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Novel Multichiral Diols and Diamines by Highly Stereoselective Pinacol Coupling of Planar Chiral [2.2]Paracyclophane Derivatives

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Abstract: The $TiCl_4$/Zn-mediated intermolecular pinacol coupling of the planar chiral carbonyl compounds [2.2]paracyclophane-4-carbaldehyde, 4-acetyl[2.2]paracyclophane (ketone) and the four regioisomeric 5-, 7-, 12- and 13-methoxy[2.2]paracyclophane-4-carbaldehydes as well as the *p*TosOH–Zn/Cu-promoted coupling of their N-substituted imines is described. Coupling of the enantiomerically pure substrates (most of carbonyl compounds and all imines) occurs stereoselectively giving rise to diastereomerically pure 1,2-diols and 1,2-diamines. Racemic aldehydes and ketone react with different degrees of stereoselectivity (depending on the substituents in certain positions) and produce one to three diastereomers. 7-Methoxy[2.2]paracyclophane-4-carbaldehyde undergoes a tandem pinacol coupling–pinacol rearrangement to yield bis-(7-methoxy[2.2]paracyclophane-4-yl)acetaldehyde. Coupling of the racemic imines produces a mixture of single racemic D,L-diamine and single *meso*-diamine in each case. The stereoselective formation of the asymmetric centres is governed by the planar chiral [2.2]paracyclophanyl moiety. The techniques elaborated are extended to the intramolecular coupling of [2.2]paracyclophane-4,13-dicarbaldehyde and its bis-N-phenylimine, resulting in stereoselective formation of the chiral triply-bridged diol and exclusive formation of the *meso*-diamine. X-Ray investigations of several diols and diamines have been carried out and the structural features of these derivatives are discussed.

Keywords: cyclophanes · diastereoselectivity · pinacol coupling · planar chirality

Introduction

The prominent role of diols and diamines as chiral inductors in a wide range of stereoselective processes is evident and well documented in the literature.[1] A notable part of these ligands are compounds possessing C_2 symmetry.[1,2] The pinacol coupling of carbonyl compounds and their imino derivatives is presently accepted as one of the most rational and convenient methods for the synthesis of such chiral diols and diamines.[3] The aim of these studies is to develop more effective catalytic systems providing chiral target compounds with high stereoselectivity and in high chemical yields. The possibility to carry out the pinacol coupling of α,ω-bis-carbonyl derivatives makes this reaction an excellent tool to prepare cyclic compounds in highly stereoselective fashion which may be useful for natural product and drug synthesis.[4] Another promising direction is the application of the pinacol coupling to the construction of novel multichiral ligands, bearing—apart from two chiral centres—additional elements of central, axial or planar chirality and/or having the diol, diamine or amino alcohol fragments incorporated in rigid frameworks. Several interesting ligands were synthesised by *intermolecular* coupling of planar chiral (η^6-arene)tricarbonylchromium complexes, ferrocenecarbaldehydes or formylphosphaferrocenes,[5] cyclopentadiene- or cyclobutene-based ketones[6] or by *intramolecular* coupling of axially chiral 2,2′-biarylcarbaldehydes and their diimines, planar chiral mono-(η^6-arene)tricarbonylchromium complexes of such biaryls, diferrocenylcarboxaldehyde and its diimine.[7] The pinacol cross-coupling of the metal-coordinated planar chiral arylaldehydes with imines has also recently been re-

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ported.[8] Selected examples of such types of ligands are presented in Figure 1 (**I**–**VI**). Reductive coupling of aromatic diimines effectively produces a variety of diazacrown esters and other nitrogen-containing macrocycles.[9]

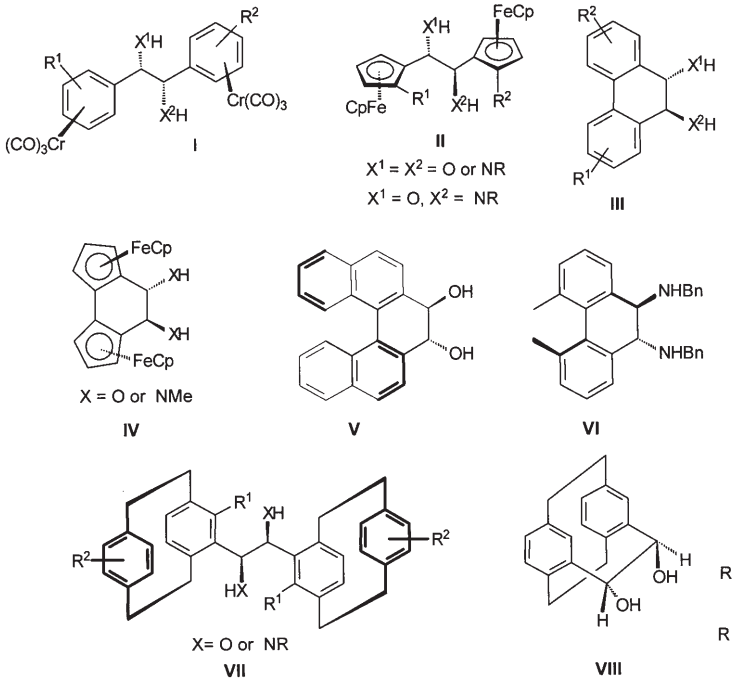


Figure 1. Selected examples of multichiral and rigid diols, diamines and amino alcohols.

4-carbaldehyde (**1**), 4-acetyl[2.2]paracyclophane (**2**, ketone) and four regioisomeric hydroxy[2.2]paracyclophane-4-carbaldehydes, all of which are chiral and have a variable substitution pattern, that is, 5-hydroxy- (*ortho*-, FHPC, **3**), 12-hydroxy- (pseudo-*ortho*-, pseudo-FHPC, **4**), 13-hydroxy- (pseudo-*gem*-, *iso*-FHPC, **5**) and 7-hydroxy-[2.2]paracyclophane-4-carbaldehydes (*para*-, *para*-FHPC, **6**) (Figure 2). This selection will help us to understand how the substituents effect reactivity and stereoselectivity of these model carbonyl compounds.

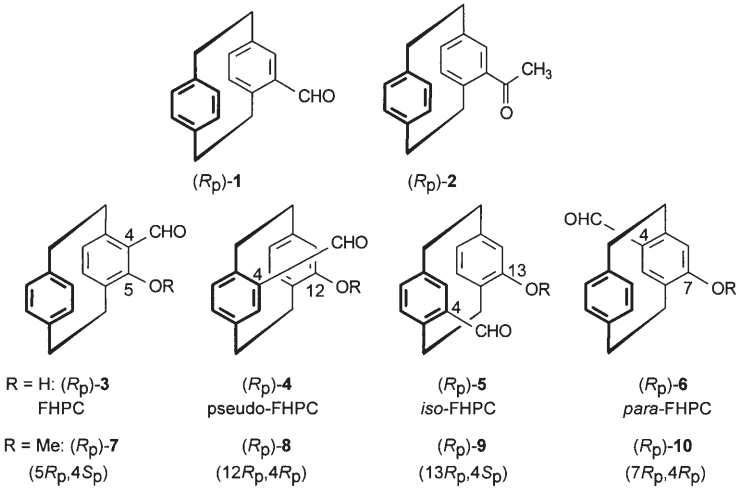


Figure 2. Carbonyl derivatives of [2.2]paracyclophane and enhanced stereochemical descriptors for disubstituted compounds.

In the course of our studies directed at the elaboration of planar chiral [2.2]paracyclophanes as ligands for asymmetric synthesis we have already reported on a number of efficient methods providing easy access to the enantiomerically pure *ortho*-acylhydroxy-, *ortho*- and pseudo-*gem*-formylhydroxy-[2.2]paracyclophanes, their imines, amino alcohols, salene-type ligands, chiral β-diketones, and others.[10] Moreover, two novel types of planar chiral bisphenols (namely, bridged and aryl [2.2]paracyclophane-type) were suggested by us recently.[11] In continuation of these studies we became interested in other chiral diols and diamines of the [2.2]paracyclophane series. Here we present the application of *intra*- and *intermolecular* pinacol coupling of planar chiral [2.2]paracyclophane carbonyl derivatives and their imines to the synthesis of novel potential ligands of type **VII** and **VIII** (Figure 1).[12] The structures and the determination of the relative configurations of these new compounds are also presented and the stereoselectivity of the coupling reactions is discussed.

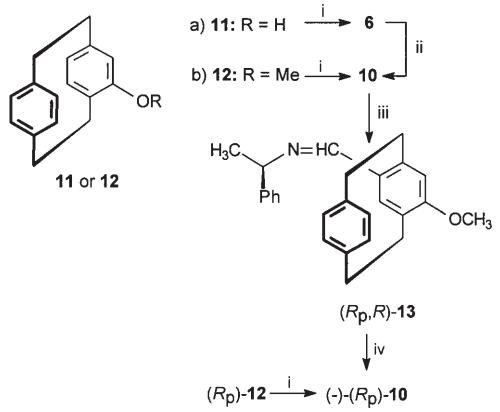
Results and Discussion

Synthesis of the starting materials: As substrates we have chosen different carbonyl compounds: [2.2]paracyclophane-

All compounds are easily available either in racemic or in enantiomerically pure form. Aldehydes *rac*- and (R_p)-**1**[13] and ketones *rac*- and (R_p)-**2**[10d] were obtained as described previously. For the synthesis of each chiral regioisomeric hydroxy[2.2]paracyclophane-4-carbaldehydes specific synthetic techniques were applied. *rac*-**3** (FHPC) was obtained from 4-hydroxy[2.2]paracyclophane in three steps with its *ortho*-regioselective oxaloylation as a key reaction.[10f] The procedure for the synthesis of *rac*-**5** (*iso*-FHPC)[10i] was based on the pseudo-*gem*-regioselective $TiCl_4$-catalysed formylation of methyl[2.2]paracyclophane-4-carboxylate with α,α-dichloromethyl methyl ether.[14] Aldehyde *rac*-**4** (pseudo-FHPC) was synthesised from 4,12-dibromo-[2.2]paracyclophane by stepwise exchange of the bromine atoms for the respective functional group.[15] All three hydroxy-substituted [2.2]paracyclophane-derived aldehydes were resolved into enantiomers through their Schiff bases by using the enantiomers of α-phenylethylamine (α-PEAM). Subsequently *rac*- and (*R*)-**3**–**5** were transformed into the respective methoxy derivatives *rac*- and (*R*)-**7**–**9** by methoxylation with methyl iodide in the presence of K_2CO_3 in acetone.[10c]

For the synthesis of 7-methoxy[2.2]paracyclophane-4-carbaldehyde (**10**) two different techniques starting from either 4-hydroxy[2.2]paracyclophane (**11**; Scheme 1, route A) or 4-

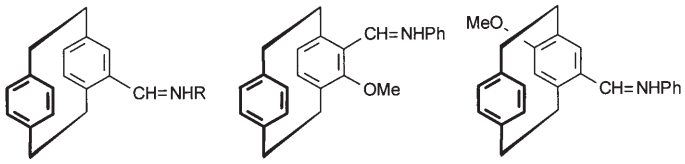
methoxy[2.2]paracyclophane (**12**; Scheme 1, route B) were investigated. We have found that formylation of phenol **11** with Cl_2CHOCH_3 (1.3 equiv $TiCl_4$, CH_2Cl_2, 2 h) was *para*-regioselective rather than *ortho*-regioselective (unlike the acylation of **11**[10e]) and thus afforded the respective 7-hydroxy-[2.2]paracyclophane-4-carbaldehyde (**6**) (*para*-FHPC, isolated yield 60%) predominantly, whereas the *ortho*-substituted compound **3** was formed only in traces (isolated yield less than 5%). At the same time formylation of **11** in the presence of other Lewis acids (1 to 5 equiv $SnCl_4$ or 1.3 equiv $FeCl_3$) was neither effective nor regioselective and produced in all cases (reaction time 2–8 h) mixtures of the corresponding *ortho*- and *para*-hydroxyaldehydes **3** and **6** together with unreacted starting phenol. From the combined reaction mixtures of these transformations we have isolated **3** (30%), **6** (36%) and the remaining **11** (25%) by preparative chromatography. Racemic **10** was obtained from **6** by the standard methoxylation procedure mentioned above. Next an alternative route to **10** was developed which included the formylation of racemic 4-methoxy[2.2]paracyclophane **12** under the conditions found by us earlier for the *para*-regioselective acylation[10e,f] of this compound. The reaction of **12** with Cl_2CHOCH_3, carried out in the presence of 1.3 equiv $TiCl_4$ in CH_2Cl_2, has provided a high level of *para*-regioselectivity and furnished **10** exclusively in a chemical yield of 90% (Scheme 1).



Scheme 1. Two routes to racemic carbaldehyde **10** and its resolution into enantiomers. i) Cl_2CHOCH_3, $TiCl_4$, CH_2Cl_2; ii) CH_3I, K_2CO_3, acetone; iii) (*R*)-PEAM, molecular sieves 4 Å, recrystallisation; iv) 2 N HCl, MeOH.

Racemic **10** was resolved into enantiomers through the diastereomeric Schiff bases **13** with enantiomers of α-PEAM (Scheme 1, the representative example is given for (*R*)-α-PEAM as a reagent). The absolute configuration of the enantiomer obtained from (R_p,*R*)-**13** (isolated in 40% chemical yield as a pure diastereomer by two successive recrystallisations from hexane) was determined as (R_p)-**10** by comparison of its specific rotation with that of an authentic sample in turn synthesised by *para*-regioselective formylation of (R_p)-**12** (Scheme 1).

Starting from aldehydes **1**, **7** and **10** we have synthesised a number of novel racemic and enantiomerically pure imines **14**–**19** (Figure 3). Phenylimines **14**, **18** and **19** were obtained



R = Ph, *rac*- or (R_p)-**14**
R = 2-Br-C_6H_4, *rac*-**15**
R = 2,6-Me_2-C_6H_3, *rac*-**16**
R = CH_2Ph, *rac*- or (R_p)-**17**

rac- or (R_p)-**18** ($5R_p$,$4S_p$)

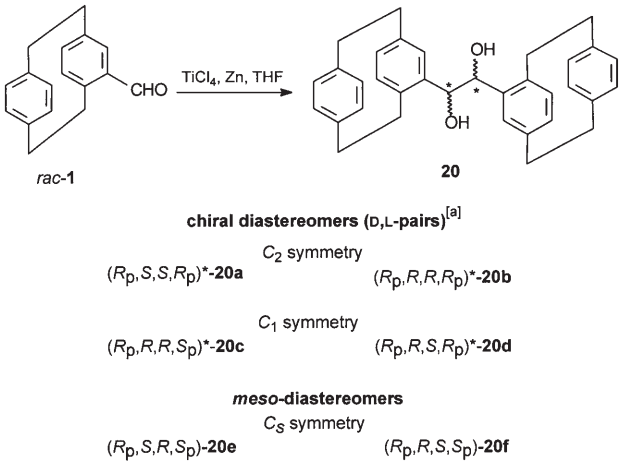
rac- or (R_p)-**19** ($7R_p$,$4R_p$)

Figure 3. Racemic and enantiomerically pure imines **14**–**19**.

from aniline hydrochloride in the presence of Et_3N, other imines **15**–**17** were synthesised from the free amines. All reactions were carried out in toluene with Et_2SnCl_2 as a catalyst[10f] allowing in all cases to reach full consumption of the starting aldehydes. Most of the compounds were found to be quite unstable on silica gel and hence were purified by recrystallisation from hexane.

For all disubstituted compounds under investigation, the absolute configurations are defined by the carbon atom to which OCH_3 group is attached (due to its priority over CHO or imino groups). In order to locate the positions of the carbonyl- or imino-substituents which are the reaction centres in the pinacol coupling reaction, we here introduce a set of enhanced stereochemical descriptors. Thus, in pseudo-*ortho*- and *para*-substituted carbonyl compounds ($12R_p$)-**8**, ($7R_p$)-**10** (Figure 2) and imine ($7R_p$)-**19** (Figure 3) the descriptors for the carbon atoms bearing CHO or CH=NHPh groups are of the same configuration (namely, $4R_p$) as the descriptor for OCH_3-substituted carbon ($12R_p$ or $7R_p$) and those of monosubstituted compounds (R_p)-**1**, (R_p)-**2** (Figure 2) and (R_p)-**14** (Figure 3). However, in the *ortho*-(($5R_p$)-**7**, ($5R_p$)-**18**) and pseudo-*gem*-derivatives (($13R_p$)-**9**) the formyl- or imino-substituted carbons could be described as $4S_p$. As will be seen below the application of these enhanced descriptors will be necessary when discussing the stereoselectivity of the coupling process. The descriptors which describe the positions for the corresponding carbonyl and imino groups will be marked there by bold letters.

