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LETTERS TO THE EDITOR

Synthesis and Properties of *N*-Phosphorylated Aminoaldehydes

M. B. Gazizov[a], R. A. Khairullin[a], A. I. Alekhina[a], L. R. Bagauva[a], and O. G. Sinyashin[b]

[a] *Kazan State Technological University,*
ul. K.Marksa 68, Kazan, Tatarstan, 420015 Russia
e-mail: mukattisg@mail.ru

[b] *Arbuzov Institute of Organic and Physical Chemistry, Kazan Research Center,*
Russian Academy of Sciences, Kazan, Tatarstan, Russia

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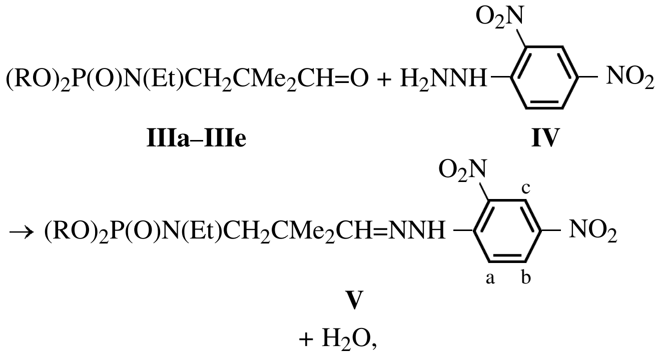
N-Phosphorylated aminoaldehydes have never been reported previously. We found that they can be synthesized by the Todd–Atterton reaction of hydrophosphoryl compounds **I** with 3-alkylamino-substituted aldehydes **II.** A mixture of aminoaldehyde and triethylamine was added dropwise with stirring at 5°C to a solution of compound **I** in CCl_4. After 1-h stirring the reaction mixture was heated to 25°C and stirred additionally for 12 h. Triethylamine hydrochloride was filtered off, and products **III** were distilled in high vacuum.

$$\underset{\textbf{I}}{R^1(R^2O)PHO} + \underset{\textbf{II}}{EtNHCH_2CMe_2CHO}$$

$$\xrightarrow{CCl_4 + B} \underset{\textbf{III}}{R^1(R^2O)P(O)N(Et)CH_2CMe_2CHO},$$

III, R^1 = MeO, R^2 = Me (**a**), R^1 = EtO, R^2 = Et (**b**), R^1 = *i*-PrO, R^2 = *i*-Pr (**c**), R^1 = BuO, R^2 = Bu (**d**), R^1 = Ph, R^2 = Me (**e**), B = Et_3N.

The structure of *N*-phosphorylated aminoaldehydes **III** was confirmed by the elemental analysis and ^{1}H and ^{31}P NMR spectra. To obtain chemical evidence for their structure and synthesize polyfunctional phosphoruscontaining compounds, aldehydes **III** were reacted with 2,4-dinitrophenylhydrazine (**IV**), *tert*-butylamine (**VI**), lithium aluminum hydride (**VII**), and hydrogen dimethyl phosphite (**Ia**). The reaction with 2,4-dinitrophenylhydrazine was carried out in ethyl acetate at 70–80°C. Crystallization from hexane gave hydrazones **V** in almost quantitative yields.



V, R = Me (**a**), Et (**b**), *i*-Pr (**c**), Bu (**d**).

The reaction of aldehydes **III** with *tert*-butylamine was carried out in toluene. The liberated water was removed by azeotropic distillation. Imines **VII** were prepared in high yields.

$$\underset{\textbf{III}}{(RO)_2P(O)N(Et)CH_2CMe_2CH{=}O} + \underset{\textbf{VI}}{H_2NBu\text{-}t}$$

$$\xrightarrow[\text{reflux}]{\text{toluene}} \underset{\textbf{VII}}{(RO)_2P(O)N(Et)CH_2CMe_2CH{=}NBu\text{-}t} + H_2O,$$

VII, R = Et (**b**), *i*-Pr (**c**), Bu (**d**).

