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Synthesis of planar chiral [2.2]paracyclophane monophosphine ligands and their application in the umpolung allylation of aldehydes

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Abstract—Chiral [2.2]paracyclophane monophosphines **8** were synthesized via resolution using chiral palladacycle **10**. Chiral phosphinite **5** was also prepared from 4-hydroxy[2.2]paracyclophane. Phosphines **8** and phosphinite **5** were used as the ligand in the umpolung allylation of aldehydes **14** with cyclohexenyl acetate **15**, giving homoallyl alcohols **16** in high diastereoselectivity and in moderate to good enantioselectivity. Palladacycle **10** was recovered by treating the palladacycle–phosphine complexes with sodium prolinate, followed by treatment with HCl in high yield.

1. Introduction

[2.2]Paracyclophane, with a unique framework of two benzene rings connected at the *para*-position by two ethylene chains, has shown its special properties in many aspects.[1] Different types of compounds derived from it have also been successfully used as novel chiral ligands in asymmetric catalysis, with excellent asymmetric induction being realized in many types of asymmetric reactions.[2,3] However, the preparation of enantiopure [2.2]paracyclophane derivatives is still quite difficult. To the best of our knowledge, there are no reports on the synthesis and applications of chiral monophosphine derivatives of [2.2]paracyclophane[4] even though chiral monophosphines are a relatively simple class of compounds and have widely been used as ligands in asymmetric catalysis.[5] We have demonstrated that planar chirality in *pseudo*-geminal disubstituted [2.2]paracyclophane ligands plays a definite role in asymmetric induction.[2c,3d] To show the role of planar chirality in [2,2]paracyclophane [2c,3d,6] and explore the applications of planar chiral cyclophane in asymmetric catalysis, we turned our attention to a study of [2.2]paracyclophane monophosphines with only planar chirality. Herein we would like to report the synthesis of [2.2]paracyclophane monophosphines and their efficient resolution using cyclopalladated compounds, as well as their application in the Pd-catalyzed asymmetric allylation of aldehydes.

2. Results and discussion

Two procedures were developed for the synthesis of chiral monophosphine ligands. Firstly, using Cram's procedure, racemic 4-hydroxy[2,2]paracyclophane **3** was prepared from [2,2]paracyclophane **1** in two steps.[7] Its resolution was realized using naproxen acid chloride instead of the more expensive camphanoyl chloride.[8] The two diastereoisomers were purified three times by crystallizations. Esters (S_p,*S*)-**4** and (R_p,*S*)-**4** were reduced with $LiAlH_4$ to produce (*S*)-**3** and (*R*)-**3** in 90% yields and in >99% ee, respectively. Treatment of (*R*)-4-hydroxy[2,2]paracyclophane **3** with chlorodiphenyl phosphine in the presence of Et_3N in toluene gave rise to the desired phosphinite **5** in 85% yield (Scheme 1). The absolute configurations of (*R*)- and (*S*)-**3** were determined by X-ray diffraction of the precursor, (R_p,*S*)-**4** (Fig. 1).

Monophosphine (*S*)-**8a** was synthesized as follows: Treatment of (*S*)-**3** with trifluoromethanesulfonic anhydride in the presence of pyridine gave triflate derivative (*S*)-**6** in 96% yield. The coupling reaction of triflate (*S*)-**6** with $Ph_2P(O)H$ using $Pd(OAc)_2$/dppp as catalyst afforded (*S*)-**7a** in 84% yield. Chiral monophosphine (*S*)-**8a** was

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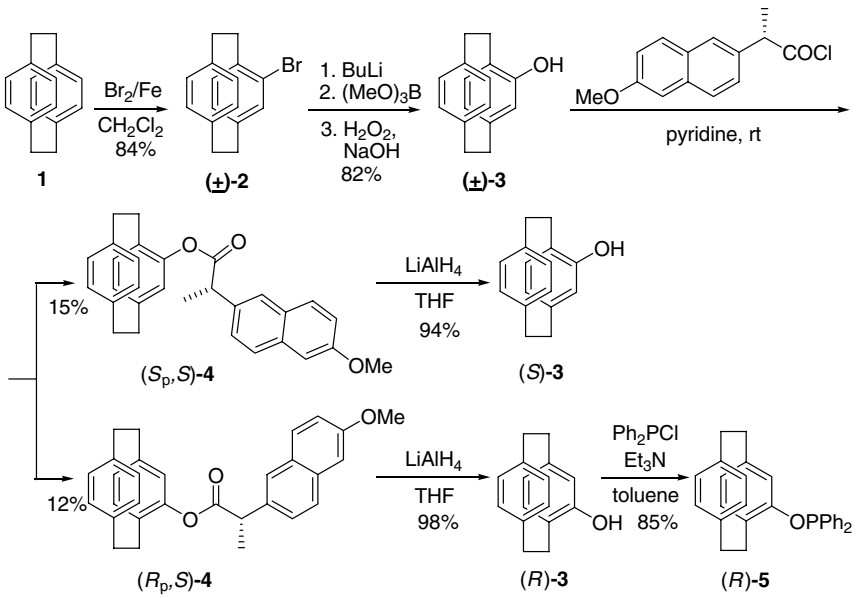


Scheme 1. Synthesis of chiral phosphinite cyclophane **5**.

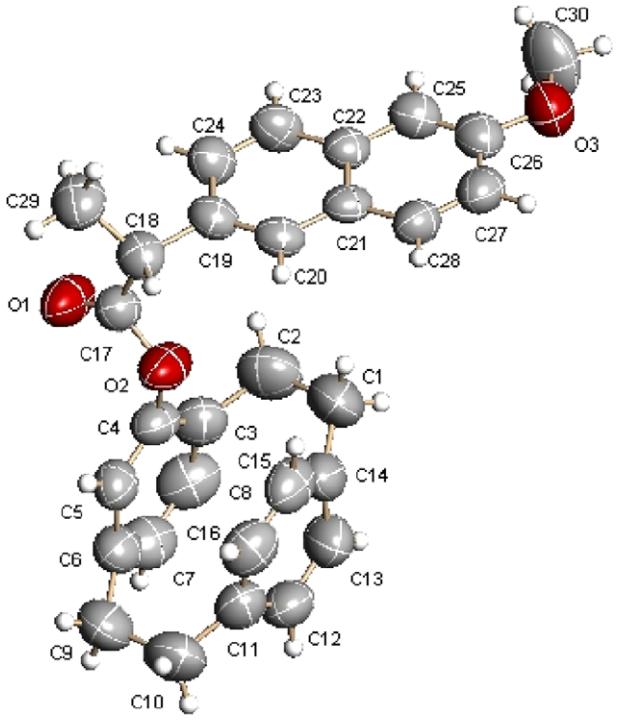
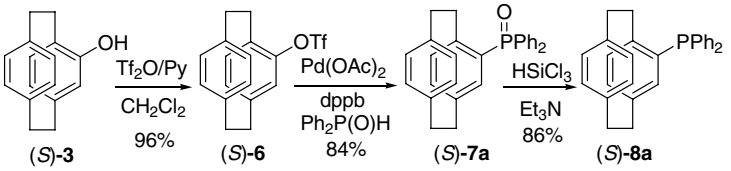


Figure 1. ORTEP diagram of the X-ray structure of (R_p,*S*)-**4**.

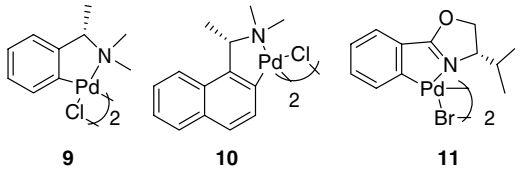
obtained in 86% yield by reduction of phosphine oxide with Cl_3SiH (Scheme 2).

