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Introduction of Axial Chirality at a Spiro Carbon Atom in the Synthesis of a Pentaerythritol – Imine Macrocycles

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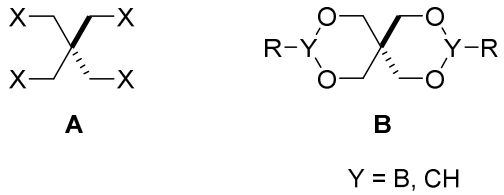
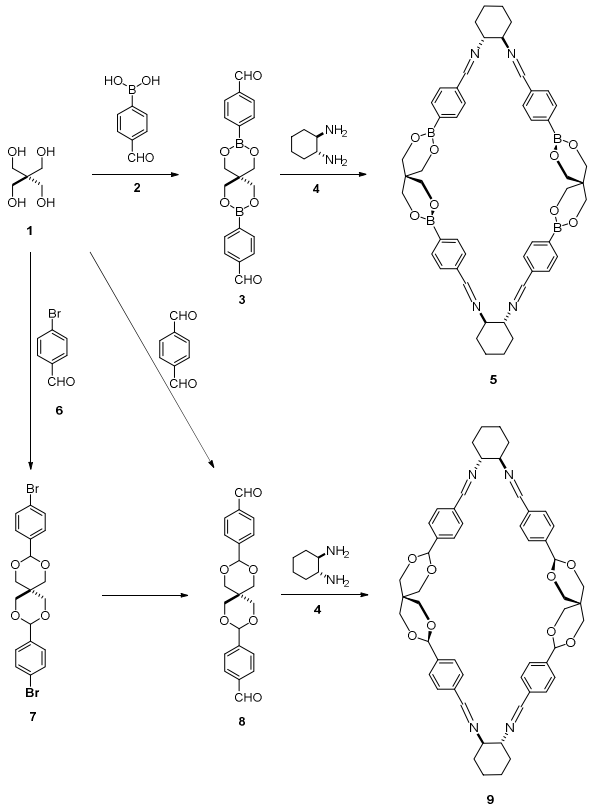
Novel chiral macrocyclic polyimines with spiro carbon atoms are described. The key feature of the synthesis is the formation of an axially chiral quaternary carbon atom having four constitutionally identical substituents. This is possible either by freezing of the labile conformation of a spiro-diboronate moiety or by diastereomeric fitting of a conformationally stable spiro-acetal moiety into a chiral framework. A general model for the description of this type of axial chirality is proposed.

Introduction

Chirality of organic molecules having a quaternary carbon atom substituted with four constitutionally identical groups can be achieved when the groups are diversified by their conformations. Whereas 2,2-dimethylpropane is achiral (T_d point group), chirality of its simple tetrasubstituted derivatives **A**, such as pentaerythritol (**1**) (X = OH), is not usually discussed, as it cannot be readily demonstrated for obvious reasons: the molecules exist as a mixture of achiral and chiral conformers, the latter as racemates. There are possible eight unique conformational permutations of the structure of **A**, including enantiomers. (see Fig. S1 of Electronic Supporting Information ESI) The idea of chiral discrimination of conformers of **A** can be brought to practice by limiting the number of accessible conformers and converting enantiomeric structures into diastereoisomers.

Diboronate (Y = B) and diacetal (Y = CH) derivatives **B** of pentaerythritol can provide a ready solution to this challenging problem. Formation of five or six-membered boronate rings from the corresponding 1,2- or 1,3-diols and boronic acids (or boroxines) are reversible reactions and proceed under thermodynamic control.[1] In fact, this and several other reactions, like imine formation,[2] provide foundation for dynamic covalent chemistry.[3] The utilization of boron and imine compounds as building blocks for the construction of macrocyclic two- and three-dimensional assemblies is currently a leading topic in supramolecular chemistry. While





Scheme 1. Synthesis of macrocycles **5** and **9**.

