Phthalocyanine-catalyzed hydrophosphorylation of hydrazones and azines*

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Benzaldehyde, acetone, and *N*-Boc-piperidone phenylhydrazones, as well as azines derived from aromatic aldehydes and ketones, react with diethyl phosphite in the presence of [tetra(*tert*-butyl)phthalocyanine]aluminum chloride to give α-hydrazino phosphonates in high yields.

Key words: α-hydrazino phosphonates, the Pudovik reaction, [tetra(*tert*-butyl)phthalocyanine]aluminum chloride, azines, phthalocyanines, hydrazones, diethyl phosphite.

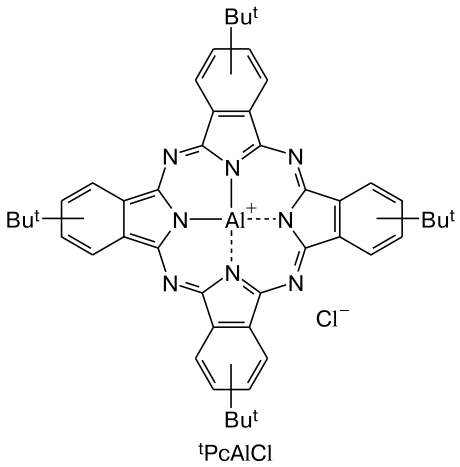
A search for new routes to α-hydrazino phosphonates, which are biologically active compounds[1—4] and structural analogs of the corresponding α-amino phosphonic acids, still attracts the attention of researchers. Known methods for the synthesis of these compounds include (1) selective reduction of α-hydrazono phosphonic acids with $NaBH_3CN$ or $BH_3 \cdot THF$,[5] (2) nucleophilic substitution in 3-methoxy-1,2,3,4-pyridazines using dimethyl phosphite in the presence of Lewis acids,[6] nucleophilic substitution in modified α-hydroxy phosphonates,[7] (3) a MeONa-catalyzed reaction of 2-nitrobenzaldehyde phenylhydrazone with dimethyl phosphite,[8] and (4) reactions of *N*,*N*-dimethylhydrazine with aldehydes and silylated phosphite in the presence of $LiClO_4$ (see Refs 9, 10).

Preparation of α-hydrazino phosphonates is based on (1) base-catalyzed reactions of aliphatic aldazines with dialkyl phosphites followed by hydrolysis (note that this method is unsuitable with aromatic aldazines)[10—12] and (2) noncatalytic addition of dialkyl phosphites to benzaldehyde azine and cyclohexanone azine.[13—17]

Thus, a quest for an efficient general route to α-hydrazino phosphonates from both aromatic aldehydes and ketones remains of current interest.

Previously, we have proposed a catalytic three-component "one pot" synthesis of α-amino phosphonates (the Kabachnik—Fields reaction) with [tetra(*tert*-butyl)phthalocyanine]aluminum chloride (^{t}PcAlCl) as a catalyst.[18,19]

We attempted to obtain α-hydrazino phosphonates in a similar way using hydrazine derivatives as the amine component. However, the three-component "one pot" synthesis in conventional solvents such as dichloromethane, alcohols, toluene, *etc.* failed because of rapid formation of insoluble hydrazones and azines. That is why we further used separately prepared hydrazones and azines in the hydrophosphorylation reaction (a version of the Pudovik reaction[20]). Recently,[21] we have published our data on the phosphorylation of some *N*-acetylhydrazones and *N*-Boc-hydrazones in the presence of ^{t}PcAlCl. In the present work, we studied methyl- and arylhydrazones and azines.



^{t}PcAlCl

We found that both the ^{t}PcAlCl-catalyzed and noncatalytic hydrophosphorylation of acetone phenylhydrazone occurs in an excess of diethyl phosphite (DEP) serving as a solvent as well. However, the presence of the catalyst increases the yield of α-hydrazino phosphonate **1** from 45 to 70%, the other conditions being the same (80 °C, 8 h) (Table 1, entries *1*, *2*). *N*-Boc-Piperidone phenylhydrazone also reacts with DEP in the presence of ^{t}PcAlCl to give the corresponding α-hydrazino phosphonate **2** in 68% yield (entry *3*).

A ^{t}PcAlCl-catalyzed reaction of benzaldehyde phenylhydrazone with an excess of DEP at 80 °C for 50 h affords α-hydrazino phosphonate **3** in 35% yield (entry *4*). At 100 °C, this reaction gives α-anilino phosphonate **4** (Scheme 2).

* Dedicated to Academician V. I. Minkin on the occasion of his 75th birthday.

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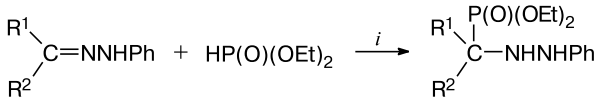
Scheme 1



1—3

i. ^{t}PcAlCl, 80 °C.

Table 1. Synthesis of α-hydrazino phosphonates

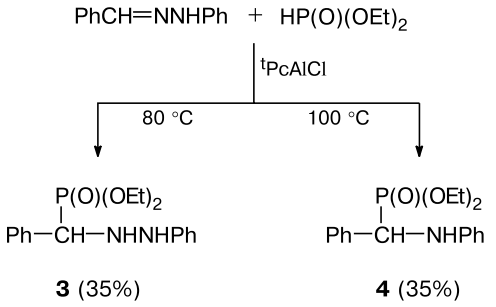
Entry	Hydrazone		H : DEP[a]	*t*/h	Product (yield (%))
	R^1	R^2			
1	Me	Me	1 : 3	8	**1** (45[b])
2	Me	Me	1 : 3	8	**1** (70)
3	$-(CH_2)_2N(Boc)(CH_2)_2-$		1 : 5	8	**2** (68)
4	Ph	H	1 : 3	50	**3** (35[c])

[a] The ratio of hydrazone to $HP(O)(OEt)_2$.
[b] The reaction was carried out in the absence of a catalyst.
[c] The yield with respect to the consumed phenylhydrazone.

