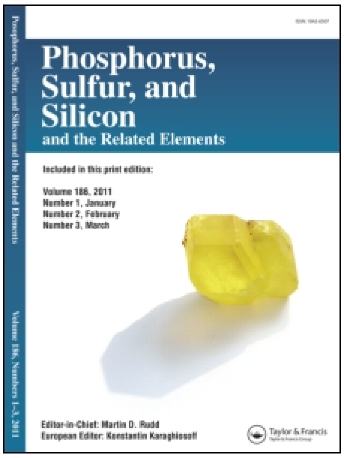

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Synthesis, Crystal Structure, and Diastereomeric Transfer of Pentacoordinated Phosphoranes Containing Valine or Iso-Leucine Residue

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SYNTHESIS, CRYSTAL STRUCTURE, AND DIASTEREOMERIC TRANSFER OF PENTACOORDINATED PHOSPHORANES CONTAINING VALINE OR ISO-LEUCINE RESIDUE

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Pentacoordinated phosphoranes containing valine or iso-leucine residue (2-phenyl-2,7^5-spiro[1,3,2-phenanthrodioxaphosphole-2,2′-1,3,2-oxazaphospholan]-5′-one) were synthesized through sequential two-step reactions, whereby the reaction products of phenyldichlorophosphine with N,O-bis(trimethylsilyl)valine or iso-leucine were followed by the addition of phenanthrenequione, and the crystals of 4a and 4b were obtained from benzene and hexane mixed solution. The x-ray structure of the crystals 4a and 4b revealed that they are distorted TBP, exhibiting R_P absolute configuration. The ^{31}P NMR spectra showed that the S_P diastereomer could transfer into the other one R_P that came out from the solution during crystallization. Correspondingly, when it was dissolved in solvents the R_P diastereomer transferred into the other one S_P, and the pair of diastereomers changed each other in solution at room temperature through a phosphonium carboxylate zwitterions intermediate.

Keywords: Crystal structure; diastereomeric transfer; pentacoordinated phosphorane

Pentacoordinted phosphorus compounds have attracted attention as models for intermediates or transition states in nonenzymatic and enzymatic phosphoryl transfer reactions.[1–3] The stereochemical

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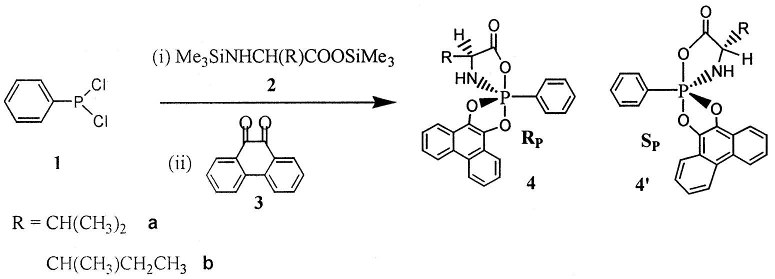
course and product distribution of phosphoryl transfer reactions have been discussed in terms of structure, stereochemistry, and pseudorotational processes of the proposed pentacoordinated phosphorus intermediates.[4,5] The structures of many nonenzymic unchiral and chiral P(V) model systems have been studied extensively by x-ray crystallography.[6–11] Akiba et al.[12] synthesized the first stable optically phosphoranes with asymmetry only at the pentacoordinated phosphorus atom from diastereomeric phosphoranes. On the other hand, the pentacoordinated phosphoranes containing amino acid residue were considered important intermediates in self-assembly reactions of N-phosphoamino acids into peptides,[13] and later the stable pentacoordinated phosphorus compounds were synthesized.[14] In this article, two pentacoordinated phosphoranes containing valine or isoleucine residue were synthesized and isolated as enantiopure diasteremer by crystallization, and the absolute configuration of the phosphorus atom in the TBP structure was determined by x-ray diffraction.