Although the products were obtained in high yields in every step, the process is cumbersome and expensive. Thus, another procedure was sought. According to the literature,[4] bromo-lithium exchange of 4-bromo[2,2]paracyclophane **2** at low temperature followed by trapping of Ph_2PCl gave racemic [2,2]paracyclophane monophosphine **8a** in good yield (71% plus 20% yield of phosphine oxide **7a**, which could be reduced to **8a** with Cl_3SiH). If monophosphine **8a** could be resolved, it would be a simple method to obtain chiral monophosphines. There are many reports of resolving monophosphines using chiral palladacycles.[9] Several palladacycles **9**–**11** were tested in resolving **8a**, amongst which palladacycle **10** was found to be the best (Scheme 3).

On mixing **8a** with (+)-dichlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato-*C*2,*N*]dipalladium(II) **10**[10] in a 2:1 molar ratio in CH_2Cl_2 at ambient temperature, two diastereomeric complexes (R_p,*S*)-**12** and (S_p,*S*)-**12** were produced after 15 min, which were readily separated by simple column chromatography. Treatment with sodium (*S*)-prolinate gave the enantiomerically pure (*R*)-(−)-**8a** (44% yield, 99% ee) and (*S*)-(−)-**8a** (48% yield, 99% ee), respectively. Reaction of compound (*S*,*S*)-**13** with HCl allowed recovery of the valuable enantiomerically pure palladacycle (*S*)-**10** in 92% yield. Recovery of proline was not studied because of its water-solubility. A variety of chiral monophosphines **8b**–**e** with different substituents on the phosphorus atom were synthesized and resolved in excellent



Scheme 2. Synthesis of chiral phosphine cyclophane **8a**.



9 **10** **11**

Scheme 3. Different palladacycles.

yields (80–96%, two steps) and in >95% ee (Scheme 4, Table 1). The absolute configurations of (*R*)- and (*S*)-**8** were determined by X-ray diffraction analysis of precursor (R_p,*S*)-**12a** (Fig. 2).

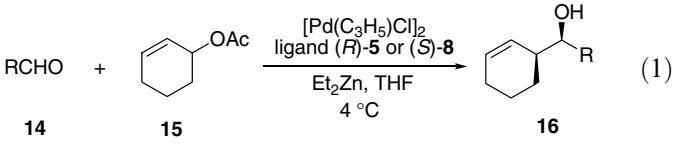
Catalytic enantioselective allylation of aldehydes represents one of the most efficient strategies for the synthesis of chiral homoallylic alcohols, which are useful intermediates in organic synthesis.[11] Zanoni et al.[12] were the first to report the asymmetric catalytic version of allylation of aldehydes by umpolung of a π-allyl palladium complex mediated by diethylzinc using chiral monodentate phosphorous as a ligand, affording products in satisfying yields with ee values of up to 70%. Subsequently, Zhou[13a] and Feringa[13b] provided further examples, in which higher enatioselectivities were realized. To examine the asymmetric induction of [2.2]paracyclophane monophosphine as a chiral ligand in asymmetric reactions, we chose the umpolung allylation of aldehydes as a model reaction.

In the presence of $[Pd(C_3H_5)Cl]_2$ (5.0 mol % Pd) and ligands (*R*)-**5** or (*S*)-**8** (10 mol %), the reaction of aldehyde **14** with cyclohexenyl acetate **15** proceeded smoothly to provide the corresponding homoallylic alcohol **16** (Eq. 1), the results are shown in Table 2. It can be seen that all reactions afforded *syn*-products in high diastereoselectivity, and the best yield (92% yield) and enantioselectivity (58% ee) were provided using **8b** as a ligand and benzaldehyde as a substrate (entry 3) while ligands (*R*)-**5** and (*S*)-dicyclohexyl[2,2]paracyclophane-4-ylphosphine **8e** showed lower reactivity and asymmetric induction than those with diarylcyclophan-4-ylphosphine ligands **8a**–**d** (entries 1 and 6 vs 2–5).

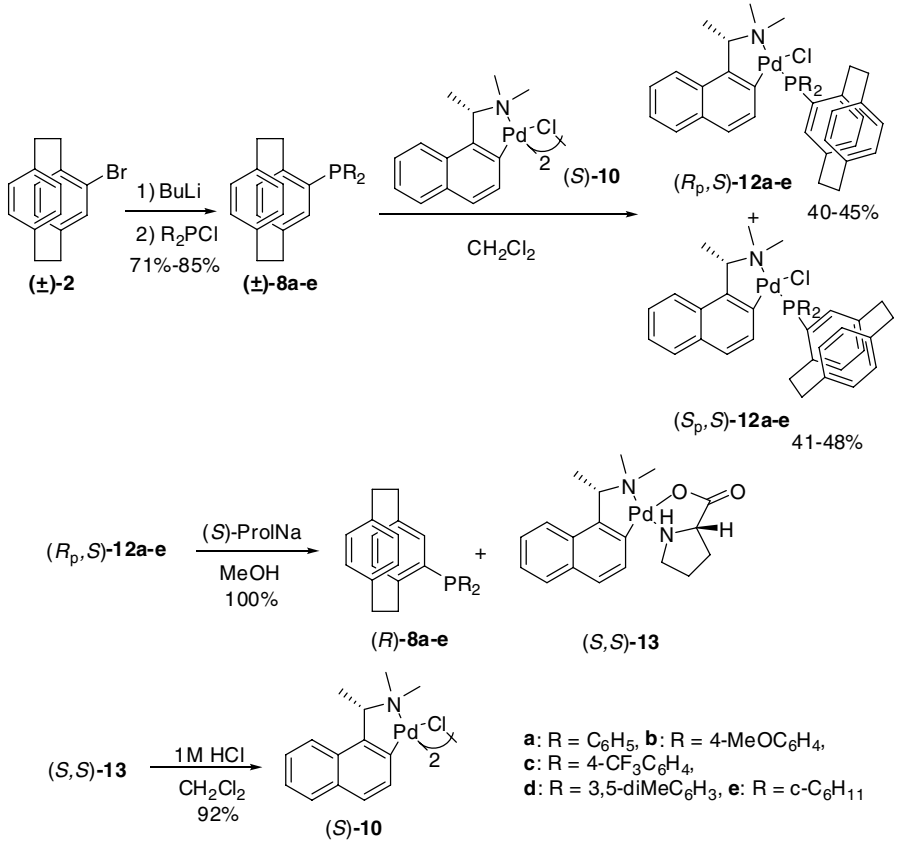
Table 1. Resolution of phosphine **8** using palladacycle **10**[a]

Entry	**8**, R	Yield[b] (%) (*R*)-**8**	ee (%) (*R*)-**8**	Yield[b] (%) (*S*)-**8**	ee (%) (*S*)-**8**
1	**a**, C_6H_5	44	99	48	99
2	**b**, 4-$MeOC_6H_4$	44	98	45	98
3	**c**, 4-$CF_3C_6H_4$	45	98	47	98
4	**d**, 3,5-$Me_2C_6H_3$	40	96	41	95
5	**e**, c-C_6H_{11}	41	99	43	99

[a] Molecular ratio: (1) phosphine **8**/palladacycle **10** = 1/1; (2) compound **12**/sodium (*S*)-prolinate = 1/1.2.
[b] Yield in two steps from racemic compound **8**.



(1)



Scheme 4. Synthesis of chiral phosphine cyclophane **8** via resolution.

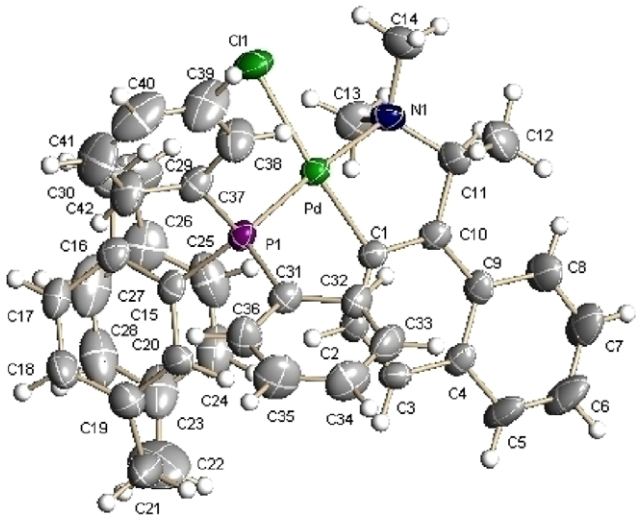


Figure 2. ORTEP diagram of X-ray structure of (R_p,*S*)-**12a**.

