3-Aryl(hetaryl)-3-hydroxy-2-phosphorus-substituted acrylonitriles. Synthesis and experimental and theoretical conformational analysis

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Under conditions of the phase transfer catalysis, acylation of (thio)phosphorylacetonitriles by (het)aroyl chlorides affords the *Z*-enol forms of *C*-acylation products in high yields. Their configurations were studied by IR spectroscopy, dipole moment measurements, and *ab initio* quantum-chemical calculations [B3LYP/6-31G(d)]. The C=C double bond and the phosphoryl or thiophosphoryl group have an *s-cis* arrangement. The possibility of strong intramolecular hydrogen bonding in these conformers is the governing factor responsible for the three-dimensional structures of the compounds under investigation. Derivatives of nicotinic acid existing in the individual form as zwitterions are the only exceptions.

Key words: (thio)phosphorylacetonitriles, phase transfer catalysis, enols, *Z* and *E* isomers, 3-aryl(hetaryl)-3-hydroxy-2-phosphorus-substituted acrylonitriles, 3-alkyl-2-(thio)phosphoryl-substituted acrylonitriles, IR spectroscopy, dipole moments, quantum-chemical calculations, conformational analysis.

Earlier,[1—4] we have reported that phosphoryl- and thiophosphorylacetonitriles **1** can be subjected to preparative acylation with alkanoyl chlorides and benzoyl chloride under the phase transfer catalysis conditions. These reactions afford C-acylation products in high yields. Under the reaction conditions (an excess of alkali), these products are transformed into chelate salts of the corresponding enol forms. After acidification, the target compounds are isolated also as enol forms of C-acyl((thio)phosphoryl)acetonitriles. According to the data from NMR spectroscopy and X-ray diffraction analysis, these compounds exist in the individual state and in solutions in aprotic solvents as cyclic *Z* isomers stabilized by strong intramolecular hydrogen bonds. In dipolar aprotic solvents (DMSO, DMF) and solvents that are prone to the formation of intermolecular hydrogen bonds (alcohols, aqueous-alcoholic media), the reaction products also exist as enol tautomers, but as two different forms of *Z* isomers (a cyclic form stabilized by an intramolecular hydrogen bond and an open form stabilized by an intermolecular hydrogen bond) and an *E* isomer. The *Z* isomer of (isopropoxymethylphosphoryl)acetylacetonitrile stabilized by an intermolecular hydrogen bond was studied by single-crystal X-ray diffraction analysis.[3]

With the aim of preparing products possessing potential biological activity, it was worthwhile to investigate acylation of compounds **1** with substituted aromatic and heterocyclic carboxylic acid halides under the phase transfer catalysis conditions. Besides, it was of interest to examine the influence of the carbocyclic or heterocyclic residue on the ability of these compounds to undergo enolization, the three-dimensional structures of the reaction products, and strength of an intramolecular hydrogen bond in the *Z* isomers of enols (in particular, for compounds containing the heterocyclic nitrogen atom, which is prone to protonation).

Earlier, we have demonstrated[2] that acylation of thiophosphorylacetonitriles with aromatic carboxylic acid chlorides afforded C,O-diacylated derivatives as by-products. Hence, we used the corresponding compounds containing the P=O group as the organophosphorus substrate in most of the syntheses of the target compounds.

C-Acylation of compounds **1a—d** with mono- and trisubstituted benzoyl chlorides **2a—d** proceeded readily and straightforward regardless of the donor-acceptor properties of substituents in the aromatic ring (Scheme 1). Sulfamidobenzoyl chloride (**2e**) can also be involved in the reaction, the sulfonamide fragment remaining intact.

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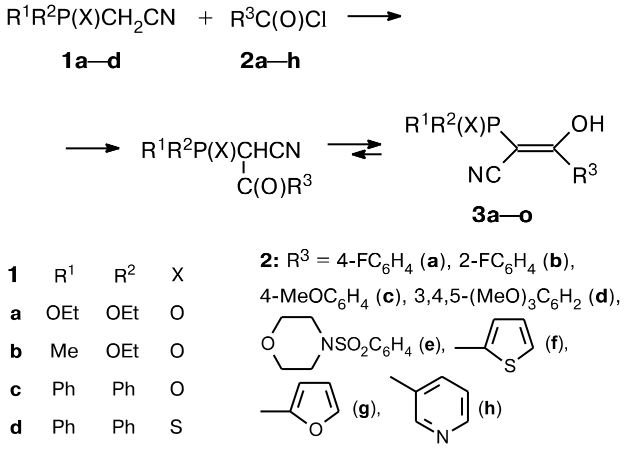
The reactions of 2-thenoyl-, 2-furoyl-, and nicotinoyl chlorides (**2f—h**) proceeded analogously.

Scheme 1



C-Acylation products **3a—o** were isolated after acidification of the reaction mixtures. Compound **3c** was obtained in lower yield compared to all other compounds due apparently to the presence of the *ortho* substituent in the aromatic ring of acid chloride **2b** and the steric hindrances that appear. The yields and physicochemical constants of the compounds thus synthesized are given in Table 1. Selected spectroscopic parameters are listed in Table 2.

The resulting compounds as well as the corresponding derivatives of aliphatic carboxylic acids occur as the only isomers of the corresponding enols as deduced from the presence of a singlet in the ^{31}P-{^{1}H} NMR spectra of compounds **3** in $CDCl_3$ or C_6D_6, the presence of one characteristic set of signals in the ^{1}H NMR spectra,* and the absence of an absorption band of the carbonyl group in the IR spectra (KBr).

