ORGANIC LETTERS

2009
Vol. 11, No. 11
2241−2244

Practical Synthesis of P-Stereogenic Diphosphacrowns

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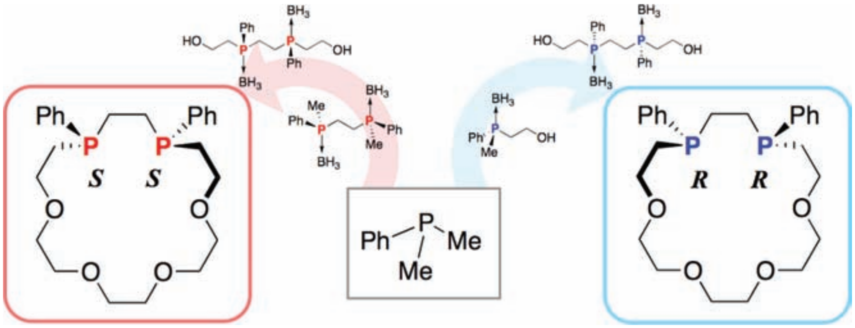
Received March 11, 2009

ABSTRACT



P-Stereogenic 18-diphosphacrown-6 derivatives containing a chiral bisphosphine unit were synthesized. This is the first practical method for the synthesis of optically pure diphosphacrowns. The diphosphacrowns have the structure of a chiral figure “8” with chiral heteroatoms that interact directly with guest ions and molecules. Pd(II) and Pt(II) complexes with the P-stereogenic diphosphacrowns were also synthesized and characterized.

Crown ethers are cyclic oligomers consisting of ethylene oxide ($-CH_2CH_2-O-$) units.[1,2] Since the landmark discovery of dibenzo-18-crown-6 by Pedersen in 1967, great progress has been made in the field of host−guest chemistry by using crown ethers because of their selective complexation of alkali metals and organic cations.[1] Various crown ether derivatives such as azacrowns containing nitrogen atoms,[2c] thiacrowns containing sulfur atoms,[2d,e] and phosphacrowns containing phosphorus atoms[2f−h] have been prepared. Moreover, optically active crown ethers have been of interest for chiral recognition. However, to the best of our knowledge, there have been no reports on the synthesis of optically pure crown ethers containing chiral heteroatoms that interact directly with guest ions and molecules.

The trivalent phosphorus atom can act as a chiral center, similar to a carbon atom, due to its high inversion energy,[3] and a wide variety of P-stereogenic phosphines have been synthesized.[4] In particular, P-stereogenic bisphosphines have played important roles as efficient chiral ligands for transition-metal-catalyzed asymmetric reactions.[4a−c] Recently, we employed P-stereogenic bisphosphines (*S*,*S*)-**1**-BH$_3$ (R = *tert*-Bu or Ph) as chiral building blocks for the synthesis of

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(1) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017–7036.

(2) (a) *Crown Ethers and Analogous Compounds, Studies in Organic Chemistry 45, M*; Hiraoka, M., Ed.; Elsevier: Amsterdam, 1992. (b) Bradshaw, J. S.; Izatt, R. M.; Bordunov, A. V.; Zhu, C. Y.; Hathaway, J. K. *Crown Ethers*; Lehn, J. M., Atwood, J. L., Davies, J. E. D., Macnicol, D. D., Vogtle, F., Eds.; Comprehensive Supramolecular Chemistry, Vol. 1; Pergamon Press: Oxford, England, 1996; Chapter 2, pp 35−95. (c) *Aza-Crown Macrocycles*; Bradshaw, J. S., Krakowiak, K. E., Izatt, R. M., Eds.; John Wiley & Sons: New York, 1993. (d) *Crown Compounds: Toward Future Applications*; Cooper, R. S., Ed.; VCH Publishers: New York, 1992; Chapters 14 and 15. (e) Adam, R. D. *Acc. Chem. Res.* **2000**, *33*, 171–178. (f) Caminade, A. M.; Majoral, J. P. *Chem. Rev.* **1994**, *94*, 1183–1213. (g) Bader, A.; Lindner, E. *Coord. Chem. Rev.* **1991**, *108*, 27–110. (h) Ciampolini, M.; Dapporto, P.; Dei, A.; Nardi, N.; Zanobini, F. *Inorg. Chem.* **1982**, *21*, 489–495.

