Structurally Diverse Second-Generation [2.2]Paracyclophane Ketimines with Planar and Central Chirality: Syntheses, Structural Determination, and Evaluation for Asymmetric Catalysis

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Dedicated to Henning Hopf, one of the pioneers of modern cyclophane chemistry, on the occasion of his 65th birthday

Abstract: A set of 20 novel [2.2]paracyclophane ketimines with planar and central chirality has been synthesized from enantiomerically pure and racemic 5-acyl-4-hydroxy[2.2]paracyclophane and α-branched chiral amines. Their X-ray structures were determined to elucidate the three-dimensional structures and the absolute configuration. The ketimines were used as catalysts in the asymmetric 1,2-addition reactions of diethylzinc with substituted benzaldehydes to furnish chiral alcohols in up to 95% *ee*.

Keywords: asymmetric catalysis · chirality · cyclophanes · ketimines · zinc

Introduction

The synthesis of enantiomerically pure compounds is one of the major challenges in organic synthesis. Today, based on the first concepts in the field of asymmetric catalysis using metal complexes, a large set of transformations can be conducted in a stereo-controlled, enantioselective, and atom-economic manner by asymmetric transition-metal catalysis. However, these syntheses rely strongly on the efficiency, selectivity, and availability of the catalysts, which are generally based on enantiomerically pure ligands. While classical ligands have mostly central chirality, planar chirality plays a pivotal role in many modern ligand systems. The tremendous success of ferrocenyl ligands as catalysts, in particular, has not been matched by any other chiral backbone to date.[1] Metallocene- and metalarene-based ligand backbones exhibit a common feature: they only adopt planar chirality upon addition of (at least) two substituents to one ring fragment. [2.2]Paracyclophanes, however, only need a single substituent to be inherently chiral. Since the initial reports by Reich and Cram,[2] the field of [2.2]paracyclophane chemistry has grown considerably.[3] The chemical behavior of [2.2]paracyclophanes is nowadays well understood, and this allows this relatively stable class of molecule to be modified as required. The most prominent example is the PHANEPHOS ligand developed by Rossen and Pye,[4] which has found several successful applications in asymmetric hydrogenation reactions. A comprehensive survey of [2.2]paracyclophane-based ligands can be found in recent reviews.[5] The use of chiral ligands with planar or central chirality based on paracyclophane systems has increased enormously since the reports by Belokon and Rozenberg et al.,[6–8] the Berkessel group,[9] and, notably, the Hopf group.[7,10] In the past few years, various new paracyclophane ligands have been introduced in asymmetric catalysis.[11–14] In particular, hydroxy[2.2]paracyclophane ketimine ligands can efficiently control the asymmetric 1,2-addition reaction of zinc reagents[15] such as alkyl-,[8,16,17] alkenyl-,[18] aryl,[19] and alkynylzinc[20] reagents to aldehydes or imines.[14,16,19]

The well-known *ortho*-acylated hydroxy[2.2]paracyclophanes **2** (R^1 = methyl, AHPC) and **3** (R^1 = phenyl, BHPC) are key intermediates for these ligands.[6,21] They can also be condensed with primary amines to give ketimines **11a** and **12a**. These first-generation ligands, pre-

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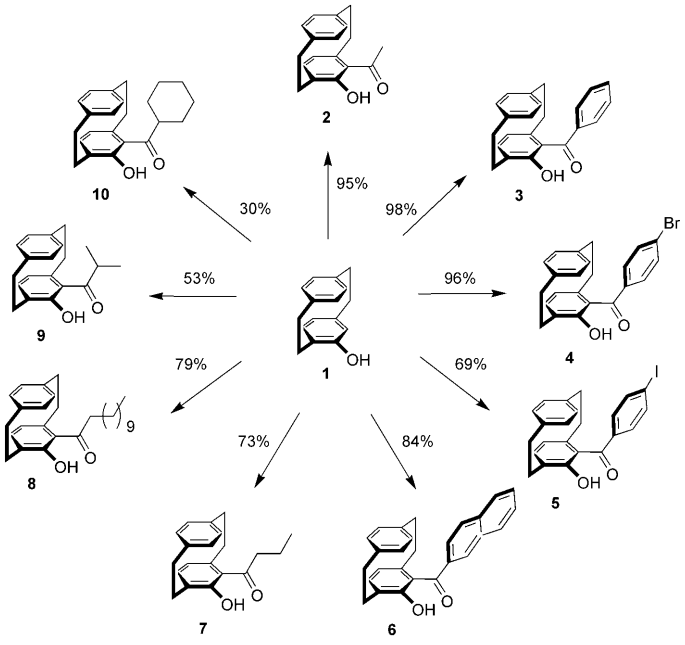
pared in the beginning by the Rozenberg group,[6] contain a 1-phenylethyl side-chain. Its ligand structure, however, ought to be vastly variable. Steric factors, such as flexibility of the backbone and side-chains, as well as electronic factors (e.g. sp^2- versus sp^3-configuration of the *N*-donors), can be easily adjusted. The introduction of central chirality by incorporation of chiral amine side-chains is also possible. The interaction of planar and central chirality, usually referred to as *chiral cooperativity*,[22–26] was thus studied in a ligand system that has elements of both planar and central chirality.

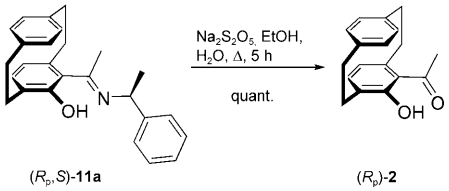
Results and Discussion

In this paper, we describe the synthesis and evaluation of second-generation[27] ketimine ligands produced from an extended set of primary amines and novel 5-acyl-4-hydroxy-[2.2]paracyclophanes. The key intermediates are the known compounds 5-acetyl-4-hydroxy[2.2]paracyclophane (AHPC, **2**) and 5-benzoyl-4-hydroxy[2.2]paracyclophane (BHPC, **3**), and the novel compounds 5-*p*-bromobenzoyl-4-hydroxy-[2.2]paracyclophane (*p*-BrBHPC, **4**), 5-*p*-iodobenzoyl-4-hydroxy[2.2]paracyclophane (*p*-IBHPC, **5**), 5-(2-naphthoyl)-4-hydroxy[2.2]paracyclophane (NHPC, **6**), 5-butyryl-4-hydroxy[2.2]paracyclophane (BuHPC, **7**), 5-lauroyl-4-hydroxy[2.2]paracyclophane (LHPC, **8**), 5-isobutyryl-4-hydroxy[2.2]paracyclophane (**9**), and 5-cyclohexanoyl-4-hydroxy[2.2]paracyclophane (**10**), all of which were synthesized by *ortho*-selective Friedel–Crafts acylation of the racemic phenol 4-hydroxy[2.2]paracyclophane (**1**) according to Scheme 1.[21,28]



Scheme 1. Synthesis of known (**2**, **3**) and novel (**4**–**10**) acyl-[2.2]paracyclophanes.

The resolution of racemic AHPC (**2**) was conducted according to the documented procedure,[21] from the ketimine **11a**,[29] by treatment with (*S*)- or (*R*)-phenylethylamine. Enantiomerically pure AHPC (**2**) could be obtained by hydrolysis of the diastereomerically pure imine **11a** (Scheme 2).[30] AHPC-based imines **11a** are more stable to-



Scheme 2. Hydrolysis of imine (R_pS)-**11a** resulting in enantiomerically pure AHPC [(R_p)-**2**].

wards acidic hydrolysis than their 5-formyl-4-hydroxy-[2.2]paracyclophane (FHPC) analogues. Therefore, the method using $Na_2S_2O_5$ published by Rozenberg et al. was employed.[21] The hydrolysis was presumed to proceed via the bisulfite addition product. Unfortunately, the hydrolysis of the more stable BHPC-based ketimines **12** is still proving to be elusive.

Our starting point for the investigation of the influence of the side-chain on the catalytic behavior of the ketimine ligands was the known intermediates AHPC (**2**) and BHPC (**3**). This allowed a direct comparison of the known ketimines **11a** and **12a**, both of which possess a phenylethyl side-chain.

From enantiomerically pure (*S*)- and (*R*)-AHPC (**2**) obtained by hydrolysis, several novel imines **11b**–**g**, **11i**, and **11k**, were prepared by condensation with chiral amines **B**–**G**, **I**, and **K**, respectively (Figure 1, Scheme 3). The reaction gave good-to-excellent yields of the products and allowed

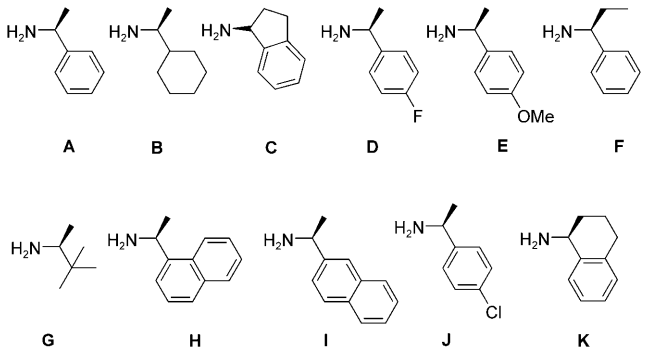
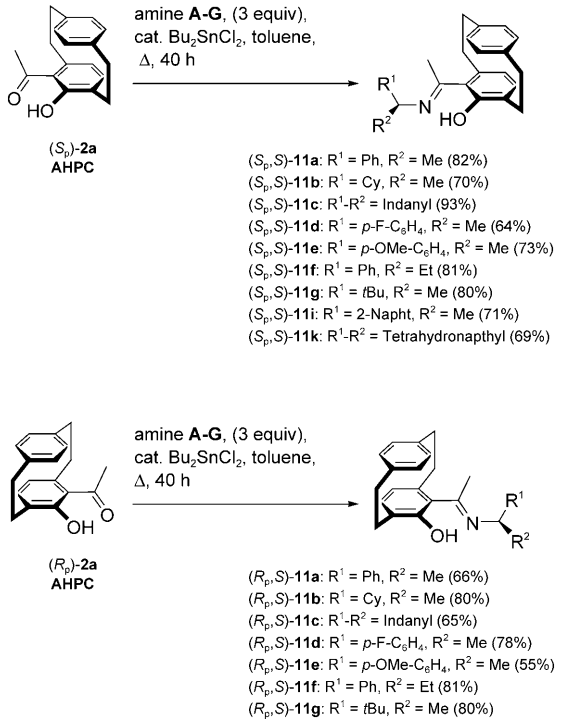


Figure 1. Chiral amines **A**–**K** used for the condensation reaction.

more in-depth studies of the influence of the size and nature of the side-chain on the catalytic performance of the ligand.

There are two advantages in using enantiomerically pure AHPC (**2**) in this condensation reaction: a tedious chromatographic separation of the diastereomers is not needed, and



Scheme 3. Syntheses of planar-chiral and central-chiral imines **11a–g**, **11i**, and **11k**.

the configuration of the desired product can be deduced from the starting materials. The configuration of the imines **11** was proven by X-ray structures of (S_P,*S*)-**11c** (Figure 2, top), (S_P,*S*)-**11i** (middle), and (S_P,*S*)-**11k** (bottom).

For the BHPC-based ligands **12**, however, which were prepared from racemic 5-benzoyl-4-hydroxy-[2.2]paracyclophane (**3**) by condensation with enantiomerically pure amines **A–C** and **G–J** in the presence of the stronger Lewis acid titanium tetrachloride (Scheme 4), the diastereomers had to be separated by flash chromatography on silica gel. The low yields in some cases can be explained by the difficulty in separating diastereomers by this method. To determine the configuration of the desired diastereomers, the crystalline materials were recrystallized from a pentane/diethyl ether mixture at room temperature and the structures determined by X-ray crystallography. This allowed their relative and absolute configurations to be established.

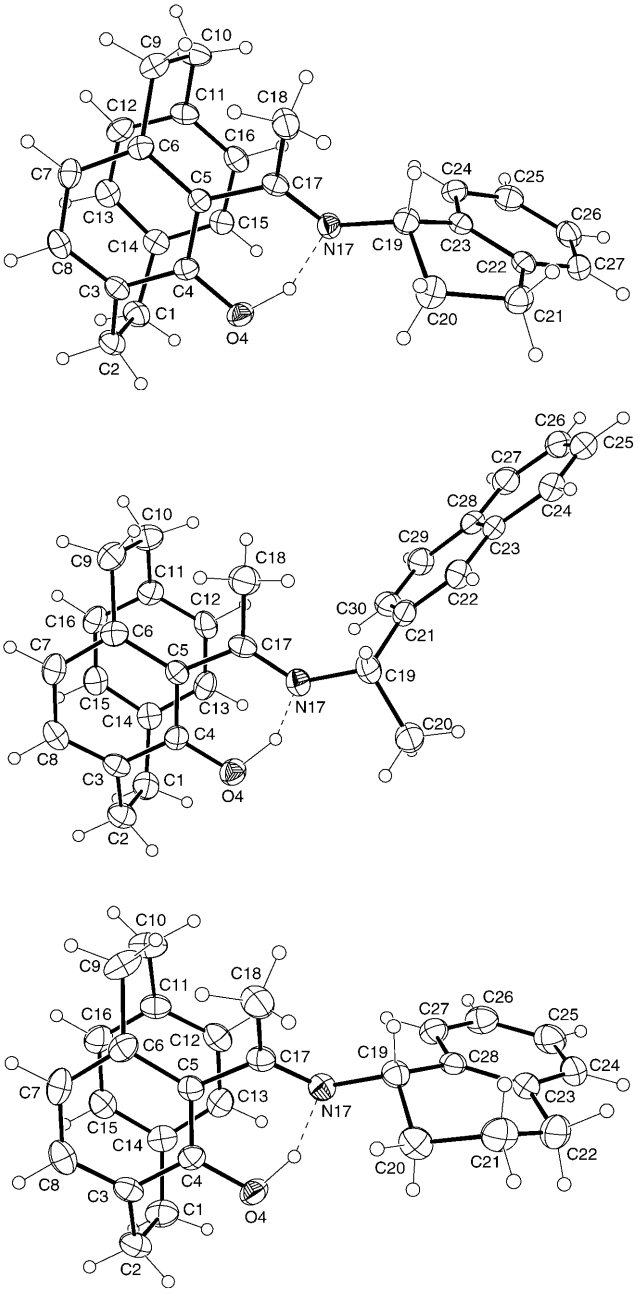
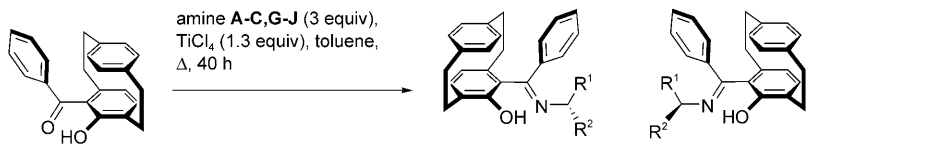


Figure 2. X-ray structures of imine (S_P,*S*)-**11c** (top), (S_P,*S*)-**11i**, (middle), and(S_P,*S*)-**11k** (bottom).



Scheme 4. Synthesis of planar-chiral and central-chiral imines **12a–c** and **12g–j**.

It was possible to acquire at least one X-ray structure of each diastereomeric pair (see Figure 3 for the structures of (S_P,*S*)-**12b**, and (S_P,*S*)- and (R_P,*S*)-**12c**, Figure 4 for the structures of (R_P,*S*)- and (S_P,*S*)-**12g**, and (R_P,*S*)-**12h**, and

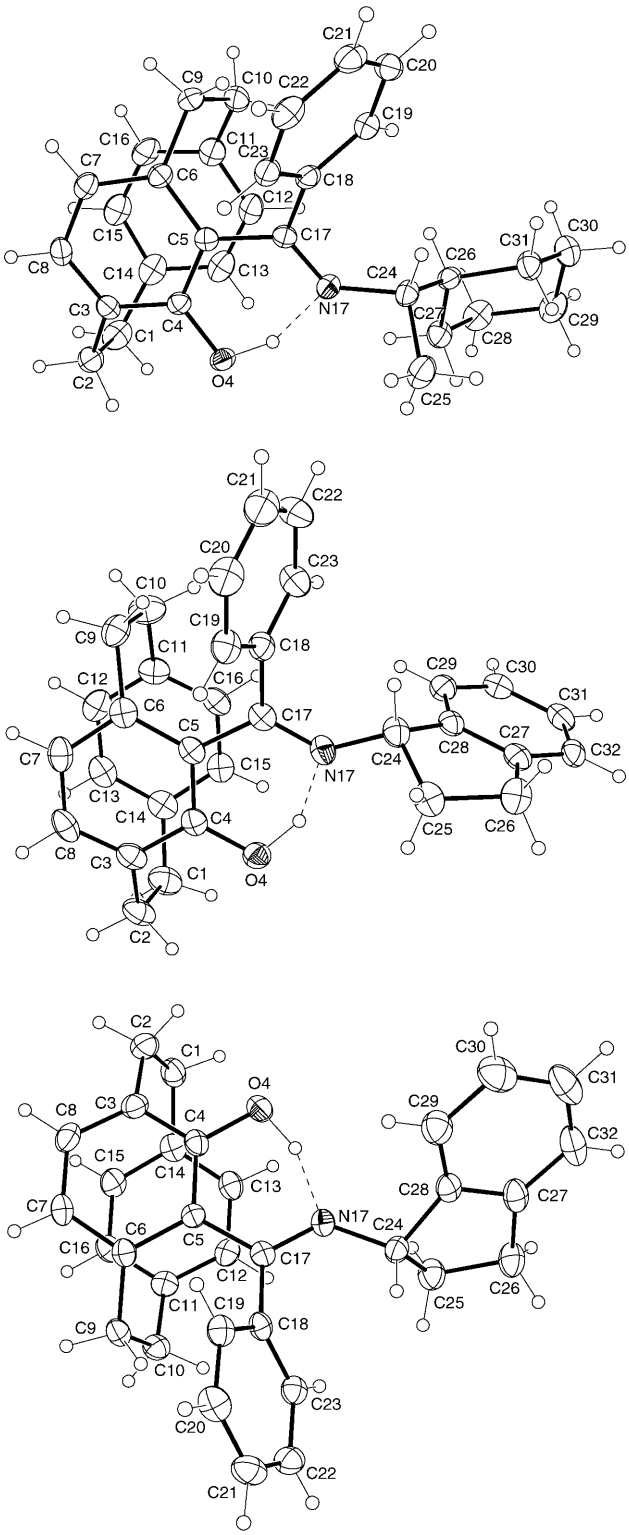


Figure 3. X-ray structure of ($S_P S$)-**12b** (top), ($S_P S$)-**12c** (middle), and ($R_P S$)-**12c** (bottom).