The three-dimensional structures of unsaturated organophosphorus compounds have been investigated in sufficient detail.[5,6] The structures of derivatives containing mainly α- or β-unsubstituted or monosubstituted vinyl or buta-1,3-dienyl group were studied. Data on the structures of polyfunctional organophosphorus compounds possessing the double bond at the phosphorus atom are very scanty.

Therefore, we carried out a detailed study of the structures of enols EtO(Me)P(O)C(CN)=C(2-furyl)OH (**3f**) and $Ph_2P(O)C(CN)$=C(2-furyl)OH (**3m**) as well as of compounds $Ph_2P(Y)C(CN)=C(Me)OH$, where Y = O (**4a**)[1] or S (**4b**),[2] which we have synthesized earlier, using IR spectroscopy and dipole moment measurements.

The crystal structures of compounds **4a**,**b** have been established by X-ray diffraction analysis.[1—3] It was found that both molecules exist as the *Z* isomers containing six-membered H-rings owing to strong intramolecular hydrogen bonds.

The IR spectra of unsaturated phosphine oxide **4a** has strong absorption bands at 1604 ($\nu_{C=C}$), 1124 ($\nu_{P=O}$), and 2200 cm^{-1} ($\nu_{C\equiv N}$) and a very broad band in the region of 2400—2800 cm^{-1} ($\nu_{P=O...H-O}$). The IR spectra of compound **4a** in Nujol (solid phase) and in solutions in CH_2Cl_2 are identical, which suggests the presence of a strong intramolecular hydrogen bond resulting in a six-membered H-ring in molecule **4a**. The IR spectrum of its thio analog (**4b**) has strong absorption bands at 1580, 1568, 1560 ($\nu_{C=C}$), and 2200 cm^{-1} ($\nu_{C\equiv N}$) and a very broad absorption band in the region of 2800—3000 cm^{-1} ($\nu_{P=S...H-O}$), which is also indicative of an intramolecular hydrogen bond. Unfortunately, the unambiguous assignment of the $\nu_{P=S}$ bands presents difficulty, because absorption bands of the benzene rings are observed in the region of 500—650 cm^{-1}. It should be noted that the wavenumbers of the characteristic absorption bands in the IR spectra of compounds **4a**,**b** (ν_{OH}, $\nu_{C=C}$, $\nu_{P=O}$) both in the solid phase and in solutions in CH_2Cl_2 are substantially smaller than the standard values for other types of compounds, which points unambiguously[7] to the presence of strong intramolecular hydrogen bonds in **4a**,**b**. Our study revealed no concentration dependence in the IR spectra, which indicates that hydrogen bonds are intramolecular.

Introduction of a furyl substituent (compound **3m**) instead of the Me group (**4a**) does not lead to a substantial change in the IR spectral pattern. The IR spectrum of **3m** in the solid state has a weak absorption band at 1595 cm^{-1}, strong absorption bands at 1584, 1560 ($\nu_{C=C}$); 1122 ($\nu_{P=O}$), and 2200 cm^{-1} ($\nu_{C\equiv N}$), and a very broad band in the region of 2400—2800 cm^{-1} ($\nu_{P=O...H-O}$). In the spectra of compound **3m** in solutions in CH_2Cl_2, the positions of the $\nu_{P=O}$ and ν_{OH} absorption bands remain unchanged, which is evidence for intramolecular hydrogen bonding. However, the character of absorption of the C=C double bond in the spectrum of a solution in CH_2Cl_2 changes (strong bands are observed at 1612, 1584, 1556, and 1536 cm^{-1}). Changes are also observed in the region of 800—1100 cm^{-1} of the IR spectrum. Compared to the spectra of solid compound **3m**, the IR spectrum of a solution has new bands at 942 and 1016 cm^{-1} as well as a new band at 1258 cm^{-1}. Presumably, the appearance of new bands in the spectrum of furyl derivative **3m** in solution is associated with specific interactions with the solvent.

The IR spectra of phosphinate **3l** in Nujol show strong absorption bands at 1606, 1530 ($\nu_{C=C}$), 1158 ($\nu_{P=O}$), 1020, 964 (ν_{P-O-C}), 2200 cm^{-1} ($\nu_{C\equiv N}$), and a very broad absorp-

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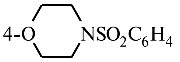
* In spite of the fact that the ^{31}P NMR spectrum of compound **3a** containing the 2-fluorophenyl substituent has the only singlet, the ^{1}H NMR spectrum of this compound contains two similar systems of signals of the corresponding fragments. We believe that these signals correspond to two different forms of the *Z* isomer, *viz*., the cyclic and open forms.

