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Synthesis of optically active oligomers consisting of chiral phosphorus atoms: capture of an intermediate between a polymer and a small molecule

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Abstract—We describe here the synthesis and properties of novel optically active oligophosphines. The effect of the number of chiral phosphorus atoms on thermal properties and conformations is documented. In this study, we captured an intermediate between a polymer and a small molecule. To the best of our knowledge, it is primarily observed that a small molecule transforms into a polymer via an amorphous small molecule during the process of the elongation of the oligomer main chain.

The preparation of optically active polymers and oligomers has been one of the most extensively studied fields in synthetic polymer chemistry and has been attracting considerable interest on several accounts. A variety of optically active polymers and oligomers have been prepared, which comprise asymmetric carbons,[1] chiral axes,[2] and one-handed helical structures.[3] Recently, we have focused on a chiral hetero atom, in particular a chiral phosphorus atom,[4] as a key component of the optically active polymers, because there have been no examples of the optically active polymers possessing the chiral phosphorus atom in the polymer main chain.[5] During our investigation of the synthesis of optically active polymers with the chiral phosphorus atom, in a previous work,[4] we successfully synthesized the optically active oligophosphines (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** comprising four and eight chiral phosphorus atoms, respectively, by means of a step-by-step reaction with chiral bisphosphine (*S*,*S*)-**1** (Chart 1). It is revealed that octaphosphine (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** commences showing the characteristics of a polymer.[6]

One of our motivations for preparing optically active oligomers containing chiral phosphorus atoms was access to hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3**, which is an intermediate between (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4**. Therefore, we describe here the synthesis and properties of the novel optically active hexaphosphine

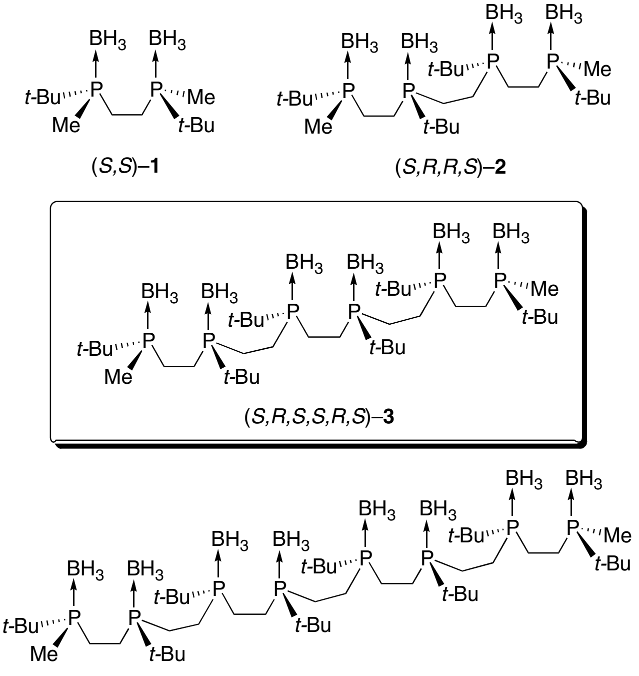

Chart 1. Optically active oligophosphines **1**–**4**.

Keywords: Chiral phosphorous atom; Optically active oligomer; Amorphous small molecule.

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(*S*,*R*,*S*,*S*,*R*,*S*)-**3** (Chart 1). The effect of the number of chiral phosphorus atoms on thermal properties and conformations in the solid state and in solution is documented. In this study, we consequently accomplished the first observation of an intermediate between a polymer and a small molecule.

