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Stereospecific Construction of a *trans*-1,4-Diphosphacyclohexane Skeleton

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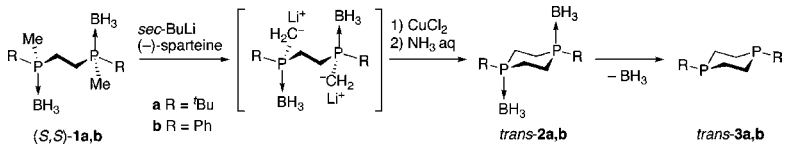
ABSTRACT

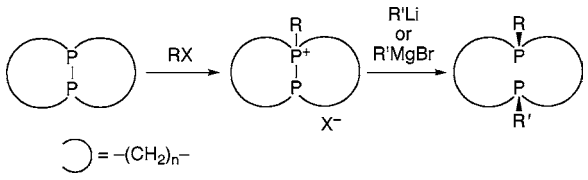


***trans*-1,4-Diphosphacyclohexanes were successfully synthesized by the stereospecific intramolecular coupling reaction of the optically active bisphosphine. This is a new route for the construction of the *trans*-1,4-diphosphacyclohexane skeleton. A cis isomer was also prepared along with the trans isomer from a mixture of *rac*- and *meso*-bisphosphines. The coordinated boranes were easily removed to afford the corresponding 1,4-diphosphacyclohexanes.**

There has been a long-standing interest in the synthesis, structure, reactivity, and coordination properties of heteroatom-containing ring systems. Among them, diphosphacycloalkanes play a considerably important role in organometallic chemistry. *cis*-Diphosphacycloalkanes are useful bidentate ligands for transition metals,[1,2] while *trans*-diphosphacycloalkanes have potential application as building blocks for the construction of metal−organic crystal architectures. In particular, porous coordination polymers, which comprise transition metals and organic ligands through a self-assembly process, are currently receiving considerable attention in view of their possible functions such as sorption, separation, guest alignment, and molecular storage.[3] Therefore, the development of new synthetic routes for *cis*- and *trans*-diphosphacycloalkanes is of considerable importance for organometallic and coordination chemistry.

Diphosphacycloalkanes reported to date are generally obtained as a mixture of stereoisomers, and they are separated by chromatography.[4] The stereoselective synthesis of *cis*-diphosphacycloalkane derivatives was attained by Alder and co-workers, in which bicyclic P−P bridged bisphosphines were ingeniously used for precursors (Scheme 1).[5] Synthetic strategy for *cis*-[1b,4e,5c,d] or *trans*-diphosphacycloalkanes[5b,d] is

Scheme 1. Stereoselective Route to *cis*-Diphosphacycloalkane Derivatives Reported by Alder and Co-workers[5]



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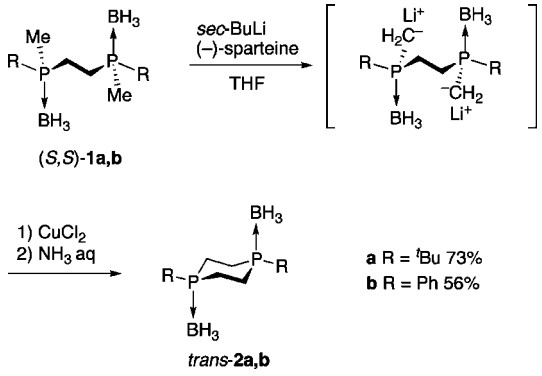
relatively undeveloped;[6] in particular, the stereoselective synthesis of *trans*-diphosphacycloalkanes remains challenging.

On the other hand, we have investigated the synthesis of optically active polymers,[7] dendrimers,[8] and oligomers[9] containing the P-chiral bisphosphine unit in their main chain, in which (*S*,*S*)-1,2-bis(boranato(*tert*-butyl)methylphosphino)-ethane (*S*,*S*)-**1a**[10,11] has been employed as the key monomer. During our studies on the incorporation of the (*S*,*S*)-**1a** skeleton into the polymer main chain, we discovered the stereospecific intramolecular coupling reaction of (*S*,*S*)-**1a** to form the *trans*-1,4-di-*tert*-butyl-1,4-diphosphacyclohexane skeleton efficiently. In this paper, we report the new synthetic route to *trans*-1,4-diphosphacyclohexane, as well as the cis stereoisomer by means of the stereospecific intramolecular oxidative coupling reaction of the optically active bisphosphine compounds.

