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Phosphorus-containing 1,3-zwitterions formed in the reaction of tributylphosphine with 3-aryl-2-cyanoacrylates

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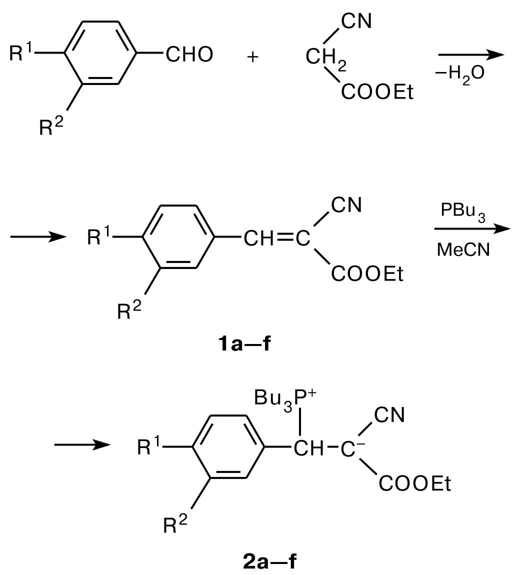
Tributylphosphine reacts with 3-aryl-2-cyanoacrylates in acetonitrile to afford adducts, *viz.*, phosphorus-containing betaines, thermodynamic stability of which depends on both the nature of the solvent and electronic and spatial characteristics of the aryl substituent in 3-aryl-2-cyanoacrylates.

Key words: tributylphosphine, 3-aryl-2-cyanoacrylates, phosphorus-containing zwitterions, X-ray diffraction analysis.

Substituted ethylenes containing electron-withdrawing substituents at the carbon atoms of the double bond easily add rather nucleophilic compounds of trivalent phosphorus to produce the corresponding phosphorus-containing 1,3-zwitterions.[1] We have described[2] the reaction of highly nucleophilic tertiary phosphines with unsubstituted alkyl 2-cyanoacrylates. This allowed involvement of alkyl 2-cyanoacrylates, which usually instantly polymerize under the action of phosphines, in the reaction with trialkylphosphines and triamidophosphites under special conditions. Reactions of 3-substituted 2-cyanoacrylates have not been studied. At the same time, synthesis of phosphorus-containing 1,3-zwitterions substituted with aryl group in the position 3 is of essential interest since it allows considerable extension of the search for the synthesis of potential medicines.

3-Aryl-2-cyanoacrylates[3] **1** were obtained by the Knoevenagel reaction of ethyl cyanoacetate with aromatic aldehydes (Scheme 1).

Scheme 1



1, 2	R1	R2	**1, 2**	R1	R2
a	H	H	**d**	Br	H
b	OH	H	**e**	H	NO_2
c	OMe	H	**f**	NO_2	H

3-Aryl-2-cyanoacrylates **1** are crystalline compounds comparatively well soluble in polar solvents. All of them are formed in a single configuration, since only one signal for the vinyl proton is observed in the ^{1}H NMR spectrum. The attempts to accomplish their reactions with triphenylphosphine or diphenylphosphine aimed at obtaining the corresponding P-zwitterions were unsuccessful. The reactants remained unchanged regardless of the solvent used. However, 3-aryl-2-cyanoacrylates **1** smoothly react with more nucleophilic tri-*n*-butylphosphine in acetonitrile to produce zwitterions **2** (see Scheme 1).

It should be noted that judging from the ^{31}P NMR spectroscopy data ethyl 3-(2,6-dichlorophenyl)-2-cyanoacrylate does not react with tributylphosphine probably due to spatial screening of the reaction center by the chlorine atoms. The yield of zwitterions **2** was almost quantitative based on the ^{31}P NMR spectra of the reaction mixtures in acetonitrile, the isolated yield was 70—90%. The structure of compounds obtained as zwitterions **2** was confirmed by elemental analysis, physicochemical characteristics and X-ray diffraction study (Fig. 1, Table 1).

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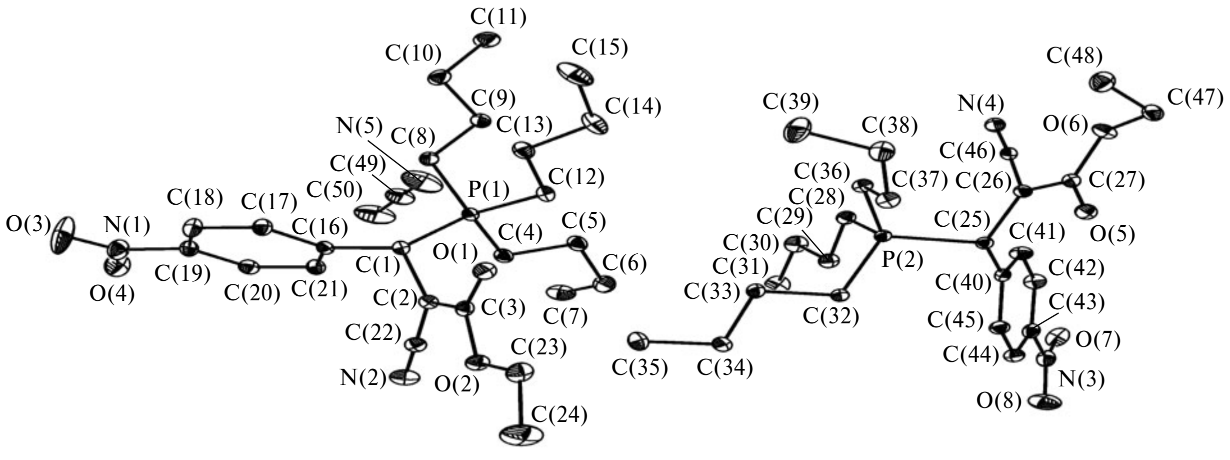

