Reviews

Acylation of phosphoryl- and thiophosphorylacetonitriles under phase transfer catalysis conditions and the keto-enol tautomerism of phosphorus-substituted acylacetonitriles

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A procedure was developed for acylation of phosphoryl- and thiophosphorylacetonitriles under phase transfer catalysis conditions. The reaction in the solid KOH/MeCN system afforded *C*-acylation products in high yields. In the individual state and in aprotic solvents, these products exist in the enol form (*Z* isomers) stabilized *via* a strong intramolecular hydrogen bond. In hydroxyl-containing media and in aprotic bipolar solvents, these compounds exist as a mixture of two geometric isomers (*E* and *Z*) of the corresponding enols. In this case, the *Z* isomer exists in two forms, namely, in the cyclic form with an intramolecular hydrogen bond and in the open form stabilized by intermolecular hydrogen bonds with the solvent. The results of X-ray diffraction analysis of both forms of *Z* isomers of the compounds containing the phosphoryl and thiophosphoryl groups are discussed.

Key words: phase transfer catalysis; phosphorylacetonitriles, thiophosphorylacetonitriles, acylation; *Z* and *E* isomers of enols, hydrogen bond; X-ray diffraction analysis; NMR spectra.

The method of phase transfer catalysis (PTC) has long been successfully used in the chemistry of organophosphorus compounds.[1] The characteristic feature of organophosphorus compounds is the fact that they can perform different functions, namely, act as substrates generating carbanions and phosphanions, as electrophilic agents participating in phosphorylation of RO, RS, and R_2N anions, and as phase-transfer catalysts (in the forms of phosphonium salts, amidophosphates, phosphoryl sulfones, phosphoryl sulfoxides, methylenediphosphonates, and some other compounds). Phase transfer catalysis is used for performing various transformations of organophosphorus compounds such as the Wittig, Horner, Atherton—Todd, and Pudovik reactions. This method has found particularly wide application in the Michaelis—Becker reaction (alkylation of phosphanions).[1] Recently,[2] this interaction under PTC conditions has also been successfully performed in the case of hydrothiophosphoryl compounds. Based on the resulting compounds, various derivatives of thioacids of phosphorus, which are difficultly accessible under classical conditions, can be synthesized in high yields.

Many works have been devoted to alkylation of carbanions of CH-acids, including phosphorus-substi-

† Deceased.

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Table 1. Equilibrium CH-acidity of phosphoryl- (**1**) and thiophosphorylacetonitriles (**2**) $R^1R^2P(X)CH_2CN$ in DMSO (K^+ as the counter ion) and the yields of acylation products $[R^1R^2P(X)](CN)C{=}C(OH)R^3$ (**5** and **6**) when the heterophase KOH(s)/MeCN system was used

Compound	R^1R^2	pK		Product	R^3	Yields of acylation products (%)[a]		
		X = O	X = S			X = O	X = S	
							without a catalyst	in the presence of Bu_4NY[b]
1a, 2a	$(EtO)_2$	17.1	15.4	**5a, 6a**	Me	93 (85)	54 (40)	80 (67)
				5b	Ph	68 (56)	—	—
1b	$(Pr^nO)_2$	17.3	—	**5c**	Me	95 (87)	—	—
				5d	Ph	66 (52)	—	—
1c, 2b	$(Bu^nO)_2$	17.5	16.3[c]	**5e**	Me	100 (90)	—	—
				5f, 6b	Et	88 (75)	54 (30)	70 (42)
				5g, 6c	Bu^t	62 (50)	—	15
1d	Me(EtO)	18.3	—	**5h**	Me	75 (63)	—	—
1e	$Me(Pr^iO)$	18.7	—	**5i**	Me	75 (58)	—	—
2c	$Me(Bu^iO)$	18.8[c]	16.7[c]	**5j, 6d**	Me	87 (76)	50 (28)	70(39)
				6e	Ph	—	—	55 (30)
1f	Et_2	19.9	—	**5k**	Me	30 (17)	—	—
1g, 2d	Ph_2	17.3	16.3	**5l, 6f**	Me	79 (70)	—	65 (37)
				5m, 6g	Bu^t	44 (36)	—	14
				5n, 6h	$PhCH_2$	55 (44)	47 (32)	67 (48)
				5o, 6i	$4\text{-}ClC_6H_4$	65 (52)	50 (26)	65(53)
				6j	Ph	—	7	43 (34)

