Highly Stereoselective Synthesis of Novel Multistereogenic Bis-Bifunctional Ligands Based on [2.2]Paracyclophane-4,7-quinone, their Structure Elucidation and Application in Asymmetric Catalysis

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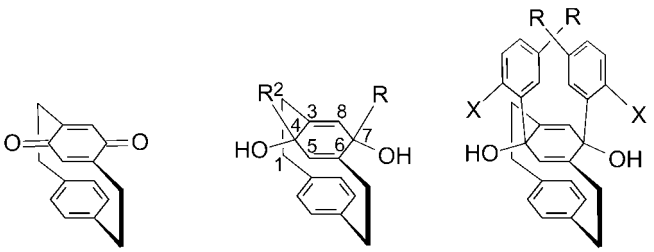
Abstract: Bis-bifunctional *cis*-4,7-diarylsubstituted-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophanes **3–6** were synthesized by a highly diastereoselective reaction of *ortho*-substituted aryllithium reagents with [2.2]paracyclophane-4,7-quinone (**1**). Enantiomerically pure diols **3–5** were tested as chiral inductors in the enantioselective addition of diethylzinc to benzaldehyde (up to 93.5% ee). Acid dehydration of *cis*-4,7-di(2-methoxyphenyl)-4,7-dihydroxy-4,7-dihydro[2.2]-paracyclophane (**3**) results in 4,7-dihydro-7,8-di(2-methoxyphenyl)[2.2]paracyclophane-4-one (**8**) – a planar chiral cyclohexadienone of the [2.2]paracyclophane series with a *para*-semiquinoid substructure. X-Ray investigations of compounds **3**, **4** and **8** were performed.

Keywords: cyclohexadienol; cyclophanes; nucleophilic addition; quinones; stereoselectivity

Introduction

A number of planar chiral [2.2]paracyclophane derivatives have been successfully applied as chiral auxiliaries and ligands for asymmetric synthesis during last decade.[1a–d] All of them have been represented by derivatives with different substitution patterns of the aromatic rings or bridges only. Meanwhile, [2.2]paracyclophane-4,7-quinone (**1**),[2] two carbonyl groups of which are built into the [2.2]paracyclophane skeleton (Figure 1) is, in our opinion, very attractive as a chiral auxiliary itself (for example, in asymmetric redox reactions), as well as a precursor for the construction of new types of ligands. In our previous papers we have described chemical transformations of quinone **1** and its derivatives.[3,4] In particular, we have shown that the nucleophilic addition of alkyl- and aryllithium reagents to *rac*-quinone **1** occurs regio- and stereospecifically (from the outer site of both carbonyl groups), resulting in the corresponding multistereogenic diols (*Rp**,4*Rc**,7*Rc**)-**2a–c** (Figure 1).[4] However, two hydroxy groups of diols **2a–c** have the *endo*-orientation and are, for this reason, not capable of chelation with metals. Therefore, we have envisaged constructing a novel series of ligands of type ***A*** (Figure 1) containing *ortho*-functionalized aryl moieties as R. In such ligands hydroxy groups bound to the [2.2]paracyclophane scaffold pairwise with functional



1 (R_p*,4R_c*,7R_c*) ***A***

2a R = Me
2b R = Bu
2c R = Ph

Figure 1. [2.2]Paracyclophane-4,7-quinone (**1**) and diols based on it.

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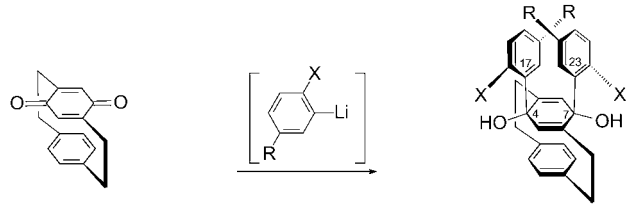
groups of the aryl fragments will form two independent systems, both of which are capable of coordination with metals and so could work as chiral promoters.

We present here the preparation and application in asymmetric synthesis of a series of multistereogenic bis-bifunctional ligands derived from enantiomerically pure [2.2]paracyclophane-4,7-quinone[3] (**1**).

Results and Discussion

First, we concentrated our studies on the regularities of the nucleophilic addition reactions of several *ortho*-functionalized aryllithium reagents,[5a, b] namely (2-methoxyphenyl)lithium, [2-(dimethylamino)phenyl]-lithium, {2-[(isopropylamino)sulfonyl]-5-methylphenyl}lithium and (2-{[(diethylamino)carbonyl]oxy}phenyl)lithium to racemic quinone **1**. All reactions were carried out by adding **1** (dissolved in toluene) to an excess of the appropriate organolithium reagent. It was found that all reactions proceeded selectively (by NMR analysis of reaction mixtures) leading to the corresponding 4,7-diarylsubstituted-4,7-dihydro-4,7-dihydroxy[2.2]-paracyclophanes (**3**–**6**) as the sole product with high yields (Scheme 1).