Noncatalytic hydrophosphorylation of benzaldehyde azine gives monoadduct **5** in 25% yield (Table 2, entry *1*; Scheme 3). With sodium ethoxide as a catalyst,[11] the yield of compound **5** does not exceed 10%, the reaction time being the same. In the presence of ^{t}PcAlCl, the yield of compound **5** increases to 77% (Table 2, entry *2*) and its analogs **7** and **9** can be obtained in 82—85% yields (Table 2, entries *4*—*7*).

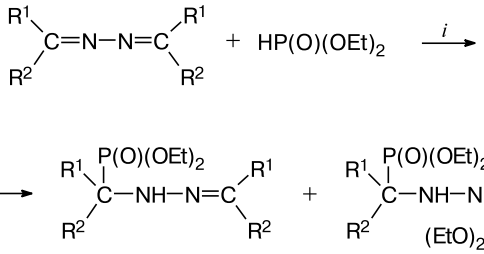
When the reaction time was increased to 70 h, diethyl phosphite added to both the imino groups of the aldazines

Scheme 2



3 (35%) **4** (35%)

Scheme 3



5, 7, 9, 11, 13, 15, 17 **6, 8, 10, 12, 14, 16**

i. ^{t}PcAlCl, 80 °C.

to give hydrazodiphosphonates **6**, **8**, and **10** in 40—55% yields; monoadducts **5**, **7**, and **9** were also isolated in 15—35% yields (Table 2, entries *3*, *5*, *7*).

α-Hydrazino phosphonates were obtained by ^{t}PcAlCl-catalyzed hydrophosphorylation of cyclopentanone, cyclo-

Table 2. Synthesis of hydrazino phosphonates and hydrazodiphosphonates

Entry	Azine		Ratio of azine : $HP(O)(OEt)_2$	*t*/h	Monophosphonate, yield (%)	Diphosphonate, yield (%)
	R^1	R^2				
1	H	Ph	1 : 3	2	**5**, 25[a]	**6**, —
2	H	Ph	1 : 3	2	**5**, 77	**6**, —
3	H	Ph	1 : 5	70	**5**, 23	**6**, 50
4	H	$2\text{-}MeOC_6H_4$	1 : 3	5	**7**, 82	**8**, —
5	H	$2\text{-}MeOC_6H_4$	1 : 5	70	**7**, 15	**8**, 55
6	H	$3\text{-}O_2NC_6H_4$	1 : 5	2	**9**, 85	**10**, —
7	H	$3\text{-}O_2NC_6H_4$	1 : 5	70	**9**, 35	**10**, 40
8	$-(CH_2)_4-$		1 : 1.2	8	**11**, 85	**12**, —
9	$-(CH_2)_4-$		1 : 5	30	**11**, 10	**12**, 40
10	$-(CH_2)_5-$		1 : 1.2	0.5	**13**, 85	—
11	$-(CH_2)_5-$		1 : 3	8	—	**14**, 80
12	$-(CH_2)_2N(Boc)(CH_2)_2-$		1 : 5	8	**15**, 30[a]	**16**, 10[a]
13	$-(CH_2)_2N(Boc)(CH_2)_2-$		1 : 5	8	**15**, 60	**16**, 20
14	$-(CH_2)_2N(Boc)(CH_2)_2-$		1 : 5	24	**15**, 10	**16**, 70
15	Me	Ph	1 : 5	50	**17**, 40[b]	—

[a] The reaction was carried out in the absence of a catalyst.
[b] The yield with respect to the consumed acetophenone azine.

hexanone, *N*-Boc-piperidone, and acetophenone azines. Depending on the reaction time and the excess of DEP, the major products were α-(cyclo)alkylidenehydrazino phosphonates **11**, **13**, **15**, and **17** or bisadducts **12**, **14**, and **16** (for their yields, see Table 2, entries *8—11*, *13—15*).

The structures of the phosphonates obtained were confirmed by IR and ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy; their molecular formulas were confirmed by elemental analysis and mass spectrometry. Diphosphonates **6**, **8**, and **10** are 1 : 1 mixtures of diastereomers (their ^{31}P, ^{1}H, and ^{13}C NMR spectra contain double sets of all signals).

The IR spectra of all the α-hydrazino phosphonates obtained show absorption bands at 1240—1270 and 3220—3270 cm^{-1} characteristic of the P=O and N—H groups, respectively.

The ^{31}P NMR spectra of monophosphonate **3**, diphosphonates **6**, **8**, and **10**, and α-arylidenehydrazino phosphonates **5**, **7**, and **9** exhibit signals for the phosphonate group at δ 19.37—22.70; in compounds **1**, **2**, and **11**—**17**, these groups resonate at δ 25.93—31.88. In the ^{1}H NMR spectra of α-hydrazino phosphonates **3**, **6**, **8**, and **10** and α-arylidenehydrazino phosphonates **5**, **7**, **9**, and **17**, the signals for the nonequivalent ethoxy groups appear as two triplets (δ 1.00—1.38) and two or three multiplets (δ 3.66—4.27). For α-hydrazino phosphonates **1**, **2**, **12**, **14**, and **16** and α-cycloalkylidenehydrazino phosphonates **11**, **13**, and **15**, the signals for the ethoxy groups appear as a triplet at δ 1.26—1.36 and a multiplet at δ 3.97—4.22. The signal for the α-CH proton is a doublet at δ 4.33—5.53 ($^2J_{H,P}$ = 20.5—22.5 Hz) for compounds **3**, **5**, and **7**, a doublet of doublets at δ 5.08 ($^2J_{H,P}$ = 22.0 Hz, $^3J_{H,H}$ = = 6.3 Hz) for compound **9**, and two doublets at δ 4.14—5.46 ($^2J_{H,P}$ = 22.5—20.9 Hz) for the diastereomers of compounds **6**, **8**, and **10**.