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.† Electronic Supplementary Information (ESI) available: NMR and MS spectra of ***3***, ***5***, ***8*** and ***9***, and description of the crystal structure of ***9***. See DOI: 10.1039/x0xx00000x

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the macrocyclic polyimines are used in the design of specific ligands, in inclusion and coordination chemistry,[4] and enantioselective catalytic reactions,[5] the borate based supramolecular architectures can be employed in applications including sensors, catalysts (nanoreactors), nano architectures, separation and delivery.[6]

Recently macrocyclic tetraol diboronates were shown to be the products of crystallization-induced dynamic self-assembly and demonstrated their potential for crystallization-based separations based on inclusion phenomena.[7] Self-assembly of molecular capsules was achieved by dynamic boronate ester formation.[8] Spiro diacetal macrocyclic compounds with polyglycol chain in macrocyclic structure were synthesized by irreversible, non-stereoselective reaction and the presence of both stable enantiomers was proven by HPLC.[9] Partial separation of enantiomers of pentaerythritol diacetals of different substituted benzaldehydes was also performed with HPLC.[10] Pathways and structural constraints for the efficient construction of imine-based macrocycles have been developed.[11,12] A combination of diol, boronic acid, aldehyde and amine functionalities has been used for condensation-based macrocyclizations.[13] Taking advantage of general synthetic utility of multicomponent macrocyclizations[14] and building on the dynamic covalent nature of both B–O and C=N bonds a methodology for the construction of pentaerythritol-based macrocycles and cages has been devised.[15]

In this report, we describe the synthesis of the first enantiomerically pure boronate–imine macrocycle **5** and the corresponding cyclic acetal macrocycle **9** (Scheme 1) in which the pentaerythritol derived structural units are of defined chirality.

Results and discussion

Synthesis

Reaction of pentaerythritol (**1**) with 4-formylphenylboronic acid **2** in THF at room temperature yielded bis-boronate **3** which was then reacted with (*R*,*R*)-1,2-diaminocyclohexane (**4**) in toluene. Macrocycle **5** was the only isolated product (yield 82% in reaction of **3** and **4** or 66% in one pot reaction) and the yield of **5** was essentially the same when all substrates were allowed to react in a one-step reaction both in solution and in the solid state using grinder mill (some byproducts were observed by the NMR spectra, apparently as a consequence of competing Petasis type reaction of aldehyde, boronic acid and amine).

Direct synthesis of **8** was performed by the reaction of acetal forming reaction in a moderate yield (30%). The reaction mixture contained also oligo- and polymeric products difficult to separate. Indirect, two step synthesis of **8** by reaction of **1** with *p*-bromobenzaldehyde (**6**) followed by formylation of aromatic rings gave a better overall yield of **8** (68%) and the product was easier to separate. Reaction of **8** with (*R*,*R*)-1,2-diaminocyclohexane (**4**) in toluene yielded macrocycle **9** in a mixture of other products of imine condensation with 98% conversion. The amount of (*R*,*R*)-**9** in reaction mixture was 30% as estimated from ^{1}H NMR spectra. As only one of two enentiomers of **8** can form diastereomeric macrocycle with enantiopure **4** the yield calculated on the base of **8** is doubled.

Structural analysis

Structure of imine-boronate macrocycle **5** was established with the aid of MS (M^+ = 884), indicating a [2+2+4] cyclocondensation of **1**, **4**, and **2**. ^{1}H NMR spectrum of **5** showed characteristic singlet of CH=N protons at 7.95 ppm and two geminally split (J = 11.4 Hz) signals at 3.98 and 4.18 ppm due to CH_2O protons, in addition to typical signals of *p*-phenylene and substituted cyclohexane protons. ^{13}C NMR spectrum of **5** also shows one signal due to CH_2O carbons at 64.9 ppm and is otherwise quite simple (11 signals); both spectra indicate D_2 symmetry of the macrocycle. Diastereotopic signals of the CH_2O groups are evidently due to a rigid structure of the pentaerythritol diboronate moiety in **5**, resulting in lowering of symmetry, in contrast to the ^{1}H NMR spectra of non-macrocyclic, conformationally unrestricted diboronate **3**, in which signals of the CH_2O protons and carbons appear as singlets, correspondingly at 4.11 and at 64.9 ppm.

