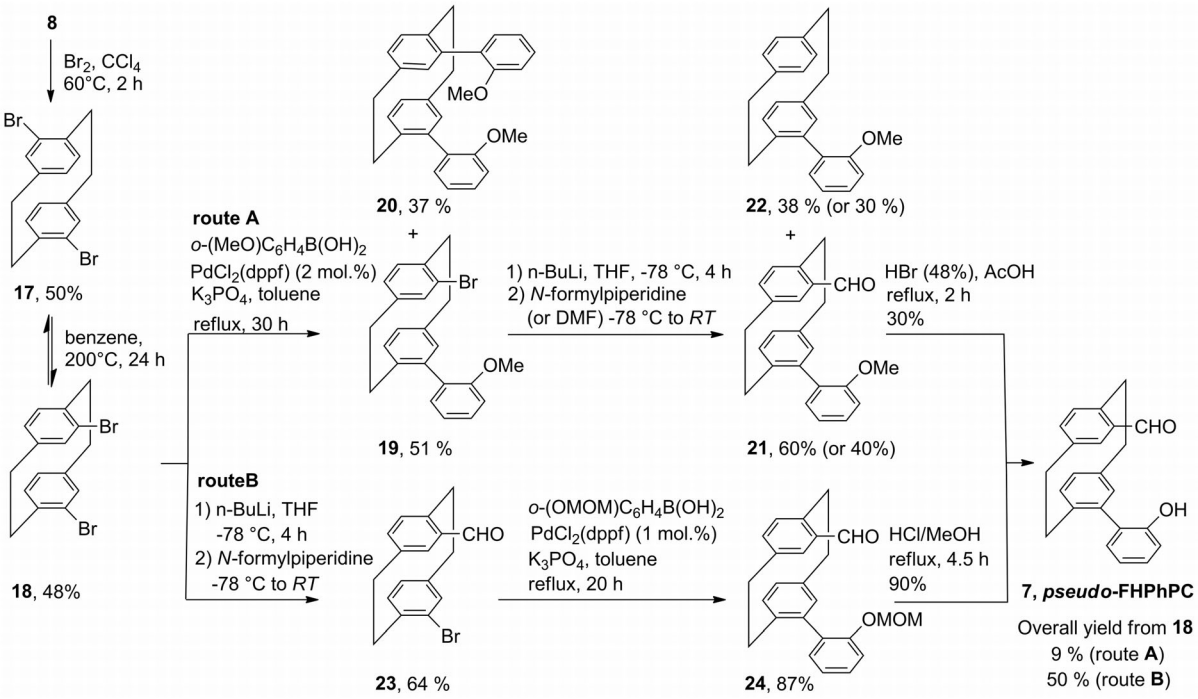
2.2. Synthesis of *pseudo*-FHPhPC 7 and Its Resolution into Enantiomers

The synthetic approach to *pseudo*-FHPhPC **7** is based on a stepwise selective exchange of the bromine substituents in *pseudo-ortho*-dibromo[2.2]paracyclophane **18** that may be accomplished in two ways: 1) bromine by phenyl via Suzuki cross-coupling followed by the other bromine moiety by formyl via monolithiation/formylation (Route **A**), and 2) the reverse approach (Route **B**, Scheme 3) followed by further transformations.

Dibromide **18** was obtained from paracyclophane **8** by a two-step procedure worked out by us earlier.[28] It comprises a non-catalytic bromination of **8**[29] followed by thermal isomerisation of the intermediate *pseudo-para*-dibromo[2.2]paracyclophane **17** into **18** in benzene in autoclave at 200 °C with a high overall yield.

Along Route **A** the aryl[2.2]paracyclophane backbone was built by Suzuki cross-coupling of **18** with anisylboronic acid under non-aqueous conditions (2 mol% of Pd(dppf)Cl_2/toluene/K_3PO_4).[21] The reaction was not chemoselective and it was accompanied by a side coupling at both bromine atoms of **18** leading to a mixture of aryl-[2.2]paracyclophane **19** and bis-aryl[2.2]paracyclophane **20** regardless of the starting dibromide/boronic acid ratio used. The maximal yield of the desired **19** (51%) was reached with three equivalents of the acid. The compound **19** was easily separated from **20** (37%) by preparative chromatography on silica gel.

To introduce the formyl group, bromide **19** was lithiated (1.2 equiv of *n*BuLi in THF at −78 °C), then treated with excess electrophile, DMF or *N*-formylpiperidine.



Scheme 3. Preparation of *pseudo*-FHPhPC **7** from [2.2]paracyclophane **8**.

With DMF, 4-formyl-12-methoxyphenyl-[2.2]paracyclophane **21** was obtained with a yield of 40%, and 4-methoxyphenyl[2.2]paracyclophane **22** (30%) was formed as a side product due to debromination of **19**. *N*-Formylpiperidine was more efficient, raising the yield of **21** up to 60% (together with 38% of **22** being formed). The last stage of Route **A**, demethylation of **21**, was carried out as described above (HBr/AcOH, under reflux) and produced the single paracyclophanyl product, *pseudo*-FHPhPC **7**, in a yield of 30% only. Consequently, the overall yield of **7** as obtained from the dibromide **18** was very poor (no more than 9%).

This unsatisfactory result prompted us to elaborate another, more efficient protocol to **7** which comprises 1) the reversed order in the lithiation/formylation and cross-coupling sequence, and 2) the use of a MOM-protecting group instead of the Me group (Scheme 3, Route **B**). Earlier[22] we had demonstrated that the formyl bromide **23** may be obtained in a yield of 40% by monolithiation[30] of **18** followed by the treatment of the reaction mixture with DMF. Replacement of DMF by *N*-formylpiperidine (in analogy with the synthesis of **21**) allowed us to raise the yield of **23** up to 64%. Suzuki coupling of **23** with *ortho*-MOMO-phenylboronic acid under standard conditions (1 mol% of $Pd(dppf)Cl_2$/toluene/K_3PO_4) produced the MOM-protected aryl[2.2]paracyclophane **24** in a yield of 87%. The MOM group was easily removed from **24** by reflux in ethanol in the presence of a few drops of 36% hydrochloric acid, leading to the target *pseudo*-FHPhPC **7** in a yield of 90%. Thus, Route **B** allowed us a fivefold increase in the overall yield of **7** (from **18)** and raised it up to 50%. The other advantage of this approach is the absence of the aryl[2.2]paracyclophane side products such as **20** or **22**. All this allows to use the Route **B** for a synthesis of *pseudo*-FHPhPC in preparative satisfactory amounts.

The hydroxyaldehyde **7** was resolved into its enantiomers in the same way as its regioisomer **6**. Reaction of the racemic **7** with (*S*)-α-PEAM produced a mixture of diastereomeric Schiff bases, (R_p,S_c)- and (S_p,S_c)-**25**, in quantitative yield (Scheme 4). Crystallization of the mixture from ethanol gave the individual diastereomer (as verified by ^{1}H NMR analysis) of **25** in a yield of 74%. The X-ray structural analysis of the appropriate single crystal allowed us to determine its configuration as (R_p,S_c)-**25** (Figure 5). A partially resolved **7** was isolated by hydrolysis of the mother liquor with 2 N HCl in ethanol. Similarly, its reaction with (*R*)-α-PEAM followed by crystallisation of the diastereomeric mixture (R_p,R_c)-/(S_p,R_c)-**25** from methanol produced diastereomerically pure (S_p,R_c)-**25** in a yield of 68%. The individual enantiomers (S_p)- and (R_p)-**7** were isolated in quantitative yield by hydrolysis of the respective Schiff bases with 2 N HCl in ethanol. Their enantiomeric purity was established as >99% by HPLC analysis on a Chiralpak AD-H column (t_R = 15.0 min for (R_p)-**7** and t_R = 18.3 min for (S_p)-**7**).

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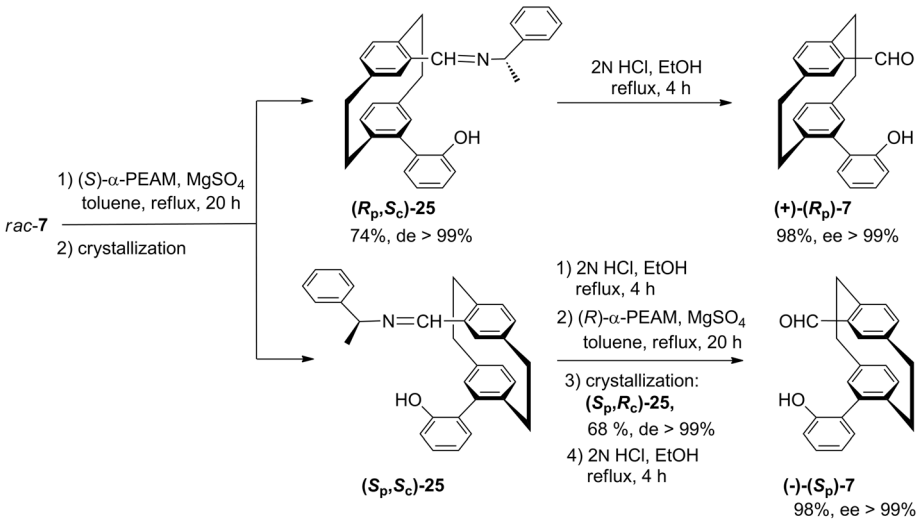


Scheme 4. Resolution of *pseudo*-FHPhPC **7** into its enantiomers.

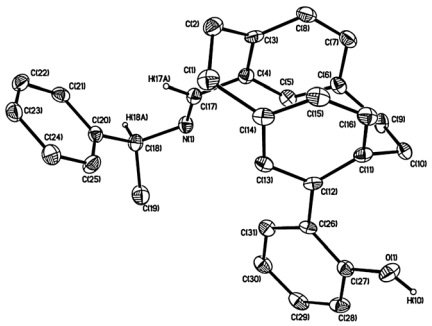


Figure 5. Molecular structure of (R_p,S_c)-**25**.

2.3. Synthesis and Application of Chiral Phenoxy-Imine Ligands Based on Enantiomers of *iso*-FHPhPC 6 and *pseudo*-FHPhPC 7

Finally, we present *iso*-FHPhPC **6** and *pseudo*-FHPhPC **7** as chiral building blocks for the construction of the first representatives of chiral phenoxy-imine ligands based on the aryl[2.2]paracyclophane backbone. During the resolution of racemic *iso*-FHPhPC **6** and *pseudo*-FHPhPC **7** only bidentate aldimines (R_p,R_c)- and (S_p,S_c)-**16** (Scheme 2) and (R_p,S_c)- and (S_p,R_c)-**25** (Scheme 4) could be obtained in enantiomerically pure form. Their diastereomers as well as the ligands **26** to **31** (Figure 6) were obtained by condensation of enantiomers **6** and **7** with the respective amino component (amines, aminoalcohols, and diamine) followed by crystallisation of the reaction mixtures. By this method a set of enantiomerically pure phenoxy-imine ligands belonging to an aryl-[2.2]paracyclophane family was obtained:

- bidentate aldimines with two stereogenic sites: (R_p,S_c)- and (S_p,R_c)-**16**, (R_p,R_c)- and (S_p,S_c)-**25** [obtained from (*S*)- or (*R*)-enantiomers of α-phenylethylamine (α-PEAM)];

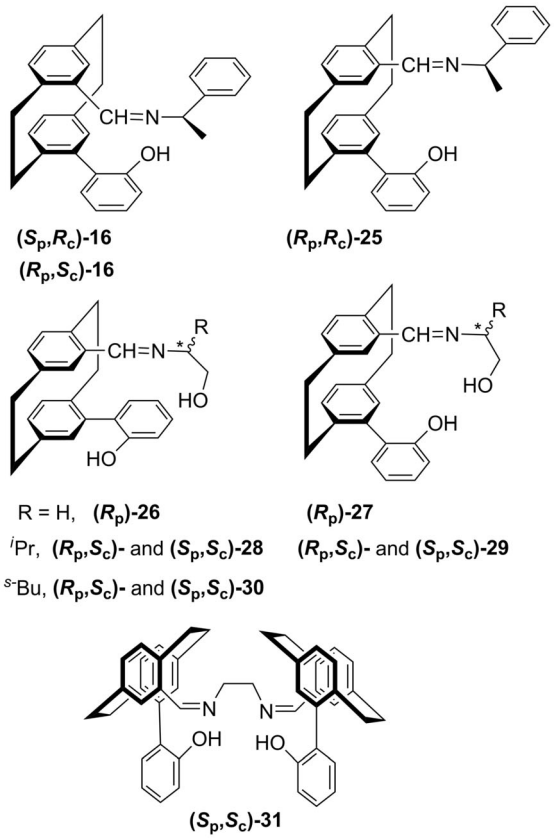


Figure 6. Chiral phenoxy-imine ligands of aryl[2.2]paracyclophane type obtained from enantiomers of **6** and **7** and various amino components.

