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Co-Metal-Free Enantioselective Conjugate Addition Reactions of Zinc Reagents

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Abstract: Asymmetric conjugate addition of diethylzinc to cinnamaldehyde in a co-metal-free fashion by using N,O-ligands with planar and central chirality is described. Different modulations of the ligand structure, including several combinations of the chiral units, indicate that a [2.2]paracyclophane backbone is essential for the activity and the enantioselectivity of the generated active catalyst. By using the optimized ligand, an isolated yield of 90% was obtained with up to 99% *ee*.

Keywords: asymmetric catalysis · conjugate addition reactions · enals · N,O-ligands · organozinc reagents

Introduction

The conjugate addition reaction (onto Michael substrates) of carbon-centered nucleophiles is one of the most important and powerful C–C bond-forming reactions in modern organic chemistry.[1] Catalytic asymmetric versions also play a significant role in the total synthesis of complex chiral natural products.[2] Asymmetric 1,4-addition reactions with hard nucleophiles generally require the presence of a co-metal, with copper or rhodium being the most used ones.

In particular, asymmetric 1,4-addition reactions of organozinc, organoaluminum, or Grignard reagents to α,β-unsaturated substrates under copper catalysis have been successfully accomplished.[3] Excellent yields and high enantioselectivities were achieved for cyclic and acyclic enones,[4] amide derivatives,[5] nitro olefins,[6] esters,[7] thioesters,[8] and malonates.[9] However, enals still constitute a challenging class of substrates since efficient systems allowing a regioselective addition are rare.

Axial chiral ligands, such as (mostly binaphthyl-based) phosphoramidites[10] or planar chiral ferrocene-based ligands,[11] are broadly used in asymmetric conjugate addition reactions. Beside these lead structures, [2.2]paracyclophanes have also been employed.[12] This class of compounds gives rapid access to planar chiral structures. Monosubstituted [2.2]paracyclophanes are, in fact, already chiral, whereas ferrocene derivatives need to be disubstituted (with achiral substituents) to become chiral. Furthermore, paracyclophanes are very stable[13] and do not racemize easily unlike some ferrocenes.[14]

Paracyclophane ligands were successfully used for asymmetric allylic substitution reactions,[15] sulfoxidation of thioethers,[16] cyclopropanation of olefins,[17] and asymmetric hydrogenation reactions.[18] Furthermore, 1,2-addition reactions of organozinc reagents to different electrophiles, for example, aldehydes or imines, were also effectively accomplished by using ligands bearing a paracyclophane scaffold.[19] Lately, even Morita–Baylis–Hillman reactions have been catalyzed by [2.2]paracyclophane-derived monophosphines.[20]

Recently, our group developed a [2.2]paracyclophane ligand-based asymmetric Michael-addition reaction of organozinc reagents to this class of compounds.[21] There is no need to add any copper salts. This is the key advantage of this ligand system, which makes it an environmentally benign process with a potential application in drug syntheses. We have newly reported the scope of this reaction. Now we present our trials to optimize the ligand structure and enhance the regioselectivity.

Results and Discussion

Nowadays, lots of different ligands are available for copper-catalyzed asymmetric 1,4-addition reactions. One of the

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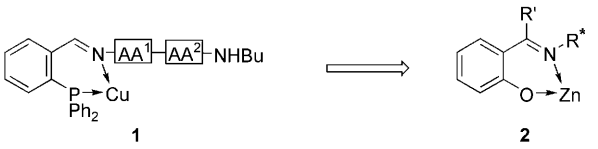
most powerful types developed by Hoveyda is based on peptidic imines bearing a phosphine moiety.[22] These ligands are particularly effective for copper co-metal catalysis due to a chelation of the copper ion by the imine and phosphine moiety. Zinc ions, in contrast, are predominately complexed by a nitrogen–oxygen chelate. That is why mostly amino alcohols are used as ligands for 1,2-addition reactions of organozinc reagents onto aldehydes.[23] With α,β-unsaturated aldehydes, it is likely that a mixture of 1,2- and 1,4-addition products is obtained, which can, however, in some cases be limited to a single product depending on whether the reaction is run under thermodynamic or kinetic control. A potential ligand **2** for such reactions is shown in Scheme 1. Its



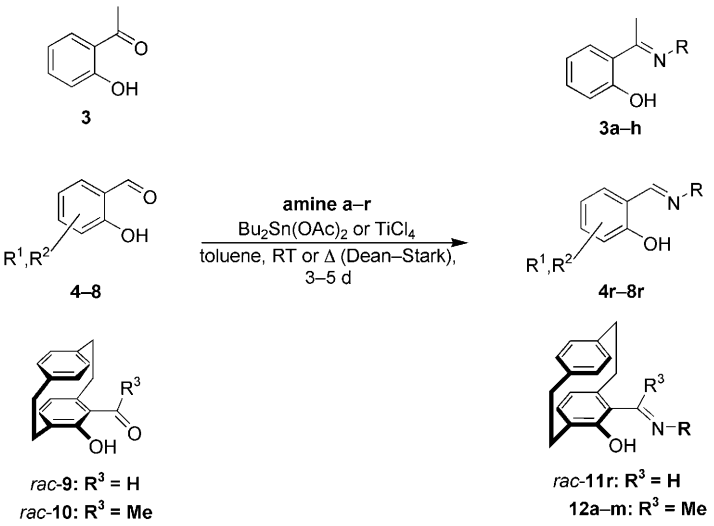
1 **2**

Scheme 1. Ligand simplification and variation of ligand **1** for zinc catalysis.

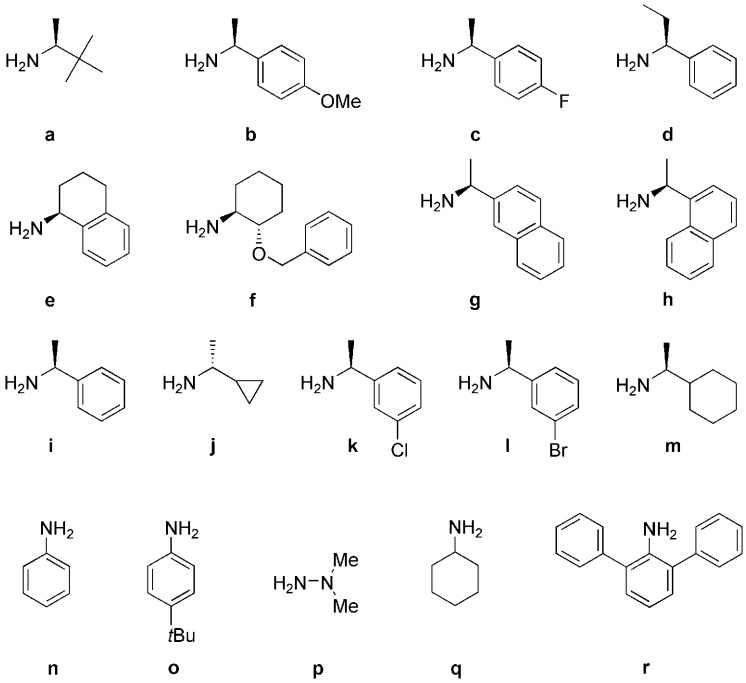
structure is based on a simplification of Hoveyda's ligand **1**. The latter has a characteristic imine functionality, which is connected to a peptide. The amino acids (AA) used bear chiral elements, which are necessary for the asymmetric induction. The N atom of the imine group serves together with the P atom as donors for the copper ion. Based on this, we proposed structure **2**, composed of an imine bearing a central chiral group and a phenol, to act as the ligand during zinc catalysis.

We first synthesized a small library of ligands **3a**–**h** (Scheme 2), by starting from readily available 2-acetylphenol (**3**), which was condensed with different enantiopure amines (compounds **a**–**r** are the different amines and hydrazines used for ligand synthesis). The obtained yields range from 40% (for **3a**) to 98% (for **3e** and **3h**).

These potential ligands were then used in an asymmetric 1,4-addition reaction. As a model reaction, we choose the copper-free Michael-addition reaction of Et_2Zn to cinnamaldehyde **13** (Scheme 3).[24–26]

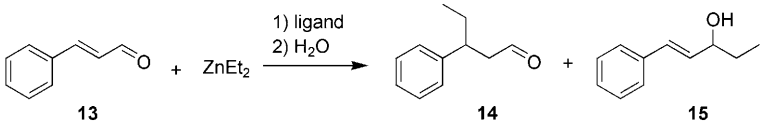


Scheme 2. General synthesis of potential ligands for zinc catalysis.



We were pleased to observe the formation of 1,4-addition product **14** in the presence of the ligands **3a**–**h** (Table 1). The tested ligands led, however, to substandard results in terms of yield, selectivity, and *ee* in almost all cases. The generated catalysts showed quite low activity ranging from 62% recovery of the starting material for **3a** (entry 1) to 88% for **3f** (entry 6) after the reaction mixture had been stirred for three days. In addition, the observed enantioselectivities for the conjugate addition products, which give in all cases (*R*)-**14**, are poor, ranging from 13 to 41%. Moreover, the desired product is most of the time either dominated by the 1,2-addition adduct (the α,β-unsaturated alcohol **15**, entries 1, 2, and 5) or is a 1:1 mixture of **14** and **15** (entries 3, 4, 6, and 8).

Because of the high electrophilicity of the aldehyde, a 1,2-addition competes most of the time with the Michael-addition reaction. However, the formation of the 1,2-addition-reaction product should be reduced, even avoided, if the reac-



13 **14** **15**

Scheme 3. Addition reaction of diethyl zinc to cinnamaldehyde **13**.

Table 1. Screening of central chiral ligands **3a–h**.[a,e]

Entry	Ligand	Starting material [%][b]	1,4-Product (**14**) [%][b]	*ee* of **14** [%][c]	1,2-Product (**15**) [%][b]
1	**3a**	62	12	41 (*R*)	15
2	**3b**	65	5	25 (*R*)	22
3	**3c**	81	6	nd[d]	5
4	**3d**	67	12	20 (*R*)	14
5	**3e**	87	4	13 (*R*)	7
6	**3f**	88	4	17 (*R*)	6
7	**3g**	80	16	nd[d]	<0.5
8	**3h**	64	15	30 (*R*)	17

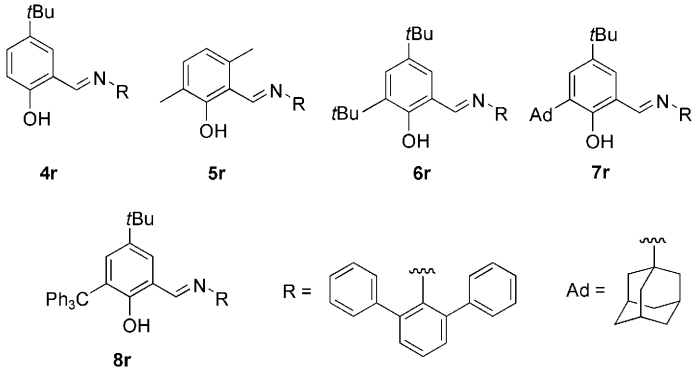
[a] Reaction conditions: ligand (2 mol%), diethylzinc (1.10 M in toluene, 2.00 equiv), toluene, −30°C, 3 d under an argon atmosphere. [b] Determined by GC analysis after workup. [c] Determined by GC analysis (chiral, Lipodex-E). [d] nd = not determined. [e] Due to side reactions, such as aldol reactions, the total amount of material does not always reach 100%.

tion is conducted at low temperature. Running the reaction at −30°C leads only in one case—in the presence of **3g**—to preferable formation of the kinetic product (Table 1, entry 7). Almost no 1,2-addition product was observed; however, the desired Michael adduct **14** was obtained in only 16% yield.

Interestingly, ligand **3h**, which is very similar to **3g** again only provides a nearly equimolar mixture of **14** and **15** (Table 1, entry 8). It might be possible to optimize the activity of ligand **3g** by means of the incorporation of different substituents onto the naphthalene part, but because of these ligands leading also to poor enantioselectivities, we did not continue with further efforts in this direction.

To better control the regioselectivity, we next investigated substituted (2,6-diphenylphenyl-2-yliminomethyl)phenols **4–8r** as ligands. Due to their steric hindrance, a 1,2-addition reaction should indeed be discriminated, especially as the substrate is thought to coordinate via the aldehyde to the generated zinc catalyst.[27]

Different substituents in the *ortho* position to the hydroxy function were tested to evaluate their influence. Therefore, several substituted α-formylphenols **4–8** were condensed with 2,6-diphenylaniline **r** (Scheme 1). Figure 1 shows X-ray structures of **5r** and Figure 2a the X-ray structure of **11r**. In both cases, a hydrogen bond between the phenolic oxygen



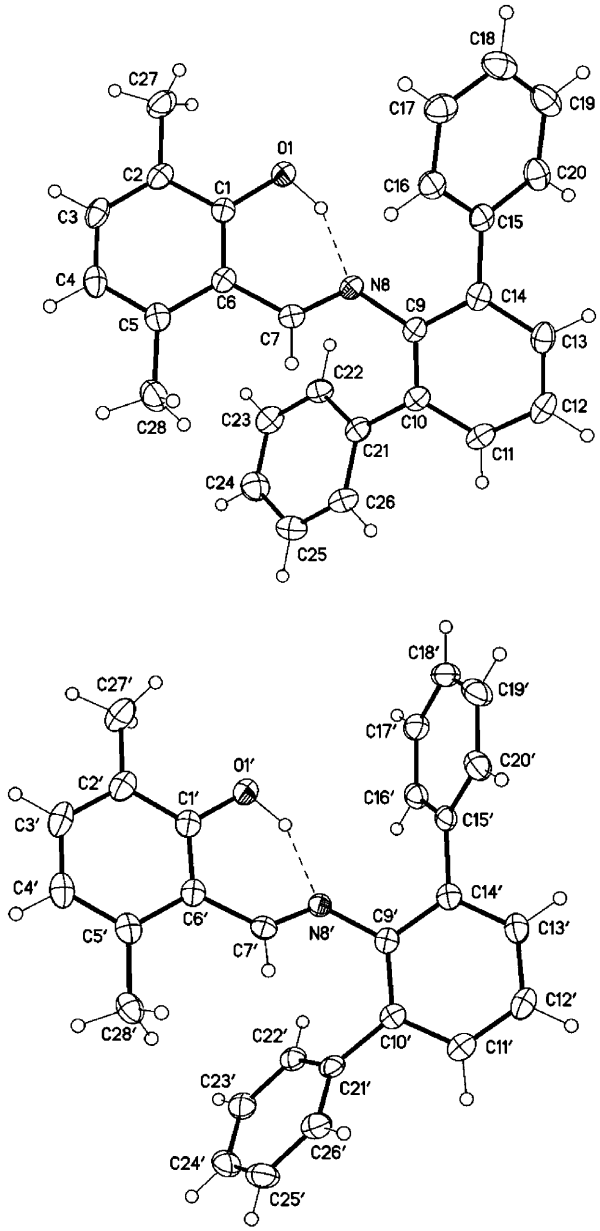


Figure 1. Molecular structure of two independent molecules of **5r**. Displacement parameters are drawn at the 50% probability level.

atom and the imine nitrogen atom is observable. In the case of **5r**, the formation of rotameric structures could be identified due to the sterically demanding 2,6-diphenylamine substituent. In **11r**, this substituent is twisted to the plane of the [2.2]paracyclophane backbone. Compounds **4–8r** were then utilized as ligands during the addition reaction of diethyl zinc to cinnamaldehyde **13** as before (Scheme 3, Table 2). In the case of ligand **4r** with a free *ortho* position, an acceptable yield and excellent regioselectivity were obtained (entry 1). Supplying 4 mol% of ligand **4r**, the regioselectivity and the product yield could even be increased (entry 2). The reaction mixture became cloudy, however, after the addition of the zinc reagents, which indicated a precipitation

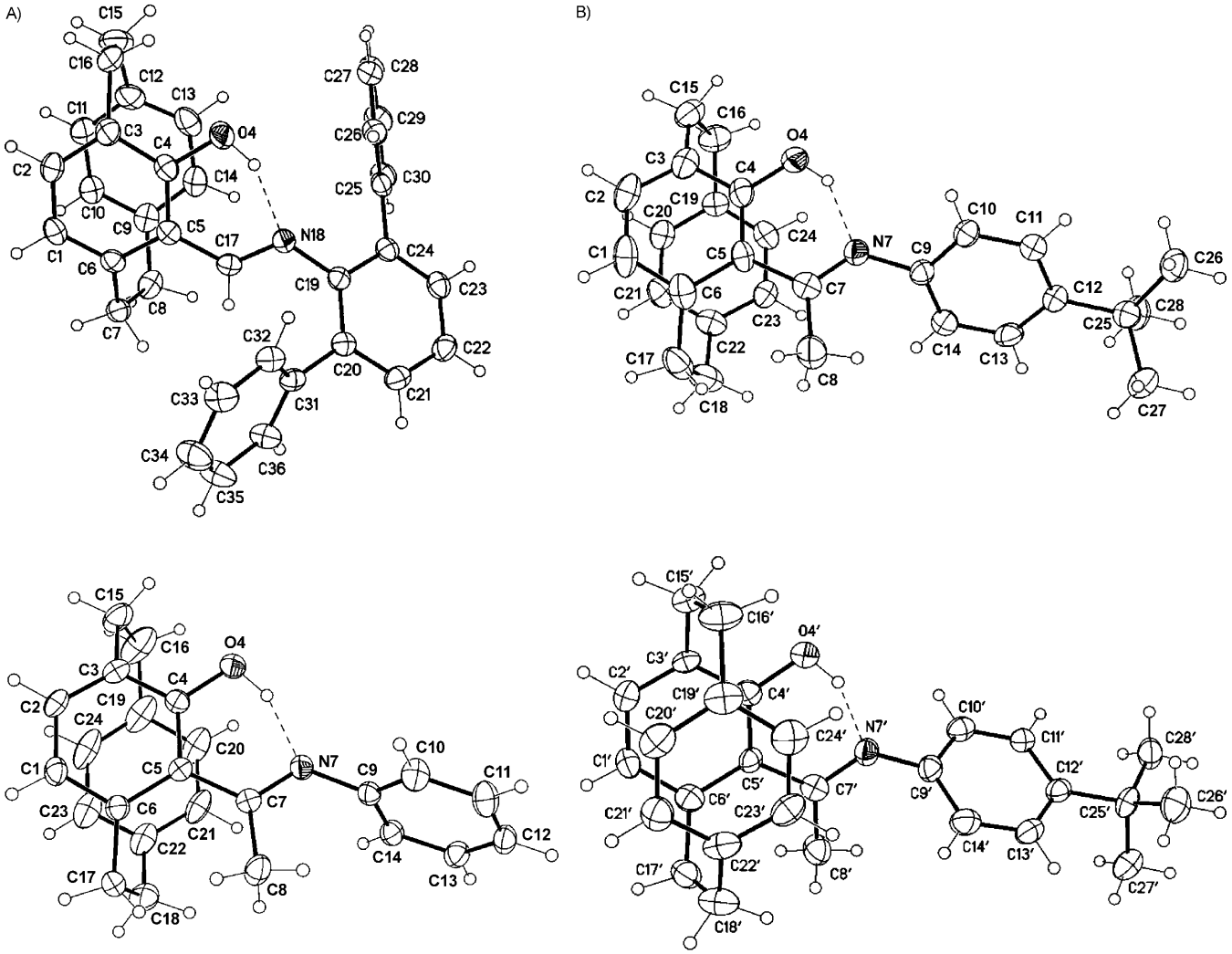


Figure 2. A) Top: Molecular structure of **11r**. Bottom: Molecular structure of **12n**. B) Molecular structure of the two independent molecules of **12o**. Displacement parameters are drawn at 50% probability level.

Table 2. Screening of *ortho*-substituted ligands **4**–**8r** derived from 2,6-diphenylaniline.[a,d]

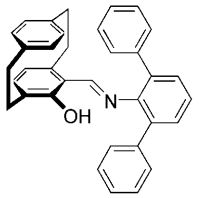
Entry	Ligand	Starting material [%][b]	1,4-Product (**14**) [%][b]	1,2-Product (**15**) [%][b]
1	**4r**	71	22	3
2	**4r**[c]	52	40	<1
3	**5r**	82	13	4
4	**6r**	80	13	<1
5	**7r**	88	3	7
6	**8r**	85	4	7

[a] Reaction conditions: ligand (2 mol%), diethylzinc (1.10 M in toluene, 2.00 equiv), toluene, −25 °C, 1.5 d under an argon atmosphere. [b] Determined by GC analysis after workup. [c] 4 mol% ligand used. [d] Due to side reactions, such as aldol reactions, the total amount of material does not always reach 100%.

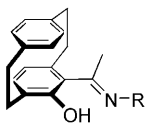
of compounds. Thus, a further optimization seemed not to be possible by increasing the ligand concentration.

When the *ortho* position becomes sterically more hindered (Table 2, entries 2–7), the yield drops and more starting material is recovered. This can be rationalized by the fact that complex generation becomes more difficult, so that less active catalyst will be formed. These results suggest that by incorporating substituents at the *ortho* position, the regioselectivity cannot be positively influenced.

We next turned to substituted [2.2]paracyclophanes bearing an imine and phenol function. Ketimines and *rac*-**12n–q** were obtained by Lewis acid catalyzed condensation of *rac*-



rac-**11r**



rac-**12n**: R = phenyl
rac-**12o**: R = 4-*t*Bu-C_6H_4
rac-**12p**: R = NMe_2
rac-**12q**: R = *c*-hexyl
(S_p)-**12q**: R = *c*-hexyl

5-acetyl-4-hydroxy[2.2]paracyclophane (*rac*-**10**) with different achiral amines or hydrazines (Scheme 2). Figure 2a and b show X-ray structures of **12n** and **12o**. The present hydrogen bond in these structures makes again sure, that the ligand structure is conformationally stable. In the case of *rac*-**11r**, which contains a sterically hindered 2,6-diphenylphenyl substituent, 5-formyl-4-hydroxy[2.2]paracyclophane (*rac*-**9**) was used as the reactant.

