σ^H-Adducts of *N*-alkylpyrazinium and quinoxalinium salts with nucleophiles. The ^1H and ^{13}C NMR spectra and the crystal structures of P-adducts*

E. V. Verbitskiy, M. V. Berezin, P. A. Slepukhin, G. L. Rusinov, and V. N. Charushin*

I. Ya. Postovsky Institute of Organic Synthesis, Ural Branch of the Russian Academy of Sciences, 22/20 ul. S. Kovalevskoi, 620041 Ekaterinburg, Russian Federation. Fax: +7 (343 2) 74 1189. E-mail: rusinov@ios.uran.ru

The previously unknown addition products of P-nucleophiles to 5-aryl- and 5-hetaryl-2,3-dicyano-1-ethylpyrazinium salts and to 5-aryl- and 5-hetaryl-1-methylquinoxalinium salts were synthesized. The three-dimensional structures of the P-σ^H-adducts of the 1,4-diazine series were established by X-ray diffraction.

Key words: 5-aryl- and 5-hetaryl-2,3-dicyano-1-ethylpyrazinium salts, 3-aryl- and 3-hetaryl-1-methylquinoxalinium salts, diethyl phosphonate, diphenyl phosphonate, σ^H-adducts with P-nucleophiles.

Pyrazines[1—4] and quinoxalines[5—8] are of interest for medical chemistry, form a skeleton of numerous natural compounds and antibiotics, and exhibit antitumor, antituberculosis, and other activities.[9—11] In recent years, the development of new methods for the synthesis and modifications of diazines, including methods based on the direct nucleophilic attack on the unsubstituted carbon atom of the azine ring, has attracted great attention.[12—19]

It is known that *N*-alkylpyrazinium and quinoxalinium salts are prone to the mono- and diaddition of O-, C-, N-, and S-nucleophiles, as well as to annulation of five- or six-membered heterocycles in reactions with a wide range of dinucleophiles.[12—14] Primary σ^H-adducts, which are generated *via* the nucleophilic attack on the α position with respect to the cationic center, were comprehensively characterized by ^1H and ^{13}C NMR spectroscopy.[20] The synthesis of 1,2-dihydro- and 1,4-tetrahydropyrazines by the addition of O- and C-nucleophiles to 1-alkyl-2,3-dicyanopyrazinium salts was also documented.[21,22] Data on the involvement of P-nucleophiles in the reactions with 1,4-diazines are lacking, although examples of the addition of P-nucleophiles to π-deficient nitroarenes[12] and azines[23—26] were reported. The structures of the P-adducts of isoquinoline,[23] phthalazine,[24] and 4,7-phenanthroline[25,26] were established by X-ray diffraction.

The aim of the present study was to synthesize relatively stable addition products of diethyl and diphenyl phosphonates to 1,4-diazinium salts, such as 5-aryl-substituted 2,3-dicyano-1-ethylpyrazinium tetrafluoroborates **1a,b** and 3-aryl-1-methylquinoxalinium iodides **2a,b** (Scheme 1). It was expected that the presence of an aryl substituent in the β position with respect to the quaternary cationic group would block the secondary addition with the result that the β attack will be the only reaction pathway.

Actually, the reactions of salts **1a,b** and **2a,b** with phosphonates **3a,b** proceed under mild conditions (20 °C, CH_3CN). It should be noted that bases are not required for the initiation of the reactions of the pyrazinium salts.

The structures of P-adducts **4a,b**, **5a,b**, and **6a,b** were confirmed by NMR spectroscopy. The structures of products **4a,b** (Figs 1 and 2, respectively) were established also by X-ray diffraction.

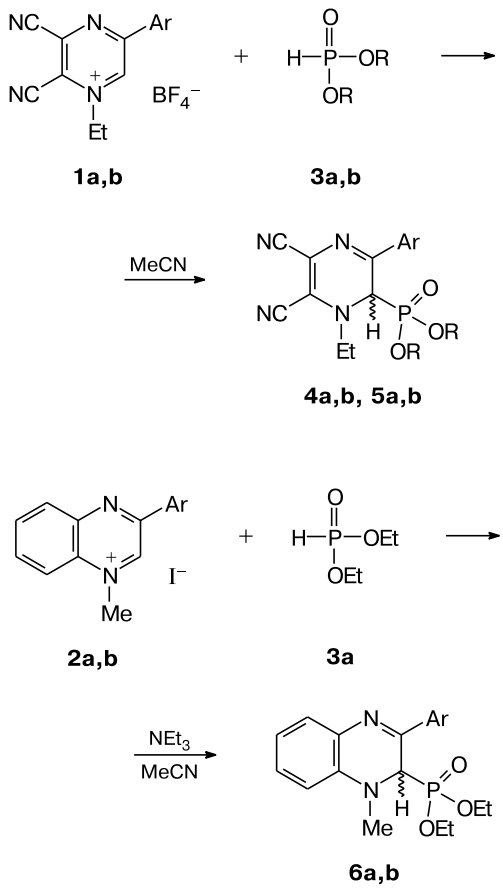
Product **4a** crystallizes in the space group $P2_1/c$ and was obtained as yellow monoclinic single crystals. The pyrazine ring adopts a pseudoenvelope conformation. The deviations of the N(1), N(2), C(1), C(2), and C(3) atoms from the mean plane are at most 0.075 Å, whereas the sp^3-hybridized C(4) atom deviates from this plane by 0.560 Å (see Fig. 1). The bond lengths in the conjugation system of the pyrazine ring C(3)=N(2)—C(2)=C(1)—N(1) differ substantially from the standard C—C, C=C, C—N, and C=N bond lengths and vary from 1.291(3) Å to 1.382(3) Å (Table 1). One ethoxy group of the diethoxyphosphoryl fragment is thermally disordered in the site 2 with occupancies of 0.5. The P—C bond length (1.836(2) Å) is close to the standard value. The overall geometry of the dialkylphosphoryl substituent in the adduct is similar to that observed for a series of dihydrobenzoazines prepared earlier.[23,24] The molecular packing consists of layers. The interlayer interactions are characterized by the absence of shortened contacts, whereas shortened intermolecular π—π contacts between the cyano groups (the transformation $-x, -y, 1-z$; the interaction length is ~3.3 Å), the