Structure of imine-acetal macrocycle **9** was established with the aid of MS (M^+ = 893), indicating a [2+2] cyclocondensation of **8**, and **4** and was confirmed by a single-crystal X-ray analysis. ^{1}H NMR spectrum of **9** showed characteristic singlet of CH=N protons at 8.14 ppm and four geminally split groups of signals from 3.59 to 4.75 ppm due to CH_2O protons in rigid cyclic structure. This structure is stabilized by intramolecular interaction between one of the equatorial CH_2O (4.74 ppm) protons and oxygen atom from the neighbouring hexamembered ring in the spiro bicyclic system. The HSQC spectrum of **9** shows signals that proves direct connection of protons at 4.78 and with carbon at 70.88 ppm and protons at 3.79 and 3.59 ppm with carbon at 70.46 ppm which is in agreement with their coupling constants in ^{1}H NMR spectrum.(2 D spectra can be found in SI). In addition to typical signals of *p*-phenylene and substituted cyclohexane protons. ^{13}C NMR spectrum of **9** also shows two signals due to CH_2O carbons at 70.5 and 70.9 ppm. As in macrocycle **5** both NMR spectra indicate D_2 symmetry of the macrocycle **9,** however the calculated conformer of the lowest energy has only C_2 symmetry and only C_1 symmetrical conformer of **9** can be found in the crystal structure.

Electronic circular dichroism (ECD) spectra of **5** and **9** (Figure 1) provide an evidence of diequatorial positions of the C=N bonds in the cyclohexane rings. This is in general agreement with others diaiminocyclohexane-based macrocyclic polyimines which displays similar pattern of Cotton effects (CE). An exciton type negative CE (Δε -26.2 at 270 nm, +20.5 at 248 nm for **5** and Δε -63.2 at 257 nm, +70.3 at 237 nm for **9**) due to the π-π* transitions within the substituted phenylimine chromophores indeed reflects a negative helicity of the vicinal C=N bonds in both macrocycles. Whereas phenylimine

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chromophores attached to one cyclohexane ring are separated 5.5 Å (phenyl rings centroid to centroid distance, see Supporting Information), the chromophores attached to two different rings are at much longer distance (at least 12.0 Å) and hence their exciton coupling is negligible. Similar negative exciton Cotton effects of (*R*,*R*)-1,2-diaminocyclohexane based diimines were previously measured. In the case of **5** an interesting observation is a red shift (*ca*. 15 nm) of the UV and ECD maxima, compared to the corresponding data for the known unsubstituted (*R*,*R*)-*N*,*N*'-bis(phenylmethylene)-1,2-cyclohexanediamine (ε 30 200 at 241 nm; Δε -88.4 at 255 nm, +72.7 at 236 nm). This is apparently due to electron deficient character of the boronic substituent in *para* position.

A detailed structure of **5** and **9** was obtained by molecular modelling using Gaussian suite of programs,[16] initially with the use of Parameterization Method 6 (PM6). Subsequently, the calculated lowest energy conformers were refined by DFT (B3LYP/631**) method. For both compounds ECD spectra were calculated by DFT (B3LYP/631**) method with 120 excited states taken into account due to large number of chromophores (calculated spectra were not scaled to fit the experimental spectra). Both spectra calculated for **5** and **9** showed the same sequence of CE's -/+, what is in good agreement with those obtained by ECD measurements.

The *P* diastereoisomer of **9** which was not found in the reaction mixture was also calculated and its CD spectrum was calculated in the same way as for the other macrocycles. Due to the similar arrangement of phenylimine chromophores the spectrum is similar to its *M*-diastereoisomer and shows a negative helicity of the vicinal C=N bonds in both macrocycles. The spiro linkers separate the chromophores to the distance that lowers their interactions and results in only minor changes visible at calculated CD spectrum.

In a commonly accepted procedure, the calculated spectra are compared with the spectra measured in one of the nonpolar aprotic solvents. However, due to the lack of solubility of **5** and **9** in any of this type of solvents the calculated spectra were directly compared with those measured in acetonitrile. Such approach can be justified by relatively high rigidity of the examined macrocycles, what makes their conformation independent on the solvent. For both macrocycles C_2 symmetry structure was obtained (Figure 2), compatible with the spectral data mentioned earlier. In contrast, the macrocycle **9** in crystal (Figure 2) does not possess the two-fold symmetry and displays more irregular shape presumably resulting from strong C-H···O intermolecular interactions that lead to partial interpenetration of the neighbouring macrocycles. For details concerning comparison of molecular conformation *in silico* and in the solid state, and intermolecular interactions in the crystals of **9** (see Tables S1 and S2, and Figs S2, S3 and S4 in ESI). Otherwise, the macrocycle of **9** maintains in crystal the basic structural features of the isolated molecule that can be described as follows. The macrocycle possesses *trans* imine bonds, equatorial C-N bonds, acetal rings in chair conformations and an *M*-helical arrangement of CH_2O groups around each of the two quaternary carbon atoms.

