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Synthesis of oligomers including eight P-chiral centers and the construction of the 12-phosphacrown-4 skeleton

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Abstract—The stepwise oxidative coupling reaction from (*S*,*S*)-**1** gave optically active oligomers, (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3**, having four and eight chiral phosphorus atoms, respectively. The behaviors of these oligomers in the solid state and in solution were investigated in detail. The first construction of a 12-phosphacrown-4 skeleton was also reported.

A number of naturally occurring macromolecules are optically active compounds possessing components of asymmetric hydrocarbon frameworks.[1] Their precisely stereoregulated higher-order structure, which is represented by a helical conformation arising from a chiral unit, plays an important role in vital functions such as molecular recognition and catalytic activity.[1] The artificial construction of the helical polymers[2] and oligomers[3] by repetition of asymmetric reactions, by using chiral units, and by external stimuli, has attracted considerable interest in the past decade. In addition, helicity induction and chiral amplification of optically inactive polymers by chiral additives were also reported.[4] Almost all of these polymers and macromolecules are composed of a carbon skeleton including the chiral carbon or the chiral axis. Although helical polysilanes consist of silicon atoms in the main chain, their helices are derived from chiral carbons in the alkyl side chain.[2k,m,5]

In this area, we focused on the chiral phosphorus atom. This is because the synthesis of the optically active polymer possessing the chiral heteroatom in the main chain is limited.[6] In addition, a trivalent phosphorus atom has the coordination ability for several transition metals. It also has the possibility to not only control the higher-order structure of the resultant P-chiral polymer by metal additives but also to exhibit a high asymmetric catalytic performance. Wild and co-workers reported the synthesis and isolation of three kinds of optically active hexaphosphines having four P-chiral centers by another approach, and a unique double-stranded parallel helicate of the copper complex was characterized.[7] We report herein the synthesis and the comparison of properties of optically active oligophosphines (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3**, which possess four and eight chiral phosphorus atoms, respectively, by the stepwise oxidative coupling reaction from (*S*,*S*)-1,2-bis(boranato-(*t*-butyl)methylphosphino)ethane (*S*,*S*)-**1**.[8] In addition, we report the successful synthesis of 12-phosphacrown-4 tetraborane **4**, which is the first example of the construction of a 12-phosphacrown-4 skeleton.

Our strategy for the construction of the P-chiral oligomer involves using (*S*,*S*)-**1** as a chiral building block, which was previously prepared by Imamoto et al.[8] The synthesis of the tetramer (*S*,*R*,*R*,*S*)-**2**[9] and the octamer (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3**[9] was accomplished by the oxidative coupling reaction from compound **1** using *sec*-BuLi and (−)-sparteine, as shown in Scheme 1. Although this procedure for the synthesis of (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** does not include an asymmetric reaction step, (−)-sparteine was used as an activator of the alkyllithium reagent. Column chromatography provided the target compounds, which were air stable in solution and in the solid state due to the coordination of boranes to phosphorus atoms.[10]

On the other hand, during the investigation of the octamer (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** synthesis, we found the first

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Keywords: Chiral phosphorus atoms; Optically active oligomer; Oxidative coupling reaction; 12-Phosphacrown-4.

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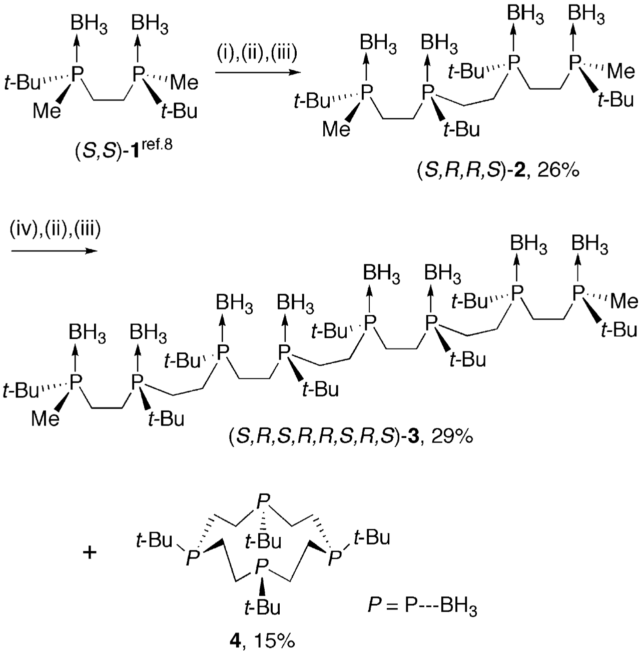
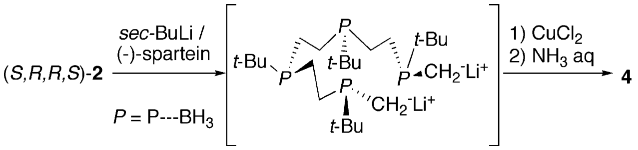


