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Synthesis, Chiral Resolution, and Absolute Configuration of Dissymmetric 4,12-Difunctionalized [2.2]Paracyclophanes

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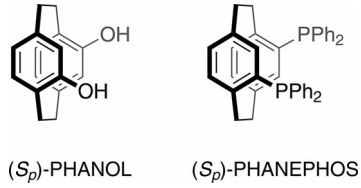
Racemic 4,12-difunctionalized [2.2]paracyclophanes were synthesized and successfully resolved by (recycling) HPLC on a stationary CHIRALPAK IA phase at a semipreparative scale. Their absolute configurations were determined by X-ray crystal structure analysis and/or by comparison of their specific optical rotations with literature data. These are valuable functionalized C_2-symmetric building blocks for the formation of more sophisticated V-shaped, chiral molecular architectures, as demonstrated by some exploratory transformations.

Introduction

Ever since [2.2]paracyclophane was synthesized in 1949 by Brown and Farthing it has fascinated chemists around the world due to the physical and chemical properties that result from its unique structure.[1] Substitution of the [2.2]-paracyclophane core often results in planar chiral compounds and some of these have already found applications in material science,[2] as supramolecular hydrogen-bond receptors,[3] or in stereoselective synthesis.[4] *Pseudo-ortho* 4,12- and *pseudo-meta* 4,15-substituted [2.2]paracyclophanes are dissymmetric molecules when they carry two identical substituents and some of these have also been successfully applied as chiral ligands or organocatalysts. Pye and Rossen, for instance, presented (R_P)-4,12-bis(diphenylphosphanyl)[2.2]paracyclophane (PHANEPHOS; Scheme 1) in 1997 and introduced the [2.2]paracyclophane scaffold as the backbone for some powerful ligands that could be used in various catalytic transformations.[5] In addition to PHANEPHOS, (±)-4,12-dihydroxy[2.2]paracyclophane (PHANOL) has been demonstrated to be a versatile organocatalyst.[6]



Scheme 1. Versatile derivatives of [2.2]paracyclophane for catalysis.

Our group is particularly interested in diastereoselective self-assembly processes of metallosupramolecular aggregates,[7] and we found dissymmetric, structurally rigid scaffolds bearing uncommon stereogenic elements such as a chiral axis,[8] stereogenic nitrogen atoms,[9] or spirocompounds[10] to be very advantageous for this purpose. Thus, dissymmetric *pseudo-ortho* 4,12- and *pseudo-meta* 4,15-substituted [2.2]paracyclophanes attracted our interest as potential building blocks for the preparation of new classes of very rigid planar-chiral ligands for the formation of oligonuclear metal complexes and, hence, we started to explore these compounds.

The main problem with this particular class of planar chiral compounds, however, is to gain access to enantiomerically pure products. In fact, there are only a rather limited number of successfully resolved 4,12-disubstituted derivatives available today.[4b,11] Pye and Rossen obtained enantiomerically pure PHANEPHOS by resolution through clathrate formation with a chiral auxiliary.[5] This could then be used as a chiral ligand in Buchwald–Hartwig amination of racemic 4,12-dibromo[2.2]paracyclophane to achieve a kinetic resolution, to some extent, since (S_P)-PHANEPHOS showed enantiomeric discrimination of (R_P)-4,12-dibromo[2.2]paracyclophane compared with its optical antipode and, hence, allowed its isolation in enantiomerically pure form.[12] In addition, there are also protocols available for the resolution of 4,12-dihydroxy[2.2]paracyclophane[13] and [2.2]paracyclophane-4,12-dicarboxylic acid.[14] Both of these are based on the formation of dia-

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stereomers with a chiral auxiliary. Very recently, Morisaki and Chujo reported another versatile auxiliary-based approach whereby they converted the racemic 4,12-dibromo[2.2]paracyclophane into a separable mixture of diastereomeric 4-bromo-12-*p*-toluene-sulfoxide[2.2]paracyclophanes upon treatment with (1*R*,2*S*,5*R*)-menthyl (*S*)-*p*-toluenesulfinate.[15] These optically pure sulfoxides could then even be transformed into the corresponding 4,12-diformyl[2.2]paracyclophanes through nucleophilic substitution. Finally, approaches that involve kinetic enzymatic resolution have also been developed.[16]

In this context, HPLC on chiral stationary phases, however, has only been reported as an analytical tool, and has not yet been applied on a (semi)preparative scale.[13–16] In most of the studies, CHIRALPAK AD and OD were employed as chiral stationary phases. In these systems the polymeric chiral selector is not covalently attached to the silica gel substrate but only physically adsorbed, which limits the range of potential eluents to a great extent. On chiral stationary phases of the next generation, the chiral selector is immobilized, which allows a broader range of eluents and also introduces new selectivity.

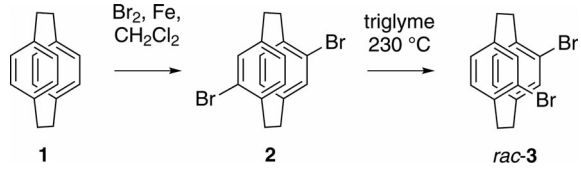
In this work we present the synthesis of [2.2]paracyclophane derivatives and a complementary resolution approach employing semipreparative HPLC on a stationary phase with a covalently attached chiral selector that allowed us to improve the resolution of planar-chiral [2.2]paracyclophanes with regard to yield and optical purity.[17] In this way we were not only able to resolve 4,12-dihydroxy[2.2]paracyclophane, 4,12-dibromo[2.2]paracyclophane, 4,12-bis(diphenylphosphane oxide)[2.2]paracyclophane, and [2.2]paracyclophane-4,12-dicarboxylic acid {indirectly after saponification of chromatographically resolved di(4-bromophenyl)[2.2]paracyclophane-4,12-dicarboxylate}, but also extended the number of successfully resolved derivatives by separating the enantiomers of 4,12-diiodo[2.2]paracyclophane, 4,12-diformyl[2.2]paracyclophane, and 4,12-di(4-hydroxyphenyl)[2.2]paracyclophane. In the case of 4,12-dihalogenated [2.2]paracyclophanes, simple HPLC failed to resolve the isomers but recycling HPLC was successful. The absolute configuration of the isomers was determined by X-ray crystal structure analysis and/or, if available, by comparison of their optical rotation with literature data.

Results and Discussion

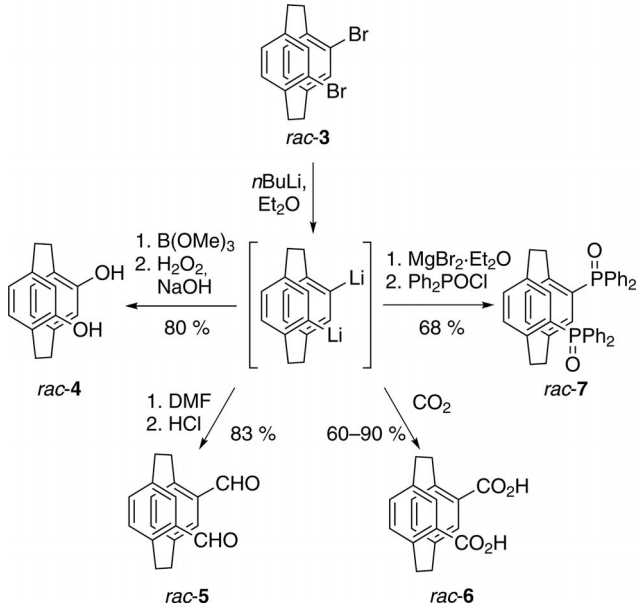
The starting material for the synthesis of all compounds was unsubstituted [2.2]paracyclophane (**1**; Scheme 2). Its bromination is well-known and several methods have been described.[18,19]

We used the method of Braddock to synthesize 4,16-dibromo[2.2]paracyclophane (**2**).[16] Heating this compound in triglyme, following the approach of Rossen and Pye, then led to *rac*-4,12-dibromo[2.2]paracyclophane (**3**).[12]

Compound *rac*-**3** was then used as the starting material for all further reactions (Scheme 3). Thanks to its high reactivity in bromine-lithium exchange reactions, we were able to insert hydroxy and formyl groups by adapting literature procedures established by Hopf[19] and Rozenberg.[20]



Scheme 2. Synthesis of 4,12-dibromo[2.2]paracyclophane [*rac*-**3**] from [2.2]paracyclophane (**1**).