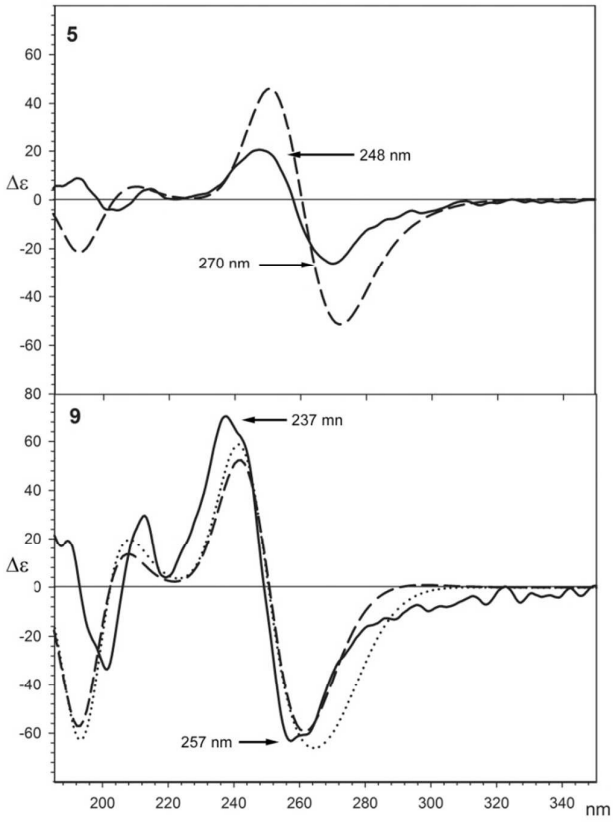

Figure 1. ECD spectra of macrocycles **5** (upper panel) and **9** (lower panel) measured in acetonitrile solution (solid linens), calculated (dashed lines) and calculated *P* diastereomer of **9** (dotted lines).

As it follows from our theoretical calculations, the diastereomeric *P*-helical diboronate spirane of **5** would be of much higher energy and therefore it was not obtained in the macrocyclization reaction. This stereoisomer tends to form a helix rather than a macrocycle (see Fig. S6 of ESI).

Configuration of the spiro system build of four constitutionally identical groups is simply described according to Figure 3. The helicity can be described by a sign of either of the two O-CH_2-C(spiro)-CH_2 torsion angles involving oxygen atoms that are at the closest distance but belong to separate rings. In a *P*-helical structure each of the two torsion angles has a positive sign and negative in an *M*-helical structure. As a consequence of planar O-B-O bonds in **5** the boronate rings are in sofa rather than chair conformation and the neighbouring aromatic rings are nearly coplanar with the O-B-O fragments (Fig. 2 (top)).

The selective formation of [2+2] rather than [3+3] cyclocondensation product can be readily rationalized by the use of connecting unit **3** or **8** having a bent structure, as previously reported for rhombimines obtained from **4** and non-linear dialdehydes.[11d,e,17] With linear connecting units (dialdehydes) and **4**, trianglimine products are formed nearly exclusively under thermodynamic conditions.[11a,b,18]

A case of chiral spiro-diboronate macrocycle was recently reported but its structure was not analysed in terms of induced axial chirality. The molecule which induced chirality