* Dedicated to Academician A. I. Konovalov on his 75th birthday.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 1, pp. 176—181, January, 2009.

1066-5285/09/5801-0176

Scheme 1



Compound	Ar	R	Compound	Ar	R
1a	Ph	—	**4a**	Ph	Et
1b	3-thienyl	—	**4b**	3-thienyl	Et
2a	3-$NO_2C_6H_4$	—	**5a**	Ph	Ph
2b	3-thienyl	—	**5b**	3-thienyl	Ph
3a	—	Et	**6a**	3-$NO_2C_6H_4$	—
3b	—	Ph	**6b**	3-thienyl	—

polar P(1)—O(1)...H—C_{sp^3}(4) contacts (x, 0.5 – y, –0.5 + z; ~2.3 Å), the shortened C_{ap}—H...N contacts (~2.6 Å, with the CN group and the N(2) atom), and some other contacts are present within the layers.

The main structural characteristics of compound **4b** (the crystal system, the space group, the unit cell parameters, the bond lengths, the molecular conformation, and the packing mode) are, on the whole, similar to those determined for the structure of **4a**.

The NMR data for σ^H-adducts of 1,4-diazinium salts with P-nucleophiles are lacking in the literature. A comparative analysis of the ^1H and ^{13}C NMR spectra of the P-adducts, the spectra of the O- and C-σ^H-adducts of 5-aryl- and 5-hetaryl-2,3-dicyano-1-ethylpyrazinium salts prepared previously,[22] and the spectra of the already known O-adducts of pyrazinium and quinoxalinium salts[20] showed that the chemical shifts of the sp^3-hybridized carbon atom and the attached proton are in good agreement with the theory[27] and available data.[20] Thus, the more electronegative is the fragment bound to the sp^3-carbon

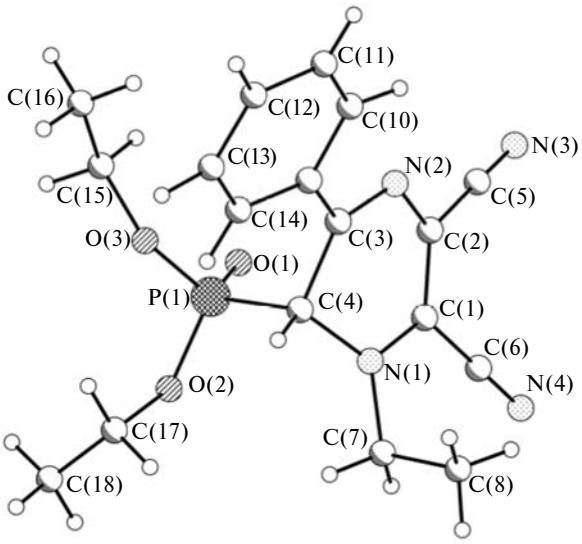


Fig. 1. Geometry of molecule **4a** in the crystal structure.

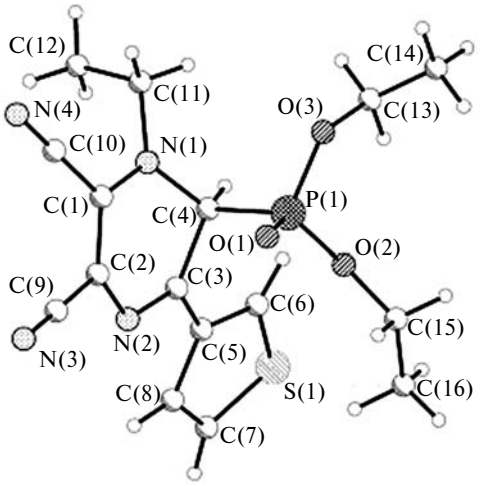


Fig. 2. Geometry of molecule **4b** in the crystal structure.