Compounds *rac*-**11r** and *rac*-**12n–q** were then used in the model 1,4-addition reaction (Scheme 2, Table 3). Compound

Table 3. Screening of planar chiral ligands.[a,e]

Entry	Ligand	Starting material [%][b]	1,4-Product (**14**) [%][b]	1,2-Product (**15**) [%][b]
1	*rac*-**11r**	90	3	4
2	*rac*-**12n**	36	41	17
3	*rac*-**12o**	35	38	19
4[c]	*rac*-**12p**	28	38	27
5	*rac*-**12q**	34	39	18
6	(S_p)-**12q**	35	39[d]	17

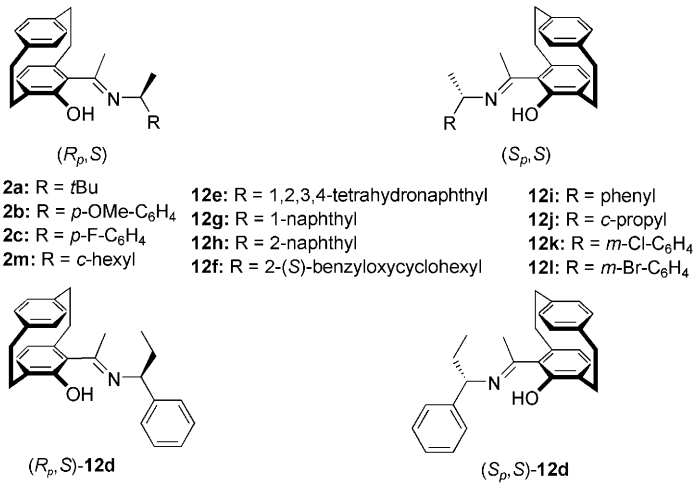
[a] Reaction conditions: ligand (2 mol%), diethylzinc (1.10 M in toluene, 2.00 equiv), toluene, −30 °C, 3 d under an argon atmosphere. [b] Determined by GC analysis after workup. [c] −20 °C, 3 d. [d] 97% *ee* for (*R*)-**14**, determined by GC (chiral, Lipodex-E). [e] Due to side reactions, such as aldol reactions, the total amount of material does not always reach 100%.

rac-**11r** bearing a bulky N substituent, led to almost no conversion (entry 1). A 2:1 mixture of **14** and **15** was obtained in all other cases (entries 2–6), which indicated that the nature of the imine substituent, as long as it is not too bulky, has no influence on the outcome of the reaction.

By using *rac*-**12p**—one of the few examples for a hydrazone based on [2.2]paracyclophane—at −20 °C instead of −30 °C, a higher conversion of the starting material was observed, but a worse regioselectivity was obtained since at higher temperatures the formation of the 1,2-product is favored (Table 3, entry 4).

To check if an enantiomerically pure ligand of this type leads to good enantioselectivities of the 1,4-addition product **14**, we tested (S_p)-**12q** (Table 3, entry 6), which was obtained by condensation of cyclohexylamine with (S_p)-**10**.[19b] We were pleased to note that (*R*)-**14** was obtained with an excellent enantiomeric excess of 97% *ee*.

Encouraged by these results, we next investigated ketimines obtained by Lewis acid catalyzed condensation of *rac*-**10** with different enantiomerically pure amines (compounds **12a–m** are synthesized planar and central chiral diastereomeric ligands based on [2.2]paracyclophanes; Scheme 2). These compounds offer with their [2.2]paracyclophane moiety the opportunity to combine the implied planar chiral unit with a central chiral part. This combination could indeed affect match–mismatch cases and lead to better enantioselectivities.



As ligand *rac*-**11r**, based on sterically demanding 2,6-diphenylaniline, led to very poor results, only sterically less-demanding chiral amines were employed.[28] Starting from *rac*-**10**,[29] two diastereomeric ketimines **12a–m** were obtained that could be separated. These structures combining a planar and central chiral unit were submitted to the 1,4-addition model reaction (Scheme 1, Table 4). The diastereomeric ligands **12** show mostly good regioselectivities and yields along with excellent enantioselectivities, which is over 90% *ee* in nearly all cases (Table 4). As we have already observed for similar cases before, the absolute configuration of the product is determined by the absolute configuration of the paracyclophane backbone (R_p or S_p), which seems to dominate the cooperation of the planar and central chiral units, present in our ligands. A (R_p)-ligand leads to the *S* product, and a (S_p)-ligand generates the *R* product.[21] Ligand **12a** with its two diastereomers shows remarkable match/mismatch characteristics. While (S_p,*S*)-**12a** produces a very high regioselectivity along with a good yield and a high *ee* (entry 2), ligand (R_p,*S*)-**12a** on the other hand has a very low activity, accompanied by a low *ee* (entry 1).

Although ligand pair **12a** remained the only relevant match/mismatch case among the whole series, we always screened both diastereomers. Ligand pair **12m** with a cyclohexylethyl substituent stands out under the tested ligands (Table 4, entries 7 and 8). When considering the yield of the desired Michael product, it was found that (R_p,*S*)-**12m** gives the highest one, up to 63% with 2 mol% ligand, along with an excellent *ee* (>99%; entry 7). Additionally, this type of ligand has an excellent regioselectivity. Almost no 1,2-addition product is formed (entries 7 and 8). This means a yield of 90% based on recovered starting material, which now provides a synthetically useful transformation. It is interesting to note that this ligand is also the optimal ligand for other transformations.[19a,b,30]

So far, all the tested ligands had a central chiral unit bearing a methyl group. To see whether this group has an influence on the outcome of the reaction, two diastereomeric ligands **12d** were tested. The latter are identical to **12i**,

Table 4. Screening of planar and central chiral diastereomeric ligands **12a**–**m**.[a,d]

Entry	Ligand	Starting material [%][b]	1,4-Product (**14**) [%][b]	*ee* of **14** [%][c]	1,2-Product (**15**) [%][b]
1	(R_p,*S*)-**12a**	82	11	86 (*S*)	2
2	(S_p,*S*)-**12a**	30	52	98 (*R*)	14
3	(R_p,*S*)-**12b**	29	46	94 (*S*)	20
4	(S_p,*S*)-**12b**	28	38	98 (*R*)	24
5	(R_p,*S*)-**12c**	37	42	96 (*S*)	15
6	(S_p,*S*)-**12c**	30	44	97 (*R*)	21
7	(R_p,*S*)-**12m**	30	63	>99 (*S*)	<1
8	(S_p,*S*)-**12m**	23	59	97 (*R*)	4
9	(R_p,*S*)-**12i**	34	39	97 (*S*)	18
10	(S_p,*S*)-**12i**	34	40	98 (*R*)	18
11	(S_p,*R*)-**12j**	34	43	96 (*R*)	19
12	(R_p,*R*)-**12j**	62	26	92 (*S*)	6
13	(R_p,*S*)-**12k**	34	44	>99 (*S*)	17
14	(S_p,*S*)-**12k**	35	41	97 (*R*)	16
15	(R_p,*S*)-**12l**	37	47	98 (*S*)	10
16	(S_p,*S*)-**12l**	32	38	97 (*R*)	17
17	(R_p,*S*)-**12e**	44	37	97 (*S*)	15
18	(S_p,*S*)-**12e**	28	42	98 (*R*)	22
19	(R_p,*S*)-**12g**	25	36	97 (*S*)	25
20	(S_p,*S*)-**12g**	25	53	97 (*R*)	18
21	(R_p,*S*)-**12h**	28	39	97 (*S*)	27
22	(S_p,*S*)-**12h**	29	37	99 (*R*)	23
23	(R_p,*S*,*S*)-**12f**	39	35	93 (*S*)	19
24	(S_p,*S*,*S*)-**12f**	28	41	98 (*R*)	23
25	(R_p,*S*)-**12d**	27	50	97 (*S*)	18
26	(S_p,*S*)-**12d**	28	43	97 (*R*)	20

[a] Reaction conditions: ligand (2 mol%), diethylzinc (1.10 M in toluene, 2.00 equiv), toluene, −25 °C, 1.5 d under an argon atmosphere. [b] Determined by GC analysis after workup. [c] Determined by GC analysis (chiral, Lipodex-E). [d] Due to side reactions, such as aldol reactions, the total amount of material does not always reach 100%.

except that the benzylic methyl group had been replaced by an ethyl group. Comparing **12d** and **12i**, similar results in terms of yields, regioselectivities, and enantioselectivities were obtained in both cases (Table 4, entries 25, 26 and 9, 10).

Taking all the results so far obtained together, it becomes clear that the planar chiral [2.2]paracyclophane unit in combination with a central chiral element is important for the activity and the selectivity of the ligand. Although, excellent enantioselectivities were observed with a [2.2]paracyclophane backbone lacking a central chiral unit, the best results in terms of yields, selectivities, and enantioselectivities are clearly obtained by combining the two chiral elements.

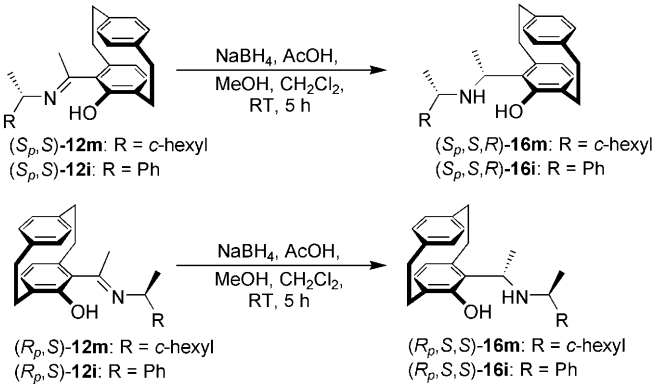
It still remains, however, unclear as to how and to what extent a central chiral unit influences the outcome of the reaction. To further explore this topic, we decided to reduce the imine double bond of the ligands. This results in the formation of an additional stereogenic center that might help us to understand the influence of central chiral units.

Reduction of imines **12m** and **12i** was easily accomplished by using sodium borohydride in combination with concentrated acetic acid in a mixture of methanol and methylene chloride (Scheme 4).[31,32] The products are isolated in good yields ranging from 70–79% (Table 5). In all cases, the half space bearing the [2.2]paracyclophane substituent, is effectively shielded from an attack of the reducing agent, so that the borohydride anion approaches from the opposite side.[33]

Thus, high to excellent diastereomeric excesses are obtained.[34] The new stereogenic centers are, therefore, in all cases independent of the central chiral center.

The absolute configuration of the ligands (R_p,*S*,*S*)-**16m**, (S_p,*S*,*R*)-**16**, (R_p,*S*,*S*)-**16i**, and (R_p,*S*,*S*)-**16i** was determined by their X-ray structures, which are presented in Figure 3. In our first communication, we assigned the structure of (R_p,*S*,*S*)-**16i** as R_p,*S*,*R*.[31,32]

These amine ligands **16m**,**i** submitted to the 1,4-addition model reaction deliver, in general, lower product yields and a lower regioselectivity than their imine analogues and what is most interesting is that the 1,2-addition compound becomes the major product (Scheme 2, Table 6). As already observed before, the absolute configuration of the 1,4-addition product **14** seems again to be mainly determined by the chiral planar unit rather than the central chiral one. The catalyst activity of the generated complexes is, however, similar to that of the ligands containing the



Scheme 4. General reduction conditions for ligands **12m** and **12i**.

Table 5. Synthesis of ligands **16**.

Entry	Ligand	Yield[a]	*de* [%][b]	Configuration[c]
1	(R_p,*S*)-**12m**	73	>99	(R_p,*S*,*S*)-**16m**
2	(S_p,*S*)-**12m**	70	>99	(S_p,*S*,*R*)-**16m**
3	(R_p,*S*)-**12i**	79	>99	(R_p,*S*,*S*)-**16i**
4	(S_p,*S*)-**12i**	79	>99	(S_p,*S*,*R*)-**16i**

[a] Isolated yield. [b] Determined by NMR spectroscopic analysis of the crude material. *de* = diastereomeric excess. [c] Determined X-ray structure analysis.

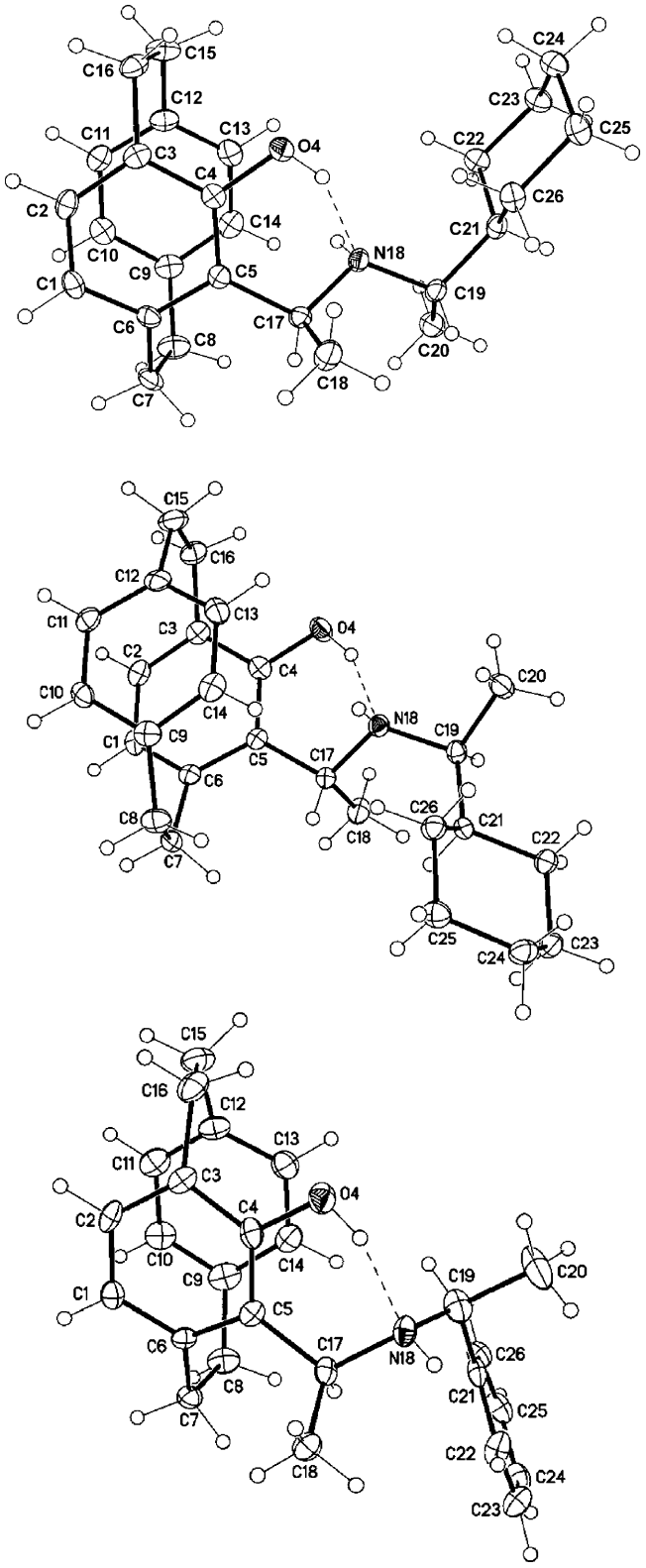


Figure 3. Top: Molecular structure of (R_p,*S*,*S*)-**16m**. Middle: Molecular structure of (S_p,*S*,*R*)-**16m**. Bottom: Molecular structure of (R_p,*S*,*S*)-**16i**. Displacement parameters are drawn at 50% probability level.

imine functionality. The use of ligand (S_p,*S*,*R*)-**16m**, which generates by far the most active catalyst, results even in only 11% starting material recovery (entry 2). In addition, high enantiomeric excesses (>90% *ee*) were obtained in all cases with ligands **16m** being the most selective ones (entries 1 and 2).

Furthermore, ligands with an S_p,*S*,*R* configuration seem to generate a slightly more active catalyst for the 1,2-addition compared to those containing an R_p,*S*,*S* configuration.

Finally, with the different amine-containing ligands **16** in hand we investigated their ability to act as ligands in the copper-mediated 1,4-addition reaction. Since secondary or tertiary amines are commonly used in N,P-ligands[35] for copper catalysis, ligands **16** should have better chelating properties than their imine analogues. The model reaction presented in Scheme 2 was used again, this time run under optimized conditions for copper catalysis.[36] The results are summarized in Table 7. 10 mol% CuCN and an equimolar amount of ligand were used in all cases (entries 1–4). As a control, identical reaction conditions without the addition of copper were applied (entries 5–8).

Concerning the copper-mediated catalysis, ligands **16m** generate a more active catalyst than **16i** (based on the recovered starting material). Ligand (S_p,*S*,*R*)-**16i** is remarkable, since almost no conversion takes place (Table 7, entry 4) and (S_p,*S*,*R*)-**16m** seems to be the most active one (entry 2).

The most dramatic change observed compared to the control experiments is, however, the pronounced difference in conversion to the desired product. Without addition of CuCN, high enantioselectivities, ranging from 70 to 89% *ee*, are obtained (Table 7, entries 5–8). But in the presence of copper, the observed enantioselectivities drop dramatically, 27% on the one hand for ligands (S_p,*S*,*R*)-**16m** and (S_p,*S*,*R*)-**16i** (entries 2 and 4) and almost no enantiomeric excess on the other hand for ligands (R_p,*S*,*S*)-**16m** and (R_p,*S*,*S*)-**16i** (entries 1 and 3).

Another interesting observation is that in the case of ligands (S_p,*S*,*R*)-**16m** and (R_p,*S*,*S*)-**16i**, the absolute configuration of **14** is switched depending on the presence or absence of copper. Even though we cannot rationalize this finding at this point, one can imagine that in the presence of copper, two opposite processes may run in parallel. On the one hand, the generated catalyst promotes the Michael addition under zinc catalysis with excellent enantioselectivities. On the other hand, there seems to be a copper-mediated pathway, which delivers the desired Michael product in high yields, but as a racemic mixture. If one assumes that the ligands do not complex copper, which is apparently the case (all efforts to obtain copper–ligand crystals by mixing either copper(I) cyanide, copper(I) iodide, copper(I) bromide, or a dimethyl sulfide complex with an equimolar amount of ligand **12i** in THF, CH_2Cl_2, and methyl *tert*-butyl ether, were unsuccessful) a transmetalation of diethylzinc to copper is likely to occur. This would generate an achiral organocopper species that is able to react in a conjugate addition reaction.

Moreover, in the control experiments without copper salt, the regioselectivity is in favor of the 1,2-addition product **14** (Table 6). The best results for an asymmetric 1,2-addition

Table 6. Screening of amine ligands **16m**,**i**.[a,d]

Entry	Ligand	Starting material [%][b]	1,4-Product (**14**) [%][b]	*ee* of **14** [%][c]	1,2-Product (**15**) [%][b]
1	(R_p,*S*,*S*)-**16m**	19	14	95 (*S*)	49
2	(S_p,*S*,*R*)-**16m**	11	12	95 (*R*)	55
3	(R_p,*S*,*S*)-**16i**	31	13	92 (*S*)	38
4	(S_p,*S*,*R*)-**16i**	30	6	91 (*R*)	45

[a] Reaction conditions: ligand (2 mol%), diethylzinc (1.10 M in toluene, 2.00 equiv), toluene, −25 °C, 1.5 d under an argon atmosphere. [b] Determined by GC analysis after workup. [c] Determined by GC analysis (chiral; Lipodex-E). [d] Due to side reactions, such as aldol reactions, the total amount of material does not always reach 100%.

Table 7. Copper-mediated and copper-free screening reactions with ligands **16m** and **16i**.[a,f]

Entry	Ligand	Starting material [%][b]	1,4-Product (**14**) [%][b]	*ee* of **14** [%][c]	1,2-Product (**15**) [%][b]	*ee* of **15** [%][d]
1	(R_p,*S*,*S*)-**16m**	29	43	1 (*S*)	19	1
2	(S_p,*S*,*R*)-**16m**	24	56	27 (*S*)	10	−6
3	(R_p,*S*,*S*)-**16i**	44	34	2 (*R*)	13	1
4	(S_p,*S*,*R*)-**16i**	82	8	27 (*R*)	6	−2
5[e]	(R_p,*S*,*S*)-**16m**	36	20	89 (*S*)	33	66
6[e]	(S_p,*S*,*R*)-**16m**	23	27	89 (*R*)	32	−48
7[e]	(R_p,*S*,*S*)-**16i**	30	16	88 (*S*)	45	75
8[e]	(S_p,*S*,*R*)-**16i**	40	17	70 (*R*)	33	−63

[a] Reaction conditions: CuCN (10 mol%), ligand (10 mol%), diethylzinc (1.00 M in *n*-hexane, 3.00 equiv), toluene, −30 °C, 1 d under an argon atmosphere. [b] Determined by GC analysis after workup. [c] Determined by GC analysis (chiral, Lipodex-E). [d] Determined by GC analysis (chiral; Hydrodex g-TBDAc). [e] No CuCN is added to the reaction. [f] Due to side reactions, such as aldol reactions, the total amount of material does not always reach 100%.

are obtained with (R_p,*S*,*S*)-**16i** in 45% yield and 75% *ee*, which makes these reduced ligands promising catalysts to address the 1,2-position of α,β-unsaturated carbonyl compounds selectively.

Concerning the amine-containing ligands, we were able to show that our zinc-catalyzed reactions indeed run under copper-free conditions and that traces of copper (present in commercially available diethylzinc solutions) mediate a concurrent racemic pathway.

Conclusion

We have demonstrated that substituted planar chiral [2.2]paracyclophanes bearing a central chiral unit are effective catalysts for asymmetric 1,4-addition reactions. Although the influence of the central chiral part cannot be fully rationalized to date, combining both chiralities results in the best catalysts. In addition, we proved that the zinc-based catalytic system is concurrently affected by copper salts and that copper-free conditions are required to obtain the desired 1,4-addition product selectively.

At this stage, it is interesting to note that depending on the paracyclophane ligand used, 1,4- or 1,2-regioselectivity is observed. In both cases with a high degree of enantioselection.

There are ongoing studies regarding this catalyst system and detailed mechanistic investigations done by in situ EXAF and IR techniques will be published in due course.

