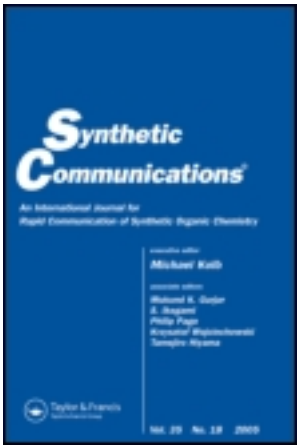


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Direct Phosphorylation of N-Protected Imidazoles and Benzoimidazoles-A Route to 1H-Imidazol(benzoimidazol)-2-yl Phosphonic and Phosphinic Acids and Their Derivatives

Igor V. Komarov [a], Aleksandr V. Strizhak [a], Mikhail Yu.Kornilov [a], Aleksandr N. Kostyuk [b] & Andrey A. Tolmachev [b]

[a] Department of Chemistry, Kiev Taras Shevchenko University, Vladimirskaya street, 64, Kiev, 252033, Ukraine

[b] Institute of Organic Chemistry of National Academy of Sciences of Ukraine, Kiev, Murmanskaya street, 5, Kiev, 252094, Ukraine

Version of record first published: 20 Aug 2006.

SYNTHETIC COMMUNICATIONS, 28(13), 2355-2370 (1998)

DIRECT PHOSPHORYLATION OF *N*-PROTECTED IMIDAZOLES AND BENZOIMIDAZOLES – A ROUTE TO 1*H*-IMIDAZOL(BENZOIMIDAZOL)-2-YL PHOSPHONIC AND PHOSPHINIC ACIDS AND THEIR DERIVATIVES

Igor V. Komarov*, Aleksandr V. Strizhak, Mikhail Yu. Kornilov,

Department of Chemistry, Kiev Taras Shevchenko University, Vladimirskaya street, 64, Kiev 252033, Ukraine

Aleksandr N. Kostyuk, Andrey A. Tolmachev

Institute of Organic Chemistry of National Academy of Sciences of Ukraine, Kiev, Murmanskaya street, 5, Kiev 252094, Ukraine

Abstract: Synthetic approaches to 1*H*-imidazol-2-yl and 1*H*-benzoimidazol-2-yl phosphinic and phosphonic acids and their derivatives are reported, based on phosphorylation of *N*-protected heterocylcles by $PhPOCl_2$ or $MePOCl_2$. Reaction of *N*-alkylbenzoimidazoles with $POCl_3$ did not lead to C-phosphorylated products in a reasonable yield, [2,2']-*bis*-benzoimidazolyles being formed instead.

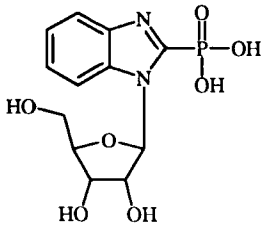


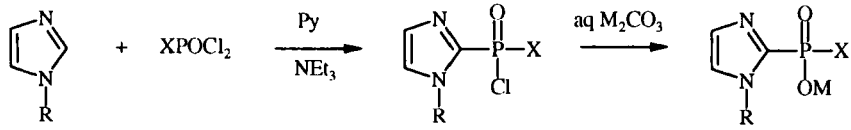
Figure 1.

Phosphinic or phosphonic acids possessing 1*H*-imidazole or 1*H*-benzoimidazole residues have attracted our attention as potential precursors to nucleotide analogues with a phosphorus-contain-

* To whom correspondence should be addressed

ing grouping attached to a carbon atom of the heterocyclic ring, an example is depicted in the Figure 1.

Firstly, direct phosphorylation of imidazole or benzoimidazole by phosphorus(V) acid chlorides was tried as a seemingly obvious way towards these targets. The analogous acylation of heterocycles by benzoyl chloride is well-documented[1]. However, our attempts at phosphorylation of unsubstituted imidazole and benzoimidazole failed. This prompted us to find appropriate protecting groups at the 1-N atom of the imidazole ring. A screening of various protecting groups has been performed. *N*-Substituted imidazoles **1–3** were subjected to reaction with $MePOCl_2$ or $PhPOCl_2$ in a pyridine-triethylamine solution. All the starting compounds readily underwent C-phosphorylation. The intermediate heteroaryl-substituted phosphinic acid chlorides **4 9** were transformed into the corresponding acids or their salts **10–15** without isolation (scheme 1):



1–3 **4–9** **10–15**

Scheme 1.

