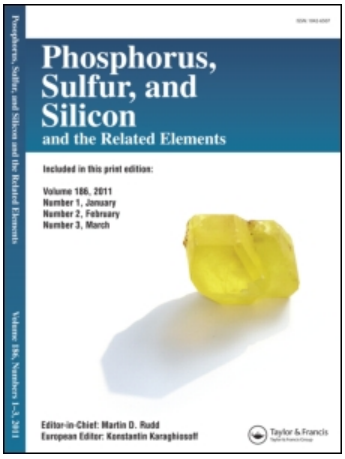

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STEREOSELECTIVE WAY TO DERIVATIVES OF N-PHOSPHORYLATED AMINO ACIDS

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In honor of Professor Reinhard Schmutzler's 60th birthday

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Stereoselective synthesis of the N-phosphor (V) substituted amino acids (**2, 3**) via the N-phosphor (III) derivatives of amino acids (**1**) are described. The diastereoisomers of N-phosphor (V) amino acids are separated by crystallization or column chromatography and used as starting compounds for preparation of chiral N-chloroamides. The prepared compounds have been characterized by NMR spectra and HPLC.

Key words: N-phosphor (III) substituted L-leucine esters, N-thiophosphor (V) substituted L-leucine esters, N-phospor (V) substituted L-leucine esters, N-chloro-N-phosphor (V) amino acids esters, diastereoisomers, stereoselectivity, NMR spectra, HPLC.

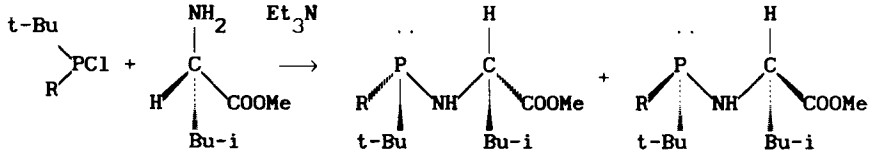
INTRODUCTION

N-Phosphorylated amino acids and proteins play important roles in the regulation of enzyme activity, protein biosynthesis, and can undergo various bio-mimic reaction.[1–5] Many of them show pharmacological properties.[2,4] Various methods for phosphorylation of amino acids and their derivatives were proposed.[1–6] However these methods possess low stereoselectivity.[7] At that time, as is known, the stereoisomers of bioactive compounds have great differences in chemical properties and biological activity. Therefore stereoselective methods for the N-phosphorylated amino acids synthesis are very important. In this work we have found that transformations of N-phosphor (III) substituted amino acids to N-phosphor (V) derivatives of amino acid are highly stereoselective, and that this reaction may be potentially a route to stereochemically pure diastereoisomers of these compounds.

RESULTS AND DISCUSSION

N-phosphor (III) amino acid esters may be easily obtained by reaction of chlorophosphines with amino acid esters. To the best of our knowledge, the N-phosphorus (III) substituted amino acid esters have not been heretofore described. The reaction of phosphinic acid chlorides with L-leucine [(+)-(R)-leucine] esters readily occurs in the presence of triethylamine at the room temperature or by heating at low

temperatures to provide very good yields of N-phospor (III) substituted L-leucine esters (**1a**, **b**).



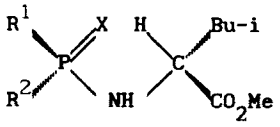
1a,b

R=i-Bu (a), Ph (b); (S,R):(R,R) 1:1

N-Phosphor (III) substituted L-leucine esters (**1a**, **b**) are stable colorless liquids distillable under reduced pressure, and can be preserved for a long time when they are carefully protected from air. The ^{31}P-{^{1}H} NMR spectra show the presence of two (RR) and (SR)-diastereoisomers of the compounds (**1a**, **b**) in the 1:1 ratio (Table I). The reaction of compounds (**1a**, **b**) with sulfur proceeds smoothly in benzene at room temperature to give with very good yields and high stereoselectivity the esters of N-thiophosphonoleucine (**2a**, **b**). Analysis of their NMR spectra (^{1}H and ^{31}P) indicated that the crude products (**2a**, **b**) were a mixture of two diastereoisomers in the ratio 94:6 (R = i-Bu) and 75:25 (R = Ph) (Table I). The diastereoisomers of N-thiophosphono-leucine (**2a**, **b**) were observed by means of the high performance liquid chromatography (HPLC). Pure major stereoisomer of (**2b**) was isolated by crystallization from hexane as a colorless stable solid in nearly