RESULTS AND DISCUSSION

Synthesis of 4,4′ and Preparation of Crystal 4a,b

Synthetic pathway of pentacoordinated phosphoranes **4**,**4**′ is shown in Scheme 1. Equiv. of N,O-bis(trimethylsilyl)amino acid (**2a** or **2b**) in benzene was added to phenyldichlorophosphine (**1**) benzene solution at room temperature under nitrogen atmosphere, 10 min later equiv. of phenanthrenequione (**3**) was added to the resulting solution, and the reactions completed in 2.5 h. The crystals of **4a** and **4b** suitable for x-ray diffraction were obtained by recrysatllization from benzene and hexane mixed solvents.



SCHEME 1 Synthetic pathway of pentacoordinated phosphoranes **4**,**4**′.

TABLE I Phosphorus Bond Lengths (Å) and Angles (deg) (Deviations from Ideal Skeletal Symmetries in Parentheses) in Compounds **4a** and **4b**

	4a	**4b**
P(1)–O(1)	1.643(3)	1.661(4)
P(1)–O(2)	1.735(3)	1.728(4)
P(1)–O(3)	1.740(3)	1.761(4)
P(1)–N(1)	1.616(3)	1.603(5)
P(1)–C(1)	1.795(5)	1.812(7)
N(1)–P(1)–O(1)	124.51° (4.51°)	127.30° (7.30°)
N(1)–P(1)–O(2)	91.00° (1.00°)	90.20° (0.20°)
O(1)–P(1)–O(2)	91.03° (1.03°)	91.40° (1.40°)
N(1)–P(1)–O(3)	88.61° (−1.39°)	89.00° (−1.00°)
O(1)–P(1)–O(3)	85.50° (−4.50°)	84.50° (−5.50°)
O(2)–P(1)–O(3)	175.50° (−4.50°)	174.10° (−5.90°)
N(1)–P(1)–C(1)	121.60° (1.60°)	119.40° (−0.60°)
O(1)–P(1)–C(1)	113.67° (−6.33°)	113.10° (−6.90°)
O(2)–P(1)–C(1)	93.09° (3.09°)	92.70° (2.70°)
O(3)–P(1)–C(1)	90.92° (0.92°)	92.70° (2.70°)

Crystal Structure of Compound 4a and 4b

The selected bond lengths and angles are listed in Table I. The data show that the phosphorus atom in pentacoordinated phosphoranes (**4a**, **4b**) is at the center of a distorted TBP, each of the two five-membered rings occupies apical-equatorial positions as shown in Figure 1.

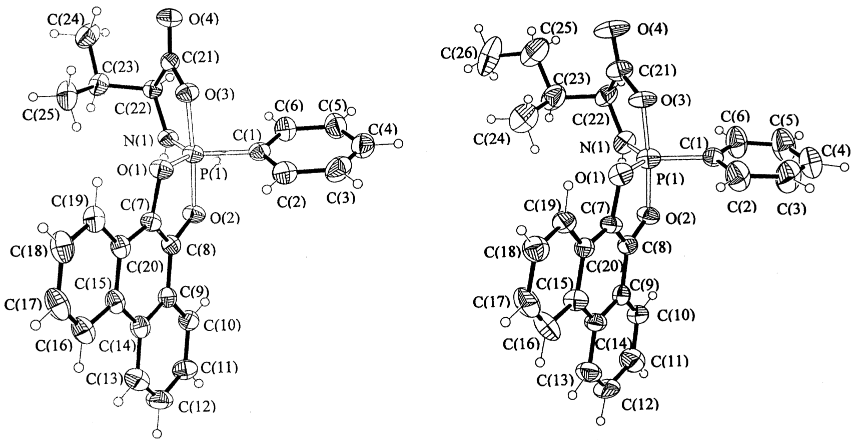


FIGURE 1 The ORTEP drawings of **4a** (left) and **4b** (right).