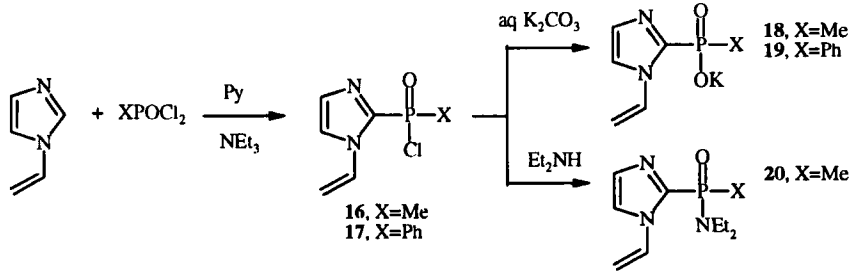
	Starting compounds			Intermediate phosphinic acid chlorides					
N⁰	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
R	Bz*	MOM*	CF_2CHFCl	Bz	Bz	MOM	MOM	CF_2CHFCl	CF_2CHFCl
X				Me	Ph	Me	Ph	Me	Ph

	Isolated phosphinic acid salts					
N°	10	11	12	13	14	15
R	Bz	Bz	MOM	MOM	CF_2CHFCl	CF_2CHFCl
X	Me	Ph	Me	Ph	Me	Ph
M	Na	Na	K	Na	Na	K

* Bz – benzyl, MOM – methoxymethyl.

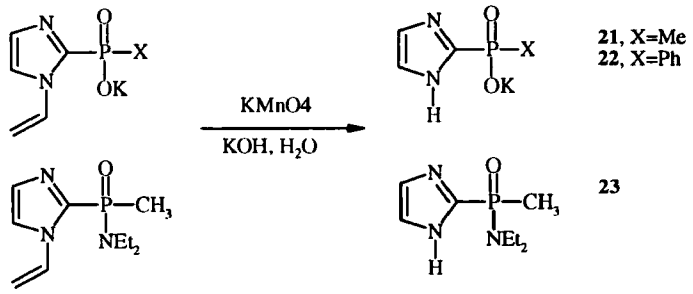
Despite the successful phosphorylation our goal was not achieved: removal of benzyl, methoxymethyl, and polyfluoroalkyl protecting groups under standard conditions was accompanied by the C–P bond scission. Other possible candidates, *N*-trityl- and *N*-dimethoxymethyl-imidaloles and benzoimidazoles simply did not react with $MePOCl_2$, $PhPOCl_2$ to give the C-phosphorylated products.

Progress was achieved with the vinyl protecting group. 1-Vinyl-1*H*-imidazole was transformed easily to the phosphinic acids or their derivatives **18–20** (scheme 2):



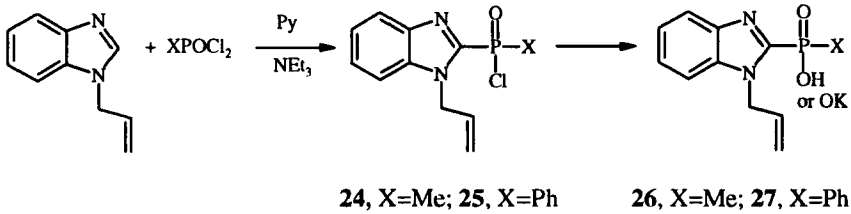
Scheme 2.

The removal of the vinyl protecting group was accomplished in water by treatment with aqueous $KMnO_4$ at pH~8, 20°C (scheme 3). The P–C bond is stable under these conditions, providing an excess of $KMnO_4$ is not used.



Scheme 3.

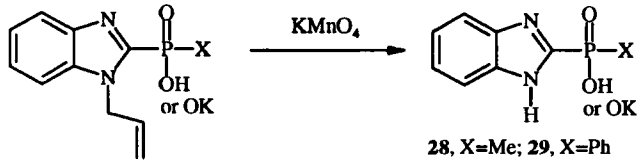
In the case of benzoimidazole, *N*-allyl protection seems to be a better choice than *N*-vinyl because the starting 1-allylbenzoimidazole is readily available. As with 1-vinilimidazoles, the phosphinic acids **26, 27** were easily obtained in moderate yield (scheme 4):



24, X=Me; **25**, X=Ph **26**, X=Me; **27**, X=Ph

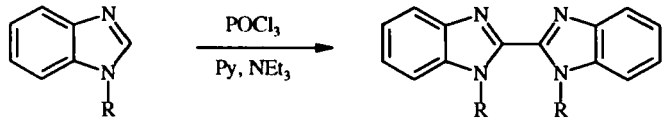
Scheme 4.