Table 1. Physicochemical characteristics and elemental analysis data for 3-aryl(hetaryl)-3-hydroxy-2-(thio)phosphorylacrylonitriles **3**

Compound	X	R^1R^2	R^3	Yield (%)	M.p./°C or B.p./°C (*p*/Torr)	Found / Calculated (%) C	H	N	Molecular formula
3a	O	$(EtO)_2$	4-FC_6H_4	61	Oil[a]	51.69 51.54	5.13 4.94	8.90 8.59	$C_{14}H_{16}FN_2O_4P$
3b	O	Ph_2	4-FC_6H_4	75	144—145 ($EtOH/Et_2O$)	69.56 69.42	4.29 4.16	3.99 3.86	$C_{21}H_{15}FNO_2P$
3c	O	$(EtO)_2$	2-FC_6H_4	37	Oil[a]	51.76 51.54	5.18 4.94	8.78 8.59	$C_{14}H_{16}FN_2O_4P$
3d	O	$(EtO)_2$	4-$MeOC_6H_4$		Oil[a]	54.36 54.02	5.99 5.83	4.75 4.50	$C_{14}H_{18}NO_5P$
3e	O	Me(EtO)	4-$MeOC_6H_4$	69	70—71 (EtOH)	55.69 55.52	5.81 5.69	5.23 4.98	$C_{13}H_{16}NO_4P$
3f	O	Me(EtO)	3,4,5-$(MeO)_3C_6H_2$	58	85—86 (MeOH)	52.85 52.79	5.87 5.87	4.05 4.11	$C_{15}H_{20}NO_6P$
3g	O	Ph_2	4-O NSO$_2$C$_6$H$_4$	62	162—163 ($EtOH/Et_2O$)	60.79 60.72	4.91 4.69	—	$C_{25}H_{23}N_2O_5PS$ [b]
3h	O	$(EtO)_2$	2-Thienyl	56	155—160(1)[a] (oil)	45.46 45.99	4.70 4.88	—	$C_{11}H_{14}NO_4PS$ [c]
3i	O	Me(EtO)	2-Thienyl	57	140—165(1)[a] (oil)	46.94 46.69	4.86 4.70	5.69 5.44	$C_{10}H_{12}NO_3PS$
3j	O	Ph_2	2-Thienyl	83	138—140 (EtOH)	64.80 64.96	3.84 3.99	3.88 3.99	$C_{19}H_{14}NO_3PS$
3k	O	$(EtO)_2$	2-Furyl	68	Oil[a]	49.03 48.71	5.18 5.17	—	$C_{11}H_{14}NO_5P$ [d]
3l	O	Me(EtO)	2-Furyl	74	139—140 ($EtOH/Et_2O$)	50.19 49.79	4.97 4.98	5.68 5.81	$C_{10}H_{12}NO_4P$
3m	O	Ph_2	2-Furyl	63	154—155 ($EtOH/Et_2O$)	68.04 68.06	4.15 4.18	4.09 4.18	$C_{19}H_{14}NO_3P$
3n	O	Ph_2	3-Pyridyl	76	220—221 (acetone)	69.09 69.36	4.39 4.37	—	$C_{20}H_{15}N_2O_2P$ [d]
3o	S	Ph_2	3-Pyridyl	63	251—252 (acetone)	65.85 66.29	4.12 4.17	7.26 7.73	$C_{20}H_{15}N_2OPS$

[a] Purified by chromatography (SiO_2, hexane—acetone 100 : 5).

[b] Found (%): S, 6.72; P, 6.16. Calculated (%): S, 6.48; P, 6.26.

[c] Found (%): S, 11.43. Calculated (%): S, 11.15.

[d] Found (%): P, 11.35 (**3k**), 9.22 (**3n**). Calculated (%): P, 11.44 (**3k**), 8.95 (**3n**).

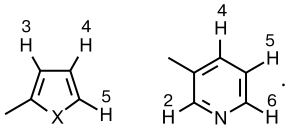
Table 2. Selected parameters of the IR (KBr or a thin layer) and NMR spectra of compounds **3a—o**

Compound	ν/cm^{-1}			δ, *J*/Hz, $CDCl_3$	
	ν_{CN}	$\nu_{P=O}$	$\nu_{C=C}$	^{31}P-{^1H}	^1H
3a	2200	1180	1575	22.36 [a]	1.40 (t, 6 H, Me, $^3J_{H,H}$ = 6.8); 4.25—4.37 (m, 4 H, CH_2O); 7.32 –7.34 (m, 2 H, C_6H_4F, $^3J_{H,H}$ = 8.8); 8.03—8.05 (2 H, C_6H_4F); 13.8 (br.s, 1 H, OH)
3b	2200	1130	1585	41.14 [b]	7.15 (t, 2 H, C_6H_4F, $^3J_{H,H}$ = 8.8); 7.55—7.59 (m, 4 H, *m*-C_6H_5P); 7.64—7.68 (m, 2 H, *p*-C_6H_5P); 7.84—7.90 (m, 4 H, *o*-C_6H_5P); 7.99—8.04 (m, 2 H, C_6H_4F); 14.2 (br.s, 1 H, OH)
3c	2200	1185	1585	20.10	*Z* cyclic: 1.41 (t, 6 H, $C\underline{H}_3CH_2$, $^3J_{H,H}$ = 6.4); 4.26—4.34 (m, 4 H, CH_2O); 7.31—7.40 (m, 2 H, Ar); 7.62—7.73 (m, 2 H, Ar); *Z* open form: 1.30 (t, 6 H, $C\underline{H}_3CH_2$, $^3J_{H,H}$ = 6.5); 4.07—4.10 (m, 4 H, CH_2O); 7.25—7.31 (m, 2 H, Ar); 7.62—7.64 (m, 1 H, Ar); 7.96—7.99 (m, 1 H, Ar); 13.9 (br.s, 1 H, OH, both forms)

(*to be continued*)

Table 2 (*continued*)