Experimental Section

General: All reactions were carried out under an argon atmosphere with oven-dried glassware. Solvents were dried under an argon atmosphere by using standard methods and were freshly distilled before use. Diethylzinc (1.10 M in toluene or 1.00 M in *n*-hexane) were purchased from commercial sources and used without further purification. *rac*-**10**, (S_p)-**10**, *rac*-**9**,[19] and 2,6-diphenylaniline[37] were synthesized according to literature procedures. The aldehydes used for the synthesis of the *ortho*-substituted salicylaldehyde derivatives were available from commercial sources or synthesized according to literature procedures. NMR spectra were analyzed according to first order and recorded on a Bruker AM 400 spectrometer. The chemical shifts (δ) are given in parts per million (ppm) relative to TMS and are referred to $CHCl_3$ with δ = 7.26 ppm. All coupling constants (*J*) are given in absolute values in Hertz (Hz). The description of signals include: s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, and ddd = doublet of dd. The signal abbreviations include: H_{ar} = aromatic proton and C_{ar} = aromatic carbon. The signal structure was analyzed by DEPT and is described as follows: p = primary C atom, s = secondary C atom, t = tertiary C atom, and q = quaternary C-atom. Gas chromatograms were recorded on a Varian CP-3900 (achiral stationary phase, capillary column Zebron ZB-5 MS, 30 m × 0.25 mm, 0.50 μm df). Enantiomeric excesses were determined by GC on a Varian CP-3800 (chiral stationary phase, capillary column Lipodex-E, 25 m × 0.25 mm and Hydrodex g-TBDAc, 25 m × 0.25 mm). In both cases, helium was used as a Carrier gas and nitrogen as the make-up gas. 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. IR spectra were recorded on a Bruker FTIR IFS-88. EIMS and HRMS were recorded on a Finnigan MAT 90 instrument. Elemental analysis was performed by using an Elementar Vario Microcube or a Heraeus CHN-O-Rapid. Flash chromatography was performed by using Machery-Nagel silica gel 60 (230–400 mesh ASTM) with the denoted solvents as the eluent. For TLC, silica-gel-coated aluminum plates (Merck, silica gel 60 with fluorescence indicator, F254) were employed. All reactions were conducted under an argon atmosphere.

X-ray crystallographic analysis: The data were collected on a Bruker-Nonius KappaCCD diffractometer at −150 °C by using $Mo_{K\alpha}$ radiation (λ = 0.71073 Å). The structures were solved by direct methods (SHELXS-97).[39] The non-hydrogen atoms were refined anisotropically, H atoms were refined by using a riding model, H (N, O) free (full-matrix least-squares refinement on F^2, SHELXL-97).[37] The absolute structure could not be determined reliably by refinement of Flack's *x* parameter.[37] For (R_p,*S*,*S*)-**16m**, (S_p,*S*,*R*)-**16m**, and (R_p,*S*,*S*)-**16i**, the absolute configuration was assigned by reference to an unchanging chiral center in the synthetic procedure. Details of data collection and refinement are given in

Tables 8 and 9. CCDC-696783 (**5r**), 696784 (**11r**), 696785 (**12n**), 696786 (**12o**), 696787 ((*R*$_p$,*S*,*S*)-**16m**), 696788 ((*S*$_p$,*S*,*R*)-**16m**), and 696789 ((*R*$_p$,*S*,*S*)-**16i**) 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

General procedure A for the conjugate addition of diethylzinc: The desired ligand (0.01 mmol, 0.02 equiv) was placed in a vial, dissolved in a diethylzinc solution (1.00 mL, toluene or *n*-hexane, 2.00 equiv) and stirred for 30 min at room temperature. After this time, the reaction mixture was cooled to the desired temperature (−30 or −25 °C) and cinnamaldehyde (0.50 mmol, 1.00 equiv) was added slowly by a syringe. The resulting reaction mixture was stirred at the mentioned temperature for the required time. The reaction was quenched with a 1 M HCl solution and diluted with diethyl ether. After separation of the organic phase, the mixture was washed twice with water and then dried over $MgSO_4$.

General procedure B for conjugate addition with ligands 16m and 16i: The desired ligand (0.01 mmol, 0.10 equiv) was placed together with CuCN (0.01 mmol, 0.10 equiv) in a vial. Then dry toluene (1.00 mL) was added and the mixture was stirred for 5 min. After this time, cinnamaldehyde (0.50 mmol, 1.00 equiv) was added. The resulting mixture was stirred for 10 min and was then cooled to −30 °C. Diethylzinc (0.30 mmol, 1.00 M solution in *n*-hexane, 3.00 equiv) was slowly added and the reaction mixture was stirred for 1 d. The reaction was quenched with a 1 M HCl solution and diluted with diethyl ether. After separation of the organic phase, the mixture was washed twice with water and then dried over $MgSO_4$.

General procedure C for imine condensation: The ketone (1.00 equiv) was dissolved in toluene (50.0 mL) and the desired amine (3.00 equiv) was added to the solution at room temperature. Then $Bu_2Sn(OAc)_2$ (cat.) was added in one portion and the reaction mixture was refluxed by using a Dean–Stark apparatus until no more starting material was detected by TLC. The mixture was allowed to cool to room temperature and the solvent was completely removed under reduced pressure. The residue was purified by flash column chromatography (*n*-pentane/diethyl ether).

Synthesis and characterization of ligands 3a–h

Table 8. Crystallographic data, structure solution, and refinement of **5r**, **11r**, **12n**, and **12o**.

Compound	**5r**	**11r**	**12n**	**12o**
formula	$C_{27}H_{23}NO$	$C_{35}H_{29}NO$	$C_{24}H_{23}NO$	$C_{28}H_{31}NO$
M_r	377.46	479.59	341.43	397.54
dimensions [mm]	0.20×0.30×0.50	0.10×0.20×0.50	0.30×0.40×0.50	0.10×0.15×0.20
crystal system	monoclinic	monoclinic	monoclinic	orthorhombic
space group	$P2_1/c$ (No.14)	$C2/c$ (No.15)	$P2_1/c$ (No.14)	$Pca2_1$ (No.29)
a [Å]	10.503(1)	30.5348(6)	11.5302(3)	16.3542(4)
b [Å]	10.069(1)	8.5751(2)	10.2977(3)	9.3885(2)
c [Å]	38.394(4)	19.1776(3)	15.4454(5)	28.4435(7)
α [°]	90	90	90	90
β [°]	90.95(1)	91.581(1)	103.463(2	90
γ [°]	90	90	90	90
V [Å^3]	4059.8(10)	5019.53(17)	1783.51(9)	4367.25(18)
Z	8	8	4	8
ρ [g cm^{-3}]	1.235	1.269	1.272	1.209
μ [mm^{-1}]	0.074	0.075	0.077	0.072
F(000)	1600	2032	728	1712
2θ max. [°]	50	50	55	55
	$-11 \le h \le 12$	$-36 \le h \le 36$	$-14 \le h \le 14$	$-16 \le h \le 21$
	$-11 \le k \le 11$	$-10 \le k \le 10$	$-13 \le k \le 12$	$-12 \le k \le 12$
	$-45 \le l \le 45$	$-22 \le l \le 22$	$-20 \le l \le 14$	$-31 \le l \le 36$
no. of measured reflns	38012	36326	13499	21099
no. of unique reflns	7052	4386	4019	8114
R_{int}	0.0378	0.0455	0.0281	0.0678
refinement on	F^2	F^2	F^2	F^2
no. of parameters/restraints	533/0	337/1	239/1	549/3
x				−1.6(19)
R [for $I > 2\sigma(I)$]	0.0461	0.0484	0.0453	0.0529
wR2 (all data)	0.1038	0.1180	0.1359	0.1197
S	1.18	1.10	1.13	0.90
max./min. difference peak [e Å^{-3}]	0.224/−0.174	0.220/−0.192	0.248/−0.246	0.258/−0.209

Table 9. Crystallographic data, structure solution, and refinement of (*R*$_p$,*S*,*S*)-**16m**, (*S*$_p$,*S*,*R*)-**16m**, and (*R*$_p$,*S*,*S*)-**16i**.

Compound	(*R*$_p$,*S*,*S*)-**16m**	(*S*$_p$,*S*,*R*)-**16m**	(*R*$_p$,*S*,*S*)-**16i**
formula	$C_{26}H_{35}NO$	$C_{26}H_{35}NO$	$C_{26}H_{29}NO$
M_r	377.55	377.55	371.50
dimensions [mm]	0.15×0.30×0.50	0.10×0.20×0.40	0.10×0.25×0.35
crystal system	orthorhombic	orthorhombic	orthorhombic
space group	$P2_12_12_1$ (No.19)	$P2_12_12_1$ (No.19)	$P2_12_12_1$ (No.19)
a [Å]	8.030(1)	7.750(1)	8.245(2)
b [Å]	14.928(3)	9.987(2)	9.093(2)
c [Å]	17.577(3)	26.354(4)	29.959(5)
α [°]	90	90	90
β [°]	90	90	90
γ [°]	90	90	90
V [Å^3]	2107.0(6)	2039.8(6)	2021.2(8)
Z	4	4	4
ρ [g cm^{-3}]	1.190	1.229	1.221
μ [mm^{-1}]	0.071	0.073	0.073
F(000)	824	824	800
2θ max. [°]	55	55	50
	$-10 \le h \le 10$	$-10 \le h \le 10$	$-9 \le h \le 9$
	$-19 \le k \le 19$	$-12 \le k \le 12$	$-10 \le k \le 10$
	$-22 \le l \le 22$	$-34 \le l \le 34$	$-32 \le l \le 31$
no. of measured reflns	43138	30119	20363
no. of unique reflns	4798	4629	2036
R_{int}	0.0382	0.0378	0.0573
refinement on	F^2	F^2	F^2
no. of parameters/restraints	259/2	259/2	259/2
x	0.4(11)	0.0(15)	−2(4)
R [for $I > 2\sigma(I)$]	0.0338	0.0418	0.0615
wR2 (all data)	0.0872	0.0871	0.1354
S	1.06	1.08	1.12
max./min. difference peak [e Å^{-3}]	0.226/−0.170	0.204/−0.187	0.278/−0.211

Synthesis of 3a: Compound **3a** was synthesized according to general procedure C with 2-hydroxyacetophenone (0.220 mL, 297 mg, 2.18 mmol) and enantiopure (*S*)-3-3-dimethyl-2-aminobutane (221 mg, 2.18 mmol). After 36 h stirring at room temperature, the raw material was purified by flash chromatography (pentane/diethyl ether 10:1). Yield: 191 mg (40%); yellow oil; $[\alpha]_D^{20}=+101.5$ ($c=0.850$ g/100 mL $CHCl_3$); $R_f=0.35$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.99$ (s, 9H; $C(CH_3)_3$), 1.17 (d, $J=6.6$ Hz, 3H; CH_3CHN), 2.37 (s, 3H; CH_3CHN), 3.57 (q, $J=6.6$ Hz, 1H; NC*H*), 6.74 (ddd, $J=1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 6.91 (dd, $J=1.1$, 8.3 Hz, 1H; H_{ar}), 7.28 (ddd, $J=1.1$, 1.6, 8.3 Hz, 1H), 7.50 ppm (dd, $J=1.6$, 8.3 Hz, 1H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 13.68 (p; CH_3CHN), 16.59 (p; CH_3CN), 26.43 (p, 3C; $C(CH_3)_3$), 34.50 (q; $C(CH_3)_3$), 62.95 (t; NCH), 116.37 (t; C_{ar}), 118.86 (q; C_{ar}), 119.27 (t; C_{ar}), 128.07 (t; C_{ar}), 132.55 (t; C_{ar}), 165.48 (q; C_{ar}, COH), 169.35 ppm (q; C=N); IR (KBr): $\tilde{\nu}=3471$ (vw), 2966 (vw), 1615 (w), 1579 (vw), 1501 (vw), 1448 (vw), 1396 (vw), 1372 (vw), 1303 (vw), 1236 (vw), 1203 (vw), 1160 (vw), 1135 (vw), 1112 (vw), 1087 (vw), 1011 (vw), 854 (vw), 837 (vw), 752 (vw), 625 (vw), 568 cm^{-1} (vw); EIMS (70 eV): *m/z* (%): 219 (15) [M^+], 162 (100), 146 (14), 120 (23), 91 (68), 57 (38), 41 (36); HR-EIMS: calcd for $C_{14}H_{21}NO$: 219.1623; found: 219.1626.

Synthesis of 3b: Compound **3b** was synthesized according to general procedure C with 2-hydroxyacetophenone (204 mg, 1.50 mmol) and enantiopure (*S*)-1-(4-methoxyphenyl)ethylamine (151 mg, 1.00 mmol). After 3 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-pentane/diethyl ether 5:1). Yield: 238 mg (59%); yellow oil; $[\alpha]_D^{20}=+326.6$ ($c=2$ g/100 mL $CHCl_3$); $R_f=0.18$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.53$ (d, $J=6.6$ Hz, 3H; CH_3CH), 2.25 (s, 3H; CH_3CN), 3.7 (s, 3H; OMe), 4.82 (q, $J=$ 6.6 Hz, 1H; CH_3CH), 6.67 (ddd, $J=1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 6.77–6.81 (m, 2H; H_{ar}), 6.86 (dd, $J=1.1$, 8.3 Hz, 1H; H_{ar}), 7.12–7.22 (m, 3H; H_{ar}), 7.41 ppm (dd, $J=1.6$, 8.3 Hz, 1H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 14.57 (p; CH_3CN), 25.24 (p; CH_3CH), 55.30 (p; OCH_3), 57.78 (t; CH_3CH), 114.19 (t, 2C; C_{ar}), 116.91 (t; C_{ar}), 118.98 (t; C_{ar}), 119.24 (q; C_{ar}), 127.39 (t, 2C; C_{ar}), 128.14 (t; C_{ar}), 132.66 (t; C_{ar}), 136.30 (q; C_{ar}), 158.69 (q; COMe), 164.60 (q; C_{ar}, COH), 170.33 ppm (q; C=N); IR (KBr): $\tilde{\nu}=3450$ (vw), 2967 (vw), 2928 (vw), 2835 (vw), 1611 (s), 1579 (w), 1511 (m), 1447 (w), 1373 (vw), 1303 (m), 1246 (m), 1177 (w), 1160 (w), 1133 (vw), 1098 (vw), 1033 (w), 972 (vw), 830 (w), 754 (w), 642 (vw), 623 (vw), 551 cm^{-1} (vw); EIMS (70 eV): *m/z* (%): 269 (36) [M^+], 135 (100); HR-EIMS: calcd for $C_{17}H_{19}NO_2$: 269.1416; found: 269.1412; elemental analysis calcd (%) for $C_{17}H_{19}NO_2$: C 75.81, H 7.11, N 5.20; found: C 75.48, H 7.11, N 5.23.

Synthesis of 3c: Compound **3c** was synthesized according to general procedure C with 2-hydroxyacetophenone (272 mg, 2.00 mmol), enantiopure (*S*)-1-(4-fluorphenyl)ethylamine (278 mg, 2.00 mmol), and a catalytic amount of $TiCl_4$. After 5 d stirring at room temperature, the raw material was purified by flash chromatography (*n*-pentane/diethyl ether 10:1). Yield: 352 mg (68%); orange/yellow oil; $[\alpha]_D^{20}=+305.9$ ($c=1.45$ g/100 mL $CHCl_3$); $R_f=0.25$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.61$ (d, $J=6.6$ Hz, 3H; CH_3CHN), 2.34 (s, 3H; CH_3CN), 4.94 (q, $J=6.6$ Hz, 1H; NC*H*), 6.79 (ddd, $J=8.3$, 1.6, 1.1 Hz, 1H; H_{ar}), 6.95 (dd, $J=8.3$, 1.1 Hz, 1H; H_{ar}), 7.03 (tt, $J=8.7$, 2.1 Hz, 2H; H_{ar}), 7.28–7.36 (m, 3H; H_{ar}), 7.51 (dd, $J=8.3$, 1.6 Hz, 1H; H_{ar}), 15.17 ppm (brs, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=14.66$ (p; CH_3CHN), 25.28 (p; CH_3CN), 57.87 (NCH), 115.53 (t; C_{ar}), 116.49 (t, d, $J_{C,F}=151.6$ Hz; C_{ar}), 118.75 (t; C_{ar}), 119.39 (q; C_{ar}), 127.87 (t, d, $J_{C,F}=$ 8.0 Hz; C_{ar}), 128.18 (t; C_{ar}), 132.68 (t; C_{ar}), 139.99 (q, $J_{C,F}=3.0$ Hz, d; C_{ar}), 161.85 (q, d, $J_{C,F}=245.3$ Hz; C_{ar}), 163.9 (q; C_{ar}, COH), 170.55 ppm (q; C=N); IR (KBr): $\tilde{\nu}=3472$ (vw), 3065 (vw), 2974 (vw), 2928 (vw), 1890 (vw), 1793 (vw), 1701 (vw), 1686 (vw), 1616 (w), 1578 (vw), 1509 (w), 1449 (vw), 1375 (vw), 1305 (vw), 1225 (vw), 1159 (vw), 1134 (vw), 1092 (vw), 1038 (vw), 1014 (vw), 937 (vw), 835 (vw), 755 (vw), 642 (vw), 623 (vw), 573 (vw), 548 (vw), 505 cm^{-1} (vw); EIMS (70 eV): *m/z* (%): 257(64) [M^+], 135 (43), 123 (100), 103 (19); HR-EIMS: calcd for $C_{16}H_{16}FNO$: 257.1216; found: 257.1213; elemental analysis calcd (%) for $C_{16}H_{16}FNO$: C 74.69, H 6.27, N 5.44; found: C 74.63, H 6.19, N 5.36.

Synthesis of 3d: Compound **3d** was synthesized according to general procedure C with 2-hydroxyacetophenone (272 mg, 2.00 mmol) and enantiopure (*S*)-phenylpropylamine (270 mg, 2.00 mmol). After 3 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-pentane/diethyl ether 10:1). Yield: 269 mg (53%); yellow oil; $[\alpha]_D^{20}=+363$ ($c=1.05$ g/100 mL $CHCl_3$); $R_f=0.36$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.88$ (t, $J=7.4$ Hz, 3H; CH_3CH_2), 1.93 (ddq, $J=14.5$, 7.4, 6.7 Hz, 2H; CH_3CH_2), 2.24 (s, 3H; CH_3CN), 4.61 (t, $J=6.7$ Hz, 1H; CH_2CH), 6.68 (ddd, $J=1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 6.88 (dd, $J=1.1$, 8.3 Hz, 1H; H_{ar}), 7.13–7.28 (m, 6H; H_{ar}), 7.42 (dd, $J=1.6$, $J=8.3$ Hz, 1H; H_{ar}), 14.72 ppm (brs, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=10.94$ (p; CH_3CH_2), 14.85 (p; CH_3CN), 32.31 (s; CH_3CH_2), 64.93 (t; CH_2CH), 116.92 (t; C_{ar}), 118.95 (t; C_{ar}), 119.28 (q; C_{ar}), 126.91 (t, 2C; C_{ar}), 127.20 (t; C_{ar}), 128.17 (t; C_{ar}), 128.70 (t, 2C; C_{ar}), 132.67 (t; C_{ar}), 142.80 (q; C_{ar}), 164.58 (q, C_{ar}; COH), 171.23 ppm (q; C=N); IR (KBr): $\tilde{\nu}=3061$ (w), 3028 (w), 2966 (m), 2930 (m), 2874 (w), 1949 (vw), 1614 (vs), 1579 (s), 1493 (m), 1450 (s), 1378 (w), 1305 (s), 1256 (m), 1236 (m), 1161 (m), 1134 (vw), 1088 (vw), 1050 (w), 1027 (w), 1005 (w), 937 (w), 838 (w), 754 (vs), 701 (s), 647 (vw), 543 (w), 522 cm^{-1} (vw); EIMS (70 eV): *m/z* (%): 253 (100) [M^+], 224 (41), 135 (38), 119 (23), 91 (81); HR-EIMS: calcd for $C_{17}H_{19}NO$: 253.1466; found: 253.1469; elemental analysis calcd (%) for $C_{17}H_{19}NO$: C 80.6, H 7.56, N 5.53; found: C 80.49, H 7.48, N 5.40.

Synthesis of 3e: Compound **3e** was synthesized according to general procedure C with 2-hydroxyacetophenone (136 mg, 1.00 mmol) and enantiopure (*S*)-1-aminotetraline (147 mg, 1.00 mmol). After 3 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-pentane/diethyl ether 10:1). Yield: 256 mg (98%); yellow solid; $[\alpha]_D^{20}=+100.6$ ($c=1.00$ g/100 mL $CHCl_3$); m.p. 77–78 °C; $R_f=0.31$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.87$–2 (m, 2H; CH_2), 2.06–2.17 (m, 2H; CH_2), 2.56 (s, 3H; CH_3), 2.82–3.03 (m, 2H; CH_2), 5–5.07 (m, 1H; NC*H*), 6.83 (ddd, $J=1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 6.92 (dd, $J=1.1$, 8.3 Hz, 1H; H_{ar}), 7.08–7.24 (m, 4H; H_{ar}), 7.31 (ddd, $J=1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 7.61 ppm (dd, $J=1.6$, 8.3 Hz, 1H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=14.27$ (p; CH_3CN), 20.46, 29.19, 31.01 (s; 3CH_2), 57.05 (t; NCH), 117.00 (t; C_{ar}), 118.88 (t; C_{ar}), 119.43 (q; C_{ar}), 126.14 (t; C_{ar}), 127.15 (t; C_{ar}), 127.90 (t; C_{ar}), 128.20 (t; C_{ar}), 129.25 (t; C_{ar}), 132.46 (t; C_{ar}), 136.77 (q; C_{ar}), 137.07 (q; C_{ar}), 164.16 (q; C_{ar}, COH), 169.79 ppm (q; C=N); IR (KBr): $\tilde{\nu}=3064$ (vw), 3017 (vw), 2933 (w), 2861 (vw), 2555 (vw), 1821 (vw), 1615 (w), 1579 (w), 1508 (w), 1491 (w), 1448 (w), 1374 (vw), 1304 (w), 1240 (w), 1163 (w), 1127 (vw), 1082 (vw), 1011 (vw), 950 (w), 853 (vw), 837 (vw), 775 (vw), 749 (w), 644 (vw), 625 (vw), 564 (vw), 531 (vw), 494 (vw), 478 (vw), 435 cm^{-1} (vw); EIMS (70 eV): *m/z* (%): 265 (54) [M^+], 135 (52), 131 (100), 91 (18); HR-EIMS: calcd for $C_{18}H_{19}NO$: 265.1467; found: 265.1465; elemental analysis calcd (%) for $C_{18}H_{19}NO$: C 81.47, H 7.22, N 5.28; found: C 81.07, H 7.12, N 5.20.

