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Iminophenol Ligands Derived from Chiral Regioisomeric Hydroxy[2.2]paracyclophane-carbaldehydes: the Influence of the Substitution Pattern on Asymmetric Induction

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Dedicated to Professor Roald Hoffmann on the occasion of his 70th birthday

Keywords: Cyclophanes / Planar chirality / Optical resolution / Absolute configuration / N,O ligands / Asymmetric catalysis

The planar-chiral 12-hydroxy[2.2]paracyclophane-4-carbaldehyde (**3**, *pseudo*-FHPC) was synthesized and resolved via its Schiff bases **9** using the enantiomers of α-phenylethylamine. The absolute configurations of the enantiomers of **3** were determined by X-ray diffraction. Derivatives **7**–**21**, representatives of cyclophane-derived iminophenols with *ortho*, *pseudo-gem* and *pseudo-ortho* arrangement of the functional groups, were prepared and studied as catalysts for the enantioselective addition of diethylzinc to benzaldehyde affording the expected alcohols in up to 97 % *ee*.

Introduction

Among the most widely applied building blocks for chiral ligands, achiral salicylaldehyde derivatives occupy a prominent place. The two functional groups located in *ortho* position with respect to each other provide for effective chelation in intermediately generated reactive complexes leading to high asymmetric differentiation along the reaction route. For many years salicylaldehyde ligands were based on achiral salicylaldehydes combined with chiral amines, alcohols and amino alcohols.[1,2] Occasionally chirality has been introduced by substitution of the aromatic moiety of the salicylaldehyde with central chiral groups as in **A** (Figure 1).[3] The next step was the creation of salicylaldehyde analogs possessing axial (**B**, Figure 1)[4] and planar chirality as in the ferrocene derived ligand **C** (Figure 1).[5]

Starting in 1994, we have developed the use of [2.2]paracyclophane derivatives as chiral promoters, and have focussed our attention particularly on the planar chiral analog of salicylaldehyde, viz. 5-hydroxy[2.2]paracyclophane-4-carbaldehyde (**1**) (FHPC = "5-formyl-4-hydroxy[2.2]paracyclophane", Figure 1).[6,7] We have suggested several efficient regioselective syntheses of this compound and have described its resolution.[8,9] A number of FHPC derivatives (such as Schiff bases, salenes and others) have found their application as effective ligands in various stereoselective processes. Meanwhile, the unique structure of [2.2]paracyclophane allows one to design structural isomers of FHPC (possessing planar chirality as well) by modification of mutual arrangement of carbonyl and hydroxy groups (Figure 1, **2** and **3**).

In continuation of our "FHPC-project", we have recently synthesized the regioisomeric formyl-hydroxy[2.2]paracyclophane with *pseudo*-geminal arrangement of the two functional groups, namely *iso*-FHPC (**2**, Figure 1).[10] In this paper we describe an efficient synthesis of a third regioisomer (12-hydroxy[2.2]paracyclophane-4-carbaldehyde **3**, *pseudo*-FHPC, Figure 1) bearing the respective functional groups in *pseudo-ortho* position, and an efficient resolution of **3** into its enantiomers. Using the three regioisomeric FHPCs (**1**–**3**) as carbonyl components, a series of bi- and tridentate iminophenol ligands was obtained with the aim to determine the influence of the substitution pattern on asymmetric induction. The efficiency of these ligands was tested in the enantioselective addition of diethylzinc to benzaldehyde.

Results and Discussion

Synthesis of Regioisomeric Formyl-hydroxy[2.2]-paracyclophanes

For the preparation and resolution into enantiomers of the chiral regioisomeric hydroxy[2.2]paracyclophane-4-carb-

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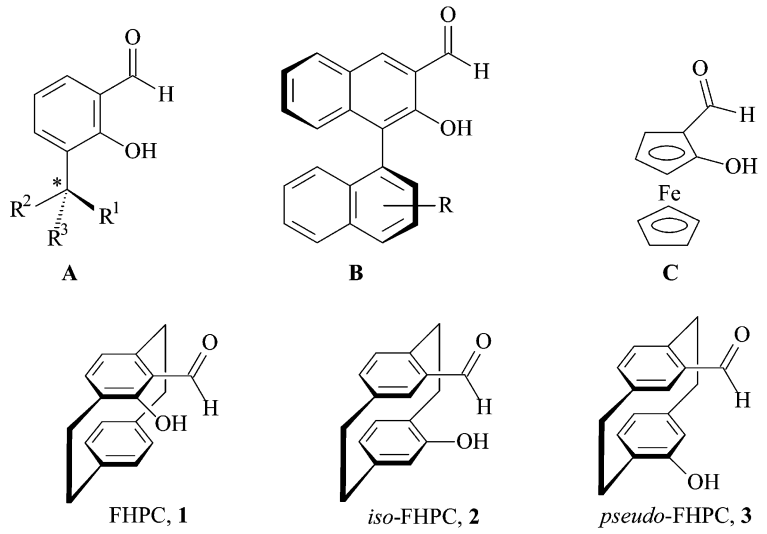


Figure 1. Chiral salicylaldehydes and their analogs.

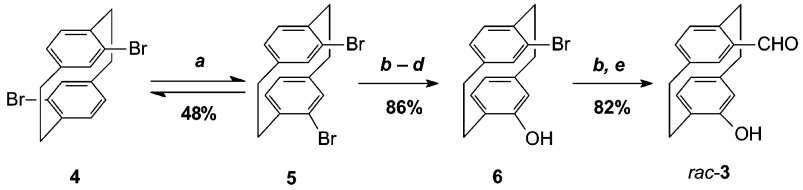
aldehydes **1** and **2** the specific synthetic techniques elaborated by us previously were applied. *rac*-**1** (FHPC) was obtained from [2.2]paracyclophane in three steps with *ortho*-regioselective oxaloylation of 4-hydroxy[2.2]paracyclophane as the key reaction.[9] The procedure for the synthesis of *rac*-**2** (*iso*-FHPC)[10] was based on the *pseudo-gem*-regioselective $TiCl_4$-catalyzed formylation of methyl[2.2]paracyclophane-4-carboxylate with α,α-dichloromethyl methyl ether.[11] Both hydroxy-substituted [2.2]paracyclophane-derived aldehydes **1** and **2** were resolved into enantiomers via their Schiff bases using the enantiomers of α-phenylethylamine (PEAM).[8,10]

For the synthesis of *rac*-**3** we started from *pseudo-ortho*-dibromo[2.2]paracyclophane (**4**), the common precursor for *pseudo-ortho*-disubstituted [2.2]paracyclophanes.[12] For the synthesis of this compound a number of synthetic approaches have been described.[13a–13c] Here we use the technique based upon isomerisation of *pseudo-para*-dibromo-[2.2]paracyclophane **4** in benzene at 200 °C in an autoclave, as described earlier by us.[14] At equilibrium in triglyme, this reaction results in a 1:1-mixture of regioiomers **4** and **5**, from which the desired **5** can be isolated quantitatively by fractional crystallization. This procedure may be repeated several times with recovered **4** (Scheme 1), thus isomerizing most of it into **5**.

The stepwise synthesis of *pseudo*-FHPC **3** from dibromide **4** is outlined in Scheme 1. The first step was the exchange of one bromine for an OH-group. For this purpose *rac*-dibromide **5** was monolithiated at low temperature (–78 °C).[15] After Li→B exchange by treatment with $B(OMe)_3$, followed by oxidation of the intermediate boronic ester with H_2O_2/NaOH, 4-bromo-12-hydroxy[2.2]-paracyclophane (**6**) was obtained in high yield.[16,17] For the introduction of the formyl group the bromophenol **6** was lithiated with excess *n*BuLi and the resulting carbanion then quenched with DMF as the electrophile. The reaction yield of this step strongly depends on the amounts of *n*BuLi and DMF employed. Thus, the usage of more than 3 equiv. of *n*BuLi and DMF, allowed us to prepare the target derivative in high chemical yield (82%). If the amounts of *n*BuLi and DMF were lower, a 65% yield of **3** was observed only. Analytically pure *pseudo*-FHPC **3** was isolated after passing the reaction mixture through a short column filled with SiO_2.

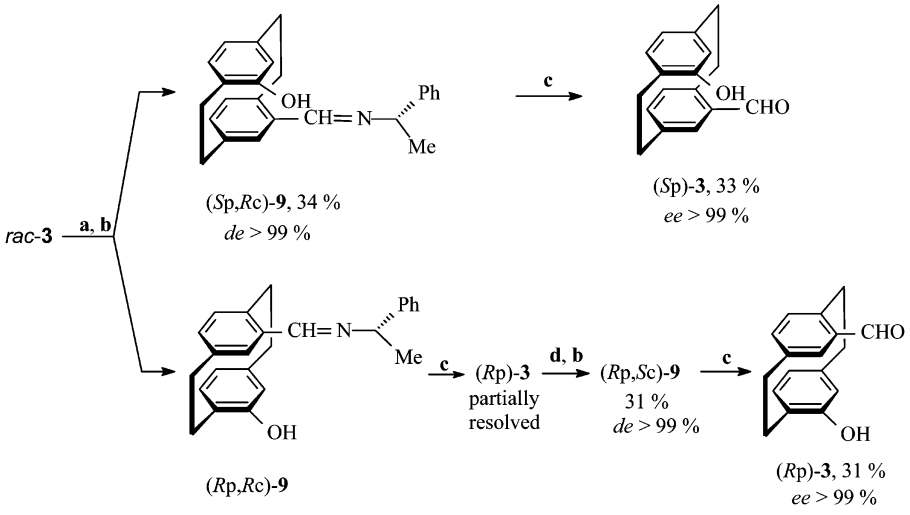
Subsequently, derivative **3** was resolved into its enantiomers using an approach successfully employed earlier for the resolution of FHPC[8] and *iso*-FHPC,[10] namely, via its diastereomeric Schiff bases (12-{[(1-phenylethyl)imino]-methyl}-(2.2)paracyclophan-4-ols, **9**) using the α-phenylethylamine enantiomers (PEAM; Scheme 2).