Scheme 3. Synthesis of functionalized racemic [2.2]paracyclophanes **4**–**6** through bromine-lithium exchange.

Compound *rac*-**4** was first synthesized by Cram in 1969 using a twofold bromine-lithium exchange followed by oxidation with $PhNO_2$.[18] Braddock improved this approach by using tetrahydrofuran (THF) instead of diethyl ether and thereby increased the yield from 16 to 35–45%.[16] Rozenberg, however, performed a stepwise substitution through monolithiation, followed by monoborylation with $B(OMe)_3$ in diethyl ether, followed by oxidation and subsequent saponification of the borate upon treatment with H_2O_2 and aqueous NaOH with the aim of resolving the resulting racemic monohydroxy-monobromo compound through diastereomeric ester formation. Subsequently, the second bromine atom was substituted by a hydroxyl group by following the same protocol, giving rise to **4** in about 46% yield (calculated only for the two substitutions).[20] When we ran this borylation/oxidation reaction in a concerted manner, i.e., a twofold substitution, we were able to dramatically increase the yield of *rac*-**4** to 80% (Scheme 3) .

Upon addition of *N*-formylpiperidine to dilithiated **3** and subsequent treatment with HCl, Hopf obtained *rac*-4,12-diformyl[2.2]paracyclophane (**5**) in yields of 60–81%

(Scheme 3).[19] When we used *N*,*N*-dimethylformamide (DMF) instead of *N*-formylpiperidine followed by quenching with aqueous HCl, we obtained *rac*-**5** in a yield of 83%.

To broaden our approach, we also prepared dicarboxylic acid *rac*-**6** and *rac*-di(phosphane oxide) *rac*-**7** according to literature protocols. Hence, *rac*-**6** could be most conveniently synthesized by the addition of dry ice to a solution of dilithiated **3**,[21] and we obtained yields of between 60 and 90% for this transformation. Compound *rac*-**7** was obtained in 68% yield from the dilithiated [2.2]paracyclophane after transmetallation and reaction with diphenylphosphinic chloride.[5]

As mentioned above, resolution of the enantiomers of **4**, **6**, and **7** has been described in the literature. Whereas the separation of *rac*-**7** could be achieved through clathrate formation with dibenzoyl-L-tartraic acid as a chiral auxiliary in a quite elegant manner[5] that only requires a simple alkalization as an additional synthetic step, the enantioseparations of *rac*-**4** and *rac*-**6** proved to be more tedious. For instance, the very long reaction time of 14 days required for Braddock's kinetic resolution of the previously synthesized acetate of **4** by transformation with a commercially available lipase of *Candida rugosa* is not attractive.[16] Thus, Jiang and Zhao developed an auxiliary-based approach whereby (±)-**4** was treated with (1*S*)-camphanoyl chloride and the resulting diastereoisomers were separated by using column chromatography.[13] In a similar approach, Jiang et al. were also able to achieve the resolution of (±)-**6** by treatment of the corresponding diacid chloride with (1*S*)-hydroxymethyl-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptanes-3-one to prepare complementary diastereomeric esters that were amenable for separation by column chromatography.[14] However, both approaches require two or three additional synthetic steps to obtain the material in optically pure form.

With our experience in HPLC-based resolutions,[9e,9i] we wanted to employ this technique for the direct separation of racemic **4**, **5**, and **7**. In fact, all these compounds could be resolved in a very efficient manner, both on an analytical and on a semipreparative scale, by using a chiral CHIRALPAK IA stationary phase and mixtures of *n*-hexane and simple alcohols such as ethanol or 2-propanol as eluent, as illustrated for **4** in Figure 1.

Comparison of the specific optical rotations of the resolved material with literature data[13–15] then allowed the configuration of (–)-(S_p)-**4**, (+)-(R_p)-**4**, (+)-(S_p)-**5**, (–)-(R_p)-**5**, (–)-(R_p)-**7**, and (+)-(S_p)-**7** to be assigned.

Unfortunately, the high polarity of (±)-**6** rendered it unsuitable for HPLC on this stationary phase. Therefore, we thought to transform this compound into the corresponding diester via its diacid chloride first. As the alcohol component, we selected 4-bromophenol for several reasons: firstly, a phenol should be a good nucleophile with which to achieve diester formation in very good yield; secondly, this diester should be easy to separate by HPLC due to its rigid structure with its moderately polar functional groups pointing in defined directions, and, thirdly, the bromine atoms provide a means with which to assign the absolute

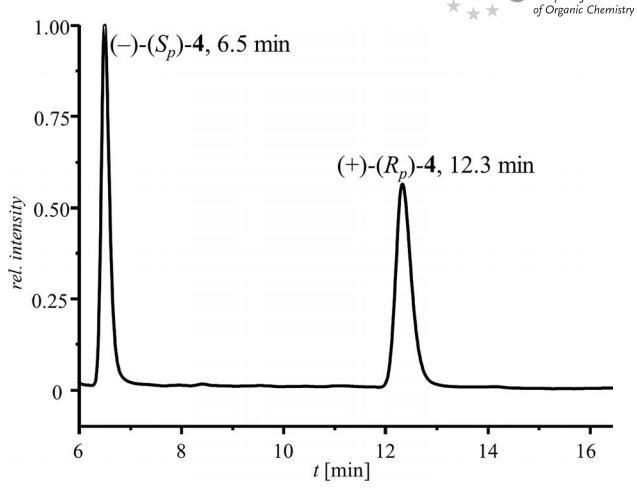
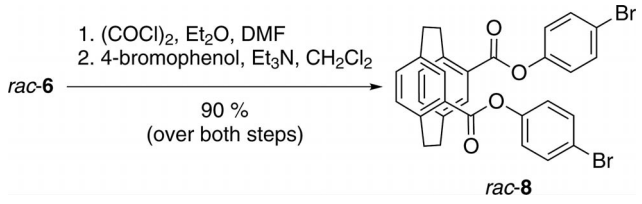


Figure 1. Chromatographic resolution of *rac*-**4** by analytical HPLC on an analytical chiral CHIRALPAK IA phase (*n*-hexane/ethanol, 75:25 v/v; flow rate 1.0 mL min^{-1}).

configuration of the resolved material through X-ray crystallography by analysis of the Flack parameter if suitable single-crystals could be grown and also to further elaborate this molecular architecture in nucleophilic substitutions. Fortunately, at least the first two points turned out to be true because we were not only able to prepare the respective di(4-bromophenyl) ester *rac*-**8** in excellent yield (Scheme 4) but could also readily resolve the enantiomers on the chiral stationary phase using *n*-hexane/ethanol (90:10 v/v) as eluent.

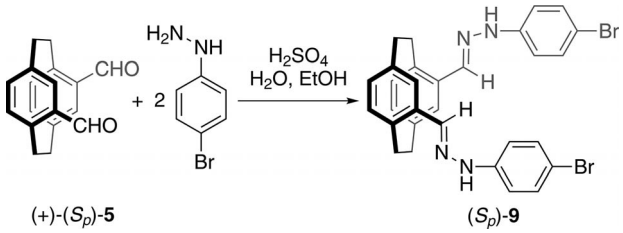


Scheme 4. Synthesis of di(4-bromophenyl) ester **8**.

