Reaction of *R*-(+)-2-benzylideneaminobutan-1-ol with ethylene phosphorochloridite. Stereospecific formation of (3*R*,5*R*)-2-(2-chloroethoxy)-5-ethyl-2-oxo-3-phenyl-1,4,2-oxazaphosphorinane

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The reaction of *R*-(+)-2-benzylideneaminobutan-1-ol with ethylene phosphorochloridite afforded phosphorus-epimeric (3*R*,5*R*)-2-(2-chloroethoxy)-5-ethyl-2-oxo-3-phenyl-1,4,2-oxazaphosphorinanes. The phosphorinane-ring closure proceeded stereospecifically and occurred only from one of the diastereofacial sides (*re*) of the C=N bond.

Key words: *R*-(+)-2-benzylideneaminobutan-1-ol, ethylene chlorophosphite, intramolecular heterocyclization, stereospecificity, 1,4,2-oxazaphosphorinanes, X-ray diffraction analysis.

The reactions of P^{III} acid halides with alcohols containing the C=N bond as the second functional group have not been adequately investigated. In several studies,[1—3] polycyclic phosphoranes were obtained by reactions of Cl—P^{III}-containing derivatives with phenols bearing the imino group in the side chain of the aromatic ring. We discovered a new pathway of the reaction performed with analogous systems. In the present study, we report the results of investigation on the pathway and stereochemistry of the reaction of *R*-(+)-2-benzylideneaminobutan-1-ol (**1**) with ethylene phosphorochloridite.

Results and Discussion

According to the ^{31}P NMR spectrum of the reaction mixture, the reaction afforded products **A** and **B** in a ratio of 2.4 : 1 (δ_P 12.4 (**A**) and 16.8 (**B**)). The major product **A** was isolated by chromatography on SiO_2 as an air-stable colorless crystalline compound. According to the X-ray diffraction data,* this product has the structure of (2*S*,3*R*,5*R*)-2-(2-chloroethoxy)-5-ethyl-2-oxo-3-phenyl-1,4,2-oxazaphosphorinane in which the Et and Ph groups are in the equatorial positions and the $ClCH_2CH_2$ group is in the axial position (Fig. 1; Table 1). We failed to isolate minor product **B** in the individual form due to the close values of R_f.

To establish the structure of product **B**, we used a fraction of the eluate containing (the ^{31}P NMR spectroscopic data) a mixture of compounds **A** and **B** in a ratio of 1 : 10. According to the results of ^1H NMR spectroscopy in CD_3CN, both compounds contain the Et groups in the equatorial positions. This is evidenced by the spin-spin coupling constants of the axial protons at the C(5) and C(6) atoms ($^3J_{H(5),H(6)}$ 11.0 (**A**) and 10.7 Hz (**B**)). The protons at the C(3) atom of products **A** and **B** have close chemical shifts and geminal constants $^2J_{HP}$ (δ 4.35 and $J = -12.5$ Hz (**A**); δ 4.37 and $J = -10.7$ Hz (**B**)). It is known[4,5] that the $^2J_{HP}$ constants in the NMR spectra of 1,4,2-oxazaphosphorinanes vary from −8.0 to −11.4 and from −15.0 to −19.2 Hz for the axial and equatorial protons, respectively. The parameters of the ^{13}C NMR spectra (CD_3CN) of prod-

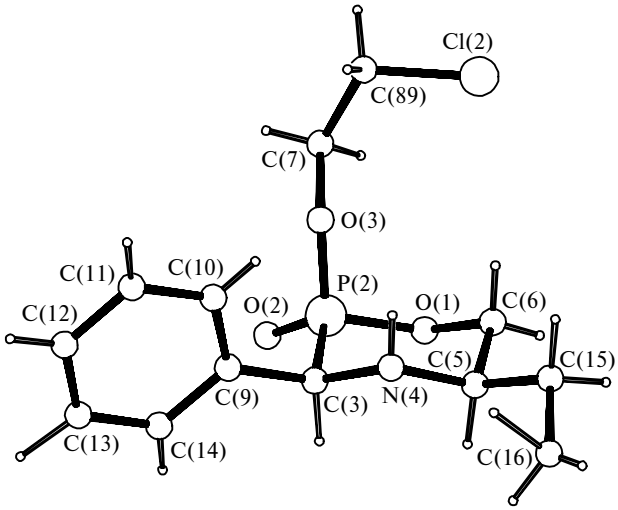

Fig. 1. Molecular geometry of product **A** in the crystal.