The reaction of racemic **3** with (*R*)-PEAM resulted in a mixture of (*R*p,*R*c)- and (*S*p,*R*c)-**9** in quantitative yield. Two successive crystallizations of the reaction mixture from methanol provided the individual diastereomer (^{1}H NMR-control) in 34% chemical yield with respect to the starting



a. benzene, 200 °C, 24h; **b.** BuLi/THF/-78 °C; **c.** $B(OCH_3)_3$; **d.** H_2O_2/NaOH; **e.** DMF

Scheme 1. Synthesis of *pseudo*-FHPC **3**.



Scheme 2. Resolution of *pseudo*-FHPC **3** into enantiomers.

racemic **3**. The X-ray structural analysis of this diastereomer revealed its (*S*p,*R*c)-configuration (Figure 2). Partially resolved **3** was recovered from the imine **9** by hydrolysis of the residual filtrates with aqueous HCl solution. It was treated with (*S*)-PEAM, and diastereomerically pure material (*R*p,*S*c)-**9** was isolated in 31% chemical yield after double recrystallization from methanol.

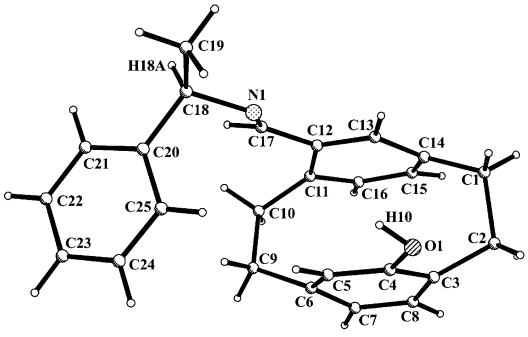


Figure 2. Molecular structure of (*S*p,*R*c)-**9**.

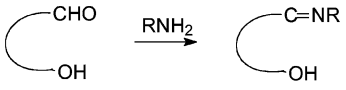
Individual enantiomers (*S*p)- and (*R*p)-**3** were released from the corresponding (*S*p,*R*c)- and (*R*p,*S*c)-**9** in practically quantitative yield by hydrolysis with 2 N HCl in methanol.

Preparation and Application in Asymmetric Synthesis of the Regioisomeric Iminophenol Ligands from FHPC, *iso*-FHPC and *pseudo*-FHPC

Enantiomerically pure formyl-hydroxy[2.2]paracyclophanes (FHPC) of type **1**, *iso*-FHPC **2** and *pseudo*-FHPC **3** were used as carbonyl components in the synthesis of the different iminophenol ligands (Figure 3). Their combination with amines and amino alcohols as amino components produced two series of bidentate and tridentate ligands, respectively. Bidentate (*R*p,*R*c)-**7**,[8] (*R*p,*S*c)-**8**[10] and (*S*p,*R*c)-**9** were isolated during resolution. Their diastereomers (*R*p,*S*c)-**7**, (*S*p,*S*c)-**8**, (*S*p,*S*c)-**9** as well as (*S*p)-**10**, (*S*p)-**11**, and (*R*p)-**12** were deliberately synthesized from the enantiomerically pure carbonyl components and amines, namely chiral PEAM and achiral, sterically hindered 2,6-dimethylaniline (DMA), respectively (Scheme 2). The second series of ligands (tridentate **13**–**21**) was obtained from (*R*p)- or (*S*p)-**1**–**3** and amino alcohols [achiral 2-ethanolamine (EA), chiral (*S*)-valinol (ValOH) and (*S*)-1-benzyl-2-hydroxy-2,2-diphenylethylimine (Ph_3AlaOH), especially prepared as a sterically hindered ValOH analog]. All FHPC derivatives were purified by simply passing the reaction mixture through a pad of silica, whereas the iminophenols derived from *iso*-FHPC and *pseudo*-FHPC were unstable on SiO_2, and were hence purified by crystallization.

The performance of the iminophenols ligands **7**–**21** was next evaluated by the reaction of diethylzinc with benzaldehyde, a useful model reaction, since it has been shown that this substrate is recognized in a different manner by various ligands.[18] In a standard experiment, the chiral zinc catalyst was prepared first from 2.2 equivalents of diethylzinc stirred with 0.1 equivalent of the chiral iminophenol in toluene at room temperature. Then one equivalent of the aldehyde was added to the catalyst solution in toluene at 0 °C, and the mixture was stirred at room temperature for 15 h. Excess Et_2Zn was destroyed by addition of 1 N HCl and after standard work-up (see Exp. Sect.), the enantiomeric excess of the resulting 1-phenylpropanol was determined by chiral GC or HPLC chromatography. The results obtained are summarized in Figures 4 and 5.

All reactions proceeded smoothly to give the respective alcohol products with high conversion ratios (>95%). We have determined the efficiency of the bidentate and tridentate ligands separately.



1, **2** or **3** **7–21**

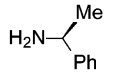
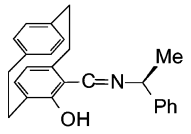
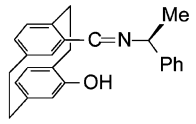
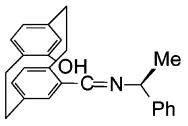
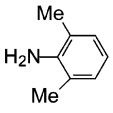
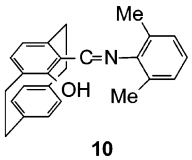
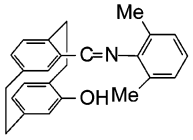
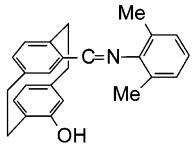
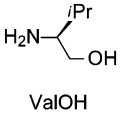
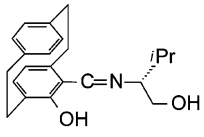
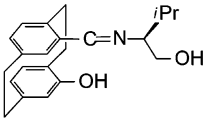
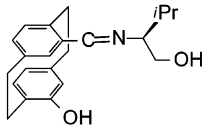
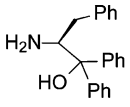
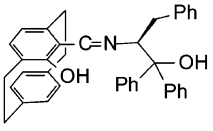
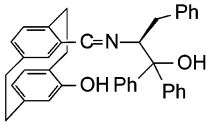
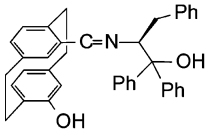
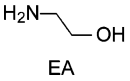
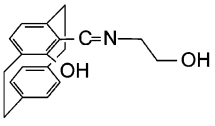
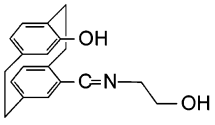
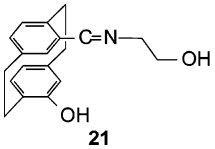
RNH_2	*ortho*	*pseudo-gem*	*pseudo-ortho*
 PEAM	 **7** (*R*p)-FHPC·(*S*)-PEAM (*R*p)-FHPC·(*R*)-PEAM	 **8** (*S*p)-*iso*-FHPC·(*S*)-PEAM (*R*p)-*iso*-FHPC·(*S*)-PEAM	 **9** (*S*p)-*pseudo*-FHPC·(*S*)-PEAM (*R*p)-*pseudo*-FHPC·(*S*)-PEAM
 DMA	 **10** (*S*p)-FHPC·DMA	 **11** (*S*p)-*iso*-FHPC·DMA	 **12** (*R*p)-*pseudo*-FHPC·DMA
 ValOH	 **13** (*R*p)-FHPC·(*R*)-ValOH (*S*p)-FHPC·(*S*)-ValOH	 **14** (*S*p)-*iso*-FHPC·(*S*)-ValOH (*R*p)-*iso*-FHPC·(*S*)-ValOH	 **15** (*R*p)-*pseudo*-FHPC·(*S*)-ValOH (Sp)-*pseudo*-FHPC·(*S*)-ValOH
 Ph_3AlaOH	 **16** (*S*p)-FHPC·(*S*)-Ph_3AlaOH (*R*p)-FHPC·(*S*)-Ph_3AlaOH	 **17** (*S*p)-*iso*-FHPC·(*S*)-Ph_3AlaOH (*R*p)-*iso*-FHPC·(*S*)-Ph_3AlaOH	 **18** (*R*p)-*pseudo*-FHPC·(*S*)-Ph_3AlaOH (*S*p)-*pseudo*-FHPC·(*S*)-Ph_3AlaOH
 EA	 **19** (*S*p)-FHPC·EA	 **20** (*R*p)-*iso*-FHPC·EA	 **21** (*R*p)-*pseudo*-FHPC·EA

Figure 3. The preparation of the iminophenol ligands.

In the case of bidentate ligands **7**–**12** (PEAM and DMA used as amine moieties) all iminophenols with *iso*-FHPC demonstrated better results, 94–97% *ee* (Figure 4). The iminophenol (*S*p)-**11** *iso*-FHPC with achiral, sterically hindered DMA also reveals high enantioselectivity (94% *ee*). Regardless of its configuration, the second chiral center present in the iminophenol structure influences the enantioselectivity of the process and the configuration of the 1-phenylpropanol formed only slightly, if at all. Thus the diastereomeric iminophenols with chiral PEAM (*R*p,*R*)- and

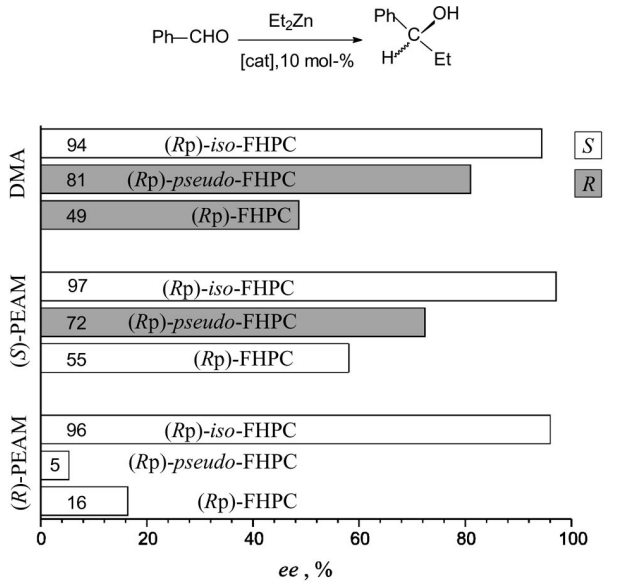


Figure 4. Enantioselective addition of diethylzinc to benzaldehyde catalysed by bidentate iminophenol ligands.