Unfortunately, we did not succeed in growing suitable crystals of the resolved diester, which would have allowed its absolute stereochemistry to be determined directly. Simple saponification of the diester under alkaline conditions, however, provided the enantiomerically pure diacid, the specific optical rotation of which could be compared with the literature data. Thus, the (–)-enantiomer of **6** could be assigned the (R_p)-configuration and the (+)-enantiomer the (S_p)-configuration. Since chiral [2.2]paracyclophanes are configurationally very stable because they do not contain α-hydrogen atoms and only begin to racemize at high temperatures of at least 150 °C or higher, depending on the substituents, it is safe to assign the same configuration to the corresponding esters, i.e., (–)-(S_p)-**8** and (+)-(R_p)-**8** (please note that the sense of rotation changes).

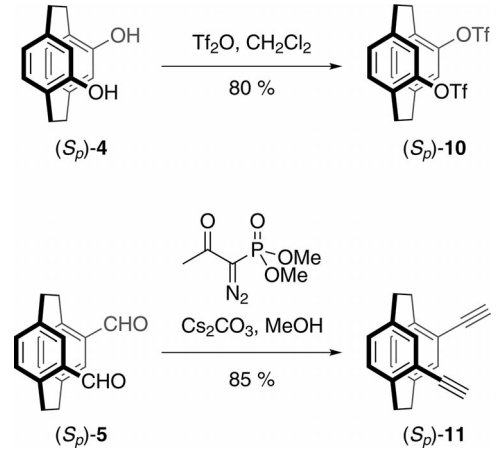
Although the sense of rotation of the enantiomers of our dialdehyde **5** nicely corresponds to the literature data,[15] we wanted to establish an additional independent proof for the

assignment. The absolute configuration of an organic molecule can either be elucidated by analysis of the Flack parameter determined through X-ray diffraction of a single crystal, or by analysis of its CD spectrum. To apply the X-ray diffraction technique, however, it is mandatory that the compound contains a heavy atom. Although dialdehyde **5** does not contain such atoms, fortunately, the first eluting enantiomer (+)-**5** could be easily transformed into its corresponding (4-bromophenyl)hydrazone **9** (Scheme 5), which readily crystallized and whose molecular structure could be determined by X-ray diffraction analysis (see Figure 3 below) and revealed the (S_p)-configuration of (+)-**5**.



Scheme 5. Synthesis of (S_p)-(4-bromophenyl)hydrazone **9** from enantiopure (+)-(S_p)-**5**.

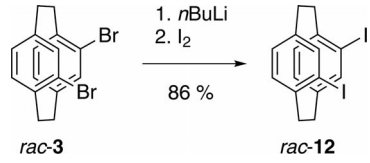
All the resolved compounds can be envisioned to act as versatile starting materials for the synthesis of more sophisticated molecular architectures, and we decided to explore this further with some of the optically pure compounds developed here. Compound **4**, for example, could be transformed into the corresponding ditriflate **10** (Scheme 6). Despite the fact that racemic dibromide **3** has already been shown to be reactive in Heck[22] and Suzuki[23] type arylations and Buchwald–Hartwig aminations,[12,24] unfortunately, it proved to be almost completely unreactive in Sonogashira like transformations in our hands.[25] Following an approach developed by Hopf,[19] however, an alternative route to 4,12-diethinyl[2.2]paracyclophane (**11**) was to treat **5** with the Bestmann–Ohira reagent[26] (Scheme 6).



Scheme 6. Synthesis of enantiomerically pure ditriflate **10** and diethynyl-substituted [2.2]paracyclophane **11**.

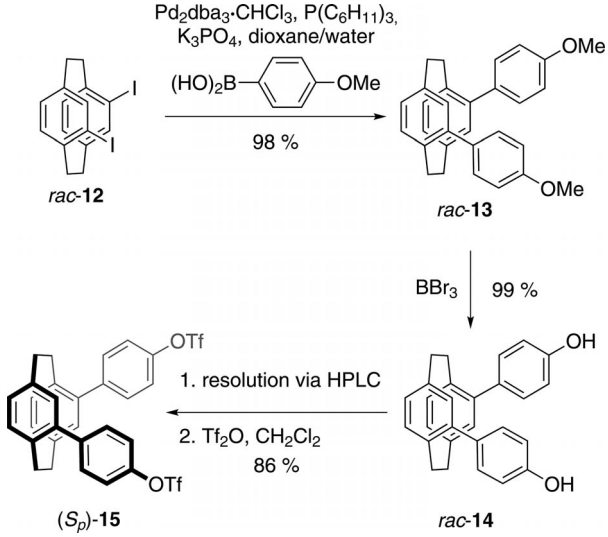
The enantiomerically pure ditriflate (+)-**10** could also be crystallized and analyzed by X-ray diffraction to reveal its (R_p)-configuration (see Figure 3 below). This provides additional experimental proof for the extraordinary high configurational stability of chiral [2.2]paracyclophanes because the precursor diol (R_p)-**4** had the same configuration.

Unfortunately, Suzuki reactions of **10** mostly produced mainly monoarylated products,[27] which might, however, be very useful for the synthesis of asymmetric derivatives. Thus, we decided to prepare the previously unknown 4,12-diiodo[2.2]paracyclophane (**12**) by quenching dilithiated **3** with iodide (Scheme 7).



Scheme 7. Synthesis of *rac*-4,12-diiodo[2.2]paracyclophane [*rac*-**12**].

To our delight, **12** showed very high reactivity in Suzuki cross-coupling reactions and led to the desired symmetrically disubstituted dissymmetric target compounds; an example is depicted in Scheme 8. The reaction of *rac*-**12** with 4-methoxyphenyl boronic acid gave the desired diarylated product *rac*-**13** in almost quantitative yield, which could be readily deprotected to give diol *rac*-**14** upon treatment with BBr_3.



Scheme 8. Synthesis of *rac*-**13**, *rac*-**14**, and enantiomerically pure ditriflate **15** (from resolved **14**).

Racemic diol **14** could then be resolved by HPLC using the chiral CHIRALPAK IA stationary phase and a mixture of *n*-hexane and 2-propanol (90:10 v/v) as eluent. The optically pure compound could then be transformed into the corresponding ditriflate **15** upon reaction with triflic anhydride. Again, **15** represents a valuable building block for the synthesis of larger V-shaped architectures and also contains

heavy atoms that can help to assign the absolute configuration by X-ray crystallographic analysis (see Figure 3 below).

Although, we were able to resolve five different 4,12-difunctionalized [2.2]paracyclophanes by using our approach, it would be preferable to resolve the two dihalogenated compounds **3** and **12** directly. In fact, Pye and Rossen were able to resolve *rac*-**3** by kinetic resolution in a Buchwald–Hartwig amination by using enantiomerically pure PHANEPHOS (**7**).[12] However, this approach provides access to only one enantiomer of **3**, with the second enantiomer being transformed irreversibly into a monoaminated paracyclophane (although this is itself useful for the preparation of asymmetric derivatives). Thus, we considered whether our HPLC approach could allow both enantiomers to be obtained in a single separation. Unfortunately, all attempts to separate the enantiomers of these compounds in a single chromatographic run failed, because the differences in retention on the chiral phase were not sufficient to achieve efficient resolution.