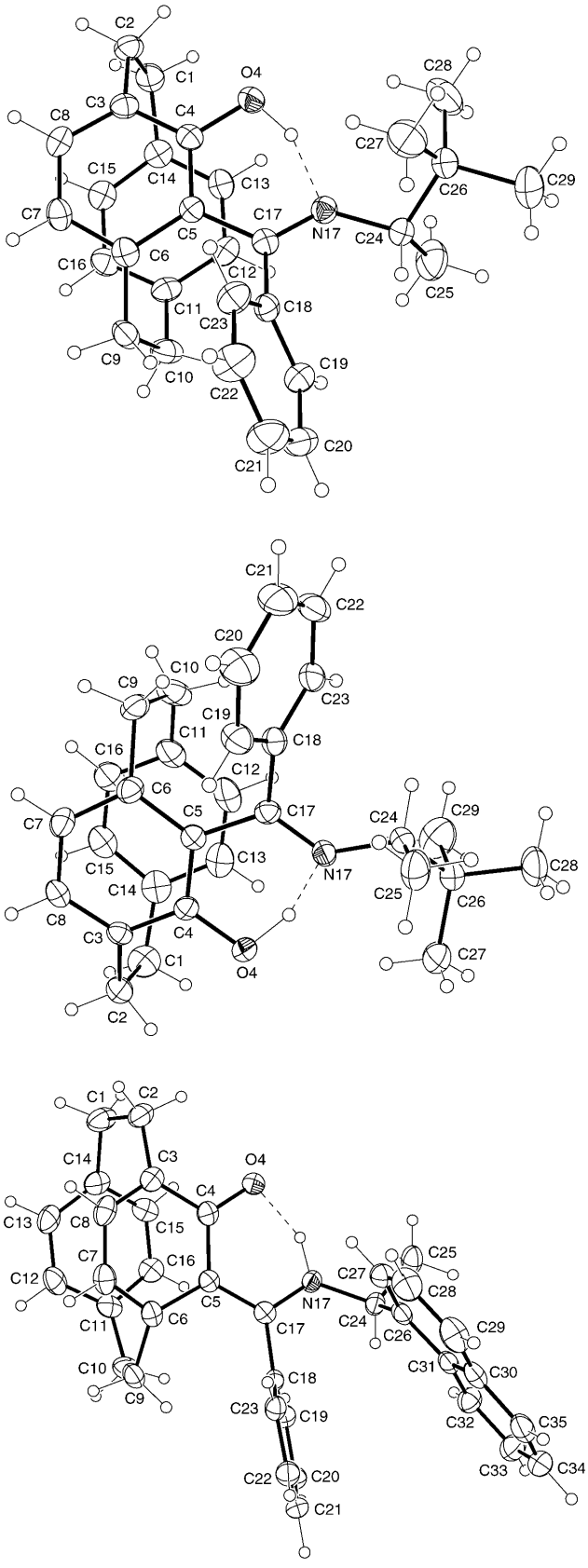


Figure 4. X-ray structure of ($R_P S$)-**12g** (top), ($S_P S$)-**12g** (middle), and ($R_P S$)-**12h** (bottom).

Figure 5 for the structures of ($R_P S$)-**12i** and ($S_P S$)-**12j**). Based on this, we were able to determine the absolute configuration of all the imines prepared and attempted to compare the catalytic results with the determined structural in-

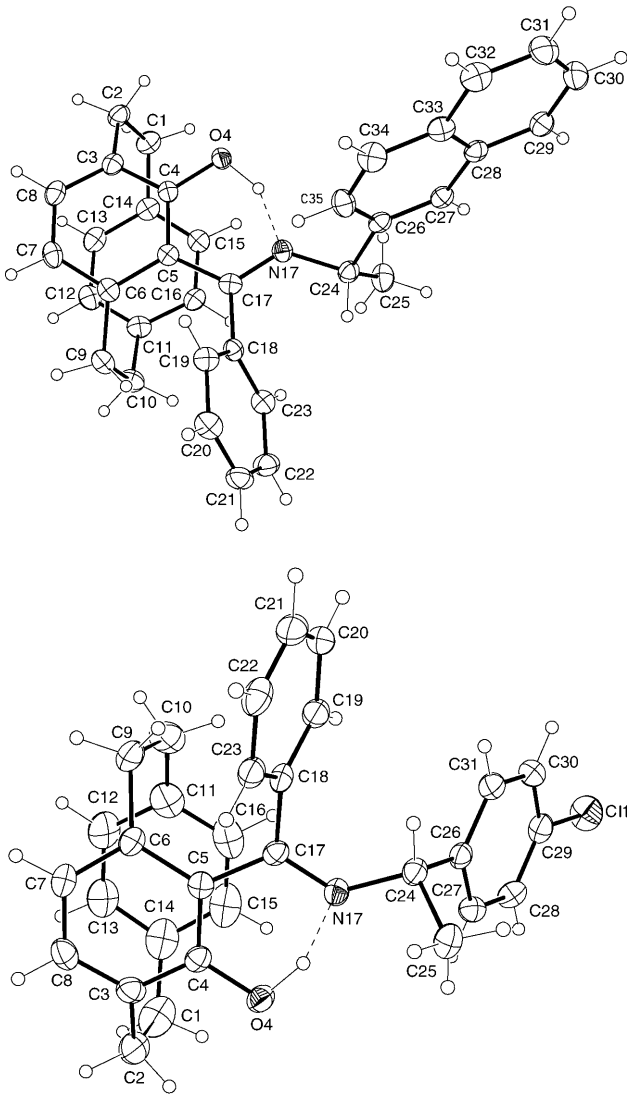
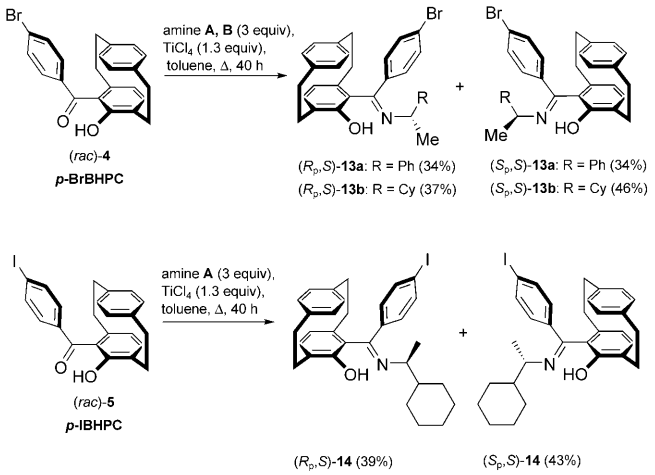


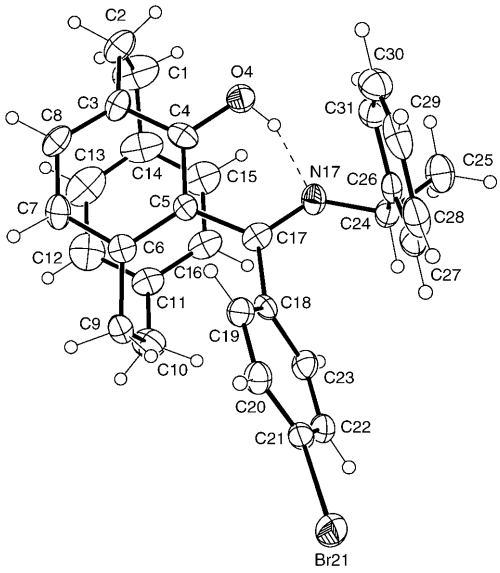
Figure 5. X-ray structure of (R_P,*S*)-**12i** (top) and (S_P,*S*)-**12j** (bottom).

formation. Unfortunately, the X-ray structures of the non-complexed ligands did not provide direct information about the structure of the catalytically active metal complex. However, they did help with the understanding and tuning of the catalysts. The X-ray structures of the imines (R_P,*S*)-**12a**[21] and (S_P,*S*)-**12a**,[21] derived from BHPC (**3**), and the imine (R_P,*S*)-**11a**,[31] derived from AHPC (**2**), have already been reported.

It was also possible to convert the new *para*-substituted ketones **4** and **5** into the corresponding ketimines **13a**,**b** and **14** with good to excellent yields (Scheme 5). The purpose of using *para*-halide-substituted ketones **4** and **5** was to create a docking position for the ligand to be attached to solid phases so that the resulting compounds could be used as immobilized catalysts.[32,33] It was possible to obtain X-ray structures for the *para*-bromo substituted ketimines **13a** and **13b**, (Figure 6), which allowed us to establish the configuration of the diastereomers. However, we were not able to obtain any single crystals that were suitable for determining



Scheme 5. Synthesis of planar-chiral and central-chiral imines **13a**,**b** and **14**.



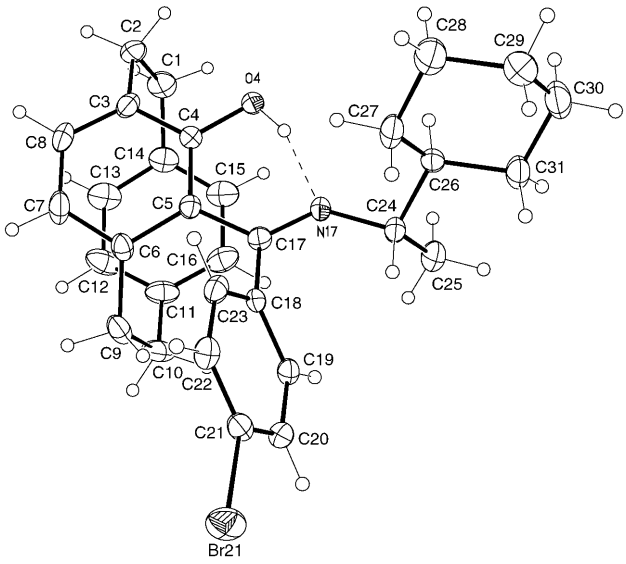


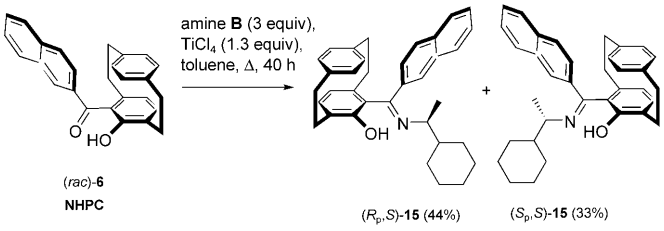
Figure 6. X-ray structure of (R_P,*S*)-**13a** (top) and (R_P,*S*)-**13b** (bottom).

the X-ray structures of the *para*-iodo-substituted ketimines **14**.

Although it was not possible to acquire X-ray structures for the diastereomers **14**, we assumed their configuration based on the ketimines **13b**, as **13b** and **14** contain the same cyclohexyl side-chain and differ only in their *para* substitution. We used the ketimines **13b** and **14** in Heck reactions with the same protected ω-alkenol to yield the same product.[33] Therefore, we were able to determine the configuration by comparing the optical rotation of the desired product. Furthermore, all S_p,S-configured diastereomers based on AHPC (**2**), BHPC (**3**), *p*-BrBHPC (**4**), or *p*-IBHPC (**5**) show negative optical rotations, while all R_p,S-configured diastereomers based on AHPC (**2**), BHPC (**3**), *p*-BrBHPC (**4**), or *p*-IBHPC (**5**) display positive optical rotations. For the following examples **15**–**17**, we were unable to obtain an X-ray structure to solve the configuration, so we determined the configuration of the diastereomers by assuming that a negative optical rotation indicates an S_p,S-configured diastereomer and a positive optical rotation, an R_p,S-configured diastereomer.

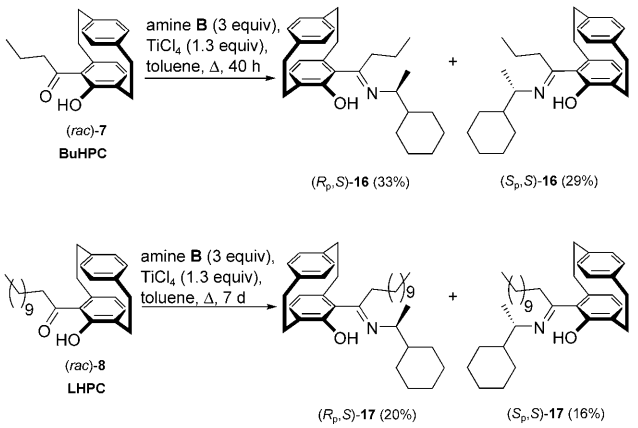
There is no relation between the R_f values and the relative configurations of the stereogenic centers. Although in most cases the R_p,S-configured diastereomers display higher R_f values, this is not the case for the diastereomeric pairs of **11e**, **12h**, and **12i**. The diastereomers of **11g** show the same R_f values, which demonstrates the need to start from enantiomerically pure ketones.

Racemic 5-(2-naphthoyl)-4-hydroxy[2.2]paracyclophane (NHPC, **6**) could be converted into the corresponding ketimines **15** in good yields under the same reaction conditions employed for the other aromatic ketones ($TiCl_4$, toluene, reflux, 40 h; Scheme 6).



Scheme 6. Synthesis of planar-chiral and central-chiral imine **15**.

In contrast to the aliphatic analogues of AHPC (**2**), it was impossible to convert the aliphatic 5-butyryl-4-hydroxy-[2.2]paracyclophane (BuHPC, **7**) and 5-lauroyl-4-hydroxy-[2.2]paracyclophane (LHPC, **8**) into the corresponding ketimines by treatment with the same Lewis acid (dibutyltin diacetate). Treatment with the stronger Lewis acid titanium tetrachloride, however, yielded the corresponding ketimines **16** and **17**, respectively, although formation of the ketimines **17** from the more-congested ketone LHPC (**8**) requires a longer reaction time of seven days (Scheme 7). It was therefore not surprising that the even more crowded 5-isobutyryl-4-hydroxy[2.2]paracyclophane (**9**) and 5-cyclohexanoyl-4-hydroxy[2.2]paracyclophane (**10**) did not react at all with an amine under the same conditions to form the corresponding ketimines.



Scheme 7. Synthesis of planar-chiral and central-chiral imines **16** and **17**.

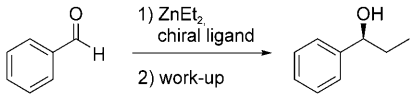
Structural discussion: A comparison of known structures with our new structures showed that they exhibit certain similarities with respect to the hydroxyimine substructure. All imines form a short hydrogen bond between the imine nitrogen and the phenolic oxygen. Interestingly, in structure (R_p,S)-**12h** (Figure 5), the distance between the phenolic oxygen atom and the hydrogen atom bound to the nitrogen N17 is shortened too. This indicates an internal salt formation. The hydrogen bonds of all ligands create a six-membered ring that is nearly planar. The only distortion occurs because of the interaction between the methyl group (C18 for (R_p,S)-**11c**) or the phenyl group ((R_p,S)-**12b**) and the [2.2]paracyclophane backbone. In the case of the zinc complexes, the zinc atom should be placed between the oxygen and the nitrogen atoms.[34]

For the ketimine diastereomers based on BHPC and related ketones, the X-ray structures show that the aryl substituent seems to be locked between the [2.2]paracyclophane backbone, and the different substitution of the amines thus prevents rotation of the arene ring. By adopting this configuration, the phenyl group ($\nu_{mn}=0.57$)[35] occupies nearly the same space as a methyl substituent ($\nu_{ef}=0.52$) or an ethyl group ($\nu_{ef}=0.56$) and is much smaller than an *i*Pr group ($\nu_{ef}=0.76$).

Evidently, the aryl- or alkylethyl group of the ligand can adopt various configurations (free rotation of the C–C bond) towards the paracyclophane unit, as shown by the different X-ray structures. This might be the reason why, in most cases, both diastereomers perform equally well in catalysis (see below) and no matched case of the stereogenic elements is apparent. Moreover, this accounts for the planar chirality as the determining stereogenic element.

Catalytic evaluation: The 1,2-addition of diethylzinc to aldehydes is a powerful method for C–C bond formation and is mechanistically well understood.[34,36] Due to the variety of

possible transition states, the reaction is very sensitive to changes in the ligand structure. For this reason, the diethylzinc addition reaction is a suitable test reaction for developing and establishing a new class of ligands (Scheme 8).



18a **19a**

Scheme 8. Diethylzinc addition to benzaldehyde (**18a**). Conditions: Benzaldehyde (0.5 mmol), ligand (2 mol%), toluene (1 mL), diethylzinc (1.0 mL, 1.0 M in hexane, 2 equiv.), 0 °C, 12 h under argon.

The novel ligands, synthesized above, were evaluated first with benzaldehyde in the 1,2-addition with diethylzinc. Thus, we were able to compare the resultant imines with those in the literature and each other to determine the influence of the changed parameter in the catalytic reactivity and selectivity. The results for the S_pS- and the R_pS-configured ligands are shown in Tables 1 and 2, respectively.

Table 1. Asymmetric 1,2-addition reactions with benzaldehyde as substrate. See Scheme 8 for conditions.

	Substrate	Ligand	Yield[a]	*ee* [%][b] (config)[c]
1	benzaldehyde	(S_pS)-**11a**	>99	83 (*R*)
2	benzaldehyde	(S_pS)-**11b**	>99	90 (*R*)
3	benzaldehyde	(S_pS)-**11c**	>99	81 (*R*)
4	benzaldehyde	(S_pS)-**11d**	>99	81 (*R*)
5	benzaldehyde	(S_pS)-**11e**	>99	78 (*R*)
6	benzaldehyde	(S_pS)-**11f**	>99	72 (*R*)
7	benzaldehyde	(S_pS)-**11g**	>99	79 (*R*)
8	benzaldehyde	(S_pS)-**11i**	>99	79 (*R*)
9	benzaldehyde	(S_pS)-**11k**	>99	80 (*R*)
10	benzaldehyde	(S_pS)-**12a**	>99	85 (*R*)
11	benzaldehyde	(S_pS)-**12b**	>99	90 (*R*)
12	benzaldehyde	(S_pS)-**12c**	>99	72 (*R*)
13	benzaldehyde	(S_pS)-**12g**	>99	88 (*R*)
14	benzaldehyde	(S_pS)-**12h**	>99	73 (*R*)
15	benzaldehyde	(S_pS)-**12i**	>95	81 (*R*)
16	benzaldehyde	(S_pS)-**13a**	>99	83 (*R*)
17	benzaldehyde	(S_pS)-**13b**	>99	87 (*R*)
18	benzaldehyde	(S_pS)-**14**	>99	88 (*R*)
19	benzaldehyde	(S_pS)-**15**	97	72 (*R*)
20	benzaldehyde	(S_pS)-**16**	68	49 (*R*)
21	benzaldehyde	(S_pS)-**17**	75	55 (*R*)

[a] Determined by GC after standard work-up. [b] Determined by GC (CP-Chirasil-Dex). [c] Determined by comparison with authentic samples.

