

Planar Chiral Tetrasubstituted [2.2]Paracyclophane: Optical Resolution and Functionalization

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S Supporting Information

ABSTRACT: We achieved optical resolution of 4,7,12,15-tetrasubstituted [2.2]paracyclophane and subsequent transformation to planar chiral building blocks. An optically active propeller-shaped macrocyclic compound containing a planar chiral cyclophane core was synthesized, showing excellent chiroptical properties such as high fluorescence quantum efficiency and a large circularly polarized luminescence dissymmetry factor.

Planar chiral [2.2]paracyclophanes provide a conformationally stable chiral environment due to suppression of the rotation of phenylenes.¹ Optical resolutions of various [2.2]paracyclophanes have been conducted,^{1–3} and the resulting optically active [2.2]paracyclophane compounds have mainly been used as chiral auxiliaries. For example, aryl-PHANEPHOS^{3a,b} are well-known commercially available compounds; they are widely used as chiral ligands for transition metal-catalyzed asymmetric reactions.

We have previously studied the planar chirality of [2.2]-paracyclophane and developed a practical optical resolution method for pseudo-*ortho*-disubstituted [2.2]paracyclophanes to be used as a chiral building block for through-space conjugated compounds.^{3i,4} There have been several reports on optical resolution of disubstituted [2.2]paracyclophane;³ however, only one report on that of a tetrasubstituted [2.2]paracyclophane compound exists.⁵ Considering the potential applications of [2.2]paracyclophane skeletons in polymer and materials chemistry,⁶ as well as organic and organometallic chemistry, further development and modification of optical resolution methods for planar chiral tetrasubstituted [2.2]paracyclophanes would be valuable. Herein, we report optical resolution of *rac*-4,7,12,15-tetrabromo[2.2]paracyclophane and subsequent transformations to produce planar chiral building blocks for through-space carbon-rich compounds.⁷ In this study, an optically active macrocycle⁸ based on a tetrasubstituted [2.2]paracyclophane was synthesized. The excellent chiroptical properties, in particular, circularly polarized luminescence (CPL), are also reported.

Optical resolution of tetrasubstituted [2.2]paracyclophane was carried out by a diastereomer method beginning with 4,7,12,15-tetrabromo[2.2]paracyclophane⁹ *rac*-1, as shown in Figure 1. One of bromides in *rac*-1 was converted to a hydroxyl group to obtain *rac*-2 in 69% isolated yield,^{3c–e} which was reacted with (–)-(1*S*,4*R*)-camphanoyl chloride **3** to obtain a mixture of diastereomers. These were readily separated by SiO₂

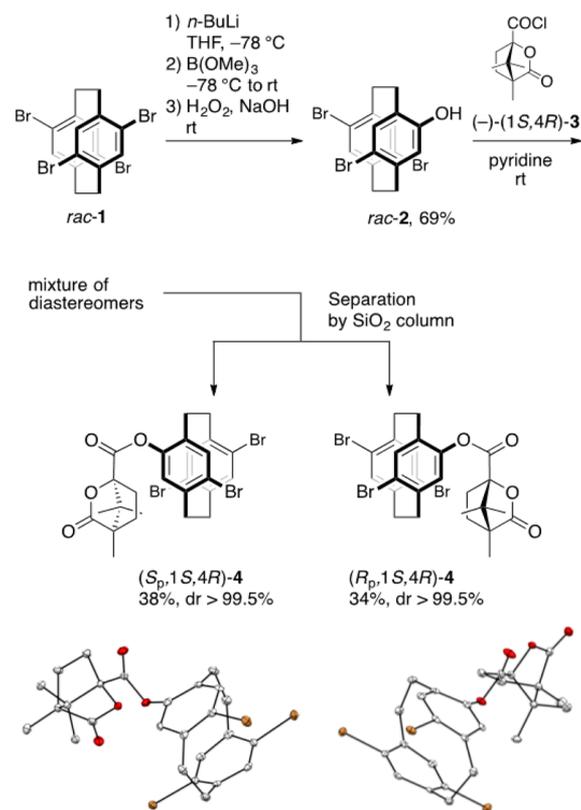


Figure 1. Optical resolution of *rac*-1. Crystal structures of (*S_p*,1*S*,4*R*)-4 and (*R_p*,1*S*,4*R*)-4 with ellipsoids at 30% probability. Hydrogen atoms and solvent (CHCl₃ in (*R_p*,1*S*,4*R*)-4) are omitted for clarity.