Table 1. Selected bond lengths in compounds **4a** and **4b** based on X-ray diffraction data

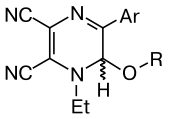
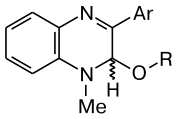
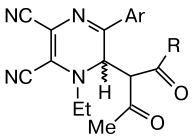
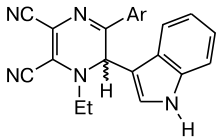
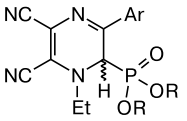
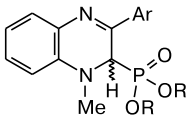
Bond	*d*/Å	
	4a	**4b**
C(1)—N(1)	1.359(3)	1.353(2)
C(2)—C(1)	1.352(3)	1.360(2)
N(2)—C(2)	1.381(3)	1.389(2)
C(3)—N(2)	1.291(3)	1.2949(19)
C(3)—C(4)	1.538(3)	1.521(2)
N(1)—C(4)	1.464(3)	1.459(2)
C(4)—P(1)	1.836(3)	1.8271(15)
P(1)—O(1)	1.4681(16)	1.4585(11)

atom, the larger are the downfield shifts. For instance, in the series of O-, C-, and P-adducts (Table 2), the chemical shifts of C_{sp^3}—H groups in the NMR spectra of the O-adducts are observed at the lowest field, whereas the corresponding chemical shifts for the P-adducts are observed at the highest field, which is consistent with the changes in the electronegativity in the series O > C ≈ P.[28]

Unlike the ^{1}H NMR spectra of the O- and C-adducts, the spectra of the P-adducts are characterized by a complex multiplet structure of the signals for the methylene protons of the NEt group due not only to their nonequivalence but also to the spin-spin coupling constants with the phosphorus atom. This is also responsible for the fact that the singlet of the hydrogen atom at C(2) characteristic of O- and C-adducts appears as a doublet in the spectra of the P-adducts. The ^{13}C NMR spectra show doubling of the signals giving rise to the corresponding doublets with the first- to fourth-order coupling constants (see the Experimental section).

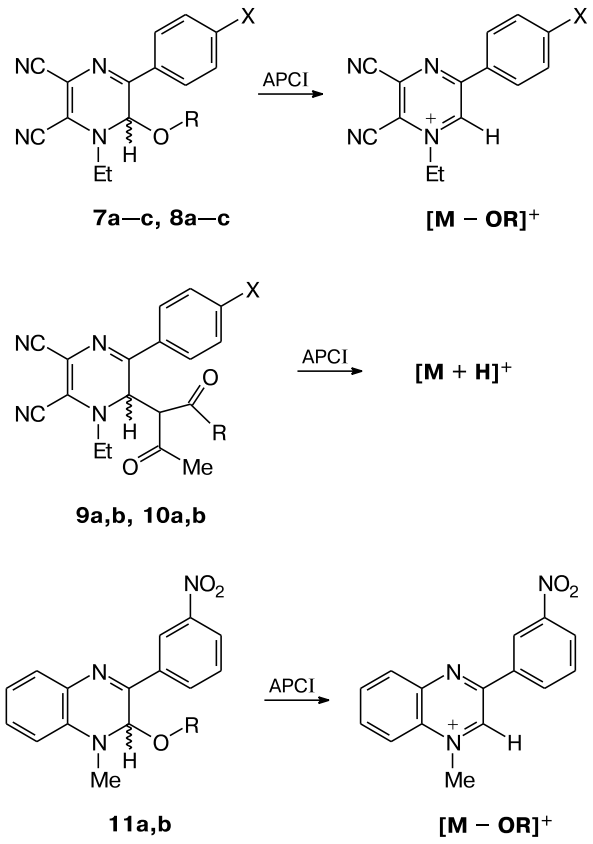
Earlier,[29] we have studied the LC/MS-chromatographic behavior of the O- and C-adducts of 2,3-dicyano-1-ethylpyrazinium. The optimal conditions for LC/MS experiments were found. The positive-ion atmospheric pressure chemical ionization (APCI) is a method of choice. Under these conditions, the O-adducts of 2,3-dicyanopyrazinium salts with water and alcohols (**7** and **8**) were shown to eliminate the alkoxy group due to thermal decomposition in the ion source (200—450 °C); however, attempts to detect the molecular ion failed (Scheme 2). The O-adducts of quinoxalinium salts

Table 2. Proton and sp^3-carbon chemical shifts in the ^{1}H and ^{13}C NMR spectra of the σ^H-adducts prepared by the addition of O-, C-, and P-nucleophiles to 1-alkyl-1,4-diazinium salts

Compound	Substituents		Solvent	δ	
	Ar	R		C(sp^3)—H	C(sp^3)
	Ph	H	DMSO-d_6—^{1}H CD_3CN—^{13}C	6.24	73.28
	Ph	Me	DMSO-d_6	6.41	—
	Ph	Et	CD_3CN	6.12	79.88
	3-NO_2—C_6H_4	H	DMSO-d_6	6.01	74.09
	3-NO_2—C_6H_4	Me	$CDCl_3$—^{1}H DMSO-d_6—^{13}C	5.98	74.19
	Ph	Me	DMSO-d_6	5.85	—
	4-F—C_6H_4	Me	$CDCl_3$	5.76	—
	3-Thienyl	Me	CD_3CN—^{1}H $CDCl_3$—^{13}C	5.65	53.83
	Ph	OEt	$CDCl_3$	5.78* (5.76)	—
	4-F—C_6H_4	OEt	$CDCl_3$	5.74* (5.71)	—
	3-Thienyl	OEt	CD_3CN	5.66* (5.63)	—
	Ph	—	DMSO-d_6	6.59	—
	3-Thienyl	—	DMSO-d_6	6.46	50.64
 **4a,b, 5a,b**	Ph	Et	$CDCl_3$	5.17	53.07
	3-Thienyl	Et	$CDCl_3$	4.97	54.29
	Ph	Ph	$CDCl_3$	5.57	53.60
	3-Thienyl	Ph	$CDCl_3$	5.37	—
 **6a,b**	3-NO_2—C_6H_4	Et	DMSO-d_6	5.77	—
	3-Thienyl	Et	DMSO-d_6	5.41	—