For all reactions, the S_pS-configured imines generate the *R*-configured alcohol and all R_pS-configured imines produce the *S*-configured alcohol. Hence, the paracyclophane backbone also determines the configuration of the desired product, as noted earlier. However, these two imines (S_pS and R_pS) can be differentiated by their yields. Nearly all examples of the S_pS-configured imines produced a 97–99% yield of the chiral alcohol, the only exception being the BuHPC-based ligand (S_pS)-**16**, which yielded the product in only 68% yield. Conversely, the diastereomeric R_pS ligands often showed a lower conversion. In addition, a high reactivity is observed for the R_pS ligands, with a high selectivity.

Table 2. Asymmetric 1,2-addition reactions with benzaldehyde as substrate. See Scheme 8 for conditions.

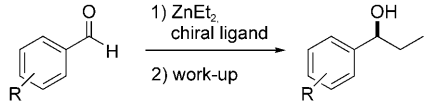
	Substrate	Ligand	Yield[a]	*ee* [%][b] (config)[c]
1	benzaldehyde	(R_pS)-**11a**	94	82 (*S*)
2	benzaldehyde	(R_pS)-**11b**	>99	90 (*S*)
3	benzaldehyde	(R_pS)-**11c**	90	70 (*S*)
4	benzaldehyde	(R_pS)-**11d**	>99	75 (*S*)
5	benzaldehyde	(R_pS)-**11e**	>99	57 (*S*)
6	benzaldehyde	(R_pS)-**11f**	95	65 (*S*)
7	benzaldehyde	(R_pS)-**11g**	>99	76 (*S*)
8	benzaldehyde	(R_pS)-**12a**	36	60 (*S*)
9	benzaldehyde	(R_pS)-**12b**	>99	79 (*S*)
10	benzaldehyde	(R_pS)-**12c**	95	33 (*S*)
11	benzaldehyde	(R_pS)-**12g**	25	42 (*S*)
12	benzaldehyde	(R_pS)-**12h**	>99	53 (*S*)
13	benzaldehyde	(R_pS)-**12i**	95	56 (*S*)
14	benzaldehyde	(R_pS)-**13a**	95	56 (*S*)
15	benzaldehyde	(R_pS)-**13b**	>99	86 (*S*)
16	benzaldehyde	(R_pS)-**14**	95	71 (*S*)
17	benzaldehyde	(R_pS)-**15**	96	74 (*S*)
18	benzaldehyde	(R_pS)-**16**	40	56 (*S*)
19	benzaldehyde	(R_pS)-**17**	69	65 (*S*)

[a] Determined by GC after standard work-up. [b] Determined by GC (CP-Chirasil-Dex). [c] Determined by comparison with authentic samples.

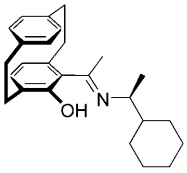
In general, the AHPC-based diastereomeric imine pairs show nearly the same selectivity, whereas the BHPC-based imine pairs often display a difference in their reactivity and selectivity. The S_pS-configured imines are more selective and reactive than their counterparts. For example, the S_pS-configured ligand **12b**, which generates an enantiomeric excess of 90% *ee* (*R*), is more selective than the R_pS-configured ligand **12b**, which only produces the chiral alcohol in 79% *ee* (*S*).

The results shown in Tables 1 and 2 show that the diastereomeric ligands (R_pS)/(S_pS)-**11b** and (S_pS)-**12b** have the highest selectivity and activity. Furthermore, it can be concluded that the imines with the (*S*)-cyclohexylethyl group in the side-chain are more selective than the other chiral amines used in this study. The highest enantiomeric excesses observed with these ligands were 90% *ee* for (*R*)- and (*S*)-1-phenylpropanol with the diastereomers (S_pS)/(R_pS)-**11b** based on AHPC with a cyclohexyl side-chain. This is an improvement of 7% and 8% *ee* over the known diastereomeric pair **11a**, which is also based on AHPC, but with a phenyl side-chain. Ligands with a cyclohexyl side-chain are more bulky and more selective than those with a phenyl side-chain. The same observation was made for the BHPC-based diastereomers **12a** in comparison with **12b**. The improvement for the S_pS-configured imine **12b** was from the earlier value of 85% *ee* to 90% *ee* in the product. The biggest improvement was observed for the R_pS-configured imine **12b**, with an increase of 19% *ee* from the original (60% *ee* to 79% *ee*).

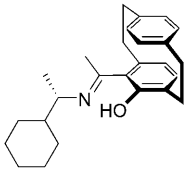
Table 3. Asymmetric 1,2-addition reactions with a range of substrates. See Scheme 8 for conditions.



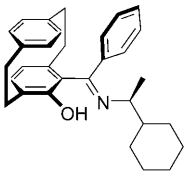
18b-f **19b-f**



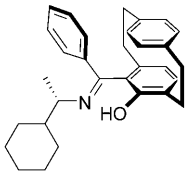
(R_p,S)-**11b**



(S_p,S)-**11b**



(R_p,S)-**12b**



(S_p,S)-**12b**

	Substrate	Ligand	Yield[a]	*ee* [%][b] (config)[c]
1	4-chlorobenzaldehyde	(S_p,S)-**11b**	>99	90 (*R*)
2	4-chlorobenzaldehyde	(R_p,S)-**11b**	>99	90 (*S*)
3	4-chlorobenzaldehyde	(S_p,S)-**12b**	96	90 (*R*)
4	4-chlorobenzaldehyde	(R_p,S)-**12b**	58	80 (*S*)
5	4-methoxybenzaldehyde	(S_p,S)-**11b**	93	69 (*R*)
6	4-methoxybenzaldehyde	(R_p,S)-**11b**	85	44 (*S*)
7	4-methoxybenzaldehyde	(S_p,S)-**12b**	82	52 (*R*)
8	4-methoxybenzaldehyde	(R_p,S)-**12b**	10	53 (*S*)
9	2-methoxybenzaldehyde	(S_p,S)-**11b**	>99	73 (*R*)
10	2-methoxybenzaldehyde	(R_p,S)-**11b**	>99	53 (*S*)
11	2-methoxybenzaldehyde	(S_p,S)-**12b**	>99	71 (*R*)
12	2-methoxybenzaldehyde	(R_p,S)-**12b**	>99	31 (*S*)
13	3,5-dimethoxybenzaldehyde	(S_p,S)-**11b**	>99	91 (*R*)
14	3,5-dimethoxybenzaldehyde	(R_p,S)-**11b**	>99	95 (*S*)
15	3,5-dimethoxybenzaldehyde	(S_p,S)-**12b**	>99	89 (*R*)
16	3,5-dimethoxybenzaldehyde	(R_p,S)-**12b**	>99	69 (*S*)
17	2-naphthaldehyde	(S_p,S)-**11b**	91	90 (*R*)
18	2-naphthaldehyde	(R_p,S)-**11b**	89	95 (*S*)
19	2-naphthaldehyde	(S_p,S)-**12b**	89	89 (*R*)
20	2-naphthaldehyde	(R_p,S)-**12b**	23	78 (*S*)

[a] Determined by GC after standard work-up. [b] Determined by GC (CP-Chirasil-Dex). [c] Determined by comparison with authentic samples.

Notable examples of the different activities and selectivities in a diastereomeric ligand pair are the imines (S_p,S)- and (R_p,S)-**12g**, which have a bulky 1-*tert*-butylethyl group at the side-chain. The S_p,S-configured imine **12g** produces the chiral alcohol with a conversion greater than 99% and an excellent 88% *ee* (*R*). In comparison, the R_p,S-configured imine **12g** yields (*S*)-1-phenylpropanol with a 25% conversion rate and with a low enantiomeric excess of 42%. In this case, a matched and an unmatched pair are formed. These results show that the choice of the side-chain is crucial to improve the system and is very sensitive towards modifications.

The next step was to evaluate these ligands with several other aromatic aldehydes. The results are shown in Table 3.

Generally, the AHPC-based ketimine **11b** shows a higher selectivity than the BHPC-based ketimine **12b**. It is interesting to note that the results with the BHPC ketimine **12b** again show a difference in the selectivity of the two diastereomers with the same substrate (for example, see entries 19 and 20). Furthermore, the *ortho*- and *para*-methoxybenzaldehydes show only a moderate enantiomeric excess: 44–73% *ee* for **11b** (entries 5, 6, 9, and 10) and 31–71% ee for **12b** (entries 7, 8, 11, and 12). This last effect cannot be rationalized by steric or electronic effects, since *meta*-substituted alkoxy or *para*-substituted chlorobenzaldehydes show good enantiomeric excesses.[17a] The other aromatic benzaldehyde derivatives show good to excellent enantiomeric excesses up to 95% *ee*.

Conclusion

In summary, we have prepared several new 5-acyl-4-hydroxy[2.2]paracyclophane **4**–**10**, which were used as key intermediates to create novel *N*,*O*-[2.2]paracyclophane ketimines with planar and central chirality. The X-ray structures of these compounds were determined. All configurations of the diastereomeric ketimines based on AHPC, BHPC, *p*-BrBHPC, and *p*-IHPC could be established by solving their X-ray structures or by using the enantiomerically pure AHPC. The new ketimines were examined with respect to their catalytic activity. It was found to be possible to tune the *N*,*O*-[2.2]paracyclophane ligands to obtain a higher enantiomeric excess of up to 95% *ee* and to increase their selectivity up to 19% *ee* during the initial generation of these ligands.

The side-chain has a strong influence on the catalytic performance. The best results are observed with the cyclohexyl-side chain, which is more crowded than the phenyl side-chain. However, using a bulkier group such as a *tert*-butyl group in the side-chain did not cause any further improvement. The BHPC derivatives show a vast difference in selectivity and activity between the diastereomeric pairs, whereas the AHPC-based diastereomeric pairs perform with similar activity and selectivity.

In future studies, we will extend this ligand system to similar ligand systems (thio analogues)[37] and novel substrates (α,β-unsaturated carbonyl compounds, imines).

Experimental Section

General: ^{1}H NMR: Bruker DP 300 (300 MHz), Bruker AM 400 (400 MHz), Bruker DRX 500 (500 MHz); $\delta = 7.26$ ppm for $CHCl_3$. The spectra were assumed to be first order. All coupling constants are absolute values. ^{13}C NMR: Bruker DP 300 (75 MHz), Bruker AM 400 (100 MHz), Bruker DRX 500 (125 MHz); $\delta = 77.00$ ppm for $CHCl_3$. IR: KBr pellets on a Bruker IFS88 IR. MS and EI-HRMS: Thermo Quest Finnegan MAT 90 (70 eV). Analytical GC (achiral stationary phase): Hewlett–Packard HP 5890 Series II, 12 m × 0.25 mm capillary column HP

I (carrier gas N_2). Enantiomeric excesses were determined by GC on a chiral stationary phase (CP-Chirasil-Dex). Optical rotations were determined on a Perkin–Elmer 241 polarimeter (Na, 589 nm). Melting points were measured with a MEL-TEMPII instrument from Laboratory Devices Inc., USA. TLC: silica gel coated aluminum plates (Merck, silica gel 60, F_{254}). Detection under UV light at 254 nm. Solvents and reagents were purchased from Acros, Aldrich, Fluka, or Merck.

Compounds **1**,[21] **2**,[21] **3**[21] and the diastereomeric pairs **11a**,[21] **11b**,[27,31] and **12a**[21] were synthesized according to literature procedures.

General procedure for diethylzinc addition to aldehydes: A 1 M solution of diethylzinc in hexane (1.0 mL) was added at room temperature to a 10 mL vial containing 0.01 mmol of the chiral ligand dissolved in 1.0 mL of dry toluene under an argon atmosphere. The mixture was stirred for 30 min at room temperature and then cooled to 0 °C. After an additional 30 min at 0 °C, the aldehyde (0.5 mmol) was added slowly and the reaction mixture was stirred for 12 h at 0 °C. The reaction mixture was then quenched with 1 M HCl and diluted with diethyl ether. The organic phase was washed twice with water and once with brine, and then dried with $MgSO_4$.

Synthesis of 4: Racemic 4-hydroxy[2.2]paracyclophane (1.13 g, 5.04 mmol) was dissolved in dry dichloromethane under argon and then cooled to 0 °C. $TiCl_4$ (6.55 mmol; 6.55 mL of a 1 M solution in dichloromethane) was added to this solution and the resulting mixture was stirred for 30 min at 0 °C. *para*-Bromobenzoylchloride (1.11 g, 5.04 mmol) was added at 0 °C with a syringe, and the solution was stirred for an additional 2 h at room temperature. The reaction was quenched with water and stirred for an additional 15 min. The phases were separated and the organic layer was washed twice with water and brine, and dried with $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield 5-*para*-bromobenzoyl-4-hydroxy[2.2]paracyclophane (2.00 g, 96 %) as a yellow solid. $R_f = 0.46$ (pentane/diethyl ether = 9:1); m.p. 122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.30$–2.55 (m, 4H), 2.70–2.80 (m, 1H), 2.95–3.05 (m, 1H), 3.08–3.16 (m, 1H), 3.35–3.44 (m, 1H), 6.20 (d, $J = 7.6$ Hz, 1H), 6.33 (dd, $J = 7.7$, 1.7 Hz, 1H), 6.39 (dd, $J = 7.8$, 1.8 Hz, 1H), 6.45 (dd, $J = 7.8$, 1.8 Hz, 1H), 6.52 (d, $J = 7.6$ Hz, 1H), 6.97 (dd, $J = 7.8$, 1.8 Hz, 1H), 7.50 (s, 4H), 11.70 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 30.21$, 33.92, 35.27, 37.05, 102.90, 126.85, 127.70, 130.93, 130.96, 131.79, 132.19, 132.86, 140.40, 127.62, 129.01, 137.86, 139.28, 140.79, 143.92, 161.93, 198.62 ppm; IR (KBr): $\tilde{\nu} = 3086$ (w), 3053 (w), 2935 (m), 2855 (m), 1923 (w), 1892 (w), 1795 (w), 1583 (m), 1415 (m), 1276 (m), 1170 (m), 1069 (m), 798 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 408/406 (5/15) [M^+], 327 (30), 309 (55), 223 (100), 195 (20); HRMS-EI: *m*/*z* calcd for $C_{23}H_{19}BrNO$: 406.0568; found: 406.0571.

Synthesis of 5: The procedure described above for the preparation of **4** was followed. Racemic 4-hydroxy[2.2]paracyclophane (0.72 g, 3.22 mmol), $TiCl_4$ (4.19 mmol of a 1 M solution in dichloromethane), and *para*-iodobenzoylchloride (0.85 g, 3.22 mmol) yielded 5-*para*-iodobenzoyl-4-hydroxy[2.2]paracyclophane as a yellow solid (1.01 g, 69 %) after purification by flash chromatography. $R_f = 0.27$ (pentane/diethyl ether = 2:1); m.p. 175 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.42$–2.50 (m, 1H), 2.53–2.68 (m, 3H), 2.89 (ddd, $J = 12.5$, 9.6, 2.3 Hz, 1H), 3.08 (ddd, $J = 12.8$, 10.6, 2.3 Hz, 1H), 3.23 (ddd, $J = 12.9$, 10.5, 5.2 Hz, 1H), 3.49 (ddd, $J = 13.0$, 10.4, 2.5 Hz, 1H), 6.35 (d, $J = 7.5$ Hz, 1H), 6.45 (dd, $J = 7.8$, 1.4 Hz, 1H), 6.51 (dd, $J = 7.8$, 1.4 Hz, 1H), 6.59 (dd, $J = 7.8$, 1.4 Hz, 1H), 6.64 (d, $J = 7.5$ Hz, 1H), 7.07 (dd, $J = 7.5$, 1.4 Hz, 1H), 7.5 (d, $J = 8.0$ Hz, 2H), 7.83 (d, $J = 8.0$ Hz, 2H), 11.79 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 30.17$, 33.87, 35.25, 37.04, 100.21, 120.82, 126.82, 127.65, 128.97, 130.84, 130.89, 131.41, 132.15, 132.83, 137.43, 137.75, 137.84, 139.79, 140.05, 140.38, 143.94, 161.91, 198.89 ppm; IR (KBr): $\tilde{\nu} = 3049$ (w), 2965 (w), 2937 (m), 2854 (w), 1894 (w), 1604 (m), 1578 (m), 1408 (m), 1237 (m), 1169 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 454 (56) [M^+], 436 (3), 349 (36), 327 (18), 223 (41), 195 (22), 165 (37), 118 (8), 104 (100), 89 (12), 43 (100); HRMS-EI: *m*/*z* calcd for $C_{23}H_{19}IO_2$: 454.0429; found: 454.0432.