The compounds **3**–**6** were isolated by preparative chromatography on silica gel as white crystals. The analysis and comparison of ^{1}H NMR data of **3**–**6** with those obtained for diols **2a**–**c**[4] allowed us to identify the newly synthesized compounds as *cis*-diols with *endo*-orientation of the hydroxyl groups. Besides, the structure and the multiplet patterns of signals in the ^{1}H and ^{13}C NMR spectra of diols **3**–**6** (similar to diols **2a**–**c**) indicate the formation of compounds of C_2-symmetry in all cases. However, in contrast with the diols **2a**–**c**, the compounds **3**–**6** contain bulky unsymmetrical aryl moieties. Therefore, the C_2-symmetry for structures **3**–**6** is possible either in the case of the restricted rotation about the corresponding C4–C17 and C7–C23 (C_{PC}–C_{Ar}) bonds together with mutual *anti*-orientation of the substituted aryl fragments, or if such a rotation is fast on the NMR time scale. The NMR experiment on dynamic behaviour of diols **3**–**6** performed in the temperature interval -100 to $+100\,^{\circ}$C showed the absence



rac-, (R_p)- or (S_p)-**1**

X = MeO, R = H — **3** (75 %)
X = Me_2N, R = H — **4** (63 %)
X = SO_2NH^iPr, R = Me — **5** (79 %)
X = $OC(O)NEt_2$, R = H — **6** (70 %)

Scheme 1.

of dynamic effects attributable to rotation of aryl moieties. This allowed us to suggest that the aryl substituents do not rotate around C_{PC}–C_{Ar} bonds and, hence, three different atropoisomers (or stereoisomers) could be formed for every diol depending on the mutual orientation of its aryl and [2.2]paracyclophanyl fragments (Figure 2). Thus, one *syn*-isomer of C_1-symmetry, and two *anti*-isomers of C_2-symmetry may, in principle, be formed while the first, *anti*^{1}-, isomer would have its X substituents directed to [2.2]paracyclophane bridges whereas in the second, *anti*^{2}-, isomer the substituents are directed to the C-5, C-8 atoms of the [2.2]paracyclophane ring.

Analysis of the ^{1}H NOESY spectrum allowed us to establish that the compound **4** is the *anti*^{2}-isomer (see Supporting Information). This structure was confirmed by X-ray analysis data (Figure 3, left structure). Unfortunately, we have found no evidences in the ^{1}H NOESY spectra of compounds **3**, **5** and **6** confirming the positioning of the aryl fragments in these compounds unambiguously. The *anti*^{2}-structure of compound **3** was proved, however, by single-crystal X-ray diffraction analysis (Figure 3, right structure).

The analysis of the geometry of **3** and **4** (according to X-ray data, see below) revealed that the rotation of the aryl fragments around C_{PC}–C_{Ar} bonds is impossible (see Supporting Information). These results are consistent with the dynamic NMR data.

Since the formation of diols **3** and **4** bearing OMe and NMe_2 groups leads stereospecifically to the formation of *anti*^{2}-isomer, we assume that diols **5** and **6** with bulky $OC(O)NEt_2$ and $S(O)_2NHCHMe_2$ groups should also have the *anti*^{2}-configuration. The values of enthalpy of formation (ΔH_f) calculated for *syn*-, *anti*^{1}- and *anti*^{2}-isomers of compounds of **3**–**6** have demonstrated that the formation of *anti*^{2}-isomers is most preferential in all cases (see Supporting Information), that is in agreement with our assumption on the *anti*^{2}-configuration of diols **5** and **6**.

Thus, we have found that all reactions occur regio- and stereospecifically (de > 99%), leading to *cis*-diols **3**–**6** with *endo*-orientation of the hydroxy-groups and *anti*^{2}-orientation of the aryl moieties. The prepared compounds **3**–**6** are unique due to a combination of different chiral elements in their molecules. These multistereogenic diols, besides a planar chiral paracyclophanyl fragment and two asymmetric centres at C(4) and C(7), possess two asymmetric axes of chirality (Figure 2, top). We suggested that one of them intersects the atoms C(4)-C(17) and the other axis, symmetrical to the former, in turn intersects the atoms C(7)-C(23) (the atoms are numbered in Scheme 1). In accordance with this, the stereochemical descriptors for potential *syn*- and *anti*^{1}-isomers of **3**–**6** should be (*Rp**,4*Rc**,7*Rc**,7,17*Ra**,4,23*Sa**)- and (*Rp**,4*Rc**7*Rc**,4,23*Sa**,7,17*Sa**)-, respectively, while the actually formed *anti*^{2}-isomers should be described as (*Rp**,4*Rc**7*Rc**,4,23*Ra**,7,17*Ra**)- (Figure 2, bot-