The skeletal symmetries of two crystal structures keep with structural principles of the relative apicophilicity (tendency occupy the axial site) of ligands in the trigonal bipyramid.[15] According to Table I the apical anhydride bond (P(1)—O(3) = 1.740 Å in **4a**, 1.761 Å in **4b**) is longer than the other apical P—O bond (P(1)—O(2) = 1.735 Å in **4a**, 1.728 Å in **4b**). In three equatorial bonds, the longest bond is P(1)—C(1) bond (1.795 Å in **4a**, 1.812 Å in **4b**), and the shortest one is P(1)—N(1) bond (1.616 Å in **4a**, 1.603 Å in **4b**). It is clearly shown that the apical P(1)—O(2) bond (1.735 Å in **4a**, 1.728 Å in **4b**) is longer than the equatorial P(1)—O(1) bond (1.643 Å in **4a**, 1.661 Å in **4b**).

The pertinent bond angles are very close to the ideal angles 180°, 120°, and 90° of the D_{3h} symmetry as shown in Table I. For example, bond angles O(2)—P(1)—O(3) in **4a**, **4b** are 175.50° and 174.10°, respectively, the corresponding deviations from ideal angle 180° are only −4.50° and −5.90°. The angles between the apical and equatorial bonds and the corresponding deviations (in parentheses) from ideal 90° are as follows: O(3)—P(1)—C(1) = 90.92° (0.92°) in **4a**, 92.70° (2.70°) in **4b**; N(1)—P(1)—O(3) = 88.61° (−1.39°) in **4a**, 89.00° (−1.00°) in **4b**; O(1)—P(1)—O(3) = 85.50° (−4.50°) in **4a**, 84.50° (−5.50°) in **4b**, correspondingly, the angles between two equatorial bonds and the corresponding deviations (in parentheses) from ideal 120°: N(1)—P(1)—O(1) = 124.51° (4.51°) in **4a**, 127.30° (7.30°) in **4b**; N(1)—P(1)—C(1) = 121.60° (1.60°) in **4a**, 119.40° (−0.60°) in **4b**; O(1)—P(1)—C(1) = 113.67° (−6.33°) in **4a**, 113.10° (−6.90°) in **4b**.

Interconversion Between the Diastereomers 4 and 4′ in Solution and Effect of Solvents to Their ^{31}P NMR Chemical Shifts

The addition of 2,2′ with 3 produced diastereomers 4,4′ corresponding to two peaks (peak area 1:1) in ^{31}P NMR spectrum, the crystal, however, was only one of the diastereomers by x-ray diffraction analysis, ^{31}P NMR of the crystal in organic solvents also showed a single peak, and the remaining mother liquid still appeared the two peaks (peak area 1:1) corresponding to the diastereomers. For example, Figure 2 showed ^{31}P NMR of reaction solution (4,4′a) (A), the crystal (**4a**) redissolved (B) and remaining mother liquid (4,4′a) (C) in benzene at room temperature (25°C). It is interesting that the crystal **4a** dissolved in benzene showed a single peak at ^{31}P NMR −29.36 ppm at starting point, with time elongating another peak at ^{31}P NMR −28.91 ppm appeared till the two peaks reached the same area in 6 h as shown in Figure 3. These results indicate that the diastereomers can transfer each other in the

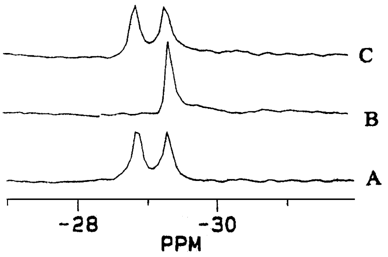


FIGURE 2 ^{31}P NMR of reaction solution with **4a**, **4′a** (A), the crystal **4a** redissolved (B) and remaining mother liquid with **4a**, **4′a** (C) in benzene.

solution at room temperature through phosphonium carboxylate zwitterions intermediate (**4″**) because carboxylate group, electron donating nitrogen at phosphorus and a NH hydrogen in **4″** can stabilized the carboxylate anion (Scheme 2).