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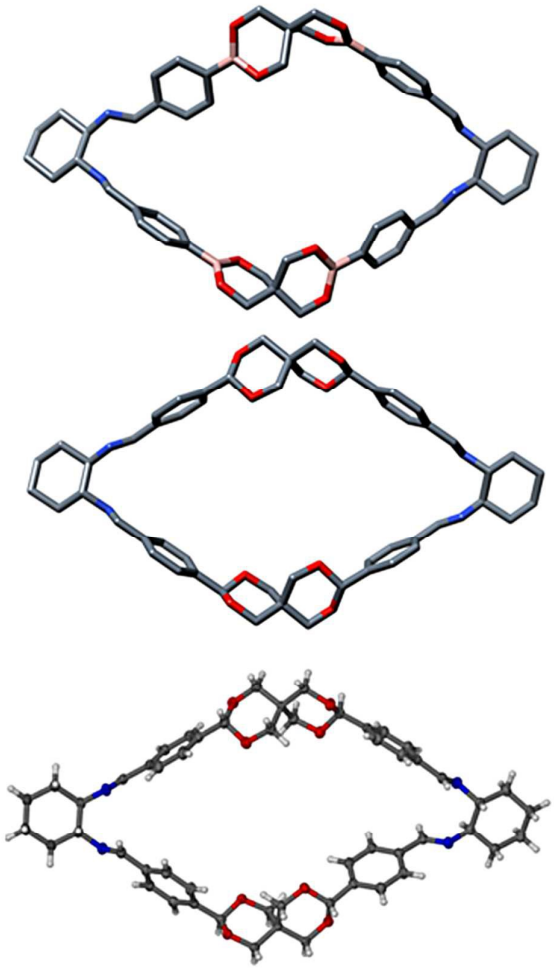

Figure 2. Calculated structures of macrocyclic tetraimines **5** (top) and **9** (middle), and the crystal structure of **9** (bottom).

was fluxionally racemic 1,1'-ferrocenediboronic acid, forming a macrocycle upon reaction with **1**. Our analysis shows that in the crystal structure of the macrocycle *M*-helical 1,1'-ferrocenediboronic acid induced *P*-helicity of pentaerythritol-derived diboronate unit.[19]

The observation of axial chirality (helicity)[20] of pentaerythritol-derived bicyclic molecules can be extended to other spiranes of the general formula shown in Figure 3. Unlike in boronic esters, the helicity change in spiro diacetals[21] cannot be easily made by a change to a boat conformation because this would lead the bulky R substituent to the axial, sterically unfavorable position. Here, a change of helicity can only be made by partial reversible acetal hydrolysis (to preserve diequatorial positions of the R substituent) which does not occur during macrocycle ring formation.

In general, axial chirality is usually associated with sp^2 hybridized molecular structures, such as atropisomeric biaryls, allenes and alkylidenecycloalkanes. Molecules of [m,n]spiranes

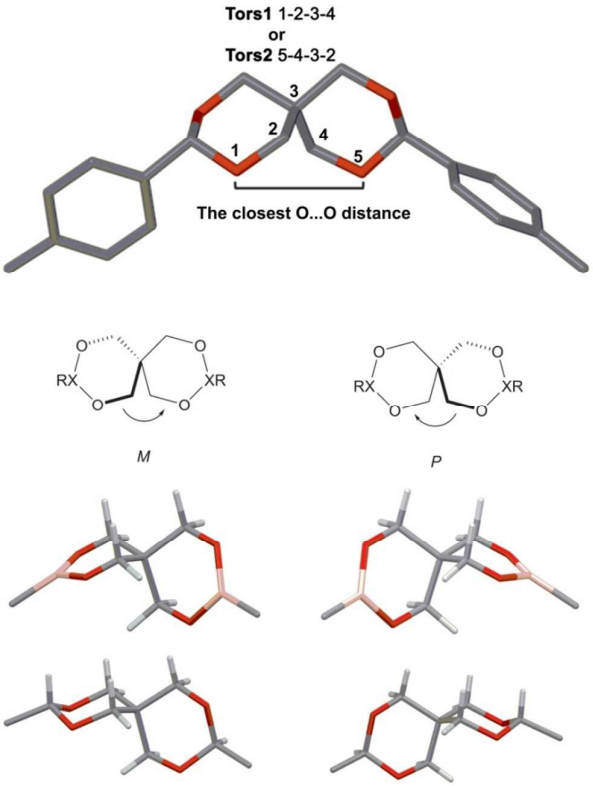

Figure 3. Definition of helicity at a spiro carbon atom in two condensed hexamembered rings of sofa-sofa and chair-chair conformations.

having both rings non-planar (*i.e.* when m, n > 2) are also chiral (devoid of symmetry plane or inversion center).