Com-pound	ν/cm^{-1}			δ, J/Hz, $CDCl_3$	
	ν_{CN}	$\nu_{P=O}$	$\nu_{C=C}$	$^{31}P-\{^1H\}$	^1H
3d	2205	1195	1580	23.39 [c]	1.07 (t, 3 H, $C\underline{H}_3CH_2$, $^3J_{H,H}$ = 6.8); 3.20 c (3 H, MeO); 3.84—3.97 (m, 4 H, CH_2O); 6.57—6.68 (m, 2 H, Ar, $^2J_{H,H}$ = 6.8); 8.21—8.24 (m, 2 H, Ar); 14.0 (br.s, 1 H, OH)
3e	2205	1180, 1190	1585, 1620	52.95 [c]	1.01 (t, 3 H, $C\underline{H}_3CH_2O$, $^3J_{H,H}$ = 6.8); 1.36 (d, 3 H, MeP, $^2J_{P,H}$ = 15.2); 3.25 (s, 3 H, MeO); 3.73—3.88 (2 H, CH_2O); 6.71 (d, 2 H, Ar, $^2J_{H,H}$ = 8.8); 8.25—8.28 (m, 2 H, Ar); 14.6 (br.s, 1 H, OH)
3f	2197	1140, 1160	1585	53.82	1.41 (t, 3 H, $C\underline{H}_3CH_2$, $^3J_{H,H}$ = 7.2); 1.82 (d, 3 H, MeP, $^2J_{P,H}$ = 15.6); 3.91 (s, 6 H, *m*-MeOAr); 3.92 (s, 3 H, *p*-MeOAr); 4.06—4.25 (m, 4 H, CH_2O); 7.27 (s, 2 H, Ar); 13.8 (br.s, 1 H, OH)
3g	2210	1190	1585, 1590	41.38	3.03—3.05 (m, 4 H, NCH_2); 3.75—3.77 (m, 4 H, OCH_2); 7.57—7.69 (m, 4 H, *m*-C_6H_5P); 7.71—7.73 (m, 2 H, *p*-C_6H_5P); 7.85—7.92 (m, overall 6 H, *o*-C_6H_5P (4 H) + $C_6H_4SO_2$ (2 H)); 8.15 (d, $C_6H_4SO_2$, 2 H, $^3J_{H,H}$ = 8.4)
3h	2205	1190	1585 (br)	21.44	1.40 (t, 6 H, Me, $^3J_{H,H}$ = 6.8); 4.16—4.26 (m, 4 H, OCH_2); 7.16 (dd, 1 H, H(4), $^3J_{H,H}$ = 5.2, $^3J_{H,H}$ = 4.0); 7.66 (d, 1 H, H(3), $^3J_{H,H}$ = 5.2); 8.29 (dd, 1 H, H(5), $^3J_{H,H}$ = 5.2, $^4J_{H,H}$ = 1.0); 13.1 (br.s, 1 H, OH)
3i	2203	1165	1580 (br)	53.31 [c]	1.01 (t, 3 H, $C\underline{H}_3CH_2O$, $^3J_{H,H}$ = 6.8); 1.24 and 1.25 (both d[d], 3 H, MeP, $^2J_{P,H}$ = 15.6); 3.59—3.80 (2 H, CH_2O); 6.62—6.65 (m, 1 H, H(4)); 6.92—6.94 (m, 1 H, H(3)); 8.50 (d, 1 H, H(5), $^3J_{H,H}$ = 3.6); 14.3 (br.s, 1 H, OH)
3j	2200	1120	1570 (br)	41.56	7.16 (dd, 1 H, H(4), $^3J_{H,H}$ = 4.8, $^3J_{H,H}$ = 4.0); 7.54—7.59 (m, 4 H, *m*-C_6H_5P); 7.64—7.68 (m, 1 H + 3 H, H(3) + *p*-C_6H_5P); 7.84—7.89 (4 H, *o*-C_6H_5P); 8.29 (dd, 1 H, H(5), $^3J_{H,H}$ = 4.0, $^4J_{H,H}$ = 1.0); 12.0 (br.s, 1 H, OH)
3k	2205	1190	1590	20.05	1.40 (t, 6 H, $C\underline{H}_3CH_2$, $^3J_{H,H}$ = 7.2); 4.16—4.26 (m, 4 H, CH_2O); 6.59 (dd, 1 H, H(4), $^3J_{H,H}$ = 4.0, $^3J_{H,H}$ = 2.0); 7.43 (dd, 1 H, H(3), $^3J_{H,H}$ = 4.0, $^4J_{H,H}$ ~1.0); 7.68—7.70 (m, 1 H, H(5)); 12.8 (br.s, 1 H, OH)
3l	2200	1158	1606, 1530	53.33	1.35 (t, 3 H, $C\underline{H}_3CH_2$, $^3J_{H,H}$ = 7.2); 1.75 (d, 3 H, MeP, $^2J_{P,H}$ = 15.6); 4.04—4.14 (m, 2 H, CH_2O); 6.56 (dd, 1 H, H(4), $^3J_{H,H}$ = 4.0, $^3J_{H,H}$ = 1.6); 7.35 (d, 1 H, H(3), $^3J_{H,H}$ = 4.0); 7.64 (dd, 1 H, H(5), $^3J_{H,H}$ = 1.6); 13.5 (br.s, 1 H, OH)
3m	2200	1122	1584, 1560	41.85	6.64 (dd, 1 H, H(4), $^3J_{H,H}$ = 3.6, $^3J_{H,H}$ = 1.6); 7.46 (d, 1 H, H(3), $^3J_{H,H}$ = 3.6); 7.59—7.64 (m, 4 H, *m*-C_6H_5P); 7.69—7.74 (m, 1 H + 3 H, H(5) + *p*-C_6H_5P); 7.89—7.95 (4 H, *o*-C_6H_5P)
3n[e]	2180	1120	1550	40.41	7.43 (dd, 1 H, H(5), $^3J_{H,H}$ = 4.8, $^3J_{H,H}$ = 8.0); 7.54—7.59 (m, 4 H, *m*-C_6H_5P); 7.64—7.67 (m, 2 H, *p*-C_6H_5P); 7.87 (dd, 2 H, *o*-C_6H_5P, $^3J_{H,H}$ = 7.2, $^3J_{H,H}$ = 13.2); 8.32 (d, 1 H, H(4), $^3J_{H,H}$ = 8.0); 8.74 (d, 1 H, H(6), $^3J_{H,H}$ = 4.8); 9.15 (br.s, 1 H, H(3)); 12.9 (br.s, 1 H, OH)
3o	2180	—	1570	37.40	7.46—7.61 (m, 1 H + 7 H, H(5) + *m*,*p*-C_6H_5P); 7.86—7.96 (m, 4 H, *o*-C_6H_5P); 8.27 (d, 1 H, H(4), $^3J_{H,H}$ = 15.6); 8.74 (d, 1 H, H(6), $^3J_{H,H}$ = 8.4); 9.15 (br.s, 1 H, H(3)), 13.0 (br.s, 1 H, OH)