TABLE I

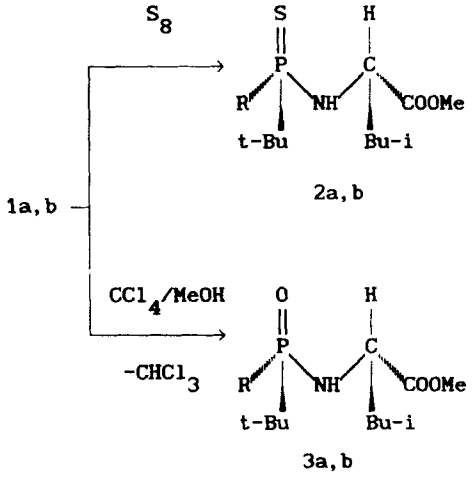
Diastereoisomeric ratios of N-phosphorylated L-leucine esters (**1–3**) determined by NMR spectra[a] and HPLC[b]



1-3

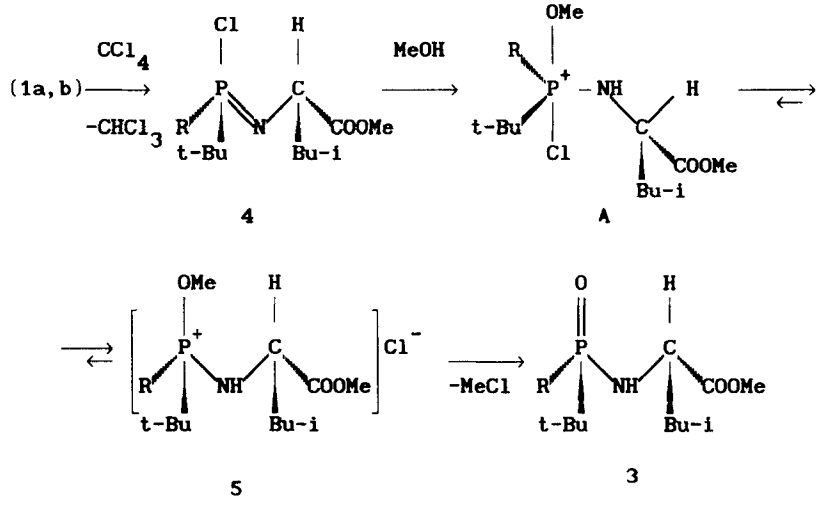
N	R^1	R^2	X	diastereo-isomeric ratios
(1a)	t-Bu	i-Bu	2e	47:53[a]
(1b)	t-Bu	Ph	2e	50:50[a]
(2a)	t-Bu	i-Bu	S	94:6[a,b]
(2b)	t-Bu	Ph	S	75:25[a,b]
(3a)	t-Bu	i-Bu	O	~100:0[a,b]
(3b)	t-Bu	Ph	O	88:12[a,b]

100% diastereoisomeric purity. Minor stereoisomer of (**2b**) was isolated as a colorless viscous liquid containing about 20% of the major diastereoisomer, which have been separated neither by crystallization nor column chromatography.