Compounds of this type are usually dynamically racemic, unless racemization process is suppressed by structural bias, such as formation of a rigid macrocycle. If this is the case, the permanently chiral molecules can be obtained, even though there is no chiral atom present in the spiro structure. *M*,*M*(*R*,*R*,*R*,*R*) diastereoisomer of **5** presents the first demonstration of a case of axial chirality due to preferential freezing of one of the conformers of the spiro moiety in a chiral macrocycle. This was made possible by the synthesis of a macrocycle in reversible reactions of boronate and imine bond formation. It may be pertinent to mention that self-assembly of a boronate macrocycle can cause inhibition of photoisomerization of an incorporated azobenzene unit, as recently reported.[18]

Conclusions

Two polyimine macrocycles **5** and **9** were synthesized with the objective to demonstrate two different types of chiral spiro moiety and helicity induction during the ring closure reaction. While **5** and **9** are structurally closely related with regard to the size and shape of macrocyclic ring, incorporation of boron atoms into 2,4,6,8-tetraoxaspiro[5,5]undecane linker affects the rigidity and conformation of the six-membered spiro rings. Both macrocycles display only one type of helicity of the spiro bicyclic part of the molecule but for different reasons. While in

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5 it was the dynamical conformational change that led only one major product, in the case of **9** chiral discrimination product was observed and a mixture of acyclic polyimines was obtained. This would explain the role of various aspects of chirality in the synthesis and structure of non-racemic macrocycles.

Experimental

General details

All commercially available reagents, except for (*R*,*R*)-1,2-diaminocyclohexane, were obtained from Sigma-Aldrich and used in reactions without further purification. The anhydrous THF used in the formation of boronate ester was distillated over potassium.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz or Varian Mercury 300 MHz at ambient temperature. All ^{1}H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to the signals for $CDCl_3$ (7.27 ppm). All ^{13}C NMR spectra were reported in ppm relative to residual $CDCl_3$ (77.0 ppm) and were obtained with ^{1}H decoupling. MS spectra were recorded on impact HD Bruker apparatus. CD spectra were recorded on JASCO J810 spectropolarimeter. Melting points were measured using open glass capillaries in a Buchi Melting Point B-545 apparatus.

Syntheses

3,9-Bis(4-formylphenyl)-2,4,8,10-tetraoxa-3,9-diboraspiro[5.5]undecane (3). A mixture of 4-formylphenylboronic acid (40mg, 0.266 mmol) and 2,2-di(hydroxymethyl)-1,3-propanediol (20 mg, 0.147 mmol) in anhydrous THF (25 ml) was stirred for 24 hours at 20 °C under argon atmosphere. Then, the solvent was evaporated under reduced pressure to give product **2** as white powder. Melting point: 230 °C. ^{1}H NMR (400 MHz, $CDCl_3$ + TMS): δ = 10.06 (s, 2H, C*H*O); 7.86-7.97 (m, 8H, arom. H); 4.11 (s, 8H, $4CH_2$) ^{13}C NMR (100 MHz, $CDCl_3$+ TMS): δ = 192.71 (*C*HO); 138.06, 134.44, 128.71 (arom. C-C), 115.87 (arom. *C*-B); 64.93 (O-*C*H_2); 36.66 (spiro-C) HRMS: *m/z* = 363.12053 (94.5%), 364.12752 (77.2%); calculated 364.12894