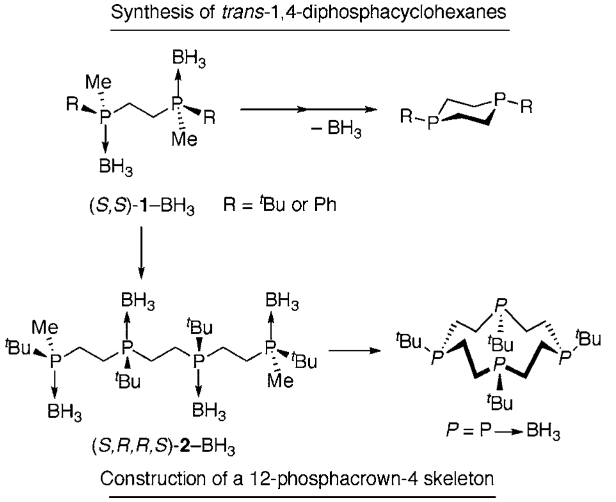
(3) Weston, R. E. *J. Am. Chem. Soc.* **1954**, *76*, 2645–2648.

(4) (a) Yamanoi, Y.; Imamoto, T. *Rev. Heteroatom. Chem.* **1999**, *20*, 227–248. (b) Crepy, K. V. L.; Imamoto, T. *Top. Curr. Chem.* **2003**, *229*, 1–40. (c) Crepy, K. V. L.; Imamoto, T. *Adv. Synth. Catal.* **2003**, *345*, 79–101. (d) Johansson, M. J.; Kann, N. C. *Mini-Rev. Org. Chem.* **2004**, *1*, 233–247. (e) Grabulosa, A.; Granell, J.; Muller, G. *Coord. Chem. Rev.* **2007**, *251*, 25–90.

10.1021/ol900504e CCC: $40.75

optically active oligomers,[5] polymers,[6] and dendrimers.[7] Further, we reported the stereospecific synthesis of *trans*-1,4-diphosphacyclohexanes[8] by the intramolecular cyclization of (*S*,*S*)-**1**-BH_3 and the construction of a 12-phosphacrown-4 skeleton[5a] by the intramolecular cyclization of (*S*,*R*,*R*,*S*)-**2**-BH_3, as shown in Scheme 1. This 12-phosphacrown-4 is the first example of a phosphacrown comprising only $-CH_2CH_2-PR-$ units;[5a,9] however, chiralities of optically active precursors (*S*,*S*)-**1**-BH_3 and (*S*,*R*,*R*,*S*)-**2**-BH_3 disappear from the ring structure. On the other hand, Lippard and coworkers reported the synthesis of 21-diphosphacrown-7 derivatives,[10] which consist of two phosphorus atoms and five oxygen atoms, and the separation of *meso* and *racemic* 21-diphosphacrown-7 derivatives from their Pd(II) complexes. Optical resolution of this *racemic* 21-diphosphacrown-7-Pd(II) complex was also achieved using Pasteur's method.[10]

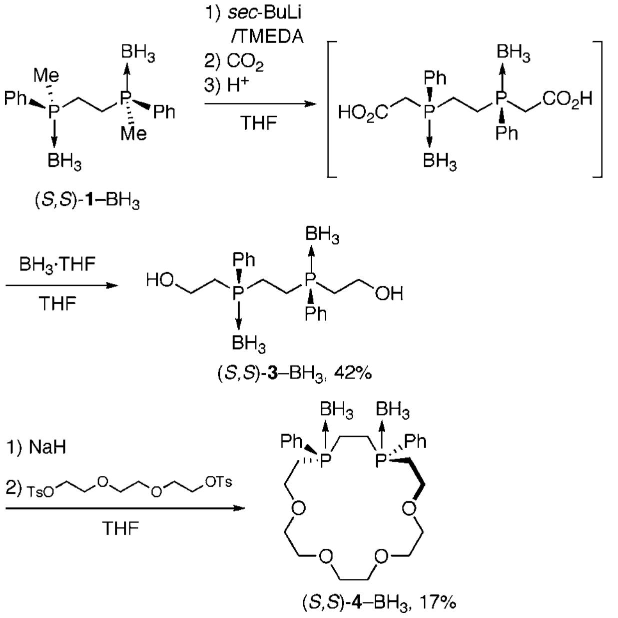
Scheme 1. Stereospecific Construction of *trans*-1,4-Diphosphacyclohexane and 12-Phosphacrown-4 Skeletons



In this communication, we report the synthesis of optically active 18-diphosphacrown-6 derivatives consisting of two chiral phosphorus atoms and four oxygen atoms. The synthesis was carried out by using P-stereogenic bisphosphines (*S*,*S*)-**3**-BH_3 and (*R*,*R*)-**3**-BH_3 as the key building blocks. This is the first practical method for the synthesis of optically pure diphosphacrowns. The synthetic procedure, characterization, and complexation with Pd(II) and Pt(II) are described.