(*R*p,*S*)-**8** lead to almost equivalent results, 97 and 96% *ee* (*R*), respectively. In all cases of the series *R*p-configuration of the *iso*-FHPC moiety leads to (*S*)-configuration of the resulting 1-phenylpropanol.

In the *pseudo*-FHPC series the best result, 81% *ee*, was observed for (*R*p)-**12** when sterically hindered DMA was used as the amine moiety. The introduction of an additional PEAM chiral centre in the (*R*p,*R*)- and (*R*p,*S*)-**9** amine moiety reduces the enantioselectivity. The (*R*p,*S*)-diastereomer demonstrates the cooperative effect of two chiral elements and furnishes 1-phenylpropanol with 72% *ee*. In contrast to the *iso*-FHPC series, (*R*p)-configuration of the *pseudo*-FHPC moiety causes production of (*R*)-1-phenylpropanol.

A mismatched effect of two chiral elements was observed in the reaction with the diastereomer (*R*p,*R*)-**9** where enantioselectivity falls dramatically to 5% *ee* only, while the respective alcohol has inverted absolute configuration, e.g. (*S*).

In the FHPC series the iminophenol with DMA (*R*p)-**10** displays 49% *ee* (*R*). The introduction of a chiral PEAM moiety in the case of iminophenols **7** leads to inversion of absolute configuration of the resulting 1-phenylpropanol also. The best result in the series was observed for (*R*p,*S*)-diastereomer (55% *ee*). The diastereomer (*R*p,*R*)-**7** demonstrates the mismatched effect of two chiral elements, which is accompanied by a significant decrease in enantioselectivity all the way down to 16% *ee*.

In our previous paper[19] we have shown for the first time that chiral tridentate iminophenol ligands bearing an additional carbinol moiety could be used as effective ligands in enantioselective Et_2Zn addition to aldehydes. However, aldimine ligands based on FHPC with achiral EA (*R*p-**19**) and chiral valinol [(*R*p,*R*)- and (*R*p,*S*)-**13**] or leucinol demonstrated very poor results[19] (displayed in part for comparison in Figure 5).

In this paper we constructed diastereomeric iminophenols (*R*p,*R*)- and (*R*p,*S*)-**16** from FHPC and sterically hindered (*S*)-triphenylalanol, which was synthesized in two steps from the corresponding enantiomers of phenylalanine. However, the results are still very poor (Figure 5).

In the series of iminophenols with achiral EA *iso*-FHPC (*R*p)-**20** demonstrates a more satisfactory result than *pseudo*-FHPC (*R*p)-**21**: 61% (*R*) and 20% *ee* (*R*), respectively.

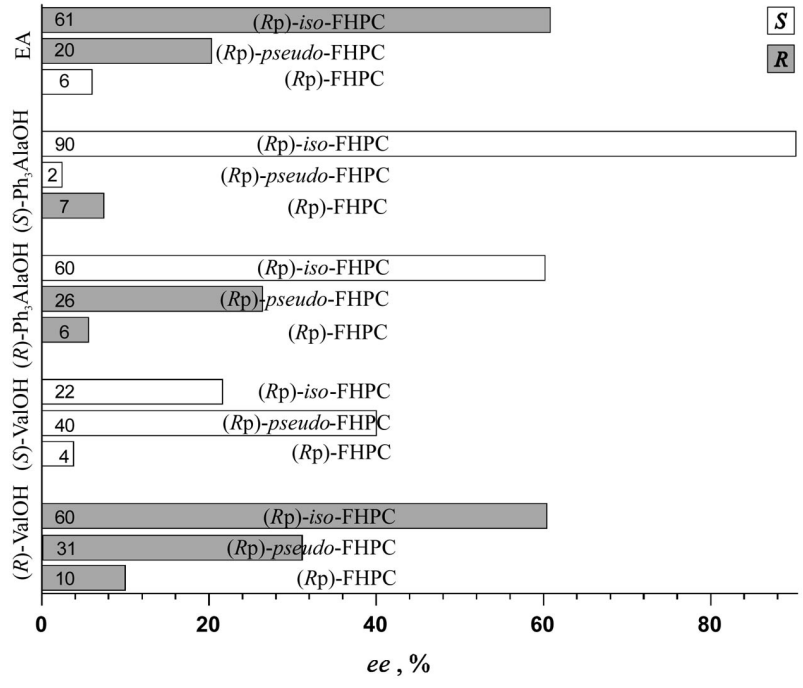


Figure 5. Enantioselective addition of diethylzinc to benzaldehyde catalysed by tridentate iminophenol ligands.

The introduction of an additional chiral center in the alkylcarbinol unit of iminophenols **14**, **15**, **17**, **18**, respectively, produced diastereomeric pairs with strong matched/mismatched effects. Thus the matched (*R*p,*R*)-**14** with *iso*-FHPC and valinole displays a medium level of 60% *ee* (*R*). For the mismatched (*R*p,*S*)-**14** the result was only 22% *ee* with simultaneous configuration inversion of the alcohol produced.

For the analogous *pseudo*-FHPC iminophenol **15**, a better result [40% *ee* (*S*)] was observed for (*R*p,*S*)-**15**. The mismatched (*R*p,*R*)-**15** diastereomer gave only 31% *ee* (*R*).

The Et_2Zn addition enantioselectivity increases when a sterically demanding fragment, triphenylalanol rather than valinol, is introduced into *iso*-FHPC. Thus for the matched diastereomer (*R*p,*S*)-**17** the best result of the whole series [90% *ee* (*S*)] was reached. Diastereomer (*R*p,*R*)-**17** demonstrates the mismatched effect of two chiral elements, which is accompanied by a significant reduction of enantioselectivity down to 60% *ee* (*S*).

The analogous *pseudo*-FHPC iminophenols **18** were even less effective than the valinol derivatives. Thus for the matched (*R*p,*R*)-**18** the observed enantioselectivity was only 26% *ee* (*R*) and practically no enantioselectivity was observed for the mismatched (*R*p,*S*)-**18** diastereomer.

Thus, in the bidentate iminophenol series we demonstrated that chiral analogs of salicyl aldehydes with functional groups located in different [2.2]paracyclophane rings (*iso*-FHPC and *pseudo*-FHPC) provide higher enantioselectivity compared with the nearest chiral analog, FHPC. The usage of *iso*-FHPC and *pseudo*-FHPC modules allows one to prepare highly efficient iminophenols even without recourse to a chiral amine moiety.

In the tridentate iminophenol series, FHPC derivatives (if compared with its non-classic analogs, Figure 4) again revealed a very low level of enantioselectivity. The ligands based on *iso*-FHPC demonstrated the highest results and were as effective as are those based on hydroxyketones of [2.2]paracyclophane series.[19]

In summary, a series of novel chiral Schiff base type N,O-ligands based on FHPC (**1**), *iso*-FHPC (**2**) and *pseudo*-FHPC (**3**) combined with different amines and amino alcohols has been synthesized. As compared to FHPC, iminophenols based on salicylic aldehydes with non-classic arrangement of the functional groups (*iso*-FHPC and *pseudo*-FHPC) produced good to excellent enantioselectivity in the diethylzinc addition to aldehydes. It should be noted that recently,[20] enantiomerically pure methoxy-derivatives of *iso*-FHPC and *pseudo*-FHPC have shown an exellent diastereoselectivity in the pinacol-coupling reaction producing the single symmetrical chiral diol in each case. Further development of chiral [2.2]paracyclophane derived ligands of the *pseudo-gem* and *pseudo-ortho*-substitution patterns is in progress in our laboratories.

Experimental Section

General: Benzene and toluene were distilled from Na. Et_2O and THF were distilled from sodium ketyl benzophenone under argon before use. NMR: Bruker AMX-400 (400.13 and 100.61 MHz, for ^1H and ^{13}C, respectively). For ^1H NMR spectroscopy the residual proton signals of the deuterated solvents were used as internal standards. MS: KRATOS MS890A (70 eV). Optical rotations: EPO-1 in thermostatted cell at 25 °C. TLC-analyses were performed on silica gel precoated plates "SORBFIL" PTLC-A-UV. Column chromatography was performed on Kieselgel 60 (Merck). 4-Hydroxy[2.2]paracyclophane-5-carbaldehyde (FHPC, **1**) and 4-hydroxy[2.2]paracyclophane-13-carbaldehyde (*iso*-FHPC, **2**) were prepared[9,10] and resolved into enantiomers according to the literature procedure.[8,10] 4-Bromo-12-hydroxy[2.2]paracyclophane (**5**) was prepared as described in ref.[16] Schiff bases **7** and **8** were synthesized according to published procedures.[8,10]

12-Hydroxy[2.2]paracyclophane-4-carbaldehyde (3): *n*BuLi (13.3 mL, 3.27 N in hexane, 0.0436 mol) was added dropwise to a solution of **6** (5 g, 0.0165 mol) in THF (200 mL) at –78 °C and the resulting mixture stirred for 5 h at this temperature. The reaction mixture was treated with DMF (3.37 mL, 0.0436 mol), warmed to room temp. and stirred overnight at this temperature. The mixture was diluted with water, the organic phase was separated, and the aqueous phase was extracted with Et_2O (3 × 100 mL). The combined organic phases were dried with Na_2SO_4. The solvent was evaporated under reduced pressure and the residue separated by silica gel column chromatography (CH_2Cl_2/Et_2O = 10:1) to afford 3.42 g (82%) of **3**. ^1H NMR ($CDCl_3$): δ = 2.60–2.74 (m, 1 H, CH_2-C*H*), 2.82–3.04 (m, 2 H, CH_2-CH_2), 3.09–3.37 (m, 3 H, CH_2-C*H*), 3.42–3.56 (m, 1 H, CH_2-C*H*), 3.94–4.10 (m, 1 H, CH_2-C*H*), 5.53 (d, ^4J = 1.8 Hz, 1 H, 5-H or 13-H), 6.20 (br. s, 1 H, O*H*), 6.32 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 7-H or 16-H), 6.45 (d, ^3J = 7.8 Hz, 1 H, 8-H or 15-H), 6.70 (s, 2 H, 16-H or 7-H and 15-H or 8-H), 7.65 (d, ^4J = 1.8 Hz, 1 H, 13-H or 5-H), 10.01 ppm (s, 1 H, C*H*O). ^{13}C NMR ($CDCl_3$): δ = 31.34, 32.98, 33.16, 34.69, 121.55, 124.16, 125.73, 131.03, 135.46, 135.75, 136.16, 139.21, 141.27, 141.70, 142.91, 154.31, 192.92 ppm (C=O). M.p. 215–216.5 °C. $C_{17}H_{16}O_2$ (252.31): calcd. C 80.93, H 6.39; found C 80.89, H 6.42.

