CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.201102511

Synthesis and Helical Structure of Spiroborate-Based Double-Stranded Helicate with Oligophenol Strands Bearing Bipyridine Units

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A large number of synthetic double helices have been developed during the past few decades because of their significant aesthetic and biomimetic appeal, and several structural motifs for double helices are now available,[1–8] including the peptide analogues of DNA,[2] transition metal complexes, namely the helicates,[3,4] aromatic oligoamides,[5] amidinium–carboxylate salt bridges,[6] and oligoresorcinols.[7] Among them, the helicates have gained popularity due to their applications in many areas, such as synthetic receptors,[9] liquid crystalline materials,[10] catalysis,[11] and DNA recognition.[12] Most of them rely on the coordination of transition metal cations to pyridine- or phenanthroline-containing molecular strands, and their three-dimensional structures are determined by the coordination geometry requirements. In contrast, helicates assembled with typical metal cations are quite rare and only a limited number of examples have been reported for the Li^+, Na^+, K^+, and B^{3+} ions.[13,14] In addition, only a few double-stranded helicates have been optically resolved into enantiomers despite the emerging interest in their inherent helical chirality.[15]

We have recently reported the synthesis of a spiroborate-based helicate ($DH1_{BNaB^-}$) from a hexaphenol ligand (**1**, H_6L1) and its optical resolution into enantiomers, which disclosed that the resolved enantiomers were stable toward racemization (Scheme 1).[14a,16] We further designed and synthesized the boron helicate ($DH2_{BNaB^-}$) containing tetraphenol strands with a biphenylene unit in the middle (**2**, H_4L2), which was also optically resolved, and achieved precise control over the ion-triggered extension–contraction motion accompanied by anisotropic twisting by using the resolved enantiomers.[14b] This study has clearly demonstrated that the linkers connecting the two biphenol units can be exchanged for other units with a shape similar to that of the biphenlyene linker. Bipyridines are obvious candidates for the substitution and of particular importance since their transition metal complexes, especially those of ruthenium,[17] osmium,[18] and rhenium,[19] exhibit interesting photophysical and photochemical properties. We now describe the design and synthesis of a new spiroborate-based helicate ($DH3_{BNa2B}$) from a tetraphenol strand bearing a bipyridine unit in the middle (**3**, H_4L3), along with the elucidation of the double helical structure and its optical resolution by chiral HPLC.

The bipyridine-containing tetraphenol (**3**) was prepared according to Scheme S1 (in the Supporting Information). The 2,2′-dimethoxybiphenyl-based monoboronic acid[14a] (**4**) and 6,6′-dibromo-2,2′-bipyridyl (**5**) were connected by Suzuki coupling to give the tetramethoxy derivative (**6**), of which the methyl groups were removed by treatment with BBr_3 to afford the tetraphenol (**3**). The bipyridine-containing helicate ($DH3_{BNa2B}$) was synthesized in the same way as those for $DH1_{BNaB^-}{\cdot}Na^+$ and $DH2_{BNaB^-}{\cdot}Na^+$ (Scheme 1).[14] The tetraphenol **3** was treated with $NaBH_4$ in 1,2-dichloroethane/ethanol (6:1, v/v) at 80 °C for one week. The reaction slowly proceeded and required a longer time to reach a reasonable conversion than those for $DH1_{BNaB^-}{\cdot}Na^+$ and $DH2_{BNaB^-}{\cdot}Na^+$. In contrast to $DH1_{BNaB^-}{\cdot}Na^+$ and $DH2_{BNaB^-}{\cdot}Na^+$, $DH3_{BNa2B}$ was sufficiently stable under silica gel chromatography conditions, therefore, $DH3_{BNa2B}$ could be isolated in 28% yield by chromatographic purification.

Single crystals suitable for an X-ray analysis were grown from an ethanol solution. The X-ray crystallographic analysis unambiguously revealed that $DH3_{BNa2B}$ adopted a double helical structure with a pseudo-D_2 symmetry, similar to those of $DH1_{BNaB^-}$ and $DH2_{BNaB^-}$, in which the two tetraphenol strands were intertwined with each other through two spiroborate bridges and the two terminal benzene rings of each tetraphenol strand were twisted by about 280° (Figure 1A). The most striking difference from $DH1_{BNaB^-}$ and $DH2_{BNaB^-}$ was that two Na^+ ions were embraced in the center of the complex coordinated by the bipyridine units and the oxygen atoms of the spiroborate moieties, thereby making the helicate electrically neutral. The two Na^+ cations were located with a very short distance of 3.1 Å, and were stabilized by the two negatively charged spiroborate groups.[20] In addition, the B–B distance of $DH3_{BNa2B}$ was 5.3 Å, which was much shorter than those of $DH1_{BNaB^-}$ (6.3 Å)[14a] and $DH2_{BNaB^-}$ (6.0 Å),[14b] as a result of the electrostatic stabilization by the two Na^+ ions (Figure 1B).