* The major diastereomer.[22]

Scheme 2



Compound	X	R	Compound	X	R
7a	H	H	**9a**	H	Me
7b	H	Me	**9b**	H	OEt
7c	H	Et	**10a**	F	Me
8a	F	H	**10b**	F	OEt
8b	F	Me	**11a**	—	H
8c	F	Et	**11b**	—	Me

behave analogously. In the case of C-adducts **9** and **10**, only the expected ions corresponding to the protonated form of the starting adduct were detected (see Scheme 2). A different behavior is observed for the P-adducts of pyrazinium salts **4** and **5**, which give primarily ions corresponding to deprotonation, the molecular ion, and its protonated form.

Hence, we showed that 2,3-dicyano-1-ethylpyrazinium and 1-methylquinoxalinium salts react with phosphorus(v) derivatives to form stable P-adducts, which were characterized by ^{1}H and ^{13}C NMR spectroscopy and X-ray diffraction.

Experimental

The solvents and reagents were dried and purified according to known procedures.[30] The NMR spectra were recorded on a Bruker DRX-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, and 162 MHz for ^{31}P) with $SiMe_4$ as the internal standard. The negative- and positive-ion electrospray LC/MS were measured in CH_3CN on a Shimadzu LCMS-2010 quadrupole LC-mass spectrometer equipped with a Supelco LC-18 column (4.6×250 mm) at a scan rate of 0.25 mL min^{-1}. The atmospheric pressure chemical ionization (APCI) or electrospray ionization (ESI) was used; the working voltage was 4.5 kV; nitrogen was used as the carrier gas; the flow rate was 2.5 L min^{-1}. The elemental analysis was carried out on an automated Perkin Elmer PE-2400 analyzer. The melting points were determined on combined Boetius stages and are uncorrected. The flash chromatography was performed with the use of silica gel Lancaster 0.040—0.063 mm (230—400 mesh).

The reaction progress was monitored and the purity of the reaction products was checked by TLC on Sorbfil plates; spots were visualized with UV light or I_2 vapor.

The X-ray diffraction study was carried out on an automated Xcalibur-3 diffractometer equipped with a CCD detector at 295(2) K (λMo-Kα, graphite monochromator, ω-scanning technique). The X-ray data for compound **4a** were collected from a piece of a yellow plate-like single crystal of dimensions 0.43×0.23×0.11 mm; for compound **4b**, from a piece of a yellow prismatic single crystal of dimensions 0.51×0.38×0.25 mm. The absorption corrections were not applied. The structures were solved by direct methods using the SHELXS-97 program package and refined with anisotropic (isotropic for hydrogen atoms) displacement parameters with the use of the SHELXL-97 program package.[31,32] The hydrogen atoms were refined using a riding model with fixed thermal parameters. The principal X-ray diffraction data collection and refinement statistics are given in Table 3. The results of the X-ray diffraction study were deposited with the Cambridge Structural Database (deposition numbers CCDC 714995 and 714996 for compounds **4a** and **4b**, respectively).*

Synthesis of (3-aryl- and 3-hetaryl-5,6-dicyano-1-ethyl-1,2-dihydropyrazin-2-yl)phosphonic acid esters (general procedure). A mixture of salt **1a** or **1b** (1 mmol) and diethyl (**3a**) or diphenyl phosphonate (**3b**) (1 mmol) in CH_3CN (5 mL) was stirred for 1 h. The solvent was distilled off *in vacuo*, and the residue was separated on silica gel using elution with a 1 : 2 ethyl acetate—benzene mixture.

Diethyl (5,6-dicyano-1-ethyl-3-phenyl-1,2-dihydropyrazin-2-yl)phosphonate (4a). Yellow-orange crystalline powder, m.p. 138—140 °C. The yield was 66%. Found (%): C, 57.97; H, 5.41; N, 14.96. $C_{18}H_{21}N_4O_3P$. Calculated (%): C, 58.06; H, 5.69; N, 15.05. ^{1}H NMR ($CDCl_3$), δ: 1.21 (t, 3 H, CH_3, J = 7.0 Hz); 1.26 (t, 3 H, CH_3, J = 7.2 Hz); 1.33 (t, 3 H, CH_3, J = 7.1 Hz); 3.64 (m, 1 H, NCH); 3.74 (m, 1 H, NCH); 4.00—4.16 (m, 4 H, OCH_2); 5.17 (d, 1 H, H(2), J = 14.2 Hz); 7.45—7.53 (m, 3 H, Ar); 7.97—7.99 (m, 2 H, Ar). ^{13}C NMR ($CDCl_3$), δ: 14.33 (s, $NCH_2\underline{C}H_3$); 16.21 (d, $OCH_2\underline{C}H_3$, ^3J = 5.8 Hz); 16.39 (d, $OCH_2\underline{C}H_3$, ^3J = 5.5 Hz); 49.39 (s, $N\underline{C}H_2$); 53.07 (d, C(2), ^1J = 162.1 Hz); 63.62 (d, $O\underline{C}H_2$, ^2J = 7.4 Hz); 63.80 (d, $O\underline{C}H_2$, ^2J = 7.6 Hz); 111.01 (s, CN (C(5)); 112.20 (d, CN (C(6)), ^4J = 2.0 Hz); 115.65 (d, C(5), ^4J = 2.5 Hz); 118.67 (d, C(6), ^3J = 3.2 Hz); 128.43 (d, C_o—Ph, ^4J = 9.3 Hz); 128.85 (s, C_m—Ph); 132.12 (s, C_p—Ph); 133.55 (d, C_{ipso}—Ph, ^3J = 2.9 Hz); 143.59 (d, C(3), ^2J = 4.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$), δ: 15.27 ($P(O)(OEt)_2$). LC/MS, m/z (I (%)): 372 $[M - H]^+$ (100), 373 $[M]^+$ (23), 374 $[M + H]^+$ (3).