We found that the relative chemical shifts between **4** and **4′** were different in different solvents as shown in Table II. According to Table II, with rise of solvent polarity ^{31}P NMR chemical shifts of pentacoordinated phosphoranes **4**,**4′** moved to low field, i.e., bigger chemical shifts (it is exception for benzene). The difference values ($\Delta\delta = \delta_{4'} - \delta_4$) of chemical shifts between the diastereomers were affected by solvents, for example 0.47 ppm in toluene, 0.00 ppm in dichloromethane and -0.14 ppm in acetone between **4a** and **4′a**. Figure 4 shows the ^{31}P NMR change of **4a** in acetone with time, the chemical shift of **4a** is bigger than that of **4′a** which is different to data in benzene (Figure 3).

CONCLUSION

Reaction of phenyldichlorophosphine with N,O-bis(trimethylsilyl)-amino acids in benzene solution was followed by the addition of phenanthrenequione in situ, this afforded crystals of **4a** and **4b**, only one of the

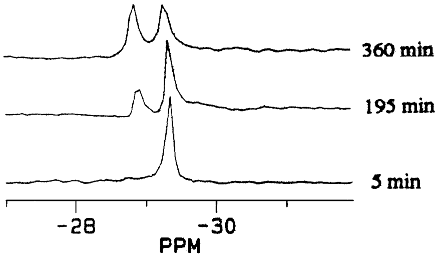
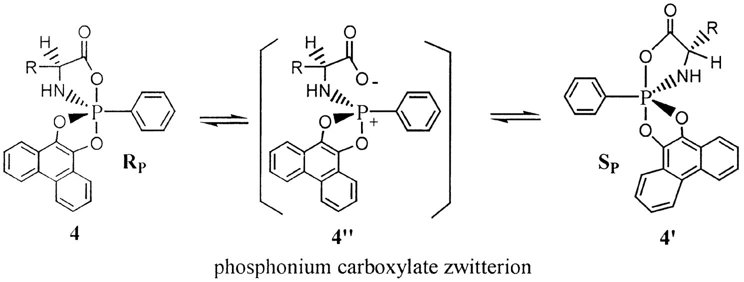


FIGURE 3 ^{31}P NMR changes of **4a** in benzene with time.



SCHEME 2 Interconversion between the diastereomers **4** and **4′** in solution at room temperature through phosphonium carboxylate zwitterion intermediate.

diastereomers by recystallizing from benzene and hexane mixed solution. X-ray structural analysis of **4a** and **4b** shows that the compounds are slight distorted TBP symmetries, each of five-membered rings occupies apical-equatorial position, and the P—O bond of the anhydride is the apical site, P—N bond the equatorial site. **4** and **4′** in solution can transfer each other at room temperature through phosphonium carboxylate zwitterions intermediate.

EXPERIMENTAL SECTION

Reagents and Procedure

Chemicals were obtained from local companies, and all solvents were dried before use. ^{1}H, ^{13}C NMR were recorded on a Bruker AM 500 spectrometer in $CDCl_3$ solvent with chemical shifts in ppm relative to tetramethysilane ($\delta = 0$). Chemical shifts for ^{31}P NMR spectra were obtained on a Bruker AC 200 p spectrometer with use of 85% H_3PO_4 ($\delta_P = 0$) as an external standard. Elemental analysis was carried out on

TABLE II ^{31}P NMR Chemical Shifts (ppm) and Difference Value ($\Delta\delta = \delta_{4'} - \delta_4$) of **4** and **4′** in Different Solvents

Compound	Carbontetro-achloride	Benzene	Toluene	Dichloro-methane	Acetone	Acetonitrile
4′a	−29.68	−28.91	−29.00	−28.00	−26.67	−26.20
4a	−30.00	−29.36	−29.47	−28.00	−26.53	−26.01
$\Delta\delta$	0.32	0.45	0.47	0.00	−0.14	−0.19
4′b	−29.82	−29.14	−29.29	−28.19	−26.81	−26.32
4b	−30.20	−29.54	−29.68	−28.19	−26.65	−26.15
$\Delta\delta$	0.38	0.40	0.39	0.00	−0.16	−0.17