Resolution of 12-Hydroxy[2.2]paracyclophane-4-carbaldehyde (3): A solution of of racemic **3** (3.42 g, 13.6 mmol) and (*R*)-α-PEAM (2.09 g, 2.2 mL, 17.3 mmol) in benzene (110 mL) was refluxed in a flask equipped with a Dean–Stark trap filled with molecular sieves (4 Å) for 13 h. The solvent was removed and the resulting mixture of diastereomeric (*S*p,*R*c)- and (*R*p,*R*c)-**9** was twice recrystallized from methanol to give 1.65 g (34%) of (*S*p*R*c)-12-{[(1-phenylethyl)-imino]methyl}[2.2]paracyclophan-4-ol (*S*p,*R*c)-**9**. M.p. 127.5–128.5 °C. $[\alpha]_D^{25}$ = +60.4 (*c* = 0.394, toluene). ^1H NMR ([D$_6$]acetone): δ = 1.70 (d, *J* = 6.5 Hz, 3 H, CH_3), 2.56–2.70 (m, 1 H, CH_2-C*H*), 2.78–3.22 (m, 5 H, CH_2-CH_2), 3.38–3.51 (m, 1 H, CH_2-C*H*), 4.19–4.33 (m, 1 H, CH_2-C*H*), 4.59 (q, *J* = 6.5 Hz, 1 H, C*H*), 5.75 (d, ^4J = 1.8 Hz, 1 H), 6.27 (dd, ^3J = 7.8, ^4J = 1.8 Hz), 6.44 (d, ^3J = 7.8 Hz, 1 H), 6.58 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.66 (d, *J* = 7.8 Hz, 1 H), 7.23–7.32 (t, ^3J = 7.5 Hz, 1 H, *p*-H, Ph), 7.34 (d, ^4J = 1.8 Hz, 1 H), 7.36–7.46 (t, ^3J = 7.5 Hz, 2 H, *m*-H, Ph), 7.51–7.62 (d, ^3J = 7.5 Hz, 2 H, *o*-H, Ph), 7.96 (br. s, 1 H, O*H*), 8.42 (s, 1 H, C*H*=N) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 24.91 (CH_3), 31.08, 32.84, 33.56, 34.34, 70.48 (N-CH), 120.62, 123.62, 125.24, 125.31, 126.59 (2 C), 128.32 (2 C), 131.19, 134.56, 135.38, 135.52, 136.07, 139.48, 140.26, 142.11, 145.93, 155.34 (C-4), 160.83 (C=N) ppm. $C_{25}H_{25}NO$ (355.48): calcd. C 84.47, H 7.09, N 3.94; found C 84.32, H 7.09, N 4.00. Compound (*S*p,*R*c)-**8** was hydrolyzed by refluxing it with aq. HCl solution in methanol. The organic material was extracted with CH_2Cl_2 (2 × 30 mL), the combined extracts were dried with Na_2SO_4, and after removal of the solvent 1.13 g (33%) of (*S*)-**3** as pale yellow crystals was isolated;

m.p. 208–209 °C. $[\alpha]_D^{25}$ = – 52.24 (*c* = 0.312, toluene). $C_{17}H_{16}O_2$ (252.31): calcd. C 80.93, H 6.39; found C 80.89, H 6.25. The combined methanol filtrates, containing partially enriched (*R*p,*R*c)-**9**, after evaporation and hydrolysis gave partially resolved (*R*)-**3** (2.12 g, 62%). This compound and 0.44 g (0.46 mL, 3.64 mmol) of (*S*)-α-PEAM afforded 0.92 g (31%) of (*R*p,*S*c)-**9**. Hydrolysis of (*R*p,*S*c)-**9** gave 0.66 g (31%) of (*R*)-**3** after crystallization from methanol.

(*S*p,*S*c)-12-{[(1-Phenylethyl)imino]methyl}[2.2]paracyclophan-4-ol [(*S*p,*S*c)-9]: Was obtained by the reaction of (*S*)-**3** (0.322 g 1.28 mmol) and (*S*)-α-PEAM (0.19 g, 0.2 mL, 1.57 mmol) in benzene (15 mL, reflux, 10 h) in 96% chemical yield (0.435 g). An analytically pure sample (0.140 g, 32%) was obtained by double recrystallization from heptane and methanol. ^{1}H NMR ([D$_6$]acetone): δ = 1.63 (d, *J* = 6.5 Hz, 3 H, C*H*$_3$), 2.53–3.26 (m, 6 H, C*H*$_2$-C*H*$_2$), 3.37–3.53 (m, 1 H, CH$_2$-CH*H*), 4.07–4.23 (m, 1 H, CH$_2$-CH*H*), 4.55–4.66 (q, *J* = 6.5 Hz, 1 H, C*H*), 5.70 (d, ^4J = 1.8 Hz, 1 H), 6.25 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.44 (d, ^3J = 7.8 Hz, 1 H), 6.58 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.66 (d, ^3J = 7.8 Hz, 1 H), 7.00 (t, ^3J = 7.5 Hz, 1 H, *p*-H, Ph), 7.37–7.48 (m, 3 H), 7.55–7.63 (d, ^3J = 7.5 Hz, 2 H, *o*-H, Ph), 7.96 (br. s, 1 H, OH), 8.48 (s, 1 H, CH=N) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 24.99 (CH$_3$), 31.12, 32.89, 33.85 (2 C), 70.57 (N-CH), 120.55, 123.60, 125.42, 126.59 (2 C), 126.63, 128.31 (2 C), 130.34, 134.56, 135.22 (2 C), 136.21, 139.53, 140.28, 141.89, 145.95, 155.33 (C-4), 160.30 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 356 (21) [M$^+$], 355 (65) [M$^+$], 236 (28), 235 (16) 234 (26), 143 (14), 132 (59), 131 (71), 130 (80), 129 (24), 121 (11), 120 (46), 106 (21), 105 (100), 104 (18), 103 (27). M.p. 110–111.5 °C. $[\alpha]_D^{25}$ = +221.5 (*c* = 0.288, toluene). $C_{25}H_{25}NO$ (355.48): calcd. C 84.47, H 7.09, N 3.94; found C 84.39, H 7.02, N 3.83.

(*S*p)-5-[(2,6-Dimethylphenylimino)methyl][2.2]paracyclophan-4-ol [(*S*p)-10]: Was obtained by the reaction of (*S*)-**1** (0.152 g 0.603 mmol) and DMA (0.32 g, 0.33 mL, 2.65 mmol) in toluene (10 mL, reflux, 24 h, catalytic amount of Et_2SnCl_2). An analytically pure sample (0.09 g, 42%) was obtained after purification by column chromatography (SiO_2, toluene) and recrystallization from toluene. ^{1}H NMR (CDCl$_3$): δ = 2.34 (s, 6 H, 2 C*H*$_3$), 2.59–3.61 (m, 8 H, C*H*$_2$-C*H*$_2$), 6.28 (d, ^3J = 7.8 Hz, 1 H, 7-H or 8-H), 6.44 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.52 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.59 (d, ^3J = 7.8 Hz, 1 H, 8-H or 7-H), 6.67 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 7.02 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 7.08 (m, 1 H, *p*-H, Ph), 7.17 (br. d, ^3J = 7.5 Hz, 2 H, *m*-H, Ph), 8.30 (s, 1 H, C*H*=N), 13.90 (br. s, 1 H, O*H*) ppm. ^{13}C NMR (CDCl$_3$): δ = 18.85 (2 CH$_3$), 29.81, 32.25, 34.03, 35.35, 119.64, 124.65, 124.96, 126.95, 128.02, 128.58 (2 C, *m*-C, Ph), 128.75, 131.11, 132.40, 133.47, 137.61, 138.53, 140.37, 143.20, 148.20, 161.44, 163.92 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 356 (42) [M$^+$], 355 (67) [M$^+$], 252 (59), 251 (94), 250 (100), 249 (14), 237 (10), 236 (40), 235 (17), 234 (35), 223 (25), 222 (61), 221 (16), 220 (14), 218 (11), 209 (11), 208 (52), 207 (18), 192 (11), 191 (11), 182 (16), 168 (12), 165 (10), 146 (10), 144 (13), 132 (14), 131 (23), 130 (17), 120 (13), 117 (18), 115 (12), 105 (38), 104 (54), 103 (49). M.p. 226.5–227 °C. $[\alpha]_D^{25}$ = –975.9 (*c* = 0.282, toluene). $C_{25}H_{25}NO$ (355.48): calcd. C 84.47, H 7.09, N 3.94; found C 84.49, H 7.12, N 3.86.

(*S*p)-13-[(2,6-Dimethylphenylimino)methyl][2.2]paracyclophan-4-ol [(*S*p)-11]: Was obtained by refluxing a solution of (*S*)-**2** (0.505 g, 2 mmol) and DMA (0.72 g, 0.75 mL, 6.10 mmol) in toluene (25 mL) with a catalytic amount of Et_2SnCl_2 for 8 h. An analytically pure sample (0.510 g, 72%) was obtained by double recrystallization from hexane. ^{1}H NMR (C$_6$D$_6$): δ = 2.34 (s, 6 H, 2 C*H*$_3$), 2.44–2.55 (m, 1 H, CH$_2$-CH*H*), 2.63–2.93 (m, 5 H, C*H*$_2$-C*H*$_2$), 3.32–3.42 (m, 1 H, CH$_2$-CH*H*), 3.58–3.68 (m, 1 H, CH$_2$-CH*H*), 4.79 (br. s, 1 H, O*H*), 5.47 (d, *J* = 1.8 Hz, 1 H, 5-H), 6.19 (d, *J* = 7.8 Hz, 1 H, 8-H or 15-H), 6.22 (dd, J_1 = 7.8, J_2 = 1.8 Hz, 1 H, 7-H or 16-H), 6.34 (d, *J* = 7.8 Hz, 1 H, 8-H or 15-H), 6.43 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 7-H or 16-H), 7.06 (t, ^3J = 7.5 Hz, 1 H, *p*-H, Ph), 7.15 (d, ^3J = 7.5 Hz, 2 H, *m*-H, Ph), 7.42 (d, *J* = 1.8 Hz, 1 H, 12-H), 8.34 (s, 1 H, C*H*=N). M.p. 169–174 °C (decomp.) ppm. $[\alpha]_D^{25}$ = –357.1 (*c* = 0.322, toluene). $C_{25}H_{25}NO$ (355.48): calcd. C 84.47, H 7.09, N 3.94; found C 84.47, H 7.20, N 3.81.