Electrospray ionization (ESI) mass measurements in the positive mode supported the structure of the boron helicate. These showed a strong signal due to the monocationic species ($[B_2Na_2(L3)_2+Na]^+$) at m/z 1580.20 along with a minor signal due to the dicationic species ($[B_2Na_2(L3)_2+2Na]^{2+}$)

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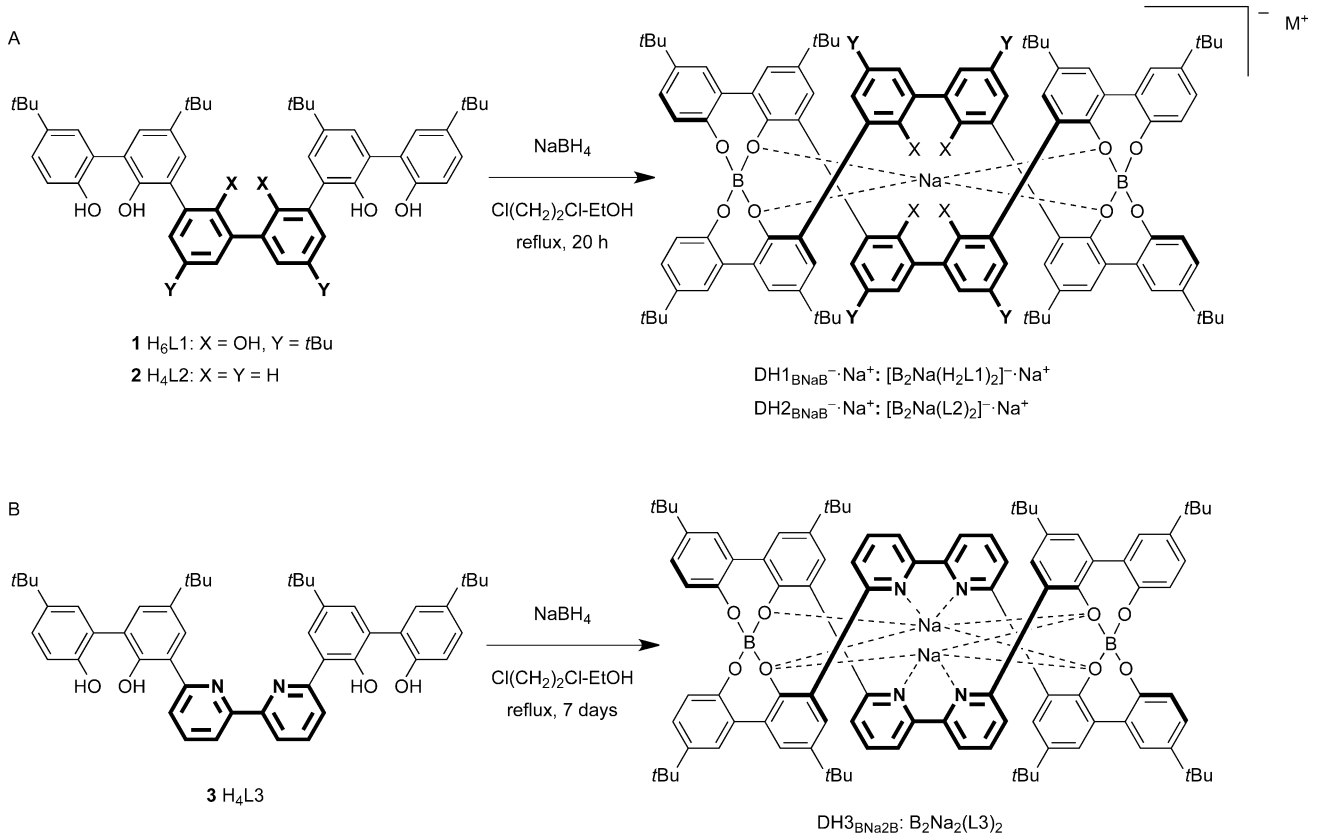
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201102511.



Scheme 1. Synthesis of: A) $DH1_{BNaB^-}{\cdot}Na^+$ and $DH2_{BNaB^-}{\cdot}Na^+$, and B) $DH3_{BNa2B}$.