The reduction with lithium aluminum hydride (**VIII**) was carried out in ether under reflux. Intermediate alkoholate **IX** was carefully decomposed with water. *N*-Phosphorylated aminoalcohols **X** were isolated pure by high-vacuum distillation.

The reaction of aldehyde **IIId** with dimethyl phosphite **Ia** was carried out under Abramov reaction

$$\underset{\textbf{IIIa, IIIb}}{4(RO)_2P(O)N(Et)CH_2CMe_2CHO} + \underset{\textbf{VIII}}{LiAlH_4}$$

$$\xrightarrow{\text{ether}} \underset{\textbf{IX}}{[(RO)_2P(O)N(Et)CH_2CMe_2CH_2O]_4^{1-}\ [AlLi]^{4+}}$$

$$\xrightarrow[-[Al(OH)_3 + LiOH]]{4H_2O} 4(RO)_2P(O)N(Et)CH_2CMe_2CH_2OH,$$

$$\textbf{X},\ R = Me\ (\textbf{a}),\ Et\ (\textbf{b}).$$

conditions. A mixture of compounds **Ia** and **IIId** was treated with a small piece of sodium. Slight heat release was initially observed, after which the reaction mixture was kept at room temperature for 24 h and neutralized with acetic acid. Volatile admixtures were removed in high vacuum, and 3-[(dibutoxyphosphoryl)ethylamino]-1-(dimethoxyphosphoryl)-2,2-dimethylpropan-1-ol (**XI**) was identified crude.

$$\underset{\textbf{I}}{(MeO)_2PHO} + \underset{\textbf{IIId}}{(BuO)_2P(O)N(Et)CH_2CMe_2CHO}$$

$$\longrightarrow \underset{\textbf{XI}}{(BuO)_2P(O)N(Et)CH_2CMe_2CH(O\ H)P(O)(OMe)_2}.$$

Reaction of hydrogen dimethyl phosphite (Ia) with 3-(ethylamino)-2,2-dimethylpropanal (II). A mixture of 13.1 g of aldehyde **II** and 10.1 g of triethylamine was added dropwise with stirring under dry nitrogen to a solution of 11.17 g of **Ia** in 80 ml of CCl_4. After 1-h stirring, the reaction mixture was heated to 25°C and stirred additionally for 12 h. The crystals formed were filtered off and twice washed with CCl_4. The solvent was removed, and the residue was distilled in high vacuum to give 14.74 g (62%) of compound **IIIa**, bp 82°C (0.09 mm Hg), n_D^{20} 1.4480. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 0.95 s (5H, CNe_2), 0.94 t (3H, NCH_2*Me*, $^1J_{HH}$ 7 Hz), 2.73 q amd 2.85 q (2H, NC*H*$_2$Me, $^3J_{HH}$ 7 Hz), 3.05 s and 3.16 s (2H, NC*H*$_2$), 3.51 d (6H, POMe, $^3J_{PH}$ 10.5 Hz), 9.5 s (1H, CHO). ^{31}P NMR spectrum, δ_P, ppm: 12.9. Found, %: N 5.88; P 13.10. $C_8H_{17}NO_3P$. Calculated, %: N 5.96; P 13.18.

3-[(Diethoxyphosphoryl)ethylamino]-2,2-dimethylpropanal (IIIb) was obtained from 16.56 g of diethyl hydrogen phosphite (**Ib**), 80 ml of CCl_4, 15 g of aldehyde **II**, and 12.12 g of triethylamine **IIIb.** Yield 20.02 g (65%), bp 92–95°C (0.09 mm Hg), n_D^{20} 1.4440. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 0.93 s (6H, CMe_2), 0.93 t (3H, NCH_2*Me*, $^3J_{HH}$ 7 Hz); 1.18 t (6H, OCH_2*Me*, $^3J_{HH}$ 7.5 Hz), 2.75 q and 2.90 q (2H, NC*H*$_2$Me, $^3J_{HH}$ 7 Hz), 3.07 s and 3.18 s (2H, NCH_2), 3.85 quintet (4H, POC*H*$_2$Me, $^3J_{HH}$ = $^3J_{PH}$ 7.5 Hz), 9.54 s (1H, CHO). ^{31}P NMR spectrum, δ, ppm: 10.2. Found, %: N 5.40; P 12.00. $C_9H_{19}NO_3P$. Calculated, %: N 5.48; P 12.16.