Diastereoselective pinacol coupling of the [2.2]paracyclophane-derived aldehydes 1, 7–10 and ketone 2: A number of efficient techniques have been described for the pinacol coupling of aldehydes and ketones, by using, for example, SmI_2 or other rare earth metal derivatives,[5a,7a–c,8,16a] low-valent Ti particles (generated in various ways)[5b,6b,16b–g] or titanocene derivatives.[16h,i] The enantioselective version of the coupling reaction was also elaborated.[16k–m] Very recently, environmentally friendly techniques of Sm^{II}-mediated pinacol coupling in water[17a] and even by sunlight[17b] were suggested. We have applied several of these techniques employing $TiCl_4$ (an inexpensive and readily available reagent) to the racemic unsubstituted aldehyde **1** (Scheme 2, Table 1). The reaction mixtures were worked up and analysed by ^1H NMR spectroscopy to determine the ratio of the diastereomers obtained.



Scheme 2. Pinacol coupling of *rac*-**1** (top), and relative configurations of six potential diastereomers of diol **20** with four chiral elements (bottom). [a] For example, (R_p,S,S,R_p)*-**20a** stands for $(R_p,S,S,R_p) + (S_p,R,R,S_p)$.

Table 1. Pinacol coupling of racemic aldehydes **1**, **7**–**10** and ketone **2** (carbonyl compound (1 equiv), $TiCl_4$ (2 equiv), Zn (4 equiv), THF).

Run	Carbonyl compound	Diol	Ratio of isomers[a] **a/b**:**c/d**:**e/f**	Isolated yield of the diol [%][b]
1[c]	**1**	**20**	22:56:22	47
2	**1**	**20**	11:54:35	72
3	**2**	**21**	67:0:33	70
4	**7**	**22**	0:25:75	72
5	**8**	**23**	62:23:15[d]	70
6	**9**	**24**	100:0:0	75
7	**10**	**25**[e]	67:33	62

[a] Determined by ^{1}H NMR analysis of the reaction mixtures. [b] In all reactions some olefinic products of the formula PC-CH=CH-PC (PC is for the respective [2.2]paracyclophane unit) were formed (as a mixture of two diastereomers) and isolated (3–7%). [c] The reaction was carried out with $[TiCl_4(thf)_2]$, Zn (4 equiv) in THF. [d] The reduction product (5%) was detected in the reaction mixture by ^{1}H NMR analysis. [e] For the structure of the product see Scheme 3.

$TiCl_4/n Bu_4NI$[16f] proved to be unsuitable for coupling of **1**. The reaction, carried out under the described conditions (CH_2Cl_2, −78 °C to room temperature, 12 h), or for a longer (up to 20 h) periods of time, or even under reflux, produced no target product, not even in traces. The reaction of **1** with the $TiCl_4/Et_3N$[16e] for 24 h proceeded only halfway and furnished a mixture of several unidentified compounds.

Satisfactory results were obtained when the reaction was promoted by the system $TiCl_4$/Zn in THF. The active species was generated in two ways here: i) by reduction with zinc of the $[TiCl_4(thf)_2]$ solution, prepared in advance, and ii) by careful addition of $TiCl_4$ to precooled THF (0 °C), producing the yellow complex in situ, followed by Zn addition (**1**/$TiCl_4$/Zn 1:2:4, modification of the reported techniques.[6b,16g]) The second approach gave higher yields of the mixture of the diastereomeric diols (cf. 72 versus 47%, Table 1, runs 2 and 1).

While beginning the discussion of the results of the coupling reaction, we would like to make the following introductory remarks. The pinacol coupling of [2.2]paracyclophane-derived carbonyl compounds (as well as their imines) produces multichiral diols (or diamines), bearing two planar chiral moieties and two newly formed chiral centres. Therefore starting from racemic compounds a mixture of six diastereomers (four chiral enantiomeric D,L-pairs and two achiral *meso*-compounds) could in principle be obtained (Scheme 2, the representative example is given for the potential diols obtained from *rac*-**1**). From these diastereomers two chiral D,L-pairs (**20a** and **b**) and two *meso*-compounds (**20e** and **f**) possess symmetry (C_2 and C_s, respectively) and hence should give a half set of NMR signals, whether in the ^{1}H or ^{13}C NMR spectrum. The diastereomeric chiral D,L-pairs **20c** and **d**, because of their C_1 symmetry should demonstrate in the spectrum a full set of signals and multiplets (with corresponding coupling constants) for the protons of the -CH(OH) fragment, however. This allows us to carry out the initial determination of the stereoselectivity of the reaction on the basis of NMR data.

Thus careful analysis of the proton spectra of the reaction mixtures showed that in both cases three compounds of the six possible were formed. Two singlets for C*H*(OH) groups at δ 4.50 and 4.56 ppm and two broad singlets of OH groups at 2.36 and 1.96, respectively, were assigned to the symmetrical chiral diol **20** and the achiral *meso*-**20**. At the same time, four signals of equal intensity, namely two doublets (J = 3.4 Hz) at 2.00 and 2.61 ppm (two nonequivalent OH protons) pairwise with two doublets (J = 3.4 Hz) at 4.87 and 5.00 ppm, respectively, (two nonequivalent C*H*(OH) protons) were attributed to the unsymmetrical chiral diol **20** according to the data of a homonuclear double proton resonance experiment. Among the three diastereomers the unsymmetrical diol was the major product in both reactions, while two symmetrical diols were formed as minor products, slightly differing in their ratio. After purification of the reaction mixtures by preparative chromatography all three diastereomers were isolated together (for they have similar chromatographic mobility) with an almost unchanged ratio. Some olefin as a mixture of two diastereomers (chiral (R_p,R_p)* and *meso* (R_p,S_p), approximately 5–7% yield) were also isolated; they were formed as a by-products of the competing McMurry reaction.

Next we turned our attention to the enantiomerically pure aldehyde (R_p)-**1** and carried out its coupling under the optimal conditions (**1** (1 equiv), $TiCl_4$ (2 equiv), Zn (4 equiv), THF). In this reaction three (all chiral) diastereomers could arise, namely two C_2-symmetrical diols differing by the configurations at the benzylic centres ((R_p,S,S,R_p)-**20** and (R_p,R,R,R_p)-**20**) and one C_1-symmetrical diastereomer (R_p,R,S,R_p)-**20**. In fact, a single C_2-symmetrical product (R_p,S,S,R_p)-**20** was produced (Table 2, run 1). This absolute configuration was assigned to **20** by comparison with that of **23** (see below). This allowed us to identify the products of the racemic reaction as one symmetrical chiral D,L-pair (R_p,S,S,R_p)*-**20**, one unsymmetrical chiral D,L-pair

(R_p,*R*,*R*,S_p)*-**20** (with the *threo*-arrangement of the newly formed asymmetric centres and configurationally different paracyclophanyl moieties) and one *meso*-compound (R_p,*S*,*R*,S_p)-**20**.

Table 2. Pinacol coupling of the carbonyl compounds (R_p)-**1**, **2**, **7**–**10** (carbonyl compound (1 equiv), $TiCl_4$ (2 equiv), Zn (4 equiv), THF)).

Run	Carbonyl compound	Descriptor for the carbonyl group	Diol (configuration)	Isolated yield [%]	$[\alpha]_D^{22}$
1	(4R_p)-**1**	**4*R*$_p$**	(R_p,***S***,***S***,R_p)-**20**[a]	77	−88.2 (*c* 0.2, $CHCl_3$)
2	(4R_p)-**2**	**4*R*$_p$**	(R_p,***R***,***R***,R_p)-**21**	52 (92)	−14.6 (*c* 0.2, $CHCl_3$)
3	(5R_p)-**7**	**4*S*$_p$**	(R_p,***S***,***S***,R_p)-**22** (R_p,***R***,***S***,R_p)-**22**	57[e] (58:42)	+116.3 (*c* 0.2, $CHCl_3$)[e]
4	(12R_p)-**8**	**4*R*$_p$**	(R_p,***S***,***S***,R_p)-**23**[b]	70	−36.6 (*c* 0.23, $CHCl_3$)
5	(13R_p)-**9**	**4*S*$_p$**	(R_p,***R***,***R***,R_p)-**24**[c]	83	+104.0 (*c* 0.3, $CHCl_3$)
6	(7R_p)-**10**	**4*R*$_p$**	(R_p,R_p)-**25**[d]	57	−69.6 (*c* 0.2, $CHCl_3$)

[a] An olefinic product was isolated in 22% yield. [b] The reduction product (14%) was detected in the reaction mixture by ^{1}H NMR analysis. [c] Olefin (10%) was detected in the reaction mixture by ^{1}H NMR analysis. [d] For the structure of the product see Scheme 3. [e] Mixture of two diastereomers.

The pinacol coupling of the racemic (Table 1) and (R_p)-enantiomers of regioisomeric aldehydes **7**–**10** and ketone (R_p)-**2** (Table 2) under similar conditions constituted the next experiments.

The coupling of the racemic methylketone **2** produced a mixture of two symmetrical diastereomers of diol **21** (chiral and *meso* according to ^{1}H NMR data, Table 1, run 3), from which the major isomer was isolated by preparative chromatography in 30% chemical yield. For the coupling of (R_p)-**2** ^{1}H NMR spectra of the reaction mixture (obtained in 92% chemical yield) revealed the formation of the single symmetrical diol **21** without any noticeable side products (Table 2, run 2). However, the isolated yield after chromatographic purification was remarkably low (52%), although small amounts (not more than 10%) of unidentified side products were isolated. The ^{1}H NMR spectra of this chiral diol **21** and maj-**21** were identical, and hence the latter constitutes the racemic chiral diol. An X-ray diffraction study, carried out for a single crystal of the optically pure sample, allowed us to determine the absolute configuration as (R_p,*R*,*R*,R_p)-**21** (see Figure 7).

In the reactions of the *ortho*-substituted aldehydes *rac*-**7** and (R_p)-**7**, mixtures of two isomers of **22** were formed in 25:75 (Table 1, run 4) and 58:42 ratios (Table 2, run 3), respectively. In both cases the ^{1}H NMR spectra of the reaction mixtures clearly displayed the dominating sharp singlets of the OCH_3 groups at 3.26 or 3.24 ppm as well as singlets at 5.19 or 5.18 ppm, attributable to -C*H*(OH) groups, thus indicating that the symmetrical diols had been generated. The second diastereomers in both cases have unsymmetrical structures. This was established by careful analysis of the ^{1}H NMR spectra of the reaction mixtures where two doublets of protons of nonequivalent C*H*(OH) groups at 4.65 and 5.05 ppm and a broadened multiplet in the range 4.77–4.87 ppm (tentatively attributed to one of OH groups) were clearly indicated. We were unable to separate the optically active diols **22** by chromatography and recrystallisation. The TLC-pure compound, with an acceptable elemental analysis, always showed the presence of two diastereomers in variable ratios in its ^{1}H NMR spectra. Recrystallisation of the reaction mixture produced by coupling of racemic **7** furnished a single crystal of the major product, suitable for X-ray analysis. This yielded the relative configuration of this diastereomer as *meso*-(R_p,*S*,*R*,S_p)-**22** (see Figure 7).

The coupling of the racemic pseudo-*ortho* substituted aldehyde **8** was as not as selective as that of *rac*-**1**, and the mixture of three diastereomers of **23** was formed again (Table 1, run 5). However, in this case the chiral symmetrical diastereomer was the dominating product. The analysis of the CH region in the ^{1}H NMR spectrum of the reaction mixture revealed the presence of two singlets at δ 4.51 and 4.66 ppm responsible for the C*H*(OH) groups of achiral *meso*-**23** and the symmetrical chiral diol **23**, respectively, and two multiplets with equal intensity at 4.43 and 4.73 ppm (two nonequivalent C*H*(OH) protons), originating from the unsymmetrical chiral diol **23**. The reaction of (R_p)-**8** produced the single chiral diol **23** (according to ^{1}H NMR analysis) which was isolated by preparative chromatography and recrystallisation (Table 2, run 4). The appropriate single crystal was subjected to X-ray analysis and the absolute configuration of **23** was established as (R_p,*S*,*S*,R_p) (see Figure 7). It should be noted that in the case of this substrate the coupling was accompanied by reduction (5 and 14% for the racemic and optically pure substrates, respectively).

The coupling of the racemic pseudo-*gem*-aldehyde *rac*-**9** occurred at a high level of stereoselectivity and resulted in a single symmetrical diol (Table 1, run 6). Enantiomerically pure (R_p)-**9** produced the single symmetrical product **24** as well (Table 2, run 5), and the ^{1}H NMR spectra of both racemic and optically pure products were identical. Both compounds were isolated by preparative chromatography, and from the latter single crystals suitable for X-ray diffraction work were obtained (see Figure 7). The absolute configuration hence determined was (R_p,*R*,*R*,R_p)-**24**.

In all reactions of **7**–**9** (as well as **1**) small amounts of the corresponding olefins (near 3–7%) were detected and were isolated as the first fractions during the chromatographic separation of the product mixtures.

Surprisingly, the reaction of racemic **10** as well as its (R_p)-enantiomer produced the aldehydes **25** (Table 1, run 7, Table 2, run 6, Scheme 3) rather than the anticipated diols, as was unambiguously confirmed by X-ray crystallography (Figure 4), ^{1}H and ^{13}C NMR spectrum, mass and IR-spectral data. The coupling of racemic **10** produced a 63:37 mixture of two isomers (maj-**25** and min-**25**), while (R_p)-**10** gave rise

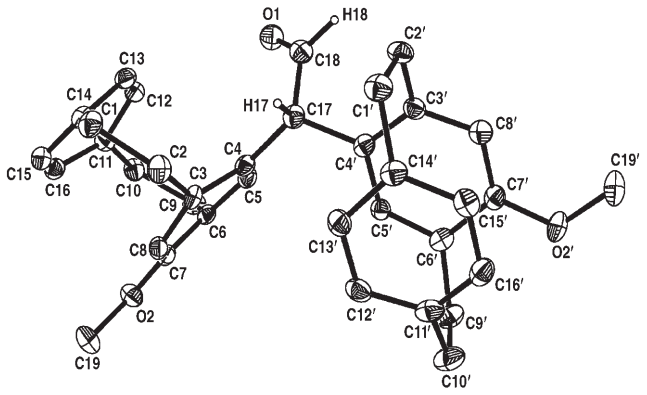


Figure 4. The structure of the aldehyde (R_p,R_p)-**25** in the crystal. Here and below the hydrogen atoms of all the aromatic rings, ethano bridges of [2.2]paracyclophanyl moieties and Me-groups are omitted for clarity. All structures are presented as ORTEP plots with ellipsoids plotted at the 30% probability level.

to (R_p,R_p)-**25**, the ^{1}H NMR spectrum of which was identical to that of the maj-**25**. We assume that in this particular case (unlike the other ones studied) a tandem pinacol coupling–Lewis acid promoted pinacol rearrangement[18] takes place. The suggested mechanism of such a sequence (similar to the one described for the coupling/rearrangement of arylketones[18a]) is summarised in Scheme 3. The expected coupling product (respective diol) would exist in the reaction mixture as the metal coordinated (Zn, Ti) cyclic intermediate, a symbolised by structure **A**. This would subsequently afford the cationic intermediate **B**, then produce the stable intermediate **C** as a result of a 1,2-migration of the 7-methoxy-[2.2]paracyclophane-4-yl-moiety and, finally, release the aldehyde **25** upon hydrolysis. The driving force of such a process could be attributed to the *para*-methoxy substituent of the starting aldehyde **6**, which should greatly facilitate the migratory aptitude of the respective [2.2]paracyclophanyl fragment.[19]

The experimental results obtained so far allow the following conclusions and generalisations:

1) Almost in all cases (except for the coupling of substrate **7**) the stereoselective formation of a single chiral symmetrical diol from an optically pure carbonyl compound was observed, correspondingly the respective D,L-pairs were produced from the racemic substrates. This supports the assumption that the planar chiral paracyclophanyl unit governs the stereoselective formation of the asymmetric centres both for the enantiomerically pure and racemic substrates.
2) With this assumption in mind two mechanisms, proposed for the pinacol coupling of carbonyl compounds mediated by low-valent Ti species, may be considered. The first mechanism (a conventional one, as referred to in the literature) assumes the generation of ketyl radicals, followed by their dimerisation in a manner, favouring the minimisation of steric interaction between aryl substituents attached to the reaction centres. The stereoselective formation of the chiral D,L-pairs is generally attributed to the additional bridging of these intermediates by the low-valent Ti species (Figure 5, left). For our case with additional planar chiral paracyclophanyl moieties such a reaction pathway determines (assuming the stereoselective formation of the anion radicals), that only symmetrical diastereomers (chiral D,L-pairs or chiral diastereomers and achiral *meso*-compounds) can be obtained. The coupling of substrates **2** and **9** (Table 1, entries 3 and 6, Table 2, entries 2 and 5) agrees with such an explanation. However, chiral unsymmetrical diastereomers found in the reaction mixtures of all other cases (for substrates **1**, **7** and **8**, Table 1, entries 1, 2, 4 and 5, Table 2, entry 3) support an alternative reaction path,[20] based on initial formation of a titanooxirane intermediate (Figure 5, right), followed by insertion of a second aldehyde into the Ti–C bond. The configuration of the second asymmetric centre formed in this case could be favoured by the more appropriate *threo*-arrangement of the bulky substituents at the two developing asymmetric centres. Accordingly, for the coupling of the racemic carbonyl derivatives of [2.2]paracyclophane (again having in mind the diastereoselective formation of the titanooxirane), all three types of diastereomers (achiral *meso*-, symmet-

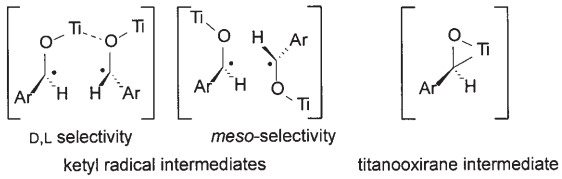
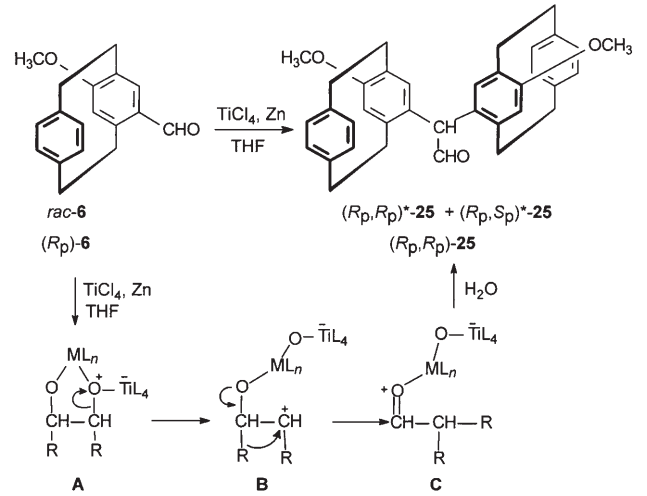


Figure 5. The possible intermediates of the pinacol coupling reaction.