- tridentate planar chiral aldimines: (R_p)-**26** and (R_p)-**27** [from ethanolamine (EA)];
- tridentate diastereomeric aldimines: (R_p,S_c)- and (S_p,S_c)-**28**, (R_p,S_c)- and (S_p,S_c)-**29**, (R_p,S_c)- and (S_p,S_c)-

30, [from (*S*)-enantiomers of valinol (ValOH) or isoleucinol (^{i}LeuOH)];
- tetradentate "salene", (S_p,S_c)-**31** (from ethylenediamine).

The aldimines **16** and **25**–**30** were next examined as chiral inductors in the Et_2Zn addition to benzaldehyde and cyclohexanecarbaldehyde. The results obtained in this work together with several previously reported ones[22] are collected in Table 1. In a standard experiment,[13] Et_2Zn (2 equiv) and the aldehyde (1 equiv) were successively added to a solution of the ligand (10 mol%) in toluene at 0 °C, and the mixture was stirred at room temperature for 15 h. Excess Et_2Zn was subsequently quenched by addition of 1 N HCl to the reaction mixture, and after standard work up the conversion rate and enantiomeric excess of the resulting secondary alcohol were determined by GC and chiral GC analysis, respectively.

It is clear from Table 1 that in the benzaldehyde series (entries 1a to 12a) the ligands derived from *iso*-FHPhPC **6** (*pseudo-gem* arrangement of functional groups) demonstrate that the stereochemical result of the addition depends on the nature and configuration of the iminomoiety. Among the diastereomeric bidentate ligands derived from (*R*)-α-PEAM, (R_p,R_c)-**16** displays better selectivity than the corresponding (R_p,S_c)-**16**, thus demonstrating a slight matched/mismatched effect in producing 1-phenylpropanol (*R*)-**32** (55 vs. 37% *ee*, entries 2a,1a).

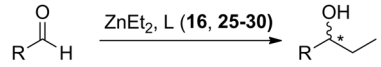
The use of the tridentate iminoalcohol ligands **28** and **30** bearing an additional asymmetric center strongly affected the enantioselectivity, providing (*S*)-**32** with good asymmetric yield with the matched ligands (S_p,*S*)-**28** and (S_p,S_c)-**30** (74 and 78% *ee*, entries 5a, 7a), while carbinol (*S*)-**32** with low enantiopurity of 13 and 5%, respectively, was obtained with the mismatched ligands (R_p,S_c)-**28** and (R_p,S_c)-**30** (entries 4a, 6a). The tridentate ligand (R_p)-**26** which has no additional chiral center showed medium selectivity [(*R*)-**32**, 49% *ee*, entry 3a] comparable to that provided by bidentate (R_p,R_c)-**16**.

Examination of the ligands derived from *pseudo*-FHPhPC **7** has revealed trends different from those provided by **6**. Thus enantiopurity of (*R*)-**32** was practically independent of α-PEAM configuration for both bidentate ligands (R_p,R_c)- and (R_p,S_c)-**25** (58 and 53% *ee*, entries 8a, 9a). In contrast to the ligands **28** and **30** derived from *iso*-FHPhPC **6**, both tridentate (R_p,S_c)- and (S_p,S_c)-**29** possessing two stereogenic sites were not so effective and led to the formation of carbinols **32** with low *ee* values and opposite configurations [(*R*)-**32**, 20% *ee*, entry 11a; (*S*)-**32**, 37% *ee*, entry 12a].

Ethanolamine planar chiral ligand (R_p)-**27** led to a result almost equivalent to that provided by its structural isomer (R_p)-**26** derived from *iso*-FHPhPC, thus giving carbinol **32** of the same configuration and enantiomeric purity [(*R*)-**32**, 50% *ee*]. A comparison of entries 10a and 3a leads to the assumption that whether the aryl paracyclophanyl fragment is *pseudo-gem* or *pseudo-ortho* positioned is not essential in the catalysis performed by these tridentate ligands, the chirality of which rests on the [2.2]paracyclophane moiety only.

In all experiments of the benzaldehyde series (if we exclude strongly mismatched (R_p,S_c)-**28** and (R_p,S_c)-**30**, entries 4a and 6a) the configuration of the resulting 1-phenylpropanol **32** was governed by the configuration of the

Table 1. Enantioselective addition of diethylzinc to aldehydes catalysed by ligands **16, 25–30** (toluene, 25 °C, 10 mol% of L).[a]



R = C_6H_5 **32**
R = C_6H_{11} **33**

Entry (a or b)[b]	FHPhPC	Amine	L	Carbinol **32**[c]	Carbinol **33**[c]
1	(R_p)-**6**	(*S*)-α-PEAM	(R_p,S_c)-**16**	37 (*R*)[d]	34 (*S*)
2	(R_p)-**6**	(*R*)-α-PEAM	(R_p,R_c)-**16**	55 (*R*)[d]	32 (*S*)
3	(R_p)-**6**	EA	(R_p)-**26**	49 (*R*)	25 (*S*)
4	(R_p)-**6**	(*S*)-ValOH	(R_p,S_c)-**28**	13 (*S*)[d]	–
5	(S_p)-**6**	(*S*)-ValOH	(S_p,S_c)-**28**	74 (*S*)[d]	31 (*R*)
6	(R_p)-**6**	(*S*)-^{i}LeuOH	(R_p,S_c)-**30**	5 (*S*)	–
7	(S_p)-**6**	(*S*)-^{i}LeuOH	(S_p,S_c)-**30**	78 (*S*)	–
8	(R_p)-**7**	(*S*)-α-PEAM	(R_p,S_c)-**25**	58 (*R*)	44 (*S*)
9	(R_p)-**7**	(*R*)-α-PEAM	(R_p,R_c)-**25**	53 (*R*)	45 (*S*)
10	(R_p)-**7**	EA	(R_p)-**27**	50 (*R*)	51 (*S*)
11	(R_p)-**7**	(*S*)-ValOH	(R_p,S_c)-**29**	20 (*R*)	–
12	(S_p)-**7**	(*S*)-ValOH	(S_p,S_c)-**29**	37 (*S*)[d]	34 (*R*)

[a] The conversions were determined by GC analysis of the reaction mixtures after standard work-up (yields: 78 to 94% for **32** and near quantitative for **33**). [b] a for benzaldehyde series, b for cyclohexanecarbaldehyde series. [c] The absolute configurations of the secondary alcohols were determined by the elution order of chiral GC analysis in comparison with standard samples. [d] Taken from previous publications[22] for comparison.

planar chiral paracyclophanyl fragment of the ligand [(*R*)-**32** as governed by (R_p) ligands, entries 1a-3a, 8a-11a, and (*S*)-**32** as governed by (S_p) ligands, entries 5a, 7a, 12a].

The efficiency of the selected *iso*-FHPhPC and *pseudo*-FHPhPC derived ligands was next evaluated in the reaction of diethylzinc with cyclohexane 1-carbaldehyde, which resulted in the formation of 1-cyclohexylpropanol **33.** The main differences between the two aldehyde series may be summarized as follows:

i) in all cases where cyclohexane carbaldehyde was applied the carbinols **33** had opposite configurations [(*S*)-**33** as governed by (R_p) ligands, entries 1b-3b, 8b–10b, and (*R*)-**33** as governed by (S_p) ligands, entries 5b, 12b];
ii) the lower enantioselectivity was observed for both series of *iso*- and *pseudo*-FHPhPC ligands (Table 1, entries 1b–3b, 5b and 8b–10b, 12b). It is noteworthy that a decrease in enantioselectivity is more evident in the *iso*-FHPhPC series. Thus, for the planar and central chiral tridentate ligand (S_p,S_c)-**28**, one of the most efficient in the benzaldehyde series, the selectivity decreased noticeably (cf. (*S*)-**32**, 74 % *ee*, entry 5a and (*R*)-**33**, 31 % *ee*, entry 5b).

3. Conclusions

We elaborated efficient routes to two novel regioisomeric chiral analogs of salicylaldehyde with an aryl-[2.2]paracyclophane backbone, namely, 4-formyl-13-(2-hydroxyphenyl)-[2.2]paracyclophane (*iso*-FHPhPC) and 4-formyl-12-(2-hydroxyphenyl)-[2.2]paracyclophane (*pseudo*-FHPhPC), and developed techniques for their optical resolution. These hydroxyaldehydes combined with amines and aminoalcohols gave rise to a set of novel enantiomerically pure bi-, tri-, and tetradentate chiral phenoxy-imino ligands.

The majority of these compounds was tested as chiral inductors in enantioselective Et_2Zn addition to aldehydes. They provide a low to good level of stereoselectivity of the reaction (up to 78 %) depending on the ligand architecture. On average, among [2.2]paracyclophane derived phenoxy-imine ligands with non-classical arrangement of the functional groups, α-phenylethylamine derivatives with *iso*- and *pseudo*-FHPhPC were less efficient than those with the respective FHPC ligands (which led to formation of **32** with *ee* values up to 97 %; see our previous paper[20]). At the same time the diastereomerically pure tridentate iminoalcohol ligand derived from (S_p)-*iso*-FHPhPC and (*S*)-ValOH was the most effective and showed a result (74 % *ee*) superior to all previously reported ones for ligands derived from enantiomers of valinol and regioisomeric FHPC **3–5** (the best results in that series are as follows: (R_p)-FHPC/(*R*)-ValOH, (*R*)-**32**, 10 % *ee*; (R_p)-*pseudo*-FHPC/(*S*)-ValOH, (*S*)-**32**, 40 % *ee*; (R_p)-*iso*-FHPC/(*R*)-ValOH, (*R*)-**32**, 60 % *ee*).[20]

We believe that the phenoxy-imine ligands constructed on the basis of a configurationally rigid and conformationally flexible backbone could find their application in various stereoselective processes. Further development of the FHPhPC project as well as the elaboration of other chiral ligands based on the aryl[2.2]paracyclophane backbone is in progress in our research group.