Synthesis of 3f: Compound **3f** was synthesized according to general procedure C with 2-hydroxyacetophenone (1.31 g, 9.60 mmol) and enantiopure 1-(*S*)-*trans*-(*S*)-2-phenylmethoxycyclohexylamine (500 mg, 2.40 mmol). After 4 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-pentane/diethyl ether 10:1). Yield: 607 mg (78%); orange oil; $[\alpha]_D^{20}=+211.4$ ($c=1.15$ g/100 mL $CHCl_3$); $R_f=0.20$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.32$–1.51 (m, 3H; *c*-hexyl), 1.57–1.67 (m, 1H; *c*-hexyl), 1.74–1.88 (m, 2H; *c*-hexyl), 1.88–1.96 (m, 1H; *c*-hexyl), 2.16–2.27 (m, 1H; *c*-hexyl), 2.38 (s, 3H; CH_3CN), 3.46–3.53 (m, 1H; *c*-hexyl), 3.71–3.77 (m, 1H; *c*-hexyl), 4.46 (d, $^2J=11.5$ Hz, 1H; CH_aH_bPh), 4.6 (d, $^2J=11.5$ Hz, 1H; CH_aH_bPh), 6.79 (ddd, $J=1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 6.97 (dd, $J=1.1$, 8.3 Hz, 1H; H_{ar}), 7.19–7.26 (m, 5H; CH_2Ph), 7.32 (ddd, $J=1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 7.53 ppm (dd, $J=1.6$, 8.3 Hz, 1H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=14.72$ (p; CH_3CN), 23.97 (s; C-*c*-hexyl), 24.03 (s; C-*c*-hexyl), 30.53 (s; C-*c*-hexyl), 32.16 (s; C-*c*-hexyl), 62.18 (t; C-*c*-hexyl), 71.99 (s; CH_2Ph), 81.83 (t; C-*c*-hexyl), 116.60 (t; C_{ar}), 119.10 (t; C_{ar}), 119.22 (q; C_{ar}), 127.47 (t; C_{ar}), 127.78 (t, 2C; C_{ar}), 128.26 (t, 3C; C_{ar}), 132.49 (t; C_{ar}), 138.59 (q; C_{ar}), 165.05 (q; C_{ar}, COH), 171.10 ppm (q; C=N); IR (KBr): $\tilde{\nu}=3061$ (w), 3030 (w), 2932 (s), 2859 (m), 1812 (vw), 1616 (vs), 1579 (m), 1497 (m), 1449 (s), 1361 (w), 1303 (m), 1259 (m), 1230 (m), 1207 (w), 1161 (m), 1093 (s), 1028 (w), 953 (w), 918 (w), 853 (w), 836 (w), 752 (s), 698 (m), 645 (vw), 620 (vw), 530 (vw), 502 cm^{-1} (vw); EIMS (70 eV): *m/z* (%): 323 (5) [M^+], 232 (20), 217 (23), 91 (100); HR-EIMS: calcd for $C_{21}H_{25}NO_2$: 323.1885; found: 323.1883.

Synthesis of 3g: Compound **3g** was synthesized according to general procedure C with 2-hydroxyacetophenone (100 μL, 136 mg, 1.00 mmol) and enantiopure (*S*)-1-(2-naphthyl)ethylamine (514 mg, 3.00 mmol). After 3 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-pentane/diethyl ether 10:1). Yield: 191 mg (66%); yellow solid; $[\alpha]_D^{20} = +494.2$ ($c = 1.15$ g/100 mL $CHCl_3$); m.p. 123–126°C; $R_f = 0.24$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 1.75 (d, $J = 6.6$ Hz, 3H; CH_3), 2.36 (s, 3H; CH_3CN), 5.11 (q, $J = 6.6$ Hz, 1H; NC*H*), 6.79 (ddd, $J = < 0.5$, 1.6, 8.3 Hz, 1H; H_{ar}), 7.01 (d, $J = 8.3$ Hz, 1H; H_{ar}), 7.33 (ddd, $J = 1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 7.54–7.55 (m, 4H; H_{ar}), 7.78–7.87 ppm (m, 4H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.83$ (p; CH_3CN), 25.25 (p; CH_3CH), 58.63 (t; CH_3CH), 117.08 (t; C_{ar}), 118.99 (t; C_{ar}), 119.32 (q; C_{ar}), 124.64 (t; C_{ar}), 124.77 (t; C_{ar}), 125.91 (t; C_{ar}), 126.31 (t; C_{ar}), 127.72 (t; C_{ar}), 127.89 (t; C_{ar}), 128.26 (t; C_{ar}), 128.80 (t; C_{ar}), 132.70 (q; C_{ar}), 132.80 (t; C_{ar}), 133.47 (q; C_{ar}), 141.58 (q; C_{ar}), 164.52 (q; C_{ar}, *C*OH), 171.05 ppm (q; *C*=N); IR (KBr): $\tilde{\nu} = 3058$ (w), 2980 (w), 2933 (w), 2555 (w), 1904 (vw), 1788 (vw), 1614 (m), 1577 (w), 1506 (w), 1445 (w), 1370 (w), 1300 (w) 1257 (w), 1165 (w), 1132 (w), 1108 (w), 1061 (w), 1011 (w), 951 (w), 898 (w), 863 (w), 836 (w), 824 (w), 751 (m), 663 (vw), 634 (w), 613 (w), 578 (w), 550 (vw), 532 (vw), 480 (w), 449 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 289 (44) [M^+], 155 (100); HR-EIMS: calcd for $C_{20}H_{19}NO$: 289.1467; found: 289.1468; elemental analysis calcd (%) for $C_{20}H_{19}NO$: C 83.01, H 6.62, N 4.84; found: C 83.24, H 6.53, N 4.65.

Synthesis of 3h: Compound **3h** was synthesized according to general procedure C with 2-hydroxyacetophenone (100 μL, 136 mg, 1.00 mmol) and enantiopure (*S*)-1-(1-naphthyl)ethylamine (422 mg, 2.50 mmol). After 4 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-pentane/diethyl ether 10:1). Yield: 328 mg (98%); brown solid; $[\alpha]_D^{20} = +563.3$ ($c = 1.20$ g/100 mL $CHCl_3$); m.p. 116°C; $R_f =$ 0.30 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.83$ (d, $J = 6.6$ Hz, 3H; CH_3), 2.26 (s, 3H; CH_3CN), 5.71 (q, $J = 6.6$ Hz, 1H; NC*H*), 6.78 (ddd, $J = 1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 7 (dd, $J = 1.1$, 8.3 Hz, 1H; H_{ar}), 7.33 (ddd, $J = 1.1$, 1.6, 8.3 Hz, 1H; H_{ar}), 7.44 (t, $J = 7.7$ Hz, 1H; H_{ar}), 7.48–7.54 (m, 3H; H_{ar}), 7.59 (ddd, $J = 1.5$, 1.5, 8.4 Hz, 1H; H_{ar}), 7.77 (d, $J = 8.1$ Hz, 1H; H_{ar}), 7.91 (dd, $J = 1.3$, 8.1 Hz, 1H; H_{ar}), 8.15 ppm (d, $J =$ 8.4 Hz, 1H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 15.19$ (p; CH_3CN), 24.70 (p; CH_3CH), 54.50 (t; CH_3CH), 116.95 (t; C_{ar}), 119.02 (t; C_{ar}), 119.22 (q; C_{ar}), 122.42 (t; C_{ar}), 123.64 (t; C_{ar}), 125.63 (t; C_{ar}), 125.89 (t; C_{ar}), 126.34 (t; C_{ar}), 127.63 (t; C_{ar}), 128.17 (t; C_{ar}), 129.23 (t; C_{ar}), 130.03 (q; C_{ar}), 132.79 (t; C_{ar}), 133.90 (q; C_{ar}), 140.33 (q; C_{ar}), 164.60 (q, C_{ar}; *C*OH), 171.71 ppm (q; *C*=N); IR (KBr): $\tilde{\nu} = 3045$ (w), 2976 (w), 2926 (w), 2865 (vw), 2548 (w), 1929 (vw), 1817 (vw), 1613 (m), 1578 (m), 1505 (m), 1450 (w), 1394 (w), 1372 (w), 1356 (w), 1323 (m), 1307 (m), 1257 (w), 1238 (w), 1171 (w), 1159 (w), 1133 (w), 1092 (w), 1016 (w), 968 (w), 938 (w), 866 (w), 834 (w), 798 (w), 779 (m), 765 (m), 659 (vw), 636 (w), 575 (vw), 533 (vw), 503 (w), 470 (vw), 457 (vw), 431 (vw), 406 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 289 (33) [M^+], 155 (100); HR-EIMS: calcd for $C_{20}H_{19}NO$: 289.1467; found: 289.1469; elemental analysis calcd (%) for $C_{20}H_{19}NO$: C 83.01, H 6.62, N 4.84; found: C 83.16, H 6.55, N 4.64.

Synthesis and characterization of precursor molecules 7r and 8r

Synthesis of 2-adamantyl-4-*tert*-butylphenol: 4-*tert*-Butylphenol (500 mg, 3.30 mmol) and adamantan-1-ol (532 mg, 3.50 mmol) were dissolved in CH_2Cl_2 (3.00 mL). Then, concentrated H_2SO_4 (180 μL) was added dropwise slowly to the reaction mixture over 10 min at room temperature. After 16 h stirring at room temperature, water (3 mL) was added and the reaction mixture was neutralized by adding a 1 M sodium hydroxide solution. This mixture was then extracted with CH_2Cl_2 (×3), and the organic phase was washed with brine and dried over sodium sulfate. After removing the solvent, purification was carried out by flash chromatography (*n*-hexane/ethyl acetate 10:1).[41] Yield: 400 mg (43%); white solid; $R_f = 0.58$ (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.30$ (s, 9H; $C(CH_3)_3$), 1.76–1.82 (m, 6H; H-Ad), 2.06–2.18 (m, 9H; H-Ad), 4.68 (br s, 1H; CO*H*), 6.58 (d, $J = 8.2$ Hz, 1H; H_{ar}), 7.07 (dd, $J = 2.4$, 8.2 Hz, 1H; H_{ar}), 7.25 ppm (d, $J = 2.4$ Hz, 1H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 29.10$ (t, 3C; C_{Ad}), 31.65 (p, 3C; $C(CH_3)_3$), 34.36 (q; C-$(CH_3)_3$), 36.89 (q; C_{ar}-$C(CH_2)_3$), 37.11 (s, 3C; C_{Ad}), 40.61 (s, 3C; C_{Ad}), 116.14 (t; C_{ar}), 123.31 (t; C_{ar}), 124.02 (t; C_{ar}), 135.53 (q; C_{ar}-$C(CH_2)_3$), 143.08 (q; *C*-*t*Bu), 152.02 ppm (q; *C*OH); IR (KBr): $\tilde{\nu} = 3489$, 3070, 2961, 2906, 2848, 2677, 2655, 1837, 1776, 1604, 1505, 1453, 1405, 1361, 1345, 1316, 1270, 1251, 1220, 1177, 1131, 1113, 1100, 1044, 1034, 977, 933, 891, 828, 806, 771, 743, 711, 672, 648, 638, 539, 494, 450 cm^{-1}; EIMS (70 eV): *m*/*z* (%): 284 [M^+] (31), 269 (100); HR-EIMS: calcd for $C_{20}H_{28}O$: 284.2140; found: 284.2137.

Synthesis of 3-adamantyl-5-*tert*-butyl-2-hydroxybenzaldehyde: 2,6-Lutidine (84.0 μL, 0.73 mmol) was added to a solution of 2-adamantan-1-yl-4-*tert*-butylphenol (259 mg, 0.91 mmol) in toluene (4.00 mL) at room temperature. Then $SnCl_4$ (1 M solution in CH_2Cl_2, 180 μL, 0.18 mmol) was added dropwise slowly over 10 min. The resulting reaction mixture was stirred for 20 min at room temperature and then paraformaldehyde (109 mg, 3.60 mmol) was added at once. It was stirred for an additional 12 h at room temperature. Then the reaction mixture was stirred for 6 h at 95°C. After cooling to room temperature, the mixture was filtered over Celite/silica gel 1:1 and washed with ethyl acetate. The filtrate was washed successively with water, 1 M HCl solution, and brine. The organic layer was then dried over sodium sulfate and evaporated. Purification was carried out by flash chromatography (*n*-hexane/ethyl acetate 15:1).[37] Yield: 251 mg (88%); colorless oil; $R_f = 0.82$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.33$ (s, 9H; $C(CH_3)_3$), 1.76–1.80 (m, 6H; H-Ad), 2.10–2.16 (m, 9H; H-Ad), 7.34 (d, $J = 2.5$ Hz, 1H; H_{ar}), 7.54 (d, $J = 2.5$ Hz, 1H; H_{ar}), 9.87 (s, 1H; C*H*O), 11.69 ppm (s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 28.99$ (t, 3C; C-Ad), 31.35 (p, 3Cp; $C(CH_3)_3$), 34.32 (q; $C(CH_3)_3$), 37.03 (s, 3C; C_{Ad}), 37.24 (q; C_{ar}-C-$(CH_2)_3$), 40.22 (s, 3C; C_{Ad}), 119.99 (q; C_{ar}-CHO), 127.73 (t; C_{ar}), 132.00 (t; C_{ar}), 137.82 (q; C_{ar}-$C(CH_2)_3$), 141.74 (q; *C*-*t*Bu), 159.39 (q; *C*OH), 197.49 ppm (t; C*H*O); IR (KBr): $\tilde{\nu} = 3881$, 3496, 2950, 2904, 2848, 2739, 2677, 2656, 1812, 1741, 1648, 1611, 1456, 1414, 1361, 1327, 1271, 1251, 1211, 1181, 1128, 1104, 1081, 1044, 976, 953, 878, 828, 818, 794, 765, 748, 705, 651, 638, 548, 520, 462, 437 cm^{-1}; EIMS (70 eV): *m*/*z* (%): 312 [M^+] (68), 297 (100); HR-EIMS: calcd for $C_{21}H_{28}O_2$: 312.2089; found: 312.2092; elemental analysis calcd (%) for $C_{21}H_{28}O_2$: C 80.73, H 9.03; found: C 80.34, H 9.12.

Synthesis of 4-*tert*-butyl-2-tritylphenol: 4-*tert*-Butylphenol (3.00 g, 19.97 mmol) and tritylchloride (1.86 g, 6.66 mmol) were heated at 220°C for 15 min. The resulting mixture was then cooled to room temperature and the obtained raw product was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). Yield: 527 mg (41%); white solid; m.p. 148–153°C; $R_f = 0.76$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.07$ (s, 9H; $C(CH_3)_3$), 4.25 (s, 1H; O*H*), 6.69 (d, $J = 8.3$ Hz, 1H; H_{ar}), 7.00 (d, $J = 2.4$ Hz, 1H; H_{ar}), 7.11–7.24 ppm (m, 16H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 31.46$ (p, 3C; $C(CH_3)_3$), 34.23 (q; C-$(CH_3)_3$), 62.93 (C-$C(C_6H_5)_3$), 117.25 (t; C_{ar}), 125.44 (t; C_{ar}), 126.75 (t; 3C; C_{trityl}), 127.88 (t, 6C; C_{trityl}), 127.93 (t; C_{ar}), 131.02 (t, 6C; C_{trityl}), 132.29 (q; C_{ar}), 142.70 (q; C_{ar}), 144.34 (q, 3C; C_{trityl}), 152.07 ppm (q; CO*H*); IR (KBr): $\tilde{\nu} = 3488$, 3393, 3055, 3027, 2961, 2903, 2865, 1955, 1891, 1816, 1661, 1596, 1490, 1444, 1406, 1363, 1332, 1269, 1208, 1186, 1124, 1082, 1036, 921, 885, 825, 748, 702, 671, 648, 632, 605, 543, 518, 496, 441, 419, 404 cm^{-1}; EIMS (70 eV): *m*/*z* (%): 392 [M^+] (100), 377 (85), 315 (39), 283 (15), 263 (23); HR-EIMS: calcd for $C_{29}H_{28}O$: 392.2140; found: 392.2143; elemental analysis calcd for $C_{29}H_{28}O$: C 88.74, H 7.19; found: C 88.82, H 7.30.

Synthesis of 5-*tert*-butyl-2-hydroxy-3-tritylbenzaldehyde: 4-*tert*-Butyl-2-tritylphenol (500 mg, 1.27 mmol), dry magnesium chloride (234 mg, 92.20 mmol), and paraformaldehyde (84.0 mg, 2.80 mmol) were suspended in THF (5.00 mL). Then, Et_3N (180 μL, 129 mg, 1.27 mmol) was added dropwise to the reaction mixture at room temperature and it was refluxed for 2 d. After complete conversion of the starting material (TLC-control), the mixture was cooled to room temperature and diluted with water. It was then extracted with CH_2Cl_2 (×3) and the combined organic layers were washed with water (×1) and brine (×2). The organic phase was dried over $MgSO_4$ and the solvent was removed. Purification was carried out by flash chromatography (*n*-hexane/ethyl acetate 40:1).[37] Yield: 214 mg (40%); white solid; m.p. 162–168°C; $R_f = 0.68$ (*n*-hexane/ethyl acetate 20:1); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.24$ (s, 9H; C-$(CH_3)_3$), 7.20–7.29 (m, 15H; H_{ar}), 7.48 (d, $J = 2.4$ Hz, 1H; H_{ar}), 7.65 (d, $J = 2.4$ Hz, 1H; H_{ar}), 9.88 (s, 1H; C*H*O), 11.22 ppm (s, 1H; CO*H*); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 31.16$ (p, 3C; $C(CH_3)_3$), 34.18 (q; C-

(CH_3)$_3$), 63.17 (C-*C*(C_6H_5)$_3$), 120.22 (q; C_{ar}, C_{ar}-CHO), 125.84 (t, 3C; C_{trityl}), 127.30 (t, 6C; C_{trityl}), 128.89 (t; C_{ar}), 130.91 (t, 6C; C_{trityl}), 135.02 (q; C_{ar}-trityl), 136.22 (t; C_{ar}), 141.51 (q; C_{ar}), 144.90 (q, 3C; C_{trityl}), 158.64 (q; CO*H*), 196.84 ppm (t; C*H*O); IR (KBr): $\tilde{\nu}$ = 3526, 3053, 3028, 2962, 2869, 1953, 1740, 1650, 1607, 1491, 1446, 1417, 1383, 1363, 1322, 1265, 1216, 1189, 1128, 1085, 1033, 1008, 950, 887, 836, 808, 748, 702, 659, 632, 617, 541, 520 cm^{-1}; EIMS (70 eV): *m*/*z* (%): 420 [*M*$^+$] (79), 343 (45), 182 (45), 105 (80), 77 (100); HR-EIMS: calcd for $C_{30}H_{28}O_2$: 420.2089; found: 420.2092; elemental analysis calcd (%) for $C_{30}H_{28}O_2$: C 85.68, H 6.71; found: C 85.36, H 6.87.

Synthesis and characterization of ligands 4–8r

Synthesis of 4r: Compound **4r** was synthesized according to general procedure C with 5-*tert*-butyl-2-hydroxybenzaldehyde (83.0 mg, 0.61 mmol) and 2,6-diphenylamine (100 mg, 0.41 mmol). After 12 h heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). Yield: 155 mg (63%); yellow solid; m.p. 163–166 °C; R_f = 0.47 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (s, 9H; C(C*H*$_3$)$_3$), 6.63 (d, *J* = 2.5 Hz, 1H; H_{ar}), 6.72 (d, *J* = 8.7 Hz, 1H; H_{ar}), 7.15–7.19 (m, 1H; H_{ar}), 7.24–7.28 (m, 5H; H_{ar}), 7.30–7.34 (m, 6H; H_{ar}), 7.85 (s, 1H; *H*C=N), 12.17 ppm (s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.30 (p, 3C; C(*C*H$_3$)$_3$), 33.83 (q; *C*-(CH_3)$_3$), 116.42 (t; C_{ar}), 118.07 (q; C_{ar}), 125.63 (t; C_{ar}), 126.91 (t, 2C; C_{ar}), 128.34 (t, 5C; C_{ar}), 129.84 (t, 4C; C_{ar}), 130.29 (t, 2C; C_{ar}), 130.34 (t; C_{ar}), 135.03 (q; 2C; C_{ar}), 139.67 (q, 2C; C_{ar}), 141.29 (q; C_{ar}), 145.24 (q; C_{ar}), 158.49 (q; *C*OH), 168.88 ppm (t; *C*=N); IR (KBr): $\tilde{\nu}$ = 3056 (w), 3027 (w), 2964 (w), 2869 (w), 1953 (vw), 1887 (vw), 1619 (w), 1580 (w), 1490 (m), 1460 (w), 1440 (w), 1407 (w), 1393 (w), 1365 (w), 1287 (w), 1264 (w), 1174 (w), 1134 (vw), 1074 (w), 1027 (vw), 986 (w), 936 (vw), 921 (vw), 896 (vw), 874 (w), 830 (w), 787 (w), 758 (m), 727 (w), 701 (m), 654 (vw), 621 (w), 593 (vw), 574 (vw), 555 (vw), 512 (vw), 493 (vw), 480 (vw), 463 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 405 (46) [*M*$^+$], 390 (27), 256 (100), 254 (26); HR-EIMS: calcd for $C_{29}H_{27}NO$: 405.2093; found: 405.2090; elemental analysis calcd (%) for $C_{29}H_{27}NO$: C 85.89, H 6.71, N 3.45; found: C 85.86, H 7.06, N 3.50.

Synthesis of 5r: Compound **5r** was synthesized according to general procedure C with 2-hydroxy-3,6-dimethylbenzaldehyde (70.0 mg, 0.47 mmol) and 2,6-diphenylamine (137 mg, 0.56 mmol). After 12 h heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). Yield: 163 mg (92%); yellow solid; m.p. 119–121 °C; R_f = 0.46 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62 (s, 3H; C*H*$_3$), 1.99 (s, 3H; C*H*$_3$), 6.24 (d, *J* = 7.5 Hz, 1H; H_{ar}), 6.84 (d, *J* = 7.5 Hz, 1H; H_{ar}), 7.11–7.15 (m, 2H; H_{ar}), 7.19–7.31 (m, 11H; H_{ar}), 8.20 (s, 1H; *H*C=N), 13.13 ppm (s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.44 (p; *C*H$_3$), 18.09 (p; *C*H$_3$), 115.82 (q; C_{ar}), 119.77 (t; C_{ar}), 124.04 (q; C_{ar}), 125.67 (t; C_{ar}), 126.94 (t, 2C; C_{ar}), 128.38 (t, 4C; C_{ar}), 129.97 (t, 4C; C_{ar}), 130.48 (t, 2C; C_{ar}), 134.02 (t; C_{ar}), 135.30 (q, 2C; C_{ar}), 137.18 (q; C_{ar}), 139.88 (q, 2C; C_{ar}), 145.60 (q; C_{ar}), 160.27 (q; *C*OH), 167.31 ppm (t; *C*=N); IR (KBr): $\tilde{\nu}$ = 3398 (vw), 3053 (w), 3027 (w), 2948 (w), 2926 (w), 1948 (vw), 1899 (vw), 1808 (vw), 1606 (m), 1578 (w), 1496 (w), 1461 (w), 1427 (w), 1413 (w), 1380 (w), 1358 (w), 1307 (vw), 1282 (w), 1254 (w), 1197 (w), 1158 (vw), 1073 (w), 1052 (w), 1027 (w), 982 (w), 917 (vw), 855 (w), 809 (w), 768 (w), 754 (m), 723 (w), 702 (m), 613 (vw), 596 (vw), 566 (vw), 535 (vw), 513 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 377 (100) [*M*$^+$], 256 (63); HR-EIMS: calcd for $C_{27}H_{23}NO$: 377.1779; found: 377.1776; elemental analysis calcd (%) for $C_{27}H_{23}NO$: C 85.91, H 6.14, N 3.71; found: C 85.82, H 6.05, N 3.65.