Allyl group removal was performed again with a $KMnO_4$ solution (scheme 5):



Scheme 5.

It should be noted that only phosphinic acids can be obtained using the reactions shown on the schemes 3, 4 and 5. Reaction of *N*-substituted imidazoles and benzoimidazoles with $POCl_3$ did not lead to the corresponding phosphonic acids or their derivatives. Instead, we have found that the main products of the reaction between benzoimidazoles and $POCl_3$ are the corresponding [2,2']-*bis*-benzoimidazolyles (scheme 6):



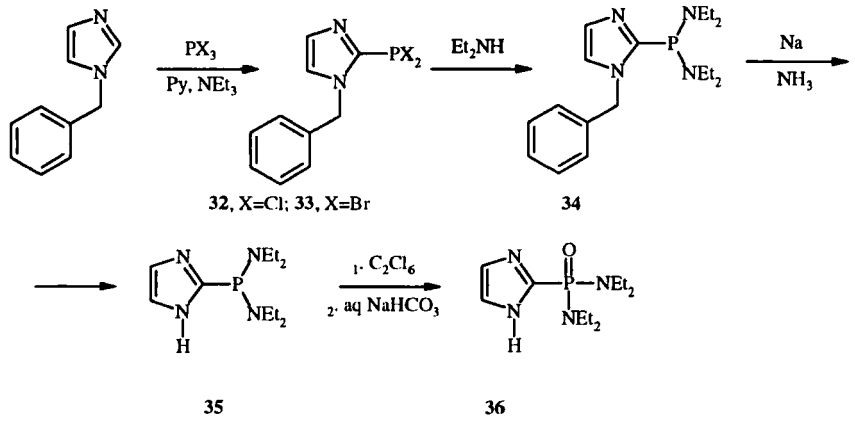
30, R=Me; **31**, R=Et

Scheme 6.

This reaction could be used for the preparative synthesis of **30, 31**. The yield was somewhat higher than that described in the literature for other reactions leading to [2,2']-*bis*-benzoimidazolyles[2-4].

For the synthesis of phosphonic acid derivatives we have developed another approach which includes *N*-benzyl group removal by sodium in liquid ammonia[5]. It seems to be impossible to apply this deprotection method to P(V) derivatives like **10** or **11** due to side reactions at phosphorus. However, for P(III) acid amides this method seemed to be feasible. We have prepared *N*-benzylimidazolyl phosphinous amide using the previously described C-phosphorylation reaction of *N*-benzylimidazole by PCl_3 or PBr_3. In contrast to other imidazol-2-yldihalo-

phosphines reported to date[6a,b], compound **32** did not polymerize in the pyridine solutions used and was characterized by its ^{31}P-NMR spectrum. Compounds **32, 33** were transformed to the corresponding amide **34** without isolation, the benzyl group was removed by sodium-liquid ammonia at -78°C. The target 1*H*-imidazol-2-yl tetraethyl diamidophosphonate **36** was obtained by oxidation (scheme 7):



Scheme 7.

EXPERIMENTAL

NMR spectra were recorded on a Bruker WP-100SY spectrometer (100.13 MHz for protons), TMS was used as an internal standard for ^{1}H and ^{13}C-NMR spectra, 85% H_3PO_4 was an external standard for ^{31}P-NMR measurements. IR spectra were measured on SP3-300 Pye Unicam infrared spectrophotometer. Melting points were measured on a hot stage and are uncorrected. Pyridine and triethylamine were dried over KOH and distilled.

Phosphorylation of 1–3, 1-vinyl-1*H*-imidazole and 1-allyl-1*H*-benzo-imidazole by $PhPOCl_2$, CH_3POCl_2 was performed using the following standard procedure. (All the operations must be carried out under a dry, inert atmosphere). To a stirred mixture of the starting heterocyclic compound (1 equiv., usually 8 mmol), triethylamine (1.2 equiv., usually 9.6 mmol) and pyridine (to obtain approximately 1M solution of the heterocyclic compound) the phosphorylating reagent (1.1 equiv.) was added dropwise during 10 min. The reaction is slightly exothermic; the formation of crystals ($NEt_3 \cdot HCl$) was observed. The course of the reaction can be easily followed by ^{31}P-NMR spectroscopy. After no changes in the ^{31}P-NMR specta were observed, the reaction mixture was worked-up as described below.