The synthesis of (*S*,*S*)-18-diphosphacrown-6 is illustrated in Scheme 2. P-Stereogenic bisphosphine (*S*,*S*)-**1**-BH_3 was prepared with >99% ee[8] from dimethylphenylphosphine by following the procedure given in the literature.[11] The dilithiation of two methyl groups of (*S*,*S*)-**1**-BH_3 by *sec*-BuLi/*N*,*N*,*N*′,*N*′-tetramethylenediamine (TMEDA) and subsequent CO_2 bubbling afforded dicarboxy acid, which was used without purification for the subsequent reaction. The reduction of two carboxylic groups with BH_3·THF yielded the optically pure dialcohol (*S*,*S*)-**3**-BH_3 in 42% isolated yield. The reaction of (*S*,*S*)-**3**-BH_3 with NaH and triethyleneglycol bis(*p*-toluenesulfonate) was carried out to obtain the corresponding optically pure 18-diphosphacrown-6 (*S*,*S*)-**4**-BH_3 in 17% isolated yield.

Scheme 2. Synthesis of (*S*,*S*)-**4**-BH_3



Next, the preparation of enantiomer (*R*,*R*)-**4**-BH_3 was attempted, as shown in Scheme 3. The enantioselective lithiation of dimethylphenylphosphine-borane by *sec*-BuLi/(−)-sparteine and the reaction with CO_2 bubbling provided the corresponding carboxylic acid, which was used without purification for the subsequent reaction. The reduction of the carboxylic acid by BH_3·THF afforded alcohol (*S*)-**5**-BH_3 in 71% yield with 87% ee.[12] The remaining methyl group in (*S*)-**5**-BH_3 was lithiated with *sec*-BuLi/TMEDA, and then it

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(5) (a) Morisaki, Y.; Ouchi, Y.; Fukui, T.; Naka, K.; Chujo, Y. *Tetrahedron Lett.* **2005**, *46*, 7011–7014. (b) Morisaki, Y.; Ouchi, Y.; Naka, K.; Chujo, Y. *Tetrahedron Lett.* **2007**, *48*, 1451–1455. (c) Morisaki, Y.; Ouchi, Y.; Naka, K.; Chujo, Y. *Chem. Asian J.* **2007**, *2*, 1166–1173.

(6) (a) Ouchi, Y.; Morisaki, Y.; Ogoshi, T.; Chujo, Y. *Chem. Asian J.* **2007**, *2*, 397–402. (b) Morisaki, Y.; Ouchi, Y.; Tsurui, K.; Chujo, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 866–872. (c) Morisaki, Y.; Ouchi, Y.; Tsurui, K.; Chujo, Y. *Polym. Bull.* **2007**, *58*, 665–671.

(7) Ouchi, Y.; Morisaki, Y.; Chujo, Y. *Polym. Bull.* **2007**, *59*, 339–349.

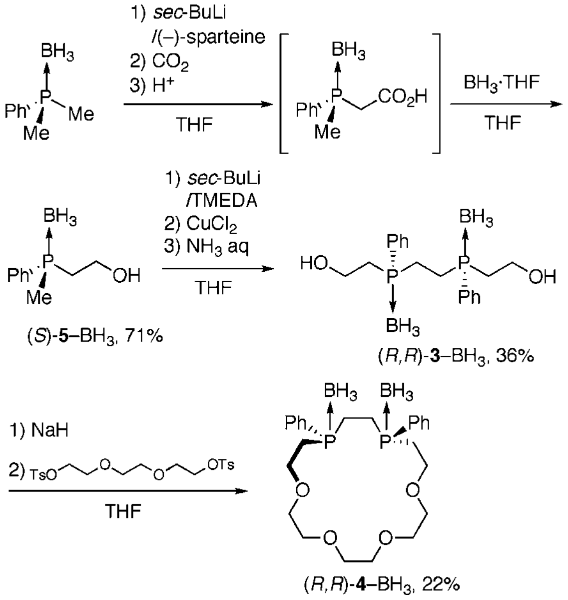
(8) Morisaki, Y.; Imoto, H.; Ouchi, Y.; Nagata, Y.; Chujo, Y. *Org. Lett.* **2008**, *10*, 1489–1492.