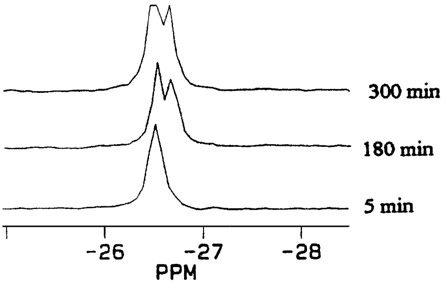


FIGURE 4 ^{31}P NMR change of **4a** in acetone with time.

a Carlo Erba 1106 CHN analyzer. Field desorption mass spectra were recorded on a Finnigan MAT 90 double-focusing mass spectrometer.

General Procedure for Preparation of 4a and 4b

To a stirred solution of phenyldichlorophosphine (**1**) (0.895 g, 5 mmol) in anhydrous benzene (8 ml) at room temperature under a nitrogen atmosphere was added dropwise N,O-bis(trimethylsilyl)valine or isoleucine[16] (5 mmol) in benzene (7 ml). After 10 min phenanthrenequione (0.93 g, 4.5 mmol) was added in small portions to the resulting solution. The reaction completed in 2.5 h as traced by ^{31}P NMR spectroscopy. Most of the solvent was removed by rotary evaporation, and the remaining solution (about 3 ml) was diluted with hexane, 3–6 days later the light yellow crystal was obtained. For compound **4a**, yield 63%. m.p. 219–211°C, Found: H 5.08 C 69.49 N 3.21, $C_{25}H_{22}NO_4P$ requires H 5.14 C 69.60 N 3.25. ^{31}P NMR δ_P −29.36 ppm (benzene). ^{1}H NMR ($CDCl_3$) δ_H 1.02 (3H, d, γ_1-CH_3, $^3J = 6.9$ Hz), 1.05 (3H, d, γ_2-CH_3, $^3J = 6.9$ Hz), 2.24 (1H, m, β-CH), 3.89 (1H, m, α-CH), 3.96 (1H, NH, $^2J_{PNH} = 15.0$ Hz), 7.32–7.38 (3H, m, o, p-Ph), 7.50–7.55 (2H, m, m-Ph), 7.83–8.65 (8H, m, —Ar). ^{13}C NMR ($CDCl_3$) δ_C 16.35 (γ_1-CH_3), 18.70 (γ_2-CH_3), 31.25 (β-CH), 60.48 (α-CH), 120.23, 120.93, 122.23, 123.02, 122.21, 124.54, 125.45, 126.07, 126.69, 127.21, 127.74, 128.25, 128.40, 130.08, 130.18, 131.23, 133.01, 134.02, 135.81, 137.92 (—Ph, —Ar), 169.62 (C=O, $^2J_{POC} = 10.0$ Hz), FDMS: M^+ m/z 431; For compound **4b**, yield 76%. M.P. 210–212°C, ^{31}P NMR δ_P −29.54 ppm (benzene). Found: H 5.40 C 70.11 N 3.07, $C_{26}H_{24}NO_4P$ requires H 5.43 C 70.11 N 3.14. ^{1}H NMR ($CDCl_3$) δ_H 0.90 (3H, t, δ-CH_3, $^3J = 7.4$ Hz), 1.04 (3H, t, γ-CH_3, $^3J = 6.9$ Hz), 1.36, 1.60 (2H, m, γ-CH_2), 1.92 (1H, m, β-CH), 3.96 (1H, m, α-CH), 4.01 (1H, NH, $^2J_{PNH} = 17.9$ Hz), 7.31–7.39 (3H, m, o,p-Ph), 7.50–7.68 (2H, m, m-Ph), 7.83–8.66 (8H, m, —Ar). ^{13}C NMR ($CDCl_3$) δ_C 11.65 (δ-CH_3), 15.29 (γ-CH_3), 24.16 (γ-CH_2), 38.20 (β-CH), 59.87 (α-CH), 120.15, 120.81, 122.21, 123.01, 123.20, 124.53, 125.44, 126.04, 126.69, 127.20, 127.71, 128.06, 128.39, 130.05, 130.14, 131.36, 132.96, 134.00, 135.80, 137.88 (–Ph, –Ar), 169.62 (C=O, $^2J_{POC} = 8.25$ Hz). FDMS: M^+ m/z 445.