[a] The yield according to the data of ^{31}P NMR spectroscopy; the yields of the purified products are given in parentheses.
[b] Y = Cl or HSO_4.
[c] Calculated according to the correlation equations for thiophosphoryl CH-acids.[8]

tuted derivatives, under phase transfer catalysis conditions.[1] However, acylation of compounds of this type under PTC conditions was described only for phosphorus-free organic compounds. Thus, the following reactions have been reported: acylation of phenylacetonitrile[3] in the $K_2CO_3(s)/C_6H_6$/dibenzo-18-crown-6 system, which occurs at the carbon atom of the CH_2 group, and *O*-acylation of β-dicarbonyl compounds[4] (2 *N* NaOH/CH_2Cl_2/Bu_4NHSO_4; the yields were 83—98%) and sterically hindered phenols[5] under conditions of ion-pair extraction (NaOH(s)/dioxane/Bu_4NHSO_4; the yields were 64—90%). The PTC method has not been previously used for acylation of phosphorus-substituted CH-acids, for example, of phosphorylacetonitrile, phosphorylacetone, or their thio analogs, although these reactions are of obvious interest as a convenient preparative procedure for the synthesis of functionally substituted phosphorylated CH-acids.

Previously,[6] acylation of potassium derivatives of dialkoxyphosphorylacetonitriles has been studied under classical conditions in nonaqueous media. According to the published data,[6,7] *C*-acylation products, which were prepared under these conditions in 15—30% yields, occurred as equilibrium mixtures of tautomers with variable contents of the ketone and enol forms.*

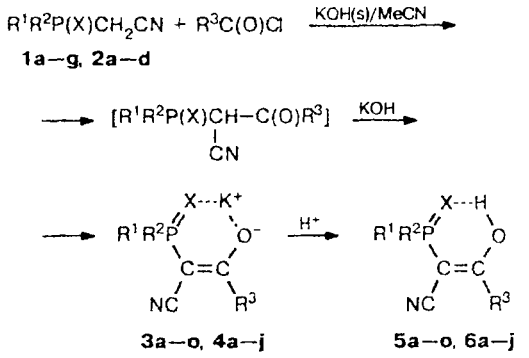
In the case of application of the PTC method to CH-acids, a knowledge of the acidity of these acids and, correspondingly, of the nucleophilicity of their carbanions, is of great importance. Because of this, the CH-acidities of the initial phosphoryl- (**1**) and thiophosphorylacetonitriles (**2**) in DMSO were measured by the indicator method.[8,9] The results of these measurements are given in Table 1. As can be seen from Table 1, compounds **1** and **2** belong to CH-acids of medium strength (pK = 15.4—19.9), and the thiophosphoryl derivatives are, on the average, one unit of pK stronger than the phosphoryl analogs. It follows from the above-mentioned data that the phosphorus-substituted acetonitriles under study belong to CH-acids that are rather highly reactive under PTC conditions.

We have established that under PTC conditions, like under classical conditions,[6,7] acylation of phosphorylacetonitriles **1** containing different substituents at the P atom occurs at the central C atom. It should be mentioned that under the reaction conditions (an excess of alkali), *C*-acyl derivatives were completely converted into chelate salts **3** of enol forms (*Z* isomers).[10,11] After the reaction mixtures were acidified, target products **5** were isolated in high yields (Scheme 1). According to the spectral data and the results of X-ray diffraction studies, products **5** exist in the corresponding enol forms.

It has been found that under optimum reaction conditions, the maximum yields of the target compounds were achieved in the two-phase KOH(s)/MeCN

* According to the results of bromometric titration and IR spectroscopy.

Scheme 1



X = O (**1**, **3**, **5**), S (**2**, **4**, **6**)

$R^1 = R^2$ = EtO, R^3 = Me (**5a**, **6a**), Ph (**5b**)
$R^1 = R^2$ = Pr^nO, R^3 = Me (**5c**), Ph (**5d**)
$R^1 = R^2$ = Bu^nO, R^3 = Me (**5e**), Et (**5f**, **6b**), Bu^t (**5g**, **6c**)
R^1 = Me, R^2 = EtO, R^3 = Me (**5h**)
R^1 = Me, R^2 = Pr^iO, R^3 = Me (**5i**)
R^1 = Me, R^2 = Bu^tO, R^3 = Me (**5j**, **6d**), Ph (**6e**)
$R^1 = R^2$ = Et, R^3 = Me (**5k**)
$R^1 = R^2$ = Ph, R^3 = Me (**5l**, **6f**), Bu^t (**5m**, **6g**), $PhCH_2$ (**5n**, **6h**), 4-ClC_6H_4 (**5o**, **6i**), Ph (**6j**)

system at a substrate : acyl halide : alkali ratio of 1.0 : 1.2 : 2.5 (see Table 1).*

Generally, the reactions with highly electrophilic normal alkanoyl chlorides are carried out at 0—10 °C. When sterically hindered pivaloyl chloride, lesser electrophilic phenacyl chloride, or aroyl chlorides are used, higher temperatures (45—60 °C) are required.