4. Experimental Section

General: THF, Et_2O, dioxane and toluene were distilled from sodium benzophenone ketyl under argon before use. DMF was distilled under reduced pressure from P_2O_5 and stored over molecular sieves 3 Å. Benzene, heptane, hexane, ethanolamine were distilled over Na before use. (*S*)- and (*R*)-α-phenylethylamines were purchased from Merck; (*S*)-valinol, (*S*)-leucinol and Et_2Zn (1 N solution in hexane) were purchased from Fluka and used without purification. Benzaldehyde and cyclohexanecarbaldehyde were purchased from Aldrich, stored and used under argon without further purification. NMR: Bruker AMX-400 (400.13 MHz) and Bruker Avance 300 (300 MHz). The ^{1}H NMR signals of the residual protons of deuterated solvents were used as internal standards. MS: KRATOS MS890 A (70 eV). Optical rotations were measured with a PerkinElmer-241 polarimeter in a thermostated cell. TLC analyses were performed on silica gel precoated SORBFIL plates PTLC-A-UV (Sorbpolimer). Column chromatography was performed on Kieselgel 60 (Merck). Enantiomeric and diastereomeric analyses were carried out by HPLC on a Chiracel-AD chiral column (hexane/*i*PrOH = 4:1, 1 mL min^{-1}). The enantioselective Et_2Zn additions to benzaldehyde were performed according to established procedures.[13]

4-Methoxycarbonyl-13-(2-methoxyphenyl)-[2.2]paracyclophane 11: A slurry of **10** (1.2 g, 3.476 mmol), *o*-anysilboronic acid (1.058 g, 6.952 mmol), $PdCl_2$(dppf) (0.050 g, 0.0695 mmol), and K_3PO_4 (1.97 g, 9.281 mmol) in abs. toluene (12 mL) was heated in an oil bath at 115–120 °C for 30 h under argon. The reaction mixture was cooled to room temperature, diluted with aq. NaCl (10 mL) and THF (10 mL) and stirred for 15 min. The mixture was extracted with THF (3 × 15 mL) and dried with Na_2SO_4. After evaporation of the solvent in vacuo and purification of the solid residue on SiO_2 (eluent benzene) the target biaryl **11** (R_f = 0.24, 1.03 g, 80 %) was isolated as well as starting material **10** (R_f = 0.32, 0.180 g, 15 %). An analytically pure sample of **11** was obtained by crystallization from ethanol. M.p. 182.5–183.5 °C; m.p. lit.[22] 182.5–183.5 °C.

4-Hydroxymethyl-13-(2-methoxyphenyl)-[2.2]paracyclophane 12: To a solution of 4-methoxycarbonyl-13-(2-methoxy-phenyl)-[2.2]paracyclophane **11** (0.2 g, 0.537 mmol) in dry Et_2O (30 mL) $LiAlH_4$ (0.122 g, 3.22 mmol) was added. The reaction mixture was refluxed for 3 h, cooled down and hydrolyzed with an excess of 2 N HCl solution. After extraction with Et_2O (2 x 15 mL) the combined organic fractions were successively washed with H_2O (2 × 20 mL), saturated aq. $NaHCO_3$ (20 mL), H_2O (15 mL) and dried with Na_2SO_4. The crude **11** (0.186 g, > 99 %) was obtained after removal of the solvent in vacuo. An analytically pure sample of **11** (0.130 g, 70 %) was obtained by crystallization from toluene. M.p. 125–127 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.75–2.86 (m, 1 H, -CHHCH$_2$-); 2.92–3.09 (m, 3 H, -CH$_2$CH$_2$-); 3.10–3.33 (m, 4 H, -CH$_2$CH$_2$-); 3.79 (s, 3 H, -OCH$_3$); 4.12 (d,

$^2J_{H,H}$=13.2 Hz, 1H, -CHHOH); 4.31 (d, $^2J_{H,H}$=13.2, 1H, -CHHOH); 6.48–6.55 (m, 2H, 7 and 15-H); 6.61 (d, ^3J=7.6, 1 H, 8-H); 6.66 (br. s, 2H, 5 and 12-H); 6.74 (br. s, 1H, 16-H); 6.94 (d, $^3J_{H,H}$=8.3 Hz, 1 H, 22-H); 7.05–7.13 (m, 1H, 20-H); 7.29–7.37 (m, 1H, 21-H); 7.47 (br d, $^3J_{H,H}$=7.3 Hz, 1 H, 19-H); MS (EI), *m/z* (rel): 326 (16, M^+-H_2O), 211 (14), 210 (48, M^+-CH_2-$C_6H_3(CH_2OH)$-CH_2), 209 (100), 208 (63), 196 (18), 195 (77), 194 (17), 181 (12), 180 (12) 178 (56), 177 (15), 176 (11), 167 (18), 166 (20), 165 (54), 152 (37), 134 (10), 131 (11), 128 (10), 119 (17), 117 (12), 115 (23), 105 (52), 103 (14). Anal. calcd for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02. Found: C, 83.68; H, 7.11.

4-Formyl-13-(2-methoxyphenyl)-[2.2]paracyclophane 13: To a stirred solution of **12** (0.100 g, 0.290 mmol) in anhydrous dioxane (6 mL) a solution of DDQ (0.066 g, 0.290 mmol) in dioxane (2.5 mL) was added dropwise at room temperature. The reaction mixture was stirred for 3 h, the precipitated $DDQH_2$ was filtered off, and the solvent was removed in vacuo. The residue was purified by preparative chromatography on SiO_2 (R_f=0.58; CH_2Cl_2) to yield **13** (0.98 g, 98%). An analytically pure sample was obtained by crystallization from ethanol (0.86 g, 86%). M.p. 140–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$,): δ=2.80–2.92 (m, 1H, -CHHCH$_2$-); 2.93–3.12 (m, 3H, -CH_2CH_2-); 3.15–3.36 (m, 3H, -CH_2CH_2-); 3.68–3.86 (m, 1H, -CHHCH$_2$-); 3.80 (s, 3H, -OCH_3); 6.53–6.77 (m, 4H, PC-arom.-H); 6.84–6.95 (m, 2H, arom.-H); 7.04–7.14 (m, 2H); 7.22–7.28 (m, 1H); 7.29–7.38 (m, 1 H, arom.-H); 9.69 (s, 1 H, CHO); MS (EI), *m/z* (rel): 342 (23, M^+), 210 (41, M^+-CH_2-C_6H_3(CHO)-CH_2), 209 (100), 195 (40, M^+-CH_2-C_6H_3(CHO)-CH_2 and CH_3), 179 (26), 178 (23). Anal. calcd for $C_{24}H_{22}O_2$: C, 84.18; H, 6.48. Found: C, 84.24; H, 6.24.

4-Formyl-13-(2-hydroxyphenyl)-[2.2]paracyclophane 6 (route **A**, from **13**): To a boiling solution of **13** (0.128 g, 0.374 mmol) in glacial acetic acid (6 mL), HBr (6 mL of 48% aq. solution) was added and the reaction mixture was refluxed for 3 h. After cooling to room temperature, the solution was concentrated in vacuo. The residue was dissolved in benzene (14 mL) and the solution washed with saturated aq. Na_2CO_3, brine, and dried with Na_2SO_4. The solvent was evaporated and the residue was purified by preparative chromatography on SiO_2 (R_f=0.38; CH_2Cl_2), to yield **6** (0.058 g, 47%). An analytically pure sample (0.49 g, 40%) was obtained by crystallization from ethanol. M.p. 199.5–202 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=2.86–2.96 (m, 1H, 2-H); 3.00–3.16 (m, 3H, 1-H, 9-H and 10-H); 3.20–3.37 (m, 3, 1-H, 9-H and 10-H); 3.79–3.88 (m, 1H, 2-H); 5.42 (s, 1H, OH); 6.62 (d, $^4J_{H,H}$=1.8 Hz, 1H, 5-H); 6.67 (dd, $^3J_{H,H}$=7.8 Hz, $^4J_{H,H}$= 1.8 Hz, 1 H, 7-H); 6.73 (d, $^3J_{H,H}$=7.8 Hz, 1 H, 15-H); 6.80 (d, $^3J_{H,H}$=7.9 Hz, 1 H, 8-H); 6.92 (br.d, 2 H, 16-H and 22-H); 7.07 (m, 1H, 21-H); 7.12 (d, $^4J_{H,H}$=1.8 Hz, 1H, 12-H); 7.25–7.34 (m, 2H, 19-H and 20-H); 9.75 (s, 1 H, CHO); MS (EI), *m/z* (rel): 328 (70, M^+), 327 (22), 197 (29), 196 (83, M^+-CH_2-C_6H_3(CHO)-CH_2), 195 (100), 194 (42), 182 (49), 181 (99), 179 (41), 178 (47), 176 (17), 167 (28), 166 (18), 165 (47), 164 (11), 153 (23), 152 (49), 151 (15), 139 (13), 133 (23), 132 (13), 131 (15), 128 (14), 127 (10), 115 (22), 105 (15), 102 (11). Anal. calcd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 83.96; H, 6.01.

13-(2-Hydroxyphenyl)-4-carboxy[2.2]paracyclophane 14: A mixture of **11** (0.700 g, 1.87 mmol) and glacial acetic acid (35 mL) was stirred at 90 °C until a clear solution was obtained (nearly 0.5 h). It was added to a hot aq. solution of 48% HBr (30 mL) and the mixture was refluxed for 3.5 h. After cooling the solvent was evaporated in vacuo, the residue was dissolved in CH_2Cl_2 (50 mL), washed with H_2O (4 x 30 mL) and dried with Na_2SO_4. The crude product was passed through a SiO_2 filled column (eluent CH_2Cl_2) to yield **14** (0.640 g, 99%), R_f=0.48 (AcOEt). An analytically pure sample (0.512 g, 80%) was obtained by crystallization from ethanol. M.p. 227–231 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ=2.80–2.92 (m, 1H, -CHHCH$_2$-); 3.01–3.39 (m, 6H, -CH_2CH_2-); 3.96–4.07 (m, 1H, -CHHCH$_2$-); 5.40 (br. s, 1H, OH); 6.60–6.68 (m, 2H); 6.73–6.85 (m, 4H); 6.89–7.01 (m, 2H); 7.41 (d, $^4J_{H,H}$=1.8 Hz, 1 H, PC-arom.-H); 7.47 (br d, $^3J_{H,H}$=7.5 Hz, 1 H); MS (EI), *m/z* (rel): 344 (25, M^+), 326 (12, M^+-H_2O), 197 (16), 196 (47, M^+-CH_2-C_6H_3(COOH)-CH_2), 195 (84), 194 (19), 182 (25), 181 (100), 179 (21), 178 (22), 177 (11), 167 (11), 165 (23), 153 (10), 152 (25), 131 (36), 115 (11), 105 (11), 103 (15). Anal. calcd for $C_{24}H_{22}O_2$: C, 80.21; H, 5.85. Found: C, 80.02; H, 5.96.