X-Ray Crystallography Experimental Section

The crystal data, data collection, and structure refinement for compounds **4a** and **4b** are summarized in Table III. The intensity data were collected at room temperature (294 ± 1°K) and monitored by three standards every hour. No decay was observed except the statistic fluctuation in the range of ±4.0%. Raw intensities were corrected for Lorentz and polarization effects, and for absorption by empirical method based on ψ-scan data.[17] The structures were solved by direct methods. Hydrogen atoms were created geometrically, ridded on their parent atoms in the refinement and included in the calculations of structure factors. All nonhydrogen atoms were subjected to anisotropic refinement. The final full-matric least-square refinement on F^2 converged with $R1 = 0.0404$ and $wR2 = 0.0836$, **4a**, 0.0482 and 0.0646, **4b**, for observed reflections [$I \geq 2\sigma(I)$]. The absolute configurations of the compounds estimated by

TABLE III Crystal Data, Data Collection, and Structure Refinement for **4a** and **4b**

Compound	**4a**	**4b**
Molecular formula	$C_{25}H_{22}NO_4P$	$C_{26}H_{24}NO_4P$
Molecular weight	431.41	445.43
Crystal size	0.50 × 0.30 × 0.20 mm	0.30 × 0.30 × 0.20 mm
Color	Light yellow	Light yellow
Crystal system, space group	Monoclinic, $P2_1$	Orthorhombic, $P2_12_12_1$
Unit cell parameters	a = 5.3430(10) Å, b = 20.438(4) Å c = 9.872(2) Å $\beta = 101.02^\circ$	a = 8.459(2) Å b = 9.722(2) Å c = 27.344(2) Å
Volume	1058.1(4) Å^3	2248.7(8) Å^3
Z, Calculated density	2, 1.354 g/cm^3	4, 1.316 g/cm^3
Diffractometer	Rigaku AFC6S	Enraf-Nonius CAD4
Absorption coefficient	0.163 mm^{-1}	0.155 mm^{-1}
Transmission factor	0.8229–0.9679	0.8244–0.9695
Data collection rang	$0 \leq h \leq 6$, $0 \leq k \leq 24$, $-11 \leq l \leq 11$	$0 \leq h \leq 10$, $0 \leq k \leq 11$, $0 \leq l \leq 32$
Reflections unique/ observed [$I \geq 2\sigma(I)$]	1921/1606	2265/830
Goodness-of-fit on F^2	1.036	1.404
Final R indices [$I > 2\sigma$ (I)]	$R_1 = 0.0386$, $wR_2 = 0.0957$	$R_1 = 0.0482$, $wR_2 = 0.0646$
R indices (all data)	$R_1 = 0.0545$, $wR_2 = 0.1056$	$R_1 = 0.1753$, $wR_2 = 0.0724$
Residual extrema in final difference map	0.175 to -0.257 e Å^{-3}	0.217 to -0.268 e Å^{-3}

Flack parameter[18] were in agreement with that of starting material, L-valine for **4a** and L-isoleucine for **4b**. Computations were performed using the SHELX97 program package[19] on an IBM PC 586 computer. Analytic expressions of atomic scattering factors were employed, and anomalous dispersion corrections were incorporated.[20]

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