The ^{13}C NMR spectra of compounds **1**—**3** and **5**—**17** show a signal for the α-C atom at δ 53.34—66.17 ($^1J_{C,P}$ = = 136.1—152.2 Hz) and signals for the C atoms of the ethoxy groups at δ 16.01—16.63 ($^3J_{C,P}$ = 4.4—6.5 Hz) and 61.52—63.63 ($^2J_{C,P}$ = 5.9—8.1 Hz).

In the conclusion, we developed a general method of catalytic hydrophosphorylation of aliphatic and aromatic hydrazones and azines for the synthesis of α-hydrazino phosphonates, α-arylidene- and α-(cyclo)alkylidenehydrazino phosphonates, and α,α′-hydrazodiphosphonates.

Experimental

^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker Avance 400 instrument (400.13, 161.98, and 100.61 MHz, respectively) in $CDCl_3$ with $SiMe_4$ as the internal standard (^{1}H, ^{13}C) and with 85% H_3PO_4 as the external standard (^{31}P). IR spectra were recorded on a UR-20 instrument in CCl_4. Elemental analysis was carried out on a Vario-II CHN-analyzer. Mass spectra were measured on a Finnigan Mat Incos 50 quadrupole mass spectrometer (EI, 70 eV, direct inlet probe).

Diethyl phosphite (Aldrich) was used as purchased. [Tetra-(*tert*-butyl)phthalocyanine]aluminum chloride was prepared according to a known procedure.[22]

Thin-layer chromatography was carried out on Silufol plates. The products were separated by column chromatography on Merck 60 silica gel (70—230 mesh ASTM).

Synthesis of α-hydrazino phosphonates 1—3, α-arylidene- and α-(cyclo)alkylidenehydrazino phosphonates 5, 7, 9, 11, 13, 15, and 17, and α,α′-hydrazodiphosphonates 6, 8, 10, 12, 14, and 16 (general procedure). Diethyl phosphite (1.2—5 mmol) and ^{t}PcAlCl (0.05 mmol) were added to a hydrazone, an azine, or a ketazine (1 mmol). The reaction mixture was stirred under argon at 80 °C until the reaction was completed (monitoring by TLC). The final reaction mixture was dissolved in a minimum amount of CH_2Cl_2—MeOH (70 : 1) and chromatographed on silica gel (column length 15 cm, diameter 1.5—2.0 cm) with the above mixed solvent as an eluent. The ratios of the reagents, the reaction times, and the yields of the compounds obtained are given in Tables 1 and 2.

Diethyl [1-methyl-1-(2-phenylhydrazino)ethyl]phosphonate (1). ^{1}H NMR, δ: 1.29 (d, 6 H, 2 Me, $^3J_{H,P}$ = 15.4 Hz); 1.36 (t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 3.76 (br.s, 1 H, NH); 4.14—4.22 (m, 4 H, 2 OCH_2); 6.02 (br.s, 1 H, NH); 6.71 (t, 1 H, arom., $^3J_{H,H}$ = 7.3 Hz); 6.90 (d, 2 H, arom., $^3J_{H,H}$ = 8.6 Hz); 7.16 (t, 1 H, arom., $^3J_{H,H}$ = 7.7 Hz). ^{31}P NMR, δ: 30.89. ^{13}C NMR, δ: 16.63 (d, Me, POEt, $^3J_{C,P}$ = 5.1 Hz); 21.56 (d, Me, $^2J_{C,P}$ = 9.0 Hz); 56.51 (d, C, $^1J_{C,P}$ = 139.0 Hz); 62.25 (d, OCH_2, $^2J_{C,P}$ = 7.3 Hz); 112.35, 118.29, 128.86, 150.62 (C_{arom}). IR, ν/cm^{-1}: 1040, 1080 (P—O—C); 1260 (P=O); 3280 (N—H). MS, *m/z*: 286 $[M]^+$, 148 $[M - P(OH)(OEt)_2 - H]^+$, 138 $[P(OH)(OEt)_2]^+$. Found (%): C, 54.47; H, 8.24; N, 9.75. $C_{13}H_{23}N_2O_3P$. Calculated (%): C, 54.54; H, 8.10; N, 9.78.

Diethyl [1-*tert*-butoxycarbonyl-4-(2-phenylhydrazino)piperidin-4-yl]phosphonate (2). ^{1}H NMR, δ: 1.29 (t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.2 Hz); 1.37 (s, 9 H, Me, Bu^t); 1.71—1.79 (m, 4 H, CH_2C, ring); 3.08—3.15 (m, 2 H, CH_2N, ring); 3.62—3.80 (m, 2 H, CH_2N, ring); 3.90 (br.s, 1 H, NH); 4.06—4.17 (m, 4 H, 2 OCH_2); 6.03 (br.s, 1 H, NH); 6.64—6.68 (m, 1 H, arom.); 6.83—6.85 (m, 2 H, arom.); 7.08—7.12 (m, 2 H, arom.). ^{31}P NMR, δ: 28.05. ^{13}C NMR, δ: 16.63 (d, Me, POEt, $^3J_{C,P}$ = 4.8 Hz); 27.65 (CH_2C, ring); 28.45 (Me, Bu^t); 38.38 (CH_2N, ring); 57.08 (d, C, $^1J_{C,P}$ = 145.3 Hz); 62.50 (d, OCH_2, $^2J_{C,P}$ = 8.1 Hz); 79.46 (s, Bu^t); 112.47, 118.67, 129.07, 149.63 (C_{arom}), 154.73 (C=O). IR, ν/cm^{-1}: 1030, 1060 (P—O—C); 1250 (P=O); 1680 (C=O); 3270 (N—H). Found (%): C, 56.48; H, 7.93; N, 9.75. $C_{20}H_{34}N_3O_5P$. Calculated (%): C, 56.19; H, 8.02; N, 9.83.