Scheme 3. Synthesis of **25** from **6** by tandem pinacol coupling–pinacol rearrangement process. R = 7-methoxy[2.2]paracyclophan-4-yl-; M = Zn or Ti; L = (THF) or Cl.

rical and unsymmetrical chiral) are in principle possible, and this was in fact observed for racemic substrates **1** and **8** (Table 1, runs 1, 2, and 5). Enantiomers of these substrates stereoselectively gave rise to the single symmetrical diols **20** and **23** (Table 2, entries 1 and 4). The selectivity of the coupling of substrate **7** contarsts that of the other derivatives because the chiral diastereomer was not formed from the racemic substrate at all, and the unsymmetrical chiral diastereomer was produced even when coupling the enantiomerically pure **7** (Table 1, run 4, Table 2, run 3). Thus it appears that both reaction pathways and participating intermediates are reasonable for different substrates and a further detailed discussion of the stereoselectivity of the pinacol coupling will have to take this duality into account.

3) We now return to the assumption that the initial formation of the intermediate (either ketyl radical or titanooxirane) occurs stereoselectively and we will discuss the role of the planar chiral [2.2]paracyclophanyl moiety more thoroughly. Here the enhanced stereochemical descriptors mentioned above will be useful. To explain the observed selectivity, we assume that the carbonyl group of each aldehyde (**4*R*$_p$**)-**1**, (12R_p,**4*R*$_p$**)-**8** or (13R_p,**4*S*$_p$**)-**9** coordinated to Ti takes up a conformation *anti* to the nearest ethano bridge, thus reducing steric interactions within the particular intermediate generated. Moreover, in the case of **8** and **9** the additional fixation of such conformations is possible by coordination of Ti with methoxy groups. In such conformations the *Si* faces of the carbonyl groups in **1** and **8**, as well as the *Re* face in **9**, are not shielded by the protons of the unsubstituted [2.2]paracyclophane ring, and in this way the intermediate species (radical anion or titanooxirane, see above) may be formed with the asymmetric centre of the opposite configuration, namely, (*S*) from (**4*R*$_p$**)-**1** and (12R_p,**4*R*$_p$**)-**8** and (*R*) from (13R_p,**4*S*$_p$**)-**9** (Table 2, runs 1, 4 and 5). At the same time for the carbonyl group of the ketone (**4*R*$_p$**)-**2** and of the *ortho*-substituted aldehyde (5R_p,**4*S*$_p$**)-**7**, the *syn* orientation with respect to the ethano bridge[21] helps to avoid undesired repulsive interactions and hence induces formation of the asymmetric centre of homonymous configuration [(*R*)- from (**4*R*$_p$**)-**2** and (*S*)- from (5R_p,**4*S*$_p$**)-**7**). Then, for practically all reactions (except for **7**, see below), either coupling between two (4R_p,*S*)- or (4R_p,*R*)-paracyclophanyl fragments or insertion of the second paracyclophanyl moiety with formation of the second asymmetric centre of the same configuration (which demands *threo* arrangement of the bulky substituents) produces the corresponding (4R_p,*R*,*R*,4R_p)- or (4R_p,*S*,*S*,4R_p)-diols. The formation of the unsymmetrical diol from (5R_p,4S_p)-**7** provides evidence for the more favourable *erythro* arrangement of two configurationally equal *ortho*-substituted paracyclophanyl moieties. Concerning the racemic compounds, it should be noted that the coupling between two stereoselectively formed ketyl radicals of opposite planar chirality ((4R_p)- and (4S_p)-) could lead to the *meso* diastereomers (4R_p,*S*,*R*,4S_p)-**20**, **22** and **23**, or (4R_p,*R*,*S*,4S_p)-**21**, whereas coupling between two homonymous fragments would produce chiral diols (R_p,*S*,*S*,R_p)*-**20** and **23** or (R_p,*R*,*R*,R_p)-**21** and **24**. If the insertion mechanism is assumed to be operative, the formation of the unsymmetrical chiral diols is governed by the more appropriate mutual arrangement of the substituents at the two asymmetric centres. It results in the formation of the *threo*-diols bearing configurationally different paracyclophanyl moieties from substrates **1** and **8**, and the *erythro*-diol with configurationally equal paracyclophanyl fragments from **7**. The presence of bulky substituents in selected positions affects the stereochemistry of the processes considerably. Thus, the formation of the chiral D,L-**21** from the racemic ketone **2** (bearing a methyl group instead of hydrogen at the carbonyl group) was approximately twice as favoured as that of *meso*-**21** (Table 1, run 3). The methoxy group in pseudo-*gem*-position of the [2.2]paracyclophane moiety (aldehyde **9**) prevents all reactions except the formation of the chiral diol D,L-**24** (Table 1, run 6). The methoxy substituent in pseudo-*ortho*-position to the carbonyl group (aldehyde **8**) causes a less pronounced influence on the stereoselectivity, but the formation of the chiral D,L-**23** still predominates (Table 1, run 5). Note that in the case of the racemic *ortho*-substituted aldehyde **3** the preferred product was *meso*-**22** (together with smaller amounts of the unsymmetrical chiral D,L-**22**), whereas the chiral C_2-symmetrical diol D,L-**22** was not formed at all, probably because of steric hindrance effects (Table 1, run 4). This awkward product was, however, obtained in the coupling reaction with (*R*)-**7**, although the contribution of the unsymmetrical D,L-**22** in this case significantly increased (Table 2, run 3).

Diastereoselective pinacol coupling of [2.2]paracyclophane-derived imines:[12] For the synthesis of chiral diamines by pinacol coupling of imino derivatives a variety of reducing agents such as SmI_2[5a,7b,7c] and its combinations with other reagents,[22] Zn-based reagents[9,23] and a few others systems[24] have been described. We have carried out the coupling reactions of imines **14**–**19** in DMF with excess Zn/Cu couple and *p*TosOH at 0 °C, followed by maintaining the reaction mixture at room temperature for 24 h. After work-up the ratio of the obtained diastereomers (Table 3) was analysed by ^{1}H NMR spectroscopy. Subsequently the diamines **26**–**31** were purified by silica gel chromatography and characterised as diastereomeric mixtures or individual compounds by the usual spectroscopic and analytical data.

According to the ^{1}H NMR data coupling of the racemic imines **14**, **15**, **17** and **19** occurs with formation of mixtures of only two diastereomers in 1:1 ratio (Table 3, entries 1, 2, 4, 6), while in the case of imines **16** and **18**, which contains bulky substituents close to the reaction centre, the ratio shifts towards one diastereomer considerably (Table 3, runs 3 and 5). No traces of the reduction product (corresponding amines) were detected. The presence of only a half set of

signals in the proton spectra of diamines **26**–**31** indicates the formation of symmetrical compounds. Diamines **26**, **30** and **31** (Table 3, runs 1, 5, 6) were isolated and characterised as mixtures of diastereomers. Recrystallisation of diamines **27** (Table 3, run 2) and **28** (Table 3, run 3), having sterically demanding N-substituents, allowed the isolation of individual crystalline diastereomers, the structures of which were determined by X-ray studies[12] as *meso*-**27** and *meso*-**28** (major) of (R_p,*S*,*R*,S_p)-relative configuration. The chromatographic separation of the mixture of the *N*-benzylimine-derived diamine **29** (Table 3, run 4) resulted in only one *meso* diastereomer in 49% yield. We have failed in the isolation of the chiral racemic isomer either by recrystallisation or preparative chromatography due to its extremely low solubility and low chromatographic mobility.

Next we have carried out the coupling of imines (R_p)-**14**, ($5R_p$,$4S_p$)-**18** and ($7R_p$,$4R_p$)-**19** (Table 4, runs 1–3) and observed in each case the stereoselective formation of the single chiral products **26**, **30**, **31**. This indicates that the second diastereomers formed in the coupling of the racemic **14**, **18** and **19** unequivocally were achiral *meso* compounds. Diamines **26**, **30** and **31** were readily purified on silica gel. The relative configuration of the diastereomerically pure **30** was determined as ($4R_p$,*S*,*S*,$4R_p$) by 2D ^{1}H NMR experiments. For diamine **31** a single crystal X-ray diffraction study revealed ($4R_p$,*S*,*S*,$4R_p$)-configuration (see Figure 7).

Relying on the established relative configurations of *meso*-**27** and **28** and chiral **30** and **31**, we assume that the planar chiral [2.2]paracyclophane moiety plays a key role in the stereochemical outcome of the reaction. It is accepted that the reaction proceeds by electron transfer from the metal to the substrate which is activated by the sulfonic acid.[20,22c] Thus if the activated imine fragments of **14**–**17** and **19** react in their *anti* conformations with respect to the nearest ethano bridge (as is also supported by the X-ray structural data of the starting imine **15**, Figure 6, top), then the *Si* faces for (**4*R*$_p$**)-**14** and ($7R_p$,**4*R*$_p$**)-**19** (as well as for racemic **15** and **16**) will not be shielded by the protons of the unsubstituted [2.2]paracyclophane ring. The coupling between (R_p)- and (S_p)-paracyclophanyl fragments should lead to the *meso* diastereomer with (R_p,*S*,*R*,S_p)-configuration as was unequivocally shown for **27** and **28**. In turn, coupling between two (R_p)- or two (S_p)-paracyclophanyl fragments should give chiral D,L-pairs (R_p,*S*,*S*,R_p)* **26**–**29** and **31** from racemic substrates **14**–**17** and **19** or (R_p,*S*,*S*,R_p)-diastereomers from (R_p)-**14** and **19**. At the same time the X-ray structure of the imine **18**[12] (Figure 6, bottom) bearing an *ortho*-substituent reveals that now the more preferable conformation of the imine fragment is the one with

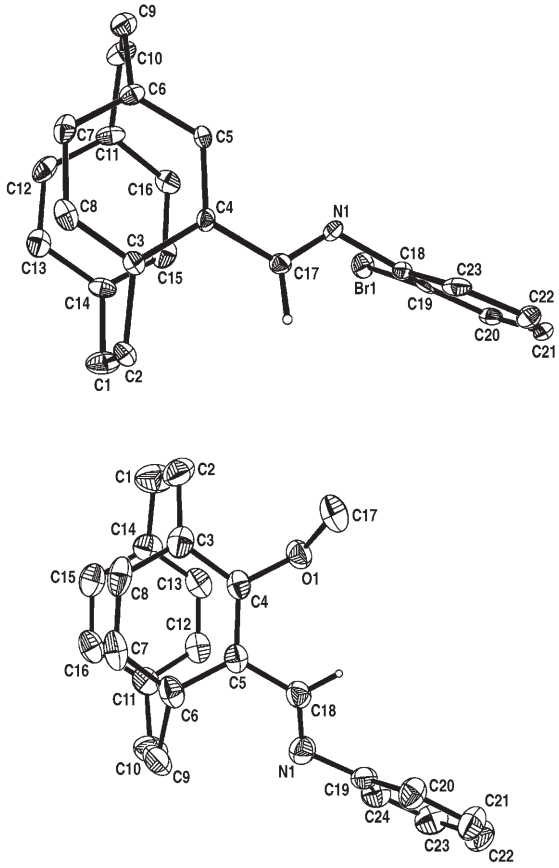
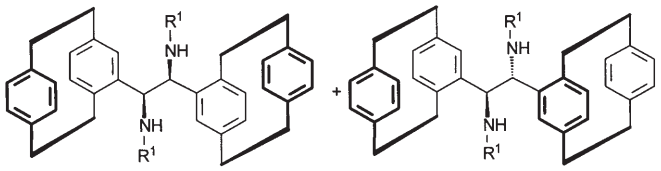


Figure 6. Structures of the imines *rac*-**15** (top) and (R_p)-**18** (bottom) in the solid state.

Table 3. Pinacol coupling of the racemic imines **14**–**19** with Zn/Cu couple and *p*TosOH.



D,L- **26 - 31** *meso* - **26 - 31**

Run	R	R^1	Imine	Diamine	Isolated yield [%]	D,L/*meso*[a]
1	H	Ph	**14**	**26**	60	50:50
2	H	2-BrC_6H_4	**15**	**27**[12]	80	51:49
3	H	2,6-Me_2-C_6H_3	**16**	**28**[12]	79	15:85
4	H	$CH_2C_6H_5$	**17**	**29**	49[b]	50:50
5	*o*-OCH_3	Ph	**18**[12]	**30**	45	25:75
6	*p*-OCH_3	Ph	**19**	**31**	64	50:50

[a] Determined by ^{1}H NMR analysis. [b] Yield of the *meso*-diamine isolated after purification on silica gel.

Table 4. Pinacol coupling of the imines (R_p)-**14**, **18** and **19** with Zn/Cu couple and *p*TosOH.