(*R*p)-12-[(2,6-Dimethylphenylimino)methyl][2.2]paracyclophan-4-ol [(*S*p)-12]: Was obtained by refluxing a solution of (*R*)-**3** (0.250 g 0.992 mmol) and DMA (0.134 g, 0.136 mL, 1.11 mmol) in toluene (10 mL) with a catalytic amount of Et_2SnCl_2 for 8 h. An analytically pure sample (0.162 g, 46%) was obtained by recrystallization from heptane. ^{1}H NMR (CDCl$_3$): δ = 2.34 (s, 6 H, 2 C*H*$_3$), 2.44–2.55 (m, 1 H, CH$_2$-CH*H*), 2.63–2.93 (m, 5 H, C*H*$_2$-C*H*$_2$), 3.32–3.42 (m, 1 H, CH$_2$-CH*H*), 3.58–3.68 (m, 1 H, CH$_2$-CH*H*), 4.79 (br. s, 1 H, O*H*), 5.47 (d, *J* = 1.8 Hz, 1 H, 5-H), 6.19 (d, *J* = 7.8 Hz, 1 H, 8-H or 15-H), 6.22 (dd, J_1 = 7.8, J_2 = 1.8 Hz, 1 H, 7-H or 16-H), 6.34 (d, *J* = 7.8 Hz, 1 H, 8-H or 15-H), 6.43 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 7-H or 16-H), 7.06 (t, ^3J = 7.5 Hz, 1 H, *p*-H, Ph), 7.15 (d, ^3J = 7.5 Hz, 2 H, *m*-H, Ph), 7.42 (d, *J* = 1.8 Hz, 1 H, 12-H), 8.34 (s, 1 H, C*H*=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 356 (29) [M$^+$], 355 (60) [M$^+$], 237 (13), 236 (58), 235 (80) 234 (100), 220 (11), 219 (13), 218 (15), 204 (10), 177 (11), 130 (11), 120 (15), 105 (11), 103 (12). M.p. 168–169 °C. $[\alpha]_D^{25}$ = –235.7 (*c* = 0.46, toluene). $C_{25}H_{25}NO$ (355.48): calcd. C 84.47, H 7.09, N 3.94; found C 84.36, H 6.91, N 3.87.

(*R*p,*S*c)-5-[(1-Hydroxymethyl-2-methylpropylimino)methyl][2.2]-paracyclophan-4-ol [(*R*p,*S*c)-13]: Was obtained by reacting (*R*)-**1** (0.088 g 0.35 mmol) and (*S*)-ValOH (0.036 g, 0.35 mmol) in toluene (6 mL, reflux, 6 h). The crude reaction mixture was passed through a short column filled with SiO_2 to provide 0.110 g (93%) of (*R*p,*S*c)-**13**. An analytically pure sample (0.093 g, 79%) was obtained by crystallization from heptane. ^{1}H NMR (CDCl$_3$): δ = 1.14 (m, 6 H, 2 C*H*$_3$), 1.68 (br. s, 1 H, O*H*), 2.05 (m, 1 H, Me$_2$C*H*), 2.51–2.66 (m, 1 H, CH$_2$-CH*H*), 2.68–3.53 (m, 8 H,-C*H*$_2$-and C*H*$_2$-C*H*$_2$), 3.67–3.73 (m, 1 H, CH$_2$-CH*H*), 3.81 (m, 1 H, N-C*H*), 6.18 (d, ^3J = 7.8 Hz, 1 H, 7-H or 8-H), 6.27 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.45 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.50 (d, ^3J = 7.8 Hz, 1 H, 8-H or 7-H), 6.62 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.86 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 8.24 (s, 1 H, C*H*=N), 14.18 (br. s, 1 H, C4-O*H*) ppm. ^{13}C NMR (CDCl$_3$): δ = 18.88 and 20.15 (2 *C*H$_3$), 29.84, 30.34 (*C*HMe$_2$), 32.16, 33.91, 35.31, 64.54, 76.91, 119.13 (q), 124.04, 126.65, 127.96 (q), 130.91, 132.15, 133.42, 137.53 (q), 137.78, 140.18 (q), 142.40 (q), 162.46 (q), 163.10 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 338 (15) [M$^+$], 337 (61) [M$^+$], 234 (28), 233 (100), 203 (11), 202 (64), 190 (20), 159 (18), 147 (44), 146 (16), 133 (12), 130 (11), 119 (10), 118 (17), 105 (13), 140 (30), 103 (17). M.p. 107.5–108.0 °C. $[\alpha]_D^{25}$ = +647.2 (*c* = 0.248, toluene). $C_{22}H_{27}NO_2$ (337.46): calcd. C 78.30, H 8.06, N 4.15; found C 78.45, H 8.02, N 4.04.

(*R*p,*S*c)-13-[(1-Hydroxymethyl-2-methylpropylimino)methyl][2.2]-paracyclophan-4-ol [(*R*p,*S*c)-14]: Was obtained by refluxing (*R*)-**2** (0.100 g, 0.400 mmol) and (*S*)-ValOH (0.045 g, 0.44 mmol) in benzene (10 mL, reflux, 6 h) in the presence of molecular sieves (4 Å) in 90% chemical yield (0.121 g). An analytically pure sample (0.100 g, 75%) was obtained by crystallization of the crude product from heptane. ^{1}H NMR ([D$_6$]acetone): δ = 1.01 (d, ^3J = 6.6 Hz, 3 H, C*H*$_3$), 1.04 (d, ^3J = 6.6 Hz, 3 H, C*H*$_3$), 1.99 (m, 1 H, C*H*Me$_2$), 2.59–2.70 (m, 1 H, CH$_2$-C*H*H), 2.88–3.05 (m, 4 H, C*H*$_2$-CH*H* and-CH*H*-), 3.12–3.24 (m, 2 H, C*H*$_2$-CH$_2$), 3.37–3.48 (m, 1 H, CH$_2$-

CHH), 3.80 (d, ^2J = 10.5 Hz, 1 H,-CHH-), 3.75–3.92 (m, 1 H, CH_2-CHH), 4.02 (m, 1 H, N-CH), 4.34 (br. s, 1 H, C4-OH), 5.99 (d, ^4J = 1.8 Hz, 1 H, 5-H), 6.22 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 7-H), 6.41 (d, ^3J = 7.8 Hz, 1 H, 8-H), 6.58 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 15-H), 6.66 (d, ^3J = 7.8 Hz, 1 H, 16-H), 7.66 (d, ^4J = 1.8 Hz, 1 H, 13-H), 8.42 (s, 1 H, CH=N) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 18.46 and 19.44 (2 CH_3), 29.89 (CH), 30.19, 32.07, 33.46 and 34.21 (C-1, –2, –9, –10), 64.44, 78.92, 120.20, 124.10, 125.53 (q), 128.76, 134.64, 134.70, 135.15, 136.31 (q), 139.23 (q), 140.63 (q), 141.45 (q), 155.57 (q), 160.51 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 338 (38) [M$^+$], 337 (78) [M$^+$], 335 (10), 322 (12), 306 (70), 294 (25), 292 (10), 278 (14), 253 (10), 252 (34), 219 (17), 218 (73), 217 (96), 216 (99), 215 (21), 187 (12), 186 (39), 174 (23), 172 (12), 171 (19), 170 (26), 169 (20), 157 (16), 156 (23), 146 (13), 145 (21), 144 (53), 143 (63), 142 (30), 141 (11), 135 (15), 133 (15), 132 (69), 131 (91), 130 (100), 129 (33), 128 (21), 121 (65), 120 (62), 119 (19), 118 (19), 117 (34), 116 (16), 115 (45), 105 (16), 104 (20), 103 (32). M.p. 127–128.5 °C. $[\alpha]_D^{25}$ = +158.4 (*c* = 0.344, toluene). $C_{22}H_{27}NO_2$ (337.46): calcd. C 78.30, H 8.06, N 4.15; found C 78.18, H 8.04, N 4.16.

(*S*p,*S*c)-13-[(1-Hydroxymethyl-2-methylpropylimino)methyl][2.2]-paracyclophan-4-ol [(*S*p,*S*c)-14]: Was obtained by reacting (*S*)-**2** (0.100 g 0.4 mmol) and (*S*)-ValOH (0.045 g, 0.44 mmol) in benzene (10 mL, reflux, 6 h) in the presence of molecular sieves (4 Å) in 91% chemical yield (0.122 g). An analytically pure sample (0.030 g, 25%) was obtained by slow crystallization from heptane. ^{1}H NMR ([D$_6$]acetone): δ = 1.01 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.04 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.99 (m, 1 H, CHMe$_2$), 2.59–2.70 (m, 1 H, CH_2-CHH), 2.88–3.05 (m, 4 H, CH_2-CHH and-CHH-), 3.12–3.24 (m, 2 H, CH_2-CH_2), 3.37–3.48 (m, 1 H, CH_2-CHH), 3.80 (d, ^2J = 10.5 Hz, 1 H,-CHH-), 3.75–3.92 (m, 1 H, CH_2-CHH), 4.02 (m, 1 H, N-CH), 4.34 (br. s, 1 H, C4-OH), 5.99 (d, ^4J = 1.8 Hz, 1 H, 5-H), 6.22 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 7-H), 6.41 (d, ^3J = 7.8 Hz, 1 H, 8-H), 6.58 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 15-H), 6.66 (d, ^3J = 7.8 Hz, 1 H, 16-H), 7.66 (d, ^4J = 1.8 Hz, 1 H, 13-H), 8.42 (s, 1 H, CH=N) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 18.46 and 19.44 (2 CH_3), 29.89 (CH), 30.19, 32.07, 33.46, 34.21 (C-1,-2,-9,-10), 64.44, 78.92, 120.20, 124.10, 125.53 (q), 128.76, 134.64, 134.70, 135.15, 136.31 (q), 139.23 (q), 140.63 (q), 141.45 (q), 155.57 (q), 160.51 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 338 (36) [M$^+$], 337 (75) [M$^+$], 322 (11), 307 (24), 306 (67), 294 (23), 278 (12), 253 (18), 252 (64), 219 (16), 218 (71), 217 (93), 216 (100), 215 (13), 187 (12), 186 (40), 174 (22), 172 (10), 171 (19), 170 (24), 169 (18), 157 (15), 156 (21), 146 (11), 145 (20), 144 (53), 143 (60), 142 (28), 141 (10), 135 (14), 133 (17), 132 (73), 131 (90), 130 (100), 129 (29), 128 (20), 121 (66), 120 (83), 119 (17), 118 (18), 117 (32), 116 (15), 115 (43), 105 (18), 104 (24), 103 (35). M.p. 124–125 °C. $[\alpha]_D^{25}$ = –334.6 (*c* = 0.126, toluene). $C_{22}H_{27}NO_2$ (337.46): calcd. C 78.30, H 8.06, N 4.15; found C 78.03, H 8.40, N 4.03.