The yields of compounds **5** change in parallel with the CH-acidity of the initial substrate, all other factors being the same. Thus, the reactions of phosphorylacetonitriles **1a—c** (with $pK \approx 17$) with acetyl chloride afforded acyl derivatives **5a,c,e** in nearly quantitative yields. For phosphorylacetonitriles with $pK \approx 18.5$ and 20, the yields were 75 and 30% (**5h,i** and **5k**), respectively. The yields of the final products also decrease as the electrophilicity decreases and steric hindrances in the molecule of the acylating agent increase. Apparently, the governing stage in this reaction involves generation of the carbanion. Consequently, steric hindrances to the formation of the intermediate state are of importance. Thus, acylation of diphenylphosphorylacetonitrile **1g** with acetyl chloride afforded the final product **5l** in 79% yield. The reaction of compound **1g** with phenacyl chloride gave product **5n** in 55% yield, while the reaction of **1g** with pivaloyl chloride gave enol **5m** in a yield of only 44%.

* When an approximately equimolar amount of alkali was used, the reaction afforded enol **5** rather than its salt (the yield was <50%), and a portion of the CH-acid remained unconsumed.

In the case of phosphorylacetonitriles **1**, the use of the systems applied for acylating purely organic compounds[3—5] affords acyl derivatives **5** in low yields (<55%). Moreover, in solvents such as benzene and dichloromethane, side reactions, namely, dealkylation of alkoxy groups at the P atom (compounds **1a—e**), hydrolysis of the nitrile group in the case of compounds containing the phosphine oxide group (**1f,g**), the cleavage of the P—C, predominate. In solvents such as DMF, dioxane, diethyl ether, and THF, a substantial portion of the initial phosphorylacetonitrile does not enter the reaction. A change from KOH to solid NaOH leads to a decrease in the yield, on the average, by 10—15%.

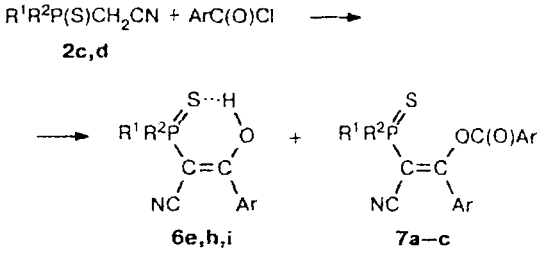
Acylation of thiophosphorylacetonitriles **2** proceeds also at the central C atom,[12] but the yields of reaction products **6** are lower than those obtained in the case of compounds containing the P=O group (see Table 1). Apparently, this is attributable to a decrease in the rate of acylation due to the lower nucleophilicity of the carbanion containing the thiophosphoryl group as well as to an increase in the steric hindrance due to the larger van der Waals radius of the S atom. Compounds **6**, like their analogs containing the phosphoryl group, exist exclusively in the enol form.

Acylation of phosphorus-substituted acetonitriles **1** and **2** occurs both in the case of catalysis with tetraalkylammonium salts (for example, Bu_4NHSO_4 or Bu_4NCl) and under phase transfer conditions without a catalyst. In the case of thiophosphorylacetonitriles **2**, the absence of a catalyst leads to a substantial decrease (by 25—30%) in the yields of the target compounds, while the presence of a catalyst has virtually no effect on the yields of their P=O analogs. Phosphorylacetonitriles **1** in themselves act as efficient catalysts of phase transfer to form, apparently, complexes with potassium ions, which readily pass into the acetonitrile volume.

As for by-products of the reactions of compounds **1** containing the P=O group in the KOH(s)/MeCN system, the cleavage of the P—C bond of the initial phosphorus component occurs to only a small extent to give R^1R^2POOH acids.[10] This hydrolysis is nontypical of thiophosphorylacetonitriles **2**, and a portion of the initial compound usually remains unconsumed. The reactions of thiophosphorylacetonitriles **2** with aroyl chlorides afforded (even when they were taken in an equimolar ratio) *C,O*-diacylation products **7** as the major by-products along with the target products **6** (Scheme 2).[11,12]

The yields of the compounds **7** increase substantially when dichloromethane rather than acetonitrile is used as the organic phase and 50% aqueous alkali is used as the base. The fact that the reaction proceeds in the above-mentioned direction only in the case of aromatic acyl halides is attributable to the ratio between the rates of two processes, namely, hydrolysis of acyl halide and *O*-acylation, under the reaction conditions: for aliphatic compounds, the rate of the former process is substan-

Scheme 2

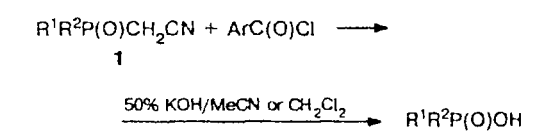


$R^1 = R^2 = Ph$; $R^1 = Me$, $R^2 = Bu^tO$; Ar = Ph, 4-ClC_6H_4

tially higher, while for aromatic compounds, the rates of two processes are, apparently, similar. Evidently, the fact that this result was observed only for the thio derivatives is attributable to the smaller strength of the P=S...M^+ bond in the chelate salt of the enol.