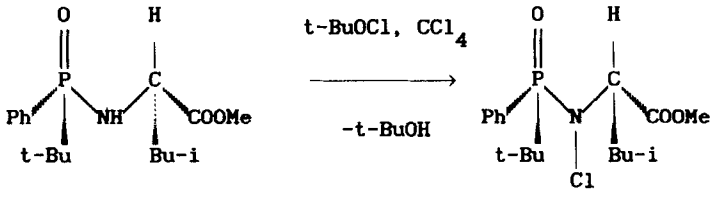


The successive treatment of the (RR) and (SR)-diastereoisomer mixture (**1**) with carbon tetrachloride and methyl alcohol afforded with very good yields and high stereoselectivity the N-phosphorylated amino acid esters (**3**). The careful analysis of the ^{1}H and ^{31}P NMR spectra shows that the crude compound (**3a**, R = i-Bu) contains only one diastereoisomer of two possible. The HPLC confirmed ~100% content of the only diastereoisomer of compound (**3a**) and absence of the other. At that time the NMR spectrum (^{1}H and ^{31}P) and HPLC of the crude product (**3b**, R = Ph) clearly indicated the presence of two diastereoisomers in the ratio 72:18. The compounds (**3a**, **b**) are rather stable and may be isolated from reaction the mixture by sublimation under reduced pressure as colorless crystalline solids with the same diastereomeric ratios. The major diastereoisomer of compound (**3b**) was separated by crystallization from hexane with 100% diastereoisomeric purity. The residual mother liquor consisted of two diastereoisomers in proportion 1:1. All efforts to achieve its further enrichment in diastereoisomer by using crystallization from different solvents were unsuccessful. However each of the two diastereoisomers of the mother liquor was isolated in pure state by silicagel column chromatography. High purity of these compounds were confirmed by ^{31}P NMR spectra which in a variety of solvents revealed exclusively a single line absorption. The ^{1}H NMR spectra of the diastereoisomers of (**3b**) were in excellent accord with their structure and clearly show the difference between them. Particularly striking is the difference between the CH_3O [$\Delta\delta(CH_3O)$ 0.2 ppm] and $(CH_3)_2C$ groups [$\Delta\delta$ [$(CH_3)_2C$] 0.14 ppm]. The ratios of these isomers as well as the purity of the isolated diastereoisomers of compound (**3b**) were confirmed by high performance liquid chromatography. The isomer with negative sign of optical rotation having a longer retention time constituted the major product, while the isomer with positive sign of optical rotation having shorter retention time was a minor component. No significant difference exists between the diastereoisomeric ratios of compounds (**2**, **3**) as estimated by ^{31}P NMR spectra and HPLC (Table I). Selectivity of separation

increases with decreasing content of methanol in the eluent for N-phosphorylated amino acid esters (**3**) and does not change for N-thiophosphorylated amino acid esters (**2**). An additional point to emphasize is that the separation of diastereoisomers of compounds (**2**) is characterized by appreciably low selectivity than that for more polar compounds (**3**). Changes in free energy of sorbtion (ΔG) of diastereoisomers on octadecyl sorbent in 65–80% aqueous methanol eluents is 0.37–0.95 kJ/mol for compounds (**3**) and 0.15–0.20 kJ/mol for compounds (**2**). It is evident that such an imbalance of diastereoisomers should not be obtained in a classical resolution. Indeed it is more reminiscent of a thermodynamic resolution. The study of the mechanism shows that the reaction proceeds via the formation of chloroiminophosphoranes (**4**), which may be verified by means of NMR spectra. The chloro-imino phosphorane (**4a**) was isolated by distillation under vacuo as a colorless liquid containing in accordance with the ^{31}P and ^{1}H NMR spectra a 1:2 mixture of two diastereoisomers. Treatment of the chloroiminophosphoranes (**4a**) with methanol at low temperature affords the alkoxyphosphonium salt (**5a**), which was verified by NMR, δ_P 84 ppm. The salt (**5a**) is converted into N-phosphorylated amino acid esters (**3a**) via the Arbusov reaction with very high stereoselectivity. In this case the equilibrium into thermodynamic products can be probably achieved through ligand rearrangement in a pentacoordinate intermediate (**A**). We are currently studying the stereochemistry and mechanism of this transformation in detail.



The N-phosphorylated amino acid esters (**3a**, **b**) are useful starting compounds for preparations of stereochemically pure chiral reagents. Thus, they can be easily converted to chiral N-chloroamides, which as we have recently showed are potential enantioselective chlorinating agents.[8] The chlorination of (**3a**, **b**) is achieved with *tert*-butylhypochlorite, a powerful chlorinating agent, easily prepared and handled.[9,10] The use of *tert*-butyl hypochlorite in CCl_4 or methanol solution leads to the N-chlorinated species (**6**) in yields which exceed 96% as measured by NMR and HPLC. The procedure allows for the ease of treatment, which does not include aqueous work up, but constitutes an evaporation at reduced pressure of solvent, with an excess of reagent and *tert*-butyl alcohol.



3 a 6

The N-chlorinated species are stable at room temperature and could be stored for weeks at 0°C. The potential for these chiral N-chlorinated compounds to effect enantioselective chlorination is currently under investigation.