Synthesis of 6r: Compound **6r** was synthesized according to general procedure C with 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (104 mg, 0.44 mmol) and 2,6-diphenylamine (211 mg, 0.86 mmol). After 1 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). Yield: 163 mg (80%); yellow solid; m.p. 118–119 °C; R_f = 0.66 (*n*-hexane/ethyl acetate 40:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 (s, 9H; C(C*H*$_3$)$_3$), 1.29 (s, 9H; C(C*H*$_3$)$_3$), 6.48 (d, *J* = 2.4 Hz, 1H; H_{ar}), 7.14–7.18 (m, 2H; H_{ar}), 7.22–7.28 (m, 6H; H_{ar}), 7.33–7.35 (m, 6H; H_{ar}), 7.84 (s, 1H; C*H*=N), 12.84 ppm (s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.30 (p, 3C; C(*C*H$_3$)$_3$), 31.36 (p, 3C; C-(*C*H$_3$)$_3$), 33.98 (q; *C*(CH$_3$)$_3$), 34.98 (q; *C*(CH$_3$)$_3$), 117.82 (q; C_{ar}), 125.49 (t; C_{ar}), 126.46 (t; C_{ar}), 126.80 (t, 2C; C_{ar}), 127.73 (t; C_{ar}), 128.29 (t, 4C; C_{ar}), 129.87 (t, 4C; C_{ar}), 130.26 (t, 2C; C_{ar}), 135.07 (q, 2C; C_{ar}), 136.49 (q; C_{ar}), 139.69 (q, 2C; C_{ar}), 139.78 (q; C_{ar}), 145.14 (q; C_{ar}), 158.06 (q; C_{ar}, *C*OH), 169.27 ppm (t; *C*H=N); IR (KBr): $\tilde{\nu}$ = 3057 (w), 3027 (w), 2955 (m), 1947 (vw), 1882 (vw), 1804 (vw), 1618 (m), 1579 (w), 1496 (vw), 1458 (m), 1438 (m), 1411 (w), 1392 (w), 1361 (w), 1319 (w), 1273 (w), 1250 (w), 1194 (w), 1168 (m), 1132 (vw), 1072 (w), 1027 (w), 980 (w), 916 (w), 865 (w), 801 (w), 760 (m), 720 w), 700 (m), 669 (vw), 644 (vw), 613 (w), 602 (vw), 577 (vw), 531 (vw), 505 (vw), 459 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 462 (57) [*M*$^+$], 446 (16), 256 (29), 234 (23), 219 (100); HR-EIMS: calcd for $C_{33}H_{35}NO$: 461.2719; found: 461.2716; elemental analysis calcd for $C_{33}H_{35}NO$: C 85.86, H 7.64, N 3.03; found: C 85.64, H 7.72, N 2.97.

Synthesis of 7r: Compound **7r** was synthesized according to general procedure C with 3-adamantan-1-yl-5-*tert*-butyl-2-hydroxybenzaldehyde (113 mg, 0.36 mmol) and 2,6-diphenylamine (123 mg, 0.50 mmol). After 20 h heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 100:1) and afterwards by preparative TLC (*n*-pentane/diethyl ether 20:1). Yield: 172 mg (73%); yellow oil; R_f = 0.30 (*n*-hexane/ethyl acetate 100:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (s, 9H; C(C*H*$_3$)$_3$), 1.79–1.85 (m, 6H; H-Ad), 2.11–2.19 (m, 9H; H-Ad), 6.56 (d, *J* = 2.38 Hz, 1H; H_{ar}), 7.24–7.28 (m, 2H; H_{ar}), 7.31–7.38 (m, 6H; H_{ar}), 7.40–7.45 (m, 6H; H_{ar}), 12.99 ppm (s, 1H; O*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.10 (t, 3C; C-Ad), 31.33 (p, 3C; C-(*C*H$_3$)$_3$), 33.99 (q; *C*(CH$_3$)$_3$), 37.14 (q; C_{ar}-*C*(CH$_2$)$_3$), 37.16 (s, 3C; C_{Ad}), 40.12 (s, 3C; C_{Ad}), 117.77 (q; C_{ar}), 125.43 (t; C_{ar}), 126.27 (t; C_{ar}), 126.74 (t, 2C; C_{ar}), 127.67 (t; C_{ar}), 128.26 (t, 4C; C_{ar}), 129.82 (t, 4C; C_{ar}), 130.20 (t, 2C; C_{ar}), 135.05 (q, 2C; C_{ar}), 136.74 (q; C_{ar}-C(CH$_2$)$_3$), 139.67 (q, 2C; C_{ar}), 139.82 (q; C_{ar}, *C*-*t*Bu), 145.10 (q, C_{ar}), 158.29 (q; C_{ar}, *C*OH), 169.27 ppm (t; *C*H=N); IR (KBr): $\tilde{\nu}$ = 3058 (w), 3027 (w), 2962 (m), 2908 (m), 2849 (m), 2678 (vw), 1946 (vw), 1712 (vw), 1647 (m), 1618 (m), 1580 (m), 1497 (w), 1458 (m), 1413 (w), 1393 (w), 1363 (w), 1317 (w), 1272 (w), 1253 (m), 1214 (w), 1194 (w), 1181 (w), 1105 (w), 1082 (w), 1028 (w), 977 (w), 908 (w), 868 (w), 796 (w), 757 (m), 700 (m), 668 (vw), 650 (vw), 638 (vw), 613 (vw), 548 (vw), 507 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 539 (71) [*M*$^+$], 524 (12), 312 (53), 297 (100), 256 (38), 245 (8); HR-EIMS: calcd for $C_{39}H_{41}NO$: 539.3188; found: 539.3187.

Synthesis of 8r: Compound **8r** was synthesized according to general procedure C with 5-*tert*-butyl-2-hydroxy-3-tritylbenzaldehyde (100 mg, 0.24 mmol) and 2,6-diphenylamine (49.0 mg, 0.20 mmol). After 20 h heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). Yield: 110 mg (71%); yellow oil; R_f = 0.50 (*n*-hexane/ethyl acetate 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (s, 9H; C(C*H*$_3$)$_3$), 6.63 (d, *J* = 2.43 Hz, 1H; H_{ar}), 7.05–7.31 (m, 29H; H_{ar}), 7.77 (s, 1H; C*H*=N), 12.71 ppm (s, 1H; O*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.15 (p, 3C; C(*C*H$_3$)$_3$), 33.93 (q; *C*(CH$_3$)$_3$, 63.30 (q; *C*Ph$_3$), 117.88 (q; C_{ar}), 125.53 (t, 2C; C_{ar}), 126.69 (t, 3C_{ar}; C-trityl), 127.06 (t, 6C_{ar}; C-trityl), 127.44 (t; C_{ar}), 127.62 (t; C_{ar}), 128.11 (t, 4C; C_{ar}), 129.77 (t, 6C; C_{ar}), 129.85 (t; C_{ar}), 131.05 (t, 6C_{ar}; C-trityl), 132.40 (t; C_{ar}), 134.07 (q; C_{ar}), 134.48 (q, 2C; C_{ar}), 139.25 (q, 2C; C_{ar}), 145.53 (q; 4C; C_{ar} + 3C-trityl), 157.69 (q; C_{ar}, *C*OH), 168.48 ppm (t; *C*H=N); IR (KBr): $\tilde{\nu}$ = 3536 (vw), 3057 (vw), 3029 (vw), 2961 (w), 2867 (vw), 1950 (vw), 1810 (vw), 1620 (w), 1598 (vw), 1581 (vw), 1493 (w), 1445 (w), 1411 (vw), 1393 (vw), 1364 (vw), 1266 (vw), 1189 (vw), 1073 (vw), 1029 (vw), 1013 (vw), 980 (vw), 916 (vw), 871 (vw), 806 (vw), 749 (w), 725 (vw), 700 (w), 659 (vw), 629 (vw), 614 (vw), 509 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 647 (100) [*M*$^+$], 420 (6), 256 (38); HR-EIMS: calcd for $C_{48}H_{41}NO$: 647.3188; found: 647.3184; elemental analysis calcd (%) for $C_{48}H_{41}NO$: C 88.99, H 6.38, N 2.16; found: C 88.74, H 6.71, N 1.81.

Synthesis and characterization of ligands *rac*-11r and 12n–q

Synthesis of *rac*-11r: Compound **11r** was synthesized according to general procedure C with *rac*-**9** (100 mg, 0.40 mmol) and 2,6-diphenylamine (194 mg, 0.79 mmol). After 1 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane). Yield: 106 mg (55%); yellow oil; R_f = 0.42 (*n*-hexane/ethyl acetate; 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.28 (ddd, *J* = 6.1, 10.3, 13.0 Hz, 1H; CH_2), 2.40–2.58 (m, 2H; CH_2), 2.71–2.98 (m, 4H; CH_2), 3.33 (ddd, *J* = 3.7, 9.7, 13.1 Hz, 1H; CH_2), 5.27 (dd, *J* = 1.83, 7.9 Hz, 1H; H_{ar}), 5.95 (d, *J* = 7.6 Hz, 1H; H_{ar}), 6.12 (dd, *J* = 1.9, 7.9 Hz, 1H; H_{ar}), 6.25 (dd, *J* = 1.9,

7.9 Hz, 1H; H_{ar}), 6.33 (d, J=7.8 Hz, 1H; H_{ar}), 6.34–6.40 (m, 1H; H_{ar}), 7.19–7.27 (m, 2H; H_{ar}), 7.32–7.47 (m, 11H; H_{ar}), 7.78 ppm (d, J=1.4 Hz, 1H; C*H*=N); ^{13}C NMR (100 MHz, $CDCl_3$): δ=28.94 (s; *C*H_2), 31.05 (s; *C*H_2), 33.07 (s; *C*H_2), 34.17 (s; *C*H_2), 118.69 (q; C_{ar}), 126.38 (t, 2C; C_{ar}), 126.65 (q; C_{ar}), 126.84 (t; C_{ar}), 127.77 (t, 4C; C_{ar}), 128.92 (t, 4C; C_{ar}), 129.03 (t; C_{ar}), 129.58 (t, 2C; C_{ar}), 130.82 (t; C_{ar}), 131.04 (t; C_{ar}), 132.09 (t; C_{ar}), 133.27 (t; C_{ar}), 134.66 (q, 2C; C_{ar}), 136.38 (q; C_{ar}), 137.84 (t; C_{ar}), 138.89 (q, 2C; C_{ar}), 139.08 (q; C_{ar}), 142.53 (q; C_{ar}), 144.63 (q; C_{ar}), 160.14 (q; C_{ar}, *C*OH), 164.51 ppm (t; C_{ar}, *C*H=N); EIMS (70 eV): *m*/*z* (%): 479 (76) [M^+], 375 (100); HR-EIMS: calcd for $C_{35}H_{29}NO$: 479.2249; found: 479.2253.

Synthesis of *rac*-12n: Compound **12n** was synthesized according to general procedure C with *rac*-**10** (100 mg, 0.38 mmol) and aniline (103 μL, 105 mg, 1.13 mmol). After 6 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-pentane/diethyl ether 20:1). Yield: 89 mg (68%); yellow solid; m.p. 136–140 °C; R_f=0.46 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.26 (s, 3H; *C*H_3), 2.54–2.62 (m, 1H; CH_2), 2.68–2.75 (m, 1H; CH_2), 2.89–3.06 (m, 1H; CH_2), 3.00–3.06 (m, 1H; CH_2), 3.12–3.24 (m, 2H; CH_2), 3.40–3.54 (m, 2H; CH_2), 6.32 (d, J=7.6 Hz, 1H; H_{ar}), 6.46–6.55 (m, 3H; H_{ar}), 6.63 (dd, J=1.8, 7.9 Hz, 1H; H_{ar}), 6.96–7.02 (m, 3H; H_{ar}), 7.18–7.24 (m, 1H; H_{ar}), 7.41–7.46 (m, 2H; H_{ar}), 14.50 ppm (s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=22.67 (p; *C*H_3), 30.40 (s; *C*H_2), 33.88 (s; *C*H_2), 35.60 (s; *C*H_2), 37.43 (s; *C*H_2), 121.11 (t; 2C_{ar}), 122.61 (q; C_{ar}), 126.06 (t; 2C_{ar}), 126.54 (t; C_{ar}), 127.33 (t; C_{ar}), 129.14 (q; C_{ar}), 129.88 (t; C_{ar}), 131.47 (t; C_{ar}), 133.01 (t; C_{ar}), 136.30 (t; C_{ar}), 137.64 (q; C_{ar}), 139.95 (q; C_{ar}), 141.19 (q; C_{ar}), 144.30 (q; C_{ar}), 147.92 (q; C_{ar}), 160.36 (q; C_{ar}, *C*OH), 171.75 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$=3033 (vw), 2928 (w), 2851 (vw), 1871 (vw), 1737 (vw), 1576 (w), 1498 (vw), 1436 (w), 1367 (vw), 1304 (vw), 1207 (vw), 1168 (vw), 1154 (vw), 1113 (vw), 1070 (vw), 1025 (vw), 981 (vw), 933 (vw), 903 (vw), 880 (vw), 864 (vw), 830 (vw), 804 (vw), 790 (vw), 764 (vw), 717 (vw), 698 (vw), 669 (vw), 615 (vw), 587 (vw), 562 (vw), 517 (vw), 440 (vw), 411 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 341 (68) [M^+], 236 (100); HR-EIMS ($C_{24}H_{23}NO$): calcd: 341.1779; found: 341.1777.

Synthesis of *rac*-12o: Compound **12o** was synthesized according to general procedure C with *rac*-**10** (100 mg, 0.38 mmol) and *tert*-butylaniline (179 μL, 168 mg, 1.13 mmol). After 6 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-pentane/diethyl ether 20:1). Yield: 85 mg (56%); yellow solid; m.p. 113–116 °C; R_f=0.51 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.34 (s, 9H; C(C*H*$_3$)$_3$), 2.29 (s, 3H; *C*H_3), 2.54–2.61 (m, 1H; CH_2), 2.66–2.75 (m, 1H; CH_2), 2.86–3.06 (m, 2H; CH_2), 3.11–3.26 (m, 2H; CH_2), 3.41–3.57 (m, 2H; CH_2), 6.31 (d, J=7.6 Hz, 1H; H_{ar}), 6.46–6.52 (m, 3H; H_{ar}), 6.63 (dd, J=1.8, 7.9 Hz, 1H; H_{ar}), 6.91–6.95 (m, 2H; H_{ar}), 6.98 (dd, J=1.8, 7.9 Hz, 1H; H_{ar}), 7.43–7.47 (m, 2H; H_{ar}), 14.77 ppm (s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=22.67 (p; *C*H_3), 30.40 (s; *C*H_2), 31.47 (p, 3C; C(*C*H$_3$)$_3$), 33.87 (s; *C*H_2), 34.50 (q; *C*(CH$_3$)$_3$), 35.59 (s; *C*H_2), 37.48 (s; *C*H_2), 120.99 (t; 2C_{ar}), 122.55 (q; C_{ar}), 124.83 (t; C_{ar}), 126.66 (t; C_{ar}), 127.37 (t; C_{ar}), 129.15 (q; C_{ar}), 129.26 (t; 2C_{ar}), 129.88 (t; C_{ar}), 131.56 (t; C_{ar}), 133.01 (t; C_{ar}), 136.46 (t; C_{ar}), 137.66 (q; C_{ar}), 139.99 (q; C_{ar}), 141.26 (q; C_{ar}), 147.29 (q; C_{ar}), 160.10 (q; C_{ar}, *C*OH), 171.75 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$=3009 (w), 2962 (m), 2929 (m), 1888 (vw), 1742 (w), 1577 (m), 1501 (w), 1435 (m), 1364 (w), 1323 (w), 1302 (w), 1267 (w), 1214 (w), 1179 (w), 1114 (w), 1016 (w), 996 (vw), 932 (w), 857 (w), 806 (w), 766 (w), 717 (w), 673 (vw), 655 (vw), 621 (vw), 577 (w), 554 (vw), 513 (w), 460 (vw), 439 (vw), 408 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 397 (77) [M^+], 293 (100), 278 (28), 248 (18); HR-EIMS: calcd for $C_{28}H_{31}NO$: 397.2406; found: 397.2403.

Synthesis of *rac*-12p: Compound **12p** was synthesized according to general procedure C with *rac*-**10** (100 mg, 0.38 mmol) and *N*,*N*-dimethylhydrazine (asym., 87.0 μL, 69.0 mg, 1.13 mmol). After 5 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). Yield: 41 mg (35%); yellow solid; m.p. 99–101 °C; R_f=0.26 (*n*-hexane/ethyl acetate 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.37 (s, 3H; C*H*$_3$C=N), 2.51–2.59 (m, 2H; CH_2), 2.74 (s, 6H; N(C*H*$_3$)$_2$), 2.79–2.88 (m, 1H; CH_2), 2.96–3.04 (m, 1H; CH_2), 3.07–3.19 (m, 2H; CH_2), 3.34–3.44 (m, 2H; CH_2), 6.28 (d, J=7.6 Hz, 1H; H_{ar}), 6.41–6.49 (m, 3H; H_{ar}), 6.58 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 6.98 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 13.25 ppm (s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=20.03 (p; *C*H$_3$C=N), 30.37 (s; *C*H_2), 33.91 (s; *C*H_2), 35.29 (s; *C*H_2), 36.82 (s; *C*H_2), 47.43 (p; 2C; N(*C*H$_3$)$_2$), 122.31 (q; C_{ar}), 126.63 (t; C_{ar}), 127.00 (t; C_{ar}), 128.54 (q; C_{ar}), 129.14 (t; C_{ar}), 131.64 (t; C_{ar}), 132.85 (t; C_{ar}), 135.15 (t; C_{ar}), 137.65 (q; C_{ar}), 139.88 (q; C_{ar}), 140.71 (q; C_{ar}), 157.71 (q; C_{ar}, *C*OH), 167.15 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$=3007 (vw), 2954 (w), 2931 (w), 2850 (w), 2819 (vw), 2773 (vw), 1873 (vw), 1593 (vw), 1571 (w), 1499 (vw), 1426 (w), 1360 (vw), 1298 (vw), 1243 (vw), 1205 (vw), 1149 (vw), 1117 (vw), 1098 (vw), 1021 (vw), 999 (vw), 967 (w), 934 (vw), 880 (vw), 844 (w), 797 (w), 717 (w), 695 (vw), 668 (vw), 612 (vw), 590 (vw), 541 (vw), 516 (vw), 477 (vw), 440 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 308 (100) [M^+], 204 (26), 161 (34); HR-EIMS: calcd for $C_{20}H_{24}N_2O$: 308.1889; found: 308.1885.

Synthesis of *rac*-12q: Compound **12q** was synthesized according to general procedure C with *rac*-**10** (100 mg, 0.38 mmol) and cyclohexylamine (113 mg, 1.13 mmol). After 3 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). Yield: 100 mg (75%); orange solid; m.p. 162–163 °C; R_f=0.53 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.36–1.74 (m, 6H; H-*c*-hexyl), 1.84–2.00 (m, 4H; H-*c*-hexyl), 2.31 (s, 3H; C*H*$_3$), 2.45–2.61 (m, 2H; CH_2), 2.79–2.89 (m, 1H; CH_2), 2.93–3.02 (m, 1H; CH_2), 3.06–3.19 (m, 2H; CH_2), 3.36–3.43 (m, 2H; CH_2), 3.56–3.67 (m, 1H; NC*H*), 6.15 (d, J=7.5 Hz, 1H; H_{ar}), 6.30 (dd, J=1.9, 7.7 Hz, 1H; H_{ar}), 6.40 (d, J=7.5 Hz, 1H; H_{ar}), 6.44–6.46 (dd, J=1.9, 7.9 Hz, 1H; H_{ar}), 6.58–6.61 (dd, J=1.8, 7.9 Hz, 1H; H_{ar}), 6.96–7.00 (dd, J=1.8, 7.7 Hz, 1H; H_{ar}), 16.32 ppm (s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=19.21 (p; *C*H_3), 24.45 (s; C-*c*-hexyl), 24.53 (s; C-*c*-hexyl), 25.58 (s; C-*c*-hexyl), 30.46 (s; *C*H_2), 33.19 (s; C-*c*-hexyl), 33.83 (s; C-*c*-hexyl), 33.87 (s; *C*H_2), 35.43 (s; *C*H_2), 37.54 (s; *C*H_2), 56.22 (t; N*C*H), 121.50 (q; C_{ar}), 125.09 (t; C_{ar}), 127.03 (t; C_{ar}), 129.59 (t; C_{ar}), 129.99 (q; C_{ar}), 131.18 (t; C_{ar}), 132.78 (t; C_{ar}), 135.90 (t; C_{ar}), 137.53 (q; C_{ar}), 139.99 (q; C_{ar}), 140.60 (q; C_{ar}), 165.06 (q; C_{ar}, *C*OH), 168.59 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$=3640 (vw), 3008 (w), 2929 (m), 2847 (m), 2665 (w), 1881 (w), 1594 (m), 1499 (w), 1439 (m), 1361 (w), 1346 (w), 1299 (w), 1232 (w), 1167 (w), 1115 (w), 1078 (w), 997 (w), 949 (w), 932 (w), 879 (w), 794 (w), 766 (w), 717 (w), 687 (w), 669 (w), 615 (w), 590 (w), 565 (vw), 537 (w), 515 (w), 465 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 347 (93) [M^+], 243 (100), 160 (29); HR-EIMS: calcd for $C_{24}H_{29}NO$: 347.2249; found: 347.2247.

Synthesis of (S_p)-12q: Yield: 60 mg (75%); $[\alpha]_D^{20}$=−698.0 (c=0.88 g/100 mL in $CHCl_3$); the remaining spectroscopic data are the same as for ligand *rac*-**6e**.