* These data can be obtained, free of charge, on application to the Cambridge Crystallographic Data Centre, www.ccdc.cam.ac.uk/datarequest/sif.

Table 3. Principal X-ray diffraction data collection and refinement statistics for compounds **4a,b**

Parameter	**4a**	**4b**
Molecular formula	$C_{18}H_{21}N_4O_3P$	$C_{16}H_{19}N_4O_3PS$
Molecular weight	372.36	378.38
T/K	295(2)	295(2)
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$
a/Å	9.9595(9)	9.6360(13)
b/Å	17.518(3)	17.8265(17)
c/Å	11.374(2)	11.1595(12)
α/deg	90.00	90.00
β/deg	101.208(11)	100.462(10)
γ/deg	90.00	90.00
V/Å^3	1946.5(5)	1885.1(4)
Z	4	4
d_{calc}	1.271	1.333
μ/мм$^{-1}$	0.166	0.279
Scan range, θ/deg	$26.37 \geq \theta \geq 2.75$	$32.52 \geq \theta \geq 2.81$
Number of measured reflections (R_{int})	3833 (0.0890)	5916 (0.0340)
Number of reflections with $I > 2\sigma$	1375	2198
Number of refined parameters	260	235
S	0.857	0.996
R_1 (based on $I > 2\sigma(I)$)	0.0497	0.0411
wR_2 (based on $I > 2\sigma(I)$)	0.0575	0.0832
R_1 (based on all reflections)	0.1972	0.1428
wR_2 (based on all reflections)	0.0698	0.0895
Residual electron density /e Å^{-3}, max/min	0.176/−0.257	0.227/−0.414

Diethyl [5,6-dicyano-1-ethyl-3-(3-thienyl)-1,2-dihydropyrazin-2-yl]phosphonate (4b). Dark-yellow crystalline powder, m.p. 136—138 °C. The yield was 69%. Found (%): C, 50.21; H, 4.81; N, 14.48. $C_{16}H_{19}N_4O_3SP \cdot 0.2H_2O$. Calculated (%): C, 50.31; H, 5.12; N, 14.67. ^{1}H NMR ($CDCl_3$), δ: 1.24 (t, 3 H, CH_3, J = 7.2 Hz); 1.26 (t, 3 H, CH_3, J = 7.3 Hz); 1.34 (t, 3 H, CH_3, J = 7.1 Hz); 3.56 (m, 1 H, NCH); 3.73 (m, 1 H, NCH); 4.03—4.16 (m, 4 H, OCH_2); 4.97 (d, 1 H, H(2), J = 13.6 Hz); 7.38 (dd, 1 H, H(5″), J = 5.2 Hz, J = 2.9 Hz); 7.66 (dd, 1 H, H(4″), J = 5.2 Hz, J = 1.3 Hz); 7.91 (dd, 1 H, H(2″), J = 2.8 Hz, J = 1.3 Hz). ^{13}C NMR ($CDCl_3$), δ: 14.18 (d, $NCH_2\underline{C}H_3$, ^4J = 7.2 Hz); 16.24 (d, $OCH_2\underline{C}H_3$, ^3J = 5.8 Hz); 16.39 (d, $OCH_2\underline{C}H_3$, ^3J = 5.6 Hz); 49.27 (s, $N\underline{C}H_2$); 54.29 (d, C(2), ^1J = 162.2 Hz); 63.63 (d, $O\underline{C}H_2$, ^2J = 7.4 Hz); 63.83 (d, $O\underline{C}H_2$, ^2J = 7.6 Hz); 111.06 (s, CN (C(5)); 112.03 (d, CN (C(6)), ^4J = 1.9 Hz); 115.68 (d, C(5), ^4J = 2.4 Hz); 118.30 (d, C(6), ^3J = 3.3); 126.96 (s, C(4″)—thienyl); 127.26 (s, C(5″)—thienyl); 130.06 (s, C(2″)—thienyl); 137.88 (d, C(3″)—thienyl, ^3J = 2.8 Hz); 139.69 (d, C(3), ^2J = 3.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$), δ: 15.04 ($P(O)(OEt)_2$). LC/MS, m/z (I (%)): 377 $[M - H]^+$ (100), 378 $[M]^+$ (21), 379 $[M + H]^+$ (8).