(1-benzyl-1*H*-imidazol-2-yl)-methyl-phosphinic acid sodium salt 10 was obtained from 2.5 g of **1** (15.8 mmol) and $MePOCl_2$. The reaction mixture obtained after the phosphorylation was poured carefully into water (about 100 ml). Solid sodium hydrocarbonate was added to the stirred mixture until no more carbon dioxide formed. The resulting solution was evaporated to dryness and the product was extracted from the formed solid with dry methanol. Crystallization from 2-propanol yielded **10** as colourless needles (3.05 g, 74 %). ^{31}P-NMR (CD_3OD, δ) 11.6 ; ^1H-NMR (CD_3OD, δ) 7.39 (m, 2H), 7.29 (m, 5H), 5.67 (s, 2H), 1.35 (d, $^2J_{P-H}$=16.5 Hz, 3H) . Anal. Calcd for $C_{11}H_{12}N_2NaO_2P$: C, 51.17; H, 4.68; N, 10.85. Found: C, 51.06; H, 4.73; N, 10.78.

(1-benzyl-1*H*-imidazol-2-yl)-phenyl-phosphinic acid sodium salt 11 was obtained from 3.0 g of **1** (19.0 mmol) and $PhPOCl_2$. The reaction mixture obtained

after the phosphorylation was poured carefully into 100 ml of 25% NaOH in H_2O. The solution was evaporated to about 20 ml and cooled. The crude product formed was collected by filtration and recrystallized from wet chloroform. The crystals were dried *in vacuo* over P_4O_{10} to obtain **11** as white powder (5.66 g, 93%). ^{31}P-NMR (CD_3OD, δ) 7, in acidic soln. 0 (in the presence of CF_3COOD); ^{1}*H*-NMR (CD_3OD, δ) 7.90–7.58 (m, 2H) 7.44–7.84 (m, 10H), 5.50 (s, 2H). Anal. Calcd for $C_{16}H_{14}N_2NaO_2P$: C, 60.01; H, 4.41; N, 8.75. Found: C, 59.96; H, 4.43; N, 8.79.

(1-methoxymethyl-1*H*-imidazol-2-yl)-methyl-phosphinic acid potassium salt 12 was obtained from 2.2 g of **2** (19.6 mmol) and $MePOCl_2$. The reaction mixture obtained after the phosphorylation was poured carefully into water (about 100 ml). Solid potassium carbonate was added until no more carbon dioxide formed. After that the solution was evaporated to dryness and the product was extracted from the solid with dry methanol. The solvent was removed under reduced pressure and the remained **12** was recrystallized from DMSO. White powder (3.04 g, 68 %). ^{31}P-NMR (CD_3OD, δ) 21; ^{1}*H*-NMR (DMSO-d_6, δ) 7.11 (s, 1H), 6.85 (s, 1H), 5.72 (s, 2H), 3.24 (s, 3H), 1.22 (d, $^2J_{P-H}$=14.7 Hz, 3H). Anal. Calcd for $C_6H_{10}KN_2O_3P$: C, 31.58; H, 4.42; N, 12.27. Found: C, 31.50; H, 4.44; N, 12.30.

(1-methoxymethyl-1*H*-imidazol-2-yl)-phenyl-phosphinic acid sodium salt 13 was obtained from 2.2 g of **2** (19.6 mmol) and $PhPOCl_2$. The reaction mixture obtained after the phosphorylation was poured carefully into solution of NaOH

(3.45 g) in water (100 ml), the solution was evaporated, dried and the product was extracted from the solid with wet chloroform. Re-precipitated from chloroform with benzene. Pale yellow powder (3.87 g, 72 %). ^{31}P-NMR (CD_3OD, δ) 8.5, in acidic soln 3.5 (in the presence of CF_3COOD); ^1H-NMR (CD_3OD, δ) 7.90–7.62 (m, 2H), 7.34–7.19 (m, 3H), 7.14 (s, 1H), 6.97 (s, 1H), 5.52 (s, 2H), 2.93 (s, 3H) . Anal. Calcd for $C_{11}H_{12}N_2NaO_3P$: C, 48.19; H, 4.41; N, 10.22. Found: C, 48.11; H, 4.74; N, 10.25.