(9) Cyclic diphosphines with a small ring size are reviewed, see: (a) Alder, R. W.; Canter, C.; Gil, M.; Gleiter, R.; Harris, C. J.; Harris, S. E.; Lange, H.; Orpen, A. G.; Taylor, P. N. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1643–1655. See also as a recent example: (b) Bates, J. I.; Gates, D. P *J. Am. Chem. Soc.* **2006**, *128*, 15998–15999.

(10) (a) Wei, L. W.; Bell, A.; Warner, S.; Williams, I. D.; Lippard, S. J. *J. Am. Chem. Soc.* **1986**, *108*, 8302–8303. (b) Wei, L. W.; Bell, A.; Ahn, K. H.; Holl, M. M.; Warner, S.; Williams, I. D.; Lippard, S. J. *Inorg. Chem.* **1990**, *29*, 825–837.

(11) Muci, A. R.; Campos, K. R.; Evans, D. A. *J. Am. Chem. Soc.* **1995**, *117*, 9075–9076.

Scheme 3. Synthesis of (*R*,*R*)-**4**-BH_3



was treated with $CuCl_2$ and aqueous NH_3 to yield a mixture of *meso*-**3**-BH_3 and *racemi*-**3**-BH_3 due to 87% ee of (*S*)-**5**-BH_3. The diastereomer *meso*-**3**-BH_3, which was formed by the coupling reaction between (*S*)- and (*R*)-**5**-BH_3, and enantiomer (*S*,*S*)-**3**-BH_3 could be removed by the repeated recrystallization (three or four times) from hot toluene and hexane and afforded optically pure dialcohol (*R*,*R*)-**3**-BH_3 in 36% isolated yield (>99% ee).[13] Optically pure diphosphacrown (*R*,*R*)-**4**-BH_3 was obtained in 22% isolated yield by following the same synthetic procedure as in the case of (*S*,*S*)-**4**-BH_3.

The structure of the optically pure 18-diphosphacrown-6 was confirmed by ^1H, ^{13}C, and ^{31}P NMR spectroscopy, mass analysis, elemental analysis,[14] and X-ray crystallography. The ORTEP drawings of (*S*,*S*)-**4**-BH_3 are shown in Figure 1; they indicate the presence of two conformations. One conformer possesses two phenyl groups on the side opposite to the diphosphacrown ring (side view I in Figure 1), and the other possesses two phenyl groups above the ring (side view II in Figure 1). In other words, two phenyl groups occupy pseudoequatorial positions (side view I) or pseudoaxial positions (side view I) to the crown ring. In solution, the ring structure of the diphosphacrown is flexible, and the rapid interconversion of two conformers occurs.[15] The optically active diphosphacrown has the structure of a chiral figure eight "8", which is formed by two chiral phosphorus atoms (front views I and II in Figure 1), and two phenyl groups at chiral phosphorus atoms are found in two diagonal quadrants. Because of the long P−C bonds (average length: approximately 1.83 Å), the ring size of 18-diphosphacrown-6 is slightly larger than that of 18-crown-6.