We attempted a synthesis of (*S*,*R*,*S*,*S*,*R*,*S*)-**3** possessing six chiral phosphorus atoms. This employed optically active bisphosphine (*S*,*S*)-**1** as a starting material, which is available with an enantiomer excess (>99%) in two steps from trichlorophosphine according to a procedure reported by Imamoto and co-workers.[7] In our previous work,[4] we reacted (*S*,*S*)-**1** with an equimolar amount of *sec*-BuLi/(−)-sparteine to produce (*S*,*R*,*R*,*S*)-**2** possessing four chiral phosphorus atoms.[8] After many trials to produce (*S*,*R*,*S*,*S*,*R*,*S*)-**3**, the best results could be obtained by treatment of (*S*,*S*)-**1** with 1.2 equiv of *sec*-BuLi/(−)-sparteine, which gave the desired (*S*,*R*,*S*,*S*,*R*,*S*)-**3** in a 14% isolated yield,[9] as shown in Scheme 1. Although this process for the synthesis of (*S*,*R*,*S*,*S*,*R*,*S*)-**3** did not include an asymmetric reaction step, (−)-sparteine was used as an activator for *sec*-BuLi. Tetraphosphine (*S*,*R*,*R*,*S*)-**2** was also obtained in 26%, which could be easily separated by simple silica gel column chromatography.

The structure of the new optically active hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3** was confirmed by ^{1}H, ^{13}C, ^{31}P NMR, and high-resolution mass spectrometry. Figure 1 shows the ^{31}P NMR spectra of (*S*,*R*,*S*,*S*,*R*,*S*)-**3** and (*S*,*S*)-**1**. The ^{31}P NMR spectrum registers three different peaks appearing at +30.4, +39.2, and +40.3 ppm. Based on the chemical shift of the phosphorus atom in (*S*,*S*)-**1** ($\delta = +30.6$ ppm, inset of Fig. 1), the peak at +30.4 ppm in (*S*,*R*,*S*,*S*,*R*,*S*)-**3** can be assigned to the terminal phosphorus atoms. Hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3** was stable on exposure to air and moisture in

$$(S,S)\text{–}\mathbf{1}\ \xrightarrow[\text{(iii) NH}_3\text{ aq.}]{\text{(i) 1.2 eq } sec\text{-BuLi/(–)-sparteine; (ii) CuCl}_2}\ \underset{26\%}{(S,R,R,S)\text{–}\mathbf{2}} + \underset{14\%}{(S,R,S,S,R,S)\text{–}\mathbf{3}}$$

Scheme 1. Synthesis of (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*S*,*R*,*S*)-**3**.[9]

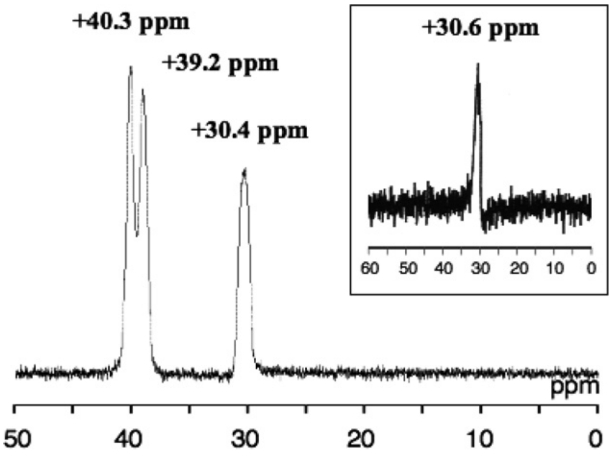


Figure 1. ^{31}P NMR spectrum of (*S*,*R*,*S*,*S*,*R*,*S*)-**3** in CDCl$_3$. Inset: ^{31}P NMR spectrum of (*S*,*S*)-**1** in CDCl$_3$.