CONCLUSIONS

The transformations of the N-phosphor (III) derivatives of amino acids (**1**) into the N-phosphor (V) substituted amino acid esters (**2**, **3**) proceeds with high stereoselectivity. Diastereoisomers of N-phosphor (V) substituted L-leucine methyl esters are separated by crystallization or column chromatography and were used for preparation of chiral N-chloro N-phosphamides (**6**). The potential for these enantioselective chlorinating reagents is currently under investigation.

EXPERIMENTAL

Melting points are uncorrected. The NMR spectra were recorded on a "Varian VXR-300" spectrometer at 300 (^{1}H) and 126.16 MHz (^{31}P). All chemical shifts are expressed in δ (ppm). ^{1}H chemical shifts are expressed relative to Me_4Si as internal standard. ^{31}P NMR spectra are referenced to external 85% H_3PO_4. All manipulations were carried out under argon, solvents were also distilled under inert atmosphere from the following drying agents: diethyl ether, hexane, heptane, benzene, CCl_4 (P_2O_5), methanol, triethylamine (sodium), ethyl acetate ($CaCl_2$). HPLC analyses were performed on a "Milichrom-1A" (Russia) and LKB (Bromma, Sweden) instruments with Ultrapack TSK ODS 120 T 5 um 250 × 4.6 mm column (65–75% aqueous methanol as eluent); Silasorb DEA column 120 × 2 mm (hexane-isopropanol mixture in 95:5 ratio as eluent); Silasorb C-18 120 × 2 mm column (50% aqueous acetonitrile as eluent); UV detector, λ_{max} 260 nm [compounds (**2b**, **3b**, **5b**)] and 220 nm [compounds (**2a**, **3a**)]. Column chromatography was performed by using Chemapol (Praha). Silicagel L 100/160. *Tert*-butylhypochlorite was obtained according to known procedure.[11] L-Leucine [(+)-(S)-leucine] was commercially available and was used without further purification: $[\alpha]_D^{23}$ +15.0° (C = 2, 5 N HCl). L-Leucine methyl ester have been prepared by the method reported in the literature.[12]

Methyl ester of N-tert-butyl-isobutylphosphine-2-amino-4-methylpentanoic acid (**1a**). To a solution of 3.61 g (0.02 mol) *tert*-butyl-isobutylchlorophosphine and 3.5 ml of triethylamine in 10 ml of benzene was added with stirring 2.9 g (0.02 mol) of L-Leucine methyl ester in 5 ml of benzene. The solution was stirred for 2–3 hours at room temperature. The reaction mixture was then refluxed for 1 hour. The precipitate of triethylamine hydrochloride was filtered off and washed with 100 ml of ether. The filtrate was evaporated and the residue was distilled under reduced pressure.

Yield 3.6 g (66%), b.p. 85–90°C (0.02 mm Hg). Colorless liquid.
NMR spectra (δ, ppm; J, Hz; $CDCl_3$):
δ_H: 0.77 d [J_{HH} 5.0, $(CH_3)_2C$]; 0.81 d [J_{HH} 7.0 $(CH_3)_2C'$]; 0.90 d [J_{HH} 12.5, $(CH_3)_3C$]; 0.8–0.9 m [$(CH_3)_2C'$]; 1.60 m (CH_2); 1.85 m (CH_2); 3.54 m (NH); 3.61 s (CH_3O); 3.66 s ($CH_3'O$). δ_P, 59.68 and 59.45 (the ratio is 1:1).
Calcd. for the $C_{15}H_{32}NO_2P$: P 10.70. Found P 10.91.

Methyl ester of N-tert-butyl-phenylphosphine-2-amino-4-methylpentanoic acid (**1b**). To a solution of 9 g (0.05 mol) of *tert*-butyl-isobutylchlorophosphine and 10 g (0.1 mol) of triethylamine in 100 ml of

benzene cooled an ice-bath was added with stirring 7.2 g (0.05 mol) of L-Leucine methyl ester. The solution was stirred for 30 min at room temperature and then the reaction mixture was refluxed for 1.5 hour. The precipitate of triethylamine hydrochloride was filtered off and washed with 100 ml of ether. The filtrate was evaporated and the residue was distilled under reduced pressure.