* The detailed results of X-ray diffraction analysis will be published elsewhere.

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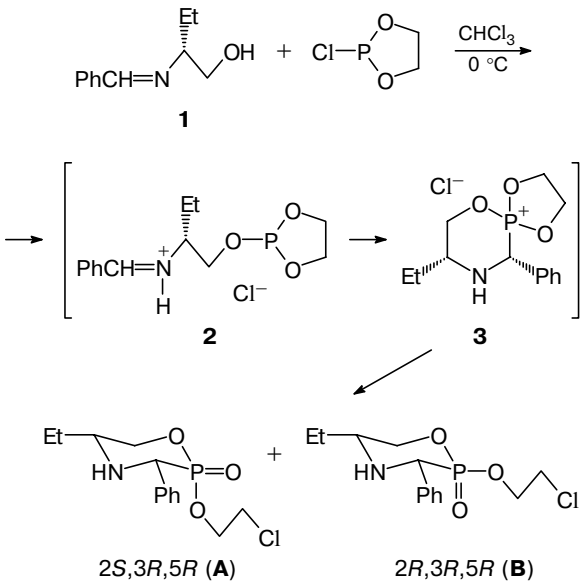
Table 1. Selected bond lengths (*d*) and bond angles (ω) in molecule **A**

Bond	*d*/Å	Angle	ω/deg
P(2)—O(1)	1.583(2)	O(1)—P(2)—O(2)	110.1(1)
P(2)—O(2)	1.466(2)	O(1)—P(2)—O(3)	106.4(1)
P(2)—O(3)	1.572(2)	O(1)—P(2)—C(3)	104.0(1)
P(2)—C(3)	1.818(2)	O(2)—P(2)—O(3)	115.7(1)
N(4)—C(3)	1.476(3)	O(2)—P(2)—C(3)	117.7(1)
N(4)—C(5)	1.467(3)	O(3)—P(2)—C(3)	101.8(1)
C(5)—C(6)	1.515(4)	P(2)—O(1)—C(6)	117.6(2)
O(1)—C(6)	1.467(4)	P(2)—O(3)—C(7)	122.4(2)
O(3)—C(7)	1.442(3)	P(2)—C(3)—N(4)	110.7(1)
Cl(2)—C(8)	1.766(3)	P(2)—C(3)—C(9)	112.8(2)
C(3)—C(9)	1.503(3)	C(3)—N(4)—C(5)	113.1(2)
C(5)—C(15)	1.525(5)	N(4)—C(3)—C(9)	113.8(2)
		N(4)—C(5)—C(6)	112.4(2)
		N(4)—C(5)—C(15)	110.4(2)
		C(6)—C(5)—C(15)	109.2(2)
		O(1)—C(6)—C(5)	110.8(2)
		O(3)—C(7)—C(8)	109.0(2)
		Cl(2)—C(8)—C(7)	112.3(2)
		C(3)—C(9)—C(10)	121.7(2)
		C(3)—C(9)—C(14)	120.2(2)
		C(10)—C(9)—C(14)	118.1(2)
		C(5)—C(15)—C(16)	112.2(3)

ucts **A** and **B** also have very close values (see Experimental). Based on comparison of the ^{1}H, ^{13}C, and ^{31}P NMR spectroscopic data, it can be stated that the H(3) proton in compound **B**, like that in compound **A**, is in the axial position, *i.e.*, the chiral C(3) atoms possess the same *R* configurations. The results of IR spectroscopy and the data from elemental analysis indicate that product **B** has the structure of (2*R*,3*R*,5*R*)-2-(2-chloroethoxy)-5-ethyl-2-oxo-3-phenyl-1,4,2-oxazaphosphorinane and differs from product **A** only in the arrangement of the substituents at the P atom. The possible scheme of the reaction (Scheme 1) involves the formation of the immonium salt, *viz.*, (*R*)-2-benzylideneammoniobutyl ethylene phosphite (**2**), its intramolecular heterocyclization to give quasiphosphonium salt **3**, and the transformation of the latter into the final reaction products (**A** and **B**) according to the Arbuzov reaction. The fact that the C(3) atom of the heterocycle has the same configuration in both products provides evidence that the ring closure proceeded stereospecifically, *i.e.*, the nucleophilic attack of the P atom on the electrophilic C atom of the imino group occurred only from one of the diastereofacial sides (*re*) of the C=N bond.