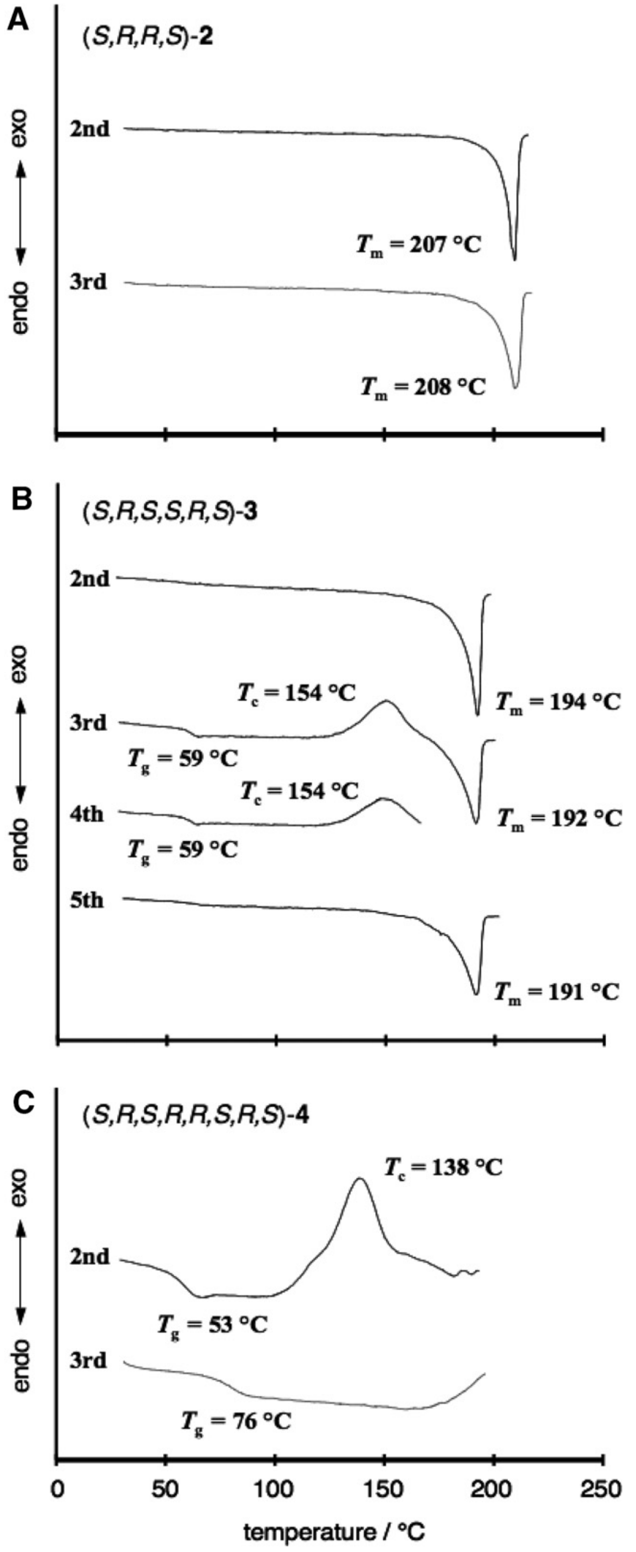


Figure 2. DSC thermograms of (A) (*S*,*R*,*R*,*S*)-**2**, (B) (*S*,*R*,*S*,*S*,*R*,*S*)-**3**, and (C) (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** at a heating rate of 10 °C/min under nitrogen.

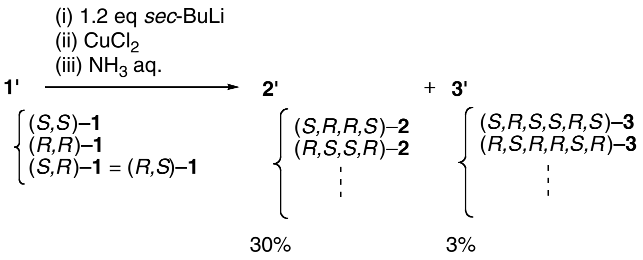
solution and in the solid state due to the coordination of boranes with the phosphorus atoms.