Diphenyl (5,6-dicyano-1-ethyl-3-phenyl-1,2-dihydropyrazin-2-yl)phosphonate (5a). Yellow powder, m.p. 114—116 °C. The yield was 45%. Found (%): C, 67.22; H, 4.49; N, 11.43. $C_{26}H_{21}N_4O_3P \cdot 1/6C_6H_6$ (PhH). Calculated (%): C, 66.98; H, 4.58; N, 11.57. ^{1}H NMR ($CDCl_3$), δ: 1.31 (t, 3 H, CH_3, J = 7.2 Hz); 3.64 (m, 1 H, NCH); 3.80 (m, 1 H, NCH); 5.57 (d, 1 H, H(2), J = 13.4 Hz); 6.80—7.52 (m, 13 H, Ar); 8.03—8.06 (m, 2 H, Ar). ^{13}C NMR ($CDCl_3$), δ: 14.40 (s, $NCH_2\underline{C}H_3$); 49.69 (s, $N\underline{C}H_2$); 53.60 (d, C(2), ^1J = 162.6 Hz); 110.75 (s, CN (C(5)), ^5J = 1.0 Hz); 112.69 (d, CN (C(6)), ^4J = 2.2 Hz); 115.21 (d, C(5), ^4J = 2.7 Hz); 118.70 (d, C(6), ^3J = 3.5 Hz); 119.70 (d, Ph, J = 4.6 Hz); 119.77 (d, Ph, J = 4.5 Hz); 125.86 (d, Ph, J = 6.7 Hz); 128.40 (s, Ph); 129.08 (s, Ph); 130.05 (d, C_o—Ph, ^4J = 10.9 Hz); 132.42 (s, Ph); 133.39 (d, C_{ipso}—Ph, ^3J = 3.1 Hz); 143.05 (d, C(3), ^2J = 4.6 Hz); 149.48 (d, Ph, J = 3.1 Hz); 149.58 (d, Ph, J = 2.6 Hz). ^{31}P NMR (162 MHz, $CDCl_3$), δ: 7.40 ($P(O)(OPh)_2$). LC/MS, m/z (I (%)): 467 $[M - H]^+$ (100), 468 $[M]^+$ (36), 469 $[M + H]^+$ (6).

Diphenyl [5,6-dicyano-1-ethyl-3-(3-thienyl)-1,2-dihydropyrazin-2-yl]phosphonate (5b). Yellow powder, m.p. 111—113 °C. The yield was 32%. Found (%): C, 61.07; H, 4.22; N, 11.67. $C_{24}H_{19}N_4O_3SP$. Calculated (%): C, 60.75; H, 4.04; N, 11.81. ^{1}H NMR ($CDCl_3$), δ: 1.31 (t, 3 H, CH_3, J = 7.2 Hz); 3.62 (m, 1 H, NCH); 3.80 (m, 1 H, NCH); 5.37 (d, 1 H, H(2), J = 12.8 Hz); 6.96—7.34 (m, 10 H, Ar); 7.42 (dd, 1 H, H(5″), J = 5.2 Hz, J = 2.8 Hz); 7.71 (dd, 1 H, H(4″), J = 5.2 Hz, J = 1.2 Hz); 7.97 (dd, 1 H, H(2″), J = 2.8 Hz, J = 1.2 Hz). ^{31}P NMR (162 MHz, $CDCl_3$), δ: 7.20 ($P(O)(OPh)_2$). LC/MS, m/z (I (%)): 473 $[M - H]^+$ (100), 474 $[M]^+$ (37), 475 $[M + H]^+$ (10).

Synthesis of diethyl (3-aryl- and 3-hetaryl-1-methyl-1,2-dihydroquinoxalin-2-yl)phosphonates. A mixture of salt **2a** or **2b** (1 mmol), diethyl phosphonate **3a** (1 mmol), and NEt_3 (1.1 mmol) in CH_3CN (5 mL) was stirred for 1.5 h. The solvent was distilled off *in vacuo*, and the residue was separated on silica gel using elution with a 1 : 2 ethyl acetate—benzene mixture.

Diethyl [1-methyl-3-(3-nitrophenyl)-1,2-dihydroquinoxalin-2-yl]phosphonate (6a). Yellow powder, m.p. 64—66 °C (decomp.). The yield was 34%. Found (%): C, 56.41; H, 5.62; N, 10.50. $C_{19}H_{22}N_3O_5P$. Calculated (%): C, 56.57; H, 5.50; N, 10.42. ^{1}H NMR (DMSO-d_6), δ: 0.89 (t, 3 H, CH_3, J = 7.0 Hz); 0.95 (t, 3 H, CH_3, J = 7.0 Hz); 3.09 (s, 3 H, CH_3); 3.60—3.83 (m, 4 H, 2 OCH_2); 5.77 (d, 1 H, H(2), J = 12.4 Hz); 6.74—6.80 (m, 2 H, Ar); 7.16—7.18 (m, 1 H, Ar); 7.29—7.31 (m, 1 H, Ar); 7.78—7.82 (m, 1 H, Ar); 8.34—8.36 (m, 1 H, Ar); 8.51—8.53 (m, 1 H, Ar); 8.90—8.91 (m, 1 H, Ar).