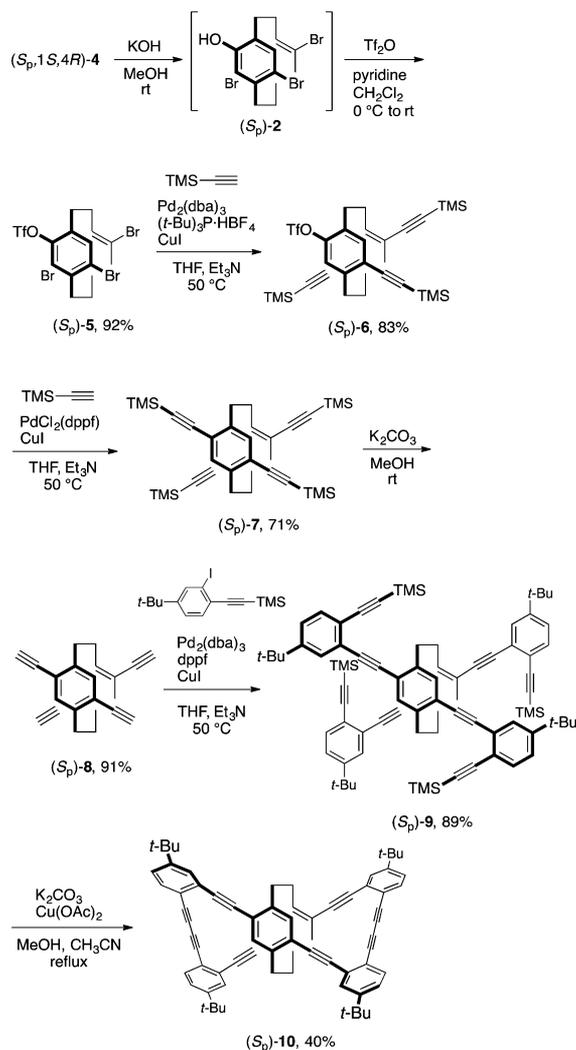
column chromatography and purified by recrystallization to obtain (*S_p*,1*S*,4*R*)-4 and (*R_p*,1*S*,4*R*)-4 in 38% and 34% isolated yield, respectively (each diastereomer ratio (dr) > 99.5%).¹⁰ The structures were confirmed by NMR spectroscopy, mass analysis, elemental analysis, and X-ray crystallography (Figure 1).

Hydrolysis and subsequent transformation of (*S_p*,1*S*,4*R*)-4 are shown in Scheme 1. Treatment of (*S_p*,1*S*,4*R*)-4 with KOH afforded (*S_p*)-2. This compound was used for the next transformation to OTf without purification, and enantiopure (*S_p*)-5 was obtained in 92% isolated yield. Sonogashira-Hagihara coupling¹¹ of (*S_p*)-5 with trimethylsilylacetylene

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Scheme 1. Synthesis of Optically Active Macrocycle



using a $\text{Pd}_2(\text{dba})_3/(\text{t-Bu})_3\text{P}$ catalysis gave only (S_p) -**6** in 83% isolated yield. Interestingly, bromide was selectively reacted, and tetra(trimethylsilylethynyl)[2.2]paracyclophane ((S_p) -**7**) was not detected by thin-layer chromatography. Reacting (S_p) -**6** with trimethylsilylacetylene using a $\text{PdCl}_2(\text{dppf})$ catalysis afforded (S_p) -**7**. Removal of the trimethylsilyl group was carried out with $\text{K}_2\text{CO}_3/\text{MeOH}$ afforded the corresponding tetrayne¹² ((S_p) -**8**) in 91% isolated yield. The enantiomer (R_p) -**8** was also synthesized by the same route.