Table 2. Pd-Catalyzed asymmetric allylation of aldehydes **14** with cyclohexenyl acetate **15**[a]

Entry	**14**, R	Ligand	Time (h)	**16**, Yield[b]	*syn*:*anti*[c] (%)	ee[d] (%)
1	**a**, Ph	(*R*)-**5**	16	**a**, 45	95:5	21
2	**a**, Ph	(*S*)-**8a**	12	**a**, 90	99:1	56
3	**a**, Ph	(*S*)-**8b**	12	**a**, 92	99:1	58
4	**a**, Ph	(*S*)-**8c**	24	**a**, 80	92:8	27
5	**a**, Ph	(*S*)-**8d**	24	**a**, 82	92:8	35
6	**a**, Ph	(*S*)-**8e**	30	**a**, 52	90:10	15
7	**b**, 1-Np	(*S*)-**8b**	12	**b**, 95	98:2	60
8	**c**, 4-$NO_2C_6H_4$	(*S*)-**8b**	12	**c**, 54	97:3	7
9	**d**, 4-$MeOC_6H_4$	(*S*)-**8b**	16	**d**, 85	99:1	57
10	**e**, 2-$MeOC_6H_4$	(*S*)-**8b**	10	**e**, 89	99:1	42
11[e]	**f**, $PhCH_2CH_2$	(*S*)-**8b**	36	**f**, 38	91:9	72

[a] Molecular ratio: $[Pd(C_3H_5)Cl]_2$/(*S*)-**8**/**14**/**15**/Et_2Zn = 2.5/10/100/120/240.
[b] Isolated yield.
[c] Determined by HPLC and/or ^{1}H NMR.
[d] Determined by HPLC.
[e] THF/toluene = 1/1 as solvent.

Using (*S*)-**8b**, the allylation of various aldehydes **14b–f** with cyclohexenyl acetate **15** was examined. The highest ee (72%) was provided when aliphatic aldehyde **14f** was used, albeit the yield was unsatisfactory (entry 11) while a high yield (95%) and good ee (60%) were found using 1-naphthaldehyde (entry 7). The reactions using benzaldehydes **14d** and **14e** with a methoxy group on the phenyl ring gave products in moderate ee (entries 9 and 10), but those with a nitro group on the phenyl ring delivered the product in much lower ee (entry 8).

3. Conclusion

In conclusion, we have developed a simple and efficient procedure for the preparation of a range of planar chiral [2.2]paracyclophane monophosphines using chiral palladacycle as a resolving reagent. This asymmetric induction ability was demonstrated in the Pd-catalyzed allylation of aldehydes. In addition, the chiral palladacycle can be recovered by treating the palladacycle–phosphine complex with sodium prolinate, followed by treatment with HCl. Further investigations on the applications of planar chiral paracyclophanes in asymmetric catalysis are in progress.

4. Experimental

General: All reactions were performed under an argon atmosphere using oven-dried glassware. Solvents were treated prior to use according to the standard method. ^{1}H NMR spectra were recorded in $CDCl_3$ or C_6D_6 at room temperature. Chemical shifts are given in parts per million relative to TMS as an internal standard. Optical rotations were measured using a thermally jacketed 10 cm cell at 20 °C (concentration c given as g/100 mL). IR spectra were measured in cm^{-1}. Ee values were determined by chiral HPLC. The commercially available reagents were used as received without further purification. Compounds **3**,[7] **9**,[14] **10**,[10] **11**,[15] Ar_2PCl,[16] were prepared using literature procedures.

4.1. Resolution of 4-hydroxy[2,2]paracyclophane 3

A mixture of racemic 4-hydroxy[2,2]paracyclophane **3** (2.24 g, 10 mmol) and naproxen acid chloride (2.98 g, 12 mmol) in pyridine (20 mL) was stirred for 4 h at room temperature. It was diluted with H_2O (200 mL), and vigorously stirred, until a white precipitate appeared. The precipitate was filtered off, washed with H_2O (5 × 100 mL) and pentane (2 × 40 mL), and dried in vacuum to give the mixture of diastereomeric esters **4** (4.09 g, 94% yield). Three fractional crystallization from ethyl acetate and hexane (1:1) gave (R_p,*S*)-**4** (0.52 g, 12% yield) and (S_p,*S*)-**4** (0.67 g, 15% yield). The filtration was combined and reused in the resolution again.

Naproxen ester (S_p,*S*)-**4**: mp 138–140 °C. $[\alpha]_D^{20} = +31.9$ (*c* 1.05, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88–7.79 (m, 3H), 7.61 (dd, $J = 8.5$, 1.7 Hz, 1H), 7.26–7.17 (m, 2H), 6.46–6.39 (m, 4H), 6.31 (dd, $J = 7.8$, 1.8 Hz, 1H), 6.17 (dd, $J = 7.7$, 1.6 Hz, 1H), 5.91 (s, 1H), 4.14 (dd, $J = 14.2$, 7.4 Hz, 1H), 3.94 (s, 3H), 3.00–2.84 (m, 6H), 2.71–2.50 (m, 2H), 1.78 (d, $J = 6.9$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1, 157.7, 148.9, 139.3, 138.9, 141.4, 135.2, 135.0, 133.8, 133.2, 132.7, 132.0, 130.7, 129.8, 129.3, 129.2, 129.0, 127.6, 127.3, 126.3, 126.1, 119.2, 105.6, 55.3, 45.9, 35.1, 34.7, 34.0, 31.4, 18.1. EIMS *m*/*z* (relative intensity %): 436 (M^+, 13), 185 (66), 91 (100). IR (KBr): 3016, 2926, 2850, 1743, 1633, 1608, 1486, 1451, 1412, 1395, 1376, 1268, 1215, 1088, 1052, 1031, 1004, 925, 901, 854, 796, 715, 652, 621, 512, 476. Anal. Calcd for $C_{30}H_{28}O_3$: C, 82.54; H, 6.46. Found: C, 82.50; H, 6.44.

Naproxen ester (R_p,*S*)-**4**: mp 145–146 °C. $[\alpha]_D^{20} = +48.5$ (*c* 0.58, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90–7.78 (m, 3H), 7.62 (dd, $J = 8.4$, 1.9 Hz, 1H), 7.26–7.18 (m, 2H), 6.62 (dd, $J = 7.8$, 2.3 Hz, 1H), 6.45–6.36 (m, 4H), 6.24 (dd, $J = 7.7$, 2.1 Hz, 1H); 5.94 (s, 1H); 4.14 (dd, $J = 14.4$, 7.5 Hz, 1H); 3.94 (s, 3H); 3.04–2.93 (m, 4H); 2.62–2.12 (m, 4H); 1.72 (d, $J = 7.0$ Hz, 1H); ^{13}C NMR

(75 MHz, $CDCl_3$): δ 172.2, 157.7, 148.8, 139.4, 138.9, 141.4, 135.4, 135.2, 133.9, 133.2, 132.8, 131.9, 131.3, 130.0, 129.2, 129.0, 127.9, 127.4, 126.3, 119.3, 105.6, 55.3, 45.6, 35.2, 34.7, 33.6, 31.4, 17.8; EIMS *m/z* (relative intensity %): 438 (M+2, 11), 410 (25), 185 (100). IR (KBr): 2929, 2852, 1744, 1607, 1508, 1486, 1413, 1394, 1267, 1234, 1152, 1107, 1031, 925, 904, 867, 822, 716, 690, 646, 514, 481. Anal. Calcd for $C_{30}H_{28}O_3$: C, 82.54; H, 6.46. Found: C, 82.50; H, 6.44.