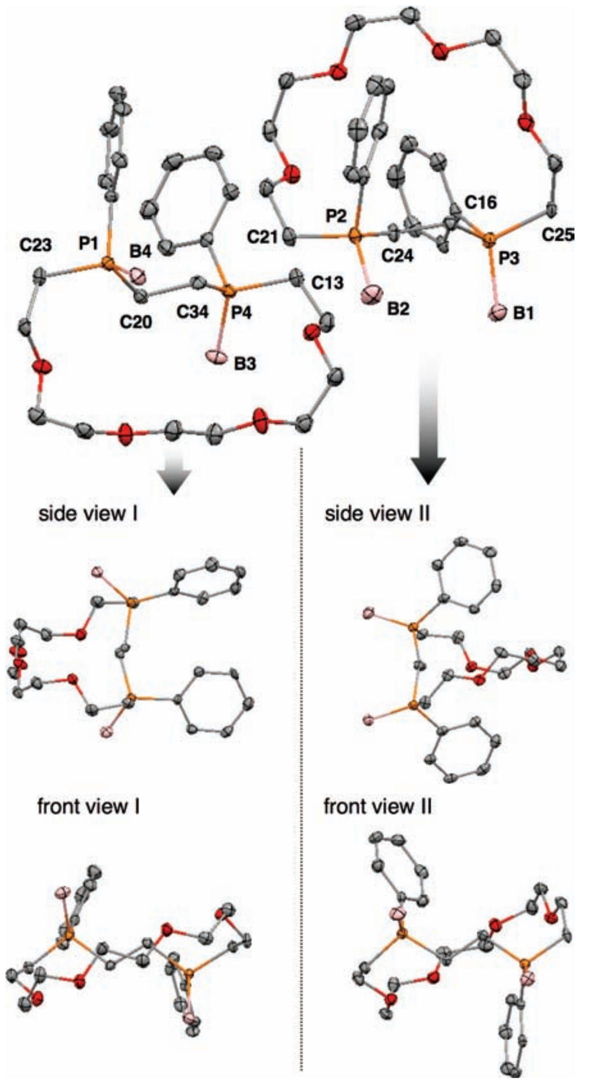


Figure 1. ORTEP drawings of (*S*,*S*)-**4**-BH_3 with 50% thermal ellipsoids. Selected bond lengths (Å) and angles (deg): P1−C20, 1.827(3); P1−C23, 1.822(4); P4−C13, 1.829(4); P4−C34, 1.827(4); P1−B4, 1.906(5); P4−B3, 1.909(4); P2−C21, 1.817(4); P2−C24, 1.810(4); P3−C16, 1.810(4); P3−C25, 1.831(4); P2−B2, 1.915(5); P3−B1, 1.917(4); C23−P1−C20, 110.03(17); C13−P4−C34, 105.26(18); C21−P2−C24, 104.82(18); C16−P3−C25, 109.68(18).

The coordinated boranes of diphosphacrown (*S*,*S*)-**4**-BH_3 could be easily removed by treatment with organic amines such as 1,4-diazabicyclo[2.2.2]octane (DABCO)[16] to afford the corresponding diphosphacrown (*S*,*S*)-**4** as an air sensitive colorless solid in 90% isolated yield. To obtain insight into the complexation behavior with transition metals as well as the asymmetric environment created by the optically active diphosphacrown (*S*,*S*)-**4**, palladium and platinum complexes

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[12] This compound was synthesized on the basis of the procedure reported in the literature by Ohashi, Imamoto, and co-workers: (a) Ohashi, A.; Kikuchi, S.; Yasutake, M.; Imamoto, T. *Eur. J. Org. Chem.* **2002**, 2535–2546. The ee value was determined by HPLC with Daicel Chiralcel OD-H column, as shown in Figure S1.

[13] Its optical purity (>99% ee) was confirmed by HPLC with Daicel Chiralcel OD-H column, as shown in Figure S2.

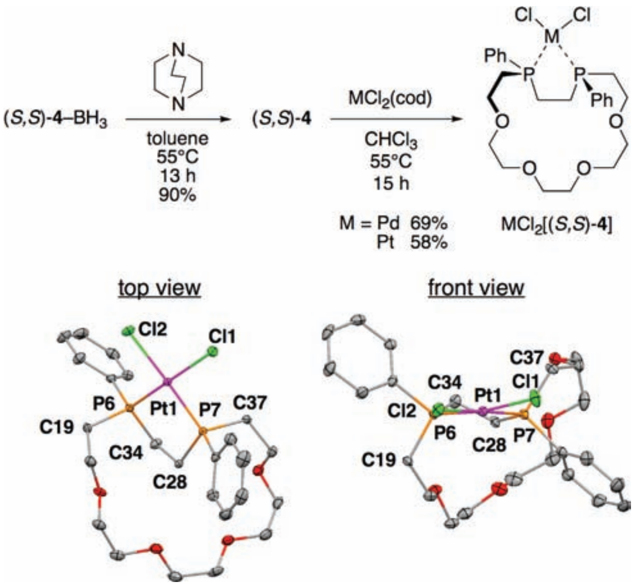
[14] See Supporting Information.

[15] ^{31}P NMR spectrum of (*S*,*S*)-**4**-BH_3 exhibits a sharp single signal with a P−B coupling, as shown in Figure S8.

[16] Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.* **1990**, *112*, 5244–5252.