The problem of low chromatographic resolution described above was finally solved by employing recycling HPLC techniques. Although the concept of recycling chromatography has been known for more than 50 years,[28] and has developed into a standard tool in gel permeation chromatography for polymer analytics,[29] it has so far received much less attention for preparative enantiomer resolution.[9i,30] With this technique we were able to resolve *rac*-**3** and *rac*-**12** on a CHIRALPAK IA stationary phase and mixtures of *n*-hexane and dichloromethane as eluent after three cycles on an analytical scale (Figure 2) and after four and five cycles on a semipreparative scale, respectively.

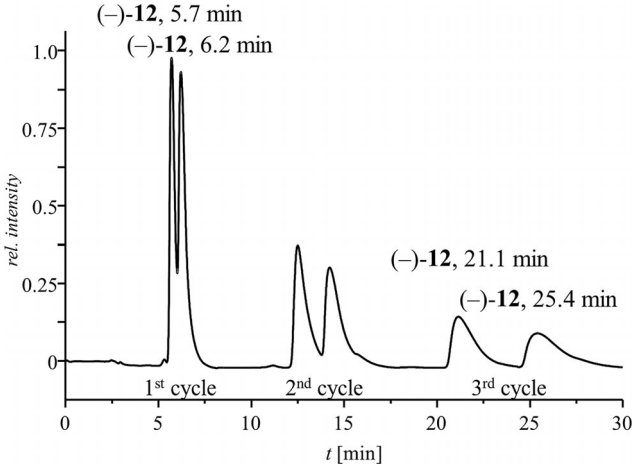


Figure 2. Chromatographic resolution of *rac*-**12** by analytical HPLC on an analytical chiral CHIRALPAK IA phase (*n*-hexane/dichloromethane, 90:10 v/v; flow rate 1.5 mL min^{-1}).

Enantiomerically pure dihalides **3** and **12** both crystallized readily and, hence, their molecular structures and absolute configurations could be determined and confirmed by X-ray diffraction (Figure 3).

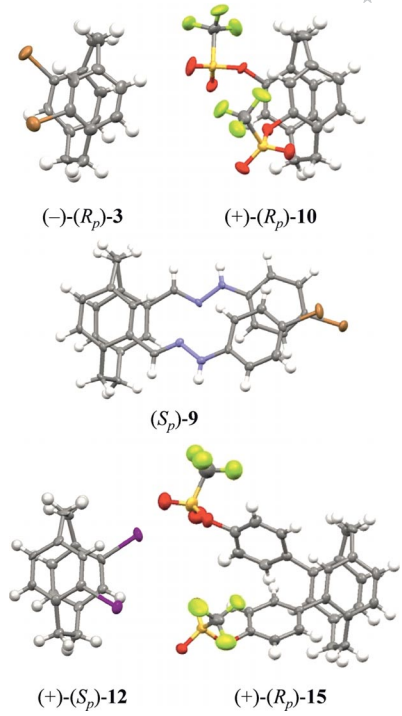


Figure 3. Molecular structures of (–)-(R_p)-**3**, (S_p)-**9**, (+)-(R_p)-**10**, (+)-(S_p)-**12**, and (+)-(S_p)-**15** as determined by X-ray diffraction analyses; carbon (grey), hydrogen (light-gray), nitrogen (blue), oxygen (red), sulfur (yellow), fluorine (green), bromine (brown), and iodine (purple).

Conclusions

We have synthesized thirteen planar chiral dissymmetric 4,12-difunctionalized [2.2]paracyclophanes. Some have previously been prepared in racemic form (**3–7**, and **11**) but some have not been synthesized before (**8**–**10** and **12**–**15**). It was possible to resolve seven of these racemic compounds (**3**–**5**, **7**, **8**, **12**, and **14**) by (recycling) HPLC techniques on an analytical and a semipreparative scale using a CHIRALPAK IA stationary phase. The absolute configurations of the separated enantiomers were determined by anomalous X-ray diffraction and/or confirmed by comparison of their specific optical rotation with literature data. All of these compounds represent interesting, configurationally very stable building blocks for the synthesis of more sophisticated molecular architectures based on the chiral V-shaped structure of the [2.2]paracyclophane scaffold in enantiomerically pure form, as demonstrated by esterification, ethynylation, arylation, and imine or hydrazone formation.

Experimental Section

General: Reactions under inert gas atmosphere were performed under argon using standard Schlenk techniques and oven-dried glassware prior to use. Thin-layer chromatography were performed on aluminum TLC plates (silica gel 60F_{254} from Merck). Detection was carried out under UV light (254 and 366 nm). Products were purified by column chromatography on silica gel 60 (70–230 mesh)

from Merck. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DRX 500 spectrometer (300 K) operating at 500.1 and 125.8 MHz, a Bruker AM 400 (298 K) operating at 400.1 MHz and 100.6 MHz, or with a Bruker Avance 300 (298 K) operating at 300.1 MHz and 75.5 MHz, respectively. ^{1}H NMR chemical shifts are reported on the δ scale (ppm) relative to residual non-deuterated solvent as the internal standard. ^{13}C NMR chemical shifts are reported on the δ scale (ppm) relative to deuterated solvent as the internal standard. Signals were assigned on the basis of ^{1}H, ^{13}C, HMQC, and HMBC NMR experiments. Mass spectra were recorded with a Finnigan MAT 212 with data system MMS-ICIS (EI) or with a Bruker micrOTOF-Q (ESI). Elemental analyses were carried out with a HeraeusVario EL. The HPLC analysis was performed using a Prominence console from Shimadzu (binary recycling system) consisting of three pumps (LC20-AT), degasser (DGU-20 A)$_3$, diode array detector (SPD-M20 A), and a fraction collector (FRC-10 A) or a smartline series from KNAUER with one S-1000 pump, autosampler S-3945, photodiode array detector S-2800, chiral detector of IBZ Meßtechnik or a smartline series from KNAUER with two S-1000 pumps, assistant 6000 with feed pump and UV-detector S-2500. Chiral analytical (4.6 × 250 mm) and semipreparative (10 × 250 mm) stationary phases CHIRALPAK IA from DAICEL were applied and solvent mixtures of *n*-heptane and dichloromethane (HPLC quality) and *n*-hexane and ethanol or 2-propanol (HPLC quality) were used.

Most solvents were dried, distilled, and stored under argon according to standard procedures. All chemicals were used as received from commercial sources. *rac*-4,16-Dibromo[2.2]paracyclophane [*rac*-**2**],[16] *rac*-4,12-dibromo[2.2]paracyclophane [*rac*-**3**],[5] *rac*-[2.2]-paracyclo-phane-4,12-dicarboxylic acid [*rac*-**6**],[21] and *rac*-4,12-bis(diphenylphosphane oxide)[2.2]paracyclophane [*rac*-**7**][5] were prepared according to literature protocols.

(R_p)- and (S_p)-4,12-Dibromo[2.2]paracyclophane [(R_p)-3 and (S_p)-3]: Separation of enantiomers by HPLC [chiral phase (semipreparative): CHIRALPAK IA; *n*-heptane/CH_2Cl_2 (90:10); f = 3.0 L min^{-1}; loading: 10 mg of racemic material per run]: R_t = 36.1 {(–)-(R_p)-**3**; $[\alpha]_D^{20}$ = –135.5 (c = 3.85 mg mL^{-1}, THF), >99.9% *ee*}, 39.2 {(+)-(S_p)-**3**; $[\alpha]_D^{20}$ = +133.4 (c = 3.75 mg mL^{-1}, THF), 99.8% *ee*} min. Suitable crystals for X-ray-diffraction analysis were grown from a mixture of dichloromethane and cyclohexane.