Note that when acylation of phosphorylacetonitriles **1** was carried out under analogous conditions (in the presence of aqueous alkali), the cleavage of the P—C bond in the molecules of the initial compounds was the predominating process (>80%). In addition, *C*-monoacylation proceeded to a small extent (Scheme 3).

Scheme 3



As mentioned above, according to our data, compounds **5** and **6** exist in the corresponding enol forms. We did not detect the presence of ketone forms, at least within the sensitivity of the methods used, although the structures of the resulting compounds were thoroughly studied both in the pure form and in solvents with different polarity (pentane, C_6D_6, $CDCl_3$, CCl_4, acetone-d_6, MeCN, DMSO, DMF, MeOH, and a 75% EtOH solution) by NMR (^1H, ^{13}C, and ^{31}P) and IR spectroscopy (Table 2) and X-ray diffraction analysis.[10—14]

The enol form in the liquid state, in aprotic solvents, and in the crystal is the only geometric cyclic *Z* isomer stabilized *via* a strong intramolecular hydrogen bond. The IR spectra of this compound have an intense absorption band in the region of 1550—1610 cm^{-1}, which is typical of a double bond in the enol forms of ketones, while the absorption band of the carbonyl group is absent. In the ^{31}P NMR spectra of compounds **5** and **6**, which were recorded in the absence of a solvent or in pentane, C_6D_6, $CDCl_3$, CCl_4, acetone-d_6, or MeCN, a single singlet signal is observed in the region corresponding to the above-mentioned environment of the P atom. The ^{13}C NMR spectra show a typical system of doublet signals for olefin carbon atoms in the regions of δ 67.4—78.9 (d, P—C(1)=) and 180.7—197.1 (d or s, =C(2)—R). The value of the direct spin-spin coupling constant $^1J_{PC}$ is 40—66 Hz larger than the value of $^1J_{PC}$ for the initial compounds **1** and **2**, which is indicative of sp^2-hybridization of the C(1) atom (according to the published data[15]). In the ^1H NMR spectra of the *C*-acetylation products (R^3 = Me), signals for the protons of the methyl group at the double bond occur as singlets, which is typical of the *trans* arrangement of this group with respect to the P atom in vinylphosphonates.[16] The position of the signal for the hydroxyl proton in the ^1H NMR spectra of compounds **5** and **6** remains unchanged as the solvents are diluted, which is indicative of the presence of an intramolecular hydrogen bond. The presence of this bond is also confirmed by the fact that the IR spectra in the above-mentioned solvents remain unchanged as the solvents were diluted repeatedly.

X-ray diffraction studies of single crystals of (diphenylphosphoryl)acetylacetonitrile **5l** and its thiophosphoryl analog **6f** (Fig. 1) confirmed the enol structures of the compounds with the *cis* orientation of the hydroxyl group and the phosphoryl (or thiophosphoryl) fragment with respect to the C(2)=C(3) double bond. The principal geometric parameters of compounds **5l** and **6f** are given in Table 3. In the molecules, a strong intramolecular hydrogen bond occurs, which leads to closure of the virtually planar six-membered ring. The length of the corresponding O—H...O=P hydrogen bond is 2.551(2) Å. The length of the O—H...S=P bond in the compound containing the P=S group is 2.991(3) and 3.033(3) Å (for two independent molecules). Taking into account the difference (0.55 Å) between the van der Waals radii of the O and S atoms (1.29 and 1.84 Å, respectively[17]), the hydrogen bond in the compound containing the thiophosphoryl group can also be assigned to strong bonds. The structural features of this hydrogen bond have been previously discussed in detail.[13] Note that the geometry of the P—C=C(OH)Me fragment remains virtually unchanged within the experimental error.

In the ^{31}P NMR spectra of compounds **5** and **6** in solvents that tend to be involved in hydrogen bonding (DMSO, DMF, and CD_3OD), two singlet signals are observed, while the ^{13}C NMR spectra have two similar systems of signals typical of the enol forms of acylated phosphoryl(thiophosphoryl)acetonitriles. The values of the intensities of the signals in the ^{31}P and ^{13}C NMR spectra correlate with each other, *i.e.*, compounds **5** and **6** in the above-mentioned solvents exist as two geometric isomers (*Z* and *E*) of the corresponding enols.*

Apparently, two forms of *Z* isomers (the cyclic form **A** stabilized *via* an intramolecular hydrogen bond and the open form **B** stabilized *via* hydrogen bonds with the

* In the ^{31}P NMR spectrum, the signal corresponding to the *E* isomer is observed at higher field than the signal of the *Z* form.