Run	Imine	Diamine	Isolated yield [%]	$[\alpha]_D^{22}$
1	(**4*R*$_p$**)-**14**	($4R_p$,***S***,***S***,$4R_p$)-**26**	64	−15.7 (*c* 0.36, C_6H_6)
2	($5R_p$,**4*S*$_p$**)-**18**	($4R_p$,***S***,***S***,$4R_p$)-**30**	52	+28.7 (*c* 0.27, C_6H_6)
3	($7R_p$,**4*R*$_p$**)-**19**	($4R_p$,***S***,***S***,$4R_p$)-**31**	46	+49.4 (*c* 0.23, C_6H_6)

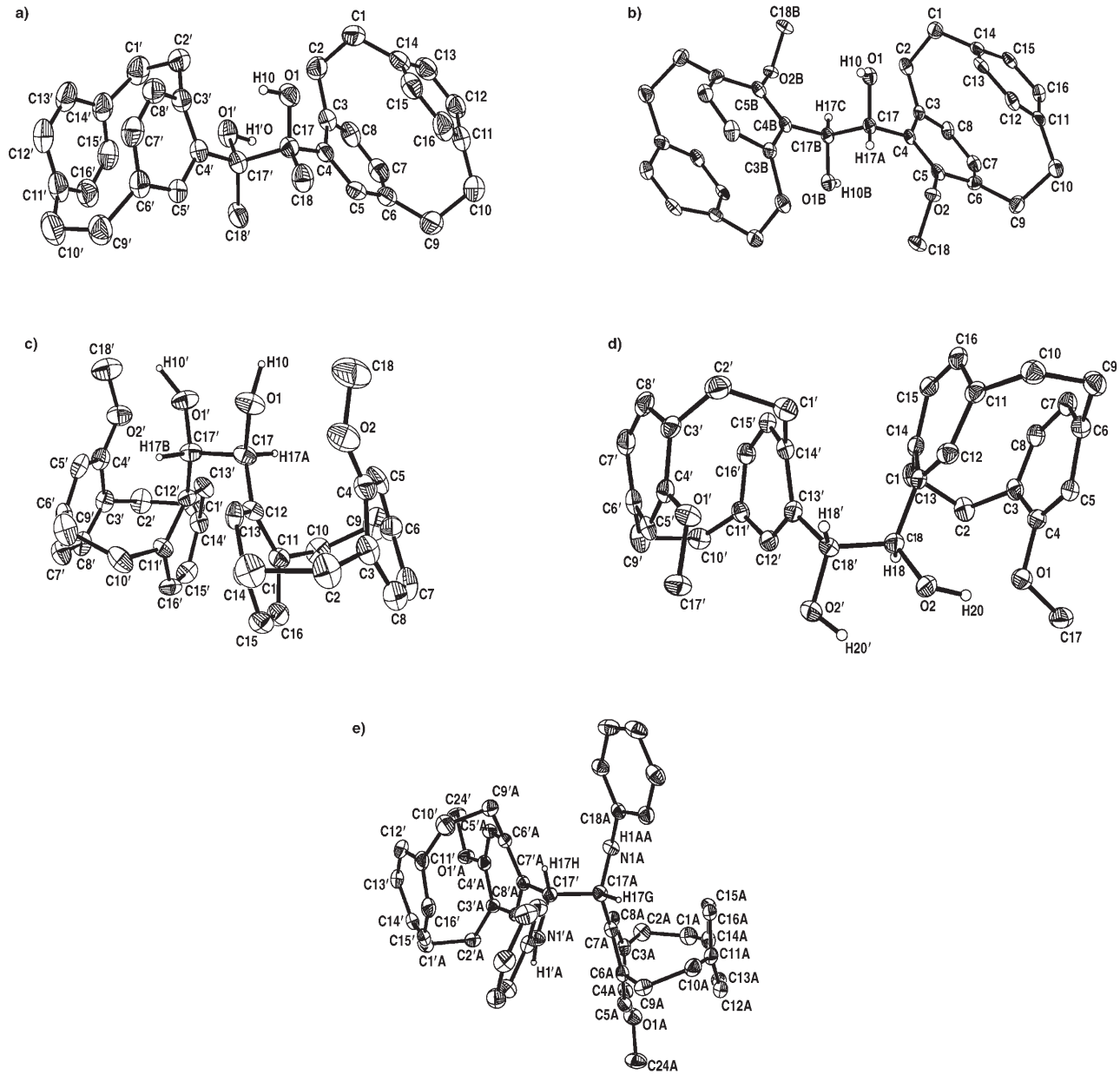


Figure 7. Structures of the diols a) (R_p,*R*,*R*,R_p)-**21**, b) (R_p,*S*,*R*,S_p)-**22**, c) (R_p,*S*,*S*,R_p)-**23**, d) (R_p,*R*,*R*,R_p)-**24**, and e) diamine (R_p,*S*,*S*,R_p)-**31** in the crystal.

the N-Ph substituent in *syn*-orientation with respect to the ethano bridge, owing to the repulsive interaction with the OCH_3 group. Thus the stereochemical result of the coupling reaction should be the opposite of that of the reaction of the imines **14**–**17** and **19**, and formation of the asymmetric centre of homonymous configuration (namely, (*R*)- from (R_p)-paracyclophanyl moiety) is expected. However, the configuration of the imine (5R_p,**4S$_p$**)-**18** (and thereby of the diamine **30**) is defined by the descriptor of the OCH_3 group. Hence the coupling of two paracyclophanyl fragments having opposite configurations should give (R_p,*S*,*R*,S_p)-**30** whereas the coupling of two paracyclophanes with the same configurations should afford (R_p,*S*,*S*,R_p)-/(S_p,*R*,*R*,S_p)-**30**.

X-ray crystallographic study and structural features of diols (R_p,*R*,*R*,R_p)-21, (R_p,*S*,*R*,S_p)-22, (R_p,*S*,*S*,R_p)-23 and (R_p,*R*,*R*,R_p)-24, and diamines *meso*-27, *meso*-28 and (R_p,*S*,*S*,R_p)-31: The general views of diols (R_p,*R*,*R*,R_p)-**21**, (R_p,*S*,*R*,S_p)-**22**, (R_p,*S*,*S*,R_p)-**23** and (R_p,*R*,*R*,R_p)-**24**, and diamine (R_p,*S*,*S*,R_p)-**31** are summarised in Figure 7. The data for diamines *meso*-**27** and *meso*-**28** are taken from ref. [12].

We have undertaken a comparative analysis of the solid-state structures of the newly synthesised diols and diamines with other similar compounds described in the literature. The structural data for compounds with the formula Ar(OH)CH–CH(OH)Ar,[25] Ar(OH)C(R)–C(R)(OH)Ar[26] and Ar(NHR^1)CH–CH(NHR^1)Ar[27] were taken from the

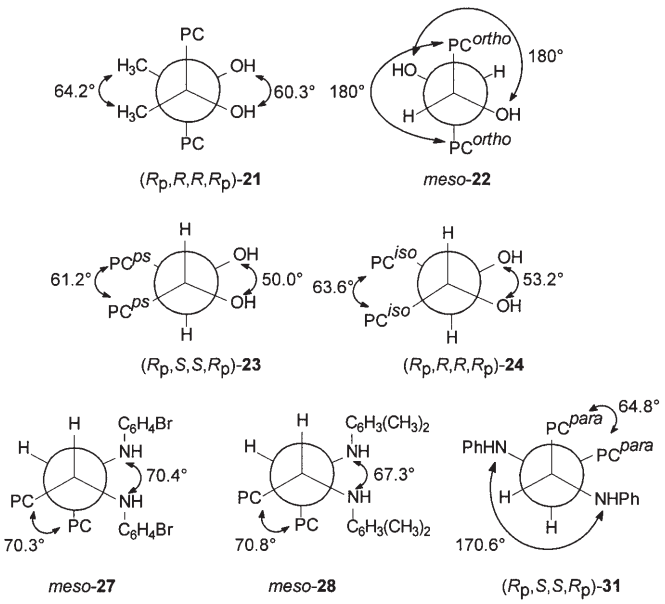


Figure 8. The conformations and characteristic torsion angles for diols and diamines in the crystal (PC: [2.2]paracyclophan-4-yl-; PC^{ortho}: 5-methoxy[2.2]paracyclophan-4-yl-; PC^{ps}: 12-methoxy[2.2]paracyclophan-4-yl-;. PC^{iso}: 13-methoxy[2.2]paracyclophan-4-yl-; PC^{para}: 7-methoxy-[2.2]paracyclophan-4-yl-).

CSD.[28] First, we have considered the conformations in the solid state of the central core of the molecules of diols **21**–**24** and diamines **27**, **28** and **31** and presented them as Newman projections with the key torsion angles (Figure 8).

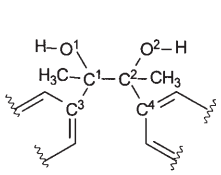
It should be noted, that all chiral compound of this type could adopt three different conformations (in order to minimise steric strain), in which one pair of the identical groups usually will be in *anti* orientation, whereas two others will pairwise be in *gauche* conformations. At the same time, for the achiral *meso* compounds two other conformations (all identical groups *anti* or all *gauche*) are preferred. From this point of view we have analysed the molecular conformations of our compounds. Thus for the centrosymmetric molecule *meso*-**22** the conformation of all substituents was *anti*. A similar conformational behaviour has been described for most *meso*-diols of the general formula Ar(OH)CH–CH(OH)Ar (Ar = 4-Br-, 4-Cl, 4-I- or 4-$CH_3C_6H_4$,[25a] 4-$OCH_3C_6H_4$ or 3,4-$(OCH_3)_2C_6H_3$[25b] or (7-*tert*-butyl-[2.2]metacyclophan-4-yl-).[25c] In only one special case[25d] (Ar = 2-$BrC_6H_4{\cdot}Cr(CO)_3$) the conformation of the corresponding *meso*-diol in the crystal was *gauche*. The solid-state structures of the chiral diols **23** and **24** are very similar to each other, with *gauche* orientations of the hydroxy groups and paracyclophanyl moieties, and *anti* orientation of the hydrogen atoms (consistent with the conformational structures of the chiral diols Ar(OH)CH–CH(OH)Ar with Ar = C_6H_5[25e] or 3,4-$(OCH_3)C_6H_3$[25f]). At the same time, the chiral diol **21** (having the formula (Ar(OH)C(R)–C(R)(OH)Ar)) revealed a *gauche* orientation of the hydroxy groups and hydrogen atoms together with an *anti* conformation of the paracyclophanyl units. Two other possible conformations were presented in the literature for diols with Ar = C_6H_5, R = CH_3,[26a] Ar = C_6H_5, R = $(CH_2)_2C(O)N(CH_2)_3$[26b] and Ar = 4-$CH_3C_6H_5$, R = $CH_2N(CH_2)_5$,[26c] (with *gauche* hydroxy and aryl groups and *anti*-alkyl substituents) and for the diol with Ar = C_6H_5, R = 2-naphthyl[26d] (where the hydroxy groups were in *anti* position). Among the *meso*-diols of such structure (Ar = C_6H_5, R = CH_3[26e] and Ar = R = C_6H_5),[26f] only *anti* conformers have been reported. Apparently, such sterically hindered diols adopt in each particular case (and depending on the substituents at the tetrahedral carbon atom) conformations that prevent unfavourable steric interactions.

The crystal structures of diamines with the formula Ar-(NHR^1)CH–CH(NHR^1)Ar are represented in the CSD database by a considerably smaller number of examples and no distinct regularities have been noticed. Thus, [2.2]paracyclophane-derived *meso*-diamines **27** and **28**[12] have all *gauche* conformations of like substituents, whereas diamines with Ar = 2-OH-C_6H_4 and R^1 = 2-ClC_6H_4[27a,b] or 4-BrC_6H_4[27a,c] prefer *anti* conformations. The crystal structure of the diamine with Ar = 4-Cl-C_6H_4 and R^1 = C_6H_5[27a,d] contains both *gauche* and *anti* conformers. Among the chiral diamines the [2.2]paracyclophane-derived **31** has *anti* conformation of the NH-R^1 substituent (R^1 = C_6H_5) as well as the diamine with Ar = C_6H_5 and R^1 = C_6F_5,[27f] whereas those with Ar = 2,6-Cl_2-C_6H_3 and R^1 = C_6H_5[27f] displays *gauche* orientation of the NH-R^1 and Ar substituents.

The key geometric parameters of the [2.2]paracyclophane-derived diols and diamines are collected in Tables 5–7. To unify the numbering of the atoms (for they have different numeration in Figure 7 due to nomenclature rules) we present a generalised view of the central fragments (see Table 5). It is clear from the data that bond lengths and dihedral angles have the values expected for the tetrahedral carbon atoms (C_{sp^3}). The only exceptions were found for the length of the central C^1–C^2 bonds in diol **21** and diamines **27**, **28** and **31**, which were clearly longer than the standard C_{sp^3}–C_{sp^3} bond (1.530 Å).[29] The greatest length of a C^1–C^2 bond was observed for diol **21** (Table 5, entry 1, 1.601 Å) with [2.2]paracyclophanyl and Me substituents at the tetrahedral carbon atoms. Similar elongations of the C^1–C^2 bond have been, for example, registered for the chiral diols (Ar(OH)C(R)–C(R)(OH)Ar) with Ar = C_6H_5, R = CH_3 (1.591 Å),[26a] Ar = C_6H_5, R = $(CH_2)_2C(O)N(CH_2)_3$ (1.594 Å),[26b] and Ar = 4-$CH_3C_6H_5$, R = $CH_2N(CH_2)_5$ (1.592 Å),[26c] and *meso*-diols with Ar = C_6H_5, R = CH_3 (1.584 Å),[26e] Ar = C_6H_5, R = 2-naphthyl-(1.619 Å),[11] and Ar = R = C_6H_5 (1.59 Å).[26f] In all these cases the lengthening of the C^1–C^2 bond is caused by the increase of the steric strain in the molecules. In [2.2]paracyclophane-derived diamines **27**, **28** and **31** the lengths of the C^1–C^2 bonds were in the range of 1.55–1.56 (Table 5, entries 5–7), similar to those of the aryl-derived diamines (1.53–1.56 Å).[27]

The values of the O^1-C^1-C^2-O^2 torsion angles for the chiral [2.2]paracyclophane-derived diols **23** and **24** (50.0 and 53.2°, Table 7, entries 3 and 4) were comparable with the angles of the parent hydrobenzoin (54.8°)[25a] and the diol with Ar = 4-$CH_3C_6H_5$, R = $CH_2N(CH_2)_5$ (53.4°),[26c] and

Table 5. Selected bond lengths [Å] for [2.2]paracyclophane-derived diols and diamines.



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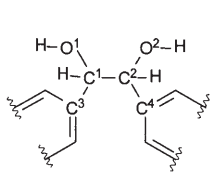

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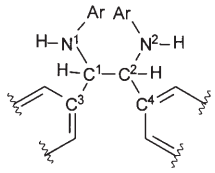


27, **28** and **31**

Entry	Bond length	C^1–C^2	C^1–C^3	C^2–C^4	O^1–C^1 or N^1–C^1	O^2–C^2 or N^2–C^2
1	(R_p,*R*,*R*,R_p)-**21**	1.601(3)	1.528(3)	1.536(3)	1.429(3)	1.433(3)
2	*meso*-**22**	1.542(7)	1.522(6)	1.522(6)	1.452(6)	1.452(6)
		1.524(8)	1.524(5)	1.524(5)	1.439(5)	1.439(5)
3	(R_p,*S*,*S*,R_p)-**23**	1.534(5)	1.508(5)	1.480(5)	1.415(4)	1.442(4)
4	(R_p,*R*,*R*,R_p)-**24**	1.538(5)	1.516(5)	1.508(5)	1.430(4)	1.448(4)
5	*meso*-**27**[12]	1.554(11)	1.533(12)	1.528(12)	1.444(10)	1.466(10)
		1.570(12)	1.537(12)	1.515(13)	1.465(11)	1.478(11)
6	*meso*-**28**[12]	1.560(3)	1.526(3)	1.523(3)	1.466(2)	1.467(2)
7	(R_p,*S*,*S*,R_p)-**31**	1.573(3)	1.534(3)	1.516(3)	1.442(2)	1.463(2)
		1.565(3)	1.505(3)	1.516(3)	1.451(2)	1.462(2)

Table 6. Selected bond angles [°] for [2.2]paracyclophane-derived diols and diamines.

Entry	Angles	O^1-C^1-C^2 or N^1-C^1-C^2	O^2-C^2-C^1 or N^2-C^2-C^1	C^3-C^1-C^2	C^4-C^2-C^1
1	(R_p,*R*,*R*,R_p)-**21**	109.9 (2)	109.3(2)	108.6(2)	110.2(2)
2	*meso*-**22**	107.6(5)	107.6(5)	111.1(4)	111.1(4)
		107.8(5)	107.8(5)	111.5(4)	111.5(4)
3	(R_p,*S*,*S*,R_p)-**23**	111.1(3)	108.7(3)	111.8(3)	113.4(3)
4	(R_p,*R*,*R*,R_p)-**24**	108.5(3)	104.6(3)	110.1(3)	113.1(3)
5	*meso*-**27**[12]	109.8(7)	112.0(7)	113.1(7)	110.7(7)
		111.1(8)	107.1(7)	109.8(7)	111.9(7)
6	*meso*-**28**[12]	105.5(2)	106.7(2)	110.1(2)	111.5(2)
7	(R_p,*S*,*S*,R_p)-**31**	112.5(2)	108.6(2)	109.8(2)	112.5(2)
		110.1(2)	109.5(2)	112.1(2)	112.0(2)

Table 7. Selected torsion angles [°] for [2.2]paracyclophane-derived diols and diamines.