Synthesis and characterization of [2.2]paracyclophane ligands

Synthesis of 12j: Compound **12j** was synthesized according to general procedure C with *rac*-**10** (154 mg, 0.58 mmol) and enantiopure (*R*)-1-cyclopropylethylamine (167 mg, 1.73 mmol). After 11 d heating (115 °C bath temperature), the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 40:1). The combined yield of both fractions was 49%.

Isomer (S_p,R)-***12j***: Yield: 47 mg (24%); orange oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.18–0.28 (m, 2H; C*H*$_2$CH$_2$), 0.50–0.60 (m, 2H; CH$_2$C*H*$_2$), 1.15–1.24 (m, 1H; CH$_2$CH$_2$C*H*), 1.45 (d, J=6.4 Hz, 3H; C*H*$_3$CH), 2.25 (s, 3H; CH$_3$CN), 2.46–2.59 (m, 2H; CH_2), 2.81–2.90 (m, 1H; CH_2), 2.94–3.02 (m, 1H; CH_2), 3.06–3.18 (m, 2H; CH_2), 3.24 (dq, J=0.8, 6.4 Hz, 1H; NC*H*), 3.34–3.45 (m, 2H; CH_2), 6.14 (d, J=7.5 Hz, 1H; H_{ar}), 6.33 (dd, J=1.9, 7.8 Hz, 1H; H_{ar}), 6.41 (d, J=7.5 Hz, 1H; H_{ar}), 6.46 (dd, J=1.9, 7.9 Hz, 1H), 6.60 (dd, J=1.8, 7.9 Hz, 1H; H_{ar}), 6.99 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 15.94 ppm (s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=2.57 (s; C-*c*-prop), 3.18 (s; C-*c*-prop), 17.95 (t; C-*c*-prop), 19.44 (p; *C*H$_3$CN), 21.56 (*C*H$_3$CHN), 30.41 (s; CH_2), 33.88 (s; CH_2), 35.45 (s; CH_2), 37.46 (s; CH_2), 57.39 (t; N*C*H), 121.89 (q; C_{ar}), 125.39 (t; C_{ar}), 127.09 (t; C_{ar}), 129.63 (t; C_{ar}), 129.67 (q; C_{ar}), 131.29 (t; C_{ar}), 132.78 (t; C_{ar}), 135.88 (t; C_{ar}), 137.55 (q; C_{ar}), 140.00 (q; C_{ar}), 140.57 (q; C_{ar}), 163.66 (q; C_{ar}, *C*OH), 168.69 ppm (q; *C*=N); EIMS: *m*/*z*: (%): 333 [M^+] (42), 229 (60), 104 (100); HR-EIMS: calcd for $C_{23}H_{27}NO$: 333.2093; found: 333.2094.

Isomer (R_p,R)-***12j***: Yield: 48 mg (25%); orange oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.31–0.44 (m, 2H; C*H*$_2$CH$_2$), 0.61–0.72 (m, 2H; CH$_2$C*H*$_2$),

1.18–1.29 (m, 1H; CH_2CH_2CH), 1.37 (d, $J=6.4$ Hz, 3H; CH_3CH), 2.25 (s, 3H; CH_3CN), 2.47–2.63 (m, 2H; CH_2), 2.83–2.90 (m, 1H; CH_2), 2.96–3.03 (m, 1H; CH_2), 3.08–3.19 (m, 2H; CH_2), 3.23 (dq, $J=0.8$, $J=6.4$ Hz 1H; NCH), 3.35–3.44 (m, 2H; CH_2), 6.18 (d, $J=7.5$ Hz, 1H; H_{ar}), 6.41 (d, $J=7.5$ Hz, 1H; H_{ar}), 6.44–6.47 (m, 2H; H_{ar}), 6.60 (dd, $J=1.8$, 7.9 Hz, 1H; H_{ar}), 7.00 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 16.07 ppm (brs, 1H; COH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=1.71$ (s; C-*c*-prop), 2.33 (s; C-*c*-prop), 17.66 (p; CH_3CN), 18.80 (t; C-*c*-prop), 20.34 (CH_3CHN), 29.60 (s; CH_2), 33.05 (s; CH_2), 34.57 (s; CH_2), 36.63 (s; CH_2), 56.61 (t; NCH), 121.00 (q; C_{ar}), 124.51 (t; C_{ar}), 126.29 (t; C_{ar}), 128.89 (q; C_{ar}), 128.96 (t; C_{ar}), 130.42 (t; C_{ar}), 131.95 (t; C_{ar}), 135.05 (t; C_{ar}), 136.71 (q; C_{ar}), 139.09 (q; C_{ar}), 139.74 (q; C_{ar}), 163.05 (q; C_{ar}, COH), 167.61 ppm (q; C=N); EIMS (70 eV): *m/z* (%): 333 [M^+] (40), 229 (57), 104 (100); HR-EIMS: calcd for $C_{23}H_{27}NO$: 333.2093; found: 333.2096.

Synthesis of 12k: Compound **12k** was synthesized according to general procedure C with *rac*-**10** (151 mg, 0.57 mmol) and enantiopure (*S*)-1-(3-chlorophenyl)ethylamine (265 mg, 2.00 mmol). After 2 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 40:1). The combined yield of both fractions was 66%.

Isomer (R_p,S)-***12k***: Yield: 71 mg (31%); orange oil; $[\alpha]_D^{20}=+560.2$ ($c=0.47$ g/100 mL in $CHCl_3$); $R_f=0.33$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.64$ (d, $J=6.6$ Hz, 3H; CH_3CHN), 2.19 (s, 3H; CH_3CN), 2.41–2.58 (m, 2H; CH_2), 2.78–2.85 (m, 1H; CH_2), 2.88–2.97 (m, 1H; CH_2), 3.03–3.13 (m, 2H; CH_2), 3.26–3.36 (m, 2H; CH_2), 4.76 (q, $J=6.6$ Hz, 1H; NCH), 6.13 (d, $J=7.5$ Hz, 1H; H_{ar}), 6.35 (d, $J=7.5$ Hz, 1H; H_{ar}), 6.33–6.42 (m, 2H; H_{ar}), 6.54 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 6.96 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 7.13–7.25 ppm (m, 4H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=19.59$ (p; CH_3CN), 24.25 (p; CH_3CHN), 29.41 (s; CH_2), 32.84 (s; CH_2), 34.43 (s; CH_2), 36.29 (s; CH_2), 56.84 (t; NCH), 121.30 (q; C_{ar}), 123.36 (t; C_{ar}), 124.85 (t; C_{ar}), 125.57 (t; C_{ar}), 126.12 (t; C_{ar}), 126.37 (t; C_{ar}), 128.40 (q; C_{ar}), 128.57 (t; C_{ar}), 129.24 (t; C_{ar}), 130.48 (t; C_{ar}), 131.77 (t; C_{ar}), 133.47 (q; C_{ar}), 135.20 (t; C_{ar}), 136.56 (q; C_{ar}), 139.01 (q; C_{ar}), 139.79 (q; C_{ar}), 144.84 (q; C_{ar}), 161.43 (q; C_{ar}, COH), 169.78 ppm (q; C=N); IR (KBr): $\tilde{\nu}=3009$ (w), 2927 (m), 2851 (w), 1595 (m), 1500 (w), 1417 (m), 1359 (w), 1340 (w), 1321 (w), 1298 (mw), 1233 (m), 1200 (w), 1155 (w), 1110 (w), 1081 (w), 1016 (vw), 993 (vw), 978 (vw), 936 (vw), 879 (w), 788 (w), 718 (w), 696 (w), 672 (vw), 621 (w), 588 (w), 568 (w), 509 cm^{-1} (w); EIMS (70 eV): *m/z* (%): 403 (69) [M^+], 299 (52), 266 (100), 162 (86), 104 (72); HR-EIMS: calcd for $C_{23}H_{26}NOCl$: 403.1703; found: 403.1701.

Isomer (S_p,S)-***12k***: Yield: 81 mg (35%); orange solid; $[\alpha]_D^{20}=-197.0$ ($c=0.51$ g/100 mL in $CHCl_3$); $R_f=0.25$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.65$ (d, $J=6.6$ Hz, 3H; CH_3CHN), 2.26 (s, 3Hp; CH_3CN), 2.40–2.47 (m, 1H; CH_2), 2.51–2.58 (m, 1H; CH_2), 2.83–2.91 (m, 1H; CH_2), 2.94–3.08 (m, 2H; CH_2), 3.15–3.28 (m, 2H; CH_2), 3.43 (ddd, $J=2.6$, 2.6, 12.8 Hz, 1H; CH_2), 4.84 (q, $J=6.6$ Hz, 1H; NCH), 6.13 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 6.21 (d, $J=7.5$ Hz, 1H; H_{ar}), 6.43 (d, $J=7.5$ Hz, 1H; H_{ar}), 6.48 (dd, $J=1.8$, 7.9 Hz, 1H; H_{ar}), 6.58 (dd, $J=1.8$, 7.9 Hz, 1H; H_{ar}), 7.02 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 7.30 (dt, $J=1.7$, 7.8 Hz, 1H; H_{ar}), 7.38 (t, $J=7.7$ Hz, 1H; H_{ar}), 7.42 (dt, $J=1.7$, 7.7 Hz, 1H; H_{ar}), 7.53 ppm (t, $J=1.7$ Hz, 1H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=20.54$ (p; CH_3CN), 24.94 (p; CH_3CHN), 30.52 (s; CH_2), 33.89 (s; CH_2), 35.41 (s; CH_2), 37.15 (s; CH_2), 57.75 (t; NCH), 122.47 (q; C_{ar}), 124.59 (t; C_{ar}), 125.93 (t; C_{ar}), 126.77 (t; C_{ar}), 127.07 (t; C_{ar}), 127.45 (t; C_{ar}), 129.27 (q; C_{ar}), 130.04 (t; C_{ar}), 130.19 (t; C_{ar}), 131.62 (t; C_{ar}), 132.72 (t; C_{ar}), 134.66 (q; C_{ar}), 136.41 (t; C_{ar}), 137.64 (q; C_{ar}), 139.967 (q; C_{ar}), 140.92 (q; C_{ar}), 146.69 (q; C_{ar}), 162.19 (q; C_{ar}, COH), 170.54 ppm (q; C=N); IR (KBr): $\tilde{\nu}=3070$ (w), 3010 (w), 2965 (w), 2927 (w), 2848 (w), 1959 (vw), 1871 (vw), 1740 (vw), 1580 (w), 1500 (w), 1471 (w), 1427 (w), 1375 (w), 1316 (vw), 1297 (w), 1242 (w), 1199 (vw), 1161 (vw), 1135 (vw), 1080 (w), 1033 (vw), 998 (vw), 983 (vw), 933 (vw), 879 (w), 838 (vw), 797 (w), 763 (vw), 717 (w), 705 (w), 666 (vw), 622 (vw), 586 (vw), 552 (vw), 532 (vw), 509 (w), 449 (vw), 422 (vw), 408 cm^{-1} (vw); EIMS (70 eV): *m/z* (%): 403 (100) [M^+], 299 (42), 160 (51); HR-EIMS: calcd for $C_{23}H_{26}NOCl$: 403.1703; found: 403.1705; elemental analysis calcd (%) for $C_{23}H_{26}NOCl$: C 77.31, H 6.49, N 3.47; found: C 77.33, H 6.49, N 3.16.

Synthesis of 12l: Compound **12l** was synthesized according to general procedure C with *rac*-**10** (152 mg, 0.57 mmol) and enantiopure (*S*)-1-(3-bromophenyl)ethylamine (343 mg, 2.67 mmol). After 2 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 40:1). The combined yield of both fractions was 60%.

Isomer (R_p,S)-***12l***: Yield: 76 mg (30%); orange oil; $[\alpha]_D^{20}=+502.4$ ($c=3.44$ g/100 mL in $CHCl_3$); $R_f=0.34$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.72$ (d, $J=6.6$ Hz, 3H; CH_3CHN), 2.27 (s, 3H; CH_3CN), 2.50–2.57 (m, 1H; CH_2), 2.59–2.67 (m, 1H; CH_2), 2.85–2.94 (m, 1H; CH_2), 2.97–3.05 (m, 1H; CH_2), 3.08–3.22 (m, 2H; CH_2), 3.34–3.46 (m, 2H; CH_2), 4.83 (q, $J=6.6$ Hz, 1H; NCH), 6.21 (d, $J=7.5$ Hz, 1H; H_{ar}), 6.41–6.44 (m, 2H; H_{ar}), 6.49 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 6.62 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 7.04 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 7.21 (t, $J=7.8$ Hz, 1H; H_{ar}), 7.29–7.31 (m, 1H; H_{ar}), 7.36–7.40 (m, 1H; H_{ar}), 7.48 ppm (t, $J=1.7$ Hz, 1H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=20.65$ (p; CH_3CN), 25.31 (p; CH_3CHN), 30.47 (s; CH_2), 33.90 (s; CH_2), 35.49 (s; CH_2), 37.36 (s; CH_2), 54.56 (t; NCH), 122.34 (q; C_{ar}, C-Br), 122.76 (q; C_{ar}), 124.87 (t; C_{ar}), 125.91 (t; C_{ar}), 127.18 (t; C_{ar}), 129.47 (q; C_{ar}), 129.54 (t; C_{ar}), 129.64 (t; C_{ar}), 130.37 (t; C_{ar}), 130.63 (t; C_{ar}), 131.54 (t; C_{ar}), 132.82 (t; C_{ar}), 136.29 (t; C_{ar}), 137.62 (q; C_{ar}), 140.06 (q; C_{ar}), 140.86 (q; C_{ar}), 146.17 (q; C_{ar}), 162.57 (q; C_{ar}, COH), 170.86 ppm (q; C=N); IR (KBr): $\tilde{\nu}=3008$ (w), 2966 (w), 2926 (m), 2851 (w), 1883 (vw), 1736 (vw), 1590 (m), 1500 (w), 1475 (w), 1419 (m), 1360 (w), 1340 (vw), 1321 (w), 1297 (w), 1234 (w), 1199 (vw), 1155 (vw), 1131 (vw), 1110 (vw), 1092 (vw), 1071 (w), 995 (vw), 979 (vw), 934 (vw), 878 (w), 785 (w), 717 (w), 696 (w), 671 (w), 619 (vw), 587 (vw), 567 (vw), 509 (vw), 442 cm^{-1} (vw); EIMS (70 eV): *m/z* (%): 449/447 (32/32) [M^+], 345/343 (23/23), 266 (88), 161 (100), 104 (77); HR-EIMS: calcd for $C_{26}H_{26}NOBr$: 447.1198; found: 447.1201.

Isomer (S_p,S)-***12l***: Yield: 76 mg (30%); orange oil; $[\alpha]_D^{20}=-113.8$ ($c=3.19$ g/100 mL in $CHCl_3$); $R_f=0.25$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.64$ (d, $J=6.6$ Hz, 3H; CH_3CHN), 2.25 (s, 3H; CH_3CN), 2.40–2.47 (m, 1H; CH_2), 2.49–2.57 (m, 1H; CH_2), 2.82–2.90 (m, 1H; CH_2), 2.95–3.07 (m, 2H; CH_2), 3.15–3.25 (m, 2H; CH_2), 3.39–3.46 (m, 1H; CH_2), 4.83 (q, $J=6.6$ Hz, 1H; NCH), 6.14 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 6.20 (d, $J=7.5$ Hz, 1H; H_{ar}), 6.43 (d, $J=7.5$ Hz, 1H; H_{ar}), 6.47 (dd, $J=1.8$, 7.9 Hz, 1H; H_{ar}), 6.58 (dd, $J=1.8$, 7.9 Hz, 1H; H_{ar}), 7.02 (dd, $J=1.8$, 7.8 Hz, 1H; H_{ar}), 7.31 (t, $J=7.8$ Hz, 1H; H_{ar}), 7.44–7.47 (m, 2H; H_{ar}), 7.70 ppm (t, $J=1.8$ Hz, 1H; H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=20.54$ (p; CH_3CN), 24.95 (p; CH_3CHN), 30.52 (s; CH_2), 33.89 (s; CH_2), 35.41 (s; CH_2), 37.15 (s; CH_2), 57.65 (t; NCH), 122.43 (q; C_{ar}, C-Br), 122.88 (q; C_{ar}), 125.05 (t; C_{ar}), 125.93 (t; C_{ar}), 127.09 (t; C_{ar}), 129.30 (q; C_{ar}), 129.68 (t; C_{ar}), 130.04 (t; C_{ar}), 130.38 (t; C_{ar}), 130.48 (t; C_{ar}), 131.62 (t; C_{ar}), 132.71 (t; C_{ar}), 136.44 (t; C_{ar}), 137.63 (q; C_{ar}), 139.96 (q; C_{ar}), 140.93 (q; C_{ar}), 146.93 (q; C_{ar}), 162.29 (q; C_{ar}, COH), 170.59 ppm (q; C=N); EIMS (70 eV): *m/z* (%): 449/447 (91/90) [M^+], 345/343 (58/59), 266 (29), 160 (100), 104 (86); HR-EIMS: calcd for $C_{26}H_{26}NOBr$: 447.1198; found: 447.1195; elemental analysis calcd (%) for $C_{26}H_{26}NOBr$: C 69.64, H 5.84, N 3.12; found: C 69.97, H 5.99, N 2.77.

Synthesis of 12e: Compound **12e** was synthesized according to general procedure C with *rac*-**10** (100 mg, 0.38 mmol) and enantiopure (*S*)-1-aminotetraline (166 mg, 1.13 mmol). After 3 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). The combined yield of both fractions was 74%.

Isomer (R_p,S)-***12e***: Yield: 54 mg (36%); orange oil; $[\alpha]_D^{20}=+119.1$ ($c=0.54$ g/100 mL $CHCl_3$); $R_f=0.50$ (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.93$–2.11 (m, 2H; $CH_2CH_2CH_2$), 2.16–2.27 (m, 2H; $CH_2CH_2CH_2$), 2.47 (s, 3H; CH_3CN), 2.46–2.53 (m, 1H; CH_2), 2.56–2.65 (m, 1H; CH_2), 2.89–3.18 (m, 6H; 2 CH_2, $CH_2CH_2CH_2$), 3.32–3.38 (m, 1H; CH_2), 3.42–3.48 (m, 1H; CH_2), 4.96 (dd, $J=4.6$, 7.4 Hz, 1H; NCH), 6.25 (d, $J=7.6$ Hz, 1H; H_{ar}), 6.39–6.41 (m, 1H; H_{ar}), 6.43 (d, $J=7.6$ Hz, 1H; H_{ar}), 6.45–6.47 (m, 1H; H_{ar}), 6.60–6.63 (m, 1H; H_{ar}), 6.93–6.95 (m, 1H; H_{ar}), 7.02 (d, $J=7.55$ Hz, 1H; H_{ar}), 7.12–7.22 (m, 3H; H_{ar}), 15.37 ppm (brs, 1H; COH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=19.98$ (p; CH_3CN), 20.80 (s; $CH_2CH_2CH_2$), 29.42 (s; $CH_2CH_2CH_2$), 30.39 (s; CH_2), 31.58 (s; $CH_2CH_2CH_2$), 33.83 (s; CH_2), 35.51 (s; CH_2), 37.47 (s; CH_2), 56.91 (t; NCH), 122.58 (q; C_{ar}), 125.87 (t; C_{ar}), 126.41 (t; C_{ar}), 127.11 (t;

C_{ar}), 127.17 (t; C_{ar}), 127.82 (t; C_{ar}), 129.25 (t; C_{ar}), 129.42 (q; C_{ar}), 129.56 (t; C_{ar}), 131.42 (t; C_{ar}), 132.84 (t; C_{ar}), 135.91 (t; C_{ar}), 136.68 (q; C_{ar}), 137.16 (q; C_{ar}), 137.55 (q; C_{ar}), 140.02 (q; C_{ar}), 140.65 (q; C_{ar}), 162.01 (q; C_{ar}, *C*OH), 169.97 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$=3301 (vw), 3019 (vw), 2932 (vw), 2859 (vw), 2285 (vw), 1660 (vw), 1585 (vw), 1500 (vw), 1433 (vw), 1361 (vw), 1299 (vw), 1263 (vw), 1234 (vw), 1157 (vw), 1111 (vw), 1021 (vw), 800 (vw), 746 (vw), 719 (vw), 672 (vw), 619 (vw), 588 (vw), 569 (vw), 510 (vw), 439 (vw), 414 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 395 (45) [M^+], 266 (83), 161 (100), 131 (80), 104 (80), 91 (46); HR-EIMS: calcd for $C_{28}H_{29}NO$: 395.2249; found: 395.2252.

Isomer (S$_p$,S)-***12e***: Yield: 53 mg (35%); yellow/orange oil; $[\alpha]_D^{20}=-557.3$ (c=0.44 g/100 mL $CHCl_3$); R_f=0.43 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.84–1.98 (m, 2H; CH_2CH$_2$CH$_2$), 2.05–2.17 (m, 2H; CH$_2$CH_2CH$_2$), 2.48 (s, 3H; CH_3CN), 2.44–2.53 (m, 1H; CH$_2$), 2.68–2.77 (m, 1H; CH$_2$), 2.84–3.17 (m, 6H; 2CH$_2$, CH$_2$CH$_2$CH_2), 3.32–3.38 (m, 1H; CH$_2$), 3.41–3.48 (m, 1H; CH$_2$), 4.91–4.95 (m, 1H; NC*H*), 6.21 (d, J=7.5 Hz, 1H; H_{ar}), 6.28 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 6.41 (d, J=7.5 Hz, 1H; H_{ar}), 6.46 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 6.61 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 6.77 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 7.20–7.30 (m, 4H; H_{ar}), 15.69 ppm (brs, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=20.08 (p; *C*H$_3$CN), 20.43 (s; *C*H$_2$CH$_2$CH$_2$), 29.32 (s; CH$_2$*C*H$_2$CH$_2$), 31.45 (s; CH$_2$CH$_2$*C*H$_2$), 30.62 (s; *C*H$_2$), 33.82 (s; *C*H$_2$), 35.61 (s; *C*H$_2$), 37.41 (s; *C*H$_2$), 56.61 (t; N*C*H), 122.22 (q; C_{ar}), 125.64 (t; C_{ar}), 126.03 (t; C_{ar}), 127.25 (t; C_{ar}), 127.33 (t; C_{ar}), 127.96 (t; C_{ar}), 129.55 (q, t; 2C_{ar}), 130.34 (t; C_{ar}), 131.48 (t; C_{ar}), 132.66 (t; C_{ar}), 136.30 (t; C_{ar}), 137.11 (q; C_{ar}), 137.17 (q; C_{ar}), 137.54 (q; C_{ar}), 140.01 (q; C_{ar}), 140.81 (q; C_{ar}), 163.10 (q; C_{ar}, *C*OH), 169.28 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$=3431 (vw), 3014 (vw), 2927 (w), 2844 (vw), 1586 (w), 1488 (vw), 1438 (w), 1353 (vw), 1295 (vw), 1238 (vw), 1159 (vw), 1124 (vw), 1069 (vw), 1006 (vw), 930 (vw), 878 (vw), 806 (vw), 754 (w), 718 (vw), 682 (vw), 589 (vw), 541 (vw), 516 (vw), 453 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 395 (51) [M^+], 266 (28), 161 (52), 131 (100); HR-EIMS: calcd for $C_{28}H_{29}NO$: 395.2249; found: 395.2246; elemental analysis calcd (%) for $C_{28}H_{29}NO$: C 85.02, H 7.39, N 3.54; found: C 84.62, H 7.40, N 3.20.