Diethyl (phenyl)(2-phenylhydrazino)methylphosphonate (3). ^{1}H NMR, δ: 1.14, 1.38 (both t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.1 Hz, $^3J_{H,H}$ = 7.0 Hz); 3.78—3.88, 3.94—4.02 (both m, 1 H each, OCH_2); 4.17—4.27 (m, 2 H, OCH_2); 4.33 (d, 1 H, CH, $^2J_{H,P}$ = = 20.5 Hz); 6.81—6.88 (m, 3 H, arom.); 7.19—7.23 (m, 2 H, arom.); 7.36—7.45 (m, 5 H, arom.). ^{31}P NMR, δ: 21.60. ^{13}C NMR, δ: 16.24, 16.53 (both d, Me, POEt, $^3J_{C,P}$ = 5.2 Hz, $^3J_{C,P}$ = 5.9 Hz); 61.16 (d, CH, $^1J_{C,P}$ = 147.1 Hz); 62.96, 63.07 (both d, OCH_2, $^2J_{C,P}$ = 7.3 Hz); 113.74, 119.82, 128.49, 128.67, 128.74, 128.88, 128.18, 129.28, 134.29, 147.84 (C_{arom}). IR, ν/cm^{-1}: 1030, 1060 (P—O—C); 1240 (P=O); 3230 (N—H). Found (%): C, 60.89; H, 6.74; N, 8.17. $C_{15}H_{20}N_3O_3P$. Calculated (%): C, 61.07; H, 6.93; N, 8.38.

Diethyl (benzylidenehydrazino)(phenyl)methylphosphonate (5), m.p. 115—116 °C (*cf.* Ref. 14: m.p. 115—116 °C). ^{1}H NMR,

δ: 1.14, 1.31 (both t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 3.75—3.85, 3.94—4.04 (both m, 1 H each, OCH_2); 4.11—4.19 (m, 2 H, OCH_2); 4.94 (d, 1 H, CH, $^2J_{H,P}$ = 22.5 Hz); 6.28 (br.s, 2 H, NH); 7.23—7.31 (m, 4 H, arom.); 7.37 (t, 2 H, arom., $^3J_{H,H}$ = 7.5 Hz); 7.47—7.48 (m, 4 H, arom.); 7.65 (s, 1 H, CH=N). ^{31}P NMR, δ: 22.08. ^{13}C NMR, δ: 16.22, 16.45 (both d, Me, POEt, $^3J_{C,P}$ = 5.1 Hz, $^3J_{C,P}$ = 5.9 Hz); 61.15 (d, CH, $^1J_{C,P}$ = 148.5 Hz); 63.09, 63.15 (both d, OCH_2, $^2J_{C,P}$ = 5.9 Hz, $^2J_{C,P}$ = 6.5 Hz); 126.17, 127.96, 128.16, 128.21, 128.43, 128.60, 135.20, 135.52 (C_{arom}); 140.19 (s, CH=N). IR, ν/cm^{-1}: 1030, 1070 (P—O—C); 1250 (P=O); 1600 (CH=N); 3230 (N—H).

Tetraethyl α,α´-hydrazobis(benzylphosphonate) (6), m.p. 92—95 °C. ^{1}H NMR, δ: 1.01, 1.03, 1.13, 1.19 (all t, 12 H, Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 3.62—3.72 (m, 2 H, OCH_2); 3.80—4.03 (m, 8 H, OCH_2, NHNH); 4.13, 4.31 (both d, 2 H, CH, $^2J_{H,P}$ = = 20.7 Hz); 7.28—7.42 (m, 10 H, arom.). ^{31}P NMR, δ: 21.22, 21.27. ^{13}C NMR, δ: 16.09—16.36 (m, Me, POEt); 60.51, 63.35 (both d, CH, $^1J_{C,P}$ = 148.5 Hz, $^1J_{C,P}$ = 147.9 Hz); 62.64, 63.14 (both d, OCH_2, $^2J_{C,P}$ = 7.3 Hz, $^2J_{C,P}$ = 6.6 Hz); 128.11, 128.55, 128.66, 128.72, 134.40, 135.50 (C_{arom}). IR, ν/cm^{-1}: 1040, 1070 (P—O—C); 1250 (P=O); 3260 (NH). Found (%): C, 54.37; H, 7.15; N, 5.56. $C_{22}H_{34}N_2O_6P_2$. Calculated (%): C, 54.54; H, 7.07; N, 5.78.

Diethyl (2-methoxyphenyl)(2-methoxybenzylidenehydrazino)-methylphosphonate (7), m.p. 109—110 °C. ^{1}H NMR, δ: 1.09, 1.32 (both t, 6 H, Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 3.70—3.81, 3.84—3.97 (both m, 1 H each, OCH_2); 3.78, 3.91 (both s, 3 H each, 2 OMe); 4.16—4.23 (m, 2 H, OCH_2); 5.53 (d, 1 H, CH, $^2J_{H,P}$ = 22.0 Hz); 6.80—6.98 (m, 4 H, arom.); 7.18—7.28 (m, 2 H, arom.); 7.46 (d, 1 H, arom., $^3J_{H,H}$ = 7.5 Hz); 7.74 (dd, 1 H, arom., $^3J_{H,H}$ = = 7.7 Hz, $^4J_{H,H}$ = 1.4 Hz); 8.02 (s, 1 H, CH=N). ^{31}P NMR, δ: 22.70. ^{13}C NMR, δ: 16.16, 16.46 (both d, Me, POEt, $^3J_{C,P}$ = = 5.9 Hz, $^3J_{C,P}$ = 6.6 Hz); 53.74 (d, CH, $^1J_{C,P}$ = 152.2 Hz); 55.51, 55.75 (both s, 2 OMe); 62.93 (d, OCH_2, $^2J_{C,P}$ = 7.4 Hz); 110.76, 110.92, 120.70, 120.89, 123.87, 125.62, 128.56, 128.86, 129.04, 129.28 156.81, 157.24 (d, $^3J_{C,P}$ = 6.5 Hz) (C_{arom}); 135.34 (s, CH=N). IR, ν/cm^{-1}: 1040, 1060 (P—O—C); 1250 (P=O); 1600 (CH=N); 3230 (N—H). Found (%): C, 59.38; H, 6.68; N, 6.85. $C_{20}H_{27}N_2O_5P$. Calculated (%): C, 59.11; H, 6.70; N, 6.89.