3-[(Diisopropoxyphosphoryl)ethylamino]-2,2-dimethylpropanal (IIIc) was obtained from 19.92 g of hydrogen diisopropyl phosphite (**Ic**), 80 ml of CCl_4, 15.66 g of aldehyde **II**, and 12.12 g of triethylamine. Yield 25.25 g (71%), bp 84–85°C (0.09 mm Hg), n_D^{20} 1.4410. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.87 s (6H, CMe_2), 0.87 t (3H, NCH_2*Me*, $^3J_{HH}$ 7 Hz), 1.1 d (12H, OCH*Me*$_2$, $^3J_{HH}$ 7.5 Hz), 2.65 q and 2.80 q (2H, NC*H*$_2$Me, $^3J_{HH}$ 7 Hz), 3.0 s and 3.11 s (2H, NCH_2), 4.33 q (2H, POC*H*Me$_2$, $^3J_{HH}$ 7.5 Hz), 9.47 s (1H, CHO). ^{31}P NMR spectrum, δ_P, ppm: 9.2. Found, %: N 5.30, P 11.69. $C_{10}H_{21}NO_3P$. Calculated, %: N 5.28; P 11.70.

3-[(Dibutoxyphosphoryl)ethylamino]-2,2-dimethylpropanal (IIId) was obtained from 23.28 g of dibutyl hydrogen phosphite (**Id**), 100 ml of CCl_4, 15.2 ml of aldehyde **II**, and 12.12 g of triethylamine. Yield 25.71 g (68%), bp 120°C (0.09 mm Hg), n_D^{20} 1.4456 ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.88 t (6H, CH_2*Me*, $^3J_{HH}$ 7 Hz), 0.99 s (6H, CMe_2); 0.98 t (3H, NCH_2*Me*, $^3J_{HH}$ 7 Hz), 1.12–1.75 m (8H, CH_2CH_2, $^3J_{HH}$ 7.5 Hz), 2.78 q and 2.93 q (2H, NC*H*$_2$Me, $^3J_{HH}$ 7 Hz), 3.1 and 3.22 s (2H, NCH_2), 3.85 q (4H, $POCH_2$, $^3J_{HH}$ = $^3J_{PH}$ 7.5 Hz), 9.57 s (1H, CHO). ^{31}P NMR spectrum, δ_P, ppm: 10.6. Found, %: N 5.05; P 11.16. $C_{11}H_{23}NO_3P$. Calculated, %: N 5.02; P 11.11.

3-[(Methoxy)phenylphosphoryl)ethylamino]-2,2-dimethylpropanal (IIIe) was obtained from 14.04 g of hydrogen methyl phenylphosphonate (**Ie**), 80 ml of CCl_4, 11.67 g of aldehyde **II**, and 9.09 g of triethylamine. Yield 15.61 g (61%), bp 130–131°C (0.08 mm Hg), n_D^{20} 1.5149. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.75 s (6H, CMe_2), 0.83 t (3H, NCH_2*Me*, $^3J_{HH}$ 7 Hz), 2.53 q and 2.65 q (2H, NC*H*$_2$Me, $^3J_{HH}$ 7 Hz), 3.0 and 3.11 s (2H, NCH_2), 3.53 d (3H, POMe, $^3J_{PH}$ 10 Hz), 7.1–7.3 m (5H, C_6H_5), 9.35 s (1H, CHO). ^{31}P NMR spectrum, δ_P, ppm: 23.4–23.6. Found, %: N 5.00, P 10.90. $C_{14}H_{22}NO_3P$. Calculated, %: N 4.95; P 10.95.