4.2. (*R*)-4-Hydroxy[2.2]paracyclophane (*R*)-3[8]

A mixture of $LiAlH_4$ (0.450 g, 11.7 mmol) and (R_p,*S*)-**4** (0.474 g, 1.17 mmol) in anhydrous THF (40 mL) was heated AT reflux for 8 h. The mixture was then cooled to 0 °C and ethyl acetate (10 mL), H_2O (10 mL), and 2 M HCl (50 mL) were successively added under stirring. The reaction mixture was extracted with Et_2O (3 × 20 mL) and the combined organic layers were washed with H_2O (2 × 50 mL) and $NaHCO_3$ solution and dried with Na_2SO_4. The solvent was removed in vacuum. The crude product was purified by flash column chromatography (CH_2Cl_2) to produce (*R*)-4-hydroxy[2.2]paracyclophane **3** 0.240 g (98% yield), mp 226–228 °C (Ref. 8 mp 232–234 °C). $[\alpha]_D^{20} = +8.4$ (*c* 1.15, $CHCl_3$), ee >99% by HPLC analysis using Chiralpak AD column, hexane/isopropanol = 90:10, flow rate 0.7 mL/min, $t_{R1} = 12.96$ min (major), $t_{R2} = 16.37$ min (minor). ^1H NMR (300 MHz, $CDCl_3$): δ 7.00 (dd, *J* = 7.9, 2.1 Hz, 1H), 6.55 (dd, *J* = 7.6, 1.8 Hz, 1H), 6.46–6.37 (m, 3H), 5.54 (d, *J* = 1.8 Hz, 1H), 4.41 (s, 1H), 3.37–2.60 (m, 8H); EIMS *m/z* (relative intensity %): 224 (M^+, 62), 120 (96), 104 (81), 91 (100).

4.3. (*S*)-4-Hydroxy[2.2]paracyclophane (*S*)-3[8]

This was obtained by the same method as that for (*R*)-**3** from (S_p,1*S*)-**3** (0.451 g, 1.11 mmol) in 94% yield (0.233 g); mp 229–230 °C (Ref. 8 mp 232–234 °). $[\alpha]_D^{20} = -8.2$ (*c* 1.05, $CHCl_3$), ee >99% by HPLC analysis using Chiralpak AD column, hexane/isopropanol = 90:10, flow rate 0.7 mL/min, $t_{R1} = 12.96$ min (minor), $t_{R2} = 16.37$ min (major).

4.4. (*R*)-Diphenyl([2.2]paracyclophan-4-yl)phosphinite (*R*)-5

To a solution of (*R*)-4-hydroxy[2.2]paracyclophane (**3**) (0.202 g, 0.90 mmol) and Et_3N (0.9 mL, 6 mmol) in toluene (10 mL) was added PPh_2Cl (0.35 mL, 1.8 mmol) dropwise at −78 °C. The mixture was stirred at room temperature overnight, concentrated in vacuum, purified by flash column chromatography (ethyl acetate/petroleum ether = 1/10) to give (*R*)-**5** as a white solid (0.312 mg, 85% yield). Mp 211–213, $[\alpha]_D^{20} = +24.1$ (*c* 1.05, $CHCl_3$), ee >99% by HPLC analysis using Chiralcel OD column, hexane/isopropanol = 90:10, flow rate 0.7 mL/min, $t_{R1} = 11.21$ min (major), $t_{R2} = 12.18$ min (minor). ^1H NMR (300 MHz, C_6D_6): δ 7.87–7.82 (m, 2H), 7.63–7.57 (m, 2H), 7.21–7.00 (m, 8H), 6.52–6.18 (m, 5H), 3.61–3.53 (m, 1H), 3.01–3.44 (m, 7H); ^{31}P NMR (161.92 MHz, C_6D_6) 107.3 ppm; EIMS *m/z* (relative intensity %): 408 (M^+, 5.0), 201 (15), 45 (100). IR (KBr): 2923, 2849, 1593, 1492, 1434, 1407, 1241, 1089, 979, 877, 805, 744, 696, 503. Anal. Calcd for $C_{28}H_{25}OP$: C, 82.33; H, 6.17. Found: C, 82.18; H, 6.15.

4.5. (*S*)-[2.2]Paracyclophan-4-yl trifluoromethanesulfonate (*S*)-6[17]

To a solution of (*S*)-4-hydroxy[2.2]paracyclophane **3** (0.175 g, 0.78 mmol) and pyridine (0.5 mL, 6 mmol) in dichloromethane (2 mL) was added trifluoromethanesulphonic anhydride (0.33 mL, 2 mmol) dropwise with stirring at 0 °C. The mixture was stirred overnight. The solution was then washed with 1 M HCl, water and saturated brine and dried over Na_2SO_4. Removal of the solvent in vacuum gave a brown solid which was purified by flash column chromatography (ethyl acetate/petroleum ether = 1/10) to give (*S*)-**6** as a white solid (0.269 g, 96% yield). $[\alpha]_D^{20} = -15.4$ (*c* 0.81, $CHCl_3$), mp 67–70 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 6.90 (dd, *J* = 8.0, 2.1 Hz, 1H), 6.60–6.45 (m, 5H), 6.17 (d, *J* = 1.2 Hz, 1H), 3.44–3.37 (m, 1H), 3.17–3.02 (m, 6H), 2.86–2.79 (m, 1H); ^{19}F NMR (56.4 MHz): −74.1 ppm; EIMS *m/z* (relative intensity %): 356 (M^+, 28), 223 (22), 104 (100), 73 (17).

4.6. (*S*)-Diphenyl([2.2]paracyclophan-4-yl)phosphine oxide (*S*)-7[18]

A mixture of dppb (49 mg, 0.114 mmol), $Pd(OAc)_2$ (17 mg, 0.076 mmol), $Ph_2P(O)H$ (307 mg, 1.51 mmol), (*S*)-4-trifluoromethylsulfonate[2.2]paracyclophane (269 mg, 0.755 mmol) in DMSO was stirred at room temperature for 10 min; *i*-Pr_2NEt (0.66 mL, 3.8 mmol) was then added, and heated to 100 °C for 12 h, then cooled to room temperature, diluted with ethyl acetate, washed with water three times and dried over Na_2SO_4. Removal of the solvent in vacuum and purification by column chromatography (ethyl acetate/petroleum ether = 1/2) to gave (*S*)-**7** as a white solid (258 mg, 84% yield). Mp 205–207. $[\alpha]_D^{20} = -24.1$ (*c* 1.05, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.72–7.65 (m, 2H), 7.57–7.33 (m, 8H), 7.16 (dd, *J* = 7.8, 1.4 Hz, 1H), 6.63–6.50 (m, 4H), 6.29–6.24 (m, 2H), 3.54–3.48 (m, 2H), 3.12–2.74 (m, 6H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 28.07 ppm. EIMS *m/z* (relative intensity %): 408 (M^+, 38), 304 (100), 225 (12), 178 (16), 99 (14).