Tetraethyl α,α´-hydrazobis(2-methoxybenzylphosphonate) (8), m.p. 44—46 °C. ^{1}H NMR, δ: 1.00—1.05 (m, 6 H, 2 Me, POEt); 1.18, 1.24 (both t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 3.66—4.09 (m, 14 H, 4 OCH_2, 2 OMe); 4.80, 4.98 (both d, 2 H, CH, $^2J_{H,P}$ = 21.5 Hz, $^2J_{H,P}$ = 21.3 Hz); 6.82—7.32 (m, 8 H, arom.). ^{31}P NMR, δ: 22.20, 22.31. ^{13}C NMR, δ: 16.05—16.42 (m, Me, POEt); 53.34, 56.06 (both d, CH, $^1J_{C,P}$ = 150.7 Hz, $^1J_{C,P}$ = 150 Hz); 55.39, 55.75 (both s, 2 OMe); 62.93 (m, 4 OCH_2); 110.53, 110.75, 120.59, 120.90, 123.84, 128.88, 126.99 (C_{arom}); 157.61, 158.00 (both d, COMe, $^3J_{C,P}$ = 7.3 Hz, $^3J_{C,P}$ = 8.1 Hz). IR, ν/cm^{-1}: 1040, 1080 (P—O—C); 1270 (P=O); 3270 (N—H). MS, *m/z*: 544 $[M]^+$, 407 $[M - P(O)(OEt)_2]^+$, 269 $[M - 2\ P(O)(OEt)_2 - H]^+$, 137 $[P(O)(OEt)_2]^+$. Found (%): C, 53.16; H, 7.20; N, 4.99. $C_{24}H_{38}N_2O_8P_2$. Calculated (%): C, 52.94; H, 7.03; N, 5.14.

Diethyl (3-nitrobenzylidenehydrazino)(3-nitrophenyl)methyl-phosphonate (9), m.p. 155—156 °C. ^{1}H NMR, δ: 1.23, 1.34 (both t, 6 H, Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 3.94—4.05, 4.05—4.13 (both m, 1 H each, OCH_2); 4.15—4.23 (m, 2 H, OCH_2); 5.08 (dd, 1 H, CH, $^2J_{H,P}$ = 22.0 Hz, $^3J_{H,H}$ = 6.3 Hz); 7.44 (t, 1 H, arom., $^3J_{H,H}$ = 8.0 Hz); 7.56 (t, 1 H, arom., $^3J_{H,H}$ = 8.0 Hz); 7.75 (s, 1 H, CH=N); 7.76 (d, 1 H, arom., $^3J_{H,H}$ = 5.9 Hz); 7.84 (d, 1 H, arom., $^3J_{H,H}$ = 8.1 Hz); 8.06 (d, 1 H, arom., $^3J_{H,H}$ = 8.5 Hz); 8.17 (d, 1 H, arom., $^3J_{H,H}$ = 8.3 Hz); 8.26 (s, 1 H, arom.); 8.37 (d, 1 H, arom., $^4J_{H,P}$ = 2.0 Hz). ^{31}P NMR, δ: 19.67. ^{13}C NMR, δ: 16.29, 16.43 (both d, Me, POEt, $^3J_{C,P}$ = 5.1 Hz, $^3J_{C,P}$ = = 5.8 Hz); 60.07 (d, CH, $^1J_{C,P}$ = 148.6 Hz); 63.47, 63.63 (both d, OCH_2, $^2J_{C,P}$ = 6.6 Hz, $^2J_{C,P}$ = 7.3 Hz); 120.69, 122.86, 123.04, 123.11, 129.44, 129.53, 131.55, 134.30 (d, $^3J_{C,P}$ = 5.1 Hz); 136.83, 137.46, 138.06, 148.43, 148.53 (C_{arom}); 143.60 (d, CH=N, $^4J_{C,P}$ = 2.9 Hz). IR, ν/cm^{-1}: 1030, 1070 (P—O—C); 1250 (P=O); 1350, 1530 (N=O, NO_2); 1600 (CH=N); 3230 (N—H). MS, *m/z*: 436 $[M]^+$, 299 $[M - P(O)(OEt)_2]^+$, 138 $[P(OH)(OEt)_2]^+$. Found (%): C, 49.60; H, 5.08; N, 12.61. $C_{18}H_{21}N_4O_7P$. Calculated (%): C, 49.55; H, 4.85; N, 12.84.

Tetraethyl α,α´-hydrazobis(3-nitrobenzylphosphonate) (10), m.p. 105—108 °C. ^{1}H NMR, δ: 1.04, 1.05, 1.13, 1.18 (all t, 12 H, Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 3.76—3.93, 3.94—4.11 (both m, 4 H each, OCH_2); 4.28 (br.s, 2 H, NHNH); 5.31, 5.46 (both d, 2 H, CH, $^2J_{H,P}$ = 22.2 Hz, $^2J_{H,P}$ = 22.5 Hz); 7.37—7.46 (m, 2 H, arom.); 7.50—7.54, 7.60—7.64 (both m, 2 H, arom.); 7.70—7.73, 7.79—7.83 (both m, 2 H, arom.); 7.86, 7.88 (both d, 2 H, arom., $^3J_{H,H}$ = 8.1 Hz). ^{31}P NMR, δ: 19.37, 19.64. ^{13}C NMR, δ: 16.01, 16.19 (both d, Me, POEt, $^3J_{C,P}$ = 5.9 Hz, $^3J_{C,P}$ = 5.1 Hz); 55.89, 57.32 (both d, CH, $^1J_{C,P}$ = 145.7 Hz, $^1J_{C,P}$ = 146.3 Hz); 62.96, 63.52 (both d, OCH_2, $^2J_{C,P}$ = 7.4 Hz); 124.74, 124.82, 128.46, 129.53 (d, $^3J_{C,P}$ = 2.2 Hz); 129.79 (d, $^3J_{C,P}$ = 2.9 Hz); 130.75, 131.11, 132.90, 133.10, 149.95, 150.02 (C_{arom}). IR, ν/cm^{-1}: 1030, 1060 (P—O—C); 1240 (P=O); 1360, 1525 (N=O); 3270 (N—H). Found (%): C, 46.18; H, 5.74; N, 9.58. $C_{22}H_{32}N_4O_{10}P_2$. Calculated (%): C, 46.00; H, 5.61; N, 9.75.