Tetrasubstituted [2.2]paracyclophanes **5** and **8** can be employed as conformationally stable chiral building blocks for various optically active carbon-rich compounds. In this study, we synthesized an optically active propeller-shaped macrocycle¹⁴ from **8**, as shown in Scheme 1. The reaction of (S_p) -**8** with 5-*tert*-butyl-2-[(trimethylsilyl)ethynyl]iodobenzene afforded the corresponding optically active compound (S_p) -**9** in 89% isolated yield. Desilylation of (S_p) -**9** with $\text{K}_2\text{CO}_3/\text{MeOH}$ and a subsequent oxidative coupling reaction using $\text{Cu}(\text{OAc})_2$ gave the target macrocycle (S_p) -**10** in 40% isolated yield. Enantiomer (R_p) -**10** was also prepared, and their structures were confirmed by NMR spectroscopy and mass analysis. A single crystal of *rac*-**10** was obtained by recrystallization with CHCl_3 and MeOH , and the molecular structure is shown in Figure S20 (Supporting Information). The enantiomers co-

crystallized into a single crystal, and the bowtie-shaped¹³ structure was confirmed from the top view. As shown in the front and side views, the structure seems like a two-blade propeller owing to the planar chiral [2.2]paracyclophane core. This structure has previously been synthesized by Hopf, Haley, and co-workers as a racemic compound,¹⁴ although the positions of the *tert*-butyl groups were different.

The optical properties of (R_p) - and (S_p) -**10** were investigated; the UV-vis absorption, circularly dichroism (CD), photoluminescence (PL), and CPL spectra of (R_p) - and (S_p) -**10** in dilute CHCl_3 solution (1.0×10^{-5} M) are shown in Figure 2. The UV-vis absorption spectrum of **10**

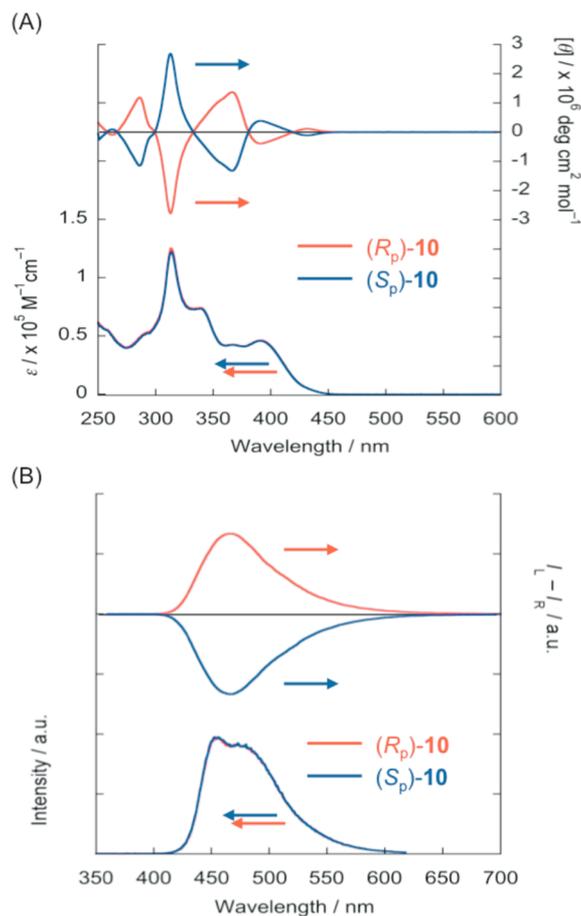


Figure 2. (A) UV-vis absorption and CD spectra of (R_p) - and (S_p) -**10** in CHCl_3 (1.0×10^{-5} M) at room temperature. (B) PL and CPL spectra of (R_p) - and (S_p) -**10** in CHCl_3 (1.0×10^{-6} M for PL and 1.0×10^{-5} for CPL) at room temperature, excited at 314 nm.