Differential scanning calorimetry (DSC) thermograms of optically active phosphines **2–4** are shown in Figure 2. As previously reported,[4] tetraphosphine (*S*,*R*,*R*,*S*)-**2** melted at 207–208 °C without glass transition point (T_g) (Fig. 2A), while octaphosphine (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** exhibited both the T_g at 53 °C and crystallization point T_c at 138 °C in the second cycle and only T_g at 76 °C in the third cycle (Fig. 2C).[10]

DSC thermograms of (*S*,*R*,*S*,*S*,*R*,*S*)-**3** are also shown in Figure 2B. In the second cycle,[11] only the melting point (T_m) at 194 °C was observed in the same manner as tetraphosphine (*S*,*R*,*R*,*S*)-**2**. The DSC thermogram in the third cycle was dramatically changed and exhibited T_g, T_c, and T_m at 59 °C, 150 °C, and 192 °C, respectively. In the NMR spectra, no differences were observed between the pristine sample of (*S*,*R*,*S*,*S*,*R*,*S*)-**3** and the sample after the DSC measurement. In addition, after the evaporation of the NMR sample, an identical DSC thermogram with only T_m at around 194 °C was obtained. Hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3** was a small molecule prior to heating; however, (*S*,*R*,*S*,*S*,*R*,*S*)-**3** behaved like a polymer in the solid state after heating. Interestingly, an initial thermogram with only a T_m at 191 °C was again observed in the fifth cycle, after the sample was heated up to 170 °C between T_c and T_m in the fourth cycle. The XRD study also implied this crystalline nature of an optically active oligomer (*S*,*R*,*S*,*S*,*R*,*S*)-**3**.

Once crystalline (*S*,*R*,*S*,*S*,*R*,*S*)-**3** is melted, it becomes amorphous; amorphous (*S*,*R*,*S*,*S*,*R*,*S*)-**3** is then recrystallized by heating above T_c just before T_m. In particular, (*S*,*R*,*S*,*S*,*R*,*S*)-**3** is observed to behave as an amorphous small molecule. Well-defined amorphous small molecules have received increasing attention.[12] Specifically, those with high T_g have found applications in organic materials such as light-emitting diodes. A number of the amorphous glassy compounds based on the small molecules have been synthesized; however, no reports indicate that the amorphous small molecules are responsible for the process of extension of the chain length of the oligomer.[13] Optically active hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3** exhibited only 'T_m' or 'T_g, T_c, and T_m successively' depending on its solid state, while optically active tetraphosphine (*S*,*R*,*R*,*S*)-**2** and octaphosphine (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** were always crystalline and amorphous irrespective of their crystal state. Thus, these observations suggest that optically active hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3** is an intermediate between a small molecule and a polymer.

On the other hand, we synthesized optically inactive hexaphosphine **3′** by treatment of optically inactive bisphosphine **1′** with 1.2 equiv *sec*-BuLi without (−)-sparteine (Scheme 2). Optically inactive bisphosphine **1′** is a mixture of (*rac*)-**1** and (*meso*)-**1**.[14] Therefore, optically inactive hexaphosphine **3′** is also a mixture of all (*rac*)-**3** and (*meso*)-**3**. Figure 3 shows the DSC trace obtained for optically inactive hexaphosphine **3′**. It revealed the T_g at 50 °C and the successive T_c at 128 °C in the second cycle as well as only T_g at 62 °C in the third cycle. This behavior resembles to that of optically active (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4**. Additionally, optically inactive tetraphosphine **2′** exhibited DSC characteristics similar to that of amorphous optically active hexaphosphine **3**. Thus, the enantiomeric purity affected the crystallinity of oligophosphines,[15] which was also supported by the XRD analysis.[16]



Scheme 2. Synthesis of optically inactive hexaphosphine **3′**.

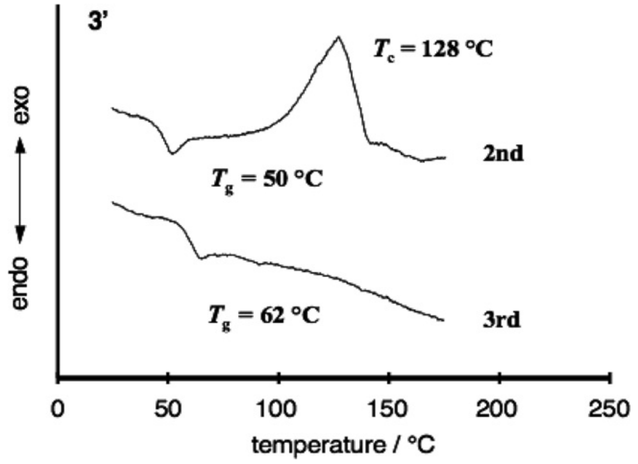


Figure 3. DSC thermograms of **3′** at a heating rate of 10 °C/min under nitrogen.