4.7. (*S*)-Diphenyl([2.2]paracyclophan-4-yl)phosphine (*S*)-8a

Compound (*S*)-**7** (250 mg, 0.59 mmol), Et_3N (0.6 mL, 4.2 mmol), toluene (5 mL) were placed in a sealed tube, and cooled to 0 °C, then added $HSiCl_3$ (0.6 mL, 5.9 mmol), and heated to 100 °C. The reaction was kept at 100 °C for 18 h, then cooled to 0 °C and quenched with 1 M NaOH, and diluted with ethyl acetate. The aqueous layer was extracted with ethyl acetate (2 × 15 mL). The combined organic layer was dried, concentrated, and purified by column chromatography (ethyl acetate/petroleum ether = 1/10) to give (*S*)-**8a** as a white solid (190 mg, 86% yield). $[\alpha]_D^{20} = -15.1$ (*c* 1.0, $CHCl_3$), mp 187–188 °C, ee = 99% by HPLC analysis using Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 7.08$ min (minor), $t_{R2} = 8.47$ min (major). ^1H NMR (300 MHz, $CDCl_3$): δ 7.40–7.39 (m, 5H), 7.25–7.20 (m, 6H), 6.54–6.43 (m, 4H), 6.20 (dd, *J* = 8.1, 2.2 Hz, 1H), 5.72 (dd, *J* = 7.3, 1.5 Hz, 1H), 3.56–3.47 (m, 2H), 3.11–2.70 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 34.2, 34.8, 35.1, 35.2, 128.3, 128.6, 129.2, 130.6, 132.2, 132.8, 133.1,

133.3, 133.5, 134.3, 135.1, 135.4, 135.8, 137.2, 139.4, 139.6, 139.8; ^{31}P NMR (161.92 MHz, $CDCl_3$) −2.46 ppm; EIMS *m*/*z* (relative intensity %): 392 (M^+, 73), 304 (47), 288 (100), 178 (34); IR (KBr): 2961, 2924, 2852, 1434, 745, 698, 501 cm^{-1}. HRMS: Anal. Calcd for $C_{28}H_{26}P^{+1}$: 393.1766. Found: 393.1765.

4.8. General procedure for the preparation of paracyclophanylphosphines

To a solution of racemic 4-bromo[2,2]paracyclophane **2** (574 mg, 2 mmol) in Et_2O (50 mL) was added *n*-BuLi (2.5 mL, 1.6 M in hexane, 4.0 mmol) dropwise at 0 °C. The resulting mixture was stirred for 2 h at this temperature. R_2PCl (4 mmol) was added and stirred for 4 h at room temperature. The mixture was quenched with dry methanol (0.5 mL), concentrated in vacuum, purified by column chromatography (ethyl acetate/petroleum ether = 1/25–3/1) to give **8** as a white solid.

4.8.1. (±)-Diphenyl([2.2]paracyclophane-4-yl)phosphine (±)-8a.[4] Compound (±)-**8a** was obtained as a white solid (71% yield). Mp 142–144 °C.

4.8.2. (±)-Di(4′-methoxyphenyl)([2.2]paracyclophane-4-yl)phosphine (±)-8b. Compound (±)-**8b** was obtained as a white solid (75% yield). Mp 122–123 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33–7.11 (m, 5H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.77 (d, *J* = 7.7 Hz, 2H), 6.51–6.42 (m, 4H), 6.20 (d, *J* = 7.9 Hz, 1H), 5.72 (dd, *J* = 7.6, 1.7 Hz, 1H), 3.84 (s, 3H), 3.74 (s, 3H), 3.51–3.47 (m, 2H), 3.05–2.92 (m, 4H), 2.75 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 34.7, 34.9, 35.1, 35.2, 55.1, 55.2, 113.8, 113.9, 114.2, 114.3, 127.5, 128.9, 130.3, 132.1, 132.7, 133.1, 134.2, 134.5, 134.7, 135.7, 136.3, 136.6, 138.4, 139.4, 139.5, 139.8, 143.3, 143.6, 159.8, 160.4; ^{31}P NMR (161.92 MHz, $CDCl_3$): −10.5 ppm; EIMS *m*/*z* (relative intensity %): 452 (M^+, 64), 346 (100), 315 (23), 239 (34), 104 (35); IR (KBr): 2926, 1593, 1497, 1284, 1245, 1093, 1029, 830, 795, 723, 528 cm^{-1}. HRMS: Anal. Calcd for $C_{30}H_{29}O_2P$: 452.1905. Found: 452.1916.

4.8.3. (±)-Di(4′-trifluoromethyl)phenyl([2.2]paracyclophane-4-yl)phosphine (±)-8c. Compound (±)-**8c** was obtained as a white solid (85% yield). Mp 135–138 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.50 (m, 4H), 7.28 (m, 2H), 7.12 (d, *J* = 8.1 Hz, 1H), 6.60–6.52 (m, 4H), 6.19 (d, *J* = 7.9 Hz, 1H), 5.67 (m, 1H), 3.50–3.43 (m, 2H), 3.12–2.96 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 34.2, 34.3, 34.7, 34.9, 35.0, 35.1, 125.1, 125.5, 130.5, 130.6, 132.0, 132.9, 133.0, 133.2, 133.3, 134.3, 134.6, 134.7, 135.5, 135.7, 139.5, 140.2, 144.0; ^{31}P NMR (161.92 MHz, $CDCl_3$) −7.56 ppm; ^{19}F NMR (56.4 MHz) −63.1 ppm; EIMS *m*/*z* (relative intensity %): 530 (M+2, 40), 426 (100), 277 (21), 104 (83), 78 (33); IR (KBr): 2927, 1606, 1396, 1324, 1169, 1128, 1060, 1016, 834, 722, 699, 599, 508 cm^{-1}. HRMS: Anal. Calcd for $C_{30}H_{23}F_6P$: 528.1442. Found: 528.1450.

4.8.4. (±)-Di(3′,5′-Dimethylphenyl)([2.2]paracyclophane-4-yl)-phosphine (±)-8d. Compound (±)-**8d** was obtained as a white solid (78% yield). Mp 173–175 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23 (m, 1H), 7.03 (m, 3H), 6.85 (m, 3H), 6.53–6.43 (m, 4H), 6.18 (d, *J* = 3.2 Hz, 1H), 5.71 (dd, *J* = 7.7, 1.7 Hz, 1H), 3.50 (m, 2H), 3.05–2.76 (m, 6H), 2.31 (s, 6H), 2.19 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.2, 21.4, 34.1, 34.8, 35.1, 35.2, 130.1, 130.4, 130.7, 131.0, 132.1, 132.6, 132.7, 133.0, 133.1, 133.3, 134.2, 135.7, 137.4, 137.5, 137.8, 137.9, 139.3, 139.8; ^{31}P NMR (161.92 MHz, $CDCl_3$) −6.70 ppm; EIMS *m*/*z* (relative intensity %): 448 (M^+, 67), 342 (42), 327 (32), 240 (34), 104 (34), 84 (28), 44 (100); IR (KBr): 2923, 2853, 1598, 1447, 1262, 1122, 1094, 900, 848, 802, 725, 694, 645, 581, 436 cm^{-1}. HRMS: Anal. Calcd for $C_{32}H_{33}P$: 448.2320. Found: 448.2328.

4.8.5. (±)-Dicyclohexyl([2.2]paracyclophane-4-yl)phosphine (±)-8e. Compound (±)-**8e** was obtained as a white solid (82%). Mp 118–120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.60–6.31 (m, 7H), 3.97 (m, 1H), 3.26–2.84 (m, 7H), 2.04–0.79 (m, 22H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.1, 26.5, 26.7, 26.9, 27.1, 27.6, 27.8, 28.8, 30.3, 34.3, 34.7, 34.9, 35.1, 35.3, 35.4, 131.9, 132.2, 132.5, 133.1, 133.3, 133.6, 134.5, 138.1, 139.1, 139.8, 144.9, 145.3; ^{31}P NMR (161.92 MHz, $CDCl_3$) −4.76 ppm; EIMS *m*/*z* (relative intensity %): 403 (M−1, 17), 322 (26), 300 (32), 240 (23), 105 (46), 91 (61), 41 (100); IR (KBr): 2922, 2847, 1578, 1477, 1263, 1175, 1112, 1000, 887, 843, 793, 726, 635, 577, 508 cm^{-1}. HRMS: Anal. Calcd for $C_{28}H_{37}P$: 404.2633. Found: 404.2632.