Yield 10.85 g (70%), b.p. 148–150°C (0.04 mm Hg). Colorless oil.
NMR spectra (δ, ppm; J, Hz; $CDCl_3$):
δ_H: 0.78 m [$(CH_3)C$]; 0.855 d [J_{HH} 10 $(CH_3)_3C$]; 0.87 d [J_{HH} 10.0 $(CH_3)_3C'$]; 1.52 m (CH_2); 1.82, spt (CH); 2.21 dd (J_{HH} 11.0, J_{HP} 11.0, NH); 3.34 s (CH_3O); 3.66 s ($CH_3'O$); 3.60 m (CHN); 7.26 m; 7.86 m (C_6H_5). δ_P: 56.98.
Calcd. for the $C_{17}H_{28}NO_2P$: P 10.01. Found P 9.81.

N-(1-carbomethoxy-3-methyl)butylamid-tert-butyl-isobutylthiophosphonic acid (**2a**). To a solution of 1.05 g (3.64 mmol) of aminophosphine (**1a**) in 3 ml of benzene was added 0.025 g (7.8 mmol) of sulfur in 10 ml of benzene. The reaction mixture was allowed to stand for 3 hours, then the solvent was evaporated and the residue dissolved in hexane. The excess of sulfur was filtered off and the hexane was evaporated. The crude product was purified by the distillation in vacuo.

Yield 0.9 g, b.p. 117–120°C (0.02 mm Hg). Colorless liquid.
NMR spectra (δ, pm; J, Hz; $CDCl_3$):
δ_H: 0.85 d [J_{HH} 5.5, $(CH_3)_2C$]; 0.87 d [J_{HH} 5.5 $(CH_3)_2C'$]; 1.05 d [J_{HH} 16.2, $(CH_3)_3C$]; 1.46 m (CH_2); 1.60 m (CH_2'); 2.2 m (CH); 2.45 dd (J_{HH} 11.0, J_{HP} 11.0, NH); 3.654 s (CH_3O); 4.26 m (CHN) (major diastereoisomer).
δ_H: 0.89 dd [$(CH_3)_2C$]; 1.08 d [J_{HH} 16.0, $(CH_3)_3C$]; 1.482 m (CH_2); 1.66 m (CH_2); 2.33 m ($C\underline{H}$); 2.487 dd (J_{HH} 11.0, J_{HP} 11.0, NH); 2.681 s (CH_3O); 4.29 (CHN) (minor diastereoisomer). δ_P: 85.14 and 81.0 (94:6).
Calcd. for the $C_{15}H_{32}NO_2PS$: N 4.36; P 9.65; S 9.97. Found N 4.42; P 9.49; S 9.55.

N-(1-carbomethoxy-3-methyl)butylamid-tert-butyl-phenyl-thiophosphonic acid (**2b**). To a solution of 3.1 g (0.01 mol) of aminophosphine (**1b**) in 5 ml of benzene was added 0.5 g (0.0155 mol) of sulfur. The reaction mixture was allowed to stand for 12 hours at room temperature, then the solvent was evaporated and the residue dissolved in hexane. The excess of sulfur was filtered off and the hexane was evaporated. The ^{31}P NMR spectrum indicated that the product was a 75:25 mixture of diastereoisomers. The crude product was then chromatographed over a column of a silica gel L 100/160 with hexane-ethylacetate (3:1) as eluent yielding two fractions of two diastereoisomers. First fraction after the evaporation of a solvent was dissolved in hexane and kept in a refrigerator for 48 hours at −20°C. A colorless crystalline solid of the major diastereoisomer was separated and dried in vacuum.

Yield 2.0 (59%), m.p. 62–62.5°C, $[\alpha]_D^{20}$ +8.1° (C = 0.01, CH_3OH).
NMR spectra (δ, ppm; J, Hz; $CDCl_3$):
δ_H: 0.83 d [J_{HH} 6.3 $(CH_3)_2C$); 0.92 d [J_{HH} 6.3 $(CH_3)_2C'$]; 1.08 d [J_{HH} 16.8, $(CH_3)_3C$]; 1.61 m (CH_2); 1.70 spt (CH); 3.0 dd (J_{HH} 11.0, J_{HP} 11.0, NH); 3.48 s (CH_3O); 4.12 m (CHN); 7.37 m; 7.78 m (C_6H_5). δ_P: 80.82.