Table 2. Selected parameters of IR spectra and ^{31}P and ^{13}C NMR spectra of the enol forms of phosphoryl(thiophosphoryl)acylacetonitriles $[R^1R^2P(X)](CN)C(1)=C(2)(OH)R^3$ **5** (X = O) and **6** (X = S)

Compound	R^1R^2	R^3	IR, νC=C /cm^{-1}	NMR, δ (*J*/Hz) in $CD_3C(O)CD_3$ (**5a—n**, **6i**), C_6D_6 (**6a**) $CDCl_3$ (**6b—h,j**)				in CD_3OD			
				Isomer	δP	δC(1) ($^1J_{PC}$)	δC(2) ($^2J_{PC}$)	Isomer	δP	δC(1) ($^1J_{PC}$)	δC(2) ($^2J_{PC}$)
5a	$(EtO)_2$	Me	1608	*Z*	20.52	71.01 (191.7)	188.22 (4.5)	*Z*	18.38	71.45 (195.0)	187.97
								E	16.58	70.58 (192.3)	186.75
5b	$(EtO)_2$	Ph	1605	*Z*	21.17	—	—	—	—	—	—
								—	—	—	—
5c	$(Pr^nO)_2$	Me	1600	*Z*	20.52	70.64 (199.3)	187.99 (4.5)	*Z*	18.40	71.97 (202.5)	187.80
								E	16.60	69.87 (200.0)	185.32 (6.7)
5d	$(Pr^nO)_2$	Ph	1605	*Z*	21.77	69.82 (187.8)	182.96 (5.9)	*Z*	19.82	82.22 (182.1)	187.52 (21.4)
								E	14.78	78.90 (162.0)	188.31 (5.0)
5e	$(Bu^nO)_2$	Me	1605	*Z*	20.58	71.20 (192.1)	188.02 (4.5)	*Z*	18.40	72.07 (198.8)	187.92
								E	16.58	69.87 (182.0)	187.41 (8.9)
5f	$(Bu^nO)_2$	Et	1585	*Z*	20.91	69.70 (191.3)	191.91 (3.7)	*Z*	19.70	—	—
								E	17.48	—	—
5g	$(Bu^nO)_2$	Bu^t	1585	*Z*	23.50	67.38 (186.9)	197.11(3.5)	*Z*	22.70	—	—
5h	Me(EtO)	Me	1605	*Z*	51.67	72.82 (129.5)	188.53	—	—	—	—
								—	—	—	—
5i	$Me(Pr^iO)$	Me	1605	*Z*	50.21	73.30 (128.9)	188.17 (9.9)	*Z*	48.55	74.20 (131.8)	187.13
								E	46.08	74.04 (125.8)	187.98
5j	Et_2	Me	1610	*Z*	63.50	69.24 (96.1)	189.49	*Z*	60.80	71.85 (101.7)	188.14
								E	52.43	71.71 (97.4)	185.40
5k	Ph_2	Me	1600	*Z*	38.47	71.81 (110.6)	189.41	*Z*	36 52	74.50 (112.4)	188.52
								E	29.34	*	*
5l	Ph_2	Bu^t	1570	—	—	—	—	*Z*	40.44	68.22 (106.4)	198.90
5m	Ph_2	$PhCH_2$	1585	*Z*	38.74	72.10 (110.7)	189.96	—	—	—	—
5n	Ph_2	4-ClC_6H_4	1580	*Z*	40.50	—	—	*Z*	38.25	—	—
6a	$(EtO)_2$	Me	1590	*Z*	71.70	78.93 (161.3)	184.88 (9.4)	*Z*	79.21	82.55 (181.7)	183.33
								E	74.32	81.04 (165.0)	183.65 (4.3)
6b	$(Bu^nO)_2$	Et	1580	*Z*	71.70	76.17 (159.2)	188.84 (7.4)	*Z*	81.05	82.22 (182.1)	187.52 (21.4)
								E	75.87	78.90 (162.0)	188.31 (5.0)
6d	$Me(Bu^iO)$	Me	1580	*Z*	77.51	76.43 (106.8)	185.53 (5.1)	*Z*	81.05	82.19 (131.8)	183.16
								E	75.87	79.81 (106.8)	184.13 (3.2)
6e	$Me(Bu^iO)$	Ph	1565	*Z*	79.83	—	—	—	—	—	—
								E	81.34	80.92 (100.0)	181.20 (3.4)
6f	Ph_2	Me	1570	*Z*	34.41	73.40 (95.0)	186.83 (2.9)	*Z*	36.52	74.50 (112.4)	188.52
								E	29.34	*	*
6h	Ph_2	CH_2Ph	1580	*Z*	38.42	71.78 (109.0)	189.50	—	—	—	—
								—	—	—	—
6i	Ph_2	4-ClC_6H_4	1550	*Z*	38.40	72.22 (103.8)	180.70 (4.0)	—	—	—	—
6j	Ph_2	Ph	1550	*Z*	37.31	72.42 (92.4)	183.50	—	—	—	—

* Signals are at the background level due to the low content of the isomer in the solution because of the low solubility of the compound in CD_3OD.

solvent) can exist in solvents that can be involved in hydrogen bonding. Two conformers, $\mathbf{B_1}$ and $\mathbf{B_2}$, may correspond to form **B**. Conformer $\mathbf{B_1}$ is formed from **A** due to the rotation about the C—O bond. Conformer $\mathbf{B_2}$ is formed due to the additional rotation about the C—P bond.