4.9. General procedure for resolution of paracyclophanylphosphines

A solution of compound (±)-**8** (0.5 mmol) and (+)-dichlorobis[(*R*)-dimethyl(1-(1-naphthyl)ethyl)aminato-*C*2,*N*]-dipalladium(II) **10** (170 mg, 0.25 mmol) in CH_2Cl_2 was stirred at room temperature for 15 min. Two diastereomers **12** were isolated by column chromatography (ethyl acetate/petroleum ether = 5/1–2/1). Sodium (*S*)-prolinate (29.5 mg, 0.24 mmol) was added to a solution of (S_p,*S*)-**12** (0.24 mmol) in methanol (10 mL) and the resulting solution stirred for 2 h. The solvent was removed to leave a yellow solid which was purified by column chromatography (ethyl acetate/petroleum ether = 1/25 to dichloromethane/methanol = 8/1) to give (*S*)-**8** (100% yield) and compound (*S*,*S*)-**13**. Compound (*S*,*S*)-**13** in CH_2Cl_2 was treated with 1 M HCl under vigorous shaking under TLC control. The combined organic layers were washed with water, dried over Na_2SO_4 and concentrated to give (*S*)-**10** (92%).

4.9.1. Resolution of diphenyl([2.2]paracyclophane-4-yl)phosphine (±)-8a. Compound (R_p,*S*)-**9a** was obtained as yellow crystals (44% yield), >98% de by ^{31}P NMR; complex (R_p,*S*)-**12a**, $[\alpha]_D^{20} = -34.0$ (*c* 1.10, $CHCl_3$), mp 147–150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (m, 1H), 7.73–7.63 (m, 5H), 7.47–7.35 (m, 2H), 7.26–7.14 (m, 8H), 6.97 (dd, *J* = 11.2, 1.4 Hz, 1H), 6.66–6.38 (m, 5H), 6.08 (d, *J* = 7.9 Hz, 1H), 4.44 (m, 2H), 3.56 (m, 1H), 3.31–2.77 (m, 12H), 2.21 (d, *J* = 6.7 Hz, 3H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 24.04 ppm; MALDIMS *m*/*z*: 696 (M^+−Cl); IR (KBr): 2921, 2851, 1733, 1573, 1435, 1184, 1093, 938, 807, 694, 579, 529, 514, 426 cm^{-1}. Anal. Calcd for $C_{42}H_{41}ClNPPd\cdot 1/2CH_2Cl_2$: C, 65.86; H, 5.46;

N, 1.81. Found: C, 65.27; H, 5.88; N, 1.49. Compound (*R*)-**8a**. $[\alpha]_D^{20} = +15.1$ (*c* 1.0, $CHCl_3$), mp 187–188 °C, ee = 99% by HPLC analysis Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 7.77$ min (major), $t_{R2} = 9.39$ min (minor).

Compound (S_p,*S*)-**12a** (48% yield), >98% de by ^{31}P NMR. Complex (S_p,*S*)-**12a**, $[\alpha]_D^{20} = -163.9$ (*c* 0.60, $CHCl_3$), mp 167–170 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 7.81–7.63 (m, 6H), 7.45–7.37 (m, 2H), 7.26–7.13 (m, 8H), 6.96 (dd, $J = 11.2$, 1.7 Hz, 1H), 6.64–6.56 (m, 5H), 6.08 (m, 1H), 4.42 (m, 2H), 3.06 (m, 1H), 2.91–2.76 (m, 12H), 2.21 (d, $J = 6.5$ Hz, 3H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 32.7 ppm; MALDIMS *m*/*z* (relative intensity %): 696 (M^+-Cl); IR (KBr): 2922, 2851, 1735, 1573, 1435, 1184, 1093, 938, 796, 740, 693, 578, 530, 512, 424 cm^{-1}. Anal. Calcd for $C_{42}H_{41}ClNPPd\cdot 1/2CH_2Cl_2$: C, 65.86; H, 5.46; N, 1.81. Found: C, 66.01; H, 5.87; N, 1.52. Compound (*S*)-**8a**. $[\alpha]_D^{20} = -15.1$ (*c* 1.0, $CHCl_3$), mp 187–188 °C, ee = 99% by HPLC analysis Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 7.08$ min (minor), $t_{R2} = 8.52$ min (major).

4.9.2. Resolution of di(4′-methoxyphenyl)([2.2]paracyclophane-4-yl)phosphine (±)-8b. Compound (R_p,*S*)-**12b** was obtained as yellow crystals (44% yield), >98% de by ^{31}P NMR; complex (R_p,*S*)-**12b**, $[\alpha]_D^{20} = -30.2$ (*c* 0.78, $CHCl_3$), mp 191–193 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 7.84–7.73 (m, 3H), 7.64 (d, $J = 7.9$ Hz, 1H), 7.41–7.31 (m, 4H), 6.99 (d, $J = 8.8$ Hz, 1H), 6.97 (d, $J = 8.5$ Hz, 2H), 6.79–6.63 (m, 6H), 6.47 (s, 2H), 6.22 (s, 1H), 4.84 (m, 1H), 4.36 (m, 1H), 3.78 (s, 3H), 3.72 (s, 3H), 3.36–3.32 (m, 2H), 2.94–2.70 (m, 10H), 2.16 (d, $J = 6.5$ Hz, 3H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 26.0 ppm; MALDIMS *m*/*z*: 756.6 (M^+), 755.6 (M^+-H); IR (KBr): 2924, 2853, 1683, 1594, 1500, 1458, 1290, 1252, 1179, 1096, 1025, 939, 798, 718, 538, 503 cm^{-1}. Compound (*R*)-**8b**. $[\alpha]_D^{20} = +37.0$ (*c* 0.20, $CHCl_3$), mp 122–123 °C, ee = 98% by HPLC analysis Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 9.72$ min (major), $t_{R2} = 11.30$ min (minor).

Compound (S_p,*S*)-**12b** (45% yield), >98% de by ^{31}P NMR. Complex (S_p,*S*)-**12b,** $[\alpha]_D^{20} = -238$ (*c* 0.97, $CHCl_3$), mp 215–218 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 7.78 (m, 2H), 7.60–7.37 (m, 6H), 7.24 (m, 2H), 6.98–6.40 (m, 10H), 6.14 (d, $J = 7.9$ Hz, 1H), 4.45 (m, 2H), 3.75 (s, 3H), 3.70 (s, 3H), 3.66–2.75 (m, 13H), 2.21 (d, $J = 5.7$ Hz, 3H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 30.4 ppm; MALDIMS *m*/*z*: 756.6 (M^+), 755.6 (M^+-H); IR (KBr): 2924, 2853, 1686, 1593, 1500, 1290, 1251, 1180, 1090, 938, 798, 720, 539, 495 cm^{-1}. Anal. Calcd for $C_{44}H_{45}ClNO_2PPd$: C, 66.67; H, 5.72; N, 1.77. Found: C, 66.70; H, 6.06; N, 1.37. Compound (*S*)-**8b**: $[\alpha]_D^{20} = -37.6$ (*c* 0.18, $CHCl_3$), mp 122–123 °C, ee = 98% by HPLC analysis Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} =$ 10.29 min (minor), $t_{R2} = 11.30$ min (major).