Scheme 1. Reagents and conditions: (i) 1 equiv of *sec*-BuLi and (−)-sparteine, THF, −78 °C; (ii) $CuCl_2$, Et_2O, −78 °C; (iii) NH_3 aq; (iv) 2 equiv of *sec*-BuLi and (−)-sparteine, THF, −78 °C.

formation of the phosphacrown framework, 12-phosphacrown-4 tetraborane **4**,[11] by an intramolecular C–C coupling reaction (15% yield), which gave a new route to phosphacrown skeletons (Scheme 1). The molecular structure of 12-phosphacrown-4 tetraborane **4** was established by X-ray structure analysis (Fig. 1).[11] *tert*-Butyl groups are located at the upper and lower sides alternately against the plane involving four phosphorus atoms (Fig. 1). Considering the stereochemistry of (*S*,*R*,*R*,*S*)-**2** (Scheme 2), only this conformation of **4** is adopted by the intramolecular oxidative coupling reaction. This is the first compound that consists of four ethylene units and four phosphorus junctions instead of oxygen atoms in 12-crownether-4.[12,13] Since the phosphorus atom has a high affinity with the late transition metals in contrast to oxygen or nitrogen atoms, 12-phosphacrown-4 would play an important role in the fields of molecular recognition chemistry as well as organometallic chemistry.



Scheme 2.

Differential scanning calorimetry (DSC) revealed the solid state behavior of the tetramer (*S*,*R*,*R*,*S*)-**2** and the octamer (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** under the heating condition. Their DSC curves are shown in Figure 2. As can be seen from the thermogram, (*S*,*R*,*R*,*S*)-**2** exhibited only one clear melting point (T_m) at 207 °C. On the other hand, (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3**, which possessed eight chiral phosphorus atoms, exhibited both a typical glass transition temperature (T_g) at 53 °C and a subsequent exothermic peak at 138 °C in the second run (Fig. 2).[14] Furthermore, (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** again exhibited T_g at a higher temperature of approximately 76 °C during the third and the fourth runs (Fig. 2).[15] In the ^{1}H NMR spectra, no differences were observed between the pristine sample of (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** and the sample after the DSC measurement. Both pristine and annealed samples of (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** exhibited an amorphous feature by X-ray powder diffraction (XRD) measurement (Fig. 3). These results imply that the exothermic phase transition peak at 138 °C can be attributed to the local crystallization peak. On the other hand, it is reported that (*S*,*S*)-**1** melts at 169–171 °C.[8] Upon increasing the number of chiral phosphorus

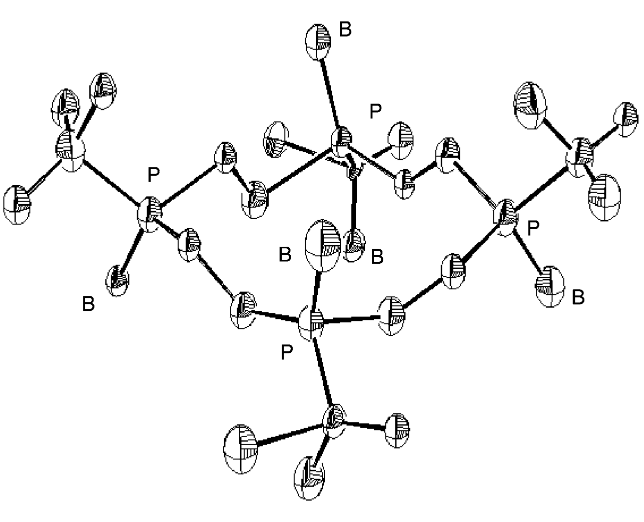


Figure 1. ORTEP drawing of 12-phosphacrown-4 tetraborane **4** with 30% thermal ellipsoids. The hydrogen atoms are omitted for clarity.