3-[(Dimethoxyphosphoryl)ethylamino]-2,2-dimethylpropanal 2,4-dinitrophenylhydrazone (IVa). To a solution of 3.36 g of 2,4-dinitrophenylhydrazine in 75 ml of ethyl acetate, 4.02 g of aldehyde **IIa** was added dropwise at 70–78°C. The resulting mixture was cooled to room temperature and left for 7 h. The crystals that formed after removal of half the solvent were filtered off, washed with hexane, and dried to obtain compound **IVa**, yield 4.6 g (65%), mp 165–166 g (from hexane). ^{1}H NMR spectrum, δ, ppm: 1.10 t (3H, NCH_2*Me*, $^3J_{HH}$ 7.5 Hz); 1.16 s (6H,

CMe_2), 2.95 q and 3.13 q (2H, NCH_2Me, $^2J_{HH}$ 7.5 Hz), 3.15 s and 3.3 s (2H, NCH_2), 3.5 d (6H, POMe, $^3J_{PH}$ 12 Hz); 7.63 s (1H, CH=N), 8.0 d ($1H^a$, $^3J_{H^aH^b}$ 10 Hz), 8.40 d.d ($1H^b$, $^3J_{H^aH^b}$ 10 Hz, $^4J_{H^cH^b}$ 2.5 Hz), 9.24 d ($1H^c$, $^4J_{H^cH^b}$ 2.5 Hz), 11.1 s (1H, NH). ^{31}P NMR spectrum, δ_P, ppm: 10.5. Found, %: N 16.50, P 7.65. $C_{15}H_{24}N_5O_5P$. Calculated, %: N 16.65, P 7.80.

3-[(Diethoxyphosphoryl)ethylamino]-2,2-dimethylpropanal 2,4-dinitrophenylhydrazone (IVb) was obtained from 3.74 g of 2,4-dinitrophenylhydrazine, 75 ml of ethyl acetate, and 5 g of aldehyde **IIIb.** Yield 5.21 g (62%), mp 139–131°C (from hexane). ^{31}P NMR spectrum, δ_P, ppm: 10.5. Found, %: N 16.9, P 6.8. $C_{17}H_{28}N_5O_5P$. Calculated, %: N 16.2; P 7.1.

3-[(Diisopropoxyphosphoryl)ethylamino]-2,2-dimethylpropanal 2,4-dinitrophenylhydrazone (IVc) was obtained from 3.04 g of 2,4-dinitriphenylhydrazine, 80 ml of ethyl acetate, and 4.5 g of aldehyde **IIIc.** Yield 4.87 g (67%), mp 94–95°C. ^1H NMR spectrum (acetone-d_6), δ, ppm: 0.98 t (3H, NCH_2Me, $^3J_{HH}$ 7 Hz), 1.04 s (6H, CMe_2), 1.08 d.d (12H, Me_2CHO, $^3J_{HH}$ 7 Hz), 2.90 q and 3.08 q (2H, NCH_2Me, $^3J_{HH}$ 7 Hz), 2.98 s and 3.1 s (2H, NCH_2), 4.3 q (2H, Me_2CH, $^3J_{HH}$ 7.5 Hz); 7.68 s (1H, CH=N), 7.88 d ($1H^a$, $^3J_{H^aH^b}$ 10 Hz), 8.23 d.d ($1H^b$, $^3J_{H^aH^b}$ 10 Hz), 8.23 d.d ($1H^b$, $^3J_{H^aH^b}$ 10 Hz, $^4J_{H^cH^b}$ 2.5 Hz), 8.98 d ($1H^c$, $^4J_{H^cH^b}$ 2.5 Hz), 11.1 s (1H, NH). ^{31}P NMR spectrum, δ_P, ppm: 10.9. Found, %: N 14.8, P 6.3. $C_{15}H_{32}N_5O_5P$. Calculated, %: N 15.2; P 6.7.