4.9.3. Resolution of di(4′-trifluoromethylphenyl)([2.2]paracyclophane-4-yl)phosphine (±)-8c. Compound (R_p,*S*)-**12c** was obtained as yellow crystals (45% yield), >98% de by ^{31}P NMR; complex (R_p,*S*)-**12c**, $[\alpha]_D^{20} = -5.1$ (*c* 1.00, $CHCl_3$), mp 138–140 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 8.03–7.96 (m, 2H), 7.74 (d, $J = 8.3$ Hz, 1H), 7.66–7.58 (m, 3H), 7.48–7.33 (m, 7H), 6.96 (d, $J = 8.8$ Hz, 1H), 6.88 (d, $J = 12.7$ Hz, 1H), 6.69 (s, 2H), 6.59 (m, 3H), 6.45 (d, $J = 7.8$ Hz, 1H), 4.67 (m, 1H), 4.43 (m, 1H), 3.49–2.82 (m, 13H), 2.16 d, $J = 6.4$ Hz, 3H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 26.3 ppm; MALDIMS *m*/*z*: 832.0 (M^+-Cl); IR (KBr): 2924, 1687, 1608, 1502, 1398, 1324, 1169, 1128, 1061, 1016, 939, 830, 700, 601, 531 cm^{-1}. Anal. Calcd for $C_{44}H_{39}ClF_6NPPd$: C, 60.84; H, 4.53; N, 1.61. Found: C, 61.22; H, 4.67; N, 1.53. Compound (*R*)-**8c**. $[\alpha]_D^{20} = +11.0$ (*c* 0.32, $CHCl_3$), mp 143–145 °C, ee = 98% by HPLC analysis Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 9.72$ min (major), $t_{R2} = 11.30$ min (minor).

Compound (S_p,*S*)-**12c** (47% yield), >98% de by ^{31}P NMR. Complex (S_p,*S*)-**12c**, $[\alpha]_D^{20} = -141.5$ (*c* 1.14, $CHCl_3$), mp 155–156 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 7.83–7.62 (m, 6H), 7.52–7.24 (m, 8H), 6.86 (m, 2H), 6.68 (m, 3H), 6.56 (m, 1H), 6.16 (d, $J = 7.4$ Hz, 1H), 4.52–4.40 (m, 2H), 3.71 (m, 1H), 3.41–3.26 (m, 2H), 3.10 (d, $J =$ 3.3 Hz, 3H), 3.03–2.85 (m, 7H), 2.22 (d, $J = 4.3$ Hz, 3H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 30.7 ppm; MALDIMS *m*/*z*: 832.0 (M^+-Cl); IR (KBr): 2924, 2854, 1687, 1608, 1502, 1398, 1324, 1169, 1128, 1061, 1016, 938, 829, 700, 601, 507 cm^{-1}. Anal. Calcd for $C_{44}H_{39}ClF_6NPPd\cdot CH_2Cl_2$: C, 58.66; H, 4.43; N, 1.54. Found: C, 58.38; H, 4.54; N, 1.58. Compound (*S*)-**8c**. $[\alpha]_D^{20} = -11.2$ (*c* 0.27, $CHCl_3$), mp 143–145 °C, ee = 98% by HPLC analysis Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 10.29$ min (minor), $t_{R2} = 11.30$ min (major).

4.9.4. Resolution of di(3′,5′-dimethyl)([2.2]paracyclophane-4-yl)phosphine (±)-8d. Compound (R_p,*S*)-**12d** was obtained as yellow crystals (40% yield), >95% de by ^{31}P NMR; complex (R_p,*S*)-**12d**, $[\alpha]_D^{20} = -30.1$ (*c* 0.56, $CHCl_3$), mp 173–175 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, $J = 8.2$ Hz, 1H), 7.62–7.54 (m, 3H), 7.46–7.26 (m, 3H), 7.18 (d, $J = 6.1$ Hz, 2H), 7.07–6.91 (m, 3H), 6.72 (m, 2H), 6.62 (m, 2H), 6.50 (m, 2H), 6.04–5.99 (m, 1H), 5.30 (m, 1H), 4.33 (m, 1H), 3.38–2.66 (m, 13H), 2.23 (s, 6H), 2.19 (d, $J = 6.4$ Hz, 3H), 2.14 (s, 6H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 25.3 ppm; MALDIMS *m*/*z*: 752.5 ($M-Cl$); IR (KBr): 2923, 2854, 1735, 1573, 1457, 1125, 938, 844, 805, 719, 692, 582, 563, 488 cm^{-1}. Anal. Calcd for $C_{46}H_{49}ClNPPd\cdot 1/2CH_2Cl_2$: C, 67.19; H, 6.06; N, 1.69. Found: C, 67.45; H, 6.36; N, 1.43. Compound (*R*)-**8d**: $[\alpha]_D^{20} = +12.6$ (*c* 0.45, $CHCl_3$), mp 203–205 °C, ee = 96% by HPLC analysis Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 3.61$ min (major), $t_{R2} = 4.01$ min (minor).

Compound (S_p,*S*)-**12d** (41% yield), >95% de by ^{31}P NMR. Complex (S_p,*S*)-**12d**, $[\alpha]_D^{20} = -231.2$ (*c* 0.82, $CHCl_3$), mp 185–186 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, $J = 8.2$ Hz, 1H), 7.67 (d, $J = 7.5$ Hz, 1H), 7.46–7.29 (m, 6H), 7.08 (m, 1H), 7.00–6.93 (m, 4H), 6.63–6.49 (m, 3H), 6.24 (m, 2H), 6.00–5.88 (m, 2H), 4.40–4.24 (m, 2H), 3.32–2.61 (m, 13H), 2.24–2.15 (m, 15H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 27.0 ppm; MALDIMS *m*/*z*: 752.5 ($M-Cl$); IR (KBr): 2921, 2853, 1573, 1458, 1255, 1125, 1075, 938, 844, 805, 719, 692, 582, 488 cm^{-1}. Compound (*S*)-**8d** $[\alpha]_D^{20} = -12.6$ (*c* 0.40, $CHCl_3$), mp 203–205 °C,

ee = 95% by HPLC analysis Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 3.65$ min (minor), $t_{R2} = 4.00$ min (major).

4.9.5. Resolution of dicyclohexyl([2.2]paracyclophane-4-yl)phosphine (±)-8e. Compound (R_p,S)-**12e** was obtained as yellow crystals (41% yield), >98% de by ^{31}P NMR; complex (R_p,S)-**12e**, $[\alpha]_D^{20} = +18.9$ (c 0. 80, $CHCl_3$), mp 225–227 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (m, 2H), 7.38–6.78 (m, 6H), 6.71 (m, 2H), 6.43 (m, 2H), 4.28 (m, 2H), 3.30 (m, 1H), 3.26–2.93 (m, 11H), 2.67 (s, 3H), 2.05–1.98 (m, 4H), 1.90–1.25 (m, 19H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 24.5 ppm; MALDIMS m/z: 708.5 (M−Cl); IR (KBr): 2920, 2849, 1573, 1443, 1365, 1174, 1073, 1010, 937, 808, 780, 740, 717, 580, 512, 494 cm^{-1}. Anal. Calcd for $C_{42}H_{53}ClNPPd$: C, 67.74; H, 7.17; N, 1.88. Found: C, 67.28; H, 7.24; N, 1.69. Compound (R)-**8e**. $[\alpha]_D^{20} = +45.0$ (c 0.20, $CHCl_3$), mp 130–132 °C, ee = 99% by HPLC analysis Chiralcel OD-H column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 12.58$ min (major), $t_{R2} = 13.32$ min (minor).

Compound (S_p,S)-**12e** (43% yield), >98% de by ^{31}P NMR. Complex (S_p,S)-**12e**, $[\alpha]_D^{20} = -22.5$ (c 0.82, $CHCl_3$), mp 236–239 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84–7.37 (m, 6H), 7.01 (d, $J = 2.2$ Hz, 1H), 6.81 (d, $J = 8.6$ Hz, 1H), 6.74 (m, 2H), 6.53–6.43 (m, 3H), 4.82 (m, 1H), 4.33 (m, 1H), 3.79 (m, 1H), 3.47–3.36 (m, 3H), 3.00 (m, 7H), 2.73–2.53 (m, 5H), 2.20 (m, 1H), 2.04 (d, $J = 6.4$ Hz, 3H), 1.81–1.12 (m, 17H); ^{31}P NMR (161.92 MHz, $CDCl_3$) 30.6 ppm; MALDIMS m/z: 708.5 (M−Cl); IR (KBr): 2932, 2848, 1571, 1073, 941, 825, 744, 719, 579, 491 cm^{-1}. Anal. Calcd for $C_{42}H_{53}ClNPPd$: C, 67.74; H, 7.17; N, 1.88. Found: C, 67.28; H, 7.22; N, 1.48. Compound (S)-**8e**: $[\alpha]_D^{20} = -44.6$ (c 0.20, $CHCl_3$), mp 130–132 °C, ee = 99% by HPLC analysis Chiralcel OD-H column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 12.43$ min (minor), $t_{R2} = 13.39$ min (major).