Synthesis of 6: The procedure described above for the preparation of **4** was followed. Racemic 4-hydroxy[2.2]paracyclophane (1.57 g, 6.54 mmol), $TiCl_4$ (8.50 mmol of a 1 M solution in dichloromethane), and 2-naphthoyl chloride (1.24 g, 6.54 mmol) yielded 5-(2-naphthoyl)-4-hydroxy[2.2]paracyclophane as a yellow solid (2.10 g, 84 %) after purification by flash chromatography. $R_f = 0.30$ (pentane/diethyl ether = 9:1); m.p. 149 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.45$–2.51 (m, 1H), 2.58–2.63 (m, 2H), 2.68 (ddd, $J = 10.6$, 5.1, 2.3 Hz, 1H), 2.81–2.88 (m, 1H), 3.12 (ddd, $J = 10.6$, 4.6, 2.6 Hz, 1H), 3.25–3.32 (m, 1H), 3.56 (ddd, $J = 10.4$, 5.6, 2.8 Hz, 1H), 6.39 (d, $J = 7.5$ Hz, 1H), 6.52–6.58 (m, 2H), 6.61 (dd, $J = 7.8$, 1.7 Hz, 1H), 6.69 (d, $J = 7.6$ Hz, 1H), 7.2 (dd, $J = 7.8$, 1.8 Hz, 1H), 7.57–7.61 (m, 1H), 7.62–7.67 (m, 1H), 7.86–7.90 (m, 1H), 7.92–7.97 (m, 3H), 8.24–8.29 (m, 1H), 11.99 ppm (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 30.26$, 33.92, 35.28, 37.07, 121.36, 126.78, 126.91, 127.70, 127.87, 128.42, 128.84, 129.52, 130.96, 132.17, 132.45, 137.79, 138.03, 140.06, 140.19, 144.32, 161.91, 199.88 ppm; IR (KBr): $\tilde{\nu} = 3049$ (m), 3012 (m), 2977 (m), 2935 (s), 2895 (m), 2852 (m), 1604 (m), 1570 (s), 1232 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 378 (20) [M^+], 273 (68), 208 (24), 145 (10), 104 (100), 58 (16), 43 (39); HRMS-EI: *m*/*z* calcd for $C_{23}H_{28}O_2$: 378.1619; found: 378.1616.

Synthesis of 7: The procedure described above for the preparation of **4** was followed. Racemic 4-hydroxy[2.2]paracyclophane (0.50 g, 2.23 mmol), $TiCl_4$ (2.90 mmol of a 1 M solution in dichloromethane), and butyryl chloride (0.23 mL, 2.23 mmol) yielded 5-butyryl-4-hydroxy-[2.2]paracyclophane as a yellow solid (0.48 g, 73 %) after purification by flash chromatography. $R_f = 0.37$ (pentane/diethyl ether = 9:1); m.p. 53 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.01$ (t, $J = 7.6$ Hz, 3H), 1.69–1.84 (m, 2H), 2.55–2.63 (m, 1H), 2.74–2.81 (m, 1H), 2.83–2.89 (m, 2H), 3.00–3.06 (m, 2H), 3.16–3.25 (m, 2H), 3.46 (ddd, $J = 12.8$, 10.2, 2.4 Hz, 1H), 3.61 (ddd, $J = 12.0$, 9.8, 2.3 Hz, 1H), 6.30–6.36 (m, 2H), 6.47 (dd, $J = 7.8$, 1.3 Hz, 1H), 6.55 (d, $J = 7.6$ Hz, 1H), 6.64 (dd, $J = 7.8$, 1.3 Hz, 1H), 7.00 (dd, $J = 7.6$, 1.5 Hz, 1H), 12.7 ppm (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 13.85$, 19.03, 30.12, 33.76, 35.61, 37.50, 44.89, 122.72, 127.14, 127.58, 131.44, 131.88, 133.03, 133.06, 137.64, 139.35, 140.17, 142.13, 161.73, 207.48 ppm; IR (KBr): $\tilde{\nu} = 3435$ (w), 3011 (w), 2963 (m), 2929 (m), 2853 (m), 1893 (w), 1731 (w), 1606 (m), 1462 (w), 1212 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 294 (68) [M^+], 279 (69), 152 (5), 208 (19), 189 (56), 147 (13), 104 (100), 91 (9), 43 (67); HRMS-EI: *m*/*z* calcd for $C_{20}H_{22}O_2$: 294.1620; found: 294.1623.

Synthesis of 8: The procedure described above for the preparation of **4** was followed. Racemic 4-hydroxy[2.2]paracyclophane (0.50 g, 2.23 mmol), $TiCl_4$ (2.90 mmol of a 1 M solution in dichloromethane), and lauroyl chloride (0.52 mL, 2.23 mmol) yielded 5-lauroyl-4-hydroxy-[2.2]paracyclophane as a yellow solid (0.71 g, 79 %) after purification by flash chromatography. $R_f = 0.54$ (pentane/diethyl ether = 9:1); m.p. 79 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.90$ (t, $J = 7.0$ Hz, 3H), 1.22–1.35 (m, 16H), 1.62–1.72 (m, 2H), 2.57 (ddd, $J = 13.2$, 10.4, 5.0 Hz, 1H), 2.76 (ddd, $J = 13.2$, 9.5, 7.0 Hz, 1H), 2.82–2.89 (m, 2H), 2.97–3.05 (m, 2H), 3.15–3.23 (m, 2H), 3.44 (ddd, $J = 13.1$, 10.2, 2.7 Hz, 1H), 3.59 (ddd, $J = 11.8$, 9.7, 2.4 Hz, 1H), 6.29–6.34 (m, 2H), 6.46 (dd, $J = 7.7$, 1.8 Hz, 1H), 6.55 (d, $J = 7.5$ Hz, 1H), 6.64 (dd, $J = 7.7$, 1.8 Hz, 1H), 6.99 (dd, $J = 7.7$, 1.8 Hz, 1H), 12.63 ppm (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 14.12$, 22.68, 25.63, 19.33, 29.34, 29.41, 29.44, 29.59, 30.12, 31.91, 33.77, 35.62, 37.50, 43.06, 127.12, 127.58, 129.34, 131.43, 131.87, 133.02, 133.03, 137.62, 139.33, 140.16, 142.09, 161.69, 207.69 ppm; IR (KBr): $\tilde{\nu} = 2927$ (m), 2854 (m), 1893 (w), 1740 (m), 1621 (m), 1585 (m), 1470 (m), 721 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 406 (1) [M^+], 279 (1), 208 (31), 104 (100), 78 (5); HRMS-EI: *m*/*z* calcd for $C_{28}H_{38}O_2$: 406.2872; found: 406.2867.

Synthesis of 9: The procedure described above for the preparation of **4** was followed. Racemic 4-hydroxy[2.2]paracyclophane (0.50 g, 2.23 mmol), $TiCl_4$ (2.90 mmol of a 1 M solution in dichloromethane), and isobutyryl chloride (0.23 mL, 2.23 mmol) yielded 5-isobutyryl-4-hydroxy-[2.2]paracyclophane as a yellow solid (0.35 g, 53 %) after purification by flash chromatography. $R_f = 0.35$ (pentane/diethyl ether = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.04$ (d, $J = 6.8$ Hz, 3H), 1.33 (d, $J = 6.8$ Hz, 3H), 2.57 (ddd, $J = 13.3$, 7.8, 2.6 Hz, 1H), 2.79–2.86 (m, 1H), 3.03–3.14 (m, 3H), 3.21 (ddd, $J = 13.0$, 7.5, 2.7 Hz, 1H), 3.33 (sept, $J = 6.8$ Hz, 1H), 3.41–3.48 (m, 2H), 6.32 (d, $J = 7.7$ Hz, 1H), 6.35 (dd, $J = 7.7$, 2.0 Hz, 1H), 6.51 (dd, $J = 7.9$, 1.6 Hz, 1H), 6.55 (d, $J = 7.5$ Hz, 1H), 6.64 (dd, $J = 7.9$, 2.0 Hz, 1H), 7.01 (dd, $J = 7.9$, 1.9 Hz, 1H), 12.02 ppm (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 18.39$, 21.78, 30.35, 33.82, 35.86, 37.08, 40.43,

122.40, 127.02, 127.70, 129.01, 131.41, 132.16, 132.76, 137.56, 139.46, 140.25, 141.99, 161.02, 212.65 ppm; IR (KBr): $\tilde{\nu}$ = 3447 (w), 2965 (m), 2931 (m), 2871 (w), 2853 (m), 1890 (w), 1616 (m), 1412 (s), 1260 (m), 1260 (m), 1221 (m), 104 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 294 (100) [M^+], 189 (67), 175 (64), 147 (16), 104 (56), 91 (7); HRMS-EI: *m/z* calcd for $C_{20}H_{22}O_2$: 294.1620; found: 294.1618.

Synthesis of 10: The procedure described above for the preparation of **4** was followed. Racemic 4-hydroxy[2.2]paracyclophane (0.50 g, 2.23 mmol), $TiCl_4$ (2.90 mmol of a 1 M solution in dichloromethane), and cyclohexanecarbonyl chloride (0.31 mL, 2.23 mmol) yielded 5-cyclohexanoyl-4-hydroxy[2.2]paracyclophane as a yellow oil (0.22 g, 30%) after purification by flash chromatography. R_f = 0.40 (pentane/diethyl ether = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25–1.31 (m, 3H), 1.32–1.40 (m, 1H), 1.61–1.67 (m, 1H), 1.71–1.80 (m, 3H), 1.90–1.96 (m, 1H), 1.98–2.05 (m, 1H), 2.57 (ddd, *J* = 13.1, 7.6, 2.6 Hz, 1H), 2.78–2.85 (m, 1H), 2.95–3.22 (m, 5H), 3.39–3.46 (m, 2H), 6.30–6.35 (m, 2H), 6.50 (dd, *J* = 7.8, 1.6 Hz, 1H), 6.54 (d, *J* = 7.6 Hz, 1H), 6.64 (dd, *J* = 7.8, 2.0 Hz, 1H), 7.01 (dd, *J* = 7.8, 2.0 Hz, 1H), 12.04 ppm (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.38, 25.76, 26.26, 28.36, 30.32, 32.01, 33.82, 35.93, 37.04, 51.19, 122.56, 126.92, 127.67, 129.02, 131.43, 132.11, 132.74, 137.55, 139.37, 140.25, 141.99, 160.98, 211.56 ppm; IR (KBr): $\tilde{\nu}$ = 3437 (w), 3010 (w), 2930 (m), 2854 (m), 1890 (w), 1611 (m), 1412 (m), 1241 cm^{-1} (w); MS (70 eV, EI): *m/z* (%): 334 (100) [M^+], 279 (8), 229 (17), 201 (10), 175 (12), 148 (16), 104 (23); HRMS-EI: *m/z* calcd for $C_{23}H_{26}O_2$: 334.1932; found: 334.1929.

Synthesis of (S_P,*S*)-11c: Enantiomerically pure (S_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 0.10 g, 0.37 mmol) was dissolved in toluene (30 mL) and (*S*)-indan-1-ylamine (**C**; 0.15 g, 1.13 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield (S_P,*S*)-**11c** as an orange solid (92 mg, 65%). R_f = 0.16 (pentane/diethyl ether = 9:1); m.p. 223 °C; $[\alpha]_D^{20}$ = −513 (*c* = 0.30 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.05–2.20 (m, 1H), 2.46 (s, 3H), 2.52–2.60 (m, 1H), 2.65–2.72 (m, 1H), 2.85–3.25 (m, 7H), 3.28–3.50 (m, 2H), 5.31 (t, *J* = 7.0 Hz, 1H), 6.21 (d, *J* = 7.8 Hz, 1H), 6.31 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.39 (d, *J* = 7.7 Hz, 1H), 6.46 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.61 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.81 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.25–7.35 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.62, 30.47, 30.95, 33.85, 34.45, 35.53, 37.31, 63.25, 122.49, 123.67, 125.09, 125.71, 126.80, 127.23, 127.84, 129.39, 129.94, 131.51, 132.70, 136.14, 137.53, 139.99, 140.68, 143.58, 162.42, 170.34 ppm; IR (KBr): $\tilde{\nu}$ = 3036(m), 3016 (m), 2963 (s), 2927 (s), 2846 (m), 1970 (w), 1579 (s), 1439 (s), 1295 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 381 (100) [M^+], 277 (15), 266 (32), 248 (12), 161 (77), 117 (62), 91 (8); HRMS-EI: *m/z* calcd for $C_{27}H_{27}NO$: 381.2093; found: 381.2086.

Synthesis of (S_P,*S*)-11d: Enantiomerically pure (S_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 0.10 g, 0.37 mmol) was dissolved in toluene (30 mL) and (*S*)-1-(4-fluorophenyl)ethylamine (**D**; 0.16 g, 1.13 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield (S_B*S*)-**11d** as an orange solid (0.11 g, 78%). R_f = 0.07 (pentane/diethyl ether = 9:1); m.p. 85 °C; $[\alpha]_D^{20}$ = −241 (*c* = 0.31 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63 (d, *J* = 6.5 Hz, 3H), 2.23 (s, 3H), 2.34–2.43 (m, 1H), 2.47–2.56 (m, 1H), 2.78–2.88 (m, 1H), 2.91–3.04 (m, 2H), 3.12–3.26 (m, 2H), 3.36–3.46 (m, 1H), 4.85 (q, *J* = 6.5 Hz, 1H), 6.06 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.17 (d, *J* = 7.6 Hz, 1H), 6.40 (d, *J* = 7.6 Hz, 1H), 6.45 (dd, *J* = 7.8, 1.6 Hz, 1H), 6.55 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.97 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.11 (t, *J* = 8.7 Hz, 2H), 7.49 ppm (dd, *J* = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.40, 24.99, 30.49, 33.92, 35.41, 37.14, 57.61, 115.58, 115.80, 122.53, 125.87, 127.06, 127.98, 128.06, 128.87, 129.31, 130.07, 131.56, 132.71, 136.31, 137.61, 139.98, 140.45, 140.48, 140.81, 160.74, 162.36, 163.18, 170.10 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −115.70 ppm; IR (KBr): $\tilde{\nu}$ = 2957 (m), 2926 (m), 2854 (m), 1881 (w), 1594 (m), 1508 (m), 1431 (m), 1226 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 387 (100) [M^+], 283 (37), 248 (5), 161 (34), 149 (6), 123 (32), 103 (10), 91 (4); HRMS-EI: *m/z* calcd for $C_{26}H_{26}FNO$: 387.1998; found: 387.1996.

Synthesis of (S_P,*S*)-11e: Enantiomerically pure (S_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 0.10 g, 0.37 mmol) was dissolved in toluene (30 mL) and (*S*)-1-(4-methoxy-phenyl)ethylamine (**E**; 0.17 g, 1.13 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield (S_P,*S*)-**11e** as an orange solid (81 mg, 55%). R_f = 0.13 (pentane/ethyl acetate = 19:1); m.p. 96 °C; $[\alpha]_D^{20}$ = −187 (*c* = 0.08 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.61 (d, *J* = 6.5 Hz, 3H), 2.21 (s, 3H), 2.33–2.43 (m, 1H), 2.46–2.55 (m, 1H), 2.74–2.83 (m, 1H), 2.90–3.04 (m, 2H), 3.15–3.25 (m, 2H), 3.38–3.45 (m, 1H), 3.79 (s, 3H), 4.79 (q, *J* = 6.5 Hz, 1H), 6.08 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.13 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.38 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.44 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.53 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.92–6.99 (m, 6H), 7.38–7.44 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.29, 25.00, 30.36, 33.92, 35.40, 37.26, 55.33, 57.40, 114.22, 122.19, 125.58, 127.06, 127.54, 129.52, 130.22, 131.45, 132.67, 136.22, 136.77, 137.64, 139.95, 140.84, 158.77, 163.49, 169.85 ppm; IR (KBr): $\tilde{\nu}$ = 2925 (s), 2854 (s), 1875 (w), 1739 (w), 1581 (m), 1461 (m), 1246 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 399 (4) [M^+], 266 (92), 220 (30), 205 (100), 162 (60), 136 (82), 108 (68), 91 (35); HRMS-EI: *m/z* calcd for $C_{27}H_{29}NO_2$: 399.2198; found: 399.2195.

Synthesis of (S_P,*S*)-11f: Enantiomerically pure (S_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 0.10 g, 0.37 mmol) was dissolved in toluene (30 mL) and (*S*)-1-phenylpropylamine (**F**; 0.15 g, 1.13 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield (S_P,*S*)-**11f** as an orange solid (0.12 g, 81%). R_f = 0.21 (pentane/diethyl ether = 9:1); m.p. 165 °C; $[\alpha]_D^{20}$ = −357 (*c* = 0.58 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.5 Hz, 3H), 1.95–2.15 (m, 2H), 2.22 (s, 3H), 2.25–2.35 (m, 1H), 2.45–2.55 (m, 1H), 2.75–2.85 (m, 1H), 2.65–2.75 (m, 1H), 2.95–3.05 (m, 1H), 3.15–3.25 (m, 2H), 3.40–3.50 (m, 1H), 4.58 (t, *J* = 6.3 Hz, 1H), 6.02 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.15 (d, *J* = 7.6, 1.7 Hz, 1H), 6.38 (d, *J* = 7.6 Hz, 1H), 6.44 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.54 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.00 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.30 (tt, *J* = 7.3, 1.5 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 2H,), 7.48 ppm (dd, *J* = 7.7, 1.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.09, 20.55, 30.49, 32.00, 33.90, 35.36, 37.28, 64.74, 122.25, 125.63, 127.03, 127.11, 127.33, 128.71, 128.86, 129.46, 130.27, 130.92, 131.47, 132.46, 136.21, 137.62, 139.93, 140.88, 143.32, 163.29, 170.77 ppm; IR (KBr): $\tilde{\nu}$ = 3651 (w), 3030 (m), 2977 (s), 2961 (s), 2927 (s), 2850 (s), 1885 (w), 1582 (s), 1435 (s), 1264 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 383 (10) [M^+], 279 (8), 233 (10), 205 (9), 149 (100); HRMS-EI: *m/z* calcd for $C_{27}H_{29}NO$: 383.2243; found: 383.2249.