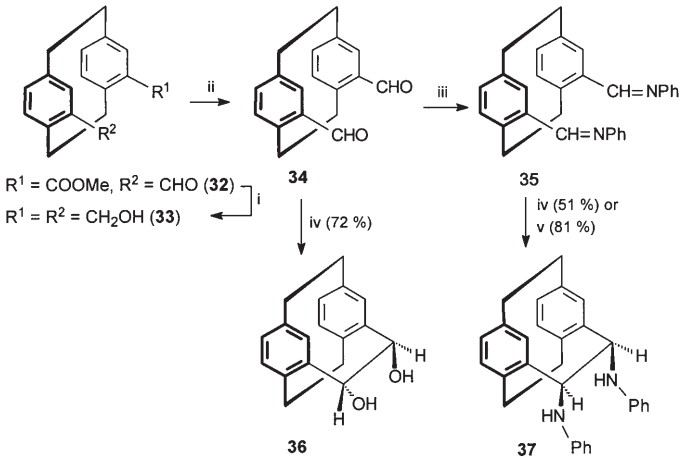
Entry	Angles	O^1-C^1-C^2-O^2 or N^1-C^1-C^2-N^2	O^2-C^2-C^1-C^3 N^2-C^2-C^1-C^3	O^1-C^2-C^1-C^4 N^1-C^2-C^1-C^4	C^3-C^1-C^2-C^4
1	(R_p,*R*,*R*,R_p)-**21**	60.4(2)	56.2(2)	56.7(2)	173.3(2)
2	*meso*-**22**	180	59.3(5)	59.3(5)	180
		180	57.8(5)	57.8(5)	180
3	(R_p,*S*,*S*,R_p)-**23**	50.0(4)	174.3(3)	174.5(3)	61.2(4)
4	(R_p,*R*,*R*,R_p)-**24**	53.2(3)	175.7(3)	173.9(2)	63.6(4)
5	*meso*-**27**[12]	71.8(9)	54.2(10)	161.5(9)	72.8(10)
		70.4(10)	55.5(1)	163.7(8)	70.3(10)
6	*meso*-**28**[12]	67.3(2)	59.1(2)	162.7(2)	70.8(2)
7	(R_p,*S*,*S*,R_p)-**31**	170.8(2)	60.9(2)	63.6(3)	64.7(3)
		165.9(2)	66.6(3)	64.4(3)	63.1(2)

notably smaller than those for other chiral diols (**21**: 60.4°, Table 7, entry 2; 3,4-$(OCH_3)_2C_6H_3$:[25b] 66.3°; Ar = C_6H_5, R = CH_3:[26a] 61.5°; Ar = C_6H_5, R = $(CH_2)_2C(O)N(CH_2)_3$:[26b] 65.2°). For diols **23** and **24** such conformations could additionally be stabilised by hydrogen bonding. Thus in the crystal of **24** both hydroxy and methoxy groups are involved in the intermolecular hydrogen bonds (parameters of the hydrogen bonds for O2–H20′···O1: O2–O1 2.81 Å, O1–H20′ 1.89 Å, O2-H20′-O1 151° and for O2′–H10′···O2: O2–O2′ 2.66 Å, O2–H10′ 2.16 Å, O2′-H10′-O2 113°). In contrast, in diol **23** only OH groups participate in intramolecular O1–H10···O1′ and O1′–H10′···O1 bonds (the parameters are: O1–O1′ 2.80 and 2.80 Å, O1–H10′ and O1–H10′ 1.81 and 2.33 Å, OHO 161 and 106° in two independent molecules) thus forming a dimeric structure, whereas the methoxy groups do not participate in the hydrogen bonding.

Intramolecular diastereoselective pinacol coupling of pseudo-*gem*-disubstituted [2.2]paracyclophanes leading to triply-bridged diols and diamines: As mentioned above several interesting examples of intramolecular coupling leading to rigid diol and diamine frameworks have been described.[7] In all these cases axial or planar chirality of the substrate has governed the stereochemistry of the reactions studied and has controlled the formation of the asymmetric centres.

We also would like to present some preliminary results on the preparation of rigid, bridged compounds by intramolecular pinacol coupling of some paracyclophane derivatives. For this purpose we have optimised the synthesis of [2.2]paracyclophane-4,13-dicarbaldehyde (**34**).[30] Following previously developed protocols[31] the procedure involves the successive reduction of the pseudo-*gem* disubstituted compound **32** with $LiAlH_4$ followed by oxidation of the resultant dicarbinol **33** with DDQ (Scheme 4). Dialdehyde **34** was converted into the corresponding bis(phenylimine) **35** as described for the synthesis of other imines; it was obtained in analytically pure form by recrystallisation. Needless to note both **34** and **35** are achiral, and only two possible diastereomers can result from the coupling, namely, a chiral D,L-pair, (*R*,*R*)*, and a *meso*-diastereomer, (*R*,*S*).

Coupling of **34** was carried out with $TiCl_4$ and Zn in THF under standard conditions. As a result of the coupling, closure of the third, vicinally hydroxy-substituted ethano bridge occurred.[32] The product was obtained in quantitative yield, ^1H and ^{13}C NMR spectra of the reaction mixture demonstrated the presence of two compounds in 77:23 ratio. Analytically pure major isomer **36** was obtained in 72% yield



Scheme 4. Preparation and stereoselective intramolecular pinacol coupling of pseudo-*gem*-disubstituted [2.2]paracyclophane derivatives **36** and **37**. i) $LiAlH_4$, THF, 95%; ii) DDQ, dioxane, 92%; iii) $PhNH_2{\cdot}HCl$, Et_3N, toluene, 79%, iv) $TiCl_4$, THF, Zn; v) Zn/Cu, *p*TosOH, DMF.

by recrystallisation of the reaction mixture from toluene. In the ^{1}H NMR spectrum of this compound two sets of signals of all characteristic protons (broad singlets of C*H* at δ 4.72 and 5.06 ppm, doublets of O*H* at 5.66 and 5.83 ppm and ABX systems of aromatic rings) were clearly visible, allowing to designate this major product as the chiral diol **36**. The structure of the second product was not established. Analytical chiral HPLC resolution of **36** showed the two peaks of the corresponding enantiomers. This diol, in principle, could be resolved into enantiomers or dissymmetry could be introduced into the starting dialdehyde by substitution of any proton in the aromatic rings or the ethano bridges.

The coupling of bisimine **35** occurs smoothly with an excess of Zn/Cu couple and *p*TosOH in DMF at 0°C for 2 h. The analysis of the reaction mixture by ^{1}H NMR spectroscopy (one set of signals of the characteristic protons) and chiral HPLC (one peak) showed that in this case the *meso*-diastereomer of the bridged diamine **37** was stereoselectively formed. The crude compound was purified by preparative chromatography on silica gel. For the pinacol coupling of aromatic oximes and azines it has been found that the application of the Zn/MsOH system affords predominantly *meso*-diamines, whereas Zn/$TiCl_4$ gave rise to D,L-diamines.[22b] This selectivity has been rationalised by differences in the nature of the active species involved. Therefore we have carried out the pinacol coupling of **35** under the reaction conditions elaborated for the coupling of aldehydes. However, in this case *meso*-**37** was formed stereoselectively again (according to ^{1}H NMR data), the isolated yield of the product was noticeably lower. Possibly with both the Zn/Cu–*p*TosOH or the Zn/$TiCl_4$ system the two imino substituents react out of conformations with the *N*Ph groups *anti* with respect to the nearest ethano bridge. Probably pinacol coupling of less hindered imino derivatives (for example, dioximes) will allow one to carry out the process with D,L-stereoselectivity.

Conclusion

The pinacol coupling of enantiomerically pure planar chiral carbonyl derivatives of [2.2]paracyclophane and their N-substituted imines occurs stereoselectively and gives rise to diastereomerically pure diols and diamines. The stereoselectivity of the coupling reaction (i.e., possible formation of one to three diastereomers) depends on the substituents of the aromatic ring for the racemic aldehydes and on the presence of a methyl substituent at the carbonyl group for the racemic ketone. In a particular case, a substituent in *para*-position to the carbonyl group induces a tandem pinacol coupling–pinacol rearrangement with formation of the corresponding acetaldehyde. Coupling of the racemic imines in each case produces a mixture of a single racemic D,L-diamine and a single *meso*-diamine. The intramolecular coupling of the pseudo-*gem*-dialdehyde stereoselectively produces a chiral racemic diol, whereas its bis-phenylimine gives rise to the *meso*-diamine exclusively. All newly synthesised chiral compounds are potential chiral ligands for a wide range of stereoselective reactions proceeding with participation of chiral diols and diamines. The application of these compounds for the construction of phosphites, phosphoroamidites, and related ligands as well as further investigation of the inter- and intramolecular coupling of appropriate [2.2]paracyclophane derivatives are currently in progress.

Experimental Section

General methods: Dichloromethane was washed successively with conc. H_2SO_4, water and saturated aq. Na_2CO_3, dried with $CaCl_2$ and successively distilled from P_2O_5 and CaH_2. THF, dioxane and toluene were distilled from sodium/benzophenone under argon before use. DMF was distilled under reduced pressure from P_2O_5 and stored over molecular sieves 3 Å. (*R*)-α-Phenylethylamine was purchased from Merck. Aldehydes *rac*- and (R_p)-**1**,[13] **3**,[10e] **4**,[15] **5**,[10i] ketones *rac*- and (R_p)-**2**[10d] and *rac*- and (R_p)-4-methoxy[2.2]paracyclophane **12**[10f] were synthesised according to described procedures. NMR: Bruker AMX-400 (400.13 for ^{1}H) and Bruker Avance 300 (75.47 MHz for ^{13}C). The ^{1}H NMR signals of the residual protons of deuterated solvents were used as internal standards. MS: KRATOS MS890 A (70 eV). Optical rotations were measured with a Perkin–Elmer-241 and EPO-1 polarimeters in a thermostated cell at 20 or 25°C. TLC analyses were performed on silica gel precoated plates Silufol UV-254 (Chemapol) and SORBFIL plates PTLC-A-UV (Sorbpolimer). Column chromatography was performed on Kieselgel 60 (Merck). Enantiomeric and diastereomeric analyses were carried out by HPLC on Chiracel-OD-H chiral column (hexane/*i*PrOH 9:1, 1 mL min^{-1}).

General procedure for the formylation of 4-hydroxy[2.2]paracyclophane (11): $TiCl_4$ (1.2 equiv, 0.05 mL, 0.087 g, 0.46 mmol) (or $SnCl_4$, $FeCl_3$ or $BF_3(OEt)_2$, 1.2 to 5 equiv) and CH_3OCHCl_2 (0.04 mL, 0.053 g, 0.46 mmol) of were added successively at 0°C to a solution of **11** (0.082 g, 0.37 mmol) in CH_2Cl_2 (3 mL) and the resulting coloured solution was stirred at room temperature for 2 to 8 h. The reaction mixture was diluted with CH_2Cl_2 (5 mL), cooled to 0°C, and water and 2N HCl were successively added to the mixture. The organic layer was washed with H_2O (2×10 mL), $NaHCO_3$ solution, and dried with Na_2SO_4. The mixture of products obtained after removal of the solvent in vacuo was separated by preparative chromatography (CH_2Cl_2).

7-Hydroxy[2.2]paracyclophane-4-carbaldehyde (6): Yield 0.056 g (60%); analytically pure sample was obtained by recrystallisation from hexane/toluene 3:2; R_f=0.2 (CH_2Cl_2); m.p. 180–181.5°C; ^{1}H NMR (400 MHz,

$CDCl_3$): $\delta = 2.64$–2.84 (m, 2H, -C*H*H-CH_2-), 2.98–3.30 (m, 4H, -C*H*H-CH_2-), 3.36–3.46 (m, 1H, -C*H*H-CH_2-), 4.00–4.12 (m, 1H, -C*H*H-CH_2-), 5.72 (s, 1H, PC aromatic 5-*H*), 5.98 (brs, 1H, OH), 6.41 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic *H*), 6.47 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic *H*), 6.54 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic *H*), 7.00 (s, 1H, aromatic 8-*H*), 7.02 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic *H*), 9.85 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 30.9$, 33.0, 33.4, 35.2 (*C*-1, 2, 9, 10), 125.1, 126.4, 128.5, 130.5, 131.8, 132.4, 132.7, 138.7, 139.6, 140.3, 146.9 (*C*-OH), 159.2 (*C*=O); MS (70 eV): *m*/*z* (%): 252 (100) [M^+], 148 (22), 104 (22); elemental analysis calcd (%) for $C_{17}H_{16}O_2$ (252.31): C 80.93, H 6.39; found: C 80.78, H 6.37.

Methoxylation of hydroxyaldehydes 3–6 was carried out by a standard procedure.[10c]

(*R*)-12-Methoxy[2.2]paracyclophane-4-carbaldehyde [(*R*)-(8)]: Yield 0.287 g (96%); analytically pure sample was obtained by recrystallisation from hexane; m.p. 176–177.5°C; $[\alpha]_D^{25} = -51.9°$ ($c = 0.27$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.58$–2.65 (m, 1H, -C*H*H-CH_2-), 2.88–2.98 (m, 2H, -C*H*H-CH_2-), 3.10–3.25 (m, 3H, -C*H*H-CH_2-), 3.43–3.50 (m, 1H, -C*H*H-CH_2-), 3.64 (s, 3H, OCH_3), 3.98–4.08 (m, 1H, -C*H*H-CH_2-), 5.62 (s, 1H, PC aromatic 5-*H*), 5.60 (d, $^4J = 1.8$ Hz, 1H, PC aromatic 5-*H*), 6.37 (dd, 1H, $^3J = 7.5$, $^4J = 1.8$ Hz, PC aromatic 7-*H*), 6.49 (d, 1H, $^3J = 7.8$ Hz, PC aromatic 8-*H*), 6.65 (d, 1H, $^3J = 7.5$, PC aromatic 16-*H*), 6.69 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic 15-*H*), 7.39 (d, $^4J = 1.8$ Hz, 1H, PC aromatic 13-*H*); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 27.7$, 29.1, 29.3, 31.2 (*C*-1, -2, -9, -10), 50.3 (OCH_3), 112.1, 119.7, 123.2, 127.05, 130.9, 131.9, 132.3, 134.7, 137.3, 138.0, 138.6, 153.4 (*C*OCH_3), 187.6 (*C*=O); MS (70 eV): *m*/*z* (%): 266 (100) [M^+], 134 (25), 104 (20); elemental analysis calcd (%) for $C_{18}H_{18}O_2$ (266.34): C 81.17, H 6.81; found 81.19, H 6.77.

Racemic 8: Yield 0.177 g (82%); m.p. 177–178°C; elemental analysis calcd (%) for $C_{18}H_{18}O_2$ (266.34): C 81.17, H 6.81; found: C 81.32, H 6.77.

(*R*)-13-Methoxy[2.2]paracyclophane-4-carbaldehyde [(*R*)-(9)]: Yield 0.42 g (90%); analytically pure sample was obtained by recrystallisation from hexane; m.p. 186–187.5°C; $[\alpha]_D^{25} = +301$ ($c = 0.2$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.66$–2.75 (m, 1H, -C*H*H-CH_2-), 2.94–3.17 (m, 5H, -C*H*H-CH_2-), 3.45–3.54 (m, 1H, -C*H*H-CH_2-), 3.48 (s, 3H, OCH_3), 3.89–3.99 (m, 1H, -C*H*H-CH_2-), 5.60 (d, $^4J = 1.8$ Hz, 1H, PC aromatic 5-*H*), 6.34 (dd, 1H, $^3J = 7.5$, $^4J = 1.8$ Hz, PC aromatic *H*), 6.48 (d, 1H, $^3J = 7.8$ Hz, PC aromatic *H*), 6.47 (d, 1H, $^3J = 7.5$ Hz, PC aromatic *H*), 6.77 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic *H*), 7.10 (d, $^4J = 1.8$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 29.8$, 30.0, 34.7, 34.9 (C-1, -2, -9, -10), 54.2 (OCH_3), 116.3, 123.8, 127.0, 130.7, 134.7, 135.8, 137.3, 139.5, 141.9, 144.2, 157.6, 189.3 (C=O); MS (70 eV): *m*/*z* (%): 266 (65) [M^+], 134 (100), 104 (96); elemental analysis calcd (%) for $C_{18}H_{18}O_2$ (266.34): C 81.17, H 6.81; found: 81.15, H 6.81.

Racemic 9: Yield 0.334 g (90%); m.p. 141–142°C; elemental analysis calcd (%) for $C_{18}H_{18}O_2$ (266.34): C 81.17, H 6.81; found: C 81.29, H 6.86.

Racemic 7-methoxy[2.2]paracyclophane-4-carbaldehyde (10) by methoxylation of 6: Yield 0.047 g (80%); analytically pure sample was obtained by recrystallisation from hexane; m.p. 141–142°C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.59$–2.69 (m, 1H, -C*H*H-CH_2-), 2.77–2.87 (m, 1H, -C*H*H-CH_2-), 3.00–3.27 (m, 4H, -C*H*H-CH_2-), 3.37–3.46 (m, 1H, -C*H*H-CH_2-), 3.80 (s, 3H, OCH_3), 4.05–4.14 (m, 1H, -C*H*H-CH_2-), 5.74 (s, 1H, PC aromatic 5-*H*), 6.38 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic *H*), 6.43 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic *H*), 6.52 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic *H*), 6.72 (dd, 1H, $^3J = 7.8$, $^4J = 1.8$ Hz, PC aromatic *H*), 7.00 (s, 1H), 9.90 (s, 1H, CHO); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 27.1$, 29.1, 29.5, 31.0 (*C*-1, -2, -9, -10), 50.0 (OCH_3), 114.9, 124.4, 126.8, 127.2, 128.7, 128.8, 134.6, 135.2, 135.7, 142.5 (*C*-OH), 157.5 (*C*-OCH_3), 185.7 (*C*=O); IR (nujol): $\tilde{\nu} = 1670$ cm^{-1} (C=O); IR (KBr): $\tilde{\nu} = 2854$ cm^{-1} (OCH_3); MS (70 eV): *m*/*z* (%): 266 (30) [M^+], 162 (44), 134 (40), 104 (100); elemental analysis calcd (%) for $C_{18}H_{18}O_2$ (266.34): C 81.17, H 6.81; found: C 81.28, H 6.75.