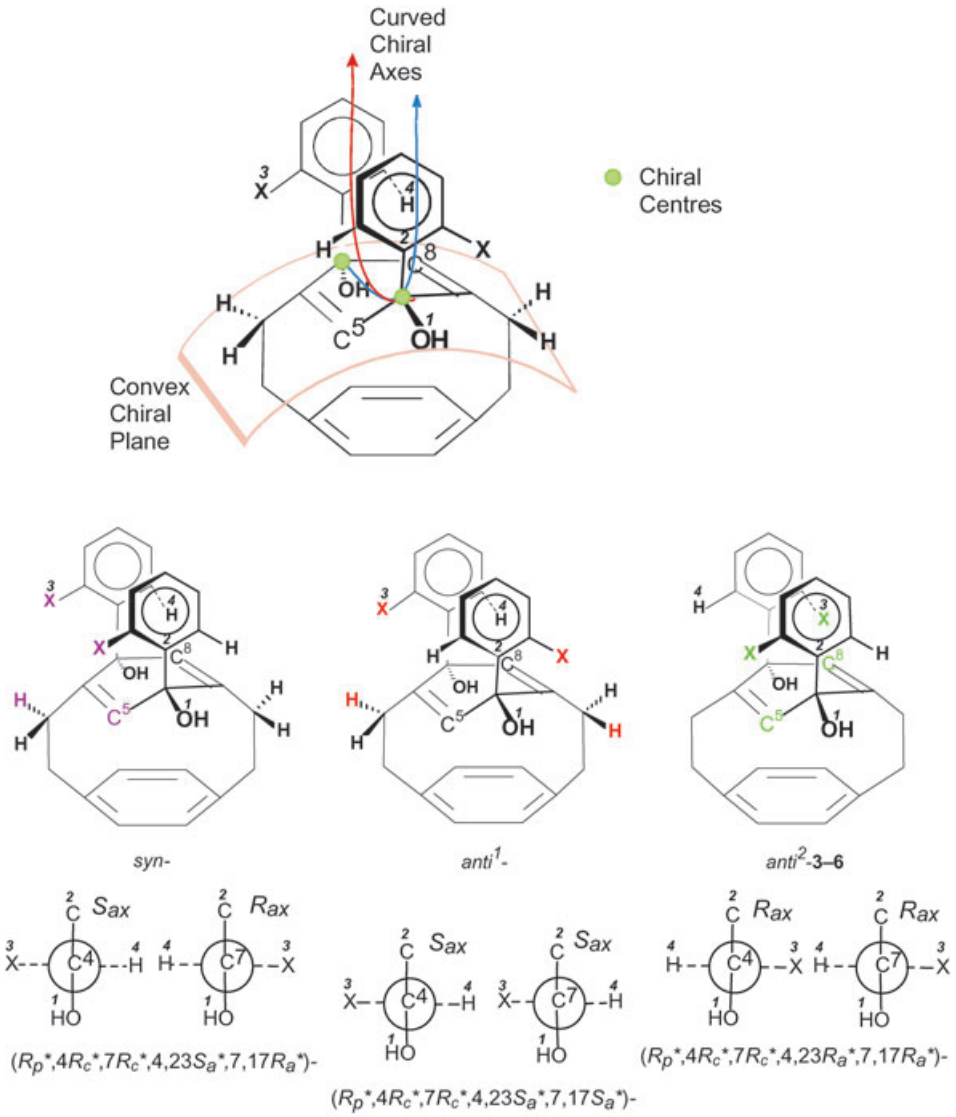
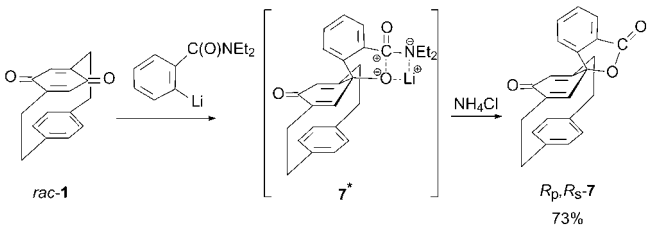


Figure 2. Five chiral elements in a molecule of a diol (top) and the relative configuration of diols **3–6** (bottom).

tom). Hence the diols **3–6** have five elements of chirality: a convex chiral plane (which is, in fact, a non-planar chiral surface), two chiral centres, and two curved chiral axes, as shown at the top of Figure 2. As such, these molecules could exist in $2^5 = 32$ different spatial configurations. However, in every case the exclusive diastereomer from this set of possible isomers was stereospecifically formed.