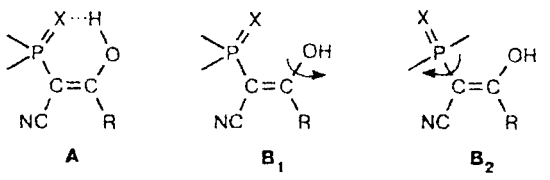


Table 3. Principal geometric parameters of the central fragments of the structures of (diphenylphosphoryl)acetylacetonitrile **5l**, its thio analog **6f**, and (isopropoxymethylphosphoryl)acetylacetonitrile **5i**

Parameter	**5l** (*Z*(A) isomer)	**6f** (*Z*(A) isomer)[a]	**5i** (*Z*(B_2) isomer)
Bond length		*d*/Å	
C(1)—C(2)	1.427(2)	1.425(6)/1.419(6)	1.425(2)
C(2)—C(3)	1.377(2)	1.368(6)/1.359(6)	1.377(2)
C(1)—N(1)	1.151(2)	1.145(6)/1.138(6)	1.147(2)
C(3)—O(2)	1.326(2)	1.330(6)/1.325(6)	1.320(2)
C(3)—C(4)	1.486(2)	1.489(6)/1.480(6)	1.491(2)
P(1)—C(2)	1.787(2)	1.799(4)/1.801(3)	1.792(2)
P(1)—X	1.501(2)	1.965(2)/1.968(2)[b]	1.489(1)
Bond angle		ω/deg	
O(1)—P(1)—C(2)	107.8(1)	112.5(1)/112.6(1)[b]	107.8(1)
P(1)—C(2)—C(3)	121.3(1)	127.5(3)/127.3(4)	123.4(1)
C(2)—C(3)—O(2)	122.3(1)	124.7(3)/123.5(4)	118.2(2)
C(1)—C(2)—P(1)	118.4(1)	114.9(3)/115.7(3)	117.2(2)
Torsion angle		φ/deg	
O(1)—P(1)—C(2)—C(3)	−16.8(2)	−2.5(2)/6.7(2)	−164.2(2)
P(1)—C(2)—C(3)—O(2)	−1.7(2)	1.9(3)/0.7(3)	−4.3(2)

[a] The data for two independent molecules are given.
[b] The parameters with the participation of the sulfur atom.

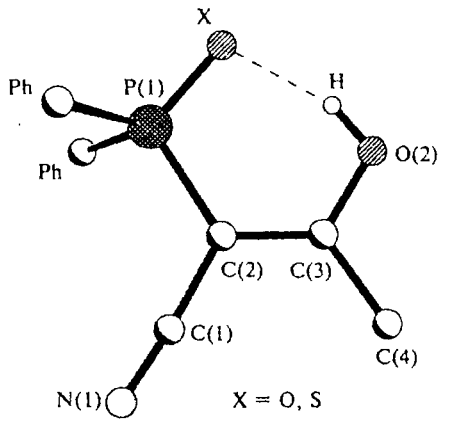


Fig. 1. Overall view of the molecules of the *Z*(A) isomers of the enols of (diphenylphosphoryl)- and (diphenylthiophosphoryl)acetylacetonitriles.

The IR spectra of (dipropoxyphosphoryl)acetylacetonitrile **5b** in methanol and in a 75% aqueous ethanol solution show two absorption bands of the P=O group, namely, the band at 1190 cm^{-1} (as in the spectra of compounds **5** in a thin film and in aprotic solvents) corresponding to the P=O group involved in intramolecular hydrogen bonding and the band at 1240 cm^{-1} corresponding to the free P=O group. In methanol, the absorption of the bonded P=O group is more intense,* while in aqueous ethanol, the more intense absorption band corresponds to the free P=O group.

Therefore, the cyclic form **A** of the *Z* isomer is partially retained in alcoholic and aqueous-alcoholic solutions. As mentioned above, the NMR spectra (^1H, ^{13}C, and ^{31}P) of compounds **5** and **6** have signals corresponding only to two isomeric enol forms. Apparently, the rates of the conformational transitions **A** $\rightleftharpoons$ $\mathbf{B_1}$ and $\mathbf{B_1}$ $\rightleftharpoons$ $\mathbf{B_2}$ are large within the NMR time scale due to which the signals of the cyclic (**A**) and linear (**B**) forms coalesce. Unfortunately, the data of IR spectroscopy also do not allow one to distinguish the *Z*(**B**) and *E* isomers because the frequencies of the P=O and OH groups in these conformers coincide.

