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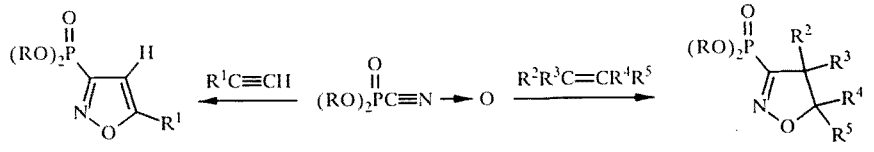
PHOSPHORYLNITRILE OXIDES. 5.* REACTIONS OF 3-(DIALKOXYPHOSPHORYL)ISOXAZOLES AND -ISOXAZOLINES WITH NUCLEOPHILIC REAGENTS

V. A. Pavlov, A. I. Kurdyukov, B. I. Gorin, F. R. Sagitova, N. V. Aristova, L. I. Deiko, and V. V. Moskva

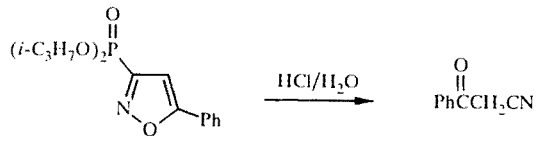
3-Phosphorylated isoxazoles and isoxazolines react with nucleophiles either with cleavage of the P—C bond and subsequent ring opening or with retention of the heterocyclic ring depending on the structure of the ring substituents, nature of the nucleophile, and reaction conditions. This permits the selective chemical modification of the starting compounds.

Heterocyclic compounds with latent functionality are commonly used in organic synthesis. Special interest in this regard is found for isoxazoles and their dihydro derivatives, isoxazolines [2, 3]. We have reported a convenient preparative synthesis for 3-(dialkoxyphosphoryl)isoxazoles II and -isoxazolines III by the 1,3-dipolar addition of phosphorylnitrile oxides I to compounds with carbon—carbon multiple bonds [4-6].



II I III

In the present work, we studied the feasibility of using some 3-phosphorylisoxazoles II and 3-phosphorylisoxazolines III as universal polyfunctional synthones for the preparation of a variety of organic structures. The ease of opening of isoxazoles, for example, by the action of bases, and also the nature of the reaction products depend on the presence and position of the ring substituents [2, 7]. Isoxazoles lacking a substituent at $C_{(3)}$ are most susceptible to the action of base. Under acid hydrolysis conditions, dialkoxyphosphorylpyridines are readily converted into the corresponding pyridylphosphonic acids [8]. Hence, we carried out the acid hydrolysis of 5-phenyl-3-(diisopropoxyphosphoryl)isoxazole (IIa, R = *i*-C_3H_7, R^1 = Ph) by heating this compound at reflux in 2 N hydrochloric acid by analogy to Redvore [8]. Benzoylacetonitrile (IV) was obtained in 86% yield along with an unidentified mixture of phosphorus compounds instead of the expected 3-isoxazolylphosphonic acid.



IIa IV

*Communication 4, see ref. [1].

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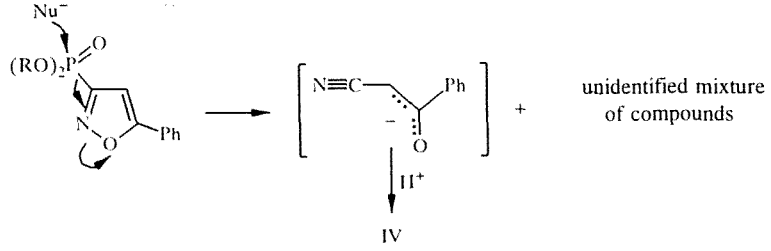
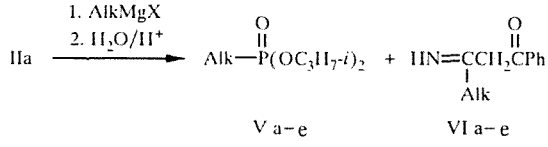
Variation in the hydrolysis conditions such as pH, solvent, temperature, and reaction time as well as alkaline hydrolysis (heating in an aqueous ethanolic solution of sodium bicarbonate) leads to analogous results, i.e., cleavage of the P—C bond and opening of the isoxazole ring. This indicates that the reaction proceeds through "irreversible deprotonation" at $C_{(3)}$ as in the case of isoxazoles unsubstituted at $C_{(3)}$, which are highly susceptible to the action of nucleophiles [2, 3]. However, in this case, we find loss of the diisopropoxyphosphoryl substituent with subsequent ring opening at the N—O bond and formation of a cyanoenol anion in the transition state.