Diethyl 1-(cyclopentylidenehydrazino)cyclopentylphosphonate (11). ^{1}H NMR, δ: 1.27 (t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.0 Hz); 1.62—1.69 (m, 4 H, ring); 1.74—1.81 (m, 4 H, ring); 1.93—2.06 (m, 4 H, ring); 2.12 (t, 2 H, ring, $^3J_{H,H}$ = 7.3 Hz); 2.29 (t, 2 H, ring, $^3J_{H,H}$ = 7.2 Hz); 4.01—4.09 (m, 4 H, 2 OCH_2); 4.71 (br.s, 1 H, NH). ^{31}P NMR, δ: 31.45. ^{13}C NMR, δ: 16.50 (d, Me, POEt, $^3J_{C,P}$ = 5.1 Hz); 24.87, 26.27, 33.16, 33.83 (d, $^2J_{C,P}$ = 5.8 Hz) (C_{ring}); 61.69 (d, OCH_2, $^2J_{C,P}$ = 7.3 Hz); 66.17 (d, C, $^1J_{C,P}$ = = 147.8 Hz); 158.47 (C=N). IR, ν/cm^{-1}: 1040, 1070 (P—O—C); 1240 (P=O); 1650 (C=N); 3250 (N—H). Found (%): C, 55.73; H, 9.22; N, 9.17. $C_{14}H_{27}N_2O_3P$. Calculated (%): C, 55.61; H, 9.00; N, 9.27.

Tetraethyl 1,1´-hydrazobis(cyclopentylphosphonate) (12). ^{1}H NMR, δ: 1.26 (t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.0 Hz); 1.58—1.82 (m, 14 H, ring); 2.04—2.14 (m, 1 H, ring); 2.30—2.34 (m, 1 H, ring); 3.73 (br.s, 2 H, NHNH); 4.03—4.11 (m, 4 H, 2 OCH_2). ^{31}P NMR, δ: 31.88. ^{13}C NMR, δ: 16.53 (d, Me, POEt, $^3J_{C,P}$ = = 5.0 Hz); 24.46 (d, $^2J_{C,P}$ = 8.1 Hz), 32.72 (d, $^3J_{C,P}$ = 11.7 Hz) (C_{ring}); 61.63 (d, OCH_2, $^2J_{C,P}$ = 7.4 Hz); 65.75 (d, C, $^1J_{C,P}$ = = 143.5 Hz). IR, ν/cm^{-1}: 1040, 1060 (P—O—C); 1250 (P=O); 3280 (N—H). MS, *m/z*: 440 $[M]^+$, 303 $[M - P(O)(OEt)_2]^+$, 165 $[M - 2P(O)(OEt)_2 - H]^+$, 138 $[P(OH)(OEt)_2]^+$. Found (%): C, 49.22; H, 8.70; N, 6.38. $C_{18}H_{38}N_2O_6P_2$. Calculated (%): C, 49.08; H, 8.70; N, 6.36.

Diethyl 1-(cyclohexylidenehydrazino)cyclohexylphosphonate (13), m.p. 90—91 °C (*cf.* Ref. 17: m.p. 87 °C). ^{1}H NMR, δ: 1.15—1.34 (m, 2 H, ring); 1.29 (t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.0 Hz); 1.42—2.07 (m, 16 H, ring); 2.20—2.25 (m, 2 H, ring), 3.98—4.20 (m, 4 H, 2 OCH_2). ^{31}P NMR, δ: 31.35. ^{13}C NMR, δ: 16.51 (d, Me, POEt, $^3J_{C,P}$ = 5.9 Hz); 20.15, 20.26, 24.98, 25.61 (d, $^3J_{C,P}$ = 5.8 Hz), 25.89, 26.98, 29.05, 35.42 (C_{ring}); 58.59

(CH, $^1J_{C,P}$ = 142.0 Hz); 61.52 (d, OCH_2, $^2J_{C,P}$ = 7.3 Hz). IR, ν/cm^{-1}: 1040, 1080 (P—O—C); 1270 (P=O); 1630 (CH=N); 3270 (N—H). MS, *m/z*: 330 $[M]^+$, 192 $[M - P(O)(OEt)_2 - H]^+$, 138 $[P(OH)(OEt)_2]^+$.

Tetraethyl 1,1′-hydrazobis(cyclohexylphosphonate) (14). ^{1}H NMR, δ: 1.17—1.34 (m, 2 H, ring); 1.31 (t, 12 H, 2 Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 1.38—1.48 (m, 4 H, ring); 1.53—1.75 (m, 10 H, ring); 1.78—1.92 (m, 4 H, ring); 4.08—4.18 (m, 8 H, 4 OCH_2). ^{31}P NMR, δ: 31.18. ^{13}C NMR, δ: 16.67 (d, Me, POEt, $^3J_{C,P}$ = 5.9 Hz); 20.34 (d, $^3J_{C,P}$ = 11.0 Hz), 25.73, 28.56 (C_{ring}); 58.67 (CH, $^1J_{C,P}$ = 136.1 Hz); 61.63 (d, OCH_2, $^2J_{C,P}$ = 8.1 Hz). IR, ν/cm^{-1}: 1040, 1070 (P—O—C); 1270 (P=O); 3260 (N—H). MS, *m/z*: 468 $[M]^+$, 330 $[M - P(O)(OEt)_2 - H]^+$, 192 $[M - 2\ P(O)(OEt)_2 - 2\ H]^+$, 138 $[P(OH)(OEt)_2]^+$. Found (%): C, 51.06; H, 9.10; N, 6.07. $C_{20}H_{42}N_2O_6P_2$. Calculated (%): C, 51.27; H, 9.04; N, 5.97.