4-Hydroxymethyl-13-(2-hydroxyphenyl)-[2.2]paracyclopane 15: A suspension of **14** (0.639 g, 1.855 mmol) and $LiAlH_4$ (0.423 g, 11.132 mmol) in dry Et_2O (80 mL) was refluxed for 6 h. After cooling, the reaction mixture was acidified with 2 N HCl, extracted with Et_2O (2 x 40 mL), successively washed with H_2O (2× 50 mL), saturated aq. $NaHCO_3$ (40 mL), H_2O (40 mL), and dried with Na_2SO_4. The solvent evaporation in vacuo yielded crude product **14** (0.607 g, 99%). An analytically pure sample of **14** (0.455 g, 75%) was obtained by crystallization from hexane. M.p. 173–174.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$,): δ=2.79–2.90 (m, 1H, -CHHCH$_2$-); 2.95–3.14 (m, 3H, -CH_2CH_2-); 3.15–3.35 (m, 4H, -CH_2CH_2-); 4.19 (d, $^2J_{H,H}$=13.0, 1H, -CHHOH); 4.37 (d, $^2J_{H,H}$=13.0 Hz, 1 H, -CHHOH); 5.60 (br s, 1H, OH); 6.55 (br s, 1H, PC-arom.-H); 6.59–6.75 (m, 5H, PC-arom.-H); 6.95 (dd, $^3J_{H,H}$=8.1 Hz, $^4J_{H,H}$=1.0 Hz, 1 H, arom.-H); 7.04–7.11 (m, 1H, arom.-H); 7.26–7.32 (m, 1H, arom.-H); 7.51 (br d, $^3J_{H,H}$=8.1 Hz, 1 H, arom.-H); MS (EI), *m/z* (rel): 312 (25, M^+-H_2O), 197 (15), 196 (47, M^+-CH_2-$C_6H_3(CH_2OH)$-CH_2), 195 (82), 194 (100), 182 (19), 181 (85), 179 (22), 178 (22), 167 (14), 165 (30), 153 (13), 152 (32), 134 (14), 128 (11). 119 (17), 118 (10), 117 (13), 115 (24), 105 (53), 104 (10). Anal. calcd for $C_{23}H_{22}O_2$: C, 83.60; H, 6.71. Found: C, 83.51; H, 6.74.

4-Formyl-13-(2-hydroxyphenyl)-[2.2]paracyclophane 6 (route **B**, from **15**): To a stirred solution of **14** (0.843 g, 2.551 mmol) in anhydrous dioxane (57 mL), a solution of DDQ (0.579 g, 2.551 mmol) in dioxane (14 mL) was added dropwise at room temperature. The reaction mixture was stirred for 3 h, the precipitated $DDQH_2$ was filtered off, and the solvent was removed in vacuo. The residue was purified by preparative chromatography on SiO_2 (R_f=0.38; CH_2Cl_2), to yield **6** (0.787 g, 94%). The analytical data agree with those of **6**, obtained by route **A**.

Resolution of 4-formyl-13-(2-hydroxyphenyl)-[2.2]paracyclophane 6: A solution of racemic **5** (0.820 g, 2.497 mmol) and (*S*)-α-PEAM (0.453 g, 0.48 mL, 3.746 mmol) in toluene (70 mL) was refluxed in a flask equipped with a Dean–Stark trap filled with $MgSO_4$ for 14 h. The solvent was evaporated and the mixture of diastereomeric aldimines (S_p,S_c)- and (R_p,S_c)-**16** was successively crystallized from a 5:4 mixture of hexane/toluene (90 mL) and ethanol (70 mL) to give aldimine (S_p,S_c)-**16** (0.313 g, 58%, *de*> 98% by ^{1}H NMR analysis). $[\alpha]_D^{20}$ +100.3 (*c* 0.60, benzene); m.p. 217–219 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ=1.36 (d, $^3J_{H,H}$=6.7 Hz, 3 H, CH_3); 2.62–2.73 (m, 1H, -CHHCH$_2$-); 2.74–2.85 (m, 1H, -CHHCH$_2$-); 2.91–3.04 (m, 3H, -CH_2CH_2-); 3.06–3.23 (m, 2H, -CH_2CH_2-); 3.63–3.74(m, 1H, -CHHCH$_2$-); 4.03 (q, $^3J_{H,H}$=6.7 Hz, 1H, 23-H); 6.50 (dd, $^3J_{H,H}$=7.8 Hz, $^4J_{H,H}$=1.8 Hz, 1H, 7-H or 16-H); 6.56–6.62 (m, 2H, 5-H and C8-H or 12-H and 15-H); 6.64 (d, $^3J_{H,H}$=7.8 Hz, 1H, 15-H or 8-H); 6.70–6.79 (m, 2H, 16-H or 7-H and 22-H); 6.85–6.92 (m, 2H, 12-H or 5-H and 20-H); 6.94–7.01 (m, 2H, 24-H and 28-H); 7.02–7.09 (m, 1, 21-H); 7.13–7.27 (m, 3H, 25-H, 26-H and 27-H); 7.31–7.40 (m, 1H, 19-H); 8.07 (s, 1H, CH=N); 9.11 (s, 1H, OH); MS (EI), *m/z*

(rel): 431 (46, M^+), 327 (19); 326 (41, $M^+-CH_3CH\text{-}C_6H_5$); 311 (20, $M^+-CH_3CHN\text{-}C_6H_5$); 235 (20, $M^+-CH_2\text{-}C_6H_3(C_6H_5OH)\text{-}CH_2$); 234 (53); 196 (20), 195 (41), 194 (20), 181(60); 179 (13); 178 (21); 177 (11); 165 (26); 152 (24); 144 (16); 143 (28); 132 (33);131 (79); 130 (99); 129 (22); 115 (20); 106 (56); 105 (100); 104 (33); 103 (45). Anal. calcd for $C_{31}H_{29}NO$: C, 86.27; H, 6.77; N, 3.25. Found: C, 86.17; H, 6.71; N, 3.24.

Compound (S_p,S_c)-**16** was hydrolyzed by reflux with 2 N HCl for 3 h (4 mL) in ethanol (35 mL). After dilution of the reaction mixture with H_2O (40 mL), the organic material was extracted with CH_2Cl_2 (4×20 mL) and dried with Na_2SO_4. Solvent removal gave (S_p)-**6** (0.234 g, 57%) as a white powder. $[\alpha]_D^{20}$ +65.6 (*c* 0.36, benzene); m.p. 213–217 °C (dec.); Anal. calcd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 83.94; H, 6.12.

The combined ethanol filtrates, containing partially resolved (R_p,S_c)-**16**, after evaporation and hydrolysis, gave partially resolved (R_p)-**6** (0.576 g, 1.752 mmol). The condensation of this compound with (*R*)-α-PEAM (0.318 g, 0.33 mL, 2.628 mmol) after two successive crystallizations of the reaction mixture from a 5:4 mixture of hexane/toluene and from ethanol afforded (R_p,R_c)-**16** (0.290 g, 54%). $[\alpha]_D^{20}$ −100.8 (*c* 0.97, benzene); m.p. 214.5–215.5 °C. Anal. calcd for $C_{31}H_{29}NO$: C, 86.27; H, 6.77; N, 3.25. Found: C, 86.16; H, 6.79; N, 3.17.

Hydrolysis of (R_p,R_c)-**16** gave (R_p)-**6** (0.219 g, 53%). $[\alpha]_D^{20}$ −63.6 (*c* 0.36, benzene); m.p. 215–217.5 °C (dec); Anal. calcd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 83.07; H, 6.09.

The enantiomeric purity of (R_p)- and (S_p)-**6** was determined as >99% by Chiral HPLC analysis (Chiralpak AD-H column, 254 nm, 1 mL min^{-1}, 9:1 mixture of hexane and 2-propanol, t_R = 22.2 min for (S_p)-**6** and t_R = 26.4 min for (R_p)-**6**).

4-Bromo-12-(2-methoxyphenyl)[2.2]paracyclophane 19: A suspension of dibromide **18** (0.4 g, 1.093 mmol), *o*-anisylboronic acid (0.498 g, 3.279 mmol), $PdCl_2$(dppf) (0.016 g, 0.022 mmol) and K_3PO_4 (0.927 g, 4.371 mmol) in abs. toluene (4 mL) was stirred for 30 h at 115–125 °C under argon. After cooling, the reaction mixture was quenched with toluene (10 mL) and 1 N NaOH (10 mL). After extraction with THF, washing the solution with 20% aq. NaCl, drying with Na_2SO_4 and solvent evaporation in vacuo, the crude product was purified by preparative column chromatography on SiO_2 (eluent CCl_4). From combined fractions with R_f = 0.1 **19**[21] (0.222 g, 52%) was obtained. An analytically pure sample (0.186 g, 44%) was prepared by crystallization from hexane.

From combined fractions with R_f = 0.09 (CCl_4) the 4,12-bis(2-methoxyphenyl)-[2.2]paracyclophane **20** (0.171 g, 37%) was isolated. An analytically pure sample (0.14 g, 30%) was obtained by crystallization from Et_2O. M.p. 159.5–160.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 2.59–2.69 (m, 2H, -CH_2CH_2-); 2.83–2.93 (m, 2H, -CH_2CH_2-); 3.06–3.20 (m, 4H, -CH_2CH_2-); 3.36 (s, 6H, OCH_3); 6.64–6.70 (m, 4 H, 5-H, 7-H, 13-H and 16-H); 6.75 (d, $^3J_{H,H}$ = 7.8 Hz, 2 H, 8-H and 15-H); 6.93 (d, $^3J_{H,H}$ = 8.1 Hz, 2 H, 22-H and 28-H); 7.00–7.07 (m, 2 H, 21-H and 27-H); 7.30–7.37 (m, 2 H, 20-H and 26-H); 7.60 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.6 Hz, 2 H, 19-H and 25-H); MS *m/z* (%): 421 (10, M^+), 420 (30, M^+), 212 (17), 211 (100), 210 (54), 209 (79), 196 (32), 195 (82), 194 (15), 181 (11), 180 (12), 179 (59), 178 (48), 177 (14), 167 (14), 166 (11), 165 (40), 152 (25). Anal. calcd for $C_{30}H_{28}O_2$: C, 85.68; H, 6.71. Found: C, 85.71; H, 6.75.

4-Formyl-12-(2-methoxyphenyl)-[2.2]paracyclophane 21: To a stirred solution of **19** (0.300 g, 0.763 mmol) in THF (4.5 mL) at −78 °C under argon, *n*BuLi (0.28 mL of 3.27 M solution in hexane, 0.915 mmol, 1.2 equiv) was added dropwise via syringe. The reaction mixture was stirred for 4 h at −78 °C and *N*-formylpiperidine (0.207 g, 0.20 mL, 1.83 mmol) was added. The reaction mixture was stirred for further 1 h at −78 °C and warmed to room temperature overnight. The crude reaction mixture was diluted with toluene (15 mL) and THF (10 mL) and quenched with 2 N HCl (15 mL). The organic material was extracted with a 3:2 mixture of toluene and THF (3×15 mL) and CH_2Cl_2 (2×15 mL), and dried with Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by preparative chromatography on SiO_2. From combined fractions with R_f = 0.47 (benzene) 4-(2-methoxyphenyl)-[2.2]paracyclo-phane **22** (0.091 g, 38%) was isolated. An analytically pure sample was obtained by crystallization from hexane. M.p. 104–106 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.73–2.92 (m, 2H, -CH_2CH_2-); 2.94–3.24 (m, 6H, -CH_2CH_2-); 3.77 (s, 3H, -OCH_3); 6.46–6.72 (m, 7 H, PC-arom.-H); 6.97 (br. d, $^3J_{H,H}$ = 8.3 Hz, 1 H, arom.-H); 7.14–7.22 (m, 1 H, arom.-H); 7.34–7.43 (m, 1 H, arom.-H); 7.58 (br. d, $^3J_{H,H}$ = 7.5 Hz, 1H, arom.-H); MS (EI), *m/z* (rel): 314 (30, M^+), 210 (23, $M^+-CH_2\text{-}C_6H_4\text{-}CH_2$), 209 (100), 195 (77, $M^+-CH_2\text{-}C_6H_4\text{-}CH_2$ and CH_3), 194(16), 179 (13), 178 (17), 165 (13). Anal. calcd for $C_{23}H_{22}O$: C, 87.86; H, 7.05. Found: C, 87.84; H, 6.98.