Scheme 1



Experimental

The starting *R*-(+)-2-benzylideneaminobutan-1-ol (**1**) with the m.p. 54—55 °C, $[\alpha]_D^{20}$ +28.0 (*c* 13.2, MeOH) (*cf.* lit. data[6]: m.p. 55—56 °C, $[\alpha]_D^{25}$ +39.3) was prepared from freshly distilled commercial *R*-(−)-2-aminobutan-1-ol (Fluka, Switzerland) with $[\alpha]_D^{20}$ −7.0 (neat) and benzaldehyde according to a procedure described previously.[6] The solvents were purified and dried according to standard procedures.[7]

The optical rotation was measured on a Polamat A polarimeter. The specific optical rotation and the concentrations of the solutions are expressed in (deg mL) (g dm)$^{-1}$ and g (100 mL)$^{-1}$, respectively. The ^{1}H NMR spectra were recorded on a Bruker WM-250 spectrometer (250 MHz) with respect to Me_4Si. The ^{13}C and ^{31}P NMR spectra were measured on a Bruker MSL-400 instrument (100 MHz for ^{13}C, with respect to Me_4Si; 162 MHz for ^{31}P, with respect to 85% H_3PO_4); CD_3CN was used as the solvent. The IR spectra were recorded on a UR-20 spectrometer.

The crystallographic data for product **A**, at +20 °C: $C_{13}H_{19}NO_3PCl$, monoclinic space group $P2_1$, a = 11.260(2) Å, b = 5.6986(3) Å, c = 11.845(2) Å, β = 106.61(1)°, V = 747.0(2) Å^3, Z = 2, M = 303.73, d_{calc} = 1.35 g cm^{-3}, μ(Mo) = 3.7 cm^{-1}, F(000) = 320. The intensities of 1746 reflections were measured on an automated Enraf—Nonius CAD-4 diffractometer at 20 °C (λ Mo-Kα, ω/2θ scanning technique, $2\theta_{max} < 53.8°$) of which 1609 reflections were with $I > 3\sigma$. The structure was solved by the direct method using the SIR program[8] and refined first isotropically and then anisotropically. The H atoms were revealed from difference electron density maps and refined isotropically at the final stage of the refinement. All calculations were carried out with the use of the MolEN program package[9] on an AlphaStation 200 computer. To establish the absolute structure and, hence, the absolute configuration of molecule **A**, we refined the "direct" and inverted structures. The reliability factors for the "direct" structure were R = 0.032, R_w = 0.046 and the corresponding values for the inverted structure were R = 0.033, R_w = 0.047. According to the Hamilton test,[10] the "direct" structure corresponds to the absolute structure with the probability of 95%. The final values of the reliability factors were as follows: R = 0.032, R_w = 0.045 using 1612 independent reflections with $F^2 \geq 3\sigma$.

(3*R*,5*R*)-2-(2-Chloroethoxy)-5-ethyl-2-oxo-3-phenyl-1,4,2-oxazaphosphorinanes (A and B). A solution of ethylene phosphorochloridite (1 g, 7.9 mmol) in anhydrous $CHCl_3$ (8 mL) was added dropwise with cooling (~0 °C) to a solution

of *R*-(+)-2-benzylideneaminobutan-1-ol (**1**) (1.4 g, 7.9 mmol) in anhydrous $CHCl_3$ (10 mL) in an atmosphere of dry argon. After warming to ~20 °C, the reaction mixture was stirred for 1 h. Then the solvent was evaporated *in vacuo* and the oily yellowish residue was chromatographed on SiO_2 (L 100/160 μm) in a 4 : 1 toluene—MeCN mixture. Product **A** was obtained in a yield of 0.62 g, a mixture of products **A** and **B** in a ratio of 2.3 : 1 was obtained in a yield of 1.24 g, and a mixture of products **A** and **B** in a ratio of 1 : 10 was obtained in a yield of 0.29 g. The total yield of compounds **A** and **B** was 90%.