In contrast to previously described examples (Scheme 1), quinone **1** reacts with an excess of {2-[(diethylamino)carbonyl]phenyl}lithium resulting in a single compound, which is an abnormal mono-addition product, namely ketolactone **7** (Scheme 2).

The structure of **7** was determined on the basis of the series of ^{1}H, ^{13}C, ^{13}C {^{1}H} NMR experiments, and IR spectroscopic data. Thus, the presence of the two different carbonyl groups in **7** is supported by characteristic bands at 1770 (−O−C=O) and 1656 (C=O) in the IR spectrum, together with the low-field signals at 169.82 (−O−C=O); 186.64 (C=O) ppm in the ^{13}C NMR spectrum. To rationalize the formation of such a product we assume that the addition of the organolithium reagent to one carbonyl group of quinone **1** occurs stereospecifically from the outer site of the carbonyl group, like the double addition to this substrate.[4] The ensuing



Scheme 2.

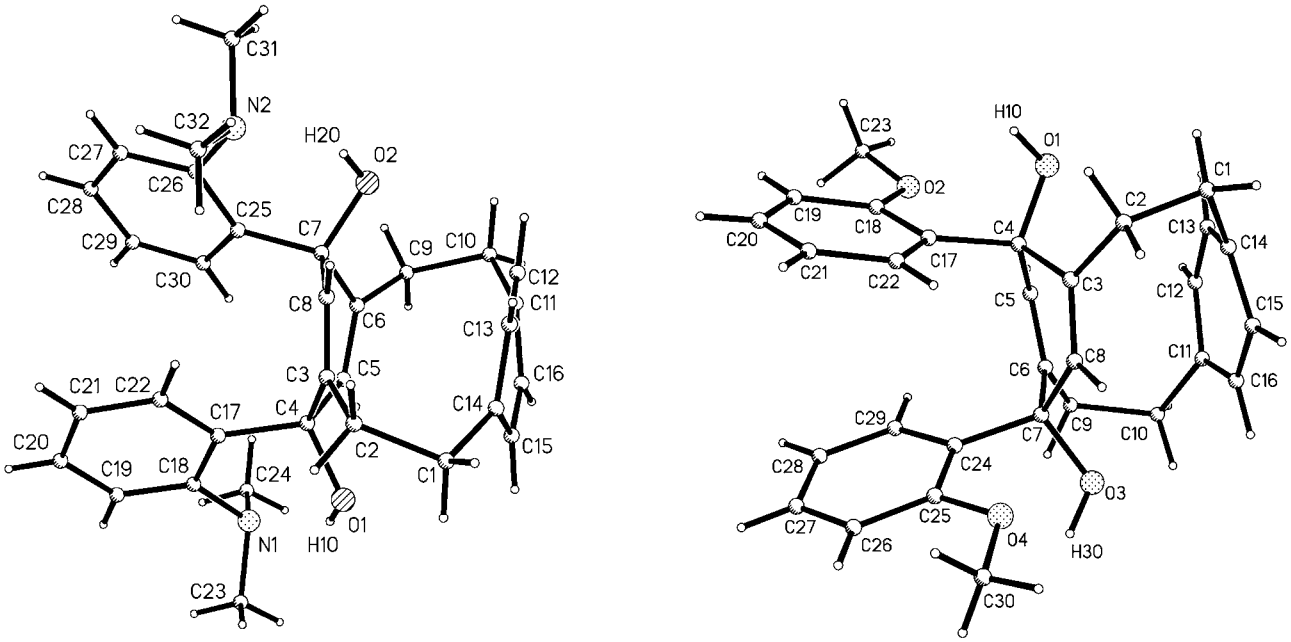
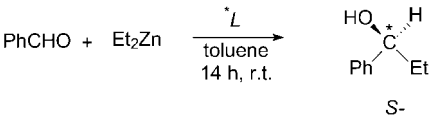


Figure 3. *Left:* Molecular structure of 4,7-bis(2-dimethylaminophenyl)-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (**4**). *Right:* Molecular structure of 4,7-bis(2-methoxyphenyl)-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (**3**).

coordination between lithium and the nitrogen atom of the proximate NEt_2 group provides the generation of the rigid intermediate **7*** which suffers the elimination of the lithium diethylamide. Further cyclization produces lactone **7** which forms, as a matter-of-course, stereospecifically and has the (*Rp*,Rc**)-relative configuration (Scheme 2). The exclusive formation of the mono-addition product could be explained if one assumes that the second carbonyl group of the paracyclophane scaffold (either in the intermediate **7*** or in the final product **7**) is shielded by the aromatic ring of paracyclophane moiety from one side, and by the aromatic ring of the substituent from the other, thus preventing the approach of the organolithium reagent to this group.