From the combined fractions with R_f = 0.22 (benzene), compound **21** (0.157 g, 60%) was obtained. M.p. 166–168.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 2.55–2.66 (m, 1H, -CH_2CHH-); 2.84–3.07 (m, 4H, -CH_2CH_2-); 3.18–3.28 (m, 1H, -CH_2CHH-); 3.33–3.42 (m, 1H, -CH_2CHH-); 3.72 (s, 3H, -CH_3); 4.09–4.17 (m, 1H, -CH_2CHH-); 6.40 (d, $^4J_{H,H}$ = 1.8, 1 H, 13-H); 6.56 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, 22-H); 6.61 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1 H, 15-H); 6.78 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, 8-H); 6.85 (dd, $^3J_{H,H}$ = 7.8, $^4J_{H,H}$ = 1.8 Hz, 1 H, 7)-H; 6.94 (br. d, $^3J_{H,H}$ = 8.3 Hz, 1 H, 22-H); 7.17–7.22 (m, 1 H, 20-H); 7.23 (d, $^4J_{H,H}$ = 1.8 Hz, 1 H, 5-H); 7.33–7.40 (m, 1, 21-H); 7.42–7.47 (dd, $^3J_{H,H}$ = 7.6 Hz, $^4J_{H,H}$ = 1.6 Hz, 1 H, 19-H); 10.13 (s, 1H, CHO); MS (EI), *m/z* (rel): 342 (20, M^+), 327 (13, M^+-CH_3); 325 (11), 324 (22), 210 (35, $M^+-CH_2\text{-}C_6H_3(CHO)\text{-}CH_2$), 209 (100), 197 (11), 196 (55), 195 (77, $M^+-CH_2\text{-}C_6H_3(CHO)\text{-}CH_2$ and CH_3), 194(23), 181 (14), 179 (24), 178 (34), 177 (11), 167 (17), 166 (13), 165 (28), 152 (20), 149 (10). Anal. calcd for $C_{24}H_{22}O_2$: C, 84.18; H, 6.48. Found: C, 84.29; H, 6.57.

4-Formyl-12-(2-hydroxyphenyl)-[2.2]paracyclophane 7 (route **A**, from **21**): To a boiling solution of **21** (0.113 g, 0.330 mmol) in glacial acetic acid (2 mL) HBr (2 mL of 48% aq. solution) was added, and the resulting mixture was refluxed for 2 h. After cooling to room temperature the solution was concentrated in vacuo, the residue was dissolved in benzene (12 mL) and the solution was successively washed with saturated aq. Na_2CO_3, brine, and finally dried with Na_2SO_4. The solvent was evaporated and the residue was purified by preparative chromatography on SiO_2 (R_f = 0.43; CH_2Cl_2) to yield **7** (0.033 g, 30%). An analytically pure sample (0.20 g, 18%) was obtained by crystallization from a 2:1 mixture of hexane/toluene. M.p. 97–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.60–2.71 (m, 1H, 9-H); 2.88–3.10 (m, 4H, 1-H, 2-H, 9-H and 10-H); 3.25–3.34 (m, 1H, 1-H); 3.35–3.44 (m, 1H, 2-H); 4.09–4.19 (m, 1H, 10-H); 5.81 (s, 1H, OH); 6.44 (d, $^4J_{H,H}$ = 1.8 Hz, 1H, 13-H); 6.64–6.71 (m, 2H, 5-H and 16-H); 6.79 (d, $^3J_{H,H}$ = 7.8, 1 H, 7-H); 6.85 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1H, 15-H); 6.95 (dd, $^3J_{H,H}$ = 8.1 Hz, $^4J_{H,H}$ = 1.1, 1H, 22-H); 7.12–7.21 (m, 1H, 21-H); 7.23–7.33 (m, 2H, 8-H and 20)-H); 7.44 (dd, $^3J_{H,H}$ = 7.7, $^4J_{H,H}$ = 1.6 Hz, 1H, 19-H); 10.14 (s, 1H, CHO); MS (EI), *m/z* (rel): 328 (11, M^+), 310 (11, M^+-H_2O), 196 (21, $M^+-CH_2\text{-}C_6H_3(CHO)\text{-}CH_2$-), 195 (46), 182 (16), 181 (100), 167 (10),

165 (11), 152 (14). Anal. calcd for $C_{23}H_{22}O_2$: C, 84.12; H, 6.14. Found: C, 84.11; H, 6.15.

4-Formyl-12-bromo[2.2]paracyclophane 23: To a stirred solution of **18** (2.500 g, 6.831 mmol) in THF (38 mL) at −78 °C under argon, *n*BuLi (2.51 mL of 3.27 M solution in hexane, 8.20 mmol, 1.2 equiv) was added dropwise via syringe. The reaction mixture was stirred for 4 h at −78 °C and *N*-formylpiperidine (1.855 g, 1.84 mL, 16.339 mmol) was added. After complete addition, the reaction mixture was stirred for 1 h at −78 °C and warmed to room temperature overnight. The crude reaction mixture was diluted with toluene (60 mL) and THF (40 mL) and quenched with 2 N HCl (50 mL). The organic material was successively extracted with a 3:2 mixture of toluene and THF (3×50 mL) and CH_2Cl_2 (2×60 mL), and dried with Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified chromatography on SiO_2 (R_f=0.40; benzene), to yield compound **23**[22] (1.380 g, 64 %).

4-Formyl-12-(2-oxymethylenemethoxyphenyl)-[2.2]paracyclophane 24: A suspension of bromide **23** (1.800 g, 5.71 mmol), *o*-anisylboronic acid (1.560 g, 8.57 mmol), Pd(dppf)Cl_2 (0.041 g, 0.057 mmol, 1 mol %) and K_3PO_4 (2.430 g, 11.42 mmol) in toluene (34 mL) under argon was stirred at reflux for 10 h. Then, a fresh portion of *o*-anisylboronic acid (0.520 g, 2.86 mmol) and K_3PO_4 (0.810 g, 3.81 mmol) were added and the reaction mixture was refluxed for an additional 10 h. After cooling down to room temperature, the reaction mixture was diluted with toluene (20 mL) and THF (30 mL) and hydrolyzed with brine (60 mL). The organic material was extracted with a 3:2 mixture of toluene and THF (3×50 mL) and dried with Na_2SO_4. The solution was concentrated in vacuo and purified by preparative chromatography on SiO_2. Elution with benzene (R_f=0.08) gave compound **24** (1.850 g, 87 %). M.p. 100–101 °C; ^{1}H NMR (400 MHz, C_6D_6, 25 °C): δ=2.51–2.61 (m, 1H, -CHHCH$_2$-); 2.63–2.91 (m, 4H, -CH$_2$CH$_2$-); 3.08–3.18 (m, 4H, -CHHCH$_2$- and OCH$_3$); 3.42–3.52 (m, 1H, -CHHCH$_2$-); 3.89–4.00 (m, 1H, -CHHCH$_2$-); 4.78 (d, $^2J_{H,H}$=10.8 Hz, 1H, -OCHHO-); 4.80 (d, $^2J_{H,H}$=10.8, 1H, -OCHHO-); 6.42 (dd, $^3J_{H,H}$=7.8 Hz, $^4J_{H,H}$=1.8 Hz, 1H, 15-H); 6.47 (d, $^3J_{H,H}$=7.8 Hz, 1H, 16-H); 6.52 (d, $^3J_{H,H}$=7.8 Hz, 1H, 8-H); 6.56 (dd, $^3J_{H,H}$=7.8 Hz, $^4J_{H,H}$=1.8 Hz, 1H, 7-H); 6.59 (d, $^4J_{H,H}$=1.8 Hz, 1H, 13-H); 7.27–7.34 (m, 2H, 21-H and 22-H); 7.38–7.47 (m, 1H, 20-H); 7.50 (d, $^4J_{H,H}$=1.8 Hz, 1H, 5-H); 7.95 (br. d, $^3J_{H,H}$=7.3 Hz, 1H, 19-H); 10.16 (s, 1H, CHO); MS (EI), *m/z* (rel): 372 (17, M^+), 340 (12, M^+-OCH_3), 240 (13, M^+-CH_2-C_6H_3(CHO)-CH_2-); 239 (27); 209 (11); 208 (25); 207 (10); 198 (21); 196 (21); 195 (92); 194 (63); 182 (17); 181 (80); 178 (13); 177 (12); 167 (11); 166 (11); 165 (39); 152 (22); 104 (13). Anal. calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.68; H, 6.57.

4-Formyl-12-(2-hydroxyphenyl)-[2.2]paracyclophane 7 (route **B**, from **24**): To a stirred solution of **24** (1.700 g, 4.964 mmol) in methanol (150 mL) four drops of concentrated HCl were added at 60 °C and the mixture was refluxed for 4.5 h. After methanol removal the residue was dissolved in CH_2Cl_2 and passed through a SiO_2 filled column. The target product **6** (1.350 g, 90 %) was obtained as a white crystalline compound. The analytical data are in agreement with those of **7**, obtained by route A.

Resolution of 4-formyl-12-(2-hydroxyphenyl)-[2.2]*para*-cyclophane 7: A solution of racemic **7** (1.363 g, 4.150 mmol) and (*S*)-α-PEAM (0.753 g, 0.79 mL, 6.223 mmol) in toluene (60 mL) was refluxed in a flask equipped with a Dean–Stark trap filled with $MgSO_4$ for 20 h. The solvent was evaporated and the mixture of the diastereomeric aldimines (R_p,S_c)- and (S_p,S_c)-**25** was crystallized from methanol (70 mL) to give imine (R_p,S_c)-**25** (0.663 g, 74 %, *de*>98 % by ^{1}H NMR analysis). $[\alpha]_D^{20}$ +179.1 (*c* 0.67, benzene); m.p. 55–56 °C; ^{1}H NMR (300 MHz, C_6D_6, 25 °C): δ=1.79 (d, $^3J_{H,H}$=6.6 Hz, 3H, CH_3); 2.44–2.79 (m, 5H, -CH_2CH_2-); 3.02–3.15 (m, 1H, -CHHCH$_2$-); 3.29–3.43 (m, 1H, -CHHCH$_2$-); 3.65–3.80 (m, 1H, -CHHCH$_2$-); 4.56 (q, $^3J_{H,H}$=6.6 Hz, 1 H, 23-H); 6.0 (br. s, 1H, OH); 6.41–6.46 (m, 2H, 7-H and 8-H, or 15-H and 16-H); 6.49 (dd, $^3J_{H,H}$=7.8 Hz, $^4J_{H,H}$=1.8 Hz, 1 H, 7-H or 15-H); 6.51–6.58 (m, 2 H, 8-H or 16-H and 13-H); 7.02–7.11 (m, 1 H, arom-H); 7.18–7.35 (m, 3 H, arom-H); 7.36–7.45 (m, 2H, 25-H and 27-H); 7.66 (d, $^4J_{H,H}$=1.8, 1 H, 5-H); 7.68–7.74 (m, 2 H, 24-H and 28-H); 7.90–7.99 (m, 1H, arom-H); 8.44 (s, 1H, CH=N); MS (EI), *m/z* (rel): 431 (92, M^+), 327 (32), 326 (63, M^+-CH_3CH-C_6H_5), 311 (28, M^+-CH_3CHN-C_6H_5), 310 (73), 309 (28), 295 (18), 293 (12), 250 (14), 236 (29), 235 (27, M^+-CH_2-C_6H_3(C_6H_5OH)-CH_2), 234 (53), 196 (15), 195 (46), 182 (19), 181 (72), 178 (13), 167 (14), 165 (20), 152 (23), 144 (13), 132 (37), 131 (69), 130 (100), 129 (13), 115 (12), 105 (61). Anal. calcd for $C_{31}H_{29}NO$: C, 86.27; H, 6.77; N, 3.25. Found: C, 86.28; H, 6.84; N, 3.17.