Note. The numbering scheme of the hydrogen atoms in the heterocyclic fragments 

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[a] Acetone-d_6 as the solvent.

[b] ^{19}F NMR: δ_F −27.60 s.

[c] C_6D_6 as the solvent.

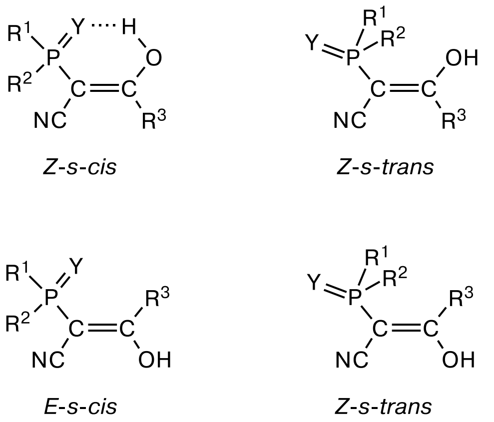
[d] Conformational isomerism.

[e] ^{13}C NMR ($CDCl_3$), δ: 70.79 (d, P—$\underline{C}$=C, $^1J_{P,C}$ = 108.5 Hz); 123.30 (CN); 128.86 (d, *m*-C_6H_5P, $^3J_{P,C}$ = 13.0 Hz); 129.13 (d, P—C, C_6H_5P, $^1J_{P,C}$ = 109.4 Hz); 131.58 (d, *o*-C_6H_5P, $^2J_{P,C}$ = 10.7 Hz); 117.85, 129.91, 136.62, 147.95, and 151.05 (five C in Py); 181.27 (d, =C(OH), $^2J_{P,C}$ = 2.0 Hz).

tion band in the region of 2400—3000 cm^{-1} ($\nu_{P=O...H—O}$). In solutions in CCl_4, the positions of the bands of the phosphoryl and hydroxy group change insignificantly (1166 and 2400—2900 cm^{-1}, respectively), which indicate that molecule **3l** has an intramolecular hydrogen bond regardless of the aggregation state of this compound. In this case, the wavenumbers of the main characteristic absorption bands are also substantially smaller than the standard values (see Ref. 7). The absorption bands of the P=O and OH groups ($\nu_{P=O}$ and ν_{OH}), which are not involved in hydrogen bonding, are absent in the spectra. The IR spectrum of compound **3l** in a solution in CCl_4 has also new absorption bands at 1554, 1558, and 1344 cm^{-1}, which may be associated with a change in the mutual arrangement of the planes of the furyl ring and the C=C bond. The IR spectrum of a solution of phosphinate **3l** in CH_2Cl_2 (like the spectrum of a solution in CCl_4) shows new absorption bands at 3512 (ν_{OH}) and 1726 cm^{-1} ($\nu_{C=O}$) compared to the spectrum of the solid sample. Therefore, the hydrogen bonds are partially cleaved in a solution of compound **3l** in CH_2Cl_2 to form, apparently, the keto tautomer, although the presence of the keto form has not been detected by $^{31}P-\{^1H\}$ and ^1H NMR spectroscopy.

Further identification of the isomers and conformers (rotational isomerism with respect to the P—C_{sp^2} bond) present in solutions of compounds **3l**,**m** and **4a**,**b** was performed based on the results of dipole moment measurements. The fact that these compounds occur as the *Z-s-cis* conformers in which intramolecular hydrogen bonds can exist was additionally confirmed by calculations according to the additive scheme as well as by experimental measurements of their dipole moments. Calculations according to the additive scheme were carried out for the isomers and conformers shown in Scheme 2.