The application of the regularities of nucleophilic addition of *ortho*-functionalized aryllithium reagents to enantiomers of quinone **1**[3,4] allowed us to synthesize compounds **3**–**5**, in which the aryl substituents have in the *ortho*-positions various groups (*N*- or *O*-functions), in optically active form. The pairwise combination of these functional groups of the aryl fragments together with the geminal hydroxy groups provides the formation of two independent (concomitantly chemically and stereochemically identical) systems, both of which are capable of chelation with metals in the course of asymmetric synthesis and catalysis. We have obtained (*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**3** and (*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**4** from the (*Sp*)-enantiomer of quinone **1**, and (*Rp*,4*Rc*,7*Rc*,4,23*Ra*,7,17*Ra*)-**5** from (*Rp*)-**1** according to the procedure elaborated for the synthesis of racemic compounds. The synthesized ligands were tested as chiral inductors in the asymmetric addition of Et_2Zn to benzaldehyde (Scheme 3). The standard experiment included the successive addition of 2 equivalents of Et_2Zn and 1 equivalent of benzaldehyde to a solution of the chiral catalyst **3**–**5** in toluene. All reactions have lead to the formation of (*S*)-1-phenylpropanol. Initially, each one of the three ligands was used at an amount of 10 mol % (Table 1, entries 1–3). The best result (93.8% ee) was obtained with the bis-bifunctional N,O-ligand (*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**4**. In further reactions with this ligand, the decrease of its amount to 3 mol % and down to 1 mol % negligibly affected the asymmetric result (Table 1, entries 4 and 5).



Scheme 3.

Table 1. Enantioselective addition of diethylzinc to benzaldehyde.[a]

Entry	L*	L*/PhCHO [%]	ee [%]	Configuration[b] of 1-phenylpropanol
1	(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**3**	10	<1	*S*
2	(*Rp*,4*Rc*,7*Rc*,4,23*Ra*,7,17*Ra*)-**5**	10	27	*S*
3	(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**4**	10	93.8	*S*
4	(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**4**	3	93.4	*S*
5	(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**4**	1	92.6	*S*

[a] The conversions were determined as > 90% by Chiral GC data.
[b] Determined by GC on a chiral stationary phase using comparison with authentic samples.

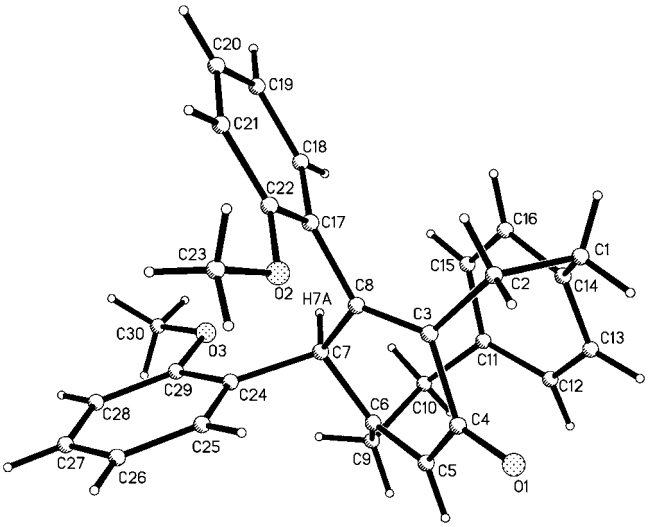
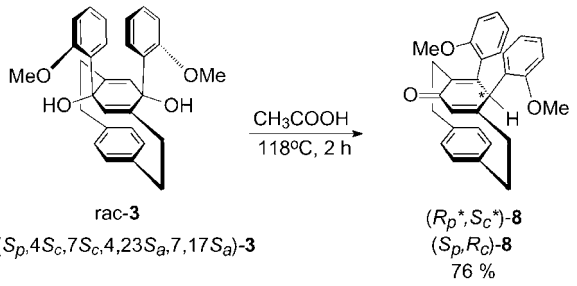


Figure 4. Molecular structure of 4,7-dihydro-7,8-di(2-methoxyphenyl)[2.2]paracyclophane-4-one (**8**).