[1-(2-chloro-1,1,2-trifluoroethyl)-1*H*-imidazol-2-yl]-methyl-phosphinic acid sodium salt 14 was prepared analogously to **12** from 2.32 g of **3** (12.6 mmol) and $MePOCl_2$. Sodium hydrocarbonate was used to neutralize the reaction mixture. White powder (2.55 g, 71 %). ^1H-NMR (DMSO-d_6, δ) 8.68 (dt, $^2J_{F-H}$=46 Hz, J_{F-H} =8.3 Hz, 1H), 7.50 (s, 1H), 7.02 (s, 1H), 1.23 (d, $^2J_{P-H}$=18 Hz, 3H). Anal. Calcd for $C_6H_6ClF_3N_2NaO_2P$: C, 25.33; H, 2.13; N, 9.85. Found: C, 25.29; H, 2.14; N, 9.88.

[1-(2-chloro-1,1,2-trifluoroethyl)-1*H*-imidazol-2-yl]-phenyl-phosphinic acid potassium salt 15 was obtained from 2.39 g of **3** (12.9 mmol) and $PhPOCl_2$. The work-up is analogous to that for **12**, the product was recrystallized from wet chloroform. Colorless needles (3.51 g, 75 %). ^{31}P-NMR (CD_3OD, δ) 9.9; ^1H-NMR (CD_3OD, δ) 8.20 (t, downfield component of dt, J_{F-H}=7.9 Hz, 0.5H), 7.86–7.56 (m, 2.5H), 7.42–7.18 (m, 4H), 7.02 (s, 1H). Anal. Calcd for $C_{11}H_8ClF_3KN_2O_2P$: C, 36.43; H, 2.22; N, 7.72. Found: C, 36.37; H, 2.23; N, 7.76.

Methyl-(1-vinyl-1*H*-imidazol-2-yl)-phosphinic acid potassium salt 18 was prepared analogously to **10** from 2.7 ml of 1-vinyl-1*H*-imidazole (29.8 mmol) and $MePOCl_2$ except that potassium carbonate was used instead of Na_2CO_3 during the work-up. Pale yellow crystals (4.45 g, 71 %). ^{31}P-NMR (CD_3OD, δ) 22; ^{1}*H*-NMR (CD_3OD, δ) 7.88 (dd, $^3J_{H-H}$=15.5 Hz, $^3J_{H-H}$=7.9 Hz, 1H), 7.53 (s, 1H), 6.97 (s, 1H), 5.34 (d, $^3J_{H-H}$=15.5 Hz, 1H), 4.86 (d, $^3J_{H-H}$=7.9 Hz, 1H), 1.50 (d, $^2J_{P-H}$=13.8 Hz, 3H). Anal. Calcd for $C_6H_8KN_2O_2P$: C, 34.28; H, 3.84; N, 13.33. Found: C, 34.21; H, 3.86; N, 13.35.

Phenyl-(1-vinyl-1*H*-imidazol-2-yl)-phosphinic acid potassium salt 19 was prepared analogously to **10** from 2.7 ml of 1-vinylimidazole (29.8 mmol) and $PhPOCl_2$. White crystals (6.49 g, 80%). ^{31}P-NMR (CD_3OD, δ) 7.2; ^{1}*H*-NMR (CD_3OD, δ) 7.98–7.68 (m, 4H), 7.65–7.24 (m, 4H), 5.65 (d, $^3J_{H-H}$=18.5 Hz, 1H), 5.25 (d, $^3J_{H-H}$=11.1 Hz, 1H). Anal. Calcd for $C_{11}H_{10}KN_2O_2P$: C, 48.52; H, 3.70; N, 10.29. Found: C, 48.56; H, 3.71; N, 10.25.