Optically active bisphosphine (*S*,*S*)-**1a**,[10] reported by Imamoto and co-workers, and (*S*,*S*)-**1b**,[12] reported by Evans and co-workers, were prepared as precursors. The treatment of (*S*,*S*)-**1** with a slightly excess of *sec*-BuLi with (−)-sparteine (2.2 equiv based on (*S*,*S*)-**1**) generated the dilithiated intermediate, as shown in Scheme 2. $CuCl_2$ was added

Scheme 2. Stereospecific Synthesis of *trans*-1,4-Diphosphacyclohexane-diborane *trans*-**2a**,**b**



to the reaction mixture, and then it was treated with aqueous NH_3. Although this scheme does not involve an asymmetric reaction, we employed (−)-sparteine to activate the alkyllithium reagent.[13] Borane coordinated to phosphorus atom enables the lithiation of the methyl group and also protects phosphine from oxidation. The crude product was purified by column chromatography on SiO_2 to obtain *trans*-1,4-di-*tert*-butyl-1,4-diphosphacyclohexane-diborane *trans*-**2a** and *trans*-1,4-diphenyl-1,4-diphosphacyclohexane-diborane *trans*-**2b** stereospecifically in 73% and 56% isolated yields, respectively.[14] On the other hand, by using 1.2 equiv of *sec*-BuLi/(−)-sparteine in the lithiation step, optically active oligomers, i.e., tetraphosphine and hexaphosphine possessing four and six chiral phosphorus atoms, respectively, were also formed through the intermolecular oxidative coupling reaction.[9b,c]

The structures of *trans*-**2** were confirmed by ^1H, ^{13}C, and ^{31}P NMR, mass analysis, elemental analysis, and X-ray crystallography. The NMR spectra of *trans*-**2** exhibited a chair conformation in solution. It is expected that bulky *tert*-butyl and phenyl groups are equatorial. X-ray crystallographic analysis revealed their structures in the solid state, and Figure 1 shows the structure of *trans*-**2b**.[15,16] Bisphosphine *trans*-**2b** adopts the chair conformation with equatorial phenyl groups and axial boranes as shown in Figure 1A. The

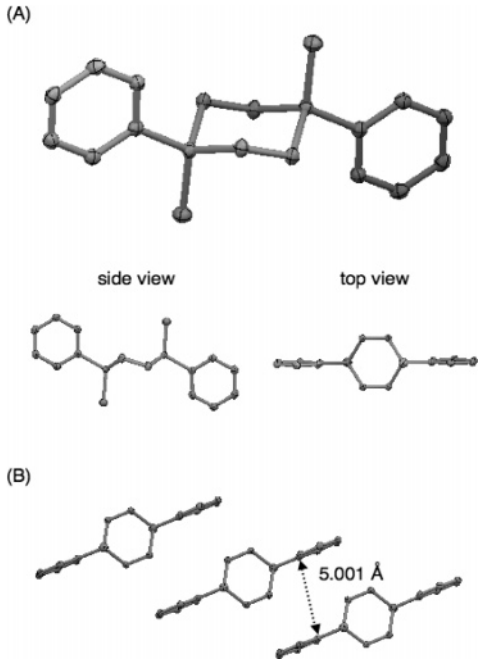


Figure 1. (A) ORTEP drawing of *trans*-**2b**. Thermal ellipsoids are drawn at the 50% probability level. (B) Top view of crystal packing structure of *trans*-**2b**. The shortest intermolecular distance of phenyl rings is included.

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(6) Recently, Gates reported the synthesis of diphosphiranium (P_2C, i.e., diphosphacyclopropane skeleton) and diphosphetanium (P_2C_2, i.e., 1,3-diphosphacyclobutane skeleton) cyclic cations from the corresponding phospha-alkenes: Bates, J. I.; Gates, D. P. *J. Am. Chem. Soc.* **2006**, *128*, 15998.