***rac*-4,12-Dihydroxy[2.2]paracyclophane [*rac*-4]:** *rac*-**3** (1.08 g, 2.80 mmol) was dissolved in anhydrous Et_2O (80 mL) and cooled to 0 °C, then *n*BuLi (2.5 M in hexane, 3.0 mL, 7.50 mmol) was slowly added by using a syringe. The solution was stirred for 1 h at 0 °C, then trimethyl borate (1.7 mL, 15.19 mmol) was added. The solution was warmed to room temperature and stirred for another 1 h, then aq. NaOH (0.5 M, 4.0 mL, 1.90 mmol) and H_2O_2 (35%, 3.0 mL, 30.38 mmol) were added and the solution was stirred for 30 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layers were washed with brine and dried with Mg_2SO_4. The solvents were evaporated and crude **4** was purified by column chromatography on silica gel (cyclohexane/ethyl acetate, 1:1 (v/v); R_f = 0.6), yield 0.568 g (2.36 mmol, 80%). The analytical data were in accordance with the literature data.[13]

Separation of Enantiomers: HPLC [chiral phase (semipreparative): CHIRALPAK IA; *n*-hexane/EtOH (75:25); f = 4.8 mL min^{-1}; loading: 40 mg of racemic material per run]: R_t = 7.10 {(–)-(S_p)-**4**; $[\alpha]_D^{20}$ = –117.0 (c = 3.44 mg mL^{-1}, THF), >99.9% *ee*}, 13.6 {(+)-(R_p)-**4**; $[\alpha]_D^{20}$ = +116.0 (c = 3.75 mg mL^{-1}, THF), >99.9% *ee*} min.

4,12-Diformyl[2.2]paracyclophane [*rac*-5]: *rac*-**3** (1.00 g, 2.73 mmol) was dissolved in anhydrous Et_2O (80 mL) and cooled to 0 °C, then *n*BuLi (2.5 M in hexane, 2.73 mL, 6.83 mmol) was slowly added by using a syringe. The solution was stirred for 1 h at 0 °C, then DMF (0.58 mL, 7.5 mmol) was added. The solution was warmed to room temperature and stirred for 1 h, then aq. HCl (4 M, 5.6 mL, 22.5 mmol) was added and the mixture was stirred for 2 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layers were washed with dilute aq. HCl, saturated $NaHCO_3$, and brine, and dried with Mg_2SO_4. The solvent was evaporated and the crude product was purified by column chromatography on silica gel [cyclohexane/ethyl acetate, 5:1 (v/v); R_f = 0.5], yield 0.600 g (2.27 mmol, 83%). The analytical data were in accordance with the literature data.[19]

Separation of Enantiomers: HPLC [chiral phase (semipreparative): CHIRALPAK IA; *n*-hexane/EtOH (75:25); f = 5.0 mL min^{-1}; loading: 20 mg of racemic material per run]: R_t = 13.3 {(+)-(S_p)-**5**; $[\alpha]_D^{20}$ = +90.0 (c = 5.70 mg mL^{-1}, THF), 99.7% *ee*}, 18.7 (–)-(R_p)-**5**; $[\alpha]_D^{20}$ = –90.5 (c = 5.30 mg mL^{-1}, THF), 99.9% *ee*} min.

(R_p)- and (S_p)-[2.2]Paracyclophane-4,12-dicarboxylic Acid [(R_p)- and (S_p)-(6)]: KO*t*Bu (0.337 g, 3.00 mmol) was dissolved in water (0.54 mL, 3.00 mmol) and THF (40 mL), and enantiomerically pure **8** (0.150 g, 0.25 mmol) was added. The resulting mixture was stirred overnight, then the THF was evaporated and water was added. The mixture was acidified with aq. HCl (2 M) and the white precipitate was filtered off and washed with water and Et_2O to give the enantiomerically pure target compound, yield 0.068 g (0.23 mmol, 92%).

Compound (+)-(S_p)-6: $[\alpha]_D^{20}$ = +149.0 (c = 4.15 mg mL^{-1}, EtOH).

Compound (–)-(R_p)-6: $[\alpha]_D^{20}$ = –150.0 (c = 4.00 mg mL^{-1}, EtOH).

(R_p)- and (S_p)-4,12-Bis(diphenylphosphane Oxide)[2.2]paracyclophane [(R_p)- and (S_p)-7]: Separation of enantiomers by HPLC [chiral phase (semipreparative): CHIRALPAK IA; *n*-hexane/2-propanol (90:10); f = 6.0 mL min^{-1}; loading: 10.5 mg of racemic material per run]: R_t = 9.4 {(–)-(R_P)-**7**; $[\alpha]_D^{20}$ = –105.0 (c = 2.00 mg mL^{-1}, ethanol), >99.9% *ee*}, 16.9 {(+)-(S_P)-**7**; $[\alpha]_D^{20}$ = +106.0 (c = 2.00 mg mL^{-1}, ethanol), >99.9% *ee*} min.

***rac*-Di(4-bromophenyl)[2.2]paracyclophane-4,12-dicarboxylate [*rac*-8]:** *rac*-**6** (0.400 g, 1.35 mmol) was dissolved in anhydrous Et_2O (60 mL) and oxalyl chloride (0.24 mL, 2.97 mmol) and one drop of DMF were added and the resulting mixture was stirred for 2 h at room temperature. The solvent was evaporated and anhydrous CH_2Cl_2 (10 mL) was added to the white residue. Triethylamine (10 mL) was added (the solution became red), then 4-bromophenol (0.584 g, 3.38 mmol) was added (the solution became yellow). The solution was stirred at room temperature overnight and then poured into ice water. The mixture was acidified and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were washed with saturated aq. $NaHCO_3$ and brine and dried with Mg_2SO_4. The product was obtained as a white powder. If required the product could be further purified by column chromatography on silica gel [cyclohexane/ethyl acetate, 2:1 (v/v); R_f = 0.8], yield 0.737 g (1.22 mmol, 90%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.88–2.96 (m, 2 H, 2-H, 10-H), 3.17–3.32 (m, 4 H, 1-H, 9-H), 4.15–4.21 (m, 2 H, 2-H, 10-H), 6.68 (d, $^3J_{8,7}$ = $^3J_{16,15}$ = 8.3 Hz, 2 H, 8-H, 16-H), 6.85 (dd, $^3J_{7,8}$ = $^3J_{15,16}$ = 8.3, $^4J_{7,5}$ = $^4J_{15,13}$ = 1.8 Hz, 2 H, 7-H, 15-H), 7.07 (d, ^3J = 8.90 Hz, 4 H, H-phenyl), 7.43 (d, $^4J_{5,7}$ = $^4J_{13,15}$ = 1.8 Hz, 2 H, 5-H, 13-H), 7.50 (d, ^3J = 8.90 Hz, 4 H, H-Ph) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 34.4 (C-1, C-9), 36.2 (C-2, C-10), 119.2 (C-21), 123.8 (C-19), 129.5 (C-4, C-12), 132.7 (C-20), 134.1 (C-5, C-13), 136.6 (C-8, C-16), 137.4 (C-7, C-15), 140.8 (C-6, C-14), 143.7 (C-3, C-11), 150.0 (C-18), 165.0 (C-17) ppm. MS (EI): *m/z*

(%) = 606.0 (15) $[C_{30}H_{22}Br_2O_4]^+$, 433.0 (80) $[C_{24}H_{18}BrO_3]^+$, 131.0 (100) $[C_9H_7O]^+$. $C_{30}H_{22}Br_2O_4$ (606.30): calcd. C 59.43, H 3.66; found C 59.35, H 4.01.

Separation of Enantiomers: HPLC [chiral phase (semipreparative): CHIRALPAK IA; *n*-hexane/EtOH (90:10); f = 5.0 mL min^{-1}; loading: 30 mg of racemic material per run]: R_t = 18.1 {(–)-(S_p)-**8**; $[a]_D^{20}$ = –59.0 (c = 5.30 mg mL^{-1}, THF), >99.9% *ee*}, 27.4 {(+)-(R_p)-**8**; $[a]_D^{20}$ = +58.0 (c = 5.85 mg mL^{-1}, THF), >99.9% *ee*} min.