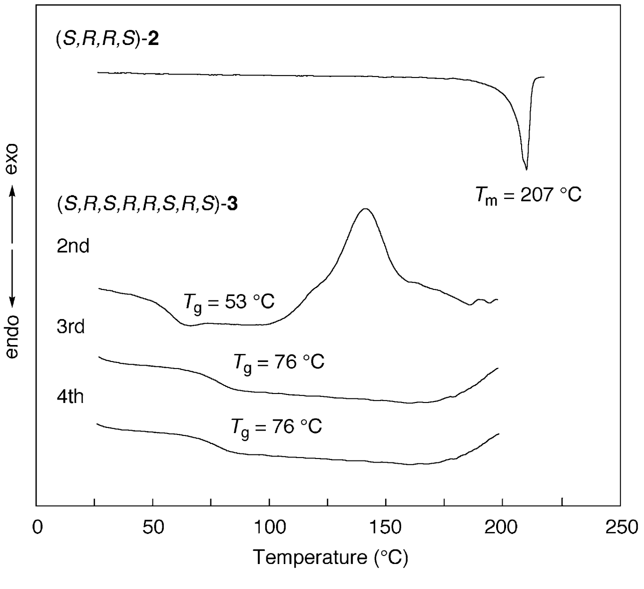


Figure 2. DSC thermograms of (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3**.

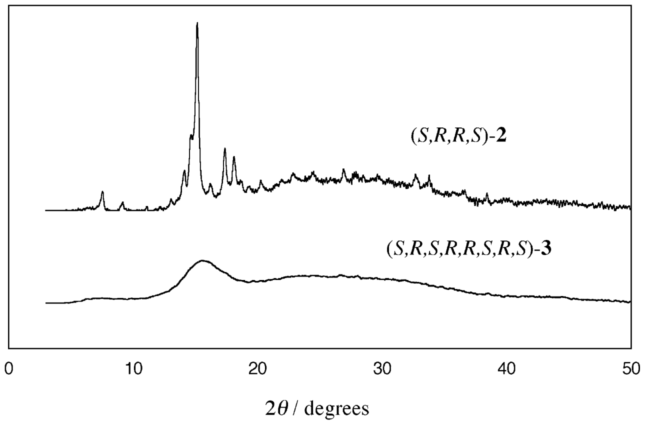


Figure 3. XRD patterns of (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3**.

atoms from four to eight, the octamer (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** showed features of a polymer.

The conformational dynamic properties of the tetramer (*S*,*R*,*R*,*S*)-**2** and the octamer (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** in $CHCl_3$ solution were investigated using the polarimeter.[16] Figure 4 shows the temperature effect of the optical rotation of (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3**. The optical rotation of (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** ($c = 1.0$) was gradually reduced at a higher temperature and increased at a lower temperature, while that of (*S*,*R*,*R*,*S*)-**2** exhibited a nearly constant value $[\alpha]_D^{17-50} = -3.4$ ($c = 1.0$) independent of the temperature.[17] Considering the reversible optical rotation changes of (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** in response to seesaw heating, it is implied that the second-order structure of (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** loosely folds at a low temperature and collapses as the temperature increases.

In conclusion, optically active oligophosphines (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** possessing four and eight chiral phosphorus atoms, respectively, have been prepared. The octamer (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** begins exhibiting behavior as a polymer, that is, the existence of T_g in the solid state and changes of the second-order structure in solution. The present study also demonstrates the first access to the construction of the 12-phosphacrown-4 skeleton. Further studies on the removal of the boranato groups from all compounds, and on the addition of transition metals to octaphosphine as well as 12-phosphacrown-4, are now underway.