The minor diastereoisomer was obtained as colorless oil, containing trace of the first diastereoisomer: Yield 0.4 g (12%).

δ_H: 0.69 d [J_{HH} 6.3, $(CH_3)_2C$]; 0.76 d [J_{HH} 6.3 $(CH_3)_2C''$]; 1.09 d [J_{HH} 17.0, $(CH_3)_3C$]; 1.45 m (CH_2); 1.70 spt (CH); 3.01 dd (J_{HH} 11.0, J_{HP} 11.0, NH); 3.68 s (CH_3O); 4.12 m (CHN); 7.37 m; 7.92 m (C_6H_5). δ_P: 81.4.
Calcd. for the $C_{17}H_{28}NO_2PS$: N 4.10; P 9.07; S 9.39. Found N 4.12; P 9.29; S 9.55.

N-(1-carbomethoxy-3-methyl)butylamid-tert-butyl-isobutylphosphonic acid (**3a**). A solution of 0.96 ml of carbon tetrachloride in 3 ml of diethyl ether was added dropwise to a solution of 1.45 g (5 mmol) of aminophosphine (**1a**) in 3 ml of the same solvent at −50°C. The reaction mixture was allowed to stand for 30 min at ambient temperature, then it was cooled to −60°C and a solvent of 0.4 ml of methyl alcohol in 2 ml of ether was added dropwise. After heating up to room temperature the reaction mixture was stirred for 30 min, the solvent was evaporated and the residue distilled under reduced pressure. Yield 1.22 g (81%), b.p. 120–130°C (0.025 mm Hg). The ^{31}P NMR spectrum and HPLC indicated that the product consisted of one diastereoisomer. The product was purified by crystallization from hexane.

Yield 70%, m.p. 141°C, $[\alpha]_D^{20}$ −22° (C = 0.01, CH_3OH).
NMR spectra (δ, ppm; J, Hz; $CDCl_3$):
δ_H: 0.87 m [$(CH_3)_2C$]; 0.95–1.05 m [$(CH_3)_2C'$]; 1.053 d [J_{HH} 14.8, $(CH_3)_3C$]; 1.459 m (CH_2); 1.60 m (CH_2); 2.00 m (NH); 3.656 s (CH_3O); 4.0 m (CHN). δ_P: 53.17.
Calcd. for the $C_{15}H_{32}NO_3P$: N 4.59; P 10.14. Found N 4.59; P 10.14.

N-(1-carbomethoxy-3-methyl)butylamid-tert-butyl-phenylphosphonic acid (**3b**). To a solution of 3.1 g (0.01 mol) of aminophosphine (**1b**) in 10 ml of ether was added dropwise 0.96 ml of carbon tetrachloride in 3 ml of the same solvent at −50°C. After heating up to room temperature the reaction mixture was stirred for 30 min and then was cooled to −60°C. After that 0.4 ml of methyl alcohol in 2 ml of ether was added to the mixture. The reaction mixture was allowed to stand for 30 min at room temperature and the solvent was evaporated. The ^{31}P NMR spectra and HPLC indicated that the crude product was a mixture of two diastereoisomers which integrated in the 88:12 ratio. The crystalline residue was recrystallized from hexane to yield the major diastereoisomer in 100% purity. The column chromatography (silica gel L 100/160) of crude product using hexane-isopropanol (95:5) as eluent yielded two fraction of two diastereoisomers in the following order:

First (minor) diastereoisomer: Yield 0.3 g (10%), m.p. 140–141.5°C (heptane), colorless needles, $[\alpha]_D^{25}$ +6° (C = 0.025, C_2H_5OH).
NMR spectra (δ, ppm; J, Hz; $CDCl_3$):
δ_H: 0.70 d [J_{HH} 6.5, $(CH_3)_2C$]; 0.79 d [J_{HH} 6.5, $(CH_3)_2C$]; 1.10 d [J_{HH} 15.0, $(CH_3)_3C$]; 1.47 m (J_{HH} 6.3, CH_2); 1.64 m (CH); 3.24 dd (J_{HH} 11, J_{HP} 11, NH); 3.71 s (CH_3O); 3.8 m (CHN); 7.46 m; 7.79 m (C_6H_5). δ_P 46.91.
Calcd. for the $C_{17}H_{28}NO_3P$: N 4.30; P 9.52. Found N 4.38; P 9.61.