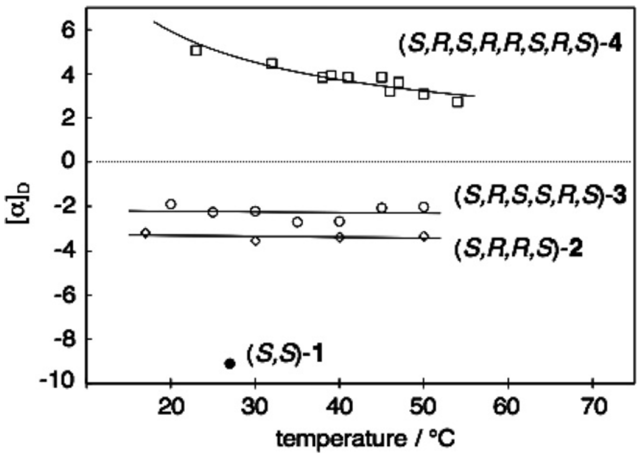


Figure 4. Optical rotation of (*S*,*S*)-**1** ($[\alpha]_D^{27}$ −9.1)[7] and optical rotation changes of (*S*,*R*,*R*,*S*)-**2**, (*S*,*R*,*S*,*S*,*R*,*S*)-**3**, and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** in CHCl$_3$.

The conformational dynamic property of (*S*,*R*,*R*,*S*)-**2**, (*S*,*R*,*S*,*S*,*R*,*S*)-**3**, and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** in CHCl$_3$ solution was investigated using a polarimeter. Figure 4 shows the temperature effect of their optical rotation. The optical rotation of (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** (*c* 1.0) was gradually reduced at a higher temperature and increased at a lower temperature reversibly, while that of (*S*,*R*,*R*,*S*)-**2** (*c* 1.0) exhibited a nearly constant value $[\alpha]_D^{17-50}$ −3.4 independent of the temperature. On the other hand, the optical rotation of (*S*,*R*,*S*,*S*,*R*,*S*)-**3** (*c* 0.5) was scattered without a tendency, and the average value was approximately $[\alpha]_D^{17-50}$ −2.0. In view of $[\alpha]_D^{27}$ −9.1 (*c* 1.0 in CHCl$_3$) of (*S*,*S*)-**1**,[7] it is speculated that chiral phosphorous atoms rotate the plane of polarized light in the counterclockwise direction, whereas the higher-ordered structure in the present system rotates it in the clockwise direction. In our system, the optical rotation $[\alpha]_D$ of the oligophosphine should reach zero with increase of the number of chiral phosphorus atoms, reminiscent of isotacitic or syndiotactic polymers. These indicate that optically active hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3** behaves like a small molecule in solution.

This work describes the synthesis of novel optically active hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3** and in detail the characterization of (*S*,*R*,*S*,*S*,*R*,*S*)-**3** as compared with a series of optically active oligophosphines (*S*,*S*)-**1**, (*S*,*R*,*R*,*S*)-**2**, (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4**, and optically inactive hexaphosphine **3′**. Bisphosphine (*S*,*S*)-**1** and tetraphosphine (*S*,*R*,*R*,*S*)-**2** are crystalline and octaphosphine (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** is amorphous, while hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3** exhibits both crystalline and amorphous states. Particularly, (*S*,*R*,*S*,*S*,*R*,*S*)-**3** behaves as an amorphous small molecule. It can be regarded that optically active hexaphosphine (*S*,*R*,*S*,*S*,*R*,*S*)-**3** is an intermediate between a small molecule and a polymer in the present system. To the best of our knowledge, it is primarily observed that the small molecule transforms into the polymer via the amorphous small molecule during the process of the elongation of the oligomer main chain.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.12.085.