(*R*p,*S*c)-12-[(1-Hydroxymethyl-2-methylpropylimino)methyl][2.2]-paracyclophan-4-ol [(*R*p,*S*c)-15]: Was obtained by refluxing a solution of (*R*)-**3** (0.090 g, 0.357 mmol) and (*S*)-ValOH (0.041 g, 0.40 mmol) in toluene (6 mL) for 12 h. An analytically pure sample (0.115 g, 95%) was obtained by crystallization from heptane. ^{1}H NMR ([D$_6$]acetone): δ = 1.01 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.04 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.99 (m, 1 H, CHMe$_2$), 2.59–2.70 (m, 1 H, CH_2-CHH), 2.88–3.05 (m, 4 H, CH_2-CHH and-CHH-), 3.12–3.24 (m, 2 H, CH_2-CH_2), 3.37–3.48 (m, 1 H, CH_2-CHH), 3.80 (d, ^2J = 10.5 Hz, 1 H,-CHH-), 3.75–3.92 (m, 1 H, CH_2-CHH), 4.02 (m, 1 H, N-CH), 4.34 (br. s, 1 H, C4-OH), 5.99 (d, ^4J = 1.8 Hz, 1 H, 5-H), 6.22 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 7-H), 6.41 (d, ^3J = 7.8 Hz, 1 H, 8-H), 6.58 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 15-H), 6.66 (d, ^3J = 7.8 Hz, 1 H, 16-H), 7.66 (d, ^4J = 1.8 Hz, 1 H, 13-H), 8.42 (s, 1 H, CH=N) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 18.46 and 19.44 (2 CH_3), 29.89 (CH), 30.19, 32.07, 33.46, 34.21 (C-1,-2,-9,-10), 64.44, 78.92, 120.20, 124.10, 125.53 (q), 128.76, 134.64, 134.70, 135.15, 136.31 (q), 139.23 (q), 140.63 (q), 141.45 (q), 155.57 (q), 160.51 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 338 (44) [M$^+$], 337 (86) [M$^+$], 306 (12), 235 (29), 234 (81), 233 (11), 219 (46), 218 (100), 217 (93), 216 (71), 206 (14), 205 (11), 191 (11), 186 (27), 174 (15), 171 (14), 170 (11), 157 (12), 156 (14), 144 (34), 143 (63), 141 (14), 133 (15), 132 (79), 131 (96), 130 (92), 129 (48), 128 (22), 121 (25), 120 (68), 119 (10), 118 (16), 117 (30), 116 (15), 115 (43), 107 (12), 105 (20), 104 (36), 103 (28). M.p. 144–144.5 °C. $[\alpha]_D^{25}$ = –107.1 (*c* = 0.35, toluene). $C_{22}H_{27}NO_2$ (337.46): calcd. C 78.30, H 8.06, N 4.15; found C 78.13, H 8.08, N 4.06.

(*S*p,*S*c)-12-[(1-Hydroxymethyl-2-methylpropylimino)methyl][2.2]-paracyclophan-4-ol [(*S*p,*S*c)-15]: Was obtained by the reaction of (*S*)-**3** (0.094 g, 0.373 mmol) and (*S*)-ValOH (0.042 g, 0.41 mmol) in toluene (6 mL, reflux, 15 h). An analytically pure sample (0.117 g, 93%) was obtained by crystallization from heptane. ^{1}H NMR ([D$_6$]acetone): δ = 1.02 (d, ^3J = 6.8 Hz, 3 H, CH_3), 1.07 (d, ^3J = 6.8 Hz, 3 H, CH_3), 2.07 (m, 1 H, CHMe$_2$), 2.55–2.69 (m, 1 H, CH_2-CHH), 2.77–3.22 (m, 7 H), 3.36–3.50 (m, 1 H), 3.75–4.00 (m, 2 H), 4.08–4.19 (m, 1 H), 5.93 (d, ^4J = 1.8 Hz, 1 H), 6.26 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.43 (d, ^3J = 7.8 Hz, 1 H), 6.57 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.65 (d, ^3J = 7.8 Hz, 1 H), 7.30 (d, ^4J = 1.8 Hz, 1 H), 7.65 (br. s, 1 H, OH), 8.26 (s, 1 H, CH=N) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 17.91 and 19.63 (2 CH_3), 29.89 (CH), 30.86, 32.92, 33.56 and 33.96 (C-1,-2,-9,-10), 63.90, 79.25, 120.38, 123.69, 125.19, 130.84, 134.24, 135.17, 135.26, 136.09, 139.36, 140.08, 142.16, 155.31, 162.14 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 338 (48) [M$^+$], 337 (82) [M$^+$], 306 (13), 236 (10), 235 (32) 234 (82), 233 (14), 219 (50), 218 (97), 217 (93), 216 (74), 206 (16), 205 (14), 191 (12), 189 (11), 187 (10), 186 (33), 174 (18), 171 (18), 170 (15), 157 (14), 156 (17), 144 (42), 143 (70), 142 (34), 141 (18), 133 (17), 132 (78), 131 (97), 130 (100), 129 (54), 128 (28), 121 (29), 120 (69), 119 (11), 118 (20), 117 (35), 116 (17), 115 (52), 107 (13), 105 (17), 104 (40), 103 (31). M.p. 125–126 °C. $[\alpha]_D^{25}$ = +16.8 (*c* = 0.31, toluene). $C_{22}H_{27}NO_2$ (337.46): calcd. C 78.30, H 8.06, N 4.15; found C 78.35, H 8.24, N 4.10.

(*R*p,*S*c)-5-[(1-Benzyl-2-hydroxy-2,2-diphenylethylimino)methyl][2.2]-paracyclophan-4-ol [(*R*p,*S*c]-16): Was obtained by refluxing a solution of (*R*)-**1** (0.090 g 0.357 mmol) and (*S*)-Ph_3AlaOH (0.108 g, 0.357 mmol) in toluene (6 mL) with a catalytic amount of Et_2SnCl_2 for 20 h. An analytically pure sample (0.143 g, 75%) was obtained after purifying the reaction mixture by column chromatography (SiO_2, CH_2Cl_2) and recrystallization from toluene/heptane. ^{1}H NMR ($CDCl_3$): δ = 1.65 (br. s, 1 H, OH), 2.19–2.33 (m, 1 H, CH_2-CHH), 2.47–2.73 (m, 2 H, CH_2-CH_2), 2.84–3.46 (m, 7 H, CH_2-CH_2 and CH_2), 4.56 (dd, ^3J = 10.5, ^3J = 2.3 Hz, 1 H, N–CH), 4.94 (dd, ^3J = 7.8, ^3J = 1.8 Hz, 1 H), 6.00 (d, *J* = 7.8 Hz, 1 H, 7-H or 8-H), 6.35 (m, 2 H), 6.47 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.56 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 7.04–7.15 (m, 1 H, *p*-H Ph), 7.15– 7.46 (m, 10 H, Ph), 7.50 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.71 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.77 (s, 1 H, CH=N), 13.34 (br. s, 1 H, OH) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.34, 31.85, 34.06, 34.91, 37.52, 78.06, 80.43, 119.24, 124.25, 126.03, 126.05, 126.83, 126.99, 127.05, 127.13, 127.29, 128.27, 128.47, 128.89, 129.15, 131.73, 131.86, 132.81, 137.31, 137.98, 139.28, 139.94, 142.54, 143.88, 144.94, 161.18, 164.47 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 538 (18) [M$^+$], 537 (41) [M$^+$], 356 (12), 355 (44), 354 (32), 262 (16), 252 (39), 251 (91) 250 (91), 249 (18), 248 (22), 236 (15), 235 (26) 234 (25), 233 (16), 183 (46), 182 (55), 181 (15), 179 (11), 178 (17), 165 (17), 161 (11), 160 (73), 159 (61), 158 (73), 152 (14), 147 (21), 146 (13), 145 (12), 133 (11), 132 (17), 131 (19), 130 (41), 129 (17), 119 (21), 118 (20), 117 (18), 115 (17), 106 (26), 105 (100), 104 (74), 103 (55).

M.p. 209.5–210.5 °C. $[a]_D^{25}$ = +389.9 (*c* = 0.298, toluene). $C_{38}H_{35}NO_2$ (537.70): calcd. C 84.88, H 6.56, N 2.60; found C 85.09, H 6.63, N 2.60.