(S_p)-4,12-Di[(4-bromophenyl)hydrazone][2.2]paracyclophane [(S_p)-9]: 4-Bromohydrazine (0.45 g) was dissolved in conc. H_2SO_4 (2 mL) and water (3 mL), EtOH (10 mL) was added and the precipitate was filtered off. Compound (S_p)-**5** (0.100 g, 0.273 mmol) was dissolved in CH_2Cl_2 (2 mL) and added to the 4-bromohydrazine solution. After standing at room temperature overnight a precipitate was formed that was filtered off and washed with water and EtOH. The crude product was recrystallized from EtOH as brownish needles that were suitable for X-ray diffraction analysis. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.86–2.93 (m, 2 H, 2-H, 10-H), 2.97–3.04 (m, 2 H, H-, 9-H), 3.15–3.21 (m, 2 H, 1-H, 9-H), 3.78–3.83 (m, 2 H, 2-H, 10-H), 6.53 (m, 4 H, 8-H, 16-H, 7-H, 15-H), 6.89 (s, 2 H, 5-H, 13-H), 6.93 (d, ^3J = 9.0 Hz, 2 H, H-Ph), 6.30 (d, ^3J = 9.0 Hz, 2 H, H-Ph), 7.60 (s, 2 H, CHN) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]-DMSO): δ = 33.1 (C-2, C-10), 34.3 (C-1, C-9), 109.3 [C-Ph(Br)], 113.8 (C-Ph), 131.0 (C-6*, C-14*), 131.4 (C-4* C-12*), 131.9 (C-Ph), 132.1 (C-3*, C-11*), 135.7 (C-8, C-16), 137.1 (C-5, C-13), 137.8 (C-7, C-15), 139.6 [C-Ph(NH)], 144.8 (C-CHN) ppm {*: assignment might be interchanged}. MS (ESI): m/z (%) = 601.06 (60) $[C_{30}H_{26}Br_2N_4 + H]^+$, 623.0 (100) $[C_{30}H_{26}Br_2N_4 + Na]^+$.

(R_p)- and (S_p)-4,12-Di(trifluoromethylsulfonyl)[2.2]paracyclophane [(R_p)- and (S_p)-10]: Enantiomerically pure **4** (0.21 g, 0.89 mmol) was dissolved in anhydrous triethylamine (1.2 mL, 8.86 mmol) and anhydrous CH_2Cl_2 (24 mL). The solution was cooled to –78 °C and triflic anhydride (0.4 mL, 2.28 mmol) was added slowly by using a syringe. The reaction mixture was warmed to room temperature, then the solution was acidified with aq. HCl (2 M) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL) and the combined organic layers were washed with saturated $NaHCO_3$ and brine, and dried with $MgSO_4$. The solvents were evaporated and the crude product was purified by column chromatography on silica gel [cyclohexane/ethyl acetate, 2:1 (v/v); R_f = 0.6], yield 0.357 (0.71 mmol, 80%). Suitable crystals for X-ray diffraction analysis were grown from a mixture of cyclohexane and ethyl acetate. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.80–2.88 (m, 2 H, 1-H, 9-H), 3.10–3.14 (m, 4 H, 2-H, 10-H), 3.41–3.47 (m, 2 H, 1-H, 9-H), 6.59–6.61 (m, 4 H, 5-H, 7-H, 13-H, 15-H), 6.67 (d, $^3J_{8,7}$ = $^3J_{16,15}$ = 7.7 Hz, 2 H, 8-H, 16-H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 31.3 (C-2, C-10), 33.3 (C-1, C-9), 118.6 [CF_3, $^1J_{C,F}$ = 320 Hz], 124.3 (C-5, C-13), 132.0 (C-3, C-11), 133.1 (C-7, C-15), 136.4 (C-8, C-16), 143.2 (C-6, C-14), 148.3 (C-4, C-12) ppm. MS (ESI): m/z (%) = 527.0 (100) $[C_{18}H_{14}F_6O_6S_2 + Na]^+$. $C_{18}H_{14}F_6O_6S_2$ (504.42): calcd. C 42.69, H 2.91, S 12.67; found C 42.86, H 2.80, S 12.71.

Compound (–)-(S_p)-10: $[a]_D^{20}$ = –20.0 (c = 4.33 mg mL^{-1}, THF).

Compound (+)-(R_p)-10: $[a]_D^{20}$ = +21.0 (c = 4.81 mg mL^{-1}, THF).

(R_P)- and (S_P)-4,12-Diethynyl[2.2]paracyclophane [(R_P)- and (S_P)-(11)]: Enantiomerically pure **5** (0.500 g, 1.89 mmol) and Cs_2CO_3 (2.407 g, 7.56 mmol) were suspended in anhydrous MeOH (40 mL) and the Bestmann–Ohira reagent (1.390 g, 7.56 mmol) was added. The resulting mixture was stirred for 24 h at room temperature, then CH_2Cl_2 and water were added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic layers were washed with brine and dried with $MgSO_4$. The solvent was evaporated and the crude product was purified by column chromatography on silica gel (ethyl acetate/cyclohexane, 5%; R_f = 0.8) to give the product as a light-yellow powder, yield 0.410 g (1.61 mmol, 85%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.79–2.86 (m, 2 H, 2-H, 10-H), 3.01–3.07 (m, 2 H, 1-H, 9-H), 3.12–3.19 (m, 2 H, 1-H, 9-H), 3.29 (s, 2 H, 18-H, 20-H), 3.55–3.62 (m, 2 H, 2-H, 10-H), 6.50 (d, $^3J_{8,7}$ = $^3J_{16,15}$ = 7.6 Hz, 2 H, 8-H, 16-H), 6.55 (dd, $^3J_{7,8}$ = $^3J_{15,16}$ = 7.6, $^4J_{7,5}$ = $^4J_{15,13}$ = 1.7 Hz, 2 H, 7-H, 15-H), 7.07 (d, $^4J_{5,7}$ = $^4J_{13,15}$ = 1.7 Hz, 2 H, 5-H, 13-H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 33.3 (C-1, C-9), 34.1 (C-2, C-10), 80.4 (C-18, C-20), 83.4 (C-17, C-19), 123.6 (C-4, C-12), 133.5 (C-7*, C-15*), 133.5 (C-8*, C-16*), 134.4 (C-5, C-13), 139.6 (C-6, C-14), 142.7 (C-3, C-11) ppm {*: assignment might be interchanged}. MS (EI): m/z (%) = 256.2 (96) $[C_{20}H_{16}]^+$, 128.1 (100) $[C_{10}H_8]^+$. $C_{20}H_{16}$ (256.34)·0.5H_2O: calcd. C 90.53, H 6.46; found C 90.97, H 6.43. The analytical data are in accordance with the reported data for the racemic compound.[19]

Compound (+)-(S_p)-11: $[a]_D^{20}$ = +50.0 (c = 1.80 mg mL^{-1}, THF).

Compound (–)-(R_p)-11: $[a]_D^{20}$ = –49.0 (c = 2.14 mg mL^{-1}, THF).