In a preceding article we have shown that the acid-catalyzed dehydration of 4,7-disubstituted-4,7-dihydro-4,7-dihydroxy[2.2]paracyclophanes of the type **2** (Figure 1) occurs stereospecifically and results in high yields of stable, planar chiral cyclohexadienones of the [2.2]paracyclophane series with an *ortho*-semiquinoid (R = Me, *n*-Bu or All) or *para*-semiquinoid (R = Ph) substructure.[3] It was quite within reason to suggest that the dehydration of aryl-substituted diol **3** would result (under the same conditions) in the formation of a carbonyl compound with a *para*-semiquinoid substructure. Diol **3** was dehydrated on reflux in glacial acetic acid that led to 7,8-di-*o*-anisyl-4,7-dihydro[2.2]paracyclophane-4-one (**8**) with 78% yield (Scheme 4). We found that **8** was formed stereospecifically (de > 99%) with the (*Rp**,*Sc**)-configuration. A *para*-semiquinoid structure of the compound **8** was determined on the basis of a series of ^{1}H, ^{13}C, ^{13}C {^{1}H}, NMR experiments, and IR spectroscopic data, and then was unambiguously proven by single-crystal X-ray diffraction analysis (Figure 4). Enantiopure cyclohexadienone (*Sp,Rc*)-**8** was synthesized from (*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**3**. Obviously the insertion of substituents in the aryl fragments does not affect the direction of the rearrangement.



Scheme 4.

Conclusion

In the present work we have investigated the nucleophilic addition of *ortho*-substituted aryllithium reagents to [2.2]paracyclophane-4,7-quinone (**1**) and found that the reactions lead to *cis*-diols **3–6** with an *endo*-orientation of the hydroxyl groups and a single *anti*-orientation of the *ortho*-substituted aryl moieties (from two *anti*- and one *syn*- alternatives). Consequently, the planar chiral compound **1** produces, in a highly regio- and stereospecific manner (de > 99%), multistereogenic compounds of the (*Rp**,4*Rc**,7*Rc**,4,23*Ra**,7,17*Ra**)-relative configurations, bearing two additional asymmetric centres and two axes of chirality. Diols **3–5** obtained in enantiomerically pure form were tested as chiral inductors in the enantioselective addition of diethylzinc to benzaldehyde, and (*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**4** (of 98% ee) has shown the best result [93.8% ee of (*S*)-1-phenylpropanol]. Regio- and stereospecific rearrangement of (*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**3** produced (*Sp*,*Rc*)-**8** which is the first optically active, planar chiral cyclohexadienone having a *para*-semiquinoid structure.

Experimental Section

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 spectrometer at 400.13 and 100.61 MHz, respectively, in $CDCl_3$. Residual signals of the solvent protons with the chemical shifts δ = 7.27 ($CDCl_3$) and 2.5 (DMSO-d_6) were used as internal standards. Mass spectra were obtained on a Kratos MS 90 mass spectrometer (70 eV) at 200 °C. TLC analysis was per-

formed using Silufol UV-254 plates (Chemapol) and "SORBFIL" plates PTLC-A-UV (Sorbpolimer), chromatographic purification and separation of diastereomers was carried out using Kieselgel 60 silica gel (Merck). Optical rotations: EPO-1. (*R*)- and (*S*)-[2.2]paracyclophane-4,7-quinone (**1**) were synthesized by a described procedure.[3] All reactions were carried out in anhydrous solvents under argon.

For spectral characteristics of compounds **3–8** and X-ray crystallographic study of compounds *rac*-**3**, *rac*-**4** and *rac*-**8**, see the Supporting Information.

cis-4,7-Bis(2-methoxyphenyl)-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (*rac*-3)

To a solution of anisole (1.8 mL, 16 mmol) in THF (20 mL) was added a 3.04 M solution of *n*-BuLi in hexane (2.63 mL, 8 mmol) at 0 °C and the mixture was stirred for 3 h. It was cooled to −78 °C and a solution of quinone **1** (0.200 g, 0.84 mmol) in toluene (200 mL) was added dropwise. The reaction mixture was allowed to warm up to room temperature and then stirred overnight. The reaction was quenched with an excess of saturated aqueous NH_4Cl solution. The organic layer was washed with H_2O and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to give the crude product, which was purified by column chromatography with benzene as eluent to afford *rac*-**3**; yield: 0.276 g (73%); decomp. temp. 172–172.5 °C; anal. calcd. (%) for $C_{30}H_{30}O_4$ (454.57): C 79.27, H 6.65; found (%): C 79.16, H 6.64.

(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-4,7-Bis(2-methoxyphenyl)-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane [(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-3]

(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**3** (ee 98%) was synthesized as described for *rac*-**3** starting from (*S*)-**1** (0.100 g, 0.42 mmol, ee 98%); isolated yield: 0.143 g (75%); $[\alpha]_D^{25}$: −286.9 (*c* 0.368, benzene); decomp. temp. 212–226 °C; anal. calcd. (%) for $C_{30}H_{30}O_4$ (454.57): C 79.27, H 6.65; found (%):C 79.15, H, 6.71. Spectroscopic data are in a good agreement with those for *rac*-**3**.

cis-4,7-Bis(2-dimethylaminophenyl)-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane, (*rac*-4)