Methyl-(1-vinyl-1*H*-imidazol-2-yl)-phosphinic acid diethylamide 20 was prepared from 5.0 ml of 1-vinylimidazole (55.2 mmol) and $MePOCl_2$. After the reaction the mixture was treated with diethylamine (16.3 ml, 158.2 mmol). The volatile products were removed under reduced pressure and **20** was extracted with benzene. The solvent was removed, and the remained oil was distilled to obtain **20** as yellow solid (b.p. 110°C/0.15 mm) which was recrystallized from hexane. Colorless needles, m.p. 79°C (7.78 g, 62 %). ^{1}*H*-NMR (CD_3OD, δ) 7.59–7.85 (m, 2H), 7.10 (s, 1H), 5.41 (dd, $^3J_{H-H}$=15.8 Hz, $^2J_{H-H}$=2 Hz, 1H), 4.94 (dd, $^3J_{H-H}$=9.0

Hz, $^2J_{H-H}$=2 Hz, 1H), 2.98 (dq, 4H), 1.77 (d, $^2J_{P-H}$=15.1 Hz, 3H), 0.92 (t, 6H); Anal. Calcd for $C_{10}H_{18}N_3OP$: C, 52.85; H, 7.98; N, 18.49. Found: C, 52.80; H, 7.96; N, 18.52.

General methods for deprotection of 18–20. A saturated aqueous $KMnO_4$ solution was added dropwise to a stirred solution of a phosphorylated heterocyclic compound in water until the colour of the mixture does not change during 30 sec after addition of a drop of $KMnO_4$. The precipitate of MnO_2 was filtered off and the filtrate was treated as described below.

(1*H*-imidazol-2-yl)-methyl-phosphinic acid potassium salt 21 was prepared from 1,6 g of **18** (7.6 mmol). After the oxidation 5 ml of conc. hydrochloric acid was added and the solution was evaporated to dryness to remove the formic acid. The remained solid was dissolved in water, solid K_2CO_3 was added until no more CO_2 was formed and the solution was evaporated to dryness. The product was extracted from the remainder with dry methanol and precipitated by three-fold excess of acetone. Pale yellow powder (0.86 g, 61%). ^{31}P-NMR (CF_3COOD, δ) 15; ^1H-NMR (CF_3COOD, δ)(s, 2H), 1.98 (d, $^2J_{P-H}$=16 Hz, 3H).Anal. Calcd for $C_4H_6KN_2O_2P$: C, 26.09; H, 3.28;N,15.21. Found: C, 26.02;H, 3.30; N, 15.25.

(1*H*-imidazol-2-yl)-phenyl-phosphinic acid 22 was prepared from 1.73 g of **19** (6.4 mmol). After oxidation the mixture was evaporated to about 10 ml and 20% hydrochloric acid was added until pH 5. The formed precipitate was collected by filtration and dried over P_4O_{10}. Colorless powder (1.32 g, 68%). ^{31}P-NMR

(DMSO-d_6, δ) 1.0; ^1H-NMR (CD_3OD, δ) 7.65–7.98 (m, 2H), 7.26–7.63 (m, 5H). Anal. Calcd for $C_9H_9N_2O_2P$: C, 51.93; H, 4.36; N, 13.46. Found: C, 51.88; H, 4.39; N, 13.49

(1*H*-imidazol-2-yl)-methyl-phosphinic acid diethylamide 23 was prepared from 1 g of **20** (4.41 mmol). After the oxidation the solution was evaporated to dryness and the product was extracted from the remained solid with benzene. The solvent was removed under reduced pressure and the remained oil was crystallized from heptane. Colorless crystals (0.62 g, 70%). ^{31}P-NMR (CD_3OD, δ) 30.5; ^1H-NMR (CD_3OD, δ) 7.23 (d, $^4J_{P-H}$=2 Hz, 2H), 3.03 (m, 4H), 1.77 (d, $^2J_{P-H}$=16 Hz, 3H), 1.01 (t, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$, δ): 142.2 (d, J_{P-H}= 170.9Hz), 130.6, 119.6, 39.2 (d, J_{P-H}=4.1), 15.0 (d, J_{P-H}=100 Hz),14.4 (d, J_{P-H} =2.1 Hz). Anal. Calcd for $C_8H_{16}N_3OP$: C, 47.76; H, 8.01; N, 20.88. Found: C, 47.70; H, 8.03; N, 20.91.

(1-allyl-1*H*-benzoimidazol-2-yl)-methyl-phosphinic acid potassium salt 26 was synthesized analogously to **12** from 2.2 g of 1-allylbenzoimidazole (13.9 mmol) and $MePOCl_2$. White powder (2.40 g, 63%). ^{31}P-NMR (CD_3OD, δ) 22; ^1H-NMR (DMSO-d_6, δ) 7.76–7.56 (m, 1H), 7.52–7.32 (m, 1H), 7.31–7.06 (m, 2H), 6.26–5.81 (m, 1H), 5.40 5.02 (m, 4H), 1.32 (d, $^2J_{P-H}$=14.8 Hz, 3H). Anal. Calcd for $C_{11}H_{12}KN_2O_2P$: C, 48.17; H, 4.41; N, 10.21. Found: C, 48.12; H, 4.44; N, 10.24.