Synthesis of (S_P,*S*)-11g: Enantiomerically pure (S_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 0.10 g, 0.37 mmol) was dissolved in toluene (30 mL) and (*S*)-3,3-dimethyl-2-aminobutane (**G**; 0.11 g, 1.13 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield (S_P,*S*)-**11g** as an orange solid (0.10 g, 80%). R_f = 0.18 (pentane/diethyl ether = 9:1); $[\alpha]_D^{20}$ = −572 (*c* = 0.28 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (s, 9H), 1.17 (d, *J* = 6.5 Hz, 3H), 2.28 (s, 3H), 2.52 (ddd, *J* = 15.8, 10.1, 5.2 Hz, 1H), 2.72 (ddd, *J* = 13.2, 9.8, 6.9 Hz, 1H), 2.92–2.99 (m, 1H), 3.00–3.11 (m, 2H), 3.19 (ddd, *J* = 12.4, 10.1, 5.2 Hz, 1H), 3.35 (ddd, *J* = 12.4, 9.2, 2.5 Hz, 1H), 3.42 (ddd, *J* = 12.9, 10.1, 2.5 Hz, 1H), 3.50 (q, *J* = 6.5 Hz, 1H), 6.16 (d, *J* = 7.2 Hz, 1H), 6.35 (dd, *J* = 7.4, 1.6 Hz, 1H), 6.41 (d, *J* = 7.2 Hz, 1H), 6.54 (dd, *J* = 7.7, 1.3 Hz, 1H), 6.65 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.00 (dd, *J* = 7.9, 1.8 Hz, 1H), 16.30 ppm (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.39, 19.68, 26.67, 30.54, 33.94, 34.70, 35.58, 37.28, 122.05, 125.02, 127.15, 129.57, 130.58, 131.64, 132.62, 136.34, 137.70, 140.21, 140.80, 164.62, 168.73 ppm; IR (KBr): $\tilde{\nu}$ = 3421 (w), 2963 (s), 2927 (s), 2853 (m), 1791 (w), 1580 (m), 1435 (m), 1261 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 349 (64) [M^+], 245 (75), 188 (87), 149 (7), 91 (10), 43 (100); HRMS-EI: *m/z* calcd for $C_{24}H_{31}NO$: 349.2406; found: 349.2409.

Synthesis of (S_P,*S*)-11i: Enantiomerically pure (S_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 0.10 g, 0.37 mmol) was dissolved in toluene (30 mL) and (*S*)-1-naphthyl-2-ylethylamine (**I**; 0.19 g, 1.13 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield (S_P,*S*)-**11i** as an orange solid (0.11 g, 71 %). R_f = 0.11 (pentane/diethyl ether = 9:1); m.p. 162 °C. $[\alpha]_D^{20} = -77$ (c = 0.26 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.74 (d, J = 6.5 Hz, 3H), 2.27 (s, 3H), 2.33–2.41 (m, 1H), 2.49–2.57 (m, 1H), 2.80–2.95 (m, 2H), 2.98–3.07 (m, 1H), 3.15–3.26 (m, 1H), 3.41–3.52 (m, 1H), 4.99 (q, J = 6.5 Hz, 1H), 6.13–6.23 (m, 2H), 6.40 (d, J = 7.4 Hz, 1H), 6.47 (dd, J = 7.8, 1.6 Hz, 1H), 6.55 (dd, J = 7.8, 1.6 Hz, 1H), 7.09 (dd, J = 7.8, 1.5 Hz, 1H), 7.45–7.53 (m, 2H), 7.63–7.67 (m, 1H), 7.83–7.89 (m, 2H), 7.90–7.95 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.49, 22.69, 30.55, 33.96, 35.40, 37.15, 58.26, 122.44, 12476, 124.91, 125.71, 125.92, 126.40, 127.15, 127.87, 129.46, 130.29, 131.59, 132.66, 136.37, 137.68, 140.05, 140.90, 142.11, 163.12, 170.48 ppm; IR (KBr): $\tilde{\nu}$ = 3036 (w), 3018 (w), 2924 (m), 2854 (m), 1583 (m), 1507 (m), 1455 (m), 1245 cm^{-1} (m). MS (70 eV, EI), *m*/*z* (%): 419 (37) [M^+], 315 (10), 161 (16), 155 (61), 58 (35), 43 (100); HRMS-EI: *m*/*z* calcd for $C_{30}H_{29}NO$: 419.2249; found: 419.2251.

Synthesis of (R_P,*S*)-11c: Enantiomerically pure (R_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 30 mg, 0.11 mmol) was dissolved in toluene (30 mL) and (*S*)-indan-1-ylamine (**C**; 50 mg, 0.33 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield 39 mg (93 %) of **11c** as a yellow-orange solid. R_f = 0.25 (pentane/diethyl ether = 9:1); m.p. 185 °C; $[\alpha]_D^{20} = +651$ (c = 0.83 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.21–2.30 (m, 1H), 2.47 (s, 3H), 2.50–2.57 (m, 1H), 2.63–2.74 (m, 2H), 2.91–3.01 (m, 2H), 3.03–3.15 (m, 3H), 3.16–3.27 (m, 1H), 3.35–3.50 (m, 2H), 5.31 (t, J = 8.2 Hz, 1H), 6.27 (d, J = 7.8 Hz, 1H), 6.40 (dd, J = 7.8, 1.9 Hz, 1H), 6.45 (d, J = 7.8 Hz, 1H), 6.49 (dd, J = 7.8, 1.9 Hz, 1H), 6.64 (dd, J = 7.8, 1.9 Hz, 1H), 6.94 (dd, J = 7.8, 1.9 Hz, 1H), 7.22–7.34 (m, 3H), 7.35–7.39 ppm (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.66, 30.41, 30.91, 33.85, 34.72, 35.48, 37.33, 63.34, 122.65, 123.84, 124.81, 125.89, 127.02, 127.23, 127.74, 129.31, 129.61, 131.48, 132.76, 136.01, 137.58, 140.03, 140.69, 143.99, 161.84, 170.77 ppm; IR (KBr): $\tilde{\nu}$ = 3020 (m), 2959 (m), 2929 (s), 1886 (w), 1595 (s), 1581 (s), 1443 (s), 1274 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 381 (70) [M^+], 358 (6), 277 (10), 266 (34), 248 (5), 161 (88), 117 (100), 58 (4), 43 (13); HRMS-EI: *m*/*z* calcd for $C_{27}H_{27}NO$: 381.2093; found: 381.2097.

Synthesis of (R_P,*S*)-11d: Enantiomerically pure (R_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 40 mg, 0.15 mmol) was dissolved in toluene (30 mL) and (*S*)-1-(4-fluorophenyl)ethylamine (**D**; 60 mg, 0.46 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield 37 mg (64 %) of **11d** as a yellow-orange solid. R_f = 0.20 (pentane/diethyl ether = 9:1); m.p. 130 °C; $[\alpha]_D^{20} = +733$ (c = 0.06 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.75 (d, J = 6.5 Hz, 3H), 2.29 (s, 3H), 2.57 (ddd, J = 10.6, 5.0, 2.2 Hz, 1H), 2.63–2.70 (m, 1H), 2.87–2.97 (m, 1H), 3.05 (dt, J = 10.8, 2.5 Hz, 1H), 3.10–3.17 (m, 1H), 3.17–3.25 (m, 1H), 3.36–3.48 (m, 2H), 4.90 (q, J = 6.5 Hz, 1H), 6.24 (d, J = 7.6 Hz, 1H), 6.46 (dd, J = 7.6, 2.6 Hz, 2H), 6.52 (dd, J = 8.0, 1.6 Hz, 1H), 6.65 (dd, J = 7.9, 1.6 Hz, 1H), 7.02–7.12 (m, 3H), 7.33–7.39 (m, 2H), 15.75 ppm (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.48, 25.46, 30.47, 30.90, 33.90, 35.48, 37.34, 57.55, 115.61, 115.78, 122.38, 125.82, 127.18, 127.82, 127.88, 129.48, 129.65, 131.53, 132.82, 136.24, 137.64, 139.58, 139.61, 140.06, 140.85, 160.89, 162.84, 170.39 ppm; ^{19}F NMR (282 MHz, $CDCl_3$): δ = −115.70 ppm; IR (KBr): $\tilde{\nu}$ = 3734 (w), 2966 (m), 2927 (s), 2851 (m), 1889 (w), 1734 (w), 1586 (m), 1508 (s), 1436 (m), 1225 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 387 (14) [M^+], 266 (100), 161 (91), 123 (22), 120 (20), 104 (92), 91 (11), 43 (33); HRMS-EI: *m*/*z* calcd for $C_{26}H_{26}NOF$: 387.1998; found: 387.1994.

Synthesis of (R_P,*S*)-11e: Enantiomerically pure (R_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 50 mg, 0.19 mmol) was dissolved in toluene (30 mL) and (*S*)-1-(4-methoxyphenyl)ethylamine (**E**; 90 mg, 0.57 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield 55 mg (73 %) of **11e** as an orange solid. R_f = 0.09 (pentane/ethyl acetate = 19:1); $[\alpha]_D^{20} = +918$ (c = 0.18 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.62 (d, J = 6.5 Hz, 3H), 2.29 (s, 3H), 2.54 (ddd, J = 12.9, 10.7, 5.3 Hz, 1H), 2.66 (ddd, J = 13.3, 9.3, 7.8 Hz, 1H), 2.90 (ddd, J = 14.1, 9.4, 7.4 Hz, 1H), 3.03 (ddd, J = 10.8, 4.4, 2.6 Hz, 1H), 3.12 (ddd, J = 13.3, 11.0, 2.8 Hz, 1H), 3.20 (ddd, J = 12.8, 10.4, 5.3 Hz, 1H), 3.37–3.47 (m, 2H), 3.80 (s, 3H), 4.85 (q, J = 6.5 Hz, 1H), 6.19 (d, J = 6.4 Hz, 1H), 6.41–6.46 (m, 2H), 6.51 (dd, J = 7.8, 1.7 Hz, 1H), 6.63 (dd, J = 7.8, 1.7 Hz, 1H), 6.89 (dt, J = 8.5, 2.1 Hz, 2H), 7.07 (dd, J = 7.8, 1.9 Hz, 1H), 7.27–7.31 (m, 2H), 16.00 ppm (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.35, 25.44, 30.48, 33.89, 35.47, 37.38, 55.29, 57.44, 114.21, 122.13, 125.53, 127.34, 129.62, 129.68, 131.42, 132.76, 135.86, 136.13, 137.62, 140.06, 140.79, 158.64, 163.62, 170.03 ppm; IR (KBr): $\tilde{\nu}$ = 3733 (w), 2964 (m), 2927 (m), 2850 (m), 1884 (w), 1762 (w), 1581 (m), 1512 (s), 1439 (m), 1246 cm^{-1} (s); MS (70 eV, EI): *m*/*z* (%): 399 (20) [M^+], 266 (10), 161 (11), 135 (100), 124 (9), 104 (17), 91 (5), 58 (26), 43 (85); HRMS-EI: *m*/*z* calcd for $C_{27}H_{29}NO_2$: 399.2198; found: 399.2194.

Synthesis of (R_P,*S*)-11f: Enantiomerically pure (R_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 40 mg, 0.13 mmol) was dissolved in toluene (30 mL) and (*S*)-1-phenylpropylamine (**F**; 50 mg, 0.39 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield 40 mg (81 %) of **11f** as an orange solid. R_f = 0.29 (pentane/diethyl ether = 9:1); m.p. 133 °C; $[\alpha]_D^{20} = +1108$ (c = 0.43 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.16 (t, J = 7.5 Hz, 3H), 2.20–2.23 (m, 2H), 2.25 (s, 3H), 2.55 (ddd, J = 12.7, 10.5, 5.1 Hz, 1H), 2.69 (ddd, J = 9.4, 7.4, 2.2 Hz, 1H), 2.93 (ddd, J = 9.4, 7.4, 2.2 Hz, 1H), 3.05 (ddd, J = 12.9, 10.5, 2.5 Hz, 1H), 3.11 (ddd, J = 12.7, 9.6, 2.2 Hz, 1H), 3.22 (ddd, J = 12.7, 10.5, 5.1 Hz, 1H), 3.40 (ddd, J = 12.1, 9.6, 2.5 Hz, 1H), 3.47 (ddd, J = 12.9, 10.1, 2.5 Hz, 1H), 4.61 (dd, J = 7.8, 5.6 Hz, 1H), 6.19 (d, J = 7.4 Hz, 1H), 6.42–6.46 (m, 1H), 6.53 (dd, J = 7.8, 1.7 Hz, 1H), 6.66 (dd, J = 7.8, 1.7 Hz, 1H), 7.08 (dd, J = 7.8, 1.7 Hz, 1H), 7.22–7.27 (m, 1H), 7.30–7.36 (m, 4H), 16.25 ppm (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.34, 20.73, 30.55, 32.68, 33.93, 35.53, 37.42, 64.65, 122.08, 125.43, 126.85, 127.15, 127.21, 128.72, 129.66, 130.03, 131.55, 132.75, 136.34, 137.67, 137.67, 140.14, 140.89, 142.39, 164.22, 171.22 ppm; IR (KBr): $\tilde{\nu}$ = 3733 (w), 3005 (m), 2967 (m), 2924 (m), 1884 (w), 1589 (m), 1450 (m), 1245 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 383 (100) [M^+], 279 (65), 250 (9), 160 (38), 119 (12), 91 (39), 58 (29), 43 (86); HRMS-EI: *m*/*z* calcd for $C_{27}H_{29}NO$: 383.2243; found: 383.2252.

Synthesis of (R_P,*S*)-11g: Enantiomerically pure (R_P)-5-acetyl-4-hydroxy-[2.2]paracyclophane (**2**; 0.10 g, 0.37 mmol) was dissolved in toluene (30 mL) and (*S*)-3,3-dimethyl-2-aminobutane (**G**; 0.11 g, 1.13 mmol) was added. After adding a catalytic amount of dibutyltin diacetate, the reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography to yield 0.10 g (80 %) of **11g** as an orange solid. R_f = 0.16 (pentane/ethyl acetate = 19:1); m.p. 102 °C; $[\alpha]_D^{20} = +408$ (c = 0.80 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 9H), 1.31 (d, J = 6.6 Hz, 3H), 2.33 (s, 3H), 2.49–2.61 (m, 2H), 2.84–2.92 (m, 1H), 3.00 (ddd, J = 13.4, 10.7, 2.7 Hz, 1H), 3.10–3.21 (m, 2H), 3.40–3.48 (m, 2H), 3.58 (q, J = 6.6 Hz, 1H), 6.21 (d, J = 7.6 Hz, 1H), 6.34 (dd, J = 7.8, 2.1 Hz, 1H), 6.43 (d, J = 7.6 Hz, 1H), 6.47 (dd, J = 7.8, 1.7 Hz, 1H), 6.61 (dd, J = 7.8, 1.8 Hz, 1H), 6.99 (dd, J = 7.6, 1.8 Hz, 1H), 15.90 ppm (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.85, 19.44, 26.58, 30.35, 33.86, 34.52, 35.47, 37.28, 62.66, 122.17, 125.55, 127.01, 129.55, 129.62, 131.21, 132.84, 135.76, 137.52, 140.01, 140.61, 163.05, 169.23 ppm; IR (KBr): $\tilde{\nu}$ = 3421 (w), 2963 (s), 2927 (s), 2853 (m), 1791 (w), 1580 (m), 1435 (m), 1261 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 349 (83) [M^+], 245 (86), 188 (100), 161 (18), 145 (11), 104 (8), 91 (2), 43 (18); HRMS-EI: *m*/*z* calcd for $C_{24}H_{31}NO$: 349.2406; found: 349.2410.

Synthesis of (R_P,*S*)- and (S_P,*S*)-12b: Racemic 5-benzoyl-4-hydroxy-[2.2]paracyclophane (**3**; 0.66 g, 2.01 mmol) was dissolved in toluene (100 mL) under argon and (*S*)-cyclohexylethylamine (**A**; 0.77 g,

6.03 mmol) and $TiCl_4$ (2.61 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the R_pS diastereomer (0.31 g, 35%) as an orange-red solid. $R_f = 0.35$ (pentane/diethyl ether = 9:1); m.p. 162 °C; $[\alpha]_D^{20} = +630$ ($c = 0.33$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.98–1.07 (m, 1H), 1.10–1.20 (m, 2H), 1.31–1.38 (m, 1H), 1.49 (d, $J = 6.4$ Hz, 3H), 1.54–1.75 (m, 7H), 2.19–2.27 (m, 1H), 2.30–2.37 (m, 1H), 2.55 (ddd, $J = 10.8$, 4.8, 2.3 Hz, 1H), 2.86 (dd, $J = 13.1$, 9.61 Hz, 1H), 3.03 (ddd, $J = 10.8$, 4.8, 2.7 Hz, 1H), 3.10–3.15 (m, 1H), 3.20–3.26 (m, 1H), 3.39 (quin, $J = 6.5$ Hz, 1H), 3.51 (ddd, $J = 10.4$, 5.1, 2.7 Hz, 1H), 6.01 (d, $J = 7.3$ Hz, 1H), 6.44–6.49 (m, 3H), 6.54–6.60 (m, 2H), 7.07–7.12 (m, 1H), 7.43–7.51 (m, 3H), 7.59–7.63 ppm (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 20.57$, 26.08, 26.14, 26.18, 29.06, 29.62, 30.27, 33.95, 35.47, 36.50, 44.40, 58.67, 124.87, 126.93, 128.75, 129.03, 129.73, 130.03, 130.07, 131.11, 133.02, 135.94, 136.81, 137.90, 139.93, 143.38, 168.24, 170.46 ppm; IR (KBr): $\tilde{\nu} = 3029$ (w), 3007 (w), 2928 (m), 2852 (m), 1892 (w), 1732 (w), 1561 (m), 1437 (m), 1238 cm^{-1} (w); MS (70 eV, EI): m/z (%): 437 (1) [M^+], 278 (2), 223 (9), 149 (100), 120 (2), 105 (3), 71 (2), 57 (5), 43 (1); HRMS-EI: m/z calcd for $C_{31}H_{35}NO$: 437.2718; found: 437.2715. The second band gave the S_pS diastereomer (0.36 g, 41%) as an orange-red solid. $R_f = 0.24$ (pentane/diethyl ether = 9:1); m.p. 130 °C; $[\alpha]_D^{20} = -878$ ($c = 0.47$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.93$ (d, $J = 6.5$ Hz, 3H), 1.20–1.48 (m, 6H), 1.63–1.71 (m, 2H), 1.79 (d, $J = 12.2$ Hz, 1H), 1.89 (d, $J = 12.2$ Hz, 1H), 1.97 (d, $J = 12.2$ Hz, 1H), 2.13 (d, $J = 12.2$ Hz, 1H), 2.20–2.27 (m, 1H), 2.31–2.40 (m, 1H), 2.55 (ddd, $J = 10.9$, 5.0, 1.7 Hz, 1H), 2.87 (dd, $J = 13.1$, 9.9 Hz, 1H), 3.01–3.08 (m, 1H), 3.21 (ddd, $J = 10.9$, 5.2, 2.4 Hz, 1H), 3.46–3.60 (m, 2H), 5.99 (d, $J = 7.3$ Hz, 1H), 6.42–6.49 (m, 3H), 6.55 (dd, $J = 7.7$, 1.3 Hz 1H), 7.07 (dd, $J = 7.7$, 1.8 Hz, 1H), 7.20–7.35 (m, 2H), 7.42 −7.55 ppm (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 19.26, 26.50, 26.52, 26.67, 29.62, 30.16, 30.36, 33.89, 35.43, 36.33, 44.09, 57.75, 120.43, 124.67, 126.87, 129.27, 129.87, 130.50, 131.15, 133.10, 135.31, 136.94, 137.86, 139.96, 143.24, 168.81, 170.72 ppm; IR (KBr): $\tilde{\nu} = 3029$ (w), 3007 (w), 2928 (m), 2853 (m), 1892 (w), 1730 (w), 1564 (m), 1437 (m), 1238 cm^{-1} (w); MS (70 eV, EI): m/z (%): 437 (100) [M^+], 333 (8), 222 (53), 194 (10), 149 (20), 111 (29), 69 (23), 43 (3); HRMS-EI: m/z calcd for $C_{31}H_{35}NO$: 437.2718; found: 437.2722.