3-[(Dibutoxyphosphoryl)ethylamino]-2,2-dimethylpropanal 2,4-dinitrophenylhydrazone (IVd) was obtained from 2.89 g of 2,4-dinitrophenylhydrazine, 80 ml of ethyl acetate, and 4.7 g of aldehyde **IIId.** Yield 4.31 g (59%), mp 97–98°C (from hexane). ^{31}P NMR spectrum, δ_P, ppm: 11.8. Found, %: N 14.8, P 6.3. $C_{19}H_{32}N_5O_5P$. Calculated, %: N 15.2, P 6.7.

Reaction of 3-[(diethoxyphosphoryl)ethylamino]-2,2-dimethylpropanal (IIIb) with *tert*-butylamine. To a solution of 0.74 g of *tert*-butylamine in 20 ml of anhydrous toluene, a solution of 3.4 g of compound **IIIb** in 10 ml of toluene was added dropwise with stirring. The reaction mixture was refluxed for 6 h with azeotropic distillation of water. The solvent was then removed, and the residue was distilled in high vacuum to give 2.56 g (63%) of *N*-*tert*-butyl-*N*-[3-[(diethoxyphosphoryl)ethylamino]-2,2-dimethylpropylidene]amine (**VIIb**), bp 92–93°C (0.08 mm Hg), n_D^{20} 1.4450. ^1H NMR spectrum (acetone-d_6), δ, ppm: 0.93 s (6H, CMe_2), 0.93 t (3H, NCH_2Me, $^3J_{HH}$ 7 Hz), 1.03 s (9H, CMe_3), 1.18 t (6H, $2OCH_2Me$, $^3J_{HH}$ 7.5 Hz), 2.78 q and 2.90 q (2H, NCH_2Me, $^3J_{HH}$ 7 Hz), 2.9 s and 3.01 s (2H, NCH_2), 3.86 quintet (4H, $POCH_2Me$, $^3J_{HH}$ = $^3J_{PH}$ 7.5 Hz), 7.5 s (1H, CH=N). Found, %: N 8.9; P 10.2. $C_{15}H_{33}N_2O_3P$. Calculated, %: N 9.1; P 10.0.

***N*-*tert*-Butyl-*N*-[3-[(diisopropoxyphosphoryl)ethylamino]-2,2-dimethylpropylidene]amine (VIIc)** was obtained from 2 g of *tert*-butylamine, 30 ml of anhydrous toluene, and 8.24 g of aldehyde **IIIc.** Yield 6.83 g (70%), bp 89°C (0.05 mm Hg), n_D^{20} 1.4403. Found, %: N 7.8, P 8.9. $C_{17}H_{37}N_2O_3P$. Calculated, %: N 8.3, P 9.2.

***N*-*tert*-Butyl-*N*-[3-[(Dibutoxyphosphoryl)ethylamino]-2,2-dimethylpropylidene]amine (VIId)** was obtained from 3 g of *tert*-butylamine, 50 ml of absolute toluene, and 9.92 g of aldehyde **IIId.** Yield 11.44 g (72%), bp 97–98°C (0.05 mm Hg), n_D^{20} 1.4480. ^1H NMR spectrum (acetone-d_6), δ, ppm: 0.85 s (6H, CMe_2), 0.85 t [6H, $O(CH_2)_3Me$, $^3J_{HH}$ 7 Hz), 0.85 t (3H, NCH_2Me, $^3J_{HH}$ 7 Hz), 1.0 s (9H, CMe_3), 1.1–1.35 m (8H, $POCH_2CH_2CH_2Me$), 2.78 q and 2.90 q (2H, NCH_2Me, $^3J_{HH}$ 7 Hz), 2.96 s and 3.07 s (2H, NCH_2), 3.79 q (4H, $POCH_2$, $^3J_{HH}$ = $^3J_{PH}$ 7 Hz), 7.48 s (1H, CH=N). Found, %: N 7.4, P 8.4. $C_{19}H_{41}N_2O_3P$. Calculated, %: N 7.7, P 8.5.