(Figure 2A) was identical to that of the cyclic compound prepared by Hopf, Haley, and co-workers.¹⁴ Thus, there was no difference in the electronic structure of the ground state between these compounds regardless of the positions of the *tert*-butyl groups.¹⁵ In the CD spectra of (R_p) - and (S_p) -**10**, intense and mirror image Cotton effects were observed in the absorption bands of the UV-vis spectra (Figure 2A). The molar ellipticity ($[\theta]$) was very large, with a $[\theta]$ for (S_p) -**10** of 2.7×10^6 deg cm^2 dmol^{-1} . The dissymmetry factor of absorbance, $g_{\text{abs}} = 2(\Delta\epsilon/\epsilon)$, is another parameter indicating chirality in the ground state; a large g_{abs} value of 0.9×10^{-2} was obtained. The specific rotation $[\alpha]_D^{25}$ (c 0.5, CHCl_3) of (S_p) -**10** was estimated to be -1494.9 , whereas that of (S_p) -**9** was $+44.1$.

In all cases, the chiroptical data for (S_p)-**10** were considerably enhanced compared with those for (S_p)-**9** in the ground state.

As shown in Figure 2B, compound **10** exhibited a vibronic emission peak at around 460 nm with an absolute PL quantum efficiency (Φ_{lum}) of 0.45 for (S_p)-**10**. The PL decay curve was fitted with a single exponential relationship ($\chi^2 = 1.18$), and the PL lifetime (τ) was calculated to be 3.71 ns (Figure S41). This efficient PL arose from criss-cross delocalization across the entire molecule via the strong through-space interaction of the [2.2]paracyclophane core.¹⁶

Intense and mirror image CPL signals for (R_p)- and (S_p)-**10** were observed in the emission region (Figure 2B) with a large CPL dissymmetry factor, $g_{\text{lum}} = 2(I_{\text{left}} - I_{\text{right}})/(I_{\text{left}} + I_{\text{right}})$, where I_{left} and I_{right} are the PL intensities of left and right CPL, respectively. The maximum $|g_{\text{lum}}|$ value was estimated to be 1.1×10^{-2} (Figure S40). It is rare that a monodispersed chiral hydrocarbon exhibits such a large g_{lum} on the order of 10^{-2} .^{17d,f,g} Recently, small molecules that exhibit CPL in dilute solution have been extensively studied; helically and axially chiral compounds have been known to have CPL with large g_{lum} values on the order of 10^{-3} – 10^{-2} .¹⁷ A conformationally stable chiral structure of the emitting species, such as a helical structure, in the excited state is essential to obtain CPL with a large g_{lum} . Macrocycle **10** possesses a conformationally stable chiral second-ordered structure (propeller-shaped structure) due to complete fixation by the [2.2]paracyclophane bridge methylenes, resulting in intense CPL with a large g_{lum} .¹⁸ There were only small differences between the g_{abs} and g_{lum} for (R_p)- and (S_p)-**10**, indicating little conformational change between the ground and the excited states.¹⁹

In conclusion, we have developed a practical method for optical resolution of planar chiral tetrasubstituted [2.2]-paracyclophane. The obtained enantiopure 4,7,12,15-tetrafunctional cyclophane was readily modified to the corresponding planar chiral compounds. In the present study, a propeller-shaped macrocyclic compound was synthesized through coupling reactions. The obtained macrocycle exhibited a chiral environment in the ground and excited state. In particular, the macrocycle exhibited PL with a high Φ_{lum} of 0.45 and CPL with a large g_{lum} of 1.1×10^{-2} . A conformationally stable higher-ordered structure in the excited state is required for CPL with a large g_{lum} , and the theoretical supports in the excited state will be the next target. From the conformational viewpoint, [2.2]paracyclophane is the ideal scaffold and provides new design guidelines for CPL materials in addition to helically and axially chiral compounds. Various functionalizations of planar chiral tetrasubstituted [2.2]paracyclophanes, such as **5** and **8**, are available to obtain a variety of optically active emissive molecules. Therefore, further investigations of [2.2]-paracyclophane-based CPL compounds and assemblies that enhance both Φ_{lum} and g_{lum} are currently underway.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, characterization data, and additional spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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(18) The CPL spectra and g_{lum} charts of (R_p)- and (S_p)-**9** are shown in Figures S26 and S27, respectively. Their g_{lum} values were sufficiently large, $|g_{\text{lum}}| = 1.2\text{--}1.3 \times 10^{-3}$.

(19) No thermochromism and solvatochromism were observed in UV, CD, PL, and CPL spectra for **10** as well as **9**; see Figures S29–S34 for **9** and S42–S47 for **10**.