4.10. Recovery of palladacycle 10[9h]

Compound (S,S)-**13** (560 mg, 1.34 mmol) in CH_2Cl_2 (30 mL) was treated with 1 M HCl (30 mL) under vigorous shaking under TLC control. The aqueous layer was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic layers were washed with water, dried over Na_2SO_4, and concentrated to give (S)-**10** (418 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.78 (m, 2H), 7.58 (m, 2H), 7.48–7.34 (m, 5H), 4.18 (m, 2H), 3.00 (d, $J = 10.0$ Hz, 6H), 2.77 (d, $J = 14.3$ Hz, 6H), 1.94–1.90 (m, 6H).

4.11. General procedure for asymmetric allylation of aldehydes

In a Schlenk tube, $[Pd(C_3H_5)Cl]_2$ (2.7 mg, 7.5 μmol), (R)-**5** or (S)-**8** (30 μmol) and THF (1.0 mL) were added under nitrogen. The reaction mixture was stirred at 0 °C for 30 min, then the fresh distilled benzaldehyde (31 μL, 0.3 mmol), cyclohexenyl acetate (50.4 mg, 0.36 mmol), and Et_2Zn (0.7 mL, 1.0 M in hexane, 0.7 mmol) were added sequentially. The mixture was allowed to warm to room temperature over 12 h before quenching with saturated NH_4Cl (aq). After stirring for 30 min, Et_2O (5 mL) was added and the organic phase separated, washed with brine (2 × 10 mL), dried over Na_2SO_4, and evaporated to give a crude homoallylic alcohol, purified by flash column chromatography (hexane/EtOAc = 10:1).

4.11.1. (1*S*,1*R*′)-(Cyclohex-2-enyl)(phenyl)methanol 16a.[13] Obtained as an oil (90% yield); absolute stereochemistry assigned by optical rotation $[\alpha]_D^{20} = +10.1$ (c 1.0, C_6H_6) (Ref. 12 +14.8); 56% ee by HPLC Chiralcel OD column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 13.41$ min (major), $t_{R2} = 14.56$ min (minor). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25–7.16 (m, 5H), 5.74–5.69 (m, 1H), 5.30–5.26 (m, 1H), 4.46 (dd, $J = 6.7$, 1.7 Hz, 1H), 2.39 (m, 1H), 1.99 (m, 1H), 1.89 (m, 2H), 1.67–1.60 (m, 2H), 1.46–1.40 (m, 2H); EIMS m/z (relative intensity %): 216 (M^+ <1), 134 (45), 91 (100).

4.11.2. (1*S*,1*R*′)-(Cyclohex-2-enyl)(1-naphthyl)methanol 16b. Obtained as a clear oil (95% yield); absolute stereochemistry assigned by analogy to compound **16a**; 60% ee by HPLC Chiralpak AD-H column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} = 22.23$ min (minor), $t_{R2} = 27.91$ min (major). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05 (m, 1H), 7.87 (m, 1H), 7.78 (m, 1H), 7.68 (m, 1H), 7.52–7.46 (m, 3H), 5.89–5.84 (m, 1H), 5.53–5.44 (m, 1H), 2.78 (m, 1H), 2.01 (m, 3H), 2.04–1.42 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.2, 23.3, 25.1, 41.8, 73.4, 123.1, 123.8, 125.2, 125.3, 125.7, 127.6, 128.5, 128.8, 130.4, 130.5, 133.6, 138.2; EIMS m/z (relative intensity %): 238 (M^+ <1), 157 (100), 129 (81). IR (Neat): 2928, 1511, 1090, 908, 779, 732, 677 cm^{-1}. HRMS: Anal. Calcd for $C_{17}H_{18}O$: 238.1358. Found: 238.1354.

4.11.3. (1*S*,1*R*′)-(Cyclohex-2-enyl)(4-nitro-phenyl)methanol 16c.[19] Obtained as a clear oil (54% yield); absolute stereochemistry assigned by analogy to compound **16a**; 7% ee by HPLC Chiralpak AS column, hexane/isopropanol = 93:7, flow rate 0.7 mL/min, $t_{R1} = 12.54$ min (minor), $t_{R2} = 14.17$ min (major). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (d, $J = 8.4$ Hz, 2H), 7.52 (d, $J = 8.4$ Hz, 2H), 5.92 (m, 1H), 5.45 (m, 1H), 4.78 (d, $J = 5.7$ Hz, 1H), 2.53 (s, 1H), 2.04–1.72 (m, 5H), 1.54–1.46 (m, 2H); EIMS m/z (relative intensity %): 233 (M^+ <1), 111 (100).

4.11.4. (1*S*,1*R*′)-(Cyclohex-2-enyl)(4-methoxy-phenyl)methanol 16d.[13] Obtained as a clear oil (85% yield); absolute stereochemistry assigned by analogy to compound **16a**; 57% ee by HPLC Chiralpak AS column, hexane/isopropanol = 90:10, flow rate 0.7 mL/min, $t_{R1} = 11.46$ min (major), $t_{R2} = 15.71$ min (minor). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27–7.24 (m, 2H), 6.89–6.86 (m, 2H), 5.81–5.76 (m, 1H), 5.37–5.33 (m, 1H), 4.50 (d, $J = 7.2$ Hz, 1H), 3.80 (s, 3H), 2.46 (m, 1H), 1.98 (m, 2H); 1.87 (m, 1H), 1.78–1.73 (m, 2H), 1.54–1.48 (m, 2H); EIMS m/z (relative intensity %): 218 (M^+ <1), 137 (100), 107 (50).

4.11.5. (1*S*,1*R*′)-(Cyclohex-2-enyl)(2-methoxy-phenyl)methanol 16e. Obtained as a clear oil (89% yield); absolute stereochemistry assigned by analogy to compound **16a**; 42% ee by HPLC Chiralpak AS column, hexane/isopropanol = 90:10, flow rate 0.7 mL/min, $t_{R1} = 8.52$ min (minor),

$t_{R2} = 9.23$ min (major). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32–7.21 (m, 2H), 6.98–6.86 (m, 2H), 5.76 (m, 1H), 5.38–5.35 (m, 1H), 4.74 (m, 1H), 3.83 (s, 1H), 2.63 (m, 1H), 2.53 (m, 1H); 1.99 (m, 2H), 1.79–1.69 (m, 2H), 1.60–1.53 (m, 2H); EIMS *m*/*z* (relative intensity %): 218 (M^+ <1), 137 (100), 107 (50).

4.11.6. (1*S*,1*R*′)-(Cyclohex-2-enyl)(3-phenyl)propan-1-ol 16f.[20] Obtained as a clear oil (36% yield); absolute stereochemistry assigned by specific rotation $[\alpha]_D^{20} = +12.6$ (*c* 0.85, C_6H_6); 72% ee by HPLC Chiralpak AD-H column, hexane/isopropanol = 95:5, flow rate 0.7 mL/min, $t_{R1} =$ 13.47 min (minor), $t_{R2} = 14.76$ min (major). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31–7.16 (m, 5H), 5.85–5.89 (m, 1H), 5.54 (dd, $J = 10.4$, 1.8 Hz, 1H), 3.61 (m, 1H), 2.87–2.80 (m, 1H), 2.71–2.61 (m, 1H); 2.24 (m, 1H), 1.98 (m, 1H), 1.84–1.71 (m, 4H), 1.59–1.44 (m, 3H); EIMS *m*/*z* (relative intensity %): 216 (M^+ <1), 134 (36), 117 (22), 91 (100).

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