Synthesis of (R_pS)- and (S_pS)-12c: Racemic 5-benzoyl-4-hydroxy-[2.2]paracyclophane (**3**; 0.11 g, 0.33 mmol) was dissolved in of toluene (50 mL) under argon, and (*S*)-indan-1-ylamine (**C**; 0.13 g, 1.00 mmol) and $TiCl_4$ (0.44 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the R_pS diastereomer (61 mg, 42%) as an orange solid. $R_f = 0.33$ (pentane/diethyl ether = 9:1); m.p. 140 °C; $[\alpha]_D^{20} = +1347$ ($c = 0.12$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.86$ (dd, $J = 13.6$, 9.5 Hz, 1H), 2.25–2.33 (m, 1H), 2.37–2.45 (m, 1H), 2.49–2.59 (m, 2H), 2.66–2.74 (m, 1H), 2.90 (dd, $J = 13.1$, 9.5 Hz, 1H), 2.96–3.04 (m, 2H), 3.10–3.17 (m, 1H), 3.20–3.28 (m, 1H), 3.40–3.47 (m, 1H), 5.08 (t, $J = 7.7$ Hz, 1H), 6.10 (d, $J = 7.5$ Hz, 1H), 6.45 (dd, $J = 7.6$, 1.8 Hz, 1H), 6.49 (d, $J = 7.6$ Hz, 1H), 6.51–6.58 (m, 2H), 6.97 (d, $J = 7.5$ Hz, 1H), 7.04 (dd, $J = 7.8$, 1.9 Hz, 1H), 7.14 (t, $J = 7.6$ Hz, 1H), 7.22 (t, $J = 7.2$ Hz, 1H), 7.28 (d, $J = 7.5$ Hz, 1H), 7.35–7.47 (m, 2H), 7.46–7.54 (m, 3H), 16.16 ppm (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 30.24$, 30.93, 33.87, 35.43, 36.39, 36.39, 63.74, 120.60, 122.99, 123.98, 124.59, 125.63, 126.88, 127.00, 127.69, 128.29, 129.16, 129.52, 129.86, 131.31, 133.09, 136.12, 136.79, 137.91, 139.91, 142.32, 143.36, 165.07, 171.93 ppm; IR (KBr): $\tilde{\nu} = 3438$ (w), 3067 (w), 2995 (m), 2942 (m), 2849 (w), 2468 (w), 1882 (w), 1561 (m), 1441 (m), 1247 cm^{-1} (m); MS (70 eV, EI): m/z (%): 443 (100) [M^+], 339 (14), 328 (29), 222 (93), 117 (93), 58 (14), 43 (56); HRMS-EI: m/z calcd for $C_{32}H_{29}NO$: 443.2249; found: 443.2248. The second band gave the S_pS diastereomer (69 mg, 47%) as an orange-red solid. $R_f = 0.27$ (pentane/diethyl ether = 9:1); m.p. 123 °C; $[\alpha]_D^{20} = -342$ ($c = 0.23$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.86$ (dd, $J = 14.0$, 9.5 Hz, 1H), 2.06–2.14 (m, 1H), 2.16–2.24 (m, 1H), 2.28–2.35 (m, 1H), 2.46–2.60 (m, 2H), 2.76–2.84 (m, 1H), 2.90–2.93 (m, 1H), 2.94–3.06 (m, 2H), 3.11–3.19 (m, 1H), 3.40–3.44 (m, 1H), 5.19 (t, $J = 7.9$ Hz, 1H), 6.08 (d, $J = 7.5$ Hz, 1H), 6.48 (dd, $J =$ 7.4, 2.2 Hz, 2H), 6.59 (dd, $J = 7.8$, 1.5 Hz, 1H), 6.65 (dd, $J = 7.6$, 1.7 Hz, 1H), 7.00 (dd, $J = 7.7$, 1.7 Hz, 1H), 7.32–7.38 (m, 2H), 7.40–7.55 (m, 6H), 7.63 ppm (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 30.07$, 30.70, 33.93, 35.56, 35.95, 36.46, 63.46, 120.83, 123.56, 125.06, 125.44, 126.87, 127.16, 127.74, 128.56, 129.36, 129.64, 130.25, 131.31, 133.09, 135.69, 137.02, 137.88, 139.92, 143.50, 144.65, 166.32, 171.10 ppm; IR (KBr): $\tilde{\nu} = 3453$ (w), 3025 (w), 2989 (w), 2925 (m), 2850 (w), 1876 (w), 1554 (m), 1438 (m), 1253 ppm (w); MS (70 eV, EI): m/z (%): 443 (37) [M^+], 339 (7), 328 (12), 222 (42), 149 (100), 117 (52), 71 (25), 57 (35), 43 (21); HRMS-EI: m/z calcd for $C_{32}H_{29}NO$: 443.2249; found: 443.2248.

Synthesis of (R_pS)- and (S_pS)-12g: Racemic 5-benzoyl-4-hydroxy-[2.2]paracyclophane (**3**; 0.30 g, 0.91 mmol) was dissolved in toluene (100 mL) under argon, and (*S*)-3,3-dimethyl-2-aminobutane (0.28 g, 2.73 mmol) and $TiCl_4$ (1.18 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the R_pS diastereomer (0.10 g, 28%) as an orange solid. $R_f = 0.37$ (pentane/diethyl ether = 9:1); m.p. 182 °C; $[\alpha]_D^{20} = +1163$ ($c =$ 0.13 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.83$ (s, 9H), 1.46 (d, $J =$ 6.6 Hz, 3H), 1.68 (dd, $J = 13.9$, 9.2 Hz, 1H), 2.17–2.25 (m, 1H), 2.29–2.36 (m, 1H), 2.57 (ddd, $J = 10.8$, 4.6, 1.8 Hz, 1H), 2.86 (dd, $J = 12.8$, 9.4 Hz, 1H), 3.02 (ddd, $J = 10.8$, 4.5, 2.9 Hz, 1H), 3.24 (ddd, $J = 10.3$, 5.0, 2.4 Hz, 1H), 3.32–3.38 (m, 1H), 3.49–3.56 (m, 1H), 5.99 (d, $J = 7.3$ Hz, 1H), 6.46 (dd, $J = 7.7$, 1.7 Hz, 3H), 6.56 (dd, $J = 7.7$, 1.7 Hz, 1H), 7.07 (dd, $J = 7.8$, 1.8 Hz, 1H), 7.40–7.54 ppm (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 18.10, 26.38, 30.09, 33.95, 34.00, 35.51, 36.58, 62.61, 120.04, 125.05, 126.94, 129.29, 129.68, 130.15, 131.15, 133.01, 136.04, 136.81, 137.91, 140.02, 143.41, 167.78, 170.53 ppm; IR (KBr): $\tilde{\nu} = 3436$ (w), 3011 (w), 2964 (m), 2928 (m), 2869 (w), 1892 (w), 1559 (m), 1438 (m), 1242 cm^{-1} (s); MS (70 eV, EI): m/z (%): 411 (5) [M^+], 307 (2), 223 (3), 85 (3), 58 (39), 43 (100); HRMS-EI: m/z calcd for $C_{29}H_{33}NO$: 411.2562; found: 411.2566. The second band gave the S_pS diastereomer (0.13 g, 34%) as an orange-red solid. $R_f = 0.31$ (pentane/diethyl ether = 9:1); m.p. 206 °C; $[\alpha]_D^{20} = -420$ ($c = 0.34$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.83$ (d, $J = 6.6$ Hz, 3H), 1.19 (s, 9H), 1.73 (dd, $J = 13.8$, 9.5 Hz, 1H), 2.19–2.27 (m, 1H), 2.34–2.44 (m, 1H), 2.51–2.62 (m, 1H), 2.83–2.91 (m, 1H), 3.06 (dt, $J =$ 10.7, 2.5 Hz, 1H), 3.25 (ddd, $J = 12.6$, 10.2, 4.8 Hz, 1H), 3.47–3.59 (m, 2H), 6.02 (d, $J = 7.9$ Hz, 1H), 6.46 (dt, $J = 7.5$, 1.9 Hz, 4H), 6.56 (dd, $J =$ 7.9, 1.9 Hz, 1H), 7.07 (dd, $J = 7.5$, 1.9 Hz, 1H), 7.44–7.58 ppm (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 16.93$, 26.99, 30.35, 33.92, 34.05, 35.46, 36.28, 61.88, 120.86, 124.89, 126.92, 129.16, 130.78, 131.20, 133.12, 135.51, 136.91, 137.90, 140.03, 143.24, 170.89 ppm; IR (KBr): $\tilde{\nu} = 3457$ (w), 2965 (m), 2926 (m), 1869 (w), 1829 (w), 1558 (m), 1438 (m), 1241 cm^{-1} (s); MS (70 eV, EI): m/z (%): 411 (5) [M^+], 307 (3), 223 (3), 58 (39), 43 (100); HRMS-EI: m/z calcd for $C_{29}H_{33}NO$: 411.2562; found: 411.2566.

Synthesis of (R_pS)- and (S_pS)-12h: Racemic 5-benzoyl-4-hydroxy-[2.2]paracyclophane (**3**; 0.21 g, 0.63 mmol) was dissolved in toluene (100 mL) under argon, and (*S*)-1-naphthyl-1-ylethylamine (0.33 g, 1.90 mmol) and $TiCl_4$ (0.82 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the S_pS diastereomer (0.15 g, 48%) as an orange solid. $R_f = 0.14$ (pentane/ethyl acetate = 19:1); m.p. 176 °C; $[\alpha]_D^{20} = -198$ ($c = 0.55$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.65$ (d, $J = 6.4$ Hz, 3H), 1.68–1.72 (m, 1H), 2.05–2.12 (m, 1H), 2.18–2.25 (m, 1H), 2.63 (ddd, $J =$ 12.7, 11.0, 4.9 Hz, 1H), 2.72 (dd, $J = 12.7$, 9.9 Hz, 1H), 3.15 (ddd, $J = 12.7$, 10.3, 2.3 Hz, 1H), 3.37 (ddd, $J = 12.7$, 10.5, 4.7 Hz, 1H), 3.61 (ddd, $J =$ 12.7, 10.3, 2.3 Hz, 1H), 5.51 (q, $J = 6.4$ Hz, 1H), 6.11 (d, $J = 7.5$ Hz, 1H), 6.19 (dd, $J = 7.6$, 1.5 Hz, 1H), 6.47–6.56 (m, 3H), 7.05–7.15 (m, 3H), 7.33 (dd, $J = 7.4$, 1.1 Hz, 2H), 7.46 (t, $J = 7.4$ Hz, 1H), 7.52 (dt, $J = 8.4$, 1.1 Hz, 1H), 7.57 (t, $J = 7.0$ Hz, 1H), 7.72 (t, $J = 7.8$ Hz, 1H), 7.82 (d, $J = 8.2$ Hz, 1H), 7.90 (d, $J = 8.0$ Hz, 1H), 7.99 (d, $J = 8.2$ Hz, 1H), 8.17 ppm (d, $J =$ 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 25.63$, 30.38, 34.00, 35.27, 36.37, 55.06, 120.93, 122.62, 123.80, 125.61, 125.73, 126.05, 126.17, 126.89, 127.70, 129.20, 129.29, 129.45, 129.66, 130.57, 131.34, 133.15, 134.17, 135.81, 137.11, 138.03, 139.87, 141.97, 143.64, 166.11, 171.09 ppm; IR (KBr): $\tilde{\nu} = 3045$ (w), 2969 (w), 2930 (m), 2851 (w), 1886 (w), 1740 (m),

1562 (s), 1436 (m), 1240 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 481 (5) [M^+], 377 (1), 222 (2), 155 (11), 77 (8), 43 (100); HRMS-EI: *m/z* calcd for $C_{35}H_{31}NO$: 481.2406; found: 481.2403. The second band gave the R_pS diastereomer (0.11 g, 38%) as an orange-red solid. R_f = 0.10 (pentane/ethyl acetate = 19:1); m.p. 198 °C; $[\alpha]_D^{20}$ = +1585 (*c* = 0.14 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.75–1.82 (m, 1H), 1.90 (d, *J* = 6.6 Hz, 3H), 2.21–2.29 (m, 1H), 2.42–2.50 (m, 1H), 2.54–2.62 (m, 1H), 2.87–2.92 (m, 1H), 3.05 (dt, *J* = 11.0, 2.8 Hz, 1H), 3.24–3.31 (m, 1H), 3.47–3.54 (m, 1H), 5.73 (q, *J* = 6.6 Hz, 1H), 6.00 (d, *J* = 7.5 Hz, 1H), 6.44 (d, *J* = 7.5 Hz, 1H), 6.50 (dd, *J* = 7.7, 1.5 Hz, 1H), 6.57–6.64 (m, 2H), 7.18–7.25 (m, 3H), 7.27–7.32 (m, 1H), 7.33–7.48 (m, 6H), 7.68 (t, *J* = 7.8 Hz, 2H), 7.76 ppm (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.86, 30.18, 33.99, 35.51, 36.53, 52.92, 120.60, 122.27, 123.99, 125. 24, 125.28, 125.67, 125.89, 127.11, 127.52, 128.32, 128.76, 129.38, 129.65, 130.18, 130.36, 131.29, 133.06, 133.61, 135.86, 137.09, 138.00, 139.83, 140.04, 143.56, 176.83, 170.96 ppm; IR (KBr): $\tilde{\nu}$ = 3044 (m), 2969 (m), 2929 (m), 2851 (w), 1886 (w), 1739 (w), 1560 (s), 1394 (m), 1241 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 481 (9) [M^+], 377 (3), 328 (3), 308 (23), 223 (4), 165 (25), 155 (100), 105 (27), 91 (17), 58 (16), 43 (40); HRMS-EI: *m/z* calcd for $C_{35}H_{31}NO$: 481.2406; found: 481.2406.

Synthesis of (R_pS)- and (S_pS)-12i: Racemic 5-benzoyl-4-hydroxy-[2.2]paracyclophane (**3**; 0.11 g, 0.33 mmol) was dissolved in toluene (100 mL) under argon, and (*S*)-1-naphth-2-ylethylamine (0.17 g, 1.00 mmol) and $TiCl_4$ (0.44 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the S_pS diastereomer (57 mg, 36%) as an orange solid. R_f = 0.27 (pentane/diethyl ether = 9:1); m.p. 183 °C; $[\alpha]_D^{20}$ = −211 (*c* = 0.37 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.60 (d, *J* = 6.4 Hz, 3H), 1.70 (dd, *J* = 13.9, 9.4 Hz, 1H), 2.09–2.17 (m, 1H), 2.18–2.27 (m, 1H), 2.67 (ddd, *J* = 12.8, 5.0, 2.1 Hz, 1H), 2.75 (dd, *J* = 12.8, 9.5 Hz, 1H), 3.13 (ddd, *J* = 12.9, 10.9, 2.3 Hz, 1H), 3.34 (ddd, *J* = 12.9, 10.0, 5.0 Hz, 1H), 3.60 (ddd, *J* = 12.8, 10.3, 2.3 Hz, 1H), 4.86 (q, *J* = 6.4 Hz, 1H), 6.10 (d, *J* = 7.6 Hz, 1H), 6.39 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.49 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.53–6.63 (m, 2H), 7.21 (d, *J* = 7.5 Hz, 2H), 7.33 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.50 (d, *J* = 7.7 Hz, 1H), 7.52–7.59 (m, 3H), 7.69 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.92–7.99 (m, 2H), 8.00 ppm (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.28, 30.42, 33.96, 35.28, 36.31, 58.93, 120.92, 124.45, 124.95, 125.63, 125.94, 126.42, 126.82, 127.83, 128.01, 128.86, 129.27, 129.68, 130.93, 131.35, 132.73, 133.75, 135.75, 137.05, 138.00, 139.85, 139.85, 143.46, 165.90, 171.09 ppm; IR (KBr): $\tilde{\nu}$ = 3446 (w), 3056 (w), 2925 (s), 2853 (m), 1728 (m), 1567 (m), 1437 (m), 1289 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 481 (4) [M^+], 377 (1), 307 (8), 279 (11), 223 (1), 149 (100), 71 (5), 43 (21); HRMS-EI: *m/z* calcd for $C_{35}H_{31}NO$: 481.2406; found: 481.2401. The second band gave the R_pS diastereomer (40 mg, 25%) as an orange-red solid. R_f = 0.21 (pentane/diethyl ether = 9:1); m.p. 205 °C; $[\alpha]_D^{20}$ = +1407 (*c* = 0.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.73–1.82 (m, 1H), 1.94 (d, *J* = 6.4 Hz, 3H), 2.20–2.27 (m, 1H), 2.39–2.46 (m, 1H), 2.53–2.59 (m, 1H), 2.85–2.93 (m, 1H), 3.01–3.07 (m, 1H), 3.21–3.28 (m, 1H), 3.49 (ddd, *J* = 12.8, 10.3, 2.3 Hz, 1H), 5.05 (q, *J* = 6.4 Hz, 1H), 6.02 (d, *J* = 7.4 Hz, 1H), 6.43 (d, *J* = 7.4 Hz, 1H), 6.46–6.50 (m, 1H), 6.55–6.60 (m, 2H), 7.17 (dd, *J* = 7.4, 2.2 Hz, 1H), 7.27–7.31 (m, 2H), 7.34–7.38 (m, 1H), 7.41–7.51 (m, 6H), 7.66–7.70 (m, 1H), 7.71–7.76 ppm (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.43, 30.18, 33.95, 35.47, 36.47, 57.89, 120.74, 124.59, 124.81, 125.41, 125.68, 125.98, 127.08, 127.54, 127.87, 128.47, 128.85, 129.40, 129.46, 130.22, 130.92, 131.29, 132.58, 133.06, 133.23, 136.01, 136.98, 137.97, 140.01, 140.82, 143.48, 166.83, 170.95 ppm; IR (KBr): $\tilde{\nu}$ = 3441 (w), 3055 (w), 2926 (s), 2853 (m), 1887 (w), 1728 (m), 1567 (m), 1437 (m), 1288 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 481 (2) [M^+], 307 (6), 279 (10), 251 (4), 149 (100), 71 (5), 57 (9), 43 (12); HRMS-EI: *m/z* calcd for $C_{35}H_{31}NO$: 481.2406; found: 481.2400.