Compound (R_p,S_c)-**25** was hydrolyzed by refluxing it with aq. 2 N HCl (6 mL) in ethanol (56 mL) for 4 h. After dilution of the reaction mixture with H_2O (50 mL), the organic material was extracted with CH_2Cl_2 (4×40 mL) and dried with Na_2SO_4. After solvent evaporation, (R_p)-**7** (0.499 g, 73 %) was obtained as a white powder. $[\alpha]_D^{20}$ +189.3 (*c* 0.56, benzene); m.p. 146.5–147.5 °C. Anal. calcd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 84.04; H, 6.09.

The combined ethanol filtrates, containing partially resolved (S_p,S_c)-**25** after evaporation and hydrolysis gave a partially resolved (S_p)-**7** (0.882 g, 2.686 mmol), which in turn was treated with (*R*)-α-PEAM (0.487 g, 0.51 mL, 4.028 mmol). The diastereomerically pure (S_p,R_c)-**25** (0.608 g, 68 %, *de*>98 % by ^{1}H NMR analysis) was obtained by crystallization from methanol. $[\alpha]_D^{20}$ −177.0 (*c* 0.50, benzene); m.p. 63–65 °C. Anal. calcd for $C_{31}H_{29}NO$: C, 86.27; H, 6.77; N, 3.25. Found: C, 86.46; H, 6.96; N, 3.23.

Hydrolysis of (S_p,R_c)-**25** gave (S_p)-**7** (0.458 g, 67 %). $[\alpha]_D^{20}$ −187.8 (*c* 0.47, benzene); m.p. 141.5–144.5 °C. Anal. calcd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 84.32; H, 6.18.

The enantiomeric purity of (R_p)-**7** and (S_p)-**7** was determined as >99 % by Chiral HPLC analysis (Chiralpak AD-H column; 254 nm, 1 mL min^{-1}, 9:1 mixture of hexane and 2-propanol; t_R= 15.0 min for (R_p)-**7** and t_R=18.3 min for (S_p)-**7**).

General procedure for preparation of aldimines from 6 and 7

Aldimine (S_p,R_c)-16: Compound (S_p)-**6** (0.050 g, 0.152 mmol) was dissolved in absolute toluene (15 mL) and (*R*)-α-PEAM (0.028 g, 0.03 mL, 0.228 mmol, 1.5 equiv) was added. The solution was refluxed in an apparatus equipped with a Dean–Stark trap filled with anhydrous $MgSO_4$ for 14 h. After solvent removal the resulting solid was purified by crystallisation from 1:3 mixture of toluene and hexane to yield (S_p,R_c)-**16** (0.045 g, 68 %). $[\alpha]_D^{20}$ +95.0 (*c* 0.70, benzene); m.p. 143.5–145 °C; ^{1}H NMR (400 MHz, C_6D_6, 25 °C): δ=1.31 (d, $^3J_{H,H}$=6.5 Hz, 3H, CH_3); 2.61–2.73 (m, 1H, -CHHCH$_2$-); 2.74–2.87 (m, 2H, -CH_2CH_2-); 2.87–3.18 (m, 3H, -CH_2CH_2-); 3.21–3.34 (m, 1H, -CHHCH$_2$-); 4.07–4.18 (m, 1H, -CHHCH$_2$-); 4.23 (q, $^3J_{H,H}$=6.5, 1H, =N-CH); 6.43 (dd, $^3J_{H,H}$=7.8 Hz, $^4J_{H,H}$=1.8 Hz, 1 H, PC-arom.-H); 6.48–6.56 (m, 2H, PC-arom.-H); 6.58 (dd, $^3J_{H,H}$=7.8 Hz, $^4J_{H,H}$=1.8 Hz, 1 H, PC-arom.-H); 6.66 (br. s, 1H, OH); 6.69–6.77 (m, 1H, arom.-H); 6.97 (br. s, 1H, PC-arom.-H); 7.09–7.34 (m, 4 H); 7.35 (m, 3 H);

7.66 (d, $^3J_{H,H}$ = 7.5 Hz, 2H, 24-H and 28-H); 8.10 (s, 1H, -CH=N); ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 1.35 (d, $^3J_{H,H}$ = 6.3 Hz, 3 H, CH_3); 2.61–2.73 (m, 1H, 2-H); 2.73–2.86 (m, 1H, 1-H); 2.89–3.04 (m, 3H, 1-H, 9-H and 10-H); 3.06–3.21 (m, 2H, 9-H and 10-H); 3.62–3.75 (m, 1H, 2-H); 4.03 (q, $^3J_{H,H}$ = 6.3 Hz, 1H, 23-H); 6.50 (d, $^3J_{H,H}$ = 7.6 Hz, 1H, 15-H); 6.55–6.62 (m, 2H, 12-H and 16-H); 6.64 (d, $^3J_{H,H}$ = 7.6 Hz, 1H, 8-H); 6.69–6.79 (m, 2H, 7-H and 22-H); 6.83–6.92 (m, 2H, C5-H and 20-H); 6.97 (d, $^3J_{H,H}$ = 7.3 Hz, 2H, 24-H and 28-H); 7.01–7.09 (m, 1H, 21-H); 7.12–7.26 (m, 3H, 25-H, 26-H and 27-H); 7.35 (br. d, $^3J_{H,H}$ = 7.3 Hz, 1H,)-H); 8.07 (s, 1H, CH = N); 9.11 (s, 1H, OH); MS (EI), *m/z* (rel): 431 (28, M^+), 430 (13), 416 (23), 327 (22), 326 (72, M^+-CH_3CH-C_6H_5), 312 (15), 311 (24, M^+-CH_3CHN-C_6H_5), 235 (18, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 234 (54), 196 (12), 195 (34), 194 (13), 185 (16), 181 (50), 178 (10), 167 (11), 165 (10), 152 (17), 149 (35), 144 (13), 143 (14), 132 (16), 131 (31), 130 (100), 129 (12), 106 (36), 105 (50), 103 (22). Anal. calcd for $C_{31}H_{29}NO$: C, 86.27; H, 6.77; N, 3.25. Found: C, 86.44; H, 6.91; N, 3.28.

Aldimine (R_p,S_c)-16 (0.067 g, 72%) was obtained from (R_p)-**6** (0.070 g, 0.213 mmol) and (*S*)-α-PEAM (0.039 g, 0.04 mL, 0.319 mmol, 1.5 equiv) after reflux for 14 h and crystallisation from a 1:3 mixture of toluene and hexane. $[\alpha]_D^{20}$ −93.0 (*c* 0.67, benzene); m.p. 141.5–143.5 °C. Anal. calcd for $C_{31}H_{29}NO$: C, 86.27; H, 6.77; N, 3.25. Found: C, 86.37; H, 6.96; N, 3.16.

Aldimine (R_p,R_c)-**25** (0.041 g, 52%) was obtained from (R_p)-**7** (0.06 g, 0.183 mmol) and (*R*)-α-PEAM (0.033 g, 0.035 mL, 0.274 mmol) after reflux for 14 h and crystallisation from a 1:3 mixture of toluene and hexane. $[\alpha]_D^{20}$ +33.9 (*c* 0.47, benzene); m.p. 155–158 °C, ^{1}H NMR (400 MHz, C_6D_6, 25 °C): δ = 1.88 (d, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_3); 2.48–2.58 (m, 1H, -CHHCH$_2$-); 2.59–2.77 (m, 4H, -CH$_2$CH$_2$-); 3.07–3.17 (m, 1H, -CHHCH$_2$-); 3.34–3.43 (m, 1H, -CHHCH$_2$-); 3.60–3.70 (m, 1H, -CHHCH$_2$-); 4.54 (q, ^3J = 6.7 Hz, 1 H, 23-H); 6.46 (br. s, 2H, 7-H and 8H, or 15-H and 16-H); 6.49 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1 H, 7-H or 15-H); 6.55 (d, $^3J_{H,H}$ = 7.8 Hz, 1 H, 8-H or 16-H); 6.69 (br. s, 1H, 13-H); 7.27–7.44 (m, 7H, 19-H, 20-H, 21H, 22-H, 25-H, 26-H, 27-H); 7.73 (d, $^3J_{H,H}$ = 7.3 Hz, 2 H, 24-H and 28-H); 7.77 (br. s, 1H, 5-H); 8.39 (br. s, 2H, CH = N and OH); MS (EI), *m/z* (rel): 431 (13, M^+), 430 (13), 326 (5, M^+-CH_3CH-C_6H_5), 311 (4, M^+-CH_3CHN-C_6H_5), 310 (8), 239 (5), 235 (5, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 234 (6), 231 (6), 209 (13), 208 (10), 194 (15), 185 (10), 181 (16), 169 (13), 167 (12), 165 (12), 155 (11), 152 (10), 149 (100), 141 (14), 139 (16), 137 (13), 131 (22), 130 (18), 127 (13), 125 (17), 121 (14), 119(13), 115 (10), 113 (22), 111 (26), 110 (10), 109 (17), 106 (15), 105 (43), 104 (11). Anal. calcd for $C_{31}H_{29}NO$: C, 86.27; H, 6.77; N, 3.25. Found: C, 86.56; H, 7.00; N, 3.33.

Aldimine (R_p)-26 (0.064 g, 81%) was obtained from (S_p)-**6** (0.070 g, 0.213 mmol) and ethanolamine (EA) (0.020 g, 0.019 mL, 0.320 mmol) after reflux for 18 h and crystallisation from heptane. $[\alpha]_D^{20}$ −86.5 (*c* 0.55, benzene); m.p. 151.5–157 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO,): δ = 2.1–2.79 (m, 1H, -CHHCH$_2$-); 2.86–2.93 (m, 1H, -CHHCH$_2$-); 2.94–3.06 (m, 3H, -CH$_2$CH$_2$- and 23-H); 3.06–3.18 (m, 3H, -CH$_2$CH$_2$-); 3.25–3.32 (m, 1H, 24-H); 3.35–3.42 (m, 1H, 23-H); 3.40–3.47 (m, 1H, 24-H); 3.62–3.64 (m, 1H, -CHHCH$_2$-); 4.04 (br.s, 1H, (C24)-OH); 6.49 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1H, 7-H); 6.55 (d, $^4J_{H,H}$ = 1.8 Hz, 1H, 5-H); 6.61 (d, $^3J_{H,H}$ = 7.8 Hz, 1H, 8-H); 6.65 (d, $^4J_{H,H}$ = 1.8 Hz, 1H, 15-H); 6.73 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1H, 16-H); 6.79–6.85 (m, 1H, 20-H or 21-H); 6.85–6.90 (m, 1H, 21-H or 20-H); 6.92(d, $^4J_{H,H}$ = 1.8 Hz, 1H, 12-H); 7.08–7.12 (m, 1H, 22-H); 7.29–7.33 (m, 1H, 19-H); 7.91 (s, 1H, CH = N); 9.13 (s, 1H, OH); MS (EI), *m/z* (rel): 371 (18, M^+), 196 (13, M^+-CH_2-$C_6H_3(CH{=}NCH_2CH_2OH)$-CH_2), 195 (27), 181 (45), 175 (46, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 174 (100), 165 (12), 152 (12), 144 (34), 143 (16), 131 (17), 130 (32), 115 (13). Anal. calcd for $C_{25}H_{25}NO_2$: C, 80.83; H, 6.78; N, 3.77. Found: C, 80.88; H, 6.90; N, 3.65.