Synthesis of 12g: Compound **12g** was synthesized according to general procedure C with *rac*-**10** (100 mg, 0.38 mmol) and enantiopure 1-(*S*)-1-(1-naphthyl)ethylamine (194 mg, 1.13 mmol). After 3 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). The combined yield of both fractions was 97%.

Isomer (R$_p$,S)-***12g***: Yield: 81 mg (51%); orange oil; $[\alpha]_D^{20}=+589.2$ (c=0.30 g/100 mL $CHCl_3$); R_f=0.46 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.91 (d, J=6.6 Hz, 3H; CH_3CHN), 2.20 (s, 3H; CH_3CN), 2.52–2.59 (m, 1H; CH$_2$), 2.64–2.72 (m, 1H; CH$_2$), 2.84–2.94 (m, 1H; CH$_2$), 3.00–3.07 (m, 1H; CH$_2$), 3.11–3.26 (m, 2H; CH$_2$), 3.35–3.51 (m, 2H; CH$_2$), 5.67 (q, J=6.6 Hz, 1H; NC*H*), 6.19 (d, J=7.5 Hz, 1H; H_{ar}), 6.50 (d, J=7.5 Hz, 1H; H_{ar}), 6.46–6.53 (m, 2H; H_{ar}), 6.65 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 7.10 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 7.39–7.43 (m, 1H; H_{ar}), 7.47–7.49 (m, 1H; H_{ar}), 7.50–7.54 (m, 1H; H_{ar}), 7.58–7.61 (m, 1H; H_{ar}), 7.74 (d, J=8.1 Hz, 1H; H_{ar}), 7.90 (dd, J=1.2, 8.1 Hz, 1H; H_{ar}), 8.14 (d, J=8.4 Hz, 1H; H_{ar}), 16.38 ppm (brs, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=20.68 (p; *C*H$_3$CN), 24.86 (p; *C*H$_3$CHN), 30.54 (s; *C*H$_2$), 33.94 (s; *C*H$_2$), 35.51 (s; *C*H$_2$), 37.51 (s; *C*H$_2$), 53.99 (t; N*C*H), 121.91 (q; C_{ar}), 122.32 (t; C_{ar}), 123.44 (t; C_{ar}), 125.48 (t; C_{ar}), 125.64 (t; C_{ar}), 126.10 (t; C_{ar}), 126.33 (t; C_{ar}), 127.22 (t; C_{ar}), 127.65 (t; C_{ar}), 129.27 (t; C_{ar}), 129.79 (t; C_{ar}), 129.98 (q; C_{ar}), 130.26 (q; C_{ar}), 131.41 (t; C_{ar}), 132.81 (t; C_{ar}), 133.87 (q; C_{ar}), 136.36 (t; C_{ar}), 137.66 (q; C_{ar}), 139.74 (q; C_{ar}), 140.11 (q; C_{ar}), 141.02 (q; C_{ar}), 164.80 (q; C_{ar}, *C*OH), 171.27 ppm (q, *C*=N); IR (KBr): $\tilde{\nu}$=2925 (m), 2854 (m), 1885, 1733 (vw), 1679 (vw), 1583 (vw), 1509 (w), 1455 (vw), 1375 (w), 1298 (w), 1259 (w), 1235 (w), 1173 (w), 1094 (vw), 1023 (vw), 933 (vw), 879 (vw), 800 (vw), 777 (w), 718 (w), 668 (vw), 645 (vw), 616 (vw), 588 (vw), 513 (vw), 447 (vw), 411 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 419 (34) [M^+], 315 (10), 155 (100); HR-EIMS: calcd for $C_{30}H_{29}NO$: 419.2249; found:419.2246.

Isomer (S$_p$,S)-***12g***: Yield: 74 mg (46%); orange oil; $[\alpha]_D^{20}=-10.8$ (c=0.40 g/100 mL $CHCl_3$); R_f=0.39 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.85 (d, J=6.6 Hz, 3H; CH_3CHN), 2.23 (s, 3H; CH_3CN), 2.35–2.43 (m, 1H; CH$_2$), 2.52–2.59 (m, 1H; CH$_2$), 2.77–2.94 (m, 2H; CH$_2$), 3.00–3.08 (m, 1H; CH$_2$), 3.12–3.27 (m, 2H; CH$_2$), 3.43–3.51 (m, 1H; CH$_2$), 5.61 (q, J=6.6 Hz, 1H; NC*H*), 6.15–6.17 (m, 2H; H_{ar}), 6.42 (d, J=7.5 Hz, 1H; H_{ar}), 6.5 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 6.58 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 7.09 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 7.50–7.67 (m, 3H; H_{ar}), 7.84–7.89 (m, 2H; H_{ar}), 7.95 (dd, J=1.0, 8.1 Hz, 1H; H_{ar}), 8.28 (d, J=8.5 Hz, 1H; H_{ar}), 16.17 ppm (brs, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=20.68 (p; *C*H$_3$CN), 24.46 (p; *C*H$_3$CHN), 30.51 (s; *C*H$_2$), 33.97 (s; *C*H$_2$), 35.42 (s; *C*H$_2$), 37.15 (s; *C*H$_2$), 54.56 (t; N*C*H), 122.26 (q; C_{ar}), 122.87 (t; C_{ar}), 124.01 (t; C_{ar}), 125.59 (t; C_{ar}), 125.77 (t; C_{ar}), 125.79 (t; C_{ar}), 126.34 (t; C_{ar}), 127.21 (t; C_{ar}), 127.86 (t; C_{ar}), 129.33 (t; C_{ar}), 129.47 (q; C_{ar}), 130.21 (q; C_{ar}), 130.57 (t; C_{ar}), 131.65 (t; C_{ar}), 132.58 (t; C_{ar}), 134.14 (q; C_{ar}), 136.57 (t; C_{ar}), 137.74 (q; C_{ar}), 140.09 (q; C_{ar}), 140.65 (q; C_{ar}), 141.09 (q; C_{ar}), 163.73 (q; C_{ar}, *C*OH), 170.90 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$=2963 (w), 2926 (w), 2855 (w), 1663 (vw), 1582 (vw), 1508 (vw), 1436 (vw), 1360 (vw), 1261 (w), 1095 (w), 1024 (w), 863 (vw), 801 (w), 718 (vw), 668 (vw), 617 (vw), 589 (vw), 510 (vw), 485 (vw), 440 (vw), 406 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 419 (100) [M^+], 315 (27), 155 (92); HR-EIMS: calcd for $C_{30}H_{29}NO$: 419.2249; found: 419.2251.

Synthesis of 12h: Compound **12h** was synthesized according to general procedure C with *rac*-**10** (100 mg, 0.38 mmol) and enantiopure (*S*)-1-(2-naphthyl-)ethylamine (194 mg, 1.13 mmol). After 3 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). The combined yield of both fractions was 78%.

Isomer (R$_p$,S)-***12h***: Yield: 59 mg (37%); orange oil; $[\alpha]_D^{20}=+601.7$ (c=1.96 g/100 mL $CHCl_3$); R_f=0.43 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.83 (d, J=6.6 Hz, 3H; CH_3CHN), 2.30 (s, 3H; CH_3CN), 2.50–2.58 (m, 1H; CH$_2$), 2.61–2.71 (m, 1H; CH$_2$), 2.85–2.93 (m, 1H; CH$_2$), 2.97–3.06 (m, 1H; CH$_2$), 3.08–3.25 (m, 2H; CH$_2$), 3.37–3.49 (m, 2H; CH$_2$), 5.05 (q, J=6.6 Hz, 1H; NC*H*), 6.19 (d, J=7.5 Hz, 1H; H_{ar}), 6.43 (d, J=7.5 Hz, 1H; H_{ar}), 6.44–6.51 (m, 2H; H_{ar}), 6.63 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 7.08 (dd, J=1.8, 7.8 Hz, 1H; H_{ar}), 7.41–7.49 (m, 2H; H_{ar}), 7.52 (dd, J=1.8, 8.5 Hz, 1H; H_{ar}), 7.73 (d, J=1.2 Hz, 1H; H_{ar}), 7.80–7.84 (m, 2H; H_{ar}), 7.85 (d, J=8.5 Hz, 1H; H_{ar}), 15.97 ppm (brs, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=20.53 (p; *C*H$_3$CN), 25.36 (p; *C*H$_3$CHN), 30.50 (s; *C*H$_2$), 33.91 (s; *C*H$_2$), 35.49 (s; *C*H$_2$), 37.41 (s; *C*H$_2$), 58.29 (t; N*C*H), 122.15 (q; C_{ar}), 124.54 (t; C_{ar}), 124.74 (t; C_{ar}), 125.63 (t; C_{ar}), 125.83 (t; C_{ar}), 126.23 (t; C_{ar}), 127.20 (t; C_{ar}), 127.67 (t; C_{ar}), 127.88 (t; C_{ar}), 128.84 (t; C_{ar}), 129.67 (q; C_{ar}), 129.71 (t; C_{ar}), 131.46 (t; C_{ar}), 132.67 (q; C_{ar}), 132.79 (t; C_{ar}), 133.42 (q; C_{ar}), 136.22 (t; C_{ar}), 137.64 (q; C_{ar}), 140.09 (q; C_{ar}), 140.86 (q; C_{ar}), 141.08 (q; C_{ar}), 163.60 (q; C_{ar}, *C*OH), 170.67 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$=3650 (vw), 3292 (vw), 3053 (w), 2927 (w), 2852 (w), 1892 (vw), 1617 (w), 1508 (w), 1438 (w), 1363 (vw), 1300 (vw), 1234 (vw), 1176 (vw), 1156 (vw), 1128 (vw), 1111 (vw), 1085 (vw), 1018 (vw), 978 (vw), 950 (vw), 894 (vw), 858 (vw), 820 (vw), 748 (vw), 718 (vw), 699 (vw), 669 (vw), 621 (vw), 589 (vw), 569 (vw), 510 (vw), 479 cm^{-1} (w); EIMS (70 eV): *m*/*z* (%): 419 (49) [M^+], 315 (16), 155 (100); HR-EIMS: calcd for $C_{30}H_{29}NO$: 419.2249; found: 419.2247.

Synthesis of 12f: Compound **12f** was synthesized according to general procedure C with *rac*-**10** (100 mg, 0.38 mmol) and enantiopure 1-(*S*)-*trans*-(*S*)-2-phenylmethoxycyclohexylamine (232 mg, 1.13 mmol). After 3 d heating at reflux temperature, the raw material was purified by flash chromatography (*n*-hexane/ethyl acetate 20:1). The combined yield of both fractions was 86%.

Isomer (R$_p$,S,S)-***12f***: Yield: 77 mg (45%); orange solid; $[\alpha]_D^{20}=+590.4$ (c=0.83 g/100 mL $CHCl_3$); m.p. 90–94 °C; R_f=0.43 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.37–1.50 (m, 3H; *c*-hexyl), 1.68–1.93 (m, 3H; *c*-hexyl), 1.95–2.08 (m, 1H; *c*-hexyl), 2.13–2.25 (m, 1H; *c*-hexyl), 2.35 (s, 3H; CH_3CN), 2.45–2.63 (m, 2H; CH$_2$), 2.81–2.9 (m, 1H; CH$_2$), 2.95–3.03 (m, 1H; CH$_2$), 3.06–3.20 (m, 2H; CH$_2$), 3.33–3.47 (m, 2H; CH$_2$), 3.47–3.57 (m, 1H; *c*-hexyl), 3.65–3.75 (m, 1H; *c*-hexyl), 4.43 (d, J=11.3 Hz, 1H; OCH*a*HbPh), 4.52 (d, J=11.3 Hz, 1H; OCHa*Hb*Ph), 6.19 (d, J=7.5 Hz, 1H; H_{ar}), 6.33 (dd, J=1.8, 7.7 Hz, 1H; H_{ar}), 6.42 (d, J=7.5 Hz, 1H; H_{ar}), 6.47 (dd, J=1.8, 7.9 Hz, 1H; H_{ar}), 6.61 (dd, J=1.8, 7.9 Hz, 1H; H_{ar}), 6.98 (dd, J=1.8, 7.7 Hz, 1H; H_{ar}), 7.14–7.24 (m, 5H; H_{ar}), 16.00 ppm (brs, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ=20.21 (p; *C*H$_3$CN), 24.09 (s; 2*C*H$_2$), 30.50 (s; *C*H$_2$), 30.55 (s; *C*H$_2$), 32.53 (s; *C*H$_2$), 33.91 (s; *C*H$_2$), 35.42 (s; *C*H$_2$), 37.43 (s; *C*H$_2$), 61.70 (t;

NCH), 71.96 (s; OCH$_2$Ph), 81.91 (t; CHOCH$_2$Ph), 122.22 (q; C$_{ar}$), 125.34 (q; C$_{ar}$), 127.04 (t; C$_{ar}$), 127.34 (t; C$_{ar}$, OCH$_2$*Ph*), 127.85 (t; 2C$_{ar}$, OCH$_2$*Ph*), 128.21 (t; 2C$_{ar}$, OCH$_2$*Ph*), 129.50 (q; C$_{ar}$), 129.57 (t; C$_{ar}$), 131.34 (t; C$_{ar}$), 132.78 (t; C$_{ar}$), 135.90 (t; C$_{ar}$), 137.64 (q; C$_{ar}$, OCH$_2$*Ph*), 138.55 (q; C$_{ar}$), 139.99 (q; C$_{ar}$), 140.72 (q; C$_{ar}$), 163.54 (q; C$_{ar}$, *C*OH), 170.76 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$ = 3011 (w), 2929 (m), 2856 (m), 1598 (w), 1499 (w), 1439 (w), 1358 (w), 1301 (w), 1233 (w), 1157 (w), 1102 (w), 1075 (w), 1027 (w), 991 (w), 927 (w), 881 (w), 863 (w), 802 (w), 745 (w), 719 (w), 700 (w), 669 (w), 623 (w), 590 (w), 551 (vw), 520 (w), 474 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 453 (37) [*M*$^+$], 349 (20), 258 (28), 91 (75), 43 (100); HR-EIMS: calcd for $C_{31}H_{35}NO_2$: 453.2668; found: 453.2664.

Isomer (S$_p$,S,S)-***12f***: Yield: 71 mg (41%); orange solid; $[\alpha]_D^{20} = -358.0$ (c = 0.50 g/100 mL $CHCl_3$); m.p. 158 °C; R_f = 0.35 (*n*-hexane/ethyl acetate 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30–1.5 (m, 3H; *c*-hexyl), 1.56–1.70 (m, 1H; *c*-hexyl), 1.74–1.92 (m, 3H; *c*-hexyl), 2.29 (s, 3H; C*H*$_3$CN), 2.31–2.39 (m, 2H; H-*c*-hexyl, C*Ha*Hb), 2.44–2.53(m, 1H; CH$_2$), 2.71–2.85 (m, 2H; CH$_2$), 2.95–3.03 (m, 1H; CH$_2$), 3.10–3.21 (m, 2H; CH$_2$), 3.34–3.44 (m, 1H; CH$_2$), 3.60–3.70 (m, 2H; NC*H*, C*H*OCH$_2$Ph), 4.61 (d, J = 11.5 Hz, 1H; OC*Ha*HbPh), 4.81 (d, J = 11.5 Hz, 1H; OCHa*Hb*Ph), 6.10 (d, J = 7.5 Hz, 1H; H$_{ar}$), 6.30 (dd, J = 1.8, 7.7 Hz, 1H; H$_{ar}$), 6.36 (d, J = 7.5 Hz, 1H; H$_{ar}$), 6.46 (dd, J = 1.8, 7.9 Hz, 1H; H$_{ar}$), 6.56 (dd, J = 1.8, 7.9 Hz, 1H; H$_{ar}$), 6.98 (dd, J = 1.8, 7.7 Hz, 1H; H$_{ar}$), 7.25–7.29 (m, 1H; OCH$_2$*Ph*), 7.31–7.35 (m, 2H; OCH$_2$*Ph*), 7.38–7.41 (m, 2H; OCH$_2$*Ph*), 16.06 ppm (br s, 1H; CO*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.40 (p; *C*H$_3$CN), 24.08 (s; *C*H$_2$), 24.17 (s; *C*H$_2$), 30.21 (s; *C*H$_2$), 30.51 (s; *C*H$_2$), 32.05 (s; *C*H$_2$), 33.96 (s; *C*H$_2$), 34.99 (s; *C*H$_2$), 37.17 (s; *C*H$_2$), 61.62 (t; NCH), 71.11 (s; OCH$_2$Ph), 81.89 (t; CHOCH$_2$Ph), 122.26 (q; C$_{ar}$), 125.11 (t; C$_{ar}$), 127.19 (t; C$_{ar}$), 127.48 (t; 2C$_{ar}$, OCH$_2$*Ph*), 127.45 (t; C$_{ar}$, OCH$_2$*Ph*), 128.38 (t; 2C$_{ar}$, OCH$_2$*Ph*), 129.29 (q; C$_{ar}$), 130.51 (t; C$_{ar}$), 131.62 (t; C$_{ar}$), 132.33 (t; C$_{ar}$), 136.26 (t; C$_{ar}$), 138.06 (q; C$_{ar}$, OCH$_2$*Ph*), 138.93 (q; C$_{ar}$), 139.94 (q; C$_{ar}$), 141.16 (q; C$_{ar}$), 163.95 (q; C$_{ar}$, *C*OH), 170.60 ppm (q; *C*=N); IR (KBr): $\tilde{\nu}$ = 3030 (w), 3008 (w), 2936 (m), 2859 (w), 1600 (w), 1498 (w), 1439 (w), 1363 (w), 1344 (w), 1293 (w), 1237 (w), 1210 (w), 1157 (w), 1134 (vw), 1112 (w), 1073 (m), 1022 (w), 991 (vw), 928 (w), 879 (w), 844 (w), 801 (w), 748 (w), 717 (w), 700 (w), 669 (w), 620 (vw), 590 (vw), 566 (w), 536 (vw), 515 (vw), 453 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 453 (24) [*M*$^+$], 349 (14), 258 (25), 91 (100), 43 (57); HR-EIMS: calcd for $C_{31}H_{35}NO_2$: 453.2668; found: 453.2664; elemental analysis calcd (%) for $C_{31}H_{35}NO_2$: C 82.08, H 7.78, N 3.09; found: C 82.39, H 8.04, N 2.95.

Synthesis and characterization of ligands 16: Ligands **16i** were synthesized according to a literature procedure.[31]

Synthesis of (*R*$_p$,*S*,*S*)-16m: Compound (*R*$_p$,*S*)-**12m** (300 mg, 0.80 mmol) was dissolved in a mixture of methanol (60 mL)/CH_2Cl_2 (30 mL) and treated at room temperature with $NaBH_4$ (112 mg, 2.96 mmol). Concentrated acetic acid (171 μL, 2.96 mmol) was then added dropwise to the yellow reaction mixture, which became immediately colorless. Stirring was maintained for 5 h at room temperature and the reaction was then quenched by the addition of water. This mixture was made basic by the addition of sodium carbonate and was then extracted with methylene chloride. The combined organic layers were dried over $MgSO_4$ and the solvent was removed completely under reduced pressure. The obtained raw material was purified by flash chromatography (*n*-pentane/diethyl ether 10:1 + 2.5% Et_3N). Yield: 220 mg (73%, >99% *de*); yellow crystals; $[\alpha]_D^{20} = +107.3$ (c = 0.60 g/100 mL acetone); m.p. 104–107 °C; R_f = 0.29 (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.09 (d, J = 6.5 Hz, 3H; *c*-hexyl-CHC*H*$_3$), 1.23 (d, J = 6.5 Hz; PhCHC*H*$_3$), 1.10–1.41 (m, 5H; H-*c*-hexyl), 1.44–1.55 (m, 1H; H-*c*-hexyl), 1.74–1.77 (m, 2H; H-*c*-hexyl), 1.85–1.96 (m, 3H; H-*c*-hexyl), 2.57 (ddd, J = 5.8, 13.0, 16.1 Hz, 1H; CH$_2$), 2.71–2.91 (m, 3H; CH$_2$), 3.06 (ddd, J = 2.7, 10.4, 13.0 Hz, 1H; CH$_2$), 3.11–3.30 (m, 3H; CH$_2$), 3.45 (ddd, J = 2.71, 9.8, 12.8 Hz, 1H; CH$_2$), 4.16 (q, J = 6.5 Hz, 1H; PhC*H*CH$_3$), 6.13 (d, J = 7.7 Hz, 1H; H$_{ar}$), 6.33 (d, J = 7.7 Hz, 1H; H$_{ar}$), 6.35 (dd, J = 1.8, 7.9 Hz, 1H; H$_{ar}$), 6.50 (dd, J = 1.8, 7.8 Hz, 1H; H$_{ar}$), 6.63 (dd, J = 1.8, 7.8 Hz, 1H; H$_{ar}$), 6.86 ppm (dd, J = 1.8, 7.9 Hz, 1H; H$_{ar}$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.04 (p; *c*-hexyl-CH*C*H$_3$), 20.29 (p; PhCH*C*H$_3$), 26.53 (s; C-*c*-hexyl), 26.62 (s; C-*c*-hexyl), 26.70 (s; C-*c*-hexyl), 29.03 (s; C-*c*-hexyl), 29.39 (s; C-*c*-hexyl), 30.28 (s; CH$_2$), 33.10 (s; CH$_2$), 34.00 (s; CH$_2$), 34.88 (s; CH$_2$), 43.91 (t; C-*c*-hexyl), 50.99 (t; Ph*C*HCH$_3$), 53.19 (t; *c*-hexyl-*C*HCH$_3$), 125.98 (t; C$_{ar}$), 126.79 (q; C$_{ar}$), 127.13 (t; C$_{ar}$), 127.95 (q; C$_{ar}$), 129.46 (t; C$_{ar}$), 132.73 (t; C$_{ar}$), 133.96 (t; C$_{ar}$), 134.49 (t; C$_{ar}$), 136.97 (q; C$_{ar}$), 138.39 (q; C$_{ar}$), 140.55 (q; C$_{ar}$), 155.91 ppm (q; C$_{ar}$, *C*-OH); IR (KBr): $\tilde{\nu}$ = 3319 (vw), 2982 (w), 2929 (w), 2850 (w), 1884 (vw), 1596 (w), 1566 (w), 1498 (vw), 1445 (w), 1401 (w), 1337 (vw), 1284 (vw), 1261 (w), 1211 (vw), 1173 (vw), 1150 (vw), 1121 (vw), 1066 (w), 1020 (vw), 1004 (vw), 981 (vw), 957 (vw), 938 (vw), 890 (vw), 863 (vw), 797 (w), 754 (vw), 717 (vw), 690 (vw), 655 (vw), 596 (vw), 572 (vw), 513 (vw), 462 (vw), 432 cm^{-1} (vw); EIMS (70 eV): *m*/*z* (%): 377 (11) [*M*$^+$], 145 (9), 104 (9), 58 (38), 43 (100); HR-EIMS: calcd for $C_{26}H_{35}NO$: 377.2719; found: 377.2721.