(2*S*,3*R*,5*R*)-Epimer (A), m.p. 104—105 °C, $[\alpha]_D^{20}$ +115.9 (*c* 2.7, MeOH). Found (%): C, 51.49; H, 6.10; Cl, 11.58; N, 4.53; P, 10.02. $C_{13}H_{19}ClNO_3P$. Calculated (%): C, 51.40; H, 6.26; Cl, 11.70; N, 4.61; P, 10.21. IR (KBr, Nujol mulls), ν/cm^{-1}: 3272 (NH); 1256 (P=O); 1047, 1035 (P—O—C). ^{1}H NMR, δ: 0.95 (t, 3 H, C(5)CH_3, $^3J_{HH}$ = 7.5 Hz); 1.42 (m, 2 H, C(5)CH_2, $^3J_{HH}$ = 7.5 Hz); 3.08 (m, 1 H, C(5)H); 3.53 (m, 2 H, CH_2Cl); 3.73—4.02 (m, 2 H, P(2)OCH_2); 4.11 (ddd, 1 H, C(6)H_{ax}, $^2J_{C(6)Hax,C(6)Heq}$ = −11.0 Hz, $^3J_{HP}$ = 1.6 Hz, $^3J_{C(6)Hax,C(5)Hax}$ = 11.0 Hz); 4.27 (ddd, 1 H, C(6)H_{eq}, $^2J_{C(6)Heq,C(6)Hax}$ = −11.0 Hz, $^3J_{HP}$ = 18.8 Hz, $^3J_{C(6)Heq,C(5)Hax}$ = 3.1 Hz); 4.35 (d, 1 H, C(3)H, $^2J_{HP}$ = −12.5 Hz); 7.35—7.50 (m, 5 H, Ph). ^{13}C NMR, δ: 59.87 (C(3), $^1J_{CP}$ = 137.42 Hz); 57.66 (C(5), $^3J_{CP}$ = 2.5 Hz); 76.00 (C(6), $^2J_{CP}$ = 8.1 Hz). ^{31}P NMR, δ: 13.6.

A mixture of the (2*S*,3*R*,5*R*)- and (2*R*,3*R*,5*R*)-epimers (A+B, 1 : 10), n_D^{20} 1.5302, $[\alpha]_D^{20}$ +16.2 (*c* 1.7, MeOH). Found (%): C, 51.55; H, 6.38; Cl, 11.89; N, 4.73; P, 10.01.

(2*R*,3*R*,5*R*)-Epimer (B). IR (KBr, thin films), ν/cm^{-1}: 3270 (NH); 1260, 1240 (P=O); 1040, 1010 (P—O—C). ^{1}H NMR, δ: 1.00 (t, 3 H, C(5)CH_3, $^3J_{HH}$ = 7.5 Hz); 1.50 (m, 2 H, C(5)CH_2, $^3J_{HH}$ = 7.5 Hz); 3.18 (m, 1 H, C(5)H, $^3J_{C(5)Hax,C(6)Hax}$ = 10.7 Hz); 3.68 (m, 2 H, CH_2Cl); 3.63—3.83 (m, 2 H, P(2)OCH_2); 4.37 (d, 1 H, C(3)H, $^2J_{HP}$ = −10.7 Hz); 5.34—5.74 (m, 2 H, C(6)H_2); 7.36—7.71 (m, 5 H, Ph). ^{13}C NMR, δ: 59.66 (C(3), $^1J_{CP}$ = 139.32 Hz); 58.01 (C(5), $^3J_{CP}$ = 0 Hz); 74.92 (C(6), $^2J_{CP}$ = 6.0 Hz). ^{31}P NMR, δ: 17.4.

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