(1-allyl-1*H*-benzoimidazol-2-yl)-phenyl-phosphinic acid 27 was synthesized from 2.2 g of 1-allylbenzoimidazole (13.9 mmol) and $PhPOCl_2$. The reaction mix-

ture obtained after the phosphorylation of by $PhPOCl_2$ was poured carefully into water (50 ml). The solution formed was evaporated by half, cooled. The product was collected by filtration and dried over P_4O_{10}. An analytical sample was recrystallized from i-PrOH. Colorless powder (3.11 g, 75%). ^{31}P-NMR (CD_3OD, δ) 4.0; ^1H-NMR (CD_3OD, δ) 8.0–7.29 (m, 9H), 5.81–5.22 (m, 2H), 4.97 (d, $^3J_{H-H}$=13.0 Hz, 1H), 4.79 (s, 2H). Anal. Calcd for $C_{16}H_{15}N_2O_2P$: C, 64.43; H, 5.07; N, 9.39. Found: C, 64.39; H, 5.11; N, 9.40.

(1*H*-benzoimidazol-2-yl)-methyl-phosphinic acid potassium salt 28. Salt **26** (2 g, 7.30 mmol) was dissolved in water and saturated solution of $KMnO_4$ (4.00 g, 28.98 mmol) was added with stirring. The mixture was then stirred for 4h at room temperature. The precipitate of MnO_2 was filtered off, the filtrate was evaporated. The product was extracted with dry methanol and was re-precipitated by three-fold excess of acetone. Yellow powder (0.94 g, 55%). ^{31}P-NMR (DMSO-d_6, δ) 15.0; ^1H-NMR (DMSO-d_6,δ) 7.82–7.60 (m, 2H), 7.48–7.30 (m, 2H), 1.52 (d, $^2J_{P-H}$ =15.0 Hz, 3H). Anal. Calcd for $C_8H_8KN_2O_2P$: C, 41.02; H, 3.44; N, 11.96. Found: C, 40.95; H, 3.48; N, 11.92.

(1*H*-benzoimidazol-2-yl)-phenyl-phosphinic acid 29. Phosphinic acid **27** (1 g , 2.97 mmol) was dissolved in water by addition of KOH and saturated solution of $KMnO_4$ (2.09 g, 13.23 mmol) was added under stirring. The mixture was then stirred for 5h at room temperature. MnO_2 was filtered off, the mixture was evaporated to about 8 ml and conc. HCl was added dropwise to the filtrate until no more precipitate was formed. The product was collected by filtration and dried

over P_4O_{10}. White powder (0.56 g, 73%). ^{31}P-NMR (CF_3COOD, δ) 4.9; ^1H-NMR (CF_3COOD, δ) 8.17–7.54 (m). Anal. Calcd for $C_{13}H_{11}N_2O_2P$: C, 60.47; H, 4.29; N, 10.85. Found: C, 60.43; H, 4.31; N, 10.83.

General methods for the preparation of 30, 31 by the oxidative coupling of benzoimidazoles. *N*-alkylbenzoimidazole (10 mmol) was dissolved in pyridine (10 ml), triethylamine (14 mmol) and $POCl_3$ (12 mmol) were added to the solution under stirring. After the reaction was complete (20 h), the mixture was poured carefully into water (50 ml), the formed solution was evaporated to about 15 ml and cooled. The crude product was collected by filtration and purified as described below.

1,1'-dimethyl-1*H*,1'*H*-[2,2']-*bis*-benzoimidazolyl 30 was recrystallized from 50% ethanol or purified by column chromatography (Silica gel Merck 60, $CHCl_3$: CH_3OH 9:1 as eluent). Yield: 68%. M.p, ^1H- and ^{13}C-NMR spectra are identical with the literature data[2,3]. Anal. Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38; N, 21.36. Found: C, 73.22; H, 5.41; N, 21.33.

1,1'-diethyl-1*H*,1'*H*-[2,2']-*bis*-benzoimidazolyl 31 was recrystallized from ethanol. Yield: 77%, m.p. 177–178 C, ^1H-NMR (DMSO-d_6, δ) 7,92–7,66 (m, 2H); 7,50–7,24 (m, 2H); 4,87 (q, 4H); 1,42 (t, 3H). Anal. Calcd for $C_{18}H_{18}N_4$: C, 74.46; H, 6.25; N, 19.30. Found: C, 74.40; H, 6.29; N, 19.27.