The lability noted for the P—C bond in 3-phosphorylisoxazoles indicated that these compounds may be used as phosphorylating agents in reactions with nucleophiles as well as in the synthesis of functional open-chain compounds. However, our attempts to carry out the reaction of isoxazole IIa with various compounds containing O-, N-,and S-nucleophilic sites (alcoholates, primary and secondary amines, substituted hydrazines, 4-substituted and unsubstituted thiosemicarbazides, and thiourea) invariably gave the ring opening product IV and an unidentified mixture of other products. We should note that, as in the case of alkaline hydrolysis, the yield of benzoylacetonitrile (IV) is significantly less and the reaction mixture contains a considerable amount of starting heterocycle IIa. In most cases, cleavage of 3,5-disubstituted isoxazoles occurs only upon the action of strong bases [2]. The introduction of a dialkoxyphosphoryl substituent at $C_{(3)}$ reduces the stability, leading under certain conditions, as noted above, to ring opening even by the action of weak bases as found for 3H-5-substituted isoxazoles.

The cleavage of isoxazoles by Grignard reagents has found limited use [9]. This method was used, for example, for cleavage of 3,5-disubstituted isoxazoles at the N—O bond with retention of the C—C bonds [10]. In light of the lability of the P—C bonds in phosphorylisoxazoles II, the reaction of these compounds with Grignard reagents, which are C-nucleophiles, should lead to new, stronger phosphorus—carbon bonds. We studied the reaction of IIa with alkylmagnesium halides, leading to diisopropyl esters of alkylphosphonic acids V and ketoimines VI.

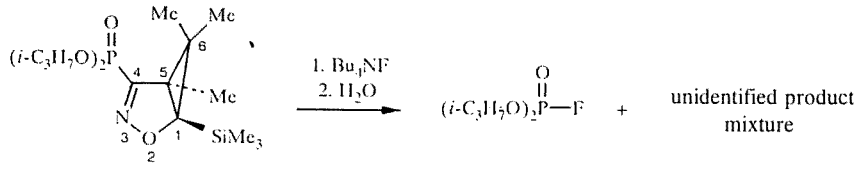


V, VI a Alk = CH_3, b Alk = C_2H_5, c Alk = C_3H_7, d Alk = *i*-C_3H_7, e Alk = C_4H_9, X = Br, I

The reaction of IIa with a two-fold excess of methylmagnesium iodide proceeds under mild conditions, leading to the diisopropyl ester of methylphosphonic acid (Va) and 1-phenyl-1-oxo-3-iminobutane (VIa) in 78% yield. However, the product yield is only 13% in the reaction of ethylmagnesium bromide with a five-fold increase in the reaction time. The reaction is even slower going to propylmagnesium bromide and only about 1% ketoimine VIc was obtained after 72 h. Variation in the reaction conditions did not lead to the substitution product and only starting compound IIa could be isolated from the reaction mixture. These findings indicate that steric hindrance due to the bulky diisopropoxyphosphoryl group to attack by the nucleophilic agents is the predominant factor in the reaction of 5-phenyl-3-(diisopropoxyphosphoryl)isoxazole (IIa) with alkylmagnesium halides.

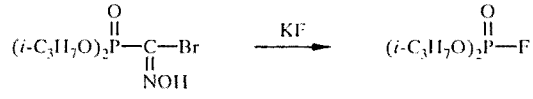
The possibility of synthesizing functional open-chain compounds by the base cleavage of isoxazolines has not been studied extensively. There have been no reports relative to 3-substituted derivatives since 1976 [11]. Ring opening at the N—O bond occurs upon the action of bases on isoxazolines unsubstituted at $C_{(3)}$. 3-Substituted isoxazolines are cleaved at the C—O bond to give enoximes [2, 3]. On the other hand, the isoxazoline ring is often stable toward the action of many reagents commonly used in organic synthesis. This permits the modification of the substituents of the isoxazoline ring, based on the capacity of this ring to undergo substitution reactions [12]. Hence, we attempted to replace the trimethylsilyl group by hydrogen in 5,6,6-trimethyl-1-trimethylsilyl-4-(diisopropoxyphosphoryl)-2-oxa-3-azabicyclo[3.1.0]hex-3-ene (IIIa, R = *i*-C_3H_7, R^2 = R^5 = $(CH_3)_2$, R^3 = CH_3, R^4 = $SiMe_3$) by the consecutive action of tetrabutylammonium fluoride and water in tetrahydrofuran. However, in this case, IIIa decomposed to give several products as indicated by thin-layer chromatography,