Scheme 2



Compound	R¹	R²	R³	Y
3l	Me	EtO	2-furyl	O
3m	Ph	Ph	2-furyl	O
4a	Ph	Ph	Me	O
4b	Ph	Ph	Me	S

Table 3. Calculated and experimental dipole moments of 3-hydroxy-2-phosphoryl(thiophosphoryl)acrylonitriles **3l**,**m** and **4a**,**b** in benzene

Compounds	μ_{calc}/D				μ_{exp}/D
	Z isomer		*E* isomer		
	s-cis	*s-trans*	*s-cis*	*s-trans*	
3l	2.51	5.89	2.02	6.46	1.89
3m	2.59	5.96	2.41	6.62	2.17
4a	2.62	6.12	2.14	7.79	2.55
4b	3.29	6.67	2.05	8.13	3.36

Actually, there are much more theoretically possible conformers (for example, conformers which differ in the rotation of the furyl ring with respect to the furyl—C_{sp^2} bond are not presented; however, their polarity is independent of the internal rotation about this bond and, hence, these conformers were not considered).

The results of calculations and experimental values are given in Table 3.

In the calculations, we used the following bond angles (ω/deg) determined by X-ray diffraction analysis of compounds **4a**,**b**:

Angle	ω/deg	
	4a	**4b**
C_{sp^2}—P=O	108	112
C=C—OH	122	124
Me—C—OH	113	112
C=C—Me	124	124
C=C—CN	120	118
C_{Ph^1}—P—C_{Ph^2}	108 [3]	106 [2]

The geometric parameters for compound **3m** were taken by analogy with compounds **4a**,**b**.

3l:

Angle	ω/deg	Angle	ω/deg
C=C—CN	120 [3]	P—O—Et	120 [10,11]
O—P—Me	104 [8]	C=C—furyl	120
O=P—C_{sp^2}	115 [9]	C=C—OH	120
O=P—Me	115 [9]		

The dipole moments of the isomers of conformers of compounds **3l**,**m** and **4a**,**b** were calculated from

Table 4. Coefficients of the equations and orientational polarizations (*P*) of compounds **3l**,**m** and **4a**,**b** in benzene

Compound	α	γ	*P*/cm³
3l	1.842	0.237	72.600
3m	1.534	0	96.624
4a	2.779	0.270	133.321
4b	4.443	0.347	230.111

the following dipole moments (μ) of the bonds and groups:

Bond	μ/D	Reference
$C_{sp^2}\rightarrow P$	0.56	5
$P\Rightarrow O$	3.40	
$P\Rightarrow S$	3.88	12
$C_6H_5\rightarrow P$	1.09	13
$C_{sp^2}\rightarrow CN$	2.81	14
$Me\rightarrow C_{sp^2}$	1.06	5
$C_{sp^2}\rightarrow OH$	0.85 (calculated from μ_{exp} of phenol)	15
$C_{sp^2}\rightarrow$furyl	0.21 (calculated from μ_{exp} of vinylfuran)	16
$Me\rightarrow P$	0.83	17
$O\rightarrow P$	0.51	12, 18
$Et\rightarrow O$	1.17	8

The dipole moments were determined in benzene at 25 °C according to a procedure described earlier.[19] The calculated and experimental dipole moments of compounds **3l**,**m** and **4a**,**b** are listed in Table 3. The coefficients of the equations used for calculations and the orientational polarizations of the compounds under consideration are given in Table 4.

It should be noted that the compounds under study possess low polarities. It is well known[7] that low dielectric permeabilities and, correspondingly, small dipole moments are typical of compounds stabilized by intramolecular hydrogen bonds, whereas large dipole moments are characteristic of compounds with intermolecular hydrogen bonds in which non-cyclic association takes place. A comparison of the experimental and calculated dipole moments provided unambiguous evidence that in none of the compounds under study do the *s-trans* conformers of the *E* and *Z* isomers occur under the above-mentioned conditions. In compounds **4a** and **4b**, the experimental dipole moments are virtually equal to those calculated for the *Z-s-cis* conformers. Therefore, hydrogen bonding plays a decisive role even in the case of the P=S bond, which is less prone to hydrogen bonding compared to the phosphoryl group. This conclusion is in complete agreement with the IR spectroscopic data. The calculated dipole moments of the *Z-s-cis* and *E-s-cis* conformers of compounds **3l**,**m** are slightly greater than the experimental values. It can only be unambiguously stated that the *s-trans* conformers (in which intramolecular hydrogen bonding cannot occur) are impossible for both the *Z* and *E* isomers of enols (see Table 3). Hence, according to the spectroscopic data, it can be assumed that the compounds under consideration exist as the *Z-s-cis* conformers in which intramolecular hydrogen bonding is possible. It should also be noted that an analogous decrease in the experimental dipole moments of molecules stabilized by intramolecular hydrogen bonds compared to those of similar compounds in which such hydrogen bonds are absent has been observed earlier.

It is evident that there are additional (although weak) interactions (in addition to intramolecular hydrogen bonding characteristic of all compounds under investigation) in solutions of compounds **3l**,**m**, containing the furyl substituent, in CH_2Cl_2 and CCl_4. According to the recent results of X-ray diffraction analysis, which will be published elsewhere, this compound and its thienyl analog adopt conformations in which the oxygen or sulfur atom of the heterocycle lies on the same side of the ring with respect to the double bond as the oxygen atoms of the P=O and OH groups (Table 5, left column, the last row), although the hydrogen atom of the hydroxy group is involved in intramolecular hydrogen bonding.