Racemic 7-methoxy[2.2]paracyclophane-4-carbaldehyde (10) by *para*-regioselective formylation of (12): $TiCl_4$ (0.6 mL, 1.04 g, 5.48 mmol) and CH_3OCHCl_2 (0.42 mL, 0.54 g, 4.7 mmol) were added successively at 0°C to a solution of **12** (1.1 g, 4.66 mmol) in CH_2Cl_2 (20 mL) and the resulting dark cherry coloured solution was stirred at room temperature for 4 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL), cooled to 0°C and then H_2O and 2N HCl were successively added to the mixture. The organic layer was washed with H_2O (2×30 mL), $NaHCO_3$ solution and dried with Na_2SO_4. The crude product obtained after removal of the solvent in vacuo was purified by preparative chromatography (silica gel, CH_2Cl_2) to yield **10** (1.15 g, 93%). Analytically pure sample was obtained by recrystallisation from hexane. M.p. 141–142°C; elemental analysis calcd (%) for $C_{18}H_{18}O_2$ (266.34): C 81.17, H 6.81; found C 80.99, H 6.80.

Resolution of 7-methoxy[2.2]paracyclophane-4-carbaldehyde (10): A solution of racemic **10** (1.15 g, 4.32 mmol) and (*R*)-α-PEAM (0.65 g, 0.67 mL, 5.39 mmol) in toluene (40 mL) was heated under reflux in a flask equipped with a Dean–Stark trap filled with molecular sieves 4 Å for 6 h. The solvent was removed and the resulting mixture of diastereomeric 7-{[(1-phenylethyl)imino]methyl}-[2.2]paracyclophan-4-ols (R_p,R_c)- and (S_p,R_c)-**13** was recrystallised from hexane. The resulting precipitate was recrystallised from hexane to give (R_p,R_c)-**13** (0.32 g, 20%) (*de* > 98% by ^{1}H NMR analysis); m.p. 172.5–173.5°C; $[\alpha]_D^{20} = -222°$ ($c = 0.27$ in C_6H_6); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 1.71$ (d, $J = 6.5$ Hz, 3H, CH_3), 2.42–2.61 (m, 2H, CH_2-CH_2), 2.90–3.10 (m, 4H, CH_2-C*H*H), 3.28 (s, 3H, OCH_3), 3.47–3.57 (m, 1H, CH_2-CH*H*), 4.00–4.14 (m, 1H, CH_2-CH*H*), 4.41–4.51 (q, $J = 6.5$ Hz, 1H, C*H*), 5.48 (s, 1H, 5-*H*), 6.30–6.39 (m, 2H), 6.62 (d, $^3J = 7.8$, 1H), 6.73 (d, $^3J = 7.8$, 1H), 7.10 (s, 1H, 8-*H*), 7.16–7.21 (t, $^3J = 7.5$ Hz, 1H, *p*-H, Ph), 7.31–7.39 (t, $^3J = 7.5$ Hz, 2H, *m*-H, Ph), 7.61–7.68 (d, $^3J = 7.5$ Hz, 2H, *o*-H, Ph), 8.28 (s, 1H, C*H*=N); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 26.0$ (CH_3), 31.6, 34.0, (2*C*), 35.2 (*C*-1, -2, -9, -10), 54.0 (OCH_3), 71.2 (N-*C*H), 118.7, 129.99, 127.03, 128.7, 129.1, 129.8, 131.7, 132.1, 133.1, 137.2, 138.9, 140.1, 143.4, 146.5, 158.5 (*C*-OCH_3), 159.4 (*C*=N); MS (70 eV): *m*/*z* (%): 369 (100) [M^+], 264 (100), 250 (16), 248 (20), 219 (8), 160 (72), 132 (25), 105 (26), 104 (11); elemental analysis calcd (%) for $C_{26}H_{27}NO$ (369.51): C 84.51, H 7.37, N 3.79; found: C 84.24, H 7.25, N 3.90.

Compound (R_p,R_c)-**13** was hydrolysed by heating under reflux with aq. HCl solution in methanol. The organic material was extracted by CH_2Cl_2 (2×30 mL), the combined extracts were dried with Na_2SO_4, and after removal of solvent (*R*)-**10** was isolated as colourless crystals (0.3 g, 19%). M.p. 138–139.5°C; $[\alpha]_D^{20} = -73°$ ($c = 0.32$ in C_6H_6); elemental analysis calcd (%) for $C_{18}H_{18}O_2$ (266.34): C 81.17, H 6.81; found: C 81.28, H 6.75.

The combined hexane filtrates, containing partially enriched (R_p,S_c)-**13**, after evaporation and hydrolysis gave partially resolved (*S*)-**10** (0.86 g, 75%). This compound and (*S*)-α-PEAM (0.41 g, 0.43 mL, 3.40 mmol) afforded (S_p,S_c)-**13** (0.31 g, 19.5%) after two successive recrystallisations of the diastereomeric mixture from hexane. M.p. 172–173°C; $[\alpha]_D^{20} = +223°$ ($c = 0.31$ in C_6H_6); elemental analysis calcd (%) for $C_{26}H_{27}NO$ (369.51): C 84.51, H 7.37, N 3.79; found: C 84.57, H 7.48, N 3.71.

Representative procedures for the synthesis of imines

From aldehyde and aniline hydrochloride

(*R*)-*N*-([2.2]Paracyclophane-4-ylmethylene)aniline (14): A mixture of (*R*)-**1** (0.49 g, 2.08 mmol), aniline hydrochloride (0.48 g, 4.15 mmol), Et_3N (0.45 g, 0.62 mL, 4.15 mmol) and a catalytic amount of Et_2SnCl_2 in toluene (12 mL) was heated under reflux for 12 h. The hydrochlorides were removed by filtration, the solvent was removed in vacuo and the solid was recrystallised from hexane to yield (*R*)-**14** as colourless crystals (0.46 g, 73%). Analytically pure material was obtained by further recrystallisation from the same solvent. M.p. 101–101.5°C; $[\alpha]_D = +351°$ ($c = 0.4$ in C_6H_6); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 2.60$–3.10 (m, 7H, -CH_2-CH_2-), 3.84 (m, 1H, -C*H*H-CH_2-), 6.34–6.46 (m, 7H, PC aromatic *H*), 6.64 (dd, $^3J = 7.8$, $^4J = 1.8$ Hz, 1H, PC aromatic 5-*H*), 7.13–7.18 (m, 1H, aromatic *p*-*H*), 7.22 (brs, 2H, aromatic *o*-*H*), 7.32 (d, $^3J = 8.0$ Hz, 2H, aromatic *m*-*H*), 8.38 (s, 1H, C*H*=N); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 30.0$, 30.9, 31.3 (2C), 116.9, 121.6, 125.3, 127.5, 128.2, 128.9, 129.3, 130.2, 131.0, 131.5, 132.5, 135.3, 136.1, 137.5, 149.6, 155.3; MS (70 eV): *m*/*z* (%): 311 (52) [M^+], 207 (95), 206 (100), 130 (17), 104 (49); elemental analysis calcd (%) for $C_{23}H_{21}N$ (311.43): C 88.71, H 6.80, N 4.50; found: C 88.75, H 6.84, N 4.34.

Racemic 14: Yield 0.605 g (96%); m.p. 99.0–100.5°C; elemental analysis calcd (%) for $C_{23}H_{21}N$ (311.43): C 88.71, H 6.80, N 4.50; found C 88.74, H 6.81, N 4.59.

(*R*)-*N*-{5-Methoxy([2.2]paracyclophane-4-yl)methylene}aniline (18): Yield 0.34 g (74%); m.p. 123.5–125°C (from hexane); $[\alpha]_D^{25} = +119°$ ($c = 0.37$ in C_6H_6); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 2.41$–2.51 (m, 1H, -CH*H*-CH$_2$-), 2.66–2.75 (m, 1H, -CH*H*-CH$_2$-), 2.78–2.89 (m, 1H, -CH*H*-CH$_2$-), 2.98–3.18 (m, 3H, -CH*H*-CH$_2$-), 3.19–3.30 (m, 1H, -C*H*H-CH$_2$-), 3.25 (s, 3H, OCH_3), 4.73–4.85 (m, 1H, -C*H*H-CH$_2$-), 6.33–6.42 (m, 3H, PC aromatic *H*), 6.53 (d, $^4J = 1.8$ Hz, 1H, PC aromatic *H*), 6.73 (d, $^4J = 1.8$ Hz, 1H, PC aromatic *H*), 7.00 (d, $^4J = 1.8$ Hz, 1H, PC aromatic *H*), 7.17 (m, 1H, aromatic *p*-*H*), 7.27–7.38 (m, 4H, aromatic *o*-*H* and *m*-*H*), 8.72 (s, 1H, C*H*=N); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 26.9$, 30.0, 30.3, 31.32, 57.2, 116.8, 121.5, 125.3, 125.3, 126.0, 126.9, 127.2, 127.7, 128.7, 129.5, 133.5, 135.0, 135. 8, 139.4, 150.0, 154.8, 157.0; MS (70 eV): *m*/*z* (%): 341 (11) [M^+], 237 (34), 236 (100), 233 (13), 222 (11), 208 (27), 195 (16), 145 (8), 104 (16), 91 (14); elemental analysis calcd (%) for $C_{24}H_{23}NO$ (341.45): C 84.42, H 6.79, N 4.10; found: C 84.25, H 6.65, N 4.14.

Racemic 17: Yield 0.257 g (88%); m.p. 139.5–140.5°C (from hexane); elemental analysis calcd (%) for $C_{24}H_{23}NO$ (341.45): C 84.42, H 6.79, N 4.10; found: C 84.49, H 6.94, N 4.10.

(*R*)-*N*-{7-Methoxy([2.2]paracyclophane-4-yl)methylene}aniline (19): Yield 0.102 g (77%) as orange coloured oil; $[\alpha]_D = -134°$ ($c = 0.56$ in C_6H_6); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 2.43$–2.57 (m, 1H, -C*H*H-CH$_2$-), 2.86–3.10 (m, 4H, -C*H*H-CH$_2$-), 3.25 (s, 3H, OCH_3), 3.45–3.55 (m, 1H, -C*H*H-CH$_2$-), 3.82–3.92 (m, 1H, -C*H*H-CH$_2$-), 5.45 (s, 1H, PC aromatic 5-*H*), 6.33 (dd, $^3J = 8.1$, $^4J = 1.87$ Hz, 1H, PC aromatic *H*), 6.36–6.43 (m, 2H, PC aromatic *H*), 6.69 (dd, $^3J = 7.78$, $^4J = 1.87$ Hz, 1H, PC aromatic *H*), 6.73 (dd, $^3J = 7.78$, $^4J = 1.87$ Hz, 1H, PC aromatic *H*), 7.10–7.19 (m, 1H, aromatic *p*-*H*), 7.31–7.41 (m, 4H, aromatic *o*-*H* and *m*-*H*), 8.44 (s, 1H, C*H*=N); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 27.3$, 29.6, 29.8, 31.2, 49.9, 114.4, 117.0, 121.2, 124.82, 125.2, 125.7, 127.4, 128.2, 128.9, 132.7, 134.5, 136.0, 140.4, 150.0, 154.7, 156.0; MS (70 eV): *m*/*z* (%): 341 (47) [M^+], 248 (17), 237 (88), 236 (100), 222 (28), 208 (75), 193 (29), 183 (9), 178 (14), 165 (20), 154 (14), 104 (58).

Racemic 19: Yield 0.188 g (68%); m.p. 105–105.5°C (from hexane); elemental analysis calcd (%) for $C_{24}H_{23}NO$ (341.45): C 84.42, H 6.79, N 4.10; found: C 84.32, H 6.83, N 3.95.

From aldehyde and pure amine

Racemic 2-bromo-*N*-([2.2]paracyclophane-4-ylmethylene)aniline (15): A mixture of racemic **1** (0.72 g, 3.05 mmol), 2-bromoaniline (0.65 g, 3.76 mmol) of and a catalytic amount of Et_2SnCl_2 in toluene (10 mL) was heated under reflux for 10 h. The solvent was removed in vacuo. The residue (pale yellow oil) was precipitated by pentane at −20°C to yield **15** (0.96 g, 81%). Analytically pure sample was obtained by recrystallisation from hexane. M.p. 105–107°C; ^{1}H NMR (400 MHz, C_6D_6): $\delta = 2.62$–3.09 (m, 7H, -CH$_2$-CH$_2$-), 3.87–4.00 (m, 1H, -C*H*H-CH$_2$-), 6.30–6.47 (m, 4H, PC aromatic *H*), 6.54 (d, 1H, $^3J = 7.8$ Hz, PC aromatic *H*), 6.70–6.79 (m, 2H, PC aromatic *H*), 6.87 (d, 1H, $^3J = 7.8$ Hz), 7.20–7.28 (m, 1H), 7.60 (d, $^3J = 7.8$ Hz, 1H), 8.10 (s, 1H, C*H*=N); ^{13}C NMR (75 MHz, C_6D_6): $\delta =$ 30.0, 30.9, 31.3, 114.6, 115.8, 122.3, 124.3, 127.9, 128.5, 129.0, 129.1, 129.2, 130.8, 131.5, 131.6, 132.0, 135.3, 135.5, 136.2, 137.9, 148.2, 156.8; MS (70 eV): *m*/*z* (%): 391 (30), 389 (30), 287 (98), 285 (100), 207 (95), 206 (23), 204 (21), 104 (38); elemental analysis calcd (%) for $C_{23}H_{20}BrN$ (390.32): C 70.78, H 5.16, Br 20.47, N 3.59; found: C 70.81, H 5.21, Br 20.52, N 3.57.

Racemic 2,6-dimethyl-*N*-([2.2]paracyclophane-4-ylmethylene)aniline (16): The title compound was obtained by treating **1** (0.246 g, 1.04 mmol) with 2,6-dimethylaniline (1.04 g, 0.62 mL, 5.04 mmol) for 8 h. The solvent was removed in vacuo and the solid was recrystallised from hexane to yield **16** (0.31 g, 87%). Analytically pure material was obtained by further recrystallisation from the same solvent. M.p. 127–128.5°C; ^{1}H NMR (400 MHz, C_6D_6): $\delta = 2.32$ (s, 6H, 2CH$_3$), 2.60–3.03 (m, 7H, -CH$_2$-CH$_2$-), 3.59–3.64 (m, 1H, -C*H*H-CH$_2$-), 6.34 (d, 1H, $^3J = 7.8$ Hz, PC aromatic *H*), 6.39–6.45 (m, 3H, PC aromatic *H*), 6.49 (d, 1H, $^3J = 7.8$ Hz, PC aromatic *H*), 6.75 (d, 1H, $^3J = 7.8$ Hz, PC aromatic *H*), 7.03–7.09 (m, 1H, aromatic *p*-*H*), 7.12–7.18 (m, 2H, aromatic *m*-*H*), 7.34 (brs, 1H, PC aromatic *H*), 8.10 (s, 1H, C*H*=N); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 14.7$, 29.4, 31.0, 31.4, 31.5, 119.7, 123.0, 124.3, 127.9, 128.3, 128.9, 129.2, 129.3, 131.3, 131.6, 132.2, 135.3, 135.4, 136.2, 137.1, 148.4, 157.4; MS (70 eV): *m*/*z* (%): 339 (70) [M^+], 236 (48), 235 (100), 233 (21), 218 (23), 204 (9), 130 (14), 104 (21); elemental analysis calcd (%) for $C_{25}H_{25}N$ (339.48): C 88.45, H 7.42, N 4.13; found C 88.21, H 7.35, N 4.05.

Racemic 1-phenyl-*N*-([2.2]paracyclophane-4-ylmethylene)methamine (17): The title compound was obtained from **1** (0.19 g, 0.805 mmol) and benzylamine (0.087 g, 0.09 mL, 0.815 mmol) after 5 h. The solvent was removed in vacuo and the solid was recrystallised from hexane to yield **17** (0.213 g, 99%). Analytically pure sample was obtained by recrystallisation from the same solvent. M.p. 95.5–97°C; ^{1}H NMR (400 MHz, C_6D_6): $\delta = 2.61$–2.70 (m, 1H, -CH*H*-CH$_2$-), 2.72–2.93 (m, 5H, -CH$_2$-CH$_2$-), 2.96–3.06 (m, 1H, -CH*H*-CH$_2$-), 3.82–3.92 (m, 1H, -CH*H*-CH$_2$-), 4.76 (s, 2H, N-C*H*$_2$), 6.33–6.43 (m, 5H, PC aromatic *H*), 6.59 (d, 1H, $^3J = 7.8$ Hz, PC aromatic *H*), 7.14–7.20 (m, 2H, PC aromatic and phenyl aromatic *H*), 7.27–7.34 (m, 2H, aromatic *H*), 7.48 (m, 2H, aromatic *H*), 8.22 (s, 1H, C*H*=N); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 30.0$, 31.0, 31.2, 31.3, 61.9, 122.9, 124.5, 127.3, 128.2, 128.9, 129.2, 130.0, 130.3, 131.4, 132.4, 135.3, 135.9, 136.4, 136.5, 156.6; MS (70 eV): *m*/*z* (%): 325 (71) [M^+], 234 (10), 224 (41), 221 (88), 220 (83), 218 (127), 104 (73); elemental analysis calcd (%) for $C_{24}H_{23}N$ (325.45): C 88.57, H 7.12, N 4.30; found: C 88.60, H 7.18, N 4.32.