Synthesis of (R_pS)- and (S_pS)-13a: Racemic 5-*para*-bromobenzoyl-4-hydroxy[2.2]paracyclophane (**4**; 0.25 g, 0.60 mmol) was dissolved in toluene (75 mL) under argon, and (*S*)-1-phenylethylamine (0.22 g, 1.80 mmol) and $TiCl_4$ (0.78 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the S_pS diastereomer (0.13 g, 43%) as an orange solid. R_f = 0.36 (pentane/diethyl ether 9:1); m.p. 108 °C; $[\alpha]_D^{20}$ = −396 (*c* = 0.28 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (d, *J* = 6.4 Hz, 3H), 1.68–1.78 (m, 1H), 2.05–2.30 (m, 2H), 2.52–2.65 (m, 1H), 2.71–2.82 (m, 1H), 3.07 (dt, *J* = 10.6, 2.7 Hz, 1H), 3.18–3.30 (m, 1H), 3.46–3.56 (m, 1H), 4.61 (dq, *J* = 6.4, 1.6 Hz, 1H), 6.07 (d, *J* = 7.7 Hz, 1H), 6.26 (dd, *J* = 7.7, 1.8 Hz, 1H), 6.41–6.52 (m, 3H), 7.01 (d, *J* = 8.5 Hz, 2H), 7.13 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.31–7.39 (m, 1H), 7.43–7.58 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.43, 30.29, 33.92, 35.26, 36.45, 59.27, 120.85, 124.04, 125.88, 125.99, 126.90, 127.31, 129.10, 129.23, 130.31, 131.34, 133.12, 134.69, 137.09, 137.75, 139.84, 143.11, 145.63, 165.11, 169.59 ppm; MS (70 eV, EI): *m/z* (%): 511/509 (21/19) [M^+], 430 (5), 405 (13), 302 (19), 167 (21), 149 (45), 105 (41), 84 (100), 47 (28); HRMS-EI: *m/z* calcd for $C_{31}H_{28}BrNO$: 509.1354; found: 509.1344. The second band gave the R_pS diastereomer (0.10 g, 34%) as an orange-red solid. R_f = 0.26 (pentane/diethyl ether 9:1); m.p. 125 °C; $[\alpha]_D^{20}$ = +790 (*c* = 0.60 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.77–1.86 (m, 1H), 1.81 (d, *J* = 6.8 Hz, 3H), 2.20–2.40 (m, 2H), 2.48–2.59 (m, 1H), 2.84–2.92 (m, 1H), 2.96–3.04 (m, 1H), 3.15–3.24 (m, 1H), 3.40–3.48 (m, 1H), 4.76 (q, *J* = 6.8 Hz, 1H), 6.20 (d, *J* = 7.6 Hz, 1H), 6.41 (d, *J* = 7.6 Hz, 1H), 6.45 (d, *J* = 1.8 Hz, 1H), 6.53 (dq, *J* = 7.8, 1.8 Hz, 2H), 7.01–7.04 (m, 2H), 7.07–7.20 (m, 6H), 7.58 (d, *J* = 8.3 Hz, 2H), 16.15 ppm (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.71, 30.37, 33.95, 35.46, 36.63, 58.13, 120.71, 123.68, 125.75, 126.24, 127.12, 127.18, 128.64, 129.45, 130.10, 131.33, 131.65, 133.11, 134.94, 137.06, 137.77, 140.02, 143.05, 166.03, 169.51 ppm; IR (KBr): $\tilde{\nu}$ = 3082 (m), 3028 (m), 3007 (m), 2966 (m), 2934 (m), 2921 (m), 2850 (m), 1871 (w), 1726 (w), 1533 (m), 1248 (m), 1032 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 511/509 (12/12) [M^+], 430 (7), 405 (9), 105 (100); HRMS-EI: *m/z* calcd for $C_{31}H_{28}BrNO$: 509.1354; found: 509.1359.

Synthesis of (R_pS)- and (S_pS)-13b: Racemic 5-*para*-bromobenzoyl-4-hydroxy[2.2]paracyclophane (**4**; 0.58 g, 1.42 mmol) was dissolved in toluene (75 mL) under argon, and (*S*)-1-cyclohexylethylamine (0.54 g, 4.26 mmol) and $TiCl_4$ (1.84 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the R_pS diastereomer (0.27 g, 37%) as an orange solid. R_f = 0.39 (pentane/diethyl ether = 9:1); m.p. 156 °C; $[\alpha]_D^{20}$ = +781 (*c* = 0.79 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.53–0.61 (m, 1H), 0.70–0.76 (m, 1H), 0.95–1.05 (m, 1H), 1.05–1.15 (m, 2H), 1.20–1.35 (m, 1H), 1.4 (s, 3H), 1.70–1.75 (m, 1H), 2.20–2.30 (m, 2H), 2.50–2.70 (m, 6H), 2.80–2.90 (m, 1H), 2.95–3.05 (m, 1H), 3.15–3.25 (m, 1H), 3.30 (q, *J* = 6.4 Hz, 1H), 3.45–3.55 (m, 1H), 6.01 (d, *J* = 7.4 Hz, 1H), 6.35 (dd, *J* = 7.8, 1.9 Hz, 1H), 6.47 (d, *J* = 2H), 6.55 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.99 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.15 (br s, 2H), 7.60 ppm (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.57, 26.08, 26.13, 26.17, 29.11, 29.92, 30.20, 33.93, 35.44, 36.64, 44.51, 59.51, 120.09, 123.58, 125.34, 126.97, 129.60, 129.93, 131.16, 133.07, 134.98, 136.82, 137.71, 139.94, 142.91, 166.85, 169.15 ppm; IR (KBr): $\tilde{\nu}$ = 3032 (w), 3008 (w), 2959 (w), 2930 (s), 2849 (m), 1732 (m), 1591 (m), 1576 (m), 1486 (m), 1242 cm^{-1} (w); MS (70 eV, EI): *m/z* (%): 517/515 (30/31) [M^+], 436 (18), 411 (23), 301 (20), 111 (100), 69 (58); HRMS-EI: *m/z* calcd for $C_{31}H_{34}BrNO$: 515.1824; found: 515.1821. The second band gave the S_pS diastereomer (0.34 g, 46%) as an orange-red solid. R_f = 0.31 (pentane/diethyl ether 9:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (d, *J* = 6.5 Hz, 3H), 1.20–1.35 (m, 6H), 1.75–1.82 (m, 2H), 1.90–1.98 (m, 3H), 2.07 (d, *J* = 12.7 Hz, 1H), 2.27–2.36 (m, 2H), 2.59 (ddd, *J* = 12.8, 10.6, 4.8 Hz, 1H), 2.86–2.93 (m, 1H), 3.05 (ddd, *J* = 12.9, 11.0, 2.4 Hz, 1H), 3.21 (ddd, *J* = 12.5, 10.2, 4.8 Hz, 1H), 3.47–3.55 (m, 2H), 6.04 (d, *J* = 7.5 Hz, 1H), 6.43 (dd, *J* = 7.9, 1.9 Hz, 1H), 6.47 (d, *J* = 7.5 Hz, 2H), 6.56 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.05 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.10–7.25 (m, 2H), 7.63 (d, *J* = 7.9 Hz, 2H), 16.70 ppm (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.23, 26.45, 26.48, 26.63, 29.65, 30.15, 30.36, 33.85, 35.41, 36.51, 44.08, 58.28, 120.50, 123.75, 125.36, 126.92, 129.83, 130.38, 131.26, 131.68, 133.17, 134.14, 137.26, 137.66, 140.01, 142.95, 169.61 ppm; IR (KBr): $\tilde{\nu}$ = 3057 (w), 3008 (w), 2959 (w), 2930 (s), 2849 (m), 1728 (m), 1591 (m), 1576 (m), 1486 (m), 1242 cm^{-1} (w); MS (70 eV, EI): *m/z* (%): 517/515 (4/4) [M^+], 293 (5), 279 (23), 167 (28), 149 (76),

113 (9), 58 (37), 43 (100); HRMS-EI: *m/z* calcd for $C_{31}H_{34}BrNO$: 515.1824; found: 515.1827.

Synthesis of (R_p,*S*)- and (S_p,*S*)-14: Racemic 4-hydroxy-5-*para*-iodobenzoyl[2.2]paracyclophane (**5**; 0.40 g, 0.88 mmol) was dissolved in toluene (75 mL) under argon, and (*S*)-1-cyclohexylethylamine (0.34 g, 2.64 mmol) and $TiCl_4$ (1.14 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the R_p,*S* diastereomer (0.19 g, 39%) as an orange solid. R_f=0.24 (pentane/diethyl ether=15:1); m.p. 177°C; $[\alpha]_D^{20}$=+917 (*c*=0.25 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.62 (dq, *J*=12.2, 3.3 Hz, 1H), 0.77 (dq, *J*=12.2, 3.3 Hz, 1H), 1.06 (tt, *J*=12.2, 3.3 Hz, 1H), 1.09–1.21 (m, 2H), 1.35–1.43 (m, 1H), 1.47 (d, *J*=6.5 Hz, 3H), 1.52–1.70 (m, 5H), 1.72–1.83 (m, 1H), 2.22–2.33 (m, 2H), 2.57 (ddd, *J*=13.0, 10.7, 4.8 Hz, 1H), 2.83–2.93 (m, 1H), 3.05 (ddd, *J*=13.5, 11.0, 3.1 Hz, 1H), 3.23 (ddd, *J*=12.7, 10.2, 4.8 Hz, 1H), 3.34 (p, *J*=6.6 Hz, 1H), 3.51 (ddd, *J*=12.7, 10.2, 2.5 Hz, 1H), 6.04 (d, *J*=7.5 Hz, 1H), 6.41 (dd, *J*=7.6, 1.7 Hz, 1H), 6.44–6.48 (m, 2H), 6.55 (dd, *J*=7.9, 1.7 Hz, 1H), 6.70–7.15 (m, 3H), 7.79 (d, *J*=7.9 Hz, 2H), 16.50 ppm (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=20.60, 26.06, 26.12, 26.14, 29.06, 29.62, 30.22, 33.91, 35.44, 36.67, 44.46, 59.19, 95.47, 119.98, 125.38, 126.95 (2C), 129.65, 129.91 (2C), 131.19, (2C), 133.08, 135.41, 146.95, 137.73, 139, 94 (2C), 142.98, 166.87, 169.32 ppm; IR (KBr): $\tilde{\nu}$=3008 (w), 2927 (s), 2851 (m), 1881 (w), 1572 (m), 1500 (w), 1436 (m), 1242 cm^{-1} (w); MS (70 eV, EI): *m/z* (%): 563 (6) [M^+], 111 (3), 58 (40), 43 (100); HRMS-EI: *m/z* calcd for $C_{31}H_{34}INO$: 563.1683; found: 563.1686. The second band gave the S_p,*S* diastereomer (0.21 g, 43%) as an orange-red solid. R_f=0.22 (pentane/diethyl ether=15:1); m.p. 115°C; $[\alpha]_D^{20}$=−685 (*c*=0.28 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.93 (d, *J*=6.6 Hz, 3H), 1.19–1.45 (m, 5H), 1.62–1.71 (m, 1H), 1.73–1.82 (m, 2H), 1.85–2.00 (m, 3H), 2.05–2.15 (m, 1H), 2.23–2.38 (m, 2H), 2.57 (ddd, *J*=12.6, 10.3, 4.8 Hz, 1H), 2.86–2.95 (m, 1H), 3.05 (ddd, *J*=13.2, 10.7, 2.3 Hz, 1H), 3.21 (ddd, *J*=12.8, 10.3, 4.8 Hz, 1H), 3.45–3.55 (m, 2H), 6.03 (d, *J*=7.4 Hz, 1H), 6.42 (dd, *J*=7.8, 2.0 Hz, 1H), 6.47 (d, *J*=7.4 Hz, 2H), 6.56 (dd, *J*=7.9, 1.7 Hz, 1H), 6.90–7.21 (m, 3H), 7.81 (d, *J*=7.9 Hz, 2H), 16.80 ppm (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=19.27, 26.46, 26.49, 26.65, 29.65, 30.16, 30.32, 33.86, 35.42, 36.53, 44.11, 58.23, 120.44, 125.23, 126.89 (2), 129.76, 130.37 (2), 131.24 (2), 133.17 (2), 134.76, 137.11, 137.68, 139.97, 142.88, 167.45, 169.61 ppm; IR (KBr): $\tilde{\nu}$=3008 (w), 2926 (s), 2851 (m), 1882 (w), 1572 (m), 1500 (w), 1436 (m), 1241 cm^{-1} (w); MS (70 eV, EI): *m/z* (%): 563 (16) [M^+], 459 (3), 111 (8), 58 (35), 43 (100); HRMS-EI: *m/z* calcd for $C_{31}H_{34}INO$: 563.1683; found: 563.1688.

Synthesis of (R_p,*S*)- and (S_p,*S*)-15: Racemic 4-hydroxy-5-(2-naphthoyl)-[2.2]paracyclophane (**6**; (0.62 g, 1.64 mmol) was dissolved in toluene (75 mL) under argon, and (*S*)-1-cyclohexylethylamine (0.63 g, 4.92 mmol) and $TiCl_4$ (2.13 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the R_p,*S* diastereomer (0.35 g, 44%) as an orange oil. R_f=0.25 (pentane/diethyl ether=9:1); $[\alpha]_D^{20}$=+1003 (*c*=0.34 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.62 (dq, *J*=12.5, 3.4 Hz, 1H), 0.74 (dq, *J*=12.2, 3.3 Hz, 1H), 0.95 (tq, *J*=12.4, 3.2 Hz, 1H), 1.07–1.18 (m, 2H), 1.37–1.46 (m, 1H), 1.55 (d, *J*=6.3 Hz, 3H), 1.58–1.70 (m, 7H), 2.11–2.18 (m, 1H), 2.31–2.42 (m, 1H), 2.55–2.63 (m, 1H), 2.79 (t, *J*=11.4 Hz, 1H), 3.05 (dt, *J*=11.0, 2.7 Hz, 1H), 3.20–3.28 (m, 1H), 3.49–3.57 (m, 1H), 6.01 (d, *J*=7.5 Hz, 1H), 6.47 (d, *J*=7.5 Hz, 2H), 6.53 (t, *J*=6.8 Hz, 2H), 7.11 (dd, *J*=7.7, 1.7 Hz, 1H), 7.55–7.78 (m, 3H), 7.86–8.05 ppm (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=20.62, 26.08, 26.13, 29.07, 29.57, 30.29, 30.94, 33.96, 35.44, 36.69, 44.46, 53.44, 58.88, 124.95, 126.87, 126.97, 127.22, 127.93, 128.60, 129.73, 130.06, 131.13, 133.03, 133.28, 136.82, 137.89, 139.95, 168.06, 170.39 ppm; IR (KBr): $\tilde{\nu}$=3010 (w), 2926 (s), 2851 (m), 2489 (w), 1738 (w), 1566 (m), 1438 (m), 1238 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 487 (12) [M^+], 383 (4), 273 (8), 111 (5), 69 (3), 58 (10), 43 (100); HRMS-EI: *m/z* calcd for $C_{35}H_{37}NO$: 487.2875; found: 487.2873. The second band gave the S_p,*S* diastereomer (0.26 g, 33%) as an orange oil. R_f=0.17 (pentane/diethyl ether=9:1); $[\alpha]_D^{20}$=−691 (*c*=0.39 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.92 (d, *J*=6.5 Hz, 3H), 1.22–1.37 (m, 2H), 1.37–1.52 (m, 3H), 1.60–1.78 (m, 2H), 1.83 (d, *J*=12.5 Hz, 1H), 1.93 (d, *J*=12.9 Hz, 1H), 2.02 (d, *J*=12.5 Hz, 1H), 2.11–2.14 (m, 3H), 2.38–2.47 (m, 1H), 2.53–2.63 (m, 1H), 2.82 (t, *J*=11.3 Hz, 1H), 3.07 (dt, *J*=11.2, 2.5 Hz, 1H), 3.21–3.30 (m, 1H), 3.50–3.56 (m, 1H), 6.02 (d, *J*=7.5 Hz, 1H), 6.46–6.51 (m, 2H), 6.56 (t, *J*=5.7 Hz, 2H), 7.13 (dd, *J*=7.4, 2.0 Hz, 1H), 7.55–7.70 (m, 3H), 7.90–8.05 ppm (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=19.34, 26.52, 26.56, 29.68, 29.68, 30.22, 30.40, 30.95, 33.93, 35.41, 36.54, 44.14, 53.45, 57.94, 124.77, 126.92, 127.24, 127.92, 128.54, 129.85, 130.50, 131.20, 133.12, 133.23, 137.00, 139.90, 168.65, 170.71 ppm; IR (KBr): $\tilde{\nu}$=3010 (w), 2926 (s), 2851 (m), 2664 (w), 1737 (w), 1567 (m), 1437 (m), 1238 cm^{-1} (m); MS (70 eV, EI): *m/z* (%): 487 (100) [M^+], 384 (7), 300 (14), 273 (56), 149 (8), 111 (26), 69 (16), 58 (20), 43 (81); HRMS-EI: *m/z* calcd for $C_{35}H_{37}NO$: 487.2875; found: 487.2878.