As can be seen from Table 4, the contents of the isomeric forms (*Z* and *E*) depend both on the nature of the substituents at the P atom and on the nature of the substituents at the β-C atom. For compounds **5** containing the phosphoryl group, the *Z* isomer predominates (up to 100%), while the content of the *E* isomer with the invariant R^3 substituent is maximum in the case of phosphonates (*Z* : *E* ≈ 80 : 20 in MeOH and 48 : 52 in DMSO). In the case of invariant substituents at the P atom, an increase in the volume of the R^3 radical at the β-C atom leads to an increase in the portion of the *Z* isomer. On the contrary, in the case of thiophosphoryl(acyl)acetonitriles **6**, the content of the *E* isomer is higher than that of the *Z* isomer, which is, apparently, attributable to the lower ability of the S atom to form strong intramolecular hydrogen bonds.

Evidently, configurational inversions in compounds **5** and **6** can occur only with the cleavage of intramolecular hydrogen bonds. These transitions can proceed either through formation of the corresponding keto form

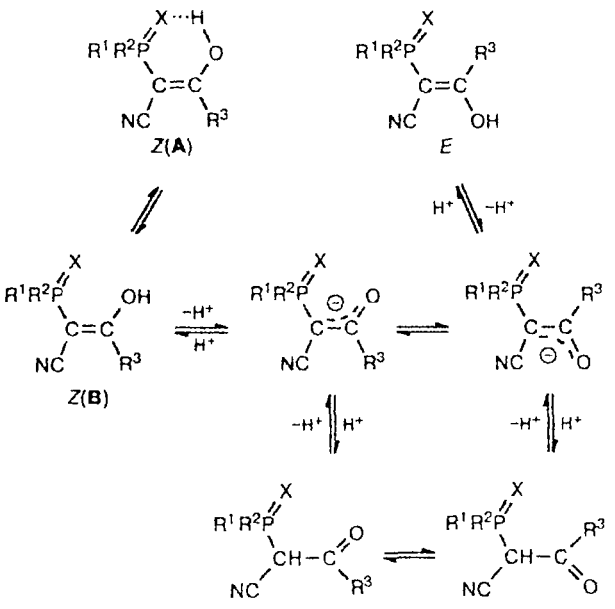
* This may be due to different solvation of the compound in these solvents as well as due to an increase in the content both of form **B** of the *Z* isomer and of the *E* isomer in the aqueous-alcoholic medium.

Table 4. Effective acidities of the enol forms of $R^1R^2P(X)(CN)C{=}C(OH)R^3$ in a 75% EtOH solution and the ratios of the *Z* and *E* isomers in CD_3OD

R^1R^2	R^3	X = O		X = S	
		pK_{eff}	*Z* : *E*	pK_{eff}	*Z* : *E*
$(EtO)_2$	Me	4.40	80 : 20	4.55	32 : 68
$Me(Bu^tO)$	Me	4.64	91 : 9	4.05	10 : 90
Et_2	Me	4.83	96 : 4	—	—
$(Bu^nO)_2$	Et	4.50	84 : 16	4.37	23 : 77
$(Bu^nO)_2$	Bu^t	4.74	100 : 0	—	—
Ph_2	Bu^t	4.40	100 : 0	—	—
Ph_2	$PhCH_2$	4.32	93 : 7	4.28	—
$(Pr^nO)_2$	Ph	4.43	97 : 3	—	—
$Me(Bu^tO)$	Ph	—	—	4.13	0 : 100
Ph_2	4-ClC_6H_4	3.89	100 : 0	3.65	—

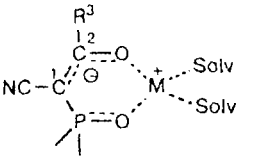
or, in the case of a sufficient acidity of the compounds, through generation of the mesomeric carbanion in which the multiplicity of the C=C bond is smaller and, therefore, conformational transitions are promoted (Scheme 4).

Scheme 4



To estimate these two possibilities, we studied the acidic dissociation of enols of phosphorus-substituted acylacetonitriles **5** and **6** by potentiometry in a 75% ethanol solution. The measured values of pK_{eff} are given in Table 4. Compounds **5** and **6** appeared to be rather strong acids (pK = 3.65—4.83). Because of this, their solutions always contain mesomeric anions at noticeable concentrations due to which the $Z \rightleftharpoons E$ transition can also occur without the participation of the keto form.