3,9-Bis(4-formylphenyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (8). Terephthalic aldehyde (2.42 g, 18 mmol), pentaerythritol (1.14 g, 8.4 mmol), *p*-TSA (0.172 g, 1 mmol) and 200 ml of chloroform was placed in 250 ml round bottom flask. The mixture was heated with stirring for 2 h. The reaction mixture was extracted with 10 % K_2CO_3 solution and organic layer was washed with H_2O and brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel (gradient: 0–10% EtOAc in DCM) to give 0.688 g of pure dialdehyde **9** in 22 % yield. Melting point: 176-178 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.03 (s, 2H, -C*H*O), 7.90 (d, *J* = 8.5 Hz, 4H, arom. H), 7.66 (d, *J* = 8.4 Hz, 4H, arom. H), 5.52 (s, 2H, acetal H), 4.85 (dd, *J* = 11.6, 2.4 Hz, 2H, -CH_2-), 3.88 (d, *J* = 11.7 Hz, 2H, -CH_2-), 3.87 (dd, *J* = 11.7, 2.6 Hz, 2H, -CH_2-), 3.69 (d, *J* = 11.7 Hz, 2H, -CH_2-). (400 MHz, DMSO-d_6) δ 10.03 (s, 2H, -C*H*O), 7.93 (d, *J* = 8.4 Hz, 4H, arom. H), 7.68 (d, *J* = 8.4 Hz, 4H, arom. H), 5.63 (s, 2H, acetal H), 4.60 (dd, *J* = 11.3, 2.0 Hz, 2H, -CH_2-), 3.97 (d, *J* = 11.5 Hz, 2H, -CH_2-), 3.86 (dd, *J* = 11.5, 2.4 Hz, 2H, -CH_2-), 3.73 (d, *J* = 11.6 Hz, 2H, -CH_2-). ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.91 (*C*HO); 143.74, 136.74,129.70, 126.78 (arom. C-C); 101.19 (acetal C); 70.95, 70.47 (-*C*H_2-); 32.59 (spiro C).

3,9-Bis(4-bromophenyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (7). 4-bromobenzaldehyde (1.14 g, 6.2 mmol), pentaerythritol (0.38 g, 2.8 mmol), *p*-toluenesulfonic acid (0.026 g, 0.15 mmol) and 45 ml of toluene was placed in 100 ml round bottom flask. The mixture was heated with stirring under Dean-Stark apparatus for 12 h. The solution was cooled to ambient temperature and the white crystals started to precipitate. After filtration, followed by washing with 5 ml of cold toluene, white crystals were obtained in 95 % yield (1.23 g, 2.6 mmol). Melting point: 215-217 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.6 Hz, 4H, arom. H), 7.38 (d, *J* = 8.4 Hz, 4H, arom. H), 5.44 (s, 2H, acetal H), 4.83 (dd, *J* = 11.6, 2.3 Hz, 2H, -OCH_2-), 3.85 (d, *J* = 11.5 Hz, 2H, -OCH_2-), 3.84 (dd, *J* = 11.6, 2.8 Hz, 2H, -OCH_2-), 3.67 (d, *J* = 11.7 Hz, 2H, -OCH_2-).

3,9-Bis(4-formylphenyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (8). 3,9-bis(4-bromophenyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (0.5 g, 1 mmol) was dissolved in 20 ml of dry THF and cooled to –78 °C under argon atmosphere. Subsequently, n-butyllithium (2.8ml, 1.6 M in hexanes, 4.5 mmol) was added dropwise and let stir for an additional 1 hour at that temperature. Dimethylformamide (0.34 ml, 4.4 mmol) was then added, and after 1 hour at –78 °C, the solution was allowed to warm to room temperature for 4 hours. The reaction was quenched by the addition of saturated NH_4Cl solution (10 ml) and stirred for 1 hour. The mixture was diluted with water (10 ml) and extracted with DCM (3 × 10 ml). The combined organic layers were washed with sat. aq. $NaHCO_3$(10ml) and brine (10 ml), dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by columnchromatography onsilica gel (gradient: 0–10% EtOAc in DCM) to give 3,9-bis(4-formylphenyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (0.267 g, 72%) as a white crystals.

Boronate–imine rhombimine (5). 100 mg (0.275 mmol) of boronate ester **2** was added to a solution of (*R,R*)-1,2-diaminocyclohexane (32 mg, 0.280 mmol) in toluene (30 ml). The mixture was heated with stirring under Dean-Stark apparatus for 2 days. The solution was cooled to ambient temperature and the solvent was removed under reduced pressure to give macrocycle **5** in 82 % yield.