***rac*-4,12-Diiodo[2.2]paracyclophane [*rac*-12]:** *rac*-**3** (0.800 g, 2.19 mmol) was dissolved in anhydrous Et_2O (40 mL) and cooled to 0 °C, then *n*BuLi (2.5 M in hexanes, 2.19 mL, 5.46 mmol) was slowly added by using a syringe and the solution was stirred for 1 h. Iodine (1.67 g, 6.57 mmol) was added, then the solution was warmed to room temperature and stirred for 2 h. The reaction mixture was diluted with CH_2Cl_2 and water and the layers separated. The organic layer was washed with Na_2SO_3, water, and brine, and dried with $MgSO_4$. The solvent was evaporated and the crude product was purified by column chromatography on silica gel (ethyl acetate/cyclohexane, 5%; R_f = 0.7) to give the product as a light-yellow powder, yield 0.867 g (1.88 mmol, 86%). Suitable crystals for X-ray diffraction analysis were grown from a mixture of dichloromethane and cyclohexane. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.88–2.99 (m, 4 H, 1-H, 9-H), 3.01–3.13 (m, 2 H, 2-H, 10-H), 3.34–3.46 (m, 2 H, 2-H, 10-H), 6.49 (d, $^3J_{8,7}$ = $^3J_{12,13}$ = 7.6 Hz, 2 H, 8-H, 16-H), 6.55 (dd, $^3J_{7,8}$ = $^3J_{13,12}$ = 7.6, $^4J_{7,5}$ = $^4J_{13,15}$ = 1.7 Hz, 2 H, 7-H, 15-H), 7.50 (d, $^4J_{5,7}$ = $^4J_{15,13}$ = 1.7 Hz, 2 H, 5-H, 13-H) ppm. ^{13}CNMR (100.6 MHz, $CDCl_3$): δ = 33.2 (C-1, C-9), 39.3 (C-2, C-10), 103.8 (C-4, C-12), 132.5 (C-7, C-15), 133.8 (C-8, C-16), 138.6 (C-5, C-13), 140.5 (C-6, C-14), 142.5 (C-3, C-11) ppm. MS (EI): m/z (%) = 360.0 (50) $[C_{16}H_{14}I_2]^+$, 230.0 (100) $[C_8H_7I]^+$. $C_{16}H_{14}I_2$ (460.09)·1/6hexane: calcd. C 43.13, H 3.26; found C 42.89, H 3.57.

Separation of Enantiomers: HPLC [chiral phase (semipreparative): CHIRALPAK IA; *n*-hexane/EtOH (90:10); f = 3.0 mL min^{-1}; loading: 10 mg of racemic material per run]: R_t = 38.48 {(–)-(R_p)-**10**; $[a]_D^{20}$ = –231.4 (c = 5.95 mg mL^{-1}, THF), >99.9% *ee*}, 41.97 {(+)-(S_p)-**10**; $[a]_D^{20}$ = +229.8 (c = 7.10 mg mL^{-1}, THF), 99.4% *ee*} min.

***rac*-4,12-Di(4-methoxyphenyl)[2.2]paracyclophane [*rac*-13]:** A round-bottom flask with reflux condenser under inert gas was charged with *rac*-**12** (0.500 g, 1.075 mmol), 4-methoxyphenyl boronic acid (0.370 g, 2.4 mmol), K_3PO_4 (3.370 g, 6.45 mmol), $Pd_2(dba)_3$·$CHCl_3$ (0.050 g, 0.05 mmol), and tricylcohexylphosphane (0.056 g, 0.20 mmol). 1,4-Dioxane (15 mL) and water (1.5 mL) were added and the degassed suspension was heated to reflux and stirred for 72 h. The reaction was quenched by addition of saturated aq. EDTA and saturated aq. Na_2CO_3. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The combined organic layers were dried with $MgSO_4$ and the solvents were evaporated. The crude product was purified by column chromatography on silica gel [cyclohexane/ethyl acetate, 4:1 (v/v); R_f = 0.5], yield 0.443 (1.05 mmol, 98%). ^{1}H NMR

(400.1 MHz, $CDCl_3$): δ = 2.69–2.76 (m, 2 H, H-1, H-9), 2.89–2.97 (m, 2 H, H-2, H-10), 3.06–3.12 (m, 2 H, H-1, H-9), 3.49–3.55 (m, 2 H, H-2, H-10), 3.87 (6 H, OMe), 6.60 (m, 4 H, H-7, H-15, H-5, H-13), 6.70 (d, $^4J_{8,7} = {}^4J_{16,15}$ = 8.2 Hz, 2 H, H-8, H-16), 6.94 (d ^3J = 8.7 Hz, 4 H, H-Ph), 7.28 (d, ^3J = 8.7 Hz, 4 H, H-Ph) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 34.6 (C-1, C-9)*, 34.6 (C-2, C-10)*, 55.5 (OMe), 113.9 (C-19), 130.0 (C-5, C-13), 130.3 (C-18), 131.8 (C-7, C-15), 133.9 (C-17), 135.6 (C-8, C-16), 136.9 (C-6, C-14), 139.7 (C-3, C-11), 140.2 (C-4, C-12), 158.7 (C-20) ppm {*: assignment might be interchanged}. MS (EI): *m/z* (%) = 420.3 (50) $[C_{30}H_{28}O_2]^+$, 211.1 (100) $[C_{15}H_{14}O]^+$. $C_{30}H_{28}O_2$ (420.54)·$^1/_3H_2O$: calcd. C 84.47, H 6.77; found C 84.50, H 6.91.

***rac*-4,12-Di(4-hydroxyphenyl)[2.2]paracyclophane [*rac*-14]:** *rac*-**13** (0.200 g, 0.47 mmol) was dissolved in anhydrous CH_2Cl_2 (20 mL) and cooled to –78 °C, then boron tribromide (1 M in CH_2Cl_2, 2.82 mL, 2.82 mmol) was added and the solution was warmed to room temperature. Water (100 mL) and CH_2Cl_2 (100 mL) were added and the solution was neutralized with aq. NaOH (6 M). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was evaporated. The crude product was purified by column chromatography on silica gel [cyclohexane/ethyl acetate, 2:1 (v/v); R_f = 0.4], yield 0.184 (0.47 mmol, 99%). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.71–2.77 (m, 2 H, H-1, H-9), 2.89–2.97 (m, 2 H, H-2, H-10), 3.06–3.12 (m, 2 H, H-1, H-9), 3.47–3.54 (m, 2 H, H-2, H-10), 5.42 (H, OH), 6.59 (m, 4 H, H-7, H-15, H-5, H-13), 6.69 (d, $^4J_{8,7} = {}^4J_{16,15}$ = 8.1 Hz, 2 H, H-8, H-16), 6.86 (d, ^3J = 8.7 Hz, 4 H, H-Ph), 7.21 (d, ^3J = 8.7 Hz, 4 H, H-Ph) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 34.5 (C-1, C-9)*, 34.5 (C-2, C-10)*, 115.4 (C-19), 130.0 (C-5, C-13), 130.5 (C-18), 131.9 (C-7, C-15), 134.0 (C-17), 135.6 (C-8, C-16), 136.9 (C-6, C-14), 139.7 (C-3, C-11), 140.1 (C-4, C-12), 154.7 (C-20) ppm {*: assignment might be interchanged}. MS (ESI): *m/z* (%) = 393.2 (80) $[C_{28}H_{24}O_2$ + H$]^+$, 415.2 (100) $[C_{28}H_{24}O_2$ + Na$]^+$. $C_{28}H_{24}O_2$ (392.49)·EtOH: calcd. C 82.16, H 6.89; found C 82.72, H 6.85.

Separation of Enantiomers: HPLC [chiral phase (semipreparative): CHIRALPAK IA; *n*-hexane/2-propanol (90:10); f = 8.0 mL min^{-1}; loading: 30 mg of racemic material per run]: R_t = 13.0 {(–)-(S_p)-**14**; $[\alpha]_D^{20}$ = –139.4 (c = 5.25 mg mL^{-1}, THF), 99.5% *ee*}, 16.9 {(+)-(R_p)-**14**; $[\alpha]_D^{20}$ = +142.0 (c = 5.70 mg mL^{-1}, THF), 99.3% *ee*} min.