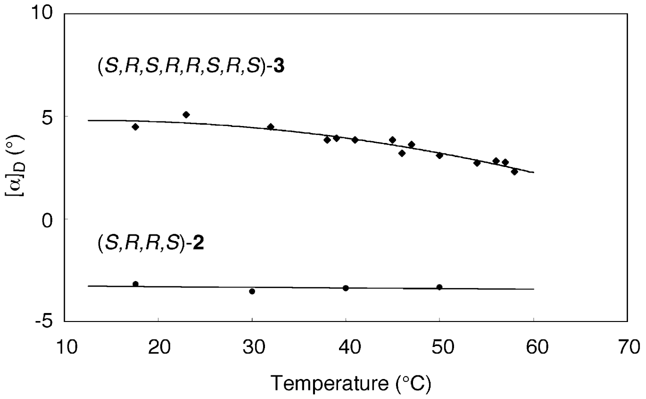


Figure 4. Optical rotation changes of (*S*,*R*,*R*,*S*)-**2** and (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** in $CHCl_3$.

Acknowledgements

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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.2005.08.039.

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9. Compound (*S*,*R*,*R*,*S*)-**2**: colorless solid; $[\alpha]_D^{25} = -3.4$ ($c = 1.0$, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$): $\delta = 0.40$ (br q, $-BH_3$, $^1J(H,B) = 98.8$ Hz, 12H), 1.17 (d, $(CH_3)_3C$, $^3J(H,P) = 13.6$ Hz, 18H), 1.20 (d, $(CH_3)_3C$, $^3J(H,P) = 13.6$ Hz, 18H), 1.24 (d, $P–CH_3$, $^2J(H,P) = 10$ Hz, 6H), 1.57–1.83 (m, $-PCH_2-$, 6H), 1.83–2.11 ppm (m, $-PCH_2-$, 6H); ^{13}C NMR (67.5 MHz, $CDCl_3$): $\delta = 5.44$ (d, $P–CH_3$, $^1J(C,P) = 35.2$ Hz), 14.7 (d, $-PCH_2-$, $^1J(C,P) = 29.2$ Hz), 14.8 (d, $-PCH_2-$, $^1J(C,P) = 29.1$ Hz), 16.0 (d, $-PCH_2-$, $^1J(C,P) = 30.4$ Hz), 25.0 ($(CH_3)_3CCH_3P-$), 25.7 ($-CH_2PC(CH_3)_3CH_2-$), 27.6 (d, $(CH_3)_3CCH_3P-$, $^1J(C,P) = 32.8$ Hz), 29.0 ppm (d, $-CH_2PC(CH_3)_3CH_2-$, $^1J(C,P) = 31.5$ Hz); $^{31}P\{^1H\}$ NMR (109.3 MHz, $CDCl_3$): $\delta = +31.5$, +39.9 ppm. HRMS (FAB) calcd for $C_{24}H_{65}P_4B_4$ $[M-H^+]$: 521.4409, found: 521.4392. Anal. Calcd for $C_{24}H_{66}P_4B_4$: C, 55.23; H, 12.74. Found: C, 55.38; H, 12.10.
   Compound (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3**: colorless solid; $[\alpha]_D^{25} = +5.2$ ($c = 1.0$, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$): $\delta = 0.01–0.90$ (br, $-BH_3$, 24H), 1.10–1.34 (br, $(CH_3)_3C$, 72H), 1.25 (s, $P–CH_3$, 6H), 1.55–2.30 ppm (br, $-PCH_2-$, 28H); ^{13}C NMR (67.5 MHz, $CDCl_3$): $\delta = 11.3$ ($P–CH_3$), 14.0–15.7 ($-PCH_2-$), 25.6 ($(CH_3)_3CP-$), 29.7 ppm ($(CH_3)_3CP-$); $^{31}P\{^1H\}$ NMR (109.3 MHz, $CDCl_3$): $\delta = +30.1$, +34.9, +39.2 ppm. LRMS (ESI) calcd 1041.8, found: 1025.8 $[M-CH_3-H^+]$. MALDI-TOF-MS (dithranol as a matrix and sodium trifluoroacetate as a cationizing agent) calcd for: $C_{48}H_{130}P_8B_8$: 1041.8, found: 1063.0 $[M+Na^+]$.
10. The removal of borane from these stable compounds was not carried out, since the primary purpose of this study was to evaluate the conformational behaviors of the optically active oligomer.