Aldimine (R_p)-27 (0.048 g, 70%) was obtained from (R_p)-**7** (0.060 g, 0.183 mmol) and EA (0.017 g, 0.017 mL, 0.274 mmol) after reflux for 12 h and crystallisation from a 3:2 mixture of toluene and hexane. $[\alpha]_D^{20}$ +124.5 (*c* 0.47, benzene); m.p. 153.5–157.5 °C; ^{1}H NMR (400 MHz, C_6D_6, 25 °C): δ = 2.50–2.81 (m, 5H, -CH$_2$CH$_2$-); 3.01–3.14 (m, 1H, -CHHCH$_2$-); 3.34–3.43 (m, 1H, -CHHCH$_2$-); 3.51–3.69 (m, 2H, 23-H and -CHHCH$_2$-); 3.71–3.81 (m, 1H, 23-H); 3.87–3.95 (m, 1H, 24-H); 3.96–4.05 (m, 1H, 24-H); 6.40–6.58 (m, 4H, 7-H, 8-H, 15-H and 16-H); 6.81 (br. s, 1 H, 13-H); 7.23–7.38 (m, 4H, 19-H, 20-H, 21-H and 22-H); 7.65 (br. s, 1 H, 5-H); 8.07 (br. s, 1 H, -C_6H_4OH); 8.31 (s, 1H, CH = N); MS (EI), *m/z* (rel): 371 (77, M^+), 354 (19), 311 (37), 310 (68), 309 (23), 295 (19), 293 (12), 196 (8, M^+-CH_2-$C_6H_3(CH{=}NCH_2CH_2OH)$-CH_2), 195 (22), 181 (52), 178 (12), 177 (21), 176 (81), 175 (76, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 174 (100), 165 (17), 152 (21), 144 (65), 143 (17), 131 (20), 130 (30), 129 (14), 128 (11), 115 (17). Anal. calcd for $C_{25}H_{25}NO_2$: C, 80.83; H, 6.78; N, 3.77. Found: C, 80.64; H, 6.77; N, 3.73.

Aldimine (R_p,S_c)-28 (0.057 g, 75%) was obtained from (R_p)-**6** (0.060 g, 0.183 mmol) and (*S*)-2-amino-3-methyl-1-buthanol ((*S*)-ValOH) (0.033 g, 0.320 mmol) after reflux for 18 h and crystallisation from a mixture of toluene and hexane. $[\alpha]_D^{20}$ +28.4 (*c* 0.37, THF); m.p. 219–222 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 0.54 (d, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_3); 0.66 (d, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_3); 1.18–1.32 (m, 1H, 25-H); 2.43–2.53 (m, 1H, 23-H); 2.63–2.75 (m, 1H, 24-H); 2.85–3.07 (m, 4H, -CH$_2$CH$_2$- and 24-H); 3.08–3.22 (m, 3H, -CH$_2$CH$_2$-); 4.00–4.12 (m, 1H, -CHHCH$_2$-); 4.26–4.36 (m, 1H, -CHHCH$_2$-); 6.48 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1H, 7-H or 16-H); 6.56–6.74 (m, 5H, 5-H, 8-H, 12-H, 15-H, and 16-H or 7-H); 6.75–6.84 (m, 1H, 19-H or 22-H); 6.87–6.97 (m, 1H, 20-H or 21-H); 7.05–7.15 (m, 1H, 21-H or 20-H); 7.34–7.45 (m, 1H, 22-H or 19-H); 7.88 (s, 1H, CH = N); 9.15 (s, 1H, OH); MS (EI), *m/z* (rel): 413 (100, M^+), 412 (11), 396 (16, M^+-H_2O), 382 (23), 312 (12), 311 (60), 310 (54), 309 (18), 295 (15), 232 (24), 219 (30), 218 (84), 217 (83, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 216 (72), 196 (19, CH_2-C_6H_3-(CH=NCH(*i*Pr)CH_2OH)-CH_2), 186 (34), 182 (10), 181 (43), 178 (10), 174 (21), 165 (13), 152 (14), 144 (12), 143 (14), 132 (18), 131 (50), 130 (61), 129 (15), 128 (11), 115 (11). Anal. calcd for $C_{28}H_{31}NO_2$: C, 81.32; H, 7.56; N, 3.39. Found: C, 81.44; H, 7.41; N, 3.34.

Aldimine (S_p,S_c)-28 (0.070 g, 80%) was obtained from (S_p)-**6** (0.070 g, 0.213 mmol) and (*S*)-ValOH (0.033 g, 0.320 mmol) after reflux for 14 h and crystallisation from a 4:1 mixture of toluene and hexane. $[\alpha]_D^{20}$ +7.9 (*c* 0.53, benzene); m.p. 140–142.5 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 0.77 (d, $^3J_{H,H}$ = 6.9 Hz, 3H, CH_3); 0.80 (d, $^3J_{H,H}$ = 6.9 Hz, 3H, CH_3); 1.86–1.98 (m, 1H, 25-H); 2.52–2.62 (m, 1H, 23-H); 2.63–2.76 (m, 1H, 24-H); 2.85–3.20 (m, 7H, -CH$_2$CH$_2$- and 24-H); 3.73–3.84 (m, 1H, -CHHCH$_2$-); 4.01–4.10 (m, 1H, -CHHCH$_2$-); 6.49 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1H, 7H or 16-H); 6.57 (d, $^4J_{H,H}$ = 1.8 Hz, 1H, 5-H or 12-H); 6.62 (d, $^3J_{H,H}$ = 7.8 Hz, 1H, 8-H or 15-H); 6.64 (d, $^4J_{H,H}$ = 1.8 Hz, 1H, 15-H or 8-H); 6.71 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1H, 16-H or 7-H); 6.75 (d, $^4J_{H,H}$ = 1.8 Hz, 1H, 12-H or 5-H); 6.79–6.92 (m, 1H, 19-H and 20-H, or 22-H and 21-H); 7.09–7.18 (m, 1H, 21-H or 20-H); 7.29–7.36 (m, 1H, 19-H or 22-H); 7.90 (s, 1H, CH = N); 9.17 (br. s, 1H, OH); MS (EI), *m/z* (rel): 413 (32, M^+), 412 (11), 382 (16), 311 (26), 219 (13), 218

(13), 217 (44, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 216 (100), 196 (14, CH_2-C_6H_3(CH=NCH(*i*Pr)CH_2OH)-CH_2), 195 (24), 182 (11), 181 (53), 178 (13), 165 (14), 152 (13), 144 (17), 143 (25), 132 (17), 131 (70), 130 (88), 129 (16), 128 (11), 115 (16). Anal. calcd for $C_{28}H_{31}NO_2$: C, 81.32; H, 7.56; N, 3.39. Found: C, 81.46; H, 7.69; N, 3.31.

Aldimine (R_p,S_c)-29 (0.071 g, 94%) was obtained from (R_p)-**7** (0.060 g, 0.183 mmol) and (*S*)-ValOH (0.028 g, 0.274 mmol) after reflux for 12 h and crystallisation from 2:5 mixture of toluene/hexane. $[\alpha]_D^{20}$ +110.1 (*c* 0.63, benzene); m.p. 170–172 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 0.93 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, CH_3); 1.04 (d, ^{3}J = 6.7 Hz, 3H, CH_3); 1.94–2.08 (m, 1H, 25-H); 2.16–2.29 (m, 1H, -CHHCH$_2$-); 2.69–2.97 (m, 3H, -CH_2CH_2-); 3.07–3.29 (m, 3H, 23-H and -CH_2CH_2-); 3.60–3.71 (m, 1H, 24-H); 3.72–3.91 (m, 2H, -CHHCH$_2$- and 24-H); 4.60–4.70 (m, 1H, -CHHCH$_2$-); 6.46–6.59 (m, 3H, PC-arom-H); 6.69 (br. s, 2H, PC-arom-H); 6.80–6.87 (m, 1H, 19-H or 22-H); 6.90–7.00 (m, 1H, 20-H or 21-H); 7.10–7.24 (m, 2H, 21-H or 20-H and PC-arom-H); 7.89–7.99 (m, 1H, 22-H or 19-H); 8.38 (s, 1H, CH=N); 9.12 (s, 1H, OH); MS (EI), *m/z* (rel): 413 (96, M^+), 412 (10), 396 (16, M^+-H_2O), 382 (28), 311 (57), 310 (57), 309 (15), 295 (18), 232 (29), 219 (33), 218 (100), 217 (87, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 216 (80), 196 (8, CH_2-C_6H_3(CH=NCH-(*i*Pr)CH_2OH)-CH_2), 195 (24), 186 (33), 182 (12), 181 (49), 178 (12), 174 (17), 165 (13), 152 (15), 144 (15), 143 (17), 132 (19), 131 (52), 130 (69), 129 (18), 128 (11), 119 (11), 115 (12). Anal. calcd for $C_{28}H_{31}NO_2$: C, 81.32; H, 7.56; N, 3.39. Found: C, 81.51; H, 7.47; N, 3.35.

Aldimine (S_p,S_c)-29 (0.054 g, 71%) was obtained from (S_p)-**7** (0.060 g, 0.183 mmol) and (*S*)-ValOH (0.028 g, 0.274 mmol) after reflux for 16 h and crystallisation from a 2:5 mixture of toluene/hexane. $[\alpha]_D^{20}$ −136.1 (*c* 0.46, benzene); m.p. 186.5–188 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 1.05 (d, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_3); 1.12 (d, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_3); 1.99–2.14 (m, 1H, 25-H); 2.15–2.28 (m, 1H, 23-H); 2.62–2.82 (m, 2H, -CHHCH$_2$- and -CH_2OH); 2.83–2.98 (m, 2H, 24-H and -CHHCH$_2$-); 3.06–3.16 (m, 1H, -CHHCH$_2$-); 3.17–3.29 (m, 2H, -CHHCH$_2$- and 24-H); 3.43–3.56 (m, 1H, -CHHCH$_2$-); 3.66–3.76 (m, 1H, -CHHCH$_2$-); 3.77–3.91 (m, 1H, -CHHCH$_2$-); 4.44–4.53 (m, 1H, -CHHCH$_2$-); 6.32 (s, 1H, 5-H or 13-H); 6.52–6.63 (m, 2H, PC-arom-H); 6.64–6.74 (m, 2H, PC-arom-H); 6.86 (d, $^3J_{H,H}$ = 8.0 Hz, 1H, 22-H); 6.90–6.98 (m, 1H, 20-H); 7.12 (s, 1H, 13-H or 5-H); 7.13–7.22 (m, 1H, 21-H); 7.76 (d, $^3J_{H,H}$ = 7.3 Hz, 1H, 19-H); 8.36 (s, 1H, CH=N); 9.14 (s, 1H, OH); MS (EI), *m/z* (rel): 413 (75, M^+), 411 (10), 396 (15, M^+-H_2O), 382 (23), 311 (50), 310 (65), 309 (20), 295 (18), 293 (13), 232 (34), 219 (27), 218 (78), 217 (100, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 216 (95), 215 (16), 214 (19), 213 (24), 196 (19, CH_2-C_6H_3(CH=NCH-(*i*Pr)CH_2OH)-CH_2), 195 (47), 186 (43), 182 (20), 181 (76), 178 (16), 174 (21), 165 (27), 152 (29), 149 (44), 144 (26), 143 (32), 132 (28), 131 (57), 130 (83), 129 (25), 128 (17), 121 (15), 119 (15), 115 (21). Anal. calcd for $C_{28}H_{31}NO_2$: C, 81.32; H, 7.56; N, 3.39. Found: C, 81.57; H, 7.62; N, 3.28.