(R_p)- and (S_p)-4,12-Di(4-trifluoromethylsulfonylphenyl)[2.2]paracyclophane [(R_p)- and (S_p)-15]: Enantiomerically pure **14** (0.110 g, 0.28 mmol) was dissolved in anhydrous CH_2Cl_2 (20 mL) and triethylamine (0.39 mL, 2.80 mmol) was added. The solution was cooled to –78 °C and triflic anhydrate was added by using a syringe. After complete addition, the solution was warmed to room temperature, then aq. HCl (2 M) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL) and the combined organic layers were washed with saturated $NaHCO_3$ and brine, and dried with $MgSO_4$. The solvent was evaporated to give **15** as a light-yellow powder, yield 0.155 g (0.24 mmol, 86%). Suitable crystals for X-ray diffraction analysis were grown from a mixture of dichloromethane and cyclohexane. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.75–2.82 (m, 2 H, H-1, H-9), 2.99–3.06 (m, 2 H, H-2, H-10), 3.13–3.20 (m, 2 H, H-1, H-9), 3.41–3.47 (m, 2 H, H-2, H-10), 6.49 (d, $^4J_{5,7} = {}^4J_{15,13}$ = 1.7 Hz, 2 H, H-5, H-13), 6.69 (dd, $^3J_{7,8} = {}^3J_{13,12}$ = 7.7, $^4J_{7,5} = {}^4J_{13,15}$ = 1.7 Hz, 2 H, H-7, H-15), 7.50 (d, $^3J_{8,7} = {}^3J_{12,13}$ = 7.7 Hz, 2 H, H-8, H-16), 7.28–7.33 (m, 8 H, H-Ph) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 34.0 (C-2, C-10), 34.6 (C-1, C-9), 118.8 ($^1J_{C,F}$ = 321 Hz, CF_3), 121.6 (C-19)*, 130.2 (C-5, C-13), 130.7 (C-18)*, 133.3 (C-7, C-15), 135.9 (C-8, C-16), 137.2 (C-3, C-11), 138.6 (C-4, C-12), 139.9 (C-6, C-14), 141.6 (C-17), 148.6 (C-20) ppm {*: assignment might be interchanged}. MS (EI): *m/z* (%) = 656.0 (60) $[C_{30}H_{28}F_6O_6S_2]^+$, 523.0 (55) $[C_{29}H_{22}F_3O_4S]^+$, 329.0 (40) $[C_{15}H_{14}F_3O_3S]^+$, 179.1 (100) $[C_{14}H_{11}]^+$.

Table 1. Crystallographic data.

	(–)-(R_P)-**3**	(S_P)-**9**	(+)-(R_P)-**10**	(+)-(S_P)-**12**	(+)-(R_P)-**15**
Formula	$C_{16}H_{14}Br_2$	$C_{30}H_{26}Br_2N_4$	$C_{18}H_{14}F_6O_6S_2$	$C_{16}H_{14}I_2$	$C_{30}H_{22}F_6O_6S_2$
M_r	366.09	602.37	504.41	460.07	656.60
T [K]	123(2)	123(2)	123(2)	123(2)	123(2)
Crystal system	trigonal	monoclinic	monoclinic	orthorhombic	orthorhombic
Space group	$P3_1$	$P2_1$	$P2_1$	$P2_12_12$	$P2_12_12_1$
Crystal dimensions [mm]	0.32 × 0.08 × 0.06	0.71 × 0.25 × 0.04	0.13 × 0.10 × 0.02	0.42 × 0.01 × 0.08	0.30 × 0.09 × 0.05
a [Å]	12.202(6)	7.7215(5)	9.5285(5)	9.2171(3)	11.6991(4)
b [Å]	12.202(6)	13.5762(13)	9.2964(7)	9.2171(3)	17.3170(8)
c [Å]	7.810(4)	24.743(2)	12.6058(8)	17.1385(4)	42.001(2)
α [°]	90	90	90	90	90
β [°]	90	93.823(3)	111.984(4)	90	90
γ [°]	120	90	90	90	90
V [Å^3]	1007.0(18)	2588.0(4)	1035.41(12)	1456.00(5)	8509.2(6)
Z	3	4	2	4	12
ρ [mg m^3]	1.811	1.546	1.618	2.099	1.538
μ [mm^{-1}]	6.016	3.159	0.345	4.300	0.272
θ range [°]	3.24–25.22	1.71–28.00	2.80–28.00	2.21–27.98	2.86–28.00
Completeness [%]	95.3	99.6	96.9	99.5	98.8
Reflections measured	6695	20149	6775	175175	65319
Unique/observed	2299/1308	11266/7690	4135/3703	3482/3334	19877/10607
Reflections (R_{int})	(0.1577)	(0.0388)	(0.0398)	(0.0664)	(0.1584)
Data/restrains/parameters	2299/19/163	11266/19/649	4135/1/289	3482/96/140	19877/104/1189
GoF on F^2	0.917	0.952	1.080	1.036	0.895
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0803	R_1 = 0.0419	R_1 = 0.0518	R_1 = 0.0362	R_1 = 0.0670
	ωR_2 0.1270	ωR_2 = 0.0727	ωR_2 = 0.1346	ωR_2 = 0.0861	ωR_2 0.1333
R indices all data	R_1 = 0.1296	R_1 = 0.0834	R_1 = 0.0582	R_1 = 0.0390	R_1 = 0.1291
	ωR_2 0.1390	ωR_2 = 0.0855	ωR_2 = 0.1378	ωR_2 = 0.0881	ωR_2 = 0.1544
Absolute structure parameter X	0.03(3)	–0.001(7)	0.07(12)	0.01(6)	0.02(8)

$C_{30}H_{28}F_6O_6S_2$ (565.61)·$^1/_3NEt_3$: calcd. C 55.67, H 3.94; found C 55.66, H 4.39.

Compound (–)-(S_p)-15: $[a]_D^{20}$ = –83.0 (c = 5.44 mg mL^{-1}, THF).

Compound (+)-(R_p)-15: $[a]_D^{20}$ = +84.0 (c = 4.05 mg mL^{-1}, THF).

Crystal Structure Determinations: X-ray crystallographic analyses of (–)-(R_p)-**3**, (S_p)-**9**, (+)-(R_p)-**10**, and (+)-(S_p)-**12**: Data were collected with a Nonius KappaCCD diffractometer equipped with a low-temperature device (Cryostream, Oxford Cryosystems, 600er series) using graphite-monochromated Mo-K_α radiation (λ = 0.71071 Å). X-ray crystallographic analysis of (+)-(R_p)-**15**: Data set was collected with an STOE IPDS2T with a low-temperature device (Cryostream, Oxford Cryosystems, 700er series) using graphite monochromatic Mo-K_α radiation (λ = 0.71071 Å). The structures were solved by direct methods (SHELXL-97) and refined by full-matrix least-squares on F^2 (SHELXL-97).[31] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms at carbon were placed in calculated positions and refined isotropically using a riding model. Crystal structures were edited with Mercury 3.0 or Diamond 3.0. For selected details of the crystallographic data see Table 1.

CCDC-927319 [for (–)-(R_p)-**3**], 927320 [for (S_p)-**9**], 927321 [for (+)-(R_p)-**10**], 927322 [for (+)-(S_p)-**12**], and 927323 [for (+)-(R_p)-**15**] contain the supplementary data for these structures. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): NMR spectra of new compounds **8**–**10** and **12**–**15** and chromatographic resolutions of racemic **3**, **5**, **7**, **8**, **12**, and **14**.

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