Quantum-chemical calculations at the B3LYP/6-31G(d) level of the hybrid density functional theory provided theoretical explanation for the preference of the *Z-s-cis* conformation stabilized by an intramolecular hydrogen bond for compounds **3k**,**l**,**m** and **4a**,**b**.* The relative energies and polarities of the possible conformers of diphenylphosphine oxide **3m** are given in Table 5 as an example. Analysis of the relative energies of the *E* and *Z* isomers unambiguously showed that these compounds exist as the *Z* isomers, the global energy minimum corresponding to the conformers with the *s-cis* orientation of the C=C and P=O or P=S bonds. It should be noted that this result for compounds **3k**—**m** containing the furyl substituent is independent of the orientation of the oxygen atom of the furyl ring with respect to the C=C double bond (*syn* or *anti*). The theoretical possibility[7,20] of the involvement of the oxygen atom of the furyl ring in hydrogen bonding with the hydroxy group was not supported by the experimental spectroscopic data for the *Z-s-cis* conformer with the mutual *anti* arrangement of this oxygen atom and the C=C bond (ΔE = 10.85 kcal mol^{-1} for phosphonate **3k**, 12.33 kcal mol^{-1} for phosphinate **3l**, and 12.72 kcal mol^{-1} for diphenylphosphine oxide **3m**). It should also be noted that the quantum-chemical calculations for compounds **3l**,**m**, **4a**, and **4b** adequately reproduce their experimental dipole moments. The experimental data on the polarity of phosphonate **3k** are lacking in the literature. However, based on the data on dipole moments of this class of compounds,[12] it can be assumed that the experimental dipole moment of **3k** is similar to μ_{exp} of compound **3l**, *i.e.*, its polarity is also adequately reproduced by quantum-chemical calculations. In addition, we carried out quantum-chemical calculations of the polarities of the same compounds in benzene, *i.e.*, in the solvent in which their experimental dipole moments were determined. In these calculations, the effect of the

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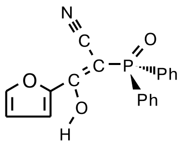
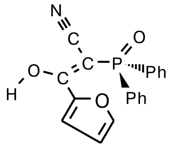
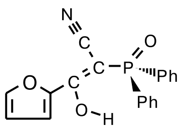
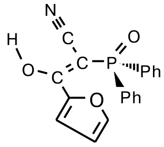
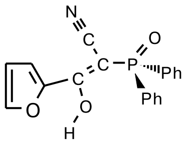
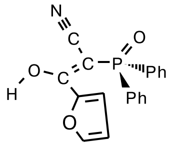
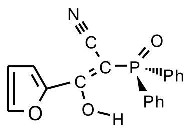
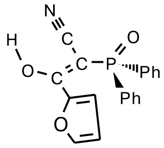
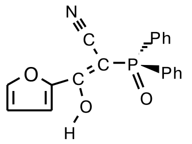
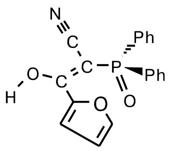
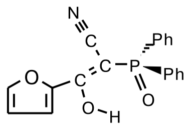
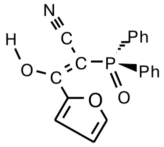
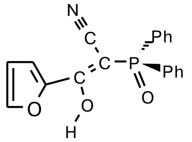
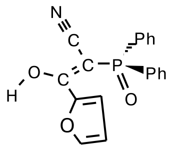
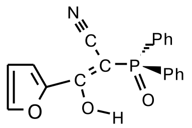
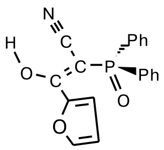
* The characteristics of the compounds (geometric parameters, frequencies, total energies, *etc.*) determined by *ab initio* calculations will be published elsewhere.

Table 5. Results of quantum-chemical calculations of the relative energies and dipole moments of diphenylphosphine oxide **3m**

Conformers of *Z* isomer	ΔE /kcal mol^{-1}	μ/D	Conformers of *E* isomer	ΔE /kcal mol^{-1}	μ/D
	19.05	9.30		22.60	10.87
	15.91	8.32		16.91	8.76
	14.59	8.76		22.78	11.51
	15.54	7.39		20.08	8.88
	17.37	6.53		17.30	4.58
	0.00	0.48		12.75	4.12
	12.72	5.56		12.87	4.26
	0.72	1.08		11.81	4.24

solvent was taken into account within the framework of the polarization continual model (IPCM).[21] The following data were obtained for the *Z-s-cis* conformers of all five compounds: 3.11 D for **3k**, 2.36 D for **3l**, 1.21 D for **3m**, 2.17 D for **4a**, and 1.52 D for **4b**. It appeared that the dipole moments calculated in solutions differ only slightly from those in the gas phase and also adequately reproduce the experimental values. This fact, along with the IR spectra and the experimental dipole moments, is additional evidence for the absence of strong interactions between the compounds under study and benzene.