which could not isolated as pure compounds. On the other hand, the ^{31}P NMR spectrum of the reaction mixture clearly showed a doublet at $\delta_P = -11.30$ ppm and $^1J_{PF} = 976.45$ Hz related to diisopropyl fluorophosphate VI, which indicates a competitive substitution reaction proceeding at the phosphorus atom:



IIIa VII

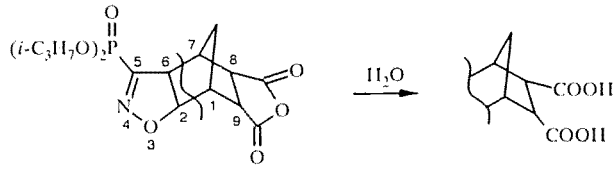
A similar cleavage of the P—C bond was observed in our attempt to replace bromine by fluorine upon treatment of the oxime of diisopropoxyphosphorylcarbonyl bromide (VIII) with potassium fluoride. We isolated diisopropyl fluorophosphate in good yield (^{19}F NMR: $\delta_F = -0.45$ m.d, $^1J_{FP} = 966.00$ Hz) instead of the expected fluoride derivative of phosphoryl-formhydroxamic acid.



VIII VII

When groups other functional substituents containing electrophilic sites are present in phosphorylated isoxazoles II and isoxazolines III in addition to the dialkoxyphosphoryl group, the reactions of these compounds with nucleophiles may also proceed without opening of the heterocycle. The nucleophilic attack in this case is directed at the alternative ring substituent.

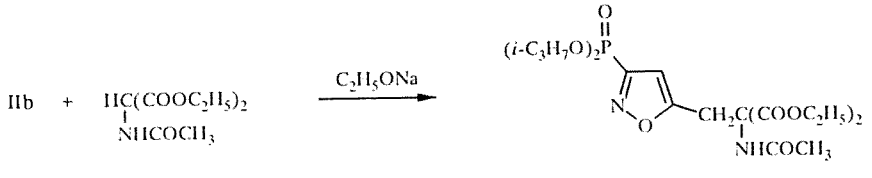
Thus, we have already shown that IIIb is readily hydrolyzed with opening of the cyclic anhydride even in the presence of atmospheric moisture to give the corresponding dicarboxylic acid IIIc [1].



IIIb IIIc

Hence, we have demonstrated the possibility of modifying functional fragments of 3-C-phosphorylated isoxazolines with retention of the unaltered isoxazoline ring.

The reaction of 5-bromomethyl-3-(diisopropoxyphosphoryl)isoxazole (IIb, R = i-C_3H_7, $R^1 = CH_2Br$) with ethyl acetamidomalonate in the presence of sodium ethylate proceeds at the 5-*exo* carbon without affecting the phosphoryl group and the isoxazole ring to give 5-[2′,2′-di(ethoxycarbonyl)-2′-N-acetamido]ethyl-3-(diisopropoxyphosphoryl)isoxazole (IIc).

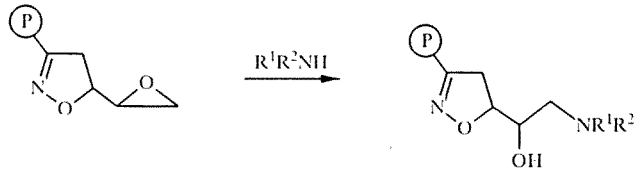


IIc

Product IIc may be used in the synthesis of analogs of agonists of α-amino acids stimulants [13].