To a solution of *N,N*-dimethylaniline (3.04 mL, 24 mmol) in hexane (4 mL) was added a 3.04 M solution of *n*-BuLi in hexane (2.63 mL, 8 mmol) at room temperature, and the mixture was then stirred at 99 °C (thermometer in the oil bath) for 20 h. It was cooled to −78 °C and a solution of quinone **1** (0.100 g, 0.42 mmol) in toluene (100 mL) was added dropwise. The reaction mixture was allowed to warm up to room temperature and was then stirred overnight. The reaction was quenched with an excess of saturated aqueous NH_4Cl solution. The organic layer was washed with H_2O and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to give the crude product, which was purified by column chromatography with CH_2Cl_2 as eluent, to afford *rac*-**4**; yield: 0.122 g (60%); decomp. temp. 255–265 °C; anal. calcd. (%) for $C_{32}H_{36}N_2O_2$ (480.65): C 79.97, H 7.55, N 5.83; found (%): C 80.22, H 7.46, N 5.73.

(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-4,7-Bis(2-dimethylaminophenyl)-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane [(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-4]

(*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**4** (ee 98%) was synthesized as described for *rac*-**4** starting from (*S*)-**1** (0.100 g, 0.42 mmol, ee 98%); isolated yield: 0.128 g (63%); $[\alpha]_D^{25}$: −258.6 (*c* 0.386, $CHCl_3$); decomp. temp. 212–222 °C; anal. calcd. (%) for $C_{32}H_{36}N_2O_2$ (480.65): C 79.97, H 7.55, N 5.83; found (%): C 80.03, H 7.43, N 5.71. Spectroscopic data are in accord with those obtained for *rac*-**4**.

cis-4,7-Bis[5-methyl-2-(isopropylsulfamido)-phenyl]-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (*rac*-5)

To a solution of tosyl-isopropylamide (1.67 g, 7.9 mmol) in THF (20 mL) was added a 3.04 M solution of *n*-BuLi in hexane (5.26 mL, 15.77 mmol) at −5 °C and the mixture was stirred for 3 h and then cooled down to −78 °C. A solution of 0.100 g (0.42 mmol) of quinone **1** in 100 mL of toluene was added dropwise. The reaction mixture was allowed to warm up to room temperature and was then stirred overnight. The reaction was quenched with excess saturated aqueous NH_4Cl solution. The organic layer was washed with H_2O, extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to give the crude product, which was purified by column chromatography with CH_2Cl_2 as eluent. Unconsumed quinone **1** was isolated in 0.010 g (10%) yield. *rac*-**5** was obtained; yield: 0.220 g (79% with respect to the total amount of **1** or 87% with respect to the consumed quinone **1**); decomp. temp. 230–232 °C; anal. calcd. (%) for $C_{36}H_{44}N_2O_6S_2$ (664.88): C 65.03, H 6.67, N 4.21, S 9.64; found (%):C 64.92, H 6.61, N 4.08, S 9.75.

(*Rp*,4*Rc*,7*Rc*,4,23*Ra*,7,17*Ra*)-4,7-Bis[5-methyl-2-(isopropylsulfamido)-phenyl]-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane [(*Rp*,4*Rc*,7*Rc*,4,23*Ra*,7,17*Ra*)-5]

The synthesis was carried out as described for *rac*-**5** from (*R*)-**1** (0.100 g, 0.42 mmol, ee > 99%). Unconsumed quinone (*R*)-**1** was isolated with 0.008 g (8%) yield. Then (*Rp*,4*Rc*,7*Rc*,4,23*Ra*,7,17*Ra*)-**5** (ee 99%) was obtained; yield: 0.203 g [72% with respect to total amount of (*R*)-**1** or 79% with respect to the consumed quinone (*R*)-**1**]; $[\alpha]_D^{25}$: +163.6 (*c* 0.209, $CHCl_3$); decomp. temp. 212–222 °C; anal. calcd. (%) for $C_{36}H_{44}N_2O_6S_2$ (664.88): C 65.03, H 6.67, N 4.21, S 9.64; found (%):C 64.95, H 6.68, N 4.19, S 9.45. Spectroscopic data are in accord with those obtained for *rac*-**5**.

cis-4,7-Bis(2-*N*,*N*-diethylcarbamoyloxyphenyl)-4,7-dihydroxy-4,7-dihydro[2.2]paracyclophane (6)

To a solution of TMEDA (1.2 mL, 8.3 mmol) in THF (25 mL) was added dropwise a 1.34 M solution of *sec*-BuLi in cyclohexane (6 mL, 8 mmol) at −78 °C. To the resulting mixture was added dropwise a solution of *N,N*-diethylcarbamoyloxybenzene (2 mL, 10.3 mmol) in THF (20 mL) and the mixture was

stirred at −78 °C for 2 h. Then a solution of quinone **1** (0.10 g, 0.4 mmol) in toluene (25 mL) was added dropwise. The reaction mixture was allowed to warm up to room temperature and was stirred overnight. The reaction was quenched with an excess of saturated aqueous NH_4Cl solution. The organic layer was washed with H_2O and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to give the crude product, which was purified by column chromatography with CH_2Cl_2 as eluent; yield of **6**: 0.183 g (70%); mp 180 °C; anal. calcd. (%) for $C_{38}H_{44}N_2O_6$ (624.78): C 73.05, H 7.10, N 4.48; found (%): C 73.04, H 7.18, N 4.28.