Diethyl [1-methyl-3-(3-thienyl)-1,2-dihydroquinoxalin-2-yl]phosphonate (6b). Yellow oil. The yield was 39%. Found (%): 56.09; H, 5.74; N, 7.45. $C_{17}H_{21}N_2O_3SP$. Calculated (%): C, 56.03; H, 5.81; N, 7.69. ^{1}H NMR (DMSO-d_6), δ: 0.93 (m, 6 H, CH_3); 3.05 (s, 3 H, CH_3); 3.53—3.78 (m, 4 H, 2 OCH_2); 5.41 (d, 1 H, H(2), J = 11.7 Hz); 6.69—6.76 (m, 2 H, Ar); 7.09—7.19 (m, 2 H, Ar); 7.60—7.71 (m, 2 H, Ar); 8.21 (dd, 1 H, H(2″), J = 2.8 Hz, J = 1.1 Hz).

1-Methyl-3-(3-nitrophenyl)-1,2-dihydroquinoxalin-2-ol (11a). A mixture of salt **1b** (100 mg, 0.254 mmol) and Na_2CO_3 (32 mg, 0.304 mmol) in H_2O (3 mL) was stirred for 1 h. The precipitate that formed was recrystallized from acetonitrile. A yellow powder with m.p. 116—118 °C was obtained. The yield was 67 mg (93%). Found (%): C, 63.48; H, 4.54; N, 14.62. $C_{15}H_{13}N_3O_3$. Calculated (%): C, 63.60; H, 4.63; N, 14.83. ^{1}H NMR (DMSO-d_6), δ: 3.19 (s, 3 H, NCH_3); 6.01 (s, 1 H, Het—H); 6.51 (s, 1 H, Het—OH); 6.88—6.92 (m, 2 H, Ar); 7.27—7.30 (m, 1 H, Ar); 7.40—7.44 (m, 1 H, Ar); 7.49—7.50 (m, 1 H, Ar); 8.31—8.33 (m, 1 H, Ar); 8.47—8.49 (m, 1 H, Ar); 8.84—8.85 (m, 1 H, Ar). ^{13}C NMR

(DMSO-d_6), δ: 34.89 (s, N$\underline{C}H_3$); 74.09 (s, C_{sp3}); 112.00 (s, Ar); 117.99 (s, Ar); 121.26 (s, Ar); 124.36 (s, Ar); 128.15 (s, Ar); 129.28 (s, Ar); 130.175 (s, Ar); 132.23 (s, Ar); 133.05 (s, Ar); 136.18 (s, Ar); 138.04 (s, Ar); 148.18 (s, Ar); 151.44 (s, Ar). LS/MS, *m/z* (*I* (%)): 266 $[M - OH]^+$ (100).

2-Methoxy-1-methyl-3-(3-nitrophenyl)-1,2-dihydroquinoxaline (11b). A mixture of salt **1b** (100 mg, 0.254 mmol) and NEt_3 (42 μl, 0.304 mmol) in methanol (3 mL) was stirred for 1 h. The precipitate that formed was recrystallized from acetonitrile. A yellow powder with m.p. 103—104 °C was obtained. The yield was 67 mg (85%). Found (%): C, 64.32; H, 4.85; N, 14.19. $C_{16}H_{15}N_3O_3$. Calculated (%): C, 64.64; H, 5.09; N, 14.13. ^{1}H NMR ($CDCl_3$), δ 2.95 (s, 3 H, NCH_3); 3.34 (s, 3 H, OCH_3); 5.98 (s, 1 H, Het—H); 6.90—7.00 (m, 2 H, Ar); 7.32—7.34 (m, 1 H, Ar); 7.60—7.67 (m, 2 H, Ar and Het); 8.28—8.30 (m, 1 H, Het); 8.47—8.49 (m, 1 H, Het); 8.95—8.97 (m, 1 H, Het). ^{13}C NMR (DMSO-d_6), δ: 34.93 (s, N$\underline{C}H_3$); 74.19 (s, C_{sp3}); 112.12 (s, Ar); 118.12 (s, Ar); 121.38 (s, Ar); 124.45 (s, Ar); 128.18 (s, Ar); 129.36 (s, Ar); 130.18 (s, Ar); 132.35 (s, Ar); 133.25 (s, Ar); 136.27 (s, Ar); 138.15 (s, Ar); 148.23 (s, Ar); 151.52 (s, Ar). LC/MS, *m/z* (*I* (%)): 266 $[M - OCH_3]^+$ (100).

This study was financially supported by the Russian Foundation for Basic Research (Project Nos 07-03-12112-ofi, 07-03-96113-r_ural_a, and 07-03-96123-r_ural_a) and the Council on Grants of the President of the Russian Federation (Program for State Support of Leading Scientific Schools of the Russian Federation, Grant NSh-3758.2008.3).