Reduction of 3-[(dimethoxyphosphoryl)ethylamino]-2,2-dimethylpropanal (III). To a suspension of 0.19 g of lithium aluminum hydride (10% excess) in 50 ml of absolute ether, a solution of 4.81 g of aldehyde **IIIa** in 20 ml of ether was added dropwise at a rate providing moderate boiling of the reaction mixture. After 2 h, the solution was cooled with ice water, and the intermediate alcoholate **IX** was decomposed with 100 ml of cold water. Metal hydroxides were filtered off, the aqueous layer was removed, and the ethereal layer was dried over $MgSO_4$. The ether was removed, and the residue was distilled in a vacuum to give 1.55 g (40%) of 3-[(dimethoxyphosphoryl)ethylamino]-2,2-dimethylpropan-1-ol (**XIa**), bp 103°C (0.09 mm Hg), n_D^{20} 1.4535. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.38 s (6H, CMe_2), 0.68 t (3H, NCH_2Me, $^3J_{HH}$ 7 Hz), 2.55 q and 2.71 q (2H, NCH_2Me, $^3J_{HH}$ 7 Hz), 2.37 and 2.49 s (2H, NCH_2), 2.74 d (2H, CH_2OH, $^3J_{HH}$ 7 Hz), 3.25 d (6H, POMe, $^3J_{HH}$ 10 Hz), 4.10 t (1H, OH, $^3J_{HH}$ 7.5 Hz). ^{31}P NMR spectrum, δ_P, ppm: 10.00. Found, %: N 5.80, P 12.95. $C_9H_{22}NO_4P$. Calculated, %: N 5.86, P 12.93.

3-[(Diethoxyphosphoryl)ethylamino]-2,2-dimethylpropan-1-ol (Xb) was obtained from 0.11 g of lithium aluminum hydride in 40 ml of ether and 3.12 g of aldehyde **IIIb** in 30 ml of ether. Yield 1.21 g (41%), bp 110°C (0.09 mm Hg), n_D^{20} 1.4432. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.7 s (6H,

CMe_2), 0.89 t (3H, NCH_2Me, $^3J_{HH}$ 7 Hz), 1.13 t (6H, $POCH_2Me$, $^3J_{HH}$ 7.5 Hz), 2.6 q and 2.73 q (2H, NCH_2Me, $^3J_{HH}$ 7 Hz), 2.99 d (2H, CH_2OH, $^3J_{HH}$ 7.5 Hz), 2.80 and 2.93 q (2H, NCH_2Me, $^3J_{HH}$ 7 Hz), 3.85 quintet (4H, $POCH_2Me$, $^3J_{HH}$ 7.5 Hz, $^3J_{PH}$ 7.5 Hz), 4.32 t (1H, OH, $^3J_{HH}$ 7.5 Hz). Found, %: N 5.30, P 11.66. $C_{11}H_{26}NO_4P$. Calculated, %: N 5.24, P 11.61.

Reaction of 3-[(dibutoxyphosphoryl)ethylamino]-2,2-dimethylpropanal (IIId) with hydrogen dimethyl phosphite. To a mixture of aldehyde **III**, 3 g, and 7 g of **Ia**, a small piece of sodium was added under argon. The reaction mixture warmed up by 5°C. It was stirred for 24 h at 20°C, neutralized with acetic acid, and volatile products were removed in high vacuum to give 3.18 g (90%) of crude 3-[(dibutoxyphosphoryl)ethylamino]-1-(dimethoxyphosphoryl)-2,2-dimethylpropan-1-ol (**XI**). ^{31}P NMR spectrum, δ_P, ppm: 12 and 26. Found, %: N 3.15, P 7.22. $C_{17}H_{39}\cdot NO_7P_2$. Calculated, %: N 3.25, P 7.19.

The ^1H NMR spectra were measured on a Tesla BS-567A spectrometer (100 MHz) against TMS. The ^{31}P NMR spectra were measured on a CPX-100 spectrometer (36.5 MHz) against 85% H_3PO_4.