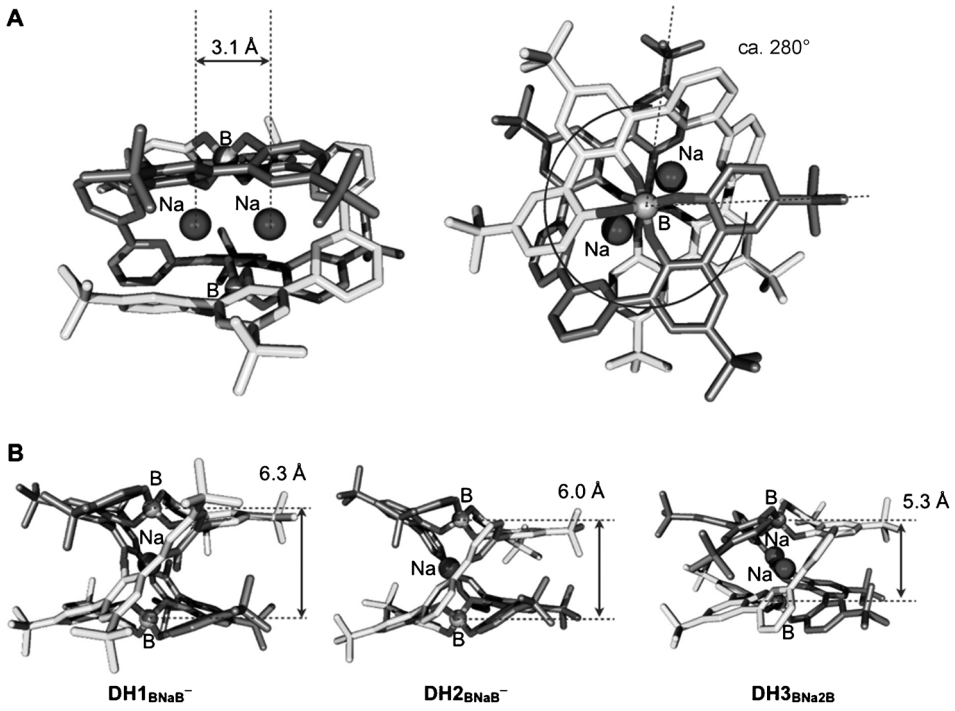


Figure 1. A) X-ray single crystal structure of $DH3_{BNa2B}$; side view (left) and top view (right). B) Comparison of the crystal structures of $DH1^-_{BNaB}$,[14a] $DH2^-_{BNaB}$,[14b] and $DH3_{BNa2B}$. Hydrogen atoms and solvent molecules are omitted for clarity.

at m/z 801.60 (Figure S1 in the Supporting Information). Moreover, no appreciable signals were observed in the negative mode measurements; this reflects the fact that the two Na^+ ions were strongly bound by the bipyridine nitrogen atoms and the spiroborate oxygen atoms. With the aim of removing the Na^+ ions, cryptand [2.2.1], which had been used to remove the Na^+ ion from $DH2_{BNaB^-}$, was added to a solution of $DH3_{BNa2B}$ in $CDCl_3$; this failed to capture the Na^+ ions even at 50 °C for 24 h. This failure to remove the Na^+ ions also supported the strong chelation of the Na^+ ions by the helicate.

The ^1H NMR spectrum of the helicate in $CDCl_3$ also revealed the pseudo-D_2 symmetric structure as was determined by the X-ray analysis in the solid state. The two *t*Bu signals and the ar-

omatic protons on the terminal benzene rings significantly shifted up-field due to the ring current effect of the benzene rings of the other strand, which was in good agreement with the crystal structure (Figure 2). In addition, the 2D NOESY