(R_p)-17: Yield 0.238 g (97%); m.p. 100–101.5°C; $[\alpha]_D = -260°$ ($c = 0.43$ in C_6H_6); elemental analysis calcd (%) for $C_{24}H_{23}N$ (325.45): C 88.57, H 7.12, N 4.30; found: C 88.61, H 7.05, N 4.26.

General procedure for pinacol coupling of aldehydes: $TiCl_4$ (0.38 g, 0.22 mL, 2 mmol) was carefully added to THF at 0°C under argon atmosphere. To the formed yellow suspension Zn (0.26 g, 4 mmol) was added and the greenish-brown mixture was stirred for 5 min. A solution of the carbonyl compound (1 mmol) in THF (3–6 mL) was added by syringe and the reaction mixture was stirred at room temperature for 2–4 h (TLC control). The mixture was diluted with CH_2Cl_2 (10 mL) and vigorously shaken with saturated aq. $NaHCO_3$ solution until the dark blue colour of the mixture vanished. The mixture was passed through a Celite pad, the organic layer was separated and dried with Na_2SO_4. The solvent was evaporated, the ratio of the products was determined by ^{1}H NMR spectroscopy, and the mixture was separated by chromatography on silica gel.

(R_p,*S*,*S*,R_p)-1,2-Bis([2.2]paracyclophane-4-yl)ethane-1,2-diol [(R_p,*S*,*S*,R_p)-20]: Yield 0.182 g (77%); m.p. 217°C (decomp); $[\alpha]_D = -88°$ ($c = 0.23$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.38$ (s, 2H, 2 OH), 2.36–2.50 (m, 4H), 2.55–2.68 (m, 2H), 2.78–2.90 (m, 2H), 2.95–3.20 (m, 12H), 4.50 (s, 2H, 2CH), 6.26 (d, $^3J = 7.8$ Hz, 2H), 6.36–6.60 (m, 10H), 6.80 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 29.3$, 30.2, 31.3, 31.4 (2*C*-1, -2, -9, -10), 71.6 (2*C*-OH), 126.4, 127.1, 128.3, 128.5 (4*C*), 129.4, 130.8, 133.0, 134.3, 135.3, 135.5, 135.8; MS (70 eV): *m*/*z* (%): 237 (27) [$^1/_2M^+$], 220 (10), 219 (14), 134 (14), 117 (12); elemental analysis calcd (%) for $C_{34}H_{34}O_2$ (474.64): C 86.04, H 7.22; found C 85.89, H 7.21.

(R_p,*R*,*R*,R_p)-2,3-Bis([2.2]paracyclophane-4-yl)-2,3-butanediol [(R_p,*R*,*R*,R_p)-21]: Yield 0.13 g (52%); m.p. 213–214.5°C; $[\alpha]_D = -15°$ ($c =$ 0.2 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.07$ (s, 6H, 2CH$_3$), 2.16 (s, 2H, 2 OH), 2.80–3.25 (m, 14H), 3.95–4.05 (m, 2H), 6.30–6.37 (m, 4H), 6.45–6.60 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 22.0$ (2CH$_3$), 31.3, 31.5, 32.7, 36.0 (2*C*-1, -2, -9, -10), 77.9 (2*C*-OH), 127.7, 128.10, 128.13, 128.7, 128.8, 128.9, 133.5, 133.8, 135.0, 135.1, 135.3, 136.6; MS (70 eV): *m*/*z* (%): 251 (20) [$^1/_2M^+$], 147 (36), 131 (28), 119 (36), 117 (27), 115 (17), 104 (100); elemental analysis calcd (%) for $C_{36}H_{38}O_2$ (502.70): C 86.02, H 7.62; found: C 86.04, H 7.65.

***meso*-1,2-Bis(5-methoxy[2.2]paracyclophane-4-yl)ethane-1,2-diol (*meso*-22)**: The title compound (0.020 g, 13%) was isolated from the mixture of diastereomers by recrystallisation from toluene. M.p. 122–124°C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.40$ (s, 2H, OH), 2.62–2.73 (m, 2H), 2.82–3.24 (m, 6H), 3.24 (s, 6H, 2OCH$_3$), 3.65–3.75 (m, 2H), 5.18 (s, 2H, 2CH), 6.11 (d, $^3J = 7.8$ Hz, 2H), 6.18 (d, $^3J = 7.8$ Hz, 2H), 6.50–6.70 (m, 8H); MS (70 eV): *m*/*z* (%): 517 (13), 500 (19), 487 (18), 415 (24), 394 (69), 291 (18), 277 (23), 267 (82) [$^1/_2M^+$], 239 (56), 205 (12), 161 (100), 104 (41); elemental analysis calcd (%) for $C_{36}H_{38}O_4$ (534.70): C 80.87, H 7.16; found C 80.93, H 7.40.

(R_p,*S*,*S*,R_p)-1,2-Bis(12-methoxy[2.2]paracyclophane-4-yl)ethane-1,2-diol [(R_p,*S*,*S*,R_p)-23]: Yield 0.07 g (62%); m.p. 269–270°C; $[\alpha]_D = -37°$ ($c =$ 0.26 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.10$ (brs, 2H, 2 OH), 2.50–2.63 (m, 2H), 2.64–2.75 (m, 2H), 2.76–2.87 (m, 2H), 2.98–3.17 (m,

8H), 3.34–3.46 (m, 2H), 3.68 (s, 6H, 2 OCH_3), 4.60 (s, 2H, 2CH), 5.77 (s, 2H, 5-*H*), 6.23 (d, ^3J=7.8 Hz, 2H), 6.38–6.50 (m, 6H), 7.02 (s, 2H, 13-*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ=31.8, 33.52, 33.54, 34.2 (2*C*-1, -2, -9, -10), 54.8 (2OCH_3), 75.3 (2*C*-OH), 116.1, 123.7, 126.2, 127.4, 132.7, 135.1, 135.2, 138.4, 140.8, 141.5, 158.0 (2*C*OCH_3); MS (70 eV): *m*/*z* (%): 534 (3) [*M*$^+$], 517 (24), 516 (20), 487 (11), 381 (13), 367 (16), 365 (17), 353 (17), 268 (54), 251 (20), 239 (31), 235 (11), 219 (22), 205 (21), 149 (37), 135 (100), 119 (10), 105 (28), 104 (16); elemental analysis calcd (%) for $C_{36}H_{38}O_4$ (534.70): C 80.87, H 7.16; found C 80.97, H 7.37.

(R_p,*R*,*R*,R_p)-1,2-Bis(13-methoxy[2.2]paracyclophane-4-yl)ethane-1,2-diol [(R_p,*R*,*R*,R_p)-24]: Yield 0.114 g (83%); m.p. 209–211°C; $[\alpha]_D$=+104° (*c*=0.3 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.00–2.11 (m, 2H), 2.35–2.49 (m, 4H), 2.87–3.17 (m, 10H), 3.63 (s, 6H, 2 OCH_3), 3.79 (brs, 2H, 2 OH), 4.60 (s, 2H, 2CH), 5.86 (s, 2H, 2*5-H*), 6.05 (d, ^3J=7.8 Hz, 2H), 6.25 (d, ^3J=7.8 Hz, 2H), 6.34 (d, ^3J=7.8 Hz, 2H), 6.40 (d, ^3J=7.8 Hz, 2H), 6.89 (s, 2H, 2 12-*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ=25.2, 27.2, 31.1, 31.3 (2*C*-1, 2, 9, 10), 54.0 (2OCH_3), 71.5 (2*C*-OH), 116.5, 122.1, 124.7, 124.9, 128.0, 130.1, 130.6, 133.8, 133.9 (4*C*), 137.9, 153.9 (2*C*OCH_3); MS (70 eV): *m*/*z* (%): 516 (76), 487 (31), 381 (20), 367 (21), 353 (30), 339 (19), 325 (17), 267 (59), 265 (16), 250 (14), 233 (14), 219 (40), 205 (66), 189 (19), 161 (16), 149 (39), 135 (100), 131 (49), 104 (82); elemental analysis calcd (%) for $C_{36}H_{38}O_4$ (534.70): C 80.87, H 7.16; found C 80.97, H 7.34.

(R_p,R_p)-Bis-(7-methoxy[2.2]paracyclophan-4-yl)acetaldehyde [(R_p,R_p)-25]: Yield 0.084 g (57%); m.p. 202.5–203.5°C; $[\alpha]_D^{25}$ = −70° (*c*=0.23 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.15–2.24 (m, 1H), 2.43–2.61 (m, 1H), 2.72–2.94 (m, 3H), 3.00–3.28 (m, 8H), 3.35–3.52 (m, 2H), 3.60–3.75 (m, 1H), 3.68 (s, 3H, 20-O*CH*$_3$), 3.80 (s, 3H, 19-O*CH*$_3$), 4.89 (d, *J*=4.7 Hz, 1H, C*H*-OH), 5.63 (s, 1H, 5′-*H*), 5.68 (s, 1H, 8′-*H*), 5.79 (dd, ^3J=7.8, ^4J=1.8 Hz, 1H, 15′-*H*), 5.81 (s, 1H, 5-*H*), 6.25 (dd, ^3J=7.8, ^4J=1.8 Hz, 1H, 16′-*H*), 6.29 (dd, ^3J=7.8, ^4J=1.8 Hz, 1H, 15-*H*), 6.37 (s, 1H, 8-*H*), 6.42 (dd, ^3J=7.8, ^4J=1.8 Hz, 1H, 12′-*H*), 6.54 (dd, ^3J=7.8, ^4J=1.8 Hz, 1H, 16-*H*), 6.58 (dd, ^3J=7.8, ^4J=1.8 Hz, 1H, 12-*H*), 6.69 (dd, ^3J=7.8, ^4J=1.8 Hz, 1H, 13′-*H*), 6.86 (dd, ^3J=7.8, ^4J=1.8 Hz, 1H, 13-*H*), 9.78 (d, *J*=4.7 Hz, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=31.3, 31.6, 33.2 (2*C*), 33.5 (2*C*), 34.4, 35.3 (C-1, -1′, -2, -2′, -9, -9′, -10, -10′), 54.2, 54.3, 55.4 (2 O*CH*$_3$, *C*H-CHO), 119.0 (C-5′), 119.1 (C-5), 126.3, 127.2, 127.5, 128.4, 128.5, 131.0 (4*C*), 131.5, 132.9, 133.1, 134.0 (C-8), 134.4, 138.1, 138.2, 140.0 (2*C*), 140.3 (C-6′), 156.4 (C-4), 156.8 (C-4′), 199.0 (*C*HO); MS (70 eV): *m*/*z* (%): 517 (21), 516 (56), 488 (50), 487 (100), 411 (14), 384 (23), 383 (65), 369 (17), 307 (8), 279 (21), 266 (11), 265 (41), 251 (16), 221 (11), 205 (16), 191 (17), 165 (11), 161 (11), 131 (15), 119 (15), 104 (42); IR (KBr): $\tilde{\nu}$=1713 cm^{-1} (HC=O); elemental analysis calcd (%) for $C_{36}H_{36}O_3$ (516.68): C 83.69, H 7.02; found C 82.80, H 7.08.

General procedure for pinacol coupling of imines: A suspension of Zn/Cu couple (0.13 g, 2 mmol) in DMF (2.5 mL) was cooled to 0°C and solutions of *p*TosOH (0.38 g, 2 mmol) in DMF (5 mL) and imines **14**–**19** (0.5 mmol) in the same solvent (1.5–3 mL) were added simultaneously dropwise during 1.5 h. The mixture was allowed to stand at room temperature for 1 h, then saturated aq. $NaHCO_3$ solution was added, and the mixture was filtered through a thin layer of silica gel or Celite pad. The filtrate was extracted with Et_2O (3×15 mL), the organic solution was thoroughly washed with H_2O (3×40 mL) and the combined extracts were dried with Na_2SO_4. The solvent was evaporated, the ratio of the products was determined by ^{1}H NMR spectroscopy, and the mixture was separated by chromatography on silica gel.

Chiral diamines **26**, **30**, and **31** were described in a previous paper.[12]

***meso*-*N*,*N*-Bis(2-bromophenyl)-1,2-bis([2.2]paracyclophane-4-yl)ethane-1,2-diamine (*meso*-27)**: Analytically pure sample (0.022 g, 28%) was obtained by recrystallisation of the mixture of diastereomers from acetone. M.p. 192°C (decomp); ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.52–2.62 (m, 2H), 2.71–3.18 (m, 14H), 4.83 (brd, 2H, 2CH), 4.98 (brd, 2H, 2NH), 5.94–6.01 (m, 4H), 6.07 (d, ^3J=7.8 Hz, 2H), 6.25 (d, ^3J=7.8 Hz, 2H), 6.34–6.43 (m, 6H), 6.62–6.70 (m, 2H), 6.93 (d, ^3J=8.0 Hz, 2H), 7.24–7.30 (m, 2H), 7.52 (d, ^3J=8.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=33.6, 34.9, 35.3 (4*C*) (2C-1, -2, -9, -10), 58.0 (2*C*H-NH), 110.7, 111.9, 118.1, 128.7, 130.7, 132.0, 132.1, 132.2, 132.5, 132.7, 133.0, 134.8, 135.4, 136.8, 138.7, 139.1, 139.2; MS (70 eV): *m*/*z* (%): 391 (49) [$^1/_2M^+$], 311 (9), 287 (100), 207 (39), 104 (67); elemental analysis calcd (%) for $C_{46}H_{42}Br_2N_2$ (782.66): C 70.59, H 5.41, Br 20.42, N 3.58; found: C 70.49, H 5.57, Br 20.00, N 3.31.

Analysis of the filtrate from recrystallisation allowed to determine the ^{1}H NMR spectrum of chiral **27**: ^{1}H NMR (400 MHz, [D$_6$]acetone): δ=2.57–2.64 (m, 2H), 2.66–2.80 (m, 2H), 2.80–3.20 (m, 10H), 3.28–3.36 (m, 2H), 4.87 (brd, 2H, 2C*H*), 5.06 (brd, 2H, 2N*H*), 5.66 (brs, 2H, 5-*H*), 5.98 (d, ^3J=7.8 Hz, 2H), 6.09 (d, ^3J=7.8 Hz, 2H), 6.38–6.48 (m, 6H), 6.52 (d, ^3J=7.8 Hz, 2H), 6.60–6.68 (m, 2H), 7.00 (d, ^3J=8.0 Hz, 2H), 7.25–7.32 (m, 2H), 7.52 (dd, ^3J=8.0, ^4J=1.3 Hz, 2H).

***meso*-*N*,*N*-Bis(2,6-dimethylphenyl)-1,2-bis([2.2]paracyclophane-4-yl)-ethane-1,2-diamine (*meso*-28)**: Analytically pure product (0.138 g, 61%) was obtained by recrystallisation of the mixture of diastereomers from EtOH/C_6H_6/AcOEt 5:2:1; m.p. 202–204°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.39–2.52 (m, 2H), 2.45 (s, 12H, 4CH_3), 2.64–2.98 (m, 12H), 3.05–3.15 (m, 2H), 4.10 (brd, *J*=11.5 Hz, 2H, 2C*H*), 5.18 (brd, *J*=11.52 Hz, 2H, 2N*H*), 5.33 (d, ^3J=7.8 Hz, 2H), 5.60 (d, ^3J=7.8 Hz, 2H), 5.98 (brs, 2H, 5-*H*), 16 (d, 2H), 6.26 (d, 2H), 6.40–6.55 (m, 4H), 6.81–6.87 (m, 2H, Ar-*para*-*H*), 7.52 (d, ^3J=7.8 Hz, 4H, Ar-*meta*-*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ=16.1 (4CH_3), 28.1, 31.3, 31.4 (4*C*) (2*C*-1, -2, -9, -10), 57.1 (2*C*H-NH), 116.5, 122.5, 125.4, 125.8, 127.7, 128.0, 128.5, 128.8, 129.2, 131.1, 132.8, 134.0, 134.1, 134.7, 134.9, 140.9 (2*C*-NH); MS (70 eV): *m*/*z* (%): 560 (11), 440 (5), 339 (35), 340 (15) [$^1/_2M^+$], 335 (10), 220 (11), 218(30), 121 (51), 104 (53); elemental analysis calcd (%) for $C_{50}H_{52}N_2$ (680.98): C 88.19, H 7.70, N 4.11; found C 87.21, H 7.71, N 3.70.