11. Compound **4**: colorless solid; ^1H NMR (270 MHz, $CDCl_3$): $\delta = 0.01–0.90$ (br, $-BH_3$, 12H), 1.11–1.30 (br, $(CH_3)_3C$, 36H), 1.70–1.83 (br, $-PCH_2CH_2P-$, 8H), 1.85–2.00 ppm (br, $-PCH_2CH_2P-$, 8H); ^{13}C NMR (67.5 MHz, $CDCl_3$): $\delta = 15.2$ (d, $-PCH_2PCH_2-$, $^1J(C,P) = 27.3$ Hz), 25.6 ($-PC(CH_3)_3-$), 28.9 ppm (d, $-PC(CH_3)_3-$, $^1J(C,P) = 33.2$ Hz); $^{31}P\{^1H\}$ NMR (109.3 MHz, $CDCl_3$): $\delta = +40.9$ ppm. HRMS (FAB) calcd for $C_{24}H_{63}P_4B_4$ $[M-H^+]$: 519.4253, found: 519.4257.
   Crystal data for **4**: $C_{24}H_{64}B_4P_4$, $M = 519.90$, crystal dimensions $0.20 \times 0.20 \times 0.20$ mm^3, orthorhombic, $a = 14.28(1)$ Å, $b = 19.04(1)$ Å, $c = 12.91(1)$, $U = 3507(1)$ Å^3, $T = 296$ K, space group $P2_12_12_1$ [No. 19], $Z = 4$, μ(Mo Kα) = 0.78 cm^{-1}, Rigaku AFC5R diffractometer, $\rho_{calcd} = 1.05$ g cm^{-3}, $\lambda = 0.71069$ Å, $\omega - 2\theta$ scan (16°/min), $2\theta_{max} = 55°$, 6543 reflections, 1410 independent, $R = 0.106$, $R_w = 0.114$. CCDC-256581 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road Cambridge CB21EZ, UK; fax: (+44) 1223 336 033; or deposit@ccdc.cam.ac.uk).
12. Successful synthesis of the first 1,4,7-triphosphacyclononane derivatives, 9-phosphacrown-3 skeleton, was reported, see: Edwards, P. G.; Newman, P. D.; Abdul Malik, K. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2922; And several polyphosphamacrocycles have been synthesized using the appropriate templates, for example, see: (a) Price, A. J.; Edwards, P. G. *Chem. Commun.* **2000**, 899; (b) Harnisch, J. A.; Angelici, R. *J. Inorg. Chim. Acta* **2000**, *300*, 273; (c) Avarvari, N.; Mézailles, N.; Ricard, L.; Floch, P. L.; Mathey, F. *Science* **1998**, *280*, 1587; (d) Mizuta, T.; Okano, A.; Sasaki, T.; Nakazawa, H.; Miyoshi, K. *Inorg. Chem.* **1997**, *36*, 200.
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14. The first cycle was heated up to 100 °C (10 °C/min) and exhibited same T_g as the second cycle.
15. The octamer (*S*,*R*,*S*,*R*,*R*,*S*,*R*,*S*)-**3** exhibited decomposition at around 220 °C according to the thermogravimetric analysis (TGA).
16. Although a circular dichromism (CD) spectrometer is a powerful tool for the studies on the dynamics of a chiral compound in solution, compounds **1**–**3** do not absorb light in the appropriate UV range.
17. Compound (*S*,*S*)-**1** shows $[\alpha]_D^{27} = -9.1$ ($c = 1.0$, $CHCl_3$): see Ref. 8. This information speculates that chiral phosphorus atoms rotate the plane of polarized light counterclockwise, and higher-order structure in the present system rotates it clockwise.