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9. A solution of (−)-sparteine (0.67 mL, 2.9 mmol) in THF (15 mL) was cooled to −78 °C under N$_2$ atmosphere. To this solution with stirring, *sec*-BuLi (1.0 M in cyclohexane and *n*-hexane solution, 2.9 mL, 2.9 mmol) was added by a syringe. After 15 min, a solution of (*S*,*S*)-**1** (0.64 g, 2.4 mmol) in THF (5.0 mL) was added dropwise, and the mixture was stirred at −78 °C over 3 h. Dry CuCl$_2$ (0.49 g, 3.7 mmol) was added in one portion with vigorous stirring, and the reaction mixture was allowed to slowly warm to room temperature. After 15 h, the reaction mixture was quenched by the addition of 28% aqueous NH$_3$ (5.0 mL) and extracted with CH$_2$Cl$_2$ (50 mL × 3). The combined extracts were washed with 5% aqueous NH$_3$, 2 M HCl, and brine. The organic layer was dried over MgSO$_4$. After the solvent was removed under

reduced pressure, the residue was purified by column chromatography on silica gel with hexane–CH_2Cl_2 (v/v = 3:1 to 0:10) to give (*S*,*R*,*R*,*S*)-**2**[4] (0.16 g, 0.31 mmol, 26%) and (*S*,*R*,*S*,*S*,*R*,*S*)-**3** (87 mg, 0.11 mmol, 14%) as colorless solids. (*S*,*R*,*S*,*S*,*R*,*S*)-**3**. Mp 191–194 °C; $R_f = 0.58$ CH_2Cl_2 100%; $[\alpha]_D^{25}$ −1.8 (*c* 0.5 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.00–0.87 (br, –BH_3, 18H), 1.17 (d, –PC(CH_3)$_3$, *J*(H,P) = 13.6 Hz, 18H), 1.19 (d, –PC(CH_3)$_3$, *J*(H,P) = 13.6 Hz, 18H), 1.20 (d, –PC(CH_3)$_3$, *J*(H,P) = 13.2 Hz, 18H), 1.25 (d, –PCH_3, *J*(H,P) = 9.6 Hz, 6H), 1.68–2.18 (br, –PCH_2–, 20H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = 5.45$ (d, –PCH_3, *J*(C,P) = 33.9 Hz) 14.6 (d, –PCH_2–, *J*(C,P) = 29.0 Hz), 14.7 (d, –PCH_2–, *J*(C,P) = 29.8 Hz), 14.8 (d, –PCH_2–, *J*(C,P) = 28.1 Hz), 14.9 (d, –PCH_2–, *J*(C,P) = 29.8 Hz), 15.9 (d, *t*-BuCH_3PCH_2–, *J*(C,P) = 30.6 Hz), 25.2 (s, (CH_3)$_3$CCH_3P–), 25.6 (s, –CH_2PC(CH_3)$_3$$CH_2$–), 25.7 (s, –$CH_2$PC($CH_3$)$_3$$CH_2$–), 27.7 (d, ($CH_3$)$_3CCH_3$P–, *J*(C,P) = 33.1 Hz), 29.0 (d, –CH_2P*C*(CH_3)$_3$$CH_2$–, *J*(C,P) = 31.5 Hz), 29.1 (d, –CH_2P*C*(CH_3)$_3$$CH_2$–, *J*(C,P) = 30.6 Hz) ppm; $^{31}P\{^1H\}$ NMR (109.3 MHz, $CDCl_3$) δ +30.4, +39.2, +40.3 ppm; HRMS (FAB) calcd for $C_{36}H_{97}B_6P_6$ $[M-H]^+$: 781.6574, found 781.6560.

10. Octaphosphine (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**4** exhibited decomposition at approximately 220 °C before melting due to the dissociation of boranes according to the thermogravimetric analysis (TGA).
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15. This point would be worth considering. The effort to clarify the crystallinity of other optically pure enantiomers is currently underway.
16. Optically inactive tetraphosphine **2′** and hexaphosphine **3′** exhibited the broad diffraction peaks and the halo peak, respectively.