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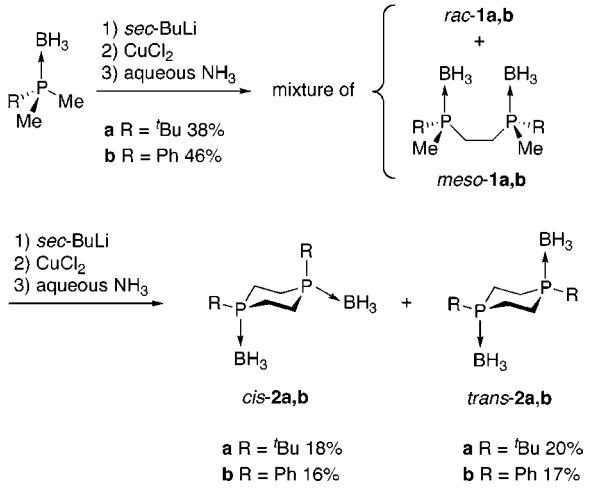
(8) Ouchi, Y.; Morisaki, Y.; Chujo, Y. *Polym. Bull.* **2007**, *59*, 339.

phenyl rings are found to be perpendicular to the diphosphacyclohexane skeleton, as shown in the side and top view in Figure 1A. In the crystal packing structure of *trans*-**2b** shown in Figure 1B, the shortest intermolecular distance of phenyl rings is 5.001 Å; therefore, there is no effective $\pi-\pi$ stacking between neighboring phenyl groups. On the other hand, *trans*-**3b** (vide infra), which does not have boranes, was synthesized by another method and characterized by X-ray crystallography.[4e] Interestingly, the ORTEP drawing shows that *trans*-**3b** adopts chair-conformation possessing the axial phenyl groups and equatorial lone pairs.[4e]

In order to construct the corresponding cis stereoisomer, optically inactive bisphosphine *meso*-**1**, i.e., (*S*,*R*)-**1** and/or (*R*,*S*)-**1**, should be prepared as a precursor.[17] Bisphosphine *meso*-**1** was synthesized by the coupling reaction of dimethylphosphine-borane without (−)-sparteine, and *rac*-bisphosphine *rac*-**1** ((*S*,*S*)-**1** and (*R*,*R*)-**1**) was also obtained simultaneously (Scheme 3). Although the isolation of the

Scheme 3. Synthesis of *cis*-1,4-Diphosphacyclohexane-diborane *cis*-**2a**,**b** and *trans*-**2a**,**b**



pure *meso*-**1** was not achieved, the intramolecular coupling reaction of a mixture of *rac*-**1** and *meso*-**1** was carried out (Scheme 3). The reaction proceeded smoothly to yield *cis*-1,4-diphosphacyclohexane-diborane *cis*-**2**, as well as *trans*-**2**. The separation of the isomers by column chromatography on SiO_2 was possible to afford the corresponding *cis*-**2a** and *trans*-**2a** in 18% and 20% yields and *cis*-**2b** and *trans*-**2b** in 16% and 17% yields (Scheme 3).

The structures of *cis*-**2** were also confirmed by ^{1}H, ^{13}C, and ^{31}P NMR, mass analysis, and elemental analysis. The ^{13}C and ^{31}P NMR spectra of *cis*-**2a** are shown in Figure 2 as representative spectra.[18] Compound *cis*-**2a** had two ethylene carbons separated clearly at 12.88 and 12.91 ppm, which

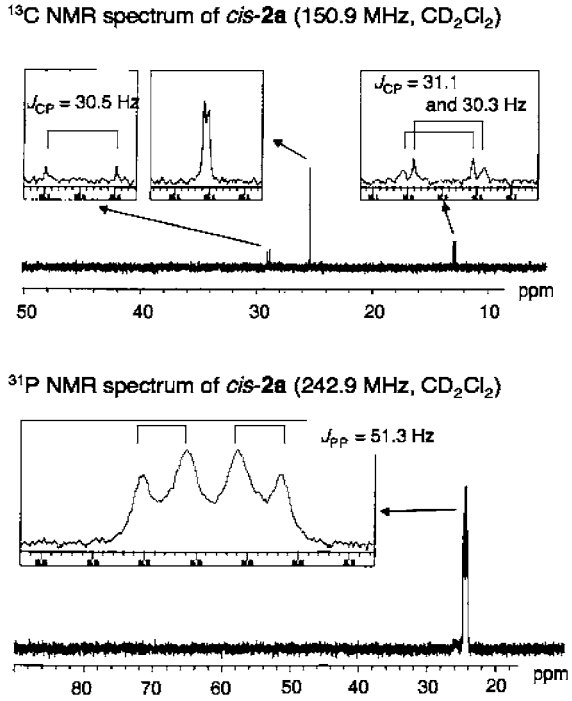


Figure 2. ^{13}C NMR (150.9 MHz, CD_2Cl_2) and ^{31}P NMR (242.9 MHz, CD_2Cl_2) spectra of *cis*-**2a**.[18]