Second (major) diastereoisomer: Yield 2.0 g (61%), m.p. 128°C (hexane), colorless prismatic crystals, $[\alpha]_D^{20}$ −68.42° (C = 0.01, C_2H_5OH). IR (liquid, ν, cm^{-1}): 1180 (P=O); 1720 (C=O); 3400 (NH).
NMR spectra (δ, ppm; J, Hz; $CDCl_3$):
δ_H: 0.87 d [J_{HH} 6.3, $(CH_3)_2C$]; 0.89 d [J_{HH} 6.3, $(CH_3)_2C'$]; 1.09 d [J_{HH} 15.0, $(CH_3)_3C$]; 1.58 m (CH_2); 1.806 spt (CH); 3.19 dd (J_{HH} 11, J_{HP} 11, NH); 3.558 s (CH_3O); 3.79 m (CHN); 7.247 m; 7.696 m (C_6H_5). δ_P 46.9.
Calcd. for the $C_{17}H_{28}NO_3P$: N 4.30; P 9.52. Found N 4.35; P 9.58.

Tert-butyl-isobutyl-chloro-N-(1-carbomethoxy-6-methylpentyl)iminophosphorane (**4a**). A solution of 1.7 ml of carbon tetrachloride in 3 ml of diethyl ether was added dropwise with stirring to a solution of 2.9 g (0.01 mol) of aminophosphine (**1a**) in 5 ml of the same solvent. After heating up to room temperature the reaction was stirred for 0.5 hour. Then the solvent was evaporated and the residue was distilled under reduced pressure.

Yield 80%, b.p. 135°C (0.03 mm Hg).
^{31}P NMR spectra (Et_2O), δ_P: 44.50 and 45.8 (35:65)
Calcd. for the $C_{15}H_{31}NO_2P$: Cl 10.95; P 9.56. Found Cl 10.69; P 9.61.

N-Chlor-N-(1-carbomethoxy-3-methyl)butylamide-tert-butyl-phenylphosphonic acid (**5**). A solution of 1.3 g (0.012 mol) of *tert*-butylhypochlorite in 5 ml of methanol was added dropwise at 0°C to a solution of 3.1 g (0.01 mol) of first diastereoisomer of (**3b**) in 10 ml of the same solvent and the reaction mixture was allowed to stand at room temperature for 6 hours under a nitrogen atmosphere in a 25 ml round-bottom flask covered with aluminum foil. The course of the reaction was monitored by means of HPLC, which showed an almost quantitative yield of N-chloroamide. After the removal of the solvent under reduced pressure the pure N-chloroamide (**5**) was obtained. Yield 3.4 g (98%).

NMR spectra (δ, ppm; J, Hz; $CDCl_3$):
δ_H: 0.83 d [J_{HH} 6.0, $(CH_3)_2C$]; 1.24 d [J_{HH} 16.0, $(CH_3)_3C$]; 1.60 m (CH_2); 3.18 s (CH_3O); 4.55 m, CHN); 7.42 m; 7.93 m (C_6H_5). δ_P: 50.86.
Calcd. for the $C_{17}H_{27}ClNO_3P$: Cl 9.85; N 3.89; P 8.61. Found Cl 9.79; N 3.91; P 8.51.

The reaction with the second diastereoisomer was performed by the same manner. Yield 98%. Colorless liquid.

NMR spectra (δ, pm; J, Hz; $CDCl_3$):
δ_H: 0.69 d [J_{HH} 6.2, $(CH_3)_2C$]; 1.26 d [J_{HH} 16.0, $(CH_3)_3C$]; 1.62 m (CH_2); 3.67 s (CH_3O); 4.56 dq [J_{HH} 6.0, J_{HP} 8.0, (CHN); 7.24 m; 7.93 m (C_6H_5). δ_P: 50.87.
Calcd. for the $C_{17}H_{27}ClNO_3P$: Cl 9.85; N 3.89; P 8.61. Found Cl 9.75; N 3.91; P 8.54.

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