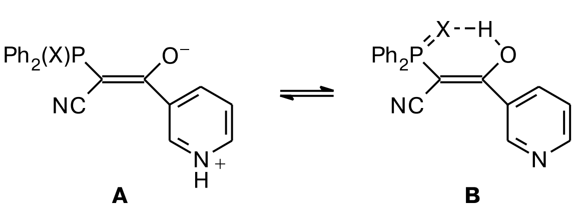
It should also be noted that, according to the results of quantum-chemical calculations, the distance between the oxygen atom of the P=O group and the hydrogen atom of the OH group in the *Z-s-cis* conformers of compounds **3m** and **4b** is 1.596 Å (the sum of the van der Waals radii of the O and H atoms is equal to 2.6 Å). The corresponding distance between the sulfur atom of the P=S group and the hydrogen atom of the OH group is 2.072 Å (the sum of the van der Waals radii of the S and H atoms is equal to 3.05 Å). These values are in good agreement with the known ranges of the geometric parameters[20] for hydrogen bonds.

To summarize, we carried out experimental and theoretical conformational analysis of 2-phosphorus-substituted acrylonitriles **3k—m** and **4a**,**b**. Information obtained by physical methods altogether (X-ray diffraction analysis, IR spectroscopy, dipole moment measurements, and quantum-chemical calculations) provided a self-consistent detailed knowledge of their fine structures in the individual form and in solution.

It should be noted that, according to the IR spectroscopic data, the structures of individual compounds **3n**,**o** differ from the structures of all other analogous acrylonitriles with both the 3-alkyl and 3-aryl(hetaryl) substituents prepared by us. The IR spectra of compounds **3n**,**o** in solutions in CH_2Cl_2 have absorption bands of the CN group at 2200 and 2195 cm^{-1}, respectively, and absorption bands of the double bond at 1565 and 1600 cm^{-1} (shoulder, 1630 cm^{-1}), which is typical of the cyclic form of the *Z* isomers of enols with such structures stabilized by intramolecular hydrogen bonds. For compound **3n**, the absorption of the P=O group is observed at 1120 cm^{-1}. In the IR spectra of these compounds in the solid state (KBr), an unusually intense absorption band of the cyano group appears already at 2180 cm^{-1} and an absorption band of the C=C bond is observed at 1550 cm^{-1}. It should be noted that similar frequencies of these functional groups have been observed earlier[22] for chelate salts of such enol forms, *i.e.*, a decrease in the frequencies of the bands of these groups is accounted for by delocalization of the negative charge over the conjugation chain. In addition, the absorption is observed as a diffuse broad signal in the region of 1900—3000 cm^{-1} corresponding to the NH group.

Taking into account that the positions of the signals and chemical shifts in the $^{31}P-\{^1H\}$ and ^1H NMR spectra of compounds **3n**,**o** are similar to those for all other compounds (see Table 2), it can be assumed that these compounds in the individual form (**A**) occur as zwitterions of the corresponding *Z* isomers of acylacetonitriles (the proton transfer to the nitrogen atom of the heterocyclic fragment), whereas the cyclic form of the *Z* isomer stabilized by an intramolecular hydrogen bond with the oxygen atom of the phosphoryl group or the sulfur atom of the thiophosphoryl group, respectively, occurs in solution (**B**) (Scheme 3). This assumption cannot be confirmed by X-ray diffraction analysis because these compounds were obtained as amorphous powders.

Scheme 3



Experimental

The NMR spectra were recorded on Bruker WP-200SY and Bruker AMX-400 instruments for solutions in $CDCl_3$ and C_6D_6 using the residual signals for the protons of the deuterated solvents as the internal standard (^1H, ^{13}C) and 85% H_3PO_4 as the external standard (^{31}P). The IR spectra were measured in KBr pellets on a Nicolet Magna-IR750 Fourier spectrometer (resolution was 2 cm^{-1}, acquisition number was 128) and for solutions in CH_2Cl_2 with concentrations c = 0.02, 0.01, and 0.004 mol L^{-1} (d = 0.5 mm) on a UR-20 instrument and on a Specord-M80 spectrometer (Nujol and solutions in CH_2Cl_2 and CCl_4).

The dipole moments were measured in benzene at 25°C on an IDM-2 instrument according to a procedure reported earlier.[19]

All calculations were carried out with the use of the GAUSSIAN 98 program (see Ref. 23) at the B3LYP level of the hybrid density functional theory with the 6-31G(d) basis set on a Pentium IV computer (1500 MHz). Calculations of the energies were performed taking into account the correction for the zero-point energy.

Acylation was carried out in MeCN without additional purification using finely dispersed solid KOH (Aldrich). Acid chlorides **2** were prepared by the reactions of the corresponding commercially available acids with $SOCl_2$ and used for acylation without additional purification.

3-Aryl(hetaryl)-3-hydroxy-2-phosphorylacrylonitriles (3) (general procedure). A solution of the corresponding acid chloride **2** (0.012 mol) in MeCN (10—15 mL) was added dropwise with stirring to a mixture of the corresponding (thio)phosphorylacetonitrile **1** (0.01 mol) and powdered KOH (0.025 mol) in MeCN (30 mL). The reactions with phosphorylacetonitriles were carried out in the absence of the catalyst (autocatalysis). In the case of acylation of compound **1d**, triethylbenzylammonium chloride or Bu_4NCl (5 mol.%) was added to a mixture of the starting organophosphorus substrate and KOH, after which the reaction mixture was additionally stirred at ~20 °C for 2 h and concentrated to dryness. Dichloromethane (50 mL) and 8% HCl (15 mL) were added to the residue. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3×25 mL). The combined extracts were dried with Na_2SO_4 and concentrated. The product was purified by chromatography (in some cases, after pre-distillation) or recrystallization (see Table 1).

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