were coupled with the phosphorus atoms with J_{CP} = 31.1 and 30.3 Hz, respectively. The methyl carbons of *tert*-butyl groups appeared at 25.40 and 25.41 ppm. The two quaternary carbons of the *tert*-butyl groups seemed to be overlapped, and they appeared at 28.9 ppm (J_{CP} = 30.5 Hz). In the ^{31}P NMR spectrum, two types of doublet peaks with J_{PP} = 51.3 Hz were observed at +24.2 and +24.7 ppm. The ^{1}H NMR spectrum also exhibited two kinds of *tert*-butyl groups, as shown in Figure S8. These spectra suggest that *cis*-**2a** adopts a chair conformation with both equatorial and axial *tert*-butyl groups in solution. Incidentally, it is reported that *cis*-**2b** acts

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

(13) The reaction without amine or with other amines such as *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) as a ligand proceede smoothly to obtain the corresponding 1,4-diphosphacyclohexane; however, the best result was obtained when (−)-sparteine was employed in the lithiation step.

(14) The oxidative intramolecular coupling reaction of enantiomer (*R*,*R*)-**1** also provides the trans isomer (*trans*-**2**) stereospecifically. Synthesis of (*R*,*R*)-**1a** was reported by Imamoto and Crépy: Imamoto, T.; Crépy K. V. L. *Tetrahedron Lett.* **2002**, *43*, 7735.

(15) The crystal data for *trans*-**2b** are as follows. $C_{16}H_{24}B_2P_2$; fw = 299.91, triclinic, *P*1 (No. 2), a = 6.761(3) Å, b = 7.616(4) Å, c = 9.075-(6) Å, b = 109.96(3)°, V = 420.3(4) Å^3, Z = 1, D_{calcd} = 1.185 g cm^{-3}. The refinement converged to R = 0.044, R_w = 0.137, GOF = 1.092.

(16) ORTEP drawing of *trans*-**2a** is shown in Figure S14 in the Supporting Information, although a desired single crystal could not be obtained.

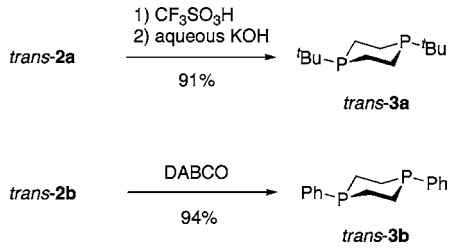
(17) The stereoselective or stereospecific synthesis of *meso*-**1** has not yet been achieved and challenged.

(18) Original spectra are shown in Figures S9 and S10 in the Supporting Information.

as a bidentate ligand for transition metals such as nickel,[2b] palladium,[2b,c] and platinum[2b,c] by adopting the boat conformation.

The removal of the coordinated boranes is demonstrated in the following deboranation reaction (Scheme 4). The boranes of *trans*-**2a** were removed by reaction with excess

Scheme 4. Removal of Boranes



trifluoromethanesulfonic acid, and subsequently with potassium hydroxide for alkylphosphine-boranes to obtain *trans*-**3a** in 91% yield.[19] Boranes of *trans*-**2b** could be easily removed under relatively mild conditions by treatment with 1,4-diazabicyclo[2.2.2]octane (DABCO) to afford the corresponding *trans*-**3b** in 94% yield.

In conclusion, we have developed the first and practical method for the construction of the *trans*-1,4-diphosphacyclohexane skeleton by the stereospecific intramolecular oxidative coupling reaction of the optically active bisphosphines (*S*,*S*)-**1**. In addition, we demonstrated that *cis*-1,4-diphosphacyclohexanes were readily obtained by the oxidative coupling reaction of the mixture of *rac*- and *meso*-bisphosphines (*rac*-**1** and *meso*-**1**). Further investigations to employ various optically active bisphosphines as a precursor and to reveal the coordination behaviors of the *trans*- and *cis*-1,4-diphosphacyclohexanes after deboranation are currently underway.

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Supporting Information Available: Experimental procedures, compound characterization data, NMR spectra, X-ray crystallographic data, and an X-ray crystallographic file (CIF) for *trans*-**2b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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