MCl$_2$[(*S*,*S*)-**4**] (M = Pd$^{\mathrm{II}}$ and Pt$^{\mathrm{II}}$) were synthesized by the reaction of MCl$_2$(cod) with (*S*,*S*)-**4** (cod = 1,5-cyclooctadiene), as shown in Scheme 4. Both the reaction with Pd$^{\mathrm{II}}$ and that with Pt$^{\mathrm{II}}$ proceeded smoothly to yield the corresponding MCl$_2$[(*S*,*S*)-**4**] complex in 69% and 58% isolated yield, respectively. Their structures were confirmed by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy, mass analysis, elemental analysis, and X-ray crystallography. In the ^{31}P NMR spectrum of PtCl$_2$[(*S*,*S*)-**4**], the typical satellite signal obtained from the phosphorus−platinum coupling ($J_{\mathrm{P-Pt}}$) was observed at δ +46.6 ppm with $J_{\mathrm{P-Pt}}$ = 3594.0 Hz.[17] The ORTEP drawing of PtCl$_2$[(*S*,*S*)-**4**] is shown in Scheme 4. The X-ray analysis revealed that (*S*,*S*)-**4** was coordinated to the platinum center, which existed outside the diphosphacrown ring (top view).

Scheme 4. Synthesis of MCl$_2$[(*S*,*S*)-**4**] (M = Pd and Pt) and ORTEP Drawings of PtCl$_2$[(*S*,*S*)-**4**] with 50% Thermal Ellipsoids[a]



[a] Selected bond lengths (Å) and angles (deg): Pt1−P6, 2.2259(10); Pt1−P7, 2.2298(9); Pt1−Cl1, 2.3641(10); Pt1−Cl2, 2.3613(8); P6−C19, 1.835(4); P6−C34, 1.834(4); P7−C28, 1.820(4); P7−C37, 1.833(4); P6−Pt1−P7, 87.22(3); P6−Pt1−Cl2, 91.30(3); P7−Pt1−Cl1, 91.79(3); Cl1−Pt1−Cl2, 89.87(3); C19−P6−C34, 108.75(18); C28−P7−C37, 109.02(18).

Two phenyl groups are also found at two diagonal quadrants and occupy *quasi*-equatorial positions (front view). This is similar to the case of a series of rhodium-(*P*-chiral bisphosphine) complexes.[4a−c,18] In addition, the corresponding palladium complex PdCl$_2$[(*S*,*S*)-**4**] also shows the same conformation around the metal center (Supporting Information, Figure S19). On the other hand, according to the ORTEP drawings of the PdCl$_2$[21-diphosphacrown-7] complex reported by Lippard and co-workers, it seems that the complex adopts the different conformation around palladium; that is, the two phenyl groups occupy quasi-axial positions in the crystal.[10] In these cases, PdCl$_2$ and PtCl$_2$ are located outside of the crown ring, and two phenyl groups at phosphorus are in the *anti* orientation with respect to the coordination plane.

In summary, we have demonstrated the practical synthesis of optically pure crown ether derivatives containing two asymmetric phosphorus atoms in the chains. We have also synthesized new P-stereogenic bisphosphines as precursors. The obtained optically pure diphosphacrowns have the structure of a chiral figure “8”, which contains chiral heteroatoms (phosphorus atoms) that interact directly with guest ions and molecules. Pd(II) and Pt(II) complexes with the diphosphacrowns were synthesized and characterized. Further studies on the synthesis of a series of optically pure diphosphacrowns with several ethylene oxide (−CH$_2$-CH$_2$O−) units and their binding properties with the guest ions are in progress. Future studies will focus on transition-metal-catalyzed asymmetric reactions involving the use of optically pure diphosphacrowns as an asymmetric ligand.

Acknowledgment. This work was supported by Grant-in-Aid for Science Research on Priority Areas (No. 20036027, Synergy of Elements) from Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information Available: Experimental procedures, compound characterization data, NMR spectra, X-ray crystallographic data, and an X-ray crystallographic files (CIFs). This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) ^{31}P NMR spectrum of PtCl$_2$[(*S*,*S*)-**4**] is shown in Figure S17.

(18) (a) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946–5952. (b) Imamoto, T.; Watanabe, J.; Wada, Y.; Masuda, H.; Yamada, H.; Tsuruta, H.; Matsukawa, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **1998**, *120*, 1635–1636.