References

1. V. M. Dembitsky, T. A. Glorizova, V. V. Poroikov, *Mini-Rev. Med. Chem.*, 2005, **5**, 319.
2. N. Sato, *Comprehensive Heterocyclic Chemistry II*, Eds A. R. Katritzky, C. W. Rees, E. F. V. Scriven, Elsevier, Oxford, 1996, **6**, 233.
3. C. G. Bonde, N. J. Gaikwad, *Bioorg. Med. Chem.*, 2004, **12**, 2151.
4. H. Gohlke, D. Gundisch, S. Schwarz, M. C. Tilotta, T. Wegge, *J. Med. Chem.*, 2002, **45**, 1064.
5. A. E. A. Porter, *Pyrazines and Their Benzo Derivatives* in *Comprehensive Heterocyclic Chemistry I*, Eds A. R. Katritzky, C. W. Rees, Pergamon Press, New York, 1984, **3**, 191.
6. A. Jaso, B. Zarranz, I. Aldana, A. Monge, *J. Med. Chem.*, 2005, **48**, 2019.
7. L. E. Seitz, W. J. Suling, R. C. Reynolds, *J. Med. Chem.*, 2002, **45**, 5604.
8. A. Carta, G. Paglietti, M. E. Rhbarnikookar, P. Sanna, L. Sechi, S. Zanetti, *Eur. J. Med. Chem.*, 2002, **37**, 355.
9. C. Betancor, R. Freire, I. Perez-Martin, T. Prange, E. Suarez, *Tetrahedron*, 2005, **61**, 2803.
10. W. Li, P. L. Fuchs, *Org. Lett.*, 2003, **5**, 2849.
11. T. G. LaCour, C. Guo, M. R. Boyd, P. L. Fuchs, *Org. Lett.*, 2000, **2**, 33.
12. O. N. Chupakhin, V. N. Charushin, H. C. van der Plas, *Nucleophilic Aromatic Substitution of Hydrogen*, Academic Press, San Diego—New York, 1994, 376 pp.
13. V. N. Charushin, O. N. Chupakhin, *Mendeleev Commun.*, 2007, **17**, 249.
14. V. N. Charushin, O. N. Chupakhin, *Pure Appl. Chem.*, 2004, **76**, 1621.
15. A. V. Gulevskaya, A. F. Pozharskii, *Adv. Heterocycl. Chem.*, 2007, **93**, 57.
16. D. V. Besedin, A. V. Gulevskaya, A. F. Pozharskii, *Chem. Heterocycl. Compd.*, 2000, **36**, 10, 1213.
17. A. V. Gulevskaya, A. F. Pozharskii, *Chem. Heterocycl. Compd.*, 2001, **37**, 12, 1461.
18. A. V. Gulevskaya, D. V. Besedin, A. F. Pozharskii, Z. A. Starikova, *Tetrahedron Lett.*, 2001, **42**, 5981.
19. A. V. Gulevskaya, O. V. Serduke, A. F. Pozharskii, D. V. Besedin, *Tetrahedron*, 2003, **59**, 7669.
20. O. N. Chupakhin, V. N. Charushin, A. R. Chernyshev, *Prog. Nucl. Magn. Res. Spectr.*, 1988, **20**, 95.
21. P. A. Slepukhin, N. N. Mochul´skaya, L. P. Sidorova, G. L. Rusinov, M. A. Ezhikova, M. I. Kodess, O. N. Kazheva, A. N. Chekhlov, O. A. D´yachenko, V. N. Charushin, *Izv. Akad. Nauk, Ser. Khim.*, 2005, 2132 [*Russ. Chem. Bull., Int. Ed.*, 2005, **54**, 2197].
22. E. V. Verbitskiy, G. L. Rusinov, P. A. Slepukhin, A. N. Grishakov, M. A. Ezhikova, M. I. Kodess, V. N. Charushin, *Zh. Org. Khim.*, 2008, **44**, 305 [*Russ. J. Org. Chem.* (*Engl. Transl.*), 2008, **44**].
23. M. Haase,W. Günther, H. Görls, E. Anders, *Synthesis*, 1999, 2071.
24. I. Takeuchi, Y. Hamada, Y. Kurono, T. Yashiro, *Chem. Pharm. Bull.*, 1990, **38**, 1504.
25. I. Takeuchi, Y. Shibata, Y. Hamada, M. Kido, *Heterocycles*, 1986, **24**, 647.
26. I. Takeuchi, Y. Hamada, Z. Taira, *Heterocycles*, 1991, **32**, 261.
27. H. Günter, *NMR Spectroscopy, An Introduction*, John Wiley and Sons, Chichester—New York—Brisbone—Toronto, 1980.
28. *Kratkii spravochnik fiziko-khimicheskikh velichin* [*Concise Handbook of Handbook of Physicochemical Quantities*], Eds A. A. Ravdel´, A. M. Ponomareva, Spetsial´naya literatura, St.-Petersburg, 1999, p. 161 (in Russian).
29. I. N. Ganebnykh, E. V. Verbitskiy, G. L. Rusinov, V. N. Charushin, O. N. Chupakhin, *Tez. dokl. III Mezhdunarodnoi konf-shkoly "Mass-spektrometriya v khimicheskoi fizike, biofizike i ekologii"* [*Abstrs. of Papers, III Intern. Conf.-School "Mass Spectrometry in Chemical Physics, Biophysics, and Ecology"*], Zvenigorod, 2007, 177—178 (in Russian).
30. F. L. Tietze, T. Eicher, *Reaktionen und Synthesen im organisch-chemischen Praktikum und Forschunglaboratorium*, Georg Thieme Verlag, Stuttgart—New York, 1991.
31. G. M. Sheldrick, *SHELXS97, Program for the Solution of Crystal Structure*, University of Göttingen, Göttingen, Germany, 1997.
32. G. M. Sheldrick, *SHELXL97, Program for the Refinement of Crystal Structure*, University of Göttingen, Göttingen, Germany, 1997.

Received July 7, 2008;
in revised form November 11, 2008