In light of the high lability of the epoxide ring, 5-oxyethenyl-3-(diisopropoxyphosphoryl)isoxazoline (IIId, R = i-C_3H_7, $R^2 = R^3 = R^4 = H$, R^5 = ) [1], which is a convenient reagent for the modification of isoxazoline through saturation of the substituent at $C_{(5)}$ by means of various functional groups, holds promise for the functionalization of phosphorylated isoxazolines. Opening of the epoxide ring by various nitrogen nucleophilic reagents permits rather facile conversion to compounds, whose preparation by other means is extremely difficult.

The reaction of IIId with secondary amines such as pyrrolidine, morpholine, and diethylamine, proceeds at the terminal carbon atom of the oxyethylene ring to give 1-[3-(diisopropoxyphosphoryl)isoxazolin-5-yl]-1-hydroxy-2-substituted ethanes IIIe-IIIg.



III d III e-h

P = $(i\text{-}C_3H_7O)_2P(O)$

III e $R^1R^2 = -(CH_2)_4-$; f $R^1R^2 = -(CH_2)_2-O-(CH_2)_2-$;

g $R^1 = R^2 = Et$; h $R^1 = H$, $R^2 = -CH(CH_3)COOH$

In the case of D-α-alanine, this reaction proceeds in the presence of excess triethylamine to give the salt of triethylamine and N-(2-[3-diisopropoxyphosphoryl)isoxazolin-5-yl]-2-hydroxy)ethyl-D-alanine (IIIh).

Hence, 3-phosphorylated isoxazoles and isoxazolines react with opening of the heterocycle preceded by cleavage of the P—C bond or retention of the heterocyclic ring depending of the structure of the ring substituents, nature of the nucleophile, and reaction conditions. This permits us to carry out the selective chemical modification of these molecules.

EXPERIMENTAL

The spin-decoupled $^{13}C—\{^1H\}$ ^{13}C NMR spectra were taken on a Bruker WM-250 Fourier spectrometer at 62.94 MHz, while the ^1H NMR spectra were taken on Varian T-60, Bruker WP-80, and Bruker WM-250 spectrometers. The ^{31}P NMR spectra were taken on a Bruker WP-80 spectrometer at 32.38 MHz and Bruker WM-250 spectrometer at 101.26 MHz. The ^{19}F NMR spectra were taken on a Bruker CXP-200 spectrometer at 188.22 MHz. The chemical shifts of the ^{13}C and ^1H nuclei were determined relative to TMS. The phosphorus chemical shifts were measured relative to H_3PO_4 as an external standard, while the fluorine chemical shifts were measured to CF_3COOH as the external standard. The IR spectra were taken on UR-20 and Bruker IFS 113V spectrometers with accumulation and computer analysis. The mass spectrum was taken on a Finnigan 4021 mass spectrometer. The reaction course was monitored and purity of the products obtained checked on Silufol UV-254 plates. The preparative chromatographic separation was carried out on Merck 9385 silica gel (dispersion 40-63 μm). The adsorbent/compound ratio was in the range from 50:1 to 100:1.

The elemental analysis data for C, H, N, and P corresponded to the calculated values.

Hydrolysis of 5-Phenyl-(2-diisopropoxyphosphoryl)isoxazole (IIa). Product IIa was obtained as in our previous work [1]. Acid hydrolysis. A solution of 0.15 g IIa in 10 ml 2 N hydrochloric acid was heated at reflux for 8 h and then extracted with chloroform or benzene. The solvent was evaporated in vacuum to give 0.06 (86%) benzoylacetonitrile (IV). ^1H NMR spectrum in $CDCl_3$: 7.95, 7.55 (5H, m, Ph), 2.62 ppm (2H, s, CH). Mass spectrum, *m/z* (*I*, %): 145(5), 105(100), 77(14). IR spectrum: 1690 (C=O), 2220 cm^{-1} (CN). Alkaline hydrolysis. A sample of 0.07 g sodium bicarbonate in 5 ml water was added to a solution of 0.3 g isoxazole IIa in 7 ml ethanol and heated at reflux for 5 h. The reaction solution was extracted with benzene and dried over anhydrous sodium sulfate. The solvent was evaporated in vacuum to give 0.04 g (28%) IV and 0.2 g (68%) IIa.