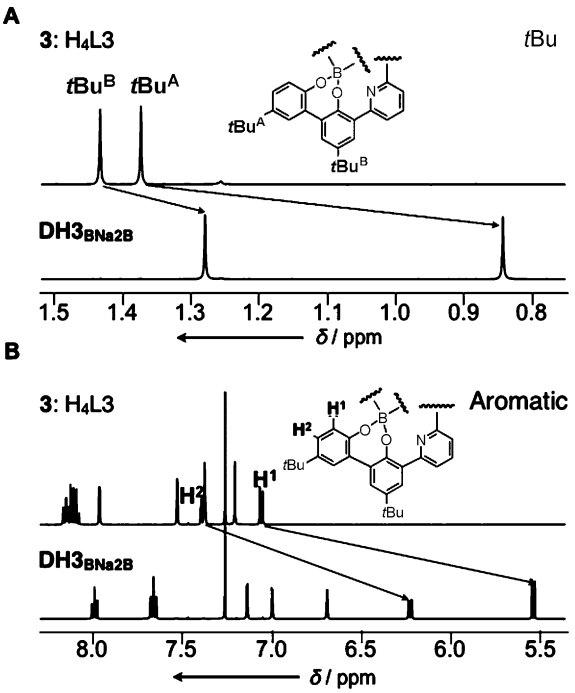


Figure 2. Partial ^{1}H NMR spectra (500 MHz) of **3** (H_4L3, upper spectrum) and $DH3_{BNa2B}$ (lower spectrum) in $CDCl_3$ at 25 °C.

experiments showed strong negative cross-peaks between the phenol rings A and C (Figures S5–S7 in the Supporting Information; for complete peak assignments, see 2D COSY, TOCSY, and NOESY spectra (Figures S2–S7)), which were attributed to the interstrand NOEs (distance approximately 2.5 Å); this indicates that the helicate retained the double-stranded helical tetranuclear structure in solution.

The optical resolution of (±)-$DH3_{BNa2B}$ was successfully achieved by chiral HPLC (Chralpak IB, Daicel, Co., Ltd.) by using hexane/$CHCl_3$ (8:2, v/v) containing diethylamine (0.1 vol%) as the eluent (Figure 3A). The resolved two fractions showed the CD spectra that are mirror images of each other, which reflect their enantiomerism (Figure 3B). The resolved enantiomers were stable and no racemization was observed even after the samples were stored in the eluent at ambient temperature for two weeks or in 1,2-dichloroethane at 80 °C for 24 h.

In conclusion, we have successfully prepared the spiroborate-based helicate with oligophenol strands bearing bipyridine units in the middle. Due to its neutral feature, both enantiomers of the racemic helicate were separated by chiral HPLC. The present results suggest that further design of the spiroborate-based helicates with functional units in the middle or at the ends is possible. The application of the helicates to chiral discrimination and asymmetric catalysis are ongoing in our laboratories.

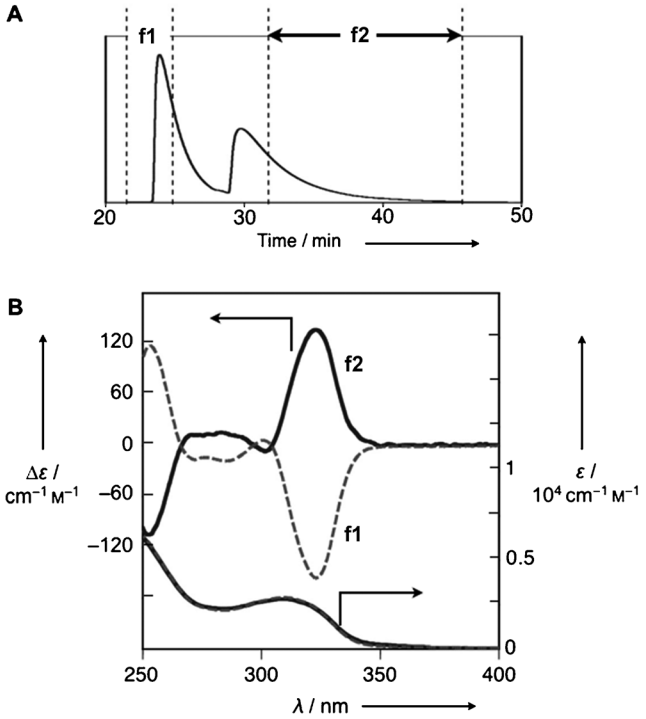


Figure 3. A) UV (254 nm) detected HPLC chromatogram of $DH3_{BNa2B}$. HPLC conditions: column, Chiralpak IB (Daicel, 2.0 f × 25 cm); eluent, hexane/$CHCl_3$ (8:2, v/v) containing diethylamine (0.1 vol%); flow rate, 8.0 mL min^{-1}; column temperature, 25 °C. B) CD and UV/Vis spectra of (+)-$DH3_{BNa2B}$ (f2) and (−)-$DH3_{BNa2B}$ (f1) in $CHCl_3$ at 25 °C.

Acknowledgements

This work was supported in part by Grant-in-Aids for Scientific Research (S) from the Japan Society for the Promotion of Science (JSPS) and for Scientific Research on Innovative Areas, "Emergence in Chemistry" from the MEXT (21111508).

Keywords: borates · helical structures · oligophenols · optical resolution

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Received: August 12, 2011
Published online: November 7, 2011