Synthesis of (R_p,*S*)- and (S_p,*S*)-16: Racemic 5-butyryl-4-hydroxy-[2.2]paracyclophane (**7**; 0.15 g, 0.45 mmol) was dissolved in toluene (75 mL) under argon, and (*S*)-1-cyclohexylethylamine (0.19 g, 1.30 mmol) and $TiCl_4$ (0.58 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 40 h. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the R_p,*S* diastereomer (60 mg, 33%) as an orange oil. R_f=0.32 (pentane/diethyl ether=9:1); $[\alpha]_D^{20}$=+230 (*c*=0.19 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.92 (t, *J*=7.5 Hz, 3H), 1.00–1.10 (m, 2H), 1.16–1.24 (m, 1H), 1.26–1.30 (m, 1H), 1.35 (d, *J*=6.5 Hz, 3H), 1.44–1.54 (m, 1H), 1.55–1.65 (m, 2H), 1.67–1.73 (m, 1H), 1.75–1.92 (m, 4H), 2.52 (ddd, *J*=10.7, 5.0, 2.3 Hz, 1H), 2.57–2.72 (m, 3H), 2.88–2.94 (m, 1H), 3.01 (ddd, *J*=13.2, 10.9, 2.6 Hz, 1H), 3.08–3.21 (m, 1H), 3.33 (ddd, *J*=11.4, 9.8, 2.0 Hz, 1H), 3.42 (ddd, *J*=13.1, 10.3, 2.6 Hz, 1H), 3.63 (p, *J*=6.5 Hz, 1H), 6.14 (d, *J*=7.5 Hz, 1H), 6.33 (dd, *J*=7.7, 1.8 Hz, 1H), 6.40 (d, *J*=7.7 Hz, 1H), 6.49 (dd, *J*=7.9, 1.8 Hz, 1H), 6.63 (dd, *J*=7.9, 1.8 Hz, 1H), 6.99 (dd, *J*=7.7, 1.8 Hz, 1H), 15.93 ppm (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=14.31, 19.94, 22.03, 26.33, 26.35, 26.44, 29.63, 29.96, 30.50, 33.52, 33.88, 35.67, 37.54, 43.91, 58.14, 120.04, 125.14, 127.07, 129.74, 129.99, 131.29, 132.70, 135.85, 137.47, 140.09, 140.32, 164.91, 173.20 ppm; IR (KBr): $\tilde{\nu}$=3418 (w), 2929 (m), 2853 (m), 1758 (w), 1582 (m), 1449 (m), 1244 cm^{-1} (w); MS (70 eV, EI): *m/z* (%): 403 (29) [M^+], 294 (59), 279 (20), 224 (55), 189 (6), 120 (61), 104 (100), 91 (4), 43 (58); HRMS-EI: *m/z* calcd for $C_{28}H_{37}NO$: 403.2875; found: 403.2872. The second band gave the S_p,*S* diastereomer (53 mg, 29%) as an orange oil. R_f=0.16 (pentane/diethyl ether=9:1); $[\alpha]_D^{20}$=−233 (*c*=0.13 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.87 (t, *J*=7.5 Hz, 3H), 1.20–1.27 (m, 2H), 1.29 (d, *J*=6.4 Hz, 3H), 1.35–1.40 (m, 2H), 1.45–1.55 (m, 2H), 1.57–1.65 (m, 2H), 1.76–1.80 (m, 1H), 1.86–1.97 (m, 3H), 1.99–2.05 (m, 1H), 2.47–2.53 (m, 1H), 2.55–2.60 (m, 1H), 2.69–2.77 (m, 2H), 2.95–3.04 (m, 2H), 3.09 (ddd, *J*=12.6, 10.0, 3.0 Hz, 1H), 3.19 (ddd, *J*=12.6, 9.4, 2.4 Hz, 1H), 3.29 (ddd, *J*=12.5, 9.6, 3.1 Hz, 1H), 3.42 (ddd, *J*=12.7, 10.3, 2.6 Hz, 1H), 3.71 (p, *J*=6.5 Hz, 1H), 6.12 (d, *J*=7.5 Hz, 1H), 6.35 (dd, *J*=7.6, 1.8 Hz, 1H), 6.40 (d, *J*=7.5 Hz, 1H), 6.52 (dd, *J*=7.8, 1.6 Hz, 1H), 6.65 (dd, *J*=7.8, 1.6 Hz, 1H), 6.99 (dd, *J*=7.8, 1.6 Hz, 1H), 16.00 ppm (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=14.22, 19.44, 22.05, 26.40, 26.41, 26.63, 29.05, 29.85, 30.67, 33.86, 34.06, 35.71, 37.37, 44.62, 57.57, 120.37, 124.83, 127.15, 129.69, 130.34, 131.60, 132.58, 136.23, 137.55, 140.19, 140.37, 165.37, 173.01 ppm; IR (KBr): $\tilde{\nu}$=3383 (w), 2929 (m), 2853 (m), 1880 (w), 1734 (w), 1582 (m), 1449 (m), 1262 cm^{-1} (w); MS (70 eV, EI): *m/z* (%): 403 (33) [M^+], 299 (16), 294 (6), 279 (5), 216 (8), 149 (16), 120 (12), 104 (17), 71 (30), 43 (100); HRMS-EI: *m/z* calcd for $C_{28}H_{37}NO$: 403.2875; found: 403.2878.

Synthesis of (R_p,*S*)- and (S_p,*S*)-17: Racemic 4-hydroxy-5-lauroyl-[2.2]paracyclophane (**8**; 0.15 g, 0.37 mmol) was dissolved in toluene (75 mL) under argon, and (*S*)-1-cyclohexylethylamine (0.14 g, 1.11 mmol) and $TiCl_4$ (0.48 mmol of a 1 M solution in dichloromethane) were added. The reaction mixture was refluxed in a Dean–Stark apparatus for 7 d. After removal of the solvent under reduced pressure, the diastereomers were separated and purified by flash chromatography. The first band gave the R_p,*S* diastereomer (39 mg, 20%) as a yellow oil. R_f=0.37 (pentane/diethyl ether=20:1); $[\alpha]_D^{20}$=+233 (*c*=0.62 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.90 (t, *J*=6.8 Hz, 3H), 1.18–1.31 (m, 26H), 1.35 (d, *J*=6.5 Hz, 3H), 2.51 (ddd, *J*=14.0, 10.8, 5.0 Hz, 1H), 2.55–2.65 (m,

Table 4. Crystallographic data, structure solution and refinement

	(S_p,S)-**11c**	(R_p,S)-**11i**	(S_p,S)-**11k**	(S_p,S)-**12b**	(R_p,S)-**12c**	(S_p,S)-**12c**
formula	$C_{27}H_{27}NO$	$C_{30}H_{29}NO$	$C_{28}H_{29}NO$	$C_{31}H_{35}NO$	$C_{32}H_{29}NO$	$C_{32}H_{29}NO$
M_r	381.50	419.54	395.52	437.60	443.56	443.56
size [mm]	0.20×0.40×0.50	0.30×0.50×0.50	0.30×0.40×0.45	0.08×0.16×0.35	0.25×0.30×0.35	0.30×0.40×0.50
crystal system	orthorhombic	orthorhombic	orthorhombic	orthorhombic	orthorhombic	orthorhombic
space group	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)
a [Å]	7.5791(1)	9.8252(2)	7.7289(1)	10.3234(1)	8.3149(1)	12.6392(2)
b [Å]	14.5153(3)	10.7048(2)	14.7952(2)	11.2280(1)	9.2324(1)	13.3797(2)
c [Å]	18.0604(4)	21.0461(5)	18.5079(3)	20.7815(2)	31.4534(4)	28.6812(4)
α [°]	90	90	90	90	90	90
β [°]	90	90	90	90	90	90
γ [°]	90	90	90	90	90	90
V [Å^3]	1986.88(7)	2213.56(8)	2116.39(5)	2408.81(4)	2414.57(5)	4850.24(13)
Z	4	4	4	4	4	8
ρ_{calcd} [g cm^{-3}]	1.275	1.259	1.241	1.207	1.220	1.215
μ [mm^{-1}]	0.076	0.075	0.074	0.071	0.073	0.072
F(000)	816	896	848	944	944	1888
$2\theta_{max}$ [°]	52	50	55	55	50	55
index range	$-9\le h\le 9$	$-11\le h\le 11$	$-10\le h\le 10$	$-13\le h\le 13$	$-9\le h\le 9$	$-15\le h\le 16$
	$-16\le k\le 17$	$-12\le k\le 12$	$-19\le k\le 19$	$-14\le k\le 14$	$-10\le k\le 10$	$-17\le k\le 17$
	$-19\le l\le 22$	$-25\le l\le 25$	$-24\le l\le 24$	$-26\le l\le 26$	$-37\le l\le 37$	$-37\le l\le 37$
measured data	12137	18652	32153	49176	26777	38572
unique data	3840	3891	4758	5524	4239	10827
R_{int}	0.0347	0.0720	0.0437	0.0431	0.0613	0.0505
parameters/restraints	266/0	293/0	275/0	301/0	310/0	619/0
x	0.1(13)	−1.0(17)	0.4(12)	0.1(10)	−0.3(13)	0.2(9)
R [$I>2\sigma(I)$]	0.0353	0.0391	0.0358	0.0338	0.0352	0.0404
$wR2$ (all data)	0.0780	0.0731	0.0895	0.0855	0.0879	0.0814
max/min difference peak [e Å^{-3}]	0.168/−0.176	0.175/−0.201	0.143/−0.176	0.170/−0.197	0.169/−0.194	0.175/−0.212

	(S_p,S)-**12g**	(R_p,S)-**12g**	(R_p,S)-**12i**	(S_p,S)-**12h**	(S_p,S)-**12j**	(R_p,S)-**13b**	(R_p,S)-**13a**
formula	$C_{29}H_{33}NO$	$C_{29}H_{33}NO$	$C_{35}H_{31}NO$	$C_{35}H_{31}NO$	$C_{31}H_{28}ClNO$	$C_{31}H_{34}BrNO$	$C_{31}H_{28}BrNO$
M_r	411.56	411.56	481.61	481.61	465.99	516.50	510.45
size [mm]	0.30×0.45×0.50	0.20×0.30×0.50	0.20×0.30×0.60	0.10×0.45×0.55	0.30×0.40×0.60	0.30×0.45×0.50	0.10×0.15×0.20
crystal system	orthorhombic	monoclinic	orthorhombic	orthorhombic	orthorhombic	monoclinic	monoclinic
space group	$P2_12_12_1$ (no. 19)	$P2_1$ (no. 4)	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)	$P2_1$ (no. 4)	$P2_1$ (no. 4)
a [Å]	10.4196(1)	8.6131(2)	9.6992(1)	11.3406(1)	10.2702(1)	9.2280(2)	8.4623(5)
b [Å]	12.3668(2)	12.6206(3)	13.1619(2)	13.9049(2)	10.7443(1)	9.4443(2)	10.9824(6)
c [Å]	18.1229(3)	11.0941(3)	20.2124(4)	16.1969(2)	22.1974(4)	14.9753(4)	13.2164(10)
α [°]	90	90	90	90	90	90	90
β [°]	90	102.582(1)	90	90	90	99.159(1)	90.095(2)
γ [°]	90	90	90	90	90	90	90
V [Å^3]	2335.26(6)	1177.00(5)	2580.31(7)	2554.09(5)	2449.40(6)	1288.49(5)	1228.28(14)
Z	4	2	4	4	4	2	2
ρ_{calcd} [g cm^{-3}]	1.171	1.161	1.240	1.252	1.264	1.331	1.380
μ [mm^{-1}]	0.070	0.069	0.073	0.074	0.180	1.619	1.698
F(000)	888	444	1024	1024	984	540	528
$2\theta_{max}$ [°]	50	50	50	50	50	55	50
index range	$-12\le h\le 12$	$-10\le h\le 10$	$-11\le h\le 9$	$-13\le h\le 13$	$-12\le h\le 12$	$-11\le h\le 11$	$-10\le h\le 8$
	$-14\le k\le 14$	$-15\le k\le 15$	$-15\le k\le 15$	$-16\le k\le 16$	$-12\le k\le 11$	$-12\le k\le 12$	$-12\le k\le 13$
	$-21\le l\le 21$	$-13\le l\le 13$	$-24\le l\le 24$	$-19\le l\le 19$	$-26\le l\le 26$	$-19\le l\le 19$	$-15\le l\le 15$
measured data	41223	20415	24885	51579	20524	13528	5832
unique data	4098	4137	4543	4499	4301	5686	4085
R_{int}	0.0516	0.0462	0.0468	0.0439	0.0418	0.0374	0.0352
parameters/restraints	284/0	283/1	338/0	337/0	310/0	310/2	310/2
X	0.1(12)	0.2(12)	0.3(12)	0.4(11)	−0.02(5)	−0.007(4)	−0.009(7)
R [$I>2\sigma(I)$]	0.0317	0.0344	0.0329	0.0285	0.0307	0.0272	0.0361
$wR2$ (all data)	0.0777	0.0721	0.0735	0.0687	0.0788	0.0537	0.0605
max/min difference peak [e Å^{-3}]	0.183/−0.159	0.182/−0.212	0.197/−0.171	0.165/−0.147	0.194/−0.267	0.300/−0.348	0.378/−0.297

3H), 2.67–2.71 (m, 1H), 2.85–2.94 (m, 1H), 2.97 (ddd, J=13.4, 10.3, 2.7 Hz, 1H), 3.05–3.12 (m, 3H), 3.17 (ddd, J=13.7, 10.3, 5.1 Hz, 1H), 3.31 (ddd, J=11.4, 9.2, 2.0 Hz, 1H), 3.43 (ddd, J=12.94 10.3, 2.4 Hz, 1H), 3.62 (p, J=6.5 Hz, 1H), 6.13 (d, J=7.5 Hz, 1H), 6.34 (dd, J=7.7, 1.7 Hz, 1H), 6.40 (d, J=7.5 Hz, 1H), 6.48 (dd, J=7.8, 1.8 Hz, 1H), 6.63 (dd, J=7.8, 1.7 Hz, 1H), 6.98 (dd, J=7.7, 1.7 Hz, 1H), 15.88 ppm (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=14.11, 19.91, 22.68, 26.35, 26.44, 28.51, 29.16, 29.31, 29.40, 29.54, 29.60, 29.63, 29.81, 29.97, 30.51, 31.63, 31.87, 33.87, 35.66, 37.57, 43.91, 58.07, 125.13, 127.07, 129.72, 129.99, 131.29, 132.68, 135.85, 137.45, 140.09, 140.30, 164.99, 173.41 ppm; IR

(KBr): $\tilde{\nu}$ = 3397 (w), 2928 (m), 2854 (m), 1883 (w), 1759 (m), 1500 (m), 1450 (m), 1262 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 515 (78) [M^+], 411 (9), 328 (11), 284 (5), 174 (8), 58 (18), 43 (100); HRMS-EI: *m*/*z* calcd for $C_{36}H_{53}NO$: 515.4127; found: 515.4131. The second band gave the (S_P,*S*)-diastereomer (30 mg, 16%) as an orange oil. R_f = 0.22 (pentane/diethyl ether = 20:1); $[\alpha]_D^{20} = -76$ (*c* = 0.25 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.9 Hz, 3H), 1.18–1.27 (m, 21H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.57–1.63 (m, 3H), 1.73–1.81 (m, 1H), 1.85–1.96 (m, 3H), 1.97–2.06 (m, 1H), 2.46–2.61 (m, 2H), 2.67–2.78 (m, 2H), 2.91–3.10 (m, 3H), 3.17–3.21 (m, 1H), 3.26 (ddd, *J* = 13.3, 8.2, 1.6 Hz, 1H), 3.41 (ddd, *J* = 12.8, 10.3, 2.4 Hz, 1H), 3.69 (p, *J* = 6.3 Hz, 1H), 6.12 (d, *J* = 7.4 Hz, 1H), 6.35 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.38 (d, *J* = 7.4 Hz, 1H), 6.52 (dd, *J* = 7.8, 1.6 Hz, 1H), 6.66 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.98 (dd, *J* = 7.7, 1.7 Hz, 1H), 15.97 ppm (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.11, 19.42, 22.68, 26.41, 26.63, 28.58, 29.05, 29.16, 29.30, 29.38, 29.53, 29.56, 29.76, 29.87, 30.68, 31.88, 32.22, 33.86, 35.71, 37.39, 44.62, 57.54, 120.41, 124.83, 127.15, 129.65, 130.34, 131.60, 132.24, 136.23, 137.55, 140.19, 140.35, 165.39, 173.23 ppm; IR (KBr): $\tilde{\nu}$ = 3435 (w), 2927 (m), 2854 (m), 1750 (m), 1653 (m), 1596 (m), 1450 (m), 1373 (w), 1262 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 515 (100) [M^+], 411 (10), 328 (13), 284 (5), 174 (9), 69 (13), 43 (29); HRMS-EI: *m*/*z* calcd for $C_{36}H_{53}NO$: 515.4127; found: 515.4131.

Crystal structure determinations: The data were collected on a Nonius Kappa CCD diffractometer at −150 °C using $Mo_{K\alpha}$ radiation (λ = 0.71073 Å). The structures were solved by direct methods (SHELXS-97).[38] The non-hydrogen atoms were refined anisotropically, and H atoms were refined using a riding model, H(N,O) free (full-matrix least-squares refinement on F^2, SHELXL-97).[39] The absolute structures were determined by refinement of Flack's x-parameter[40] for (R_P,*S*)-**13a**, (R_P,*S*)-**13b**, and (S_P,*S*)-**12j**. For the other structures, only the relative configuration was determined from the known chiral center. An empirical absorption correction was applied for (R_P,*S*)-**13b** and (R_P,*S*)-**13a**. For (R_P,*S*)-**12i** an extinction correction was applied. Details of data collection and refinement are given in Table 4. CCDC-261588 [(S_P,*S*)-**11c**], CCDC-261600 [(R_P,*S*)-**11i**], CCDC-261599 [(S_P,*S*)-**11k**], CCDC-261589 [(S_P,*S*)-**12b**], CCDC-261591 [(R_P,*S*)-**12c**], CCDC-261590 [(S_P,*S*)-**12c**], CCDC-261592 [(S_P,*S*)-**12g**], CCDC-261593 [(R_P,*S*)-**12g**], CCDC-261595 [(R_P,*S*)-**12j**], CCDC-261594 [(R_P,*S*)-**12j**), CCDC-261598 [(S_P,*S*)-**12j**], CCDC-261597 [(R_P,*S*)-**13b**], and CCDC-261596 [(R_P,*S*)-**13a**] contain the supplementary crystallographic data for this paper. 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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