Aldimine (R_p,S_c)-30 (0.072 g, 92%) was obtained from (R_p)-**6** (0.060 g, 0.183 mmol) and (*S*)-2-amino-3-methyl-1-penthanol ((*S*)-^{t}LeuOH) (0.032 g, 0.274 mmol) after reflux for 17 h and crystallisation from 1:3 mixture of toluene/hexane. $[\alpha]_D^{20}$ −51.4 (*c* 0.36, $CHCl_3$); m.p. 189.5–191.5 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 0.60 (d, $^3J_{H,H}$ = 6.0 Hz, 3H, 26-H); 0.74–0.82 (m, 3H, 28-H); 0.83–0.94 (m, 2H, 25-H and 27-H); 1.17–1.29 (m, 1H, 27-H); 2.50–2.58 (m, 1H, 23-H); 2.62–2.73 (m, 1H, -CHHCH$_2$-); 2.87–3.22 (m, 7H, -CH_2CH_2- and 24-H); 4.04–4.14 (m, 1H, -CHHCH$_2$-); 4.20–4.27 (m, 1H, -CHHCH$_2$-); 6.47 (dd, $^3J_{H,H}$ = 7.8 Hz, ^{4}J = 1.8 Hz, 1H, 16-H); 6.58–6.73 (m, 5H, PC-arom-H); 6.78–6.84 (m, 1H, 22-H); 6.88–6.95 (m, 1H, 20-H); 7.06–7.13 (m, 1H, 21-H); 7.35–7.43 (m, 1H, 19-H); 7.86 (s, 1H, CH=N); 9.15 (s, 1H, OH); MS (EI), *m/z* (rel): 427 (21, M^+), 426 (15), 397 (28), 396 (100), 370 (19), 368 (19), 354 (29), 328 (15), 327 (10), 326 (24), 312 (14), 311 (60), 233 (12), 231 (18, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 230 (36), 209 (12), 197 (14), 196 (14, CH_2-C_6H_3(CH=NCH(*s*Bu)CH_2OH)-CH_2), 195 (48), 194 (15), 182 (16), 181 (70), 178 (19), 174 (27), 165 (13), 152 (15), 144 (19), 143 (35), 132 (13), 131 (35), 130 (57), 117 (12), 115 (14). Anal. calcd for $C_{29}H_{33}NO_2$: C, 81.46; H, 7.78; N, 3.28. Found: C, 81.44; H, 7.88; N, 3.04.

Aldimine (S_p,S_c)-30 (0.053 g, 62%) obtained from (S_p)-**5** (0.066 g, 0.201 mmol) and (*S*)-^{t}LeuOH (0.035 g, 0.301 mmol) after reflux for 17 h and crystallisation from a 4:1 mixture of toluene and hexane. $[\alpha]_D^{20}$ +16.7 (*c* 0.58, benzene); m.p. 118.5–121 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 1.05 (d, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_3); 1.12 (d, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_3); 1.99–2.14 (m, 1H, 25-H); 2.15–2.28 (m, 1H, 23-H); 2.62–2.82 (m, 2H, -CHHCH$_2$- and -CH_2OH); 2.83–2.98 (m, 2H, 24-H and -CHHCH$_2$-); 3.06–3.16 (m, 1H, -CHHCH$_2$-); 3.17–3.29 (m, 2H, -CHHCH$_2$- and 24-H); 3.43–3.56 (m, 1H, -CHHCH$_2$-); 3.66–3.76 (m, 1H, -CHHCH$_2$-); 3.77–3.91 (m, 1H, -CHHCH$_2$-); 4.44–4.53 (m, 1H, -CHHCH$_2$-); 6.32 (s, 1H, 5-H or 13-H); 6.52–6.63 (m, 2H, PC-arom.-H); 6.64–6.74 (m, 2H, PC-arom-H); 6.86 (d, $^3J_{H,H}$ = 8.0 Hz, 1H, 22-H); 6.90–6.98 (m, 1H, 20-H); 7.12 (s, 1H, 13-H or 5-H); 7.13–7.22 (m, 1H, 21-H); 7.76 (d, $^3J_{H,H}$ = 7.3 Hz, 1H, 19-H); 8.36 (s, 1H, CH=N); 9.14 (s, 1H, OH); MS (EI), *m/z* (rel): 427 (24, M^+), 397 (32), 396 (100), 370 (26), 326 (28), 312 (22), 311 (83), 231 (14, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 230 (23), 196 (23, CH_2-C_6H_3(CH=NCH-(*s*Bu)CH_2OH)-CH_2), 195 (58), 194 (25), 181 (90), 174 (40), 167 (22), 149 (37), 144 (28), 143 (40), 131 (44), 130 (58). Anal. calcd for $C_{29}H_{33}NO_2$: C, 81.46; H, 7.78; N, 3.28. Found: C, 81.44; H, 8.04; N, 3.79.

Aldimine (S_p,S_c)-31 (0.049 g, 22%) was obtained from (S_p)-**7** (0.217 g, 0.661 mmol) and ethylenediamine (0.028 g, 0.031 mL, 0.462 mmol) after reflux for 34 h and repeated crystallization from toluene/ethyl acetate. $[\alpha]_D^{20}$ −72.2 (*c* 0.20, benzene); m.p. 222.5–225 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 2.17–2.35 (m, 2H, -CH_2CH_2-); 2.68–2.99 (m, 8H, -CH_2CH_2-);3.08–3.29 (m, 4H, -CH_2CH_2-); 3.72–3.89 (m, 2H, -CH_2CH_2-); 4.07–4.23 (m, 2H, =N-CH_2); 4.25–4.40 (m, 2H, =N-CH_2); 6.37 (s, 2 H, 5-H or 13-H); 6.51–6.62 (m, 4H, PC-arom-H); 6.65–6.75 (m, 4H, PC-arom-H); 6.81–6.93 (m, 4H, 20-H and 22-H); 7.08–7.18 (m, 2H, 21-H); 7.20 (s, 2 H, 13-H or 5-H); 7.71–7.81 (m, 2H, 19-H); 8.62 (s, 2H, CH=N); 9.15 (br. s, 2 H, OH); MS (EI), *m/z* (rel): 680 (34, M^+), 679 (12), 663 (15, M^+-OH), 483 (25, M^+-CH_2-$C_6H_3(C_6H_5OH)$-CH_2), 370 (14), 356 (11), 355 (23), 354 (22), 353 (14), 340 (17), 339 (10), 338 (18), 328 (16), 327 (16), 326 (35), 325 (13), 324 (17), 312 (19), 311 (76), 310 (90), 309 (41), 297 (12), 296 (11), 295 (36), 293 (17), 289 (10), 209 (15), 197 (15), 196 (19), 195 (56), 194 (20), 185 (19), 182 (20), 181 (100), 178 (19), 175 (20), 174 (20), 173 (22), 167 (16), 165 (25), 160 (31), 159 (25), 158 (91), 157 (18), 152 (24), 145 (18), 144 (80), 143 (42), 132 (19), 131 (40), 130 (79), 129 (22), 128 (22), 117 (22), 115 (22). Anal. calcd for $C_{48}H_{44}N_2O_2$: C, 84.67; H, 6.51; N, 4.11. Found: C, 84.72; H, 6.66; N, 4.58.

Enantioselective diethylzinc addition to aldehydes catalyzed by phenoxy-imines 16, 25–30

Typical experimental procedure: To a solution of aldimine **16, 25–30** (0.007 mmol) in toluene (0.28 mL), Et_2Zn (0.142 mmol, 0.140 mL of 1 N solution in hexane) and aldehyde (benzaldehyde

or cyclohexanecarbaldehyde, 0.071 mmol) were successively added by syringe at 0 °C. The resulting yellow solution was warmed to room temperature and allowed to stir for an additional 15 h period. The excess of Et_2Zn was hydrolyzed with 1 N HCl (0.25 mL); the reaction mixture was then diluted with Et_2O (4 mL), and H_2O (3 mL). The organic layer was separated and the aqueous fraction was additionally extracted with Et_2O (5× 4 mL). The combined organic fractions were washed with brine (2 mL) and dried with Na_2SO_4. After solvent removal the oily residue without further purification was subjected to GC and Chiral GC for conversion and enantiomeric excess analysis. The conversion was determined by GC analysis (Hewlett–Packard HP 5890 Series II gas chromatograph) on an HP-1 (12 m× 0.25 mm) with N_2 (15 psi) as carrier gas, split ratio 75:1. Inject temperature 200 °C, detector FID 250 °C, temperature program: 40 °C (1 min), heat rate 30 °C min^{-1}, end temperature 250 °C (10 min). Enantiomeric analysis of secondary alcohols was performed by GC analysis (Sigma 2000 (PerkinElmer) on a Gamma cyclodextrin Trifluoracetyl (G-TA) column (30 m × 0.25 mm) (1-phenylpropanol) and on the Beta cyclodextrin Dimethyl B-DM column (30 m × 0.25 mm) (1-cyclohexylpropanol) with He (15 psi) as carrier gas, split ratio 75:1. Temperature data for 1-phenylpropanol: inject temperature 220 °C, detector FID 220 °C, column temperature 120 °C; the retention times (min) were 11.60 (*S*) and 12.20 (*R*). Temperature data for 1-cyclohexylpropanol: inject temperature 200 °C, detector FID 220 °C, temperature program: 40 °C (1 min), heat rate 20 °C min^{-1}, end temperature 190 °C (5 min); the retention times (min) were 18.70 (*S*) and 19.40 (*R*).

X-ray crystallography: Single crystals were grown by slow evaporation from MeOH solution. Diffraction data were collected on a Syntex $P2_1$ diffractometer [$\lambda(MoK_\alpha) = 0.71072$ Å, $\theta/2\theta$-scans] at 298 K for (R_p,R_c)-**16** and on a Bruker SMART 1000 CCD diffractometer [$\lambda(MoK_\alpha) = 0.71072$ Å, ω-scans] at 120 K for (R_p,S_c)-**25**. The structures were solved by direct methods and refined by the full-matrix least-squares technique against F^2 in the anisotropic-isotropic approximation. The hydrogen atoms of the hydroxy group in both structures were located in the Fourier density synthesis while all other hydrogen atoms were calculated from the geometrical point of view and refined with the riding model. All calculations were performed with the SHELXTL software package.[31] Crystal data and structure refinement parameters are listed in Table 2.

Table 2. Crystal and structure refinement data for (R_p,R_c)-**16** and (R_p,S_c)-**25**.

	(R_p,R_c)-**16**	(R_p,S_c)-**25**
Formula	$C_{31}H_{29}NO$	$C_{31}H_{29}NO$, CH_4O
M_r	431.55	463.59
$F(000)$	460	496
T, K	120	298
Crystal system, Space group	Monoclinic, $P2_1$	Monoclinic, $P2_1/c$
$Z(Z')$	2(1)	2(1)
a, Å	7.716(2)	7.542(2)
b, Å	10.122(3)	17.129(6)
c, Å	14.517(4)	9.952(3)
β, °	90.283(7)	102.68(2)
V, Å^3	1133.9(6)	1254.3(6)
ρ, g cm^{-3}	1.264	1.163, 3.33
μ, cm^{-1}	0.75	0.75
$2\Theta_{max}$, °	60	52
Reflections measured	9839	2772
Independent reflections	5073	2523
Observed reflections [$I > 2\sigma(I)$]	1872	1717
R_1	0.0643	0.0560
wR_2	0.1726	0.1285
GOF	0.755	0.995
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.267, −0.191	0.271, −0.224

Crystallographic data for (R_p,R_c)-**16** and (R_p,S_c)-**25** have been deposited with the Cambridge Crystallographic Data Centre (CCDC), deposition numbers 601914 and 601915, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-335-033; e-mail: deposit @ccdc.cam.ac.uk.

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