Reaction of 5-Phenyl-3-(diisopropoxyphosphoryl)isoxazole (IIa) with Alkylmagnesium Halides. A solution of 10 mmoles isoxazole IIa in ether was added dropwise with stirring to a freshly prepared solution of 20 mmoles alkylmagnesium halide in 15 ml absolute ether. The mixture was heated at reflux for 5-72 h and cooled. Then, 10 ml saturated aqueous ammonium chloride was added followed by hydrochloric acid until the precipitate completely dissolved. The ethereal layer was separated and dried over anhydrous sodium sulfate. The products obtained were separated by preparative column chromatography. The reaction with methylmagnesium iodide over 5 h gave 1.4 g (78%) of the diisopropyl ester of methylphosphonic acid (Va, $C_7H_{17}PO_3$), *m/z* (*I*, %): 181(9), 165(3), 123(58), 97(100), 79(26), and 1.26 g (78%) 1-phenyl-1-oxo-3-iminobutane (VIa, $C_{10}H_{11}NO$), *m/z* (*I*, %): 161(49), 160(100), 145(8), 144(4), 105(12), 84(81), 77(18), 65(4). IR spectrum: 1640 (HN=C—CH—C=O), 3300 cm^{-1} (NH). The reaction with ethylmagnesium bromide over 24 h gave

0.23 g (13%) 1-phenyl-1-oxo-3-iminopentane (VIb, $C_{11}H_{13}NO$), *m/z* (*I*, %): 175(32), 174(100), 159(12), 158(10), 105(10), 98(60), 79(14), 77(21). IR spectrum: 1642 (HN=C—CH—C=O), 3310 cm^{-1} (NH). The reaction with propylmagnesium bromide over 72 h gave 0.02 g (1%) 1-phenyl-1-oxo-3-iminohexane (VIc, $C_{12}H_{15}NO$), *m/z* (*I*, %): 189(52), 188(100), 173(15), 174(8), 105(12), 84(95), 77(28).

5,6,6-Trimethyl-1-trimethylsilyl-4-(diisopropoxyphosphoryl)-2-oxa-3-azabicyclo[3.1.0]hex-3-ene (IIIa, $C_{16}H_{32}NO_4PSi$). A solution of 0.46 g (3 mmoles) 1,3,3-trimethyl-2-trimethylsilylcyclopropene [14] in 15 ml absolute ether was added over 2 min to a solution of 0.53 g (2.55 mmoles) diisopropoxyphosphorylnitrile oxide obtained according to our previous procedure [1] in 40 ml absolute ether at −60°C. The reaction mixture was stirred for 1 h at −60°C and then for an additional 16 h with gradual warming to room temperature. The solvent was evaporated in vacuum. The residue was subjected to chromatography on a silica gel column using 1:2 ethyl acetate—hexane as the eluent to give 0.7 g (81%), oily IIIa. ^1H NMR spectrum in $CDCl_3$: 1.28-1.33 (12H, m, $2(C\underline{H}_3)_2CH$), 4.72 (2H, m, $2(CH_3)_2C\underline{H}$), 0.78 3H, s, *endo*-CH_3), 1.14 (2H, s, *exo*-CH_3), 1.42 (3H, s, 5-CH_3), 0.12 ppm, $^2J_{HSi}$ = 6.8 (9H, s, $Si(CH_3)_3$). ^{13}C NMR spectrum in $CDCl_3$: 23.62, 23.76, 23.87, 24.05 ($(CH_3)_2CH$), 72.17, 72.27, $^2J_{POC}$ = 5.8 ($CH(CH_3)_2$), 11.08 (*endo*-CH_3), 17.95 (*exo*-CH_3), 18.47 (5-CH_3), −1.05, $^1J_{CSi}$ = 53.0 ($Si(CH_3)_3$), 79.59, $^1J_{CSi}$ = 64.1, $^3J_{CP}$ = 4.2 ($C_{(1)}$), 155.77, $^1J_{PC}$ = 209.2 ($C_{(4)}$), 49.93, $^2J_{PC}$ = 24.2 ($C_{(5)}$), 15.68 ppm ($C_{(6)}$). ^{31}P NMR spectrum in $CDCl_3$: 3.34 ppm (s). IR spectrum: 2978.7, 2935.2, 2875.2, 2875.9, 2237.0, 1735.7, 1546.9, 1467.2, 1453.8, 1385.6, 1375.3, 1252.1, 1179.2, 1142.2, 1105.7, 998.0, 927.9, 842.3, 770.2, 733.3, 625.7, 585.6 cm^{-1}.