(*Sp*,*Sc*)-5-[(1-Benzyl-2-hydroxy-2,2-diphenylethylimino)methyl][2.2]-paracyclophan-4-ol [(*Sp*,*Sc*]-16): Was obtained by refluxing (*R*)-**1** (0.100 g 0.400 mmol) and (*S*)-Ph_3AlaOH (0.128 g, 042 mmol) in benzene (10 mL) with Et_2SnCl_2 as a catalyst for 48 h. The crude reaction mixture was passed through a short column filled with SiO_2 to result in 0.200 g (93%) of (*Sp*,*Sc*)-**15**. An analytically pure sample (0.035 g, 16%) was obtained by slow crystallization from heptane. ^{1}H NMR ($CDCl_3$): δ = 1.85 (br. s, 1 H, O*H*), 2.19–2.33 (m, 1 H, CH_2-CH*H*), 2.47–2.73 (m, 2 H, CH_2-CH_2), 2.84–3.46 (m, 7 H, CH_2-CH_2, C*H*, C*H*H), 4.56 (dd, ^2J = 10.5, ^3J = 2.3 Hz, C*H*H), 4.94 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.00 (d, ^3J = 7.8 Hz, 1 H), 6.35 (m, 2 H), 6.47 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.56 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 7.10 (t, ^3J = 7.5 Hz, 1 H, *p*-H Ph), 7.15–7.46 (m, 10 H, Ph), 7.50 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.71 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.77 (s, 1 H, C*H*=N), 13.34 (br. s, 1 H, C(4)O*H*) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.34, 31.85, 34.06, 34.92, 37.52, 78.06, 80.43, 119.24, 124.25, 126.03, 126.05, 126.83, 126.99, 127.05, 127.13, 127.29, 128.27, 128.47, 128.89, 129.15, 131.73, 131.86, 132.81, 137.31, 137.98, 139.28, 139.94, 142.54, 143.88, 144.94, 161.18, 164.47 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 538 (14) [M$^+$], 537 (33) [M$^+$], 355 (28), 354 (20), 262 (14), 252 (25), 251 (94) 250 (96), 249 (12), 248 (14), 235 (16) 234 (15), 192 (11), 183 (25), 182 (45), 181 (11), 178 (12), 165 (10), 160 (53), 159 (37), 158 (53), 147 (16), 132 (10), 131 (10), 130 (19), 120 (11), 119 (14), 118 (123), 117 (10), 106 (16), 105 (100), 104 (69), 103 (28). M.p. 192.5–193.5 °C. $[a]_D^{25}$ = –567.3 (*c* = 0.266, toluene). $C_{38}H_{35}NO_2$ (537.70): calcd. C 84.88, H 6.56, N 2.60; found C 84.69, H 6.52, N 2.43.

(*Rp*,*Sc*)-13-[(1-Benzyl-2-hydroxy-2,2-diphenylethylimino)methyl]-[2.2]paracyclophan-4-ol [(*Rp*,*Sc*]-17): Was obtained by the reaction of (*R*)-**2** (0.245 g 0.97 mmol) and (*S*)-Ph_3AlaOH (0.13 g, 1.07 mmol) in benzene (10 mL) in 96% (0.333 g) chemical yield (reflux, 6 h). An analytically pure sample (0.158 g, 46%) was obtained by crystallization from hexane. ^{1}H NMR ($CDCl_3$): δ = 1.75 (br. s, 1 H, O*H*), 2.19–2.33 (m, 1 H, CH_2-CH*H*), 2.47–2.73 (m, 2 H, CH_2-CH_2), 2.84–3.46 (m, 7 H, CH_2-CH_2, C*H*, C*H*H), 4.56 (dd, ^2J = 10.5, ^3J = 2.3 Hz, C*H*H), 4.94 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.00 (d, ^3J = 7.8 Hz, 1 H), 6.35 (m, 2 H), 6.47 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.56 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 7.10 (t, ^3J = 7.5 Hz, 1 H, *p*-H Ph), 7.15–7.46 (m, 10 H, Ph), 7.50 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.71 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.77 (s, 1 H, C*H*=N), 13.34 (br. s, 1 H, C(4)O*H*) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.34, 31.85, 34.06, 34.92, 37.52, 78.06, 80.43, 119.24, 124.25, 126.03, 126.05, 126.83, 126.99, 127.05, 127.13, 127.29, 128.27, 128.47, 128.89, 129.15, 131.73, 131.86, 132.81, 137.31, 137.98, 139.28, 139.94, 142.54, 143.88, 144.94, 161.18, 164.47 (C=N) ppm. $C_{38}H_{35}NO_2$ (537.70): calcd. C 84.88, H 6.56, N 2.60; found C 84.05, H 6.49, N 2.41.

(*Sp*,*Sc*)-13-[(1-Benzyl-2-hydroxy-2,2-diphenylethylimino)methyl]-[2.2]paracyclophan-4-ol [(*Sp*,*Sc*]-17): Was obtained (reflux, 6 h) by the reaction of (*R*)-**2** (0.078 g, 0.27 mmol) and (*S*)-Ph_3AlaOH (0.062 g, 0.24 mmol) in benzene (10 mL) with Et_2SnCl_2 as a catalyst with 96% chemical yield (0.145 g). An analytically pure sample (0.067 g, 46%) was obtained by crystallization from heptane/ethyl acetate = 3/1. ^{1}H NMR ($CDCl_3$): δ = 2.19–2.33 (m, 1 H, CH_2-CH*H*), 2.47–2.73 (m, 2 H, CH_2-CH_2), 2.84–3.46 (m, 7 H, CH_2-CH_2, C*H*, C*H*H), 4.56 (dd, ^2J = 10.5, ^3J = 2.3 Hz, C*H*H), 4.94 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.00 (d, ^3J = 7.8 Hz, 1 H), 6.35 (m, 2 H), 6.47 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.56 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 7.10 (t, ^3J = 7.5 Hz, 1 H, *p*-H Ph), 7.15–7.46 (m, 10 H, Ph), 7.50 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.71 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.77 (s, 1 H, C*H*=N), 13.34 (br. s, 1 H, C(4)O*H*) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.34, 31.85, 34.06, 34.92, 37.52, 78.06, 80.43, 119.24, 124.25, 126.03, 126.05, 126.83, 126.99, 127.05, 127.13, 127.29, 128.27, 128.47, 128.89, 129.15, 131.73, 131.86, 132.81, 137.31, 137.98, 139.28, 139.94, 142.54, 143.88, 144.94, 161.18, 164.47 (C=N) ppm. $C_{38}H_{35}NO_2$ (537.70): calcd. C 84.88, H 6.56, N 2.60; found C 84.49, H 6.50, N 2.42.

(*Rp*,*Sc*)-12-[(1-Benzyl-2-hydroxy-2,2-diphenylethylimino)methyl]-[2.2]paracyclophan-4-ol [(*Rp*,*Sc*]-18): Was obtained by the reaction of (*R*)-**3** (0.14 g, 0.556 mmol) and (*S*)-Ph_3AlaOH (0.17 g, 0.56 mmol) in benzene (10 mL, reflux, 8 h). An analytically pure sample (0.117 g, 39%) was obtained by crystallization from hexane/*i*PrOH. ^{1}H NMR (C_6D_6): δ = 2.30–2.45 (m, 3 H, C*H*H-CH_2), 2.64–2.96 (m, 3 H, C*H*H-CH_2), 3.04 (m, 2 H,-CH_2), 3.06–3.21 (m, 1 H, CH_2-CH*H*), 3.44–3.56 (m, 1 H, CH_2-CH*H*), 3.90 (br. s, 1 H, O*H*), 4.27 (d, ^4J = 1.8 Hz, 1 H, 5-H), 4.41 (m, 1 H, C*H*), 4.63 (s, 1 H, C(4)O*H*), 6.08 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H, 7-H), 6.23 (d, ^3J = 7.8 Hz, 1 H, 8-H), 6.27 (m, 2 H, 15-H and 16-H), 6.85 (t, ^3J = 7.5 Hz, 1 H, *p*-H Ph), 6.90–7.06 (m, 5 H, Ph), 7.07–7.18 (m, 3 H, Ph), 7.33 (t, ^3J = 7.5 Hz, 1 H, *m*-H Ph), 7.61 (s, 1 H, C*H*=N), 7.70 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.84 (d, ^4J = 1.8 Hz, 1 H, 13-H), 7.95 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph) ppm. MS (EI, 70 eV): *m*/*z* (%) = 538 (18) [M$^+$], 537 (40) [M$^+$], 356 (15), 355 (48), 354 (35), 286 (32), 237 (12), 236 (53), 235 (61) 234 (63), 233 (26), 232 (16), 195 (10), 192 (14), 191 (17), 183 (35), 182 (66), 181 (24), 178 (15), 167 (18), 165 (18), 154 (11), 153 (10), 152 (20), 145 (12), 143 (73), 142 (58), 132 (17), 131 (28), 130 (53), 129 (28), 128 (16), 121 (22), 120 (55), 118 (16), 117 (27), 116 (14), 115 (43), 107 (14), 105 (100), 104 (29), 103 (26). M.p. 146–149.5 °C (decomp.). $[a]_D^{25}$ = –250.7 (*c* = 0.308, toluene). $C_{38}H_{35}NO_2$ (537.70): calcd. C 84.88, H 6.56, N 2.60; C 85.07, H 6.61, N 2.47.

(*Sp*,*Sc*)-12-[(1-Benzyl-2-hydroxy-2,2-diphenylethylimino)methyl]-[2.2]paracyclophan-4-ol [(*Sp*,*Sc*)-18]: Was obtained by the reaction of (*R*)-**3** (0.14 g, 0.556 mmol) and (*S*)-Ph_3AlaOH (0.17 g, 0.56 mmol) in of benzene (10 mL, reflux, 8 h). An analytically pure sample (0.1 g, 33%) was obtained by crystallization from hexane/*i*PrOH. ^{1}H NMR (C_6D_6): δ = 2.19–2.33 (m, 1 H, CH_2-CH*H*), 2.47–2.73 (m, 2 H, CH_2-CH_2), 2.84–3.46 (m, 7 H, CH_2-CH_2, C*H*, C*H*H), 4.56 (dd, ^2J = 10.5, ^3J = 2.3 Hz, C*H*H), 4.94 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.00 (d, ^3J = 7.8 Hz, 1 H), 6.35 (m, 2 H), 6.47 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.56 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 7.10 (t, ^3J = 7.5 Hz, 1 H, *p*-H Ph), 7.15–7.46 (m, 10 H, Ph), 7.50 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.71 (d, ^3J = 7.5 Hz, 2 H, *o*-H Ph), 7.77 (s, 1 H, C*H*=N), 13.34 (br. s, 1 H, C(4)O*H*) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.34, 31.85, 34.06, 34.92, 37.52, 78.06, 80.43, 119.24, 124.25, 126.03, 126.05, 126.83, 126.99, 127.05, 127.13, 127.29, 128.27, 128.47, 128.89, 129.15, 131.73, 131.86, 132.81, 137.31, 137.98, 139.28, 139.94, 142.54, 143.88, 144.94, 161.18, 164.47 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 538 (21) [M$^+$], 537 (45) [M$^+$], 356 (15), 355 (51), 354 (38), 286 (36), 237 (11), 236 (51), 235 (61) 234 (62), 233 (25), 232 (15), 195 (10), 192 (11), 191 (14), 183 (28), 182 (65), 181 (18), 178 (11), 167 (15), 165 (14), 152 (14), 145 (10), 143 (71), 142 (54), 132 (15), 131 (26), 130 (50), 129 (23), 128 (12), 127 (20), 120 (48), 118 (15), 117 (23), 116 (12), 115 (34), 107 (18), 106 (26), 105 (100), 104 (26), 103 (22). M.p. 177–180 °C (decomp.). $[a]_D^{25}$ = –187.2 (*c* = 0.226, toluene). $C_{38}H_{35}NO_2$ (537.70): calcd. C 84.88, H 6.56, N 2.60; found C 88.71, H 6.65, N 2.61.