(1-benzyl-1*H*-imidazol-2-yl)-phosphonous acid *bis*-diethylamide 34 (all operations were carried out under a dry nitrogen atmosphere) was obtained from

2.37 g of (15.0 mmol), 1.43 ml of PBr_3 or 1.31 ml of PCl_3 (15.0 mmol) and 2.49 ml of NEt_3 (18.0 mmol). In case of the reaction with PCl_3 the ^{31}P-NMR signal of the formed **(1-benzyl-1*H*-imidazol-2-yl)-dichlorophosphine 32** appears at 120 ppm (pyridine-d_5). After the phosphorylation (24 h) diethylamine (9.2 ml, 90 mmol) was added to the reaction mixture. The volatile products were removed under reduced pressure and the product was extracted with benzene, ammonium salts were filtered off. The solvent was removed under reduced pressure, the oily residue was dissolved in heptane. The heptane solution was cooled to about 0°C, decanted from non-soluble dark oil and freeze-dried. Pale yellow oil (4.59 g, 92%). ^{31}P-NMR (CD_3CN, δ) 71; ^{1}*H*-NMR (CD_3CN, δ) 7.66–7.26 (m, 7H), 5.56 (s, 2H), 2.41 (dq, 8H), 1.30 (dt, 12H). Anal. Calcd for $C_{18}H_{29}N_4P$: C, 65.04; H, 8.79; N, 16.85. Found: C, 64.82; H, 8.96; N, 16.88.

(1*H*-imidazol-2-yl)-phosphonic acid *bis*-diethylamide 36. To a solution of sodium (0.56 g, 24.22 mmol) in liquid ammonia (25 ml) a solution of amide **34** (4.02 g, 12.11 mmol) in toluene was added dropwise under stirring at -78°C. The reaction was complete after 10–12 min which can be easily determined by the color of the solution which changed from blue to light-red. Ammonium chloride (1.30 g, 24.22 mmol) was added and the reaction mixture was allowed to evaporate. A solution of hexachloroethane (2.79 g, 12.11 mmol) in benzene (30 ml) was added afterwards, the formed mixture was washed with 10% $NaHCO_3$. The aqueous layer was washed with chloroform (3×30 ml), the combined organic layers were dried ($CaCl_2$) and evaporated to dryness *in vacuo*. The oily residue was dried *in vacuo*

(0.1 mm Hg, 80°C, 5 h). Pale yellow oil (2.97 g, 95%). ^1H-NMR (CD_3OD, δ) 7.19 (s, 2H), 3.02 (dq, 8H), 1.02 (dt, 12 H). Anal. Calcd for $C_{11}H_{23}N_4OP$: C, 51.15; H, 8.97; N, 21.69. Found: C, 50.91; H, 9.21; N, 21.74.

ACKNOWLEDGEMENTS

Financial support from INTAS, the International Association for the promotion of cooperation with scientists in the independent states of the former Soviet Union, (Grant INTAS-93-3532) is gratefully acknowledged.

LITERATURE AND NOTES

1. Regel, E.; Buchel, K.-H. *Lieb. Ann. Chem.* **1977**, 145.
2. Khristich, B.I.; Bondarenko, E.V. *Khim.Heterotsikl.Soedinenii* **1987**, 339.
3. Khristich, B.I.; Simonov, A.M.; Shepelenko, E.N.; Yatsimirski, V.A. *Khim. Heterotsikl. Soedinenii* **1983**, 98.
4. Ro, J.S.; Iyengar, D.S.; Bhalerao, U.T.; Rao, S.N.*Heterocycles* **1987**, *26* (5), 1161.
5. Tolmachev, A.A.; Kozlov, E.S.; Pinchuk, A.M. *Zhurn. Obshch. Khim.* **1982**, *52* (10), 2352.
6. a. Tolmachev, A.A.; Yurchenko, A.A.; Rozhenko, A.V.; Semenova, M.G. *Zh. Org. Khim.* **1993**, *63* (8), 1911.
   b. Tolmachev, A.A.; Yurchenko, A.A.; Merkulov, A.S.; Pinchuk, A.M.*Heteroatom.* , in press

(Received in the UK 31 October 1997)