Fluorination of the Oxime of (Diisopropoxyphosphoryl)carbonyl Bromide (VIII). The synthesis of oximes of (dialkoxyphosphoryl)carbonyl halides has been described in our previous work [15, 16]. A solution of 4.0 g (40 mmoles) potassium fluoride in 15 ml was added with stirring to a solution of 6.0 g (20 mmoles) oxime of (diisopropoxyphosphoryl)carbonyl bromide (VIII) in 15 ml acetone. The temperature of the reaction mixture rose to 36-37°C. The solution was stirred for 3 h at room temperature and extracted with chloroform. The solvent was evaporated in vacuum to give 3.0 g (79%) diisopropyl fluorophosphate (VII). ^{31}P NMR spectrum: −11.5 ppm (d), $^1J_{PF}$ 989.4. ^{19}F NMR spectrum in acetone-d_6: −0.45 ppm (d), $^1J_{FP}$ 966.0.

5-[2,2-Di(ethoxycarbonyl)-2-N-acetamido]ethyl-3-(diisopropoxyphosphoryl)isoxazole (IIc, $C_{19}H_{31}N_2O_9P$). A sample of 2.2 g (10 mmoles) ethyl N-acetamidomalonate was added to a solution of 0.23 g (10 mmoles) metallic sodium in 45 ml absolute ethanol. The mixture was stirred for 10 min. A solution of 3.6 g (10 mmoles) 5-bromomethyl-3-(diisopropoxyphosphoryl)isoxazole (IIb) obtained according to our previous procedure [1] in 5 ml absolute ethanol was added. The mixture was stirred for 4 h at 60-65°C until the starting reagents were consumed as indicated by thin-layer chromatography using 3:2 hexane—acetone as the eluent. The solvent was evaporated in vacuum and the residue was dissolved in chloroform. The KBr precipitate was filtered off and chloroform was removed. The residual oil was purified by preparative chromatography on a silica gel column using 1:1 chloroform—ether as the eluent to give 4.0 g (78%) IIc as colorless crystals, mp 55-57°C. ^1H NMR spectrum in $CDCl_3$: 1.30 (18H, m, $(C\underline{H}_3)_2CH$, $C\underline{H}_3CH_2$), 1.95 (3H, s, CH_3CO), 3.87 (2H, s, CH_2), 4.20 (4H, q, $C\underline{H}_2CH_3$), 4.73 (2H,m, $C\underline{H}(CH_3)_2$), 6.20 (1H, s, NH), 6.75 ppm (1H, s, 4-CH). ^{31}P NMR spectrum in acetone-d_6: 3.70 ppm (s).

1-[3-(Diisopropoxyphosphoryl)isoxazolin-5-yl]-1-hydroxy-2-N-pyrrolidinylethane (IIIe, $C_{15}H_{29}N_2O_5P$). A sample of 5 ml ethanol and a solution of 0.13 ml (1.5 mmoles) pyrrolidine in 5 ml benzene was added to a solution of 0.42 g (1.5 mmole) 5-oxyethenyl-3-(diisopropoxyphosphoryl)isoxazoline (IIId) in 10 ml benzene. The solution was heated at reflux for 2 h. Chromatography on a silica gel column with acetonitrile as the eluent gave 0.39 g (62%) IIIe as an oil. ^1H NMR spectrum in $CDCl_3$: 1.38 (d), 1.40 (d), $^3J_{HH}$ 7.0 (12H, $CH(C\underline{H}_3)_2$), 1.82 (4H, m, $—CH_2CH_2—$), 2.65 (6H, m, $N(CH_2)_3$), 3.22 (2H,m, 4-CH_2), 3.85 (1H, m, —CHOH), 4.63 (1H, m, 5-CH), 4.79 (2H, m, $CH(CH_3)_2$), 5.17 ppm (1H, s, OH). ^{31}P NMR spectrum in $CDCl_3$: 3.04 ppm (s).