(*Rp*)-13-[(2-Hydroxyethylimino)methyl][2.2]paracyclophan-4-ol [(*Rp*)-20]: Was obtained by the reaction of (*R*)-**2** (0.100 g, 0.400 mmol) and of EA (0.03 g, 0.03 mL, 0.44 mmol) in benzene (10 mL, reflux, 7 h) with molecular sieves (4 Å) in 95% chemical

yield (0.111 g). An analytically pure sample (0.087 g, 74%) was obtained by crystallization from toluene. ^{1}H NMR ([D$_6$]acetone): δ = 2.59–2.76 (m, 1 H, CH$_2$-CH*H*), 2.50–3.22 (m, 5 H, C*H*$_2$-C*H*$_2$), 3.40–3.56 (m, 1 H, CH$_2$-CH*H*), 3.61–3.77 (m, 1 H, CH$_2$-CH*H*), 3.77–4.10 (m, 4 H, C*H*$_2$-C*H*$_2$), 5.76 (d, ^4J = 1.8 Hz, 1 H), 6.25 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.47 (d, ^3J = 7.8 Hz, 1 H), 6.51 (d, ^3J = 7.8 Hz, 1 H), 6.68 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 7.36 (d, ^4J = 1.8 Hz, 1 H), 8.72 (s, 1 H, C*H*=N) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 30.23 (2 C), 34.59, 34.79, 61.81, 63.43, 121.19, 123.94, 125.19, 131.69, 134.58, 134.82, 134.87, 135.14, 138.94, 140.73, 141.35, 155.72, 160.84 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 296 (24) [M$^+$], 295 (66) [M$^+$], 177 (11), 176 (65), 175 (89), 174 (100), 157 (12), 156 (13), 132 (20), 131 (39), 130 (65), 129 (19), 128 (10), 121 (27), 120 (37), 118 (9), 117 (22), 116 (15), 115 (33), 104 (10), 103 (19), 102 (11). M.p. 180–181 °C. $[\alpha]_D^{25}$ = +282.8 (*c* = 0.232, acetone). C$_{19}$H$_{21}$NO$_2$ (295.38): calcd. C 77.26, H 7.17, N 4.74; found C 77.16, H 7.21, N 4.73.

(*R*p)-12-[(2-Hydroxyethylimino)methyl][2.2]paracyclophan-4-ol [(*R*p)-21]: Was obtained by the reaction of (*R*)-**3** (0.100 g, 0.400 mmol) and EA (0.03 g, 0.03 mL, 0.44 mmol) in benzene (10 mL, reflux, 7 h) in 100% chemical yield (0.117 g). An analytically pure sample (0.082 g, 70%) was obtained by crystallization from toluene. ^{1}H NMR ([D$_6$]acetone): δ = 2.54–2.71 (m, 1 H, CH$_2$-CH*H*), 2.78–3.24 (m, 6 H, C*H*$_2$-C*H*$_2$), 3.33–3.48 (m, 1 H, CH$_2$-CH*H*), 3.69–4.08 (m, 4 H, C*H*$_2$-C*H*$_2$), 4.22 (br. s, 1 H, OH), 5.89 (d, ^4J = 1.8 Hz, 1 H), 6.23 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.42 (d, ^3J = 7.8 Hz, 1 H), 6.59 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1 H), 6.65 (d, ^3J = 7.8 Hz, 1 H), 7.55 (d, ^4J = 1.8 Hz, 1 H), 7.80 (br. s, 1 H, OH), 8.42 (s, 1 H, C*H*=N) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 30.49, 32.81, 33.18, 34.06, 61.83, 63.89, 120.12, 123.78, 125.35, 128.98, 134.62, 134.93, 135.27, 136.15, 139.40, 140.51, 141.63, 155.48, 161.99 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 296 (49) [M$^+$], 295 (84) [M$^+$], 235 (39), 234 (86), 206 (20), 205 (17), 191 (17), 189 (15), 178 (15), 177 (55), 176 (97), 175 (100), 174 (98), 165 (11), 157 (12), 156 (12), 147 (13), 145 (44), 144 (95), 143 (76), 142 (33), 141 (16), 132 (28), 131 (64), 130 (83), 129 (47), 128 (25), 121 (24), 120 (72), 119 (13), 118 (17), 117 (47), 116 (29), 115 (62), 107 (10), 105 (13), 104 (23), 103 (40), 102 (22). M.p. 163–164 °C. $[\alpha]_D^{25}$ = –47.1 (*c* = 0.244, acetone). C$_{19}$H$_{21}$NO$_2$ (295.38): calcd. C 77.26, H 7.17, N 4.74; found C 77.14, H 7.19, N 4.70.

Enantioselective Addition of Diethylzinc to Benzaldehyde Catalyzed by Compounds 6–20

Typical Procedure: To a solution of the respective Schiff base (0.01 mmol) in toluene (0.28 mL), 1.1 M solution of Et$_2$Zn in toluene (0.2 mL, 0.22 mmol) was added in one portion at 0 °C followed by the benzaldehyde (0.1 mmol) added dropwise. The mixture was stirred for 15 h at room temp. and quenched by addition of a 1 N HCl solution (0.45 mL), diluted with Et$_2$O (2 mL) and H$_2$O (1 mL). The organic layer was separated and the aqueous fraction was extracted with Et$_2$O (3 × 2 mL) or CH$_2$Cl$_2$. The combined organic fractions were washed with aq. NaHCO$_3$ (3 mL) and dried with Na$_2$SO$_4$. After solvent removal, the oily residue was subjected to chiral GC or HPLC analysis without further purification.

Enantiomeric analysis of 1-phenylpropanol was performed by GC on Gamma Cyclodextrin Trifluoracetyl (G-TA) (30 m × 0.25 mm) using He as carrier gas. Temperature program for 1-phenylpropanol: split temperature 220 °C, detector FID 220 °C, column temperature 120 °C; the retention times were 11.3 (*S*) and 11.7 min (*R*), respectively. Enantiomeric analysis of 1-phenylpropanol was performed by HPLC (Varian 5000 LC) on Chiracel OD (250 mm × 4.6 mm) with hexane/2-propanol 100/4 as eluent, flow rate 1 mL/min, temperature 20 °C, detector UV 254 nm, the retention times were 9.4 (*S*) and 11.1 min (*R*), respectively.

Crystal Data: (*S*p,*R*)-**9**, C$_{26}$H$_{29}$NO$_2$ (*M* = 387.50), C$_{25}$H$_{25}$NO·CH$_3$OH, monoclinic, space group *P*2$_1$, *a* = 9.475(3), *b* = 8.122(2), *c* = 13.449(4) Å, β = 102.910(7)°, *V* = 1008.8(5) Å^3, *Z* = 2, d_{calc} = 1.276 g cm^{-3}, μ = 0.080 mm^{-1}, *F*(000) = 416, crystal size 0.25 × 0.2 × 0.15 mm. Single-crystal X-ray diffraction experiments were carried out with a Bruker SMART 1000 CCD area detector (graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å), ω-scans with a 0.3° step in ω and 10 s per frame exposure, θ_{max} = 25.50°) at 120 K. Reflection intensities were integrated using SAINT software [SMART V5.051 and SAINT V5.00, area detector control and integration software, 1998, Bruker AXS Inc., Madison, WI 53719, USA] and semi-empirical method SADABS [G. M. Sheldrick, SADABS, 1997, Bruker AXS Inc., Madison, WI 53719, USA].

A total of 4764 reflections were measured, 3159 (R_{int} = 0.0462) independent reflections were used in further calculations and refinement. The structures were solved by direct methods and refined by the full-matrix least-squares against F^2 in anisotropic (for non-hydrogen atoms) and isotropic (for H atoms) approximation. All hydrogen atoms (with the exception of the H atoms of OH groups) were placed in geometrically calculated positions and included in the final refinement using the riding model with the U_{iso}(H) parameters equal to 1.2U_{eq}(C$_i$) or 1.5U_{eq}(C$_{ii}$), where U(C$_i$) and U(C$_{ii}$) are the equivalent thermal parameters of the sp^2 and sp^3 carbon atoms to which the respective H atoms are bonded. The H atoms in OH-groups were located from the difference Fourier syntheses and included in the final refinement using the riding model with the U_{iso}(H) parameters equal to 1.2U_{eq}(O$_i$), where U(O$_i$) are the equivalent thermal parameters of the oxygen atoms to which the respective H atoms are bonded.

The final refinements were converged to *R*1 = 0.0628 [for 2185 unique reflections with $I > 2\sigma(I)$] and *wR*2 = 0.1276 (from all 3159 unique reflections); the number of the refined parameters is 263.

All calculations were performed on an IBM PC/AT using the SHELXTL software [G. M. Sheldrick, SHELXTL-97, Version 5.10, Bruker AXS Inc., Madison, WI 53719, USA].

CCDC-655748 contains the supplementary crystallographic data (atomic coordinates, bond lengths, bond angles and termal parameters) for (*S*p,*R*)-**9**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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