***meso*-*N*,*N*-Dibenzyl-1,2-bis([2.2]paracyclophane-4-yl)ethane-1,2-diamine (*meso*-29)**: Yield 0.049 g (49%); m.p. 210–211.5°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.82 (brs, 2H, 2N*H*), 2.45–2.55 (m, 2H), 2.72–3.10 (m, 14H), 4.06 (brs, 2H, 2C*H*-NH), 4.06–4.16 (m, 4H, 2CH_2-NH), 6.15 (d, ^3J=7.8 Hz, 2H), 6.19 (brs, 2H, 5-*H*), 6.25 (brd, ^3J=7.8 Hz, 2H), 6.31 (brd, ^3J=7.8 Hz, 2H), 6.36 (brd, ^3J=7.8 Hz, 2H), 6.45–6.53 (m, 4H), 7.31–7.38 (m, 2H, Ar-*para*-*H*), 7.40–7.47 (m, 4H, Ar-*meta*-*H*), 7.52 (m, 4H, Ar-*ortho*-*H*), ^{13}C NMR (75 MHz, $CDCl_3$): δ=25.7 (2CH_2-NH), 29.3, 31.0, 31.3, 31.4 (2*C*-1, -2, -9, -10), 49.2 (*C*H$_2$-NH), 58.8 (2*C*H-NH), 123.1, 124.2, 124.6, 126.1, 127.2, 127.60, 128.1, 128.3, 129.0, 130.9, 132.9, 134.6, 134.7, 135.4, 135.5, 137.3; MS (70 eV): *m*/*z* (%): 326 (27) [$^1/_2M^+$], 221 (83), 220 (56), 104 (45), 91 (100); elemental analysis calcd (%) for$C_{48}H_{48}N_2$ (652.92): C 88.30, H 7.41, N 4.29; found C 88.10, H 7.61, N 4.12.

[2.2]Paracyclophane-4,13-dicarbaldehyde (34): $LiAlH_4$ (1.2 g, 50 mmol) was added under argon to a solution of **32** (3.7 g, 12.6 mmol) in anhydrous THF (300 mL). The reaction mixture was stirred at 60°C for 5 h. Unreacted $LiAlH_4$ was destroyed by addition of wet AcOEt and water, and the reaction mixture was acidified with 2N aqueous HCl solution until the precipitate had entirely dissolved. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3×100 mL). The combined organic solutions were washed with water, saturated aq. $NaHCO_3$ solution, water (15 mL), and dried with $MgSO_4$. The solvent was evaporated to yield diol **33** (3.20 g, 95%). This compound (11.9 mmol) was dissolved in anhydrous dioxane (180 mL) and a solution of DDQ (2.70 g, 11.9 mmol) in anhydrous dioxane (120 mL) was added dropwise at room temperature. The reaction mixture was stirred at room temperature for 3 h, and the precipitated $DDQH_2$ was filtered off. The solvent was removed in vacuo, the residue was dissolved in CH_2Cl_2 and separated from the remaining $DDQH_2$ by filtration. Silica gel column chromatography (CH_2Cl_2) gave dialdehyde **34** (2.90 g, 92%). Analytically pure sample was obtained by recrystallisation from cyclohexane. M.p. 209–210°C (lit.[26] m.p. 207–209°C).

***N*,*N*′-{[2.2]Paracyclophane-4,13-diyldimethylylidene}dianiline (35)** was obtained as described above from **34** and aniline hydrochloride in quantitative yield. Analytically pure product was obtained by recrystallisation from heptane: Yield 0.37 g (79%). M.p. 123°C; ^{1}H NMR (400 MHz, C_6D_6): δ=2.78–2.95 (m, 6H, -CH_2-C**H$_2$**-), 4.16–4.25 (m, 2H, -CH_2-C**H$_2$**-), 6.43 (dd, ^3J=7.8, ^4J=1.8 Hz, 2H,), 6.47 (d, ^3J=7.8 Hz, 2H, PC aromatic *H*), 7.02–7.12 (m, 10H, phenyl aromatic *H*), 7.31 (d, ^4J=1.8 Hz, 2H, PC aromatic *H*), 8.40 (s, 2H, C*H*=N); ^{13}C NMR (75 MHz, C_6D_6): δ = 32.9 (2C), 34.8 (2C), 121.2 (4C), 125.6 (2C), 129.1 (4C), 133.6 (2C), 135.1 (2C), 135.6 (2C), 136.8 (2C), 139.7 (2C), 141.3 (2C), 152.5 (2C), 159.2

(2C); MS (70 eV): *m/z* (%): 414 (21) [M^+], 337 (30), 322 (18), 209 (8), 207 (100) [$^1/_2M^+$], 77 (8); elemental analysis calcd (%) for $C_{30}H_{26}N_2$ (414.55): C 86.92, H 6.32, N 6.76; found C 86.95, H 6.21, N 6.58.

1,2-Dihydroxy[2.2.2][1,2,4]cyclophane (36): $TiCl_4$ (12.08 mmol, 1.33 mL, 2.30 g) was carefully added to THF (15 mL) at 0°C under argon. Then Zn (30.02 mmol, 1.96 g) was added to the yellow suspension, and the greenish-brown mixture was stirred for 5 min. A solution of dialdehyde **34** (0.82 g, 3.11 mmol) in THF (30 mL) was added dropwise and the reaction mixture was stirred at room temperature for 3 h (TLC control). The mixture was diluted with Et_2O (40 mL), the organic layer was washed with saturated aq. $NaHCO_3$, H_2O and dried with Na_2SO_4. The solvent was evaporated to yield crude **36** (0.82 g, 98%). Analytically pure material was obtained by purification of the reaction mixture on silica gel ($CHCl_3$) and recrystallisation from toluene. Yield 0.60 g (72%); m.p. 232–234°C (lit.[27] m.p. 234°C); ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.57–2.63 (m, 1H, CH_2), 2.70–2.83 (m, 1H, CH_2), 2.88–3.17 (m, 5H, CH_2), 3.66–3.76 (m, 1H, CH_2), 4.72 (brs, 1H, C*H*), 5.06 (brs, 1H, C*H*), 5.66 (d, $J_{CH\text{-}OH}$ = 3.9 Hz, 1H, OH), 5.83 (d, $J_{CH\text{-}OH}$ = 2.9 Hz, 1H, OH), 6.13 (d, ^4J = 1.8 Hz, 1H, 5- or 12-*H*), 6.18 (d, ^3J = 7.8 Hz, 1H, 8- or 15-*H*), 6.19 (d, ^3J = 7.8 Hz, 1H, 8- or 15-*H*), 6.41 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1H, 7- or 16-*H*), 6.46 (dd, ^3J = 7.8, ^4J = 1.8 Hz, 1H, 7- or 16-*H*), 6.56 (d, ^4J = 1.8 Hz, 1H, 5- or 12-*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.5, 33.8, 36.1, 36.2 (*C*-1, -2, -9, -10), 80.3 and 89.5 (2*C*-OH), 129.2, 131.2, 133.6, 133.9, 134.6, 136.6, 137.5, 139.5, 140.1, 140.6, 145.1, 146.1; MS (70 eV): *m/z* (%): 266 (52) [M^+], 249 (24), 219 (12), 205 (16), 190 (8), 133 (100) [$^1/_2M^+$], 119 (80), 105 (87); IR (KBr): $\tilde{\nu}$ = 2947 and 2926 cm^{-1} (OH); elemental analysis calcd (%) for $C_{18}H_{18}O_2$ (266.34): C 81.17, H 6.81; found: C 81.04, H 6.87; analytical HPLC resolution: t_R = 17:56.0 and 21:56.4 min, respectively.

1,2-Bis(*N*-phenylamino)[2.2.2][1,2,4]cyclophane (37): A suspension of Zn/Cu couple (0.047 g, 0.73 mmol) in DMF (1 mL) was cooled to 0°C and solutions of *p*TosOH (0.14 g, 0.73 mmol) in DMF (1.5 mL) and bisimine **35** (0.1 g, 0.24 mmol) in the same solvent (1.5 mL) were added simultaneously dropwise during 0.5 h. The mixture was allowed to stand at room temperature for 2 h. The reaction mixture was diluted with H_2O, extracted twice with CH_2Cl_2, the combined organic layers were washed with H_2O and dried with Na_2SO_4. The solvent was evaporated and excess DMF was removed under reduced pressure to yield crude **37** in quantitative yield. The ^{1}H NMR spectrum of this product showed the formation of a single *meso*-isomer. An analytically pure sample (0.08 g, 80%) was obtained after chromatography on silica gel (toluene). M.p. 192°C (decomp); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.80–2.90 (m, 2H, 1-H^b, 2-H^b), 2.95–3.03 (m, 2H, 9-H^b, 10-H^b), 3.09–3.16 (m, 2H, 9-H^a, 10-H^a), 3.33–3.41 (m, 2H, 1-H^a, 1-H^a), 5.00 (brs, 2H, 2NH), 5.20 (brs, 2H, 17-H,

Table 8. Summary of crystal data, data collection and refinement parameters for the structures of the compounds reported in this paper.

	(R_p,*R*,*R*,R_p)-**21**	(R_p,*S*,*R*,S_p)-**22**	(R_p,*S*,*S*,R_p)-**23**	(R_p,*R*,*R*,R_p)-**24**	(R_p,R_p)-**25**	(R_p,*S*,*S*,R_p)-**31**	**15**
formula	$C_{36}H_{38}O_2$	$C_{43}H_{46}O_4$	$C_{36}H_{39}O_4 \cdot 0.5H_2O$	$C_{36}H_{38}O_4$	$C_{35}H_{35}O_3 \cdot CHCl_3$	$C_{48}H_{48}N_2O_2 \cdot 0.125(C_6H_{14})$	$C_{23}H_{20}BrN$
M_r	502.66	626.80	543.67	534.66	636.02	695.66	390.31
crystal habit	colourless prism	colourless needle	colourless plate	colourless plate	colourless plate	colourless prism	colourless plate
crystal size [mm]	0.1×0.3×0.5	0.3×0.2×0.05	0.4×0.5×0.6	0.4×0.3×0.2	0.3×0.4×0.5	0.3×0.5×0.5	0.4×0.3×0.2
crystal system	monoclinic	triclinic	orthorhombic	orthorhombic	monoclinic	monoclinic	orthorhombic
space group	$P2_1$	$P\bar{1}$	$P2_12_12$	$P2_12_12_1$	$P2_1$	$C2/c$	$P2_12_12_1$
cell constants							
a [Å]	8.0035(12)	9.893(5)	17.535(7)	9.397(11)	12.5390(7)	20.126(3)	7.697(2)
b [Å]	11.4165(16)	13.598(6)	17.728(7)	15.68(2)	8.5160(5)	19.473(4)	13.155(4)
c [Å]	15.367(2)	13.786(5)	9.152(4)	19.18(2)	28.6420(17)	38.962(7)	17.508(4)
α [°]	90	72.89(3)	90	90	90	90	90
β [°]	102.455(4)	88.45(4)	90	90	91.690(1)	94.457(5)	90
γ [°]	90	72.81(4)	90	90	90	90	90
V [Å^3]	1371.0(3)	1689.6(13)	2845(2)	2825(6)	3057.1(3)	15224(5)	1772.7(7)
Z	2	2	4	4	4	16	4
ρ_{calcd} [mg m^{-3}]	1.218	1.232	1.269	1.257	1.382	1.214	1.462
T [K]	293	163	120	110	120	110	163
$2\theta_{max}$ [°]	56.1	46.5	58.0	56.2	52.0	56.0	52.0
μ(Mo$_{K\alpha}$) [mm^{-1}]	0.073	0.077	0.082	0.080	0.338	0.073	2.323
absorption correction	semiempirical from equivalents	none		semiempirical from equivalents			none
T_{min}/T_{max}	0.499/0.969	–	0.123/0.928	0.478/0.968	0.607/0.862	0.797/0.928	–
no. indep. reflns	6850	3754	24251	16629	21549	54480	3709
R_{int}	0.0191	0.0477	0.1087	0.586	0.0541	0.0803	0.0388
no. reflns refined	5659	3429	7470	6823	10505	18115	3244
no. obsd reflns ($I > 2\sigma(I)$)	3241	2016	2593	3330	6827	6268	2389
abs. structure parameter	−0.2(2)	–	−6.0(2)	−0.8(2)	0.4(8)	–	0.02(2)
no. parameters	343	432	371	479	829	964	226
R_1 (on F for obsd reflns)[a]	0.0545	0.0606	0.0735	0.0601	0.0656	0.598	0.0565
wR^2 (on F^2 for all reflns)[b]	0.1331	0.1536	0.1266	0.1228	0.1267	0.0757	0.1228
weighting scheme			$w^{-1} = 1/[\sigma^2(F_o^2) + (aP)^2 + bP,\ P = {}^1/_3(F_o^2 + 2F_c^2)$				
a	0.0611	0.0853	0.0155	0.0400	0.0132	0.0016	0.0481
b	–	0.3174	–	0.2800	3.5110	0.0500	2.9500
F(000)	540	672	1164	1144	1336	5956	
GOOF	1.020	1.013	0.981	0.984	1.013	0.977	0.972
largest diff. peak/hole [e Å^{-3}]	0.169/ −0.133	0.257/ −0.268	0.339/ −0.346	0.328/ −0.186	0.573/ −0.479	0.923/ −0.249	1.450/ −0.621

[a] $R_1 = \Sigma||F_o| - \Sigma F_c||/|(F_o)$ for observed reflections. [b] $wR_2 = \{[w(F_o^2 - F_c^2)^2/[w(F_o^2)^2]\}^{0.5}$ for all reflections.

18-H), 6.36 (d, $^3J=7.8$ Hz, 2H, 8-H, 15-H), 6.47 (dd, $^3J=7.8$, $^4J=1.8$ Hz, 2H, 7-H, 16-H), 6.64 (d, $^4J=1.8$ Hz, 2H, 5-H, 12-H), 6.69 (br d, 4H, 4-*o*-H-Phenyl), 6.73–6.78 (m, 2H, 2-*p*-H-Phenyl), 7.12–7.20 (m, 4H, 4-*m*-H-Phenyl); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=33.1$ (2*C*), 36.6 (2*C*) (*C*-1, -2, -9, -10), 60.2 (2*C*H-NH), 114.3 (4*C*), 118.4 (2*C*), 129.2 (4*C*), 130.2 (2C), 133.4 (2C), 134.2 (2C), 138.0 (2C), 141.3 (2C), 142.9 (2C), 147.9 (2C); MS (70 eV): *m*/*z* (%): 416 (27) [M^+], 415 (45), 339 (66), 324 (100), 297 (15), 206 (73), 191 (28), 104 (20), 77 (15); elemental analysis calcd (%) for $C_{30}H_{28}N_2$ (416.57): C 86.50, H 6.77, N 6.72; found: C 86.48, H 6.71, N 6.64; analytical HPLC resolution: $t_R=10$:41.6 min.

X-ray crystallographic study of imine 15, diols 21–24, aldehyde 25 and diamine 31: Single-crystal X-ray diffraction experiments for **21**–**25** and **31** were carried out with a Bruker SMART 1000 CCD area detector, using graphite monochromated $Mo_{K\alpha}$ radiation ($\lambda=0.71073$ Å, ω scans with a 0.3° step in ω and 10 s per frame exposure, $2\theta<60°$) at 110–120 K with the exception of **21** (at 293 K). The low temperature of the crystals was maintained with a Cryostream (Oxford Cryosystems) open-flow N_2 gas cryostat. Reflection intensities were integrated using SAINT software[33] and semiempirical method SADABS.[34] Single-crystal X-ray diffraction experiments for **22** and **15** were carried out with a rebuilt Syntex $P2_1$ four-circle diffractometer, using graphite monochromated $Mo_{K\alpha}$ radiation (q/2q scans) at 163 K, the reflection intensities were integrated using Siemens P3/PC software.[35]

The structures were solved by direct methods and refined by the full-matrix least-squares against F^2 in anisotropic (for non-hydrogen atoms) approximation. The hydrogen atoms of the OH and NH groups were located from the difference Fourier syntheses and refined in isotropic approximation in rigid model, the positions of the hydrogen atoms of CH_2 and CH_3 groups and the phenyl rings were calculated and included in the refinement using the riding model approximation with the $U_{iso}(H)=1.2\,U_{eq}(C)$ for the methyne and $U_{iso}(H)=1.5\,U_{eq}(C)$ for methylene and methyl groups, where the $U_{eq}(C)$ is the equivalent isotropic temperature factor of the carbon atom bonded to the corresponding H atom.

All calculations were performed on an IBM PC/AT using the SHELXTL software.[36]

The crystallographic data for compounds **15**, **21**–**25** and **31** are represented in the Table 8. Some geometrical parameters are represented in the Tables 5–7.

CCDC-266839 (**15**), -266840 (**21**), -266841 (**22**), -266842 (**23**), -266843 (**24**), -266844 (**25**) and -266845 (**31**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif/

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