1-[3-(Diisopropoxyphosphoryl)isoxazolin-5-yl]-1-hydroxy-2-N-morpholinylethane (IIIf, $C_{15}H_{29}N_2O_6P$). The synthesis of IIIf was analogous to the synthesis of IIIe. The reaction was carried out with 0.49 g (1.75 mmole) isoxazoline IId and 0.16 g (1.75 mmole) morpholine. Preparative column chromatography using acetonitrile as the eluent gave 0.35 g (53%) IIIf, n_D^{20} 1.4533. ^1H NMR spectrum in $CDCl_3$: 1.35 (d), 1.38 (d), $^1J_{HH}$ 7.2 (12H, $CH(C\underline{H}_3)_2$), 2.40-2.80 (6H, m, $N(CH_2)_3$), 3.21 (2H, m, 4-CH_2), 3.69 (4H, m, CH_2OCH_2), 3.92 (1H, m, CHOH), 4.47 (1H, s, OH), 4.68 (1H, m, 5-CH), 4.76 ppm (2H, m, $C\underline{H}(CH_3)_2$. ^{31}P NMR spectrum in acetone—d_6: 5.13 ppm (s). IR spectrum: 3400, 2990, 2945, 2860, 1820, 1740, 1580, 1460, 1390, 1380, 1300, 1300, 1260, 1185, 1140, 1125, 1080, 1020, 945, 910, 890, 875, 810, 780, 760, 590, 540 cm^{-1}.

1-[3-(Diisopropoxyphosphoryl)isoxazolin-5-yl]-1-hydroxy-2-N-diethylaminoethane (IIIg, $C_{15}H_{31}N_2O_5P$). The synthesis of IIIg was analogy to the synthesis of IIIe. The reaction of 1.09 g (4 mmoles) isoxazoline IIId and 0.4 g (4 mmoles) diethylamine gave 0.45 g (33%) IIIh as an oil, which was purified by preparative chromatography on a silica gel column using ethyl acetate as the eluent, n_D^{20} 1.4740. ^{1}H NMR spectrum of $CDCl_3$: 1.10, $^3J_{HH}$ = 7.0 (6H, t, $CH_2C\underline{H}_3$), 1.41, $^3J_{HH}$ = 7.0 (12H, d, $CH(C\underline{H}_3)_2$), 2.40-2.90 (6H, m, $N(CH_2)_3$), 3.21 (1H, m, 4-CH_2), 3.31 (1H, m, 4-CH_2), 3.50-3.90 (2H, m, CHOH), 4.40-4.97 ppm (3H, m, 5-H, $C\underline{H}(CH_3)_2$). ^{31}P NMR spectrum in acetone-d_6: 5.20 ppm (s). IR spectrum: 3400, 2985, 2940, 2880, 2830, 1740, 1580, 1470, 1460, 1390, 1380, 1260, 1185, 1150, 1110, 1010, 945, 910, 890, 780, 750, 590 cm^{-1}.

Triethylamine Salt of N-(2-[3-Diisopropoxyphosphoryl)isoxazolin-2-yl]-2-hydroxy)ethyl-D-alanine (IIIh, $C_{20}H_{42}N_3O_7P$). A solution of 0.92 g (3.5 mmoles) isoxazoline IIIh in 2 ml acetone, 0.5 ml triethylamine, 10 ml water, and 0.3 g (3.5 mmoles) D-α-alanine were mixed. After 24 h, the reaction mixture was washed with ether and water was removed on a rotary evaporator. The colorless crystals isolated were washed with acetone to give 0.35 g (23%) IIIh, mp 196-198°C. ^{1}H NMR spectrum in DMSO-d_6: 1.25 (24H, m, CH_3, $CH_2C\underline{H}_3$, $CH(C\underline{H}_3)_2$), 2.70-2.90 (2H, m, NCH_2), 2.90-3.52 (8H, m, 4-CH_2, $N(C\underline{H}_2CH_3)_3$), 3.52-3.90 (2H, m, CHOH), 3.65 (4H, m, 5-CH, $C\underline{H}(CH_3)_2$), 4.80-6.00 ppm (2H, NH, NH^+). ^{31}P NMR spectrum in H_2O: 6.11 ppm (s). IR spectrum: 3350, 3100, 3200-2400, 2600, 1625, 1580, 1415, 1380, 1370, 1310, 1260, 1180, 1150, 1110, 1000, 900, 860, 780 cm^{-1}.

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