Diethyl {1-*tert*-butoxycarbonyl-4-[1-(*tert*-butoxycarbonyl)-piperidin-4-ylidenehydrazino]piperidin-4-yl}phosphonate (15), m.p. 64—66 °C. ^{1}H NMR, δ: 1.26 (t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = = 7.1 Hz); 1.43 (both s, 18 H, 6 Me, Bu^t); 1.83—2.02 (m, 4 H, ring); 2.32—2.55 (m, 4 H, ring); 2.97—3.28 (br.m, 2 H, ring); 3.33—3.68 (m, 4 H, ring); 3.72—3.95 (br.m, 2 H, ring); 3.97—4.05 (m, 4 H, 2 OCH_2); 4.92 (br.s, 1 H, NH). ^{31}P NMR, δ: 28.85. ^{13}C NMR, δ: 16.48 (d, Me, POEt, $^3J_{C,P}$ = 5.1 Hz); 25.66 (C_{ring}); 28.40 (s, Me, Bu^t); 28.61, 33.09 (C_{ring}); 56.79 (d, C, $^1J_{C,P}$ = 146.4 Hz); 61.87 (d, OCH_2, $^2J_{C,P}$ = 7.3 Hz); 79.34, 79.80 (both s, C, Bu^t); 147.35 (C=N); 154.91 (C=O). IR, ν/cm^{-1}: 1040, 1060 (P—O—C); 1260 (P=O); 1690 (C=O); 3280 (N—H). MS, *m/z*: 532 $[M]^+$, 395 $[M - P(O)(OEt)_2]^+$, 337 $[M - P(OH)(OEt)_2 - Bu^t]^+$, 138 $[P(OH)(OEt)_2]^+$, 57 $[Bu^t]^+$. Found (%): C, 54.20; H, 8.47; N, 10.34. $C_{24}H_{45}N_4O_7P$. Calculated (%): C, 54.12; H, 8.52; N, 10.52.

Tetraethyl 4,4′-hydrazobis{[1-(*tert*-butoxycarbonyl)piperidin-4-yl]phosphonate} (16). ^{1}H NMR, δ: 1.32 (t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 1.44 (s, 18 H, 6 Me, Bu^t); 1.81—1.95 (br.m, 8 H, ring); 2.99—3.21 (br.m, 4 H, ring); 3.66—3.87 (br.m, 4 H, ring); 3.66—3.87 (br.s, 2 H, NHNH); 4.09—4.17 (m, 4 H, 2 OCH_2). ^{31}P NMR, δ: 28.32. ^{13}C NMR, δ: 16.61 (d, Me, POEt, $^3J_{C,P}$ = 5.2 Hz); 28.08, 28.10 (C_{ring}); 28.42 (s, Me, Bu^t); 56.64 (d, C, $^1J_{C,P}$ = 142.7 Hz); 62.11 (d, OCH_2, $^2J_{C,P}$ = 7.3 Hz); 79.47 (s, C, Bu^t); 154.66 (C=O). IR, ν/cm^{-1}: 1030, 1050 (P—O—C); 1260 (P=O); 1690 (C=O); 3280 (N—H). MS, *m/z*: 670 $[M]^+$, 533 $[M - P(O)(OEt)_2]^+$, 395 $[M - 2\ P(O)(OEt)_2 - H]^+$, 339 $[M - 2\ P(O)(OEt)_2 - Bu^t]^+$, 57 $[Bu^t]^+$. Found (%): C, 49.93; H, 8.48; N, 8.23. $C_{28}H_{56}N_4O_{10}P_2$. Calculated (%): C, 50.14; H, 8.42; N, 8.35.

Diethyl 1-phenyl-1-(1-phenylethylidene)hydrazinoethylphosphonate (17). ^{1}H NMR, δ: 1.17, 1.25 (both t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = 7.1 Hz); 2.02 (d, 3 H, Me, $^3J_{H,P}$ = 15.9 Hz); 2.22 (s, 3 H, Me); 3.80—3.87, 3.93—4.01 (both m, 1 H each, OCH_2); 4.03—4.12 (m, 2 H, OCH_2); 7.24—7.30 (m, 3 H, arom.); 7.34—7.39 (m, 5 H, arom.); 7.45—7.50 (m, 2 H, arom.). ^{31}P NMR, δ: 25.93. ^{13}C NMR, δ: 12.23 (s, Me); 16.34 (both d, Me, POEt, $^3J_{C,P}$ = 6.5 Hz); 22.22 (s, Me); 62.72 (d, C, $^1J_{C,P}$ = = 140.0 Hz); 63.01, 63.15 (both d, OCH_2, $^2J_{C,P}$ = 7.3 Hz); 125.51, 127.63, 128.00, 128.07, 128.32, 128.58, 133.13, 139.34, 140.35 (C_{arom}), 144.96 (s, C=N). IR, ν/cm^{-1}: 1040, 1060 (P—O—C); 1250 (P=O); 1600 (C=N); 3220 (N—H). MS, *m/z*: 374 $[M]^+$, 237 $[M - P(O)(OEt)_2]^+$, 138 $[P(OH)(OEt)_2]^+$. Found (%): C, 64.05; H, 7.13; N, 7.28. $C_{20}H_{27}N_2O_3P$. Calculated (%): C, 64.16; H, 7.27; N, 7.48.