Attempts to purify **5** by crystallization or chromatography were unsuccessful. Melting point: >300 °C decomposition. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (s, 4 -N=C*H*-); 7.70-7.72 (d, 8H, arom. H); 7.41-7.43 (d, 8H, arom. H); 4.17-4.19 (d, *J* = 11.4 Hz, 8H, -OCH_2-); 3.97-4.00 (d, *J* = 11.4 Hz, 8H, -OCH_2-); 3.27-3.29 (m, 4H, =N-C*H*-); 0.86-2.02 (m, 16H, -CH_2-) ^{13}C NMR (100 MHz,$CDCl_3$): δ = 162.75 (-N=*C*H-); 138.36, 133.99, 126.90

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(arom. C-C); 127.36 (arom. *C*-B); 72.71 (-CH-N), 64.95 (-O*C*H$_2$-); 36.79, 32.41, 24.44 (aliph. C); 33.07 (spiro C)
EI MS: *m/z* = 884.2 (calc: 884.4)

One pot synthesis ofboronate–imine rhombimine (5). The mixture of 4-formylphenylboronic acid (100 mg, 0.669 mmol), 2,2-di(hydroxymethyl)-1,3-propanediol (46 mg, 0.338 mmol) and (*R*,*R*)-1,2-diaminocyclohexane (40 mg, 0.350 mmol) in anhydrous THF (40 ml) was stirred for 24 hours at 20°C under argon atmosphere. Then, the solvent was removed under reduced pressure. Attempts to purify **5** by crystallization or chromatography were unsuccessful. Spectral data were identical to the one described for macrocycle **5** in previous reaction.

Diacetal spirorombimine (9). The mixture of dialdehyde **9** (0.45 g, 1.2 mmol), (*R,R*)-1,2-diaminocyclohexane (0.14 g, 1.2 mmol), catalytic amount of *p*-toluenesulfonic acid and toluene (60 ml) was placed in round-bottom flask (under argon). The mixture was heated with stirring under Dean-Stark apparatus for one day. The solution was cooled to ambient temperature and the solvent was removed under reduced pressure to give macrocycle **9** in almost quantitative yield. Crystals suitable for X-ray spectroscopy were obtained by slow Et_2O vapour diffusion to $CHCl_3$/EtOH solution of **9**. Melting point: > 290 °C decomposition. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 4H, -N=C*H*-), 7.53 (d, *J* = 8.2 Hz, 8H, arom. H), 7.40 (d, *J* = 8.1 Hz, 8H, arom. H), 5.40 (s, 4H, acetal H), 4.75 (d, *J* = 10.9 Hz, 4H, -OC*H*$_2$-), 3.79 (dd, *J* = 11.4, 2.1 Hz, 4H, -OC*H*$_2$-), 3.78 (d, *J* = 11.5 Hz, 4H, -OC*H*$_2$-), 3.59 (d, *J* = 11.7 Hz, 4H, -OC*H*$_2$-), 3.40 – 3.31 (m, 4H, =N-C*H*-), 1.94 – 1.40 (m, 16H, -C*H*$_2$-). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.04 (-N=*C*H-); 139.77, 136.83, 127.80, 126.38 (arom. C); 101.89 (acetal C); 77.22, 73.70, 70.88, 70.46 (-O*C*H$_2$-); 32.70, 32.51, 24.49 (aliph. C). ESI MS: *m/z* = 893 (calc. 892.4).

X-ray diffraction

Crystals of **9** suitable for single-crystal X-ray diffraction were obtained from the slow evaporation of a mixture of dichloromethane (DCM) and methanol (MeOH) in ratio 1:2 (DCM:MeOH). Reflection intensities were measured on a SuperNova diffractometer equipped with Cu microfocus source (λ=1.54178 Å) and 135 mm Atlas CCD detector. The temperature of the crystal (150K) was controlled with an Oxford Instruments Cryosystem cold nitrogen-gas blower. Data reduction and analysis were carried out with the CrysAlisPro software. The structures were solved by direct methods using SIR-2011[22] and refined by the full-matrix least-squares techniques with SHELXL-2014.[23] All heavy atoms were refined anisotropically. The hydrogen atoms bound to C atoms were placed at calculated positions and refined using a riding model, and their isotropic displacement parameters were given a value 20% higher than the isotropic equivalent for the atom to which the H atoms were attached.
The relevant crystal data and refinement parameters are listed in Table S3.

Graphical images were produced in Xseed[24] using Pov-Ray[25] and Mercury[26] programs.

CCDC 1567710 contains 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%5Frequest/cif

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