Synthesis of (*S*$_p$,*S*,*R*)-16m: Compound (*S*$_p$,*S*,*R*)-**16m** was prepared and purified according to the procedure for (*R*$_p$,*S*,*S*)-**16m** from (*S*$_p$,*S*)-**12m** (153 mg, 0.53 mmol), $NaBH_4$ (57.0 mg, 1.51 mg), and concentrated acetic acid (87.0 μL, 91.0 mg, 1.51 mmol). Yield: 134 mg (67%, >99% *de*); white crystals; $[\alpha]_D^{20} = -76.7$ (c = 0.55 g/100 mL acetone); m.p. 150–154 °C; R_f = 0.50 (*n*-hexane/ethyl acetate 5:1 + 2.5% Et_3N); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (d, J = 6.7 Hz, 3H; *c*-hexyl-CHC*H*$_3$), 1.20 (d, J = 6.6 Hz, 3H; PhCHC*H*$_3$), 1.15–1.29 (m, 3H; H-*c*-hexyl), 1.31–1.44 (m, 2H; H-*c*-hexyl), 1.64–1.98 (m, 6H; H-*c*-hexyl), 2.57 (ddd, J = 5.5, 10.5, 13.0 Hz, 1H; CH$_2$), 2.74–2.83 (m, 1H; CH$_2$), 2.87–2.96 (m, 2H; CH$_2$), 3.04 (ddd, J = 2.7, 10.4, 13.0 Hz, 1H; CH$_2$), 3.11–3.27 (m, 3H; CH$_2$, *c*-hexylC*H*CH$_3$), 3.42 (ddd, J = 2.9, 10.0, 12.9 Hz, 1H; CH$_2$), 4.10 (q, J = 6.6 Hz, 1H; PhC*H*CH$_3$), 6.08 (d, J = 7.6 Hz, 1H, H$_{ar}$), 6.30 (d, J = 7.6 Hz, 1H; H$_{ar}$), 6.44 (dd, J = 1.8, 7.9 Hz, 1H; H$_{ar}$), 6.51 (dd, J = 1.8, 7.8 Hz, 1H, H$_{ar}$), 6.64 (dd, J = 1.8, 7.8 Hz, 1H; H$_{ar}$), 6.90 ppm (dd, J = 1.8, 7.9 Hz, 1H; H$_{ar}$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.10 (p; *c*-hexyl-CH*C*H$_3$), 22.84 (p; PhCH*C*H$_3$), 26.43 (s; C-*c*-hexyl), 26.73 (s; C-*c*-hexyl), 26.75 (s; C-*c*-hexyl), 27.10 (s; C-*c*-hexyl), 30.09 (s; C-*c*-hexyl), 30.23 (s; CH$_2$), 32.85 (s; CH$_2$), 34.10 (s; CH$_2$), 34.85 (s; CH$_2$), 41.22 (t; C-*c*-hexyl), 52.66 (t; Ph*C*HCH$_3$), 54.78 (t; *c*-hexyl-*C*HCH$_3$), 125.79 (t; C$_{ar}$), 126.39 (q; C$_{ar}$), 127.61 (t; C$_{ar}$), 127.90 (q; C$_{ar}$), 129.65 (t; C$_{ar}$), 132.71 (t; C$_{ar}$), 133.96 (t; C$_{ar}$), 134.08 (t; C$_{ar}$), 137.04 (q; C$_{ar}$), 138.31 (q; C$_{ar}$), 140.60 (q; C$_{ar}$), 156.16 ppm (q; C$_{ar}$, *C*-OH); IR (KBr): $\tilde{\nu}$ = 3321 (m), 2926 (s), 2855 (s), 1857 (w), 1598 (m), 1567 (m), 1498 (m), 1459 (s), 1438 (s), 1376 (m), 1325 (m), 1283 (m), 1252 (m), 1211 (m), 1167 (m), 1120 (m), 1103 (m), 1073 (m), 1058 (m), 1016 (m), 973 (m), 938 (m), 891 (m), 868 (m), 838 (w), 787 (m), 770 (m), 716 (m), 686 (w), 657 (m), 632 (vw), 589 (m), 562 (w), 516 (m), 477 (vw), 459 (vw), 417 cm^{-1} (w); EIMS (70 eV): *m*/*z* (%): 377 (81) [*M*$^+$], 145 (46), 104 (100); HR-EIMS: calcd for $C_{26}H_{35}NO$: 377.2719; found: 377.2720.

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[1] a) F. López, B. L. Feringa in *Asymmetric Synthesis-The Essentials* (Eds.: M. Christmann, S. Bräse), Wiley-VCH, Weinheim, **2008**; b) A. Alexakis, C. Benhaim, *Eur. J. Org. Chem.* **2002**, 3221–3236; c) N. Krause, A. Hoffmann-Röder, *Synthesis* **2001**, 171–196; d) P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis, Tetrahedron Organic Chemistry Series 9*, Pergamon, Oxford, **1992**.

[2] A few selected examples: a) S. R. Harutyunyan, Z. Zhao, T. den Hartog, K. Bouwmeester, A. J. Minnaard, B. L. Feringa, F. Govers, *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 8507–8512; b) E. P. Balskus, E. N. Jacobsen, *J. Am. Chem. Soc.* **2006**, *128*, 6810–6812; c) A. K. Miller, C. C. Hughes, J. J. Kennedy-Smith, S. N. Gradl, D. Trauner, *J. Am. Chem. Soc.* **2006**, *128*, 17057–17062; d) N. Ohyabu, T. Nishikawa, M. Isobe, *J. Am. Chem. Soc.* **2003**, *125*, 8798–8805; e) L. A. Arnold, R. Naasz, A. J. Minnaard, B. L. Feringa, *J. Am. Chem. Soc.* **2001**, *123*, 5841–5842; f) K. C. Nicolaou, F. P. J. T. Rutjes, E. A. Theodorakis, J. Tiebes, M. Sato, E. Untersteller, *J. Am. Chem. Soc.* **1995**, *117*, 10252–10263.

[3] With organozinc reagents: K. Soai, S. Niwa, *Chem. Rev.* **1992**, *92*, 833–856; L. Pu, H.-B. Yu, *Chem. Rev.* **2001**, *101*, 757–824; with organoaluminum reagents: a) M. d'Augustin, A. Alexakis, *Tetrahedron Lett.* **2007**, *48*, 7408–7412; b) A. Alexakis, V. Albrow, K. Biswas, M. d'Augustin, O. Prieto, S. Woodward, *Chem. Commun.* **2005**, *22*, 2843–2845; with Grignard reagents: F. López, A. Minnaard, B. L. Feringa, *Acc. Chem. Res.* **2007**, *40*, 179–188.
[4] For cyclic enones: a) H. Clavier, L. Coutable, J.-C. Guillemin, M. Mauduit, *Tetrahedron: Asymmetry* **2005**, *16*, 921–924; b) D. Pena, F. López, S. R. Harutyunyan, A. J. Minnaard, B. L. Feringa, *Chem. Commun.* **2004**, 1836–1837; c) S. J. Degrado, H. Mizutani, A. H. Hoveyda, *J. Am. Chem. Soc.* **2002**, *124*, 13362–13363; d) S. J. Degrado, H. Mizutani, A. H. Hoveyda, *J. Am. Chem. Soc.* **2001**, *123*, 755–756; for acyclic enones: e) A. P. Duncan, J. L. Leighton, *Org. Lett.* **2004**, *6*, 4117–4119; f) H. Mizutani, S. J. Degrado, A. H. Hoveyda, *J. Am. Chem. Soc.* **2002**, *124*, 779–781.
[5] a) A. El-Batta, M. Bergdahl, *Tetrahedron Lett.* **2007**, *48*, 1761–1765; b) A. Hajra, N. Yoshikai, E. Nakamura, *Org. Lett.* **2006**, *8*, 4153–4155; c) M. Pineschi, F. Del Moro, V. Di Bussolo, F. Macchia, *Adv. Synth. Catal.* **2006**, *348*, 301–304; d) A. W. Hird, A. H. Hoveyda, *Angew. Chem.* **2003**, *115*, 1314–1317; *Angew. Chem. Int. Ed.* **2003**, *42*, 1276–1279.
[6] a) F. Valleix, K. Nagai, T. Soeta, M. Kuriyama, K.-i. Yamada, K. Tomioka, *Tetrahedron* **2005**, *61*, 7420–7424; b) D. Polet, A. Alexakis, *Tetrahedron Lett.* **2005**, *46*, 1529–1532; c) A. Duursma, A. J. Minnaard, B. L. Feringa, *J. Am. Chem. Soc.* **2003**, *125*, 3700–3701; d) A. Alexakis, C. Benhaim, *Org. Lett.* **2000**, *2*, 2579–2581.
[7] a) F. López, S. R. Harutyunyan, A. Meetsma, A. J. Minnaard, B. L. Feringa, *Angew. Chem.* **2005**, *117*, 2812–2816; *Angew. Chem. Int. Ed.* **2005**, *44*, 2752–2756; b) J.-F. Paquin, C. R. J. Stephenson, C. Defieber, E. M. Carreira, *Org. Lett.* **2005**, *7*, 3821–3824.
[8] a) B. M. Ruiz, K. Geurts, M. À. Fernández-Ibánez, B. ter Horst, A. J. Minnaard, B. L. Feringa, *Org. Lett.* **2007**, *9*, 5123–5126; b) R. Des Mazery, M. Pullez, F. López, S. R. Harutyunyan, A. J. Minnaard, B. L. Feringa, *J. Am. Chem. Soc.* **2005**, *127*, 9966–9967.
[9] a) J. Schuppan, A. J. Minnaard, B. L. Feringa, *Chem. Commun.* **2004**, 792–793; b) T. Watanabe, T. F. Knöpfel, E. M. Carreira, *Org. Lett.* **2003**, *5*, 4557–4558; c) A. Alexakis, C. Benhaim, *Tetrahedron: Asymmetry* **2001**, *12*, 1151–1157.
[10] a) A. J. Minnaard, B. L. Feringa, L. Lefort, J. G. de Vries, *Acc. Chem. Res.* **2007**, *40*, 1267–1277; b) O. Pamies, M. Diéguez, C. Claver, *Adv. Synth. Catal.* **2007**, *349*, 836–840; c) H. Du, W. Yuan, B. Zhao, Y. Shi, *J. Am. Chem. Soc.* **2007**, *129*, 11688–11689; d) C. J. Diez-Holz, C. Böing, G. Franció, M. Hölscher, W. Leitner, *Eur. J. Org. Chem.* **2007**, 2995–3002; e) D. Polet, A. Alexakis, K. Tissot-Croset, C. Corminboeuf, K. Ditrich, *Chem. Eur. J.* **2006**, *12*, 3596–3609; f) C. A. Falciola, K. Tissot-Croset, A. Alexakis, *Angew. Chem.* **2006**, *118*, 6141–6144; *Angew. Chem. Int. Ed.* **2006**, *45*, 5995–5998; g) S. A. Moteki, D. Wu, K. L. Chandra, D. S. Reddy, J. M. Takacs, *Org. Lett.* **2006**, *8*, 3097–3100; h) B. L. Feringa, *Acc. Chem. Res.* **2000**, *33*, 346–353.
[11] Reviews: a) R. G. Arrayás, J. Adrio, J. C. Carretero, *Angew. Chem.* **2006**, *118*, 7836–7878; *Angew. Chem. Int. Ed.* **2006**, *45*, 7674–7715; b) L.-X. Dai, T. Tu, S.-L. You, W.-P. Deng, X.-L. Hou, *Acc. Chem. Res.* **2003**, *36*, 659–667.
[12] a) P. J. Pye, K. Rossen, R. A. Reamer, N. N. Tsou, R. P. Volante, P. J. Reider, *J. Am. Chem. Soc.* **1997**, *119*, 6207–6208; b) *Modern Cyclophane Chemistry* (Eds.: R. Gleiter, H. Hopf), Wiley-VCH, Weinheim, **2004**; c) K. Krohn, H. Rieger, H. Hopf, D. Barrett, P. G. Jones, D. Doring, *Chem. Ber.* **1990**, *123*, 1729–1732; d) T. Danilova, V. Rozenberg, E. Vorontsov, Z. A. Starikova, H. Hopf, *Tetrahedron: Asymmetry* **2003**, *14*, 1375.
[13] D. J. Cram, N. L. Allinger, *J. Am. Chem. Soc.* **1955**, *77*, 6289–6294.
[14] H. J. Reich, D. J. Cram, *J. Am. Chem. Soc.* **1969**, *91*, 3517–3526.
[15] X.-W. Wu, K. Yuan, W. Sun, M.-J. Zhang, X.-L. Hou, *Tetrahedron: Asymmetry* **2003**, *14*, 107–112.
[16] A. H. Vetter, A. Berkessel, *Tetrahedron Lett.* **1998**, *39*, 1741–1744.
[17] D. S. Masterson, T. L. Hobbs, D. T. Glatzhofer, *J. Mol. Catal. A* **1999**, *145*, 75–81.
[18] a) T. Focken, G. Raabe, C. Bolm, *Tetrahedron: Asymmetry* **2004**, *15*, 1693–1706; b) D. Chaplin, P. Harrison, J. P. Henschke, I. C. Lennon, G. Meek, P. Moran, C. J. Pilkington, J. A. Ramsden, S. Watkins, A. Zanotti-Gerosa, *Org. Process Res. Dev.* **2003**, *7*, 89–94; c) A. Zanotti-Gerosa, C. Malan, D. Herzberg, *Org. Lett.* **2001**, *3*, 3687–3690.
[19] a) F. Lauterwasser, J. Gall, S. Höfener, S. Bräse, *Adv. Synth. Catal.* **2006**, *348*, 2068–2074; b) F. Lauterwasser, M. Nieger, H. Mansikkamäki, K. Nättinen, S. Bräse, *Chem. Eur. J.* **2005**, *11*, 4509–4525; c) S. Bräse, S. Dahmen, S. Höfener, F. Lauterwasser, M. Kreis, R. E. Ziegert, *Synlett* **2004**, 2647–2669; d) N. Hermanns, S. Dahmen, C. Bolm, S. Bräse, *Angew. Chem.* **2002**, *114*, 3844–3846; *Angew. Chem. Int. Ed.* **2002**, *41*, 3692–3694; e) S. Dahmen, S. Bräse, *J. Am. Chem. Soc.* **2002**, *124*, 5940–5941; f) S. Dahmen, S. Bräse, *Chem. Commun.* **2002**, 26–27; g) S. Dahmen, S. Bräse, *Org. Lett.* **2001**, *3*, 4119–4122.
[20] T.-Z. Zhang, L.-X. Dai, X.-L. Hou, *Tetrahedron: Asymmetry* **2007**, *18*, 1990–1994.
[21] S. Bräse, S. Höfener, *Angew. Chem.* **2005**, *117*, 8091–8093; *Angew. Chem. Int. Ed.* **2005**, *44*, 7879–7881.
[22] a) S. J. Degrado, J. Mizutani, A. H. Hoveyda, *J. Am. Chem. Soc.* **2001**, *123*, 755–756; b) H. Mizutani, S. J. Degrado, A. H. Hoveyda, *J. Am. Chem. Soc.* **2002**, *124*, 779–781; c) S. J. Degrado, H. Mizutani, A. H. Hoveyda, *J. Am. Chem. Soc.* **2002**, *124*, 13362–13363; d) A. W. Hird, A. H. Hoveyda, *J. Am. Chem. Soc.* **2005**, *127*, 14988–14989.
[23] L. Pu, H.-B. Yu, *Chem. Rev.* **2001**, *101*, 757–824.
[24] See, for example: a) J. A. Marshall, M. Herold, H. S. Eidam, P. Eidam, *Org. Lett.* **2006**, *8*, 5505–5508; b) B. G. Kelly, D. G. Gilheany, *Tetrahedron Lett.* **2002**, *43*, 887–890.
[25] Other asymmetric approaches to aldehyde **14**: a) S. G. Ouellet, J. B. Tuttle, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, *127*, 32–33; b) K. Tanaka, G. C. Fu, *J. Org. Chem.* **2001**, *66*, 8177–8186; c) T. Mukaiyama, H. Hayashi, T. Miwa, K. Narasaka, *Chem. Lett.* **1982**, 1637–1640; d) H. Rakotoarisoa, R. G. Perez, P. Mangeney, A. Alexakis, *Organometallics* **1996**, *15*, 1957–1959; e) H. Ahlbrecht, D. Enders, L. Santowski, G. Zimmerman, *Chem. Ber.* **1989**, *122*, 1995–2004.
[26] Asymmetric addition to **13** (selection): a) C. Palomo, A. Landa, A. Mielgo, M. Oiarbide, A. Puente, S. Vera, *Angew. Chem.* **2007**, *119*, 8583–8587; *Angew. Chem. Int. Ed.* **2007**, *46*, 8431–8435; b) H. Gotoh, H. Ishikawa, Y. Hayashi, *Org. Lett.* **2007**, *9*, 5307–5309; c) S. E. Denmark, J. R. Heemstra, Jr., *J. Org. Chem.* **2007**, *72*, 5668–5688; d) L. Hojabri, A. Hartikka, F. M. Moghaddam, P. I. Arvidsson, *Adv. Synth. Catal.* **2007**, *349*, 740–748; e) S. Brandau, A. Landa, J. Franzen, M. Marigo, K. A. Jorgensen, *Angew. Chem.* **2006**, *118*, 4411–4415; *Angew. Chem. Int. Ed.* **2006**, *45*, 4305–4309; f) W. Wang, H. Li, J. Wang, *Org. Lett.* **2005**, *7*, 1637–1639; g) D. Seebach, U. Misslitz, P. Uhlmann, *Angew. Chem.* **1989**, *101*, 484–485; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 472–473; h) T. Ooi, K. Doda, K. Maruoka, *J. Am. Chem. Soc.* **2003**, *125*, 9022–9023.
[27] For mechanistic investigations on the 1,2-addition reaction of dialkylzinc reagents to aldehydes, see: M. Kitamura, S. Okada, S. Suga, R. Noyori, *J. Am. Chem. Soc.* **1989**, *111*, 4028–4036.
[28] These [2.2]paracyclophane-based ligands were used before in our group (see reference [19]).
[29] (*rac*)-**10** is synthesized in three steps by starting from commercially available [2.2]paracyclophane (see reference [19c]).
[30] a) S. Dahmen, *Org. Lett.* **2004**, *6*, 2113–2116; b) S. Höfener, F. Lauterwasser, S. Bräse, *Adv. Synth. Catal.* **2004**, *346*, 755–759; c) F. Lauterwasser, S. Vanderheiden, S. Bräse, *Adv. Synth. Catal.* **2006**, *348*, 443–448; d) R. E. Ziegert, S. Bräse, *Synlett* **2006**, 2119–2123.
[31] V. I. Rozenberg, T. I. Danilova, E. V. Sergeeva, I. A. Shouklov, Z. A. Starikova, H. Hopf, K. Kuhlein, *Eur. J. Org. Chem.* **2003**, 432–440.
[32] S. Dahmen, S. Bräse, *Tetrahedron: Asymmetry* **2001**, *12*, 2845–2850.
[33] For some models regarding the reduction of imines with borohydride, see: a) M. Periasamy, A. Devasagayaraj, N. Satyanarayana, C. Narayana, *Synth. Commun.* **1989**, *19*, 565–573; b) J. C. Fuller, C. M. Belisle, C. T. Goralski, B. Singaram, *Tetrahedron Lett.* **1994**, *35*, 5389–5392. Salicylimines gave: c) G. Palmieri, *Eur. J. Org. Chem.*

1999, 805–811; d) E. P. Kündig, C. Botuha, G. Lemercier, P. Romanens, L. Saudan, S. Thibault, *Helv. Chim. Acta* **2004**, *87*, 561–579.
[34] For an alternative approach, see: a) D. Enders, S. Noll, J. W. Bats, *Synlett* **2005**, 2679–2681; b) D. Enders, S. Noll, G. Raabe, J. Runsink, *Synthesis* **2008**, 1288–1296; c) M. Kreis, M. Nieger, S. Bräse, *J. Organomet. Chem.* **2006**, *691*, 2171–2181; d) T. I. Danilova, V. I. Rozenberg, Z. A. Starikova, S. Bräse, *Tetrahedron: Asymmetry* **2004**, *15*, 223–229; e) T. I. Danilova, V. I. Rozenberg, E. V. Sergeeva, Z. A. Starikova, S. Bräse, *Tetrahedron: Asymmetry* **2003**, *14*, 2013–2019.
[35] P. J. Guiry, C. P. Saunders, *Adv. Synth. Catal.* **2004**, *346*, 497–537.
[36] According to reference [4f] three equivalents of diethylzinc were used.
[37] M. A. Zuideveld, P. Wehrmann, C. Röhr, S. Mecking, *Angew. Chem.* **2004**, *116*, 887–891; *Angew. Chem. Int. Ed.* **2004**, *43*, 869–873.
[38] G. M. Sheldrick, *Acta Crystallogr.* **2008**, *A64*, 112–122.
[39] H. D. Flack, *Acta Crystallogr.* **1983**, *A39*, 876–881.
[40] In analogy to: K. Gademann, D. E. Chavez, E. N. Jacobsen, *Angew. Chem.* **2002**, *114*, 3185–3187; *Angew. Chem. Int. Ed.* **2002**, *41*, 3059–3061.
[41] T. Vidar Hansen, L. Skattebol, *Tetrahedron Lett.* **2005**, *46*, 3829–3830.

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