7-(2-Carbonyloxyphenyl)spirolactone-4,7-dihydro[2.2]paracyclophane-4-one (7)

To a solution of TMEDA (1.2 mL, 8.3 mmol) in THF (25 mL) was added dropwise a 1.34 M solution of *sec*-BuLi in cyclohexane (4.9 mL, 6.5 mmol) at −78 °C. The mixture was treated with *N,N*-diethylbenzylamide (1.33 g, 7.50 mmol) in THF (20 mL) and stirred for 2 h at −78 °C. Then a solution of quinone **1** (0.15 g, 0.6 mmol) in toluene (25 mL) was added dropwise. The reaction mixture was allowed to warm up to room temperature and was stirred overnight. The reaction was quenched with excess saturated aqueous NH_4Cl solution. The organic layer was washed with H_2O and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to give the crude product, which was purified by column chromatography with CH_2Cl_2 as eluent; yield of **7**: 0.157 g (73%); mp 273.5–274 °C; anal. calcd. (%) for $C_{23}H_{18}O_3$ (342.39): C 80.68, H 5.30; found (%): C 80.45, H 5.23.

4,7-Dihydro-7,8-di(2-methoxyphenyl)-[2.2]paracyclophane-4-one (*rac*-8)

To the diol **3** (0.181 g, 0.4 mmol), glacial acetic acid (10 mL) was added, and the reaction mixture was refluxed in a flask equipped with a Dean–Stark trap and filled with $MgSO_4$ for 2 h. Acetic acid was removed under vacuum and the reaction mixture was washed with pentane and dried under vacuum. The reaction mixture was purified by column chromatography with benzene/ethyl acetate mixture (7/3) as eluent.; yield of *rac*-**8**: 0.136 g (78%); decomp. temp. 217 °C; anal. calcd. (%) for $C_{30}H_{28}O_3$ (436.55): C 82.54, H 6.46; found (%): C 82.53, H 6.40.

(*Sp,Rc*)-4,7-Dihydro-7,8-di(2-methoxyphenyl)-[2.2]paracyclophane-4-one (*Sp,Rc*)-8

The synthesis was carried out as described for *rac*-**8** from (*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17*Sa*)-**3** (0.04 g, 0.09 mmol, ee 98%) in glacial acetic acid to afford the isolated product (*Sp,Rc*)-**8**; yield: 0.058 g (76%, ee 98%); $[\alpha]_D^{25}$: +112.2 (*c* 0.300, THF); mp 217 °C; anal. calcd. (%) for $C_{30}H_{28}O_3$ (436.55): C 82.54, H 6.46; found (%): C 82.21, H 6.54. Spectroscopic data are in accord with those obtained for *rac*-**8**.

Enantioselective Diethylzinc Addition to Benzaldehyde Catalyzed by Compounds (*Rp*,4*Rc*,7*Rc*,4,23*Ra*,7,17*Ra*)-3, (*Sp*,4*Sc*,7*Sc*,4,23*Sa*,7,17S*a*)-4, (*Rp*,4*Rc*,7*Rc*,4,23*Ra*,7,17*Ra*)-5; Typical Procedure

To a solution of a diol (0.0021 mmol) in toluene (0.28 mL), a 1.1 M solution of Et_2Zn in toluene (0.140 mL, 0.142 mmol) was added in one portion at 0 °C followed by the benzaldehyde (0.071 mmol) added dropwise, and the mixture was stirred for 14 h at room temperature. It was quenched by addition of 1 N HCl solution (0.25 mL), diluted with Et_2O (4 mL) and H_2O (3 mL). The organic layer was separated and the aqueous fraction was additionally extracted with Et_2O (5 × 4 mL) or CH_2Cl_2. The combined organic fractions were washed with brine (2 mL) and dried over Na_2SO_4. After solvent removal the oily residue without further purification was subjected to the chiral GC. Enantiomeric analysis of 1-phenylpropanol was performed by GC on a Gamma Cyclodextrin Trifluoroacetyl (G-TA) column (30 m × 0.25 mm) with He as carrier gas. Temperature data for 1-phenylpropanol: split temperature 220 °C, detector FID 220 °C, column temperature 120 °C; the retention times (min) were 12.1 (*S*) and 12.6 (*R*).

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