Diethyl (anilino)(phenyl)methylphosphonate (4).[23] Diethyl phosphite (3 mmol) and ^{t}PcAlCl (0.05 mmol) were added to benzaldehyde phenylhydrazone (1 mmol). The reaction mixture was stirred under argon at 100 °C for 30 h. Further workup of the reaction mixture followed the general procedure for the synthesis of α-hydrazino phosphonates. The yield of α-anilino phosphonate **4** was 35% (with respect to the consumed phenylhydrazone). ^{1}H NMR, δ: 1.13, 1.30 (both t, 6 H, 2 Me, POEt, $^3J_{H,H}$ = = 7.1 Hz); 3.92—4.14 (m, 4 H, 2 OCH_2); 4.94 (d, 1 H, CH, $^2J_{H,P}$ = 24.3 Hz); 6.60—7.49 (m, 10 H, arom.). ^{31}P NMR, δ: 22.80. ^{13}C NMR, δ: 16.26, 16.41 (both d, Me, POEt, $^3J_{C,P}$ = 5.1 Hz, $^3J_{C,P}$ = 5.9 Hz); 61.95 (d, CH, $^1J_{C,P}$ = 150.1 Hz); 63.23, 63.44 (both d, OCH_2, $^2J_{C,P}$ = 6.6 Hz, $^2J_{C,P}$ = 6.5 Hz); 126.25, 128.30, 128.84, 129.10, 129.14, 136.59, 139.48 (C_{arom}). IR, ν/cm^{-1}: 1030, 1070 (P—O—C); 1250 (P=O); 3230 (N—H). MS, *m/z*: 319 $[M]^+$, 182 $[M - P(O)(OEt)_2]^+$, 137 $[P(O)(OEt)_2]^+$.

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References

1. P. Diel, L. Maier, *Eur. Pat. Appl. EP*, 1985, 143 078; *Chem. Abstr.*, 1985, **103**, 215544m.
2. N. Lange, W. Kochmann, G. Wolter, K. Peter, A. Seidel, P. Thomas, H. Hennig, *Ger. (East).*, 1990, DD 285284, A5 19901212.
3. T. E. McNeel, M. S. Whittemore, S. D. Bryant, G. H. Vunk, *PCT Int. Appl.*, 1999, WO 9906325 A1 19990211.
4. C. Cannizzaro, J. M. Chen, C. Xiaowu, A. Cho, L. S. Chong, M. Desai, M. Fardis, T. Kirschberg, R. L. Mackman, S. Swaminathan, US Pat., 2008, US 7417055.
5. C. Yuan, S. Chen, R. Xie, H. Feng, *Phosphorus, Sulfur, Silicon, Relat. Elem.*, 1995, **106**, 115.
6. M. Kaname, K. Yoshinaga, Y. Arakawa, S. Youshifuji, *Tetrahedron Lett.*, 1999, **40**, 7993.
7. C. Yuan, C. Li, *Synthesis*, 1996, 507.
8. L. V. Ryapisova, L. B. Kashevarova, S. V. Fridland, I. G. Shaikhiev, *Zh. Obshch. Khim.*, 2000, **70**, 1631 [*Russ. J. Gen. Chem.* (*Engl. Transl.*), 2000, **70**].
9. A. Heydari, A. Javidan, M. Schaffie, *Tetrahedron Lett.*, 2001, **42**, 8071.
10. A. Heydari, M. Mehrdad, M. Schaffie, M. Abdolrezaie, R. Hajinassirei, *Chem. Lett.*, 2002, **31**, 1146.
11. J. Racon, C. Wasielevski, *Rocz. Chem.*, 1976, **50**, 447.
12. J. Racon, C. Wasielevski, *Tetrahedron Lett.*, 1978, 1609.
13. A. N. Pudovik, R. R. Shagidullin, V. K. Khairullin, I. I. Vandyukova, A. V. Chernova, A. M. Kibardin, M. A. Pudovik, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 2063 [*Russ. Chem. Bull.* (*Engl. Transl.*), 1996, **45**, 1956].
14. V. K. Khairullin, M. A. Pudovik, R. R. Shagidullin, R. M. Mukhamadeeva, I. Kh. Shakirov, A. N. Pudovik, *Zh. Obshch. Khim.*, 1994, **64**, 613 [*J. Gen. Chem.* (*Engl. Transl.*), 1994, **64**].
15. E. E. Nifant′ev, N. V. Zyk, M. P. Koroteev, *Zh. Obshch. Khim.*, 1974, **45**, 1455 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1974, **45**].

16. E. E. Nifant´ev, N. V. Zyk, M. P. Koroteev, V. N. Abramov, *Zh. Obshch. Khim.*, 1974, **45**, 2162 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1974, **45**].
17. E. E. Nifant´ev, N. V. Zyk, M. P. Koroteev, *Dokl. Akad. Nauk SSSR*, 1974, **218**, 1371 [*Dokl. Chem.* (*Engl. Transl.*), 1974].
18. E. D. Matveeva, T. A. Podrugina, E. V. Tishkovskaya, N. S. Zefirov, *Synlett*., 2003, 2321.
19. E. D. Matveeva, T. A. Podrugina, M. V. Prisyazhnoi, N. S. Zefirov, *Izv. Akad. Nauk, Ser. Khim*., 2006, 1164 [*Russ. Chem. Bull., Int. Ed.*, 2006, **55**, 1209].
20. A. N. Pudovik, *Usp. Khim.*, 1954, **27**, 169 [*Russ. Chem. Rev.* (*Engl. Transl.*), 1954, **27**].
21. E. D. Matveeva, T. A. Podrugina, I. N. Kolesnikova, M. V. Prisyazhnoi, G. G. Karateev, N. S. Zefirov, *Izv. Akad. Nauk*, *Ser. Khim.,* 2010, 409 [*Russ. Chem. Bull., Int. Ed.*, 2010, **59**, 2].
22. S. A. Mikhalenko, S. V. Barkanova, O. L. Lebedev, E. A. Luk´yanets, *Zh. Obshch. Khim.*, 1971, **41**, 2735 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1971, **41**].
23. Changtao Qian, Taisheng Huang, *J. Org. Chem*., 1998, **63**, 4125.

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