Using (diethoxyphosphoryl)acetylacetonitrile **5a** as an example, we also examined stereochemical ratios for salts of enols **5** in different solvents by NMR spectroscopy (^{31}P and ^{13}C). Potassium salt **3a** in acetonitrile exists as a single stereoisomer, namely, as the chelate similar to the cycle having an intramolecular hydrogen bond, with the delocalized negative charge (Solv is the solvent).[10]



Note that the ^{13}C NMR spectrum of this compound is similar to the spectrum of the corresponding enol,[10] but the value of $^1J_{PC}$ is even larger (213.8 Hz), which is indicative of sp^2-hybridization of the C(1) atom. In methanol, in which the salt dissociates, two isomeric forms of the enol are observed in a *Z* : *E* ratio of 40 : 60. For the tetrabutylammonium salt that forms only ionic pairs (apparently, contact ionic pairs exist in acetonitrile, while in methanol the pairs are separated by the solvent), the ratios of the *Z* and *E* isomers are 50 : 50 and 40 : 60 in CD_3CN and CD_3OD, respectively, *i.e.*, in the latter case, this ratio is identical to that observed in the case of the potassium salt in the same solvent. Apparently, this ratio corresponds to the isomer ratio in the mesomeric anion.

It is known that in ether, Cu^{2+} ions interact with *C*-acylated phosphorylacetonitriles to form chelate salts.[18] Because the chelate ring is formed *via Z* anions, we believed that it is possible to use complexation with copper salts for obtaining pure *E* isomers or solvents enriched with *E* isomers from aqueous-ethanolic solutions. However, when half the amount of $CuCl_2$ was used in the reaction with (isopropoxymethylphosphoryl)acetylacetonitrile **5i**, we obtained a crystalline compound whose composition is identical to that of the initial compound but whose melting point is higher (81—82 °C), along with the corresponding copper complex. In the case of the *Z* isomer of this enol stabilized *via* an intramolecular hydrogen bond, the melting point is 64—65 °C.[10]

X-ray diffraction analysis of the resulting compound demonstrated that it exists as conformer $\mathbf{B_2}$ of the *Z* isomer, *i.e.*, it is stabilized *via* intermolecular hydrogen bonds rather than *via* intramolecular hydrogen bonds (Fig. 2). In the crystal, molecules are linked in chains along the *a* axis through hydrogen bonds. Note that the geometry of the P(CN)C=C(OH)—Me fragment remains virtually unchanged on going from conformer **A** to $\mathbf{B_2}$ of the *Z* isomer, *i.e.*, for all compounds, the geometry of this fragment remains virtually unchanged within the experimental error.

Our data on the structures of the products of *C*-acylation of phosphorylacetonitriles are inconsistent with published data on compounds of this type (the content of the keto form varies from 7 to 63%), while the physicochemical constants for compounds with the corresponding radicals are identical,[6,7] which gave impetus to verification of the results of bromometric titra-

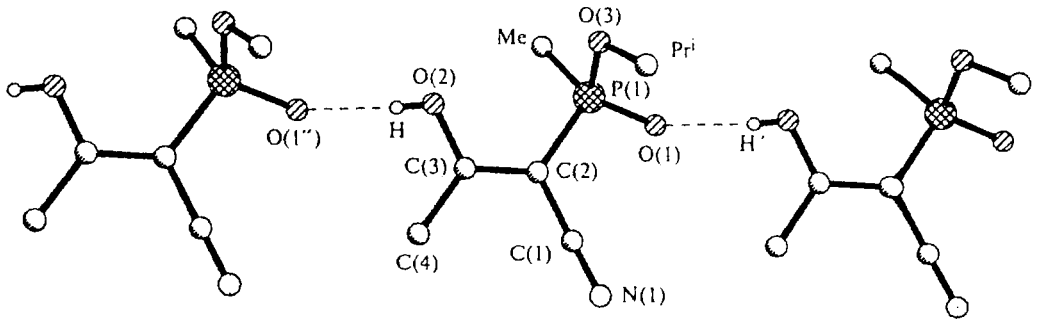


Fig. 2. Scheme of formation of intermolecular hydrogen bonds in the crystal of the $Z(B_2)$ isomer of the enol form of (isopropoxymethylphosphoryl)acetylacetonitrile **5i**.

tion reported in the above-mentioned works. We have established that the results of direct and back bromometric titration of compounds **5** are substantially different. The content of the enol form determined by direct titration is 98%, which agrees with our data on the structures of the compounds under study. The results of reverse titration agree with the data reported in Refs. 6 and 7. It is known[19] that in the case of complex structures the method of reverse bromometric titration can give erroneous results due to incomplete isolation of iodine from KI under the action of the bromination product. Apparently, this is the cause of the erroneous results obtained in Refs. 6 and 7.

* * *

Therefore, we have developed a simple and efficient procedure for acylation of phosphorus-substituted acetonitriles under phase transfer catalysis conditions. The enol structures of the resulting compounds were established by physicochemical methods. The synthesized phosphoryl(thiophosphoryl)acylacetonitriles may be of interest as potential biologically active compounds and synthons for preparing various organic and organophosphorus compounds.

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