Fig. 1. Molecular structure of zwitterion **2f**.

Table 1. Selected bond lengths (*d*) and bond angles (ω) in molecule **2f**

Parameter	Value
Bond	*d*/Å
O(1)—C(3)	1.2352(13)
O(2)—C(3)	1.3802(13)
N(2)—C(22)	1.1549(15)
C(1)—C(2)	1.5165(14)
C(2)—C(3)	1.4134(14)
C(2)—C(22)	1.4057(14)
O(5)—C(27)	1.2390(12)
O(6)—C(27)	1.3710(12)
N(4)—C(46)	1.1647(14)
C(25)—C(26)	1.5088(14)
C(26)—C(27)	1.4110(14)
C(26)—C(46)	1.4051(14)
Angle	ω/deg
C(1)—C(2)—C(3)	118.66(9)
C(1)—C(2)—C(22)	120.12(9)
C(3)—C(2)—C(22)	121.12(9)
C(25)—C(26)—C(27)	117.84(9)
C(25)—C(26)—C(46)	121.67(9)
C(27)—C(26)—C(46)	120.35(9)

Table 2. Percentage of the zwitterion **2** in various solvents

Solvent	ε	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**
MeCN	37.5	91.3	98.8	96.9	100.0	100.0	100.0
DMSO	48.9	87.9	94.3	95.9	97.7	96.8	98.2
Me_2CO	20.70	40.0	21.6	30.7	21.4	27.9	29.2
$CHCl_3$	4.806	1.1	3.1	1.7	2.5	2.8	3.3
THF	7.4	0	3.8	1.3	2.6	2.2	3.1

The IR spectra show absorption bands of the cyano- and ethoxycarbonyl groups of compound **2** at lower frequencies than analogous ones for the starting cyanoacrylates. Thus, this is the evidence of considerable delocalization of the negative charge in zwitterions **2**. The signals for the methylene protons of the ethoxycarbonyl group appear as two quartets due to the presence of a asymmetric center in molecules **2**. The methylene protons at the phosphorus atom appear as complex multiplets.

All zwitterions obtained undergo dissociation in organic solvents to certain extent to produce the starting tributylphosphine and the corresponding acrylate. Dissociation of these compounds is minimal in acetonitrile and dimethyl sulfoxide, in less polar solvents the degree of dissociation depends on the solvent polarity. The degree of dissociation of zwitterions **2** was determined based on the integrated ratio of signals for the phosphorus atoms in the solution for zwitterion **2** and tributylphosphine. The percentage of zwitterion **2** in the solution after dissolution of crystalline zwitterion **2** in one or another solvent is given in Table 2.

The structure of compound **2f** was determined by X-ray diffraction analysis (see Fig. 1). Compound **2f** contains a chiral carbon atom and crystallizes in the triclinic space group $P1^-$ with two crystallographically independent molecules in the unit cell. Two crystallographically independent molecules differ only in the conformation of the ethoxy group in the carboxylate substituent (the torsion angles C(3)—O(2)—C(23)—C(24) and C(27)—O(6)—C(47)—C(48) are 173.6(1) and −89.8(1)°, respectively). Compound **2f** is a zwitterion containing positive phosphonium and negative carbanion centers. Zwitterionic structure of compound **2f** is stabilized due to the delocalization of the negative charge over the O=C—C—C≡N fragment (see Table 1).

In the crystal, the molecules of compound **2f** are linked through weak hydrogen bonds: C—H...O [C(1)—H(1A)...O(1) (1 − *x*, 2 − *y*, 1 − *z*), C...O 3.338(2), H...O 2.37 Å, angle C—H...O is 162°; C(1)—H(17A)...O(1) (1 − *x*, 2 − *y*, 1 − *z*), C...O 3.205(2), H...O 2.33 Å, angle C—H...O is 153°; C(32)—H(32B)...O(5) (2 − *x*, 2 − *y*, −*z*), C...O 3.135(2), H...O 2.30 Å, angle C—H...O is 141°; C(45)—H(45A)...O(5) (2 − *x*, 2 − *y*, −*z*), C...O 3.282(2), H...O 2.42 Å, angle C—H...O is 151°] and C—H...N

[C(28)—H(28A)...N(4) $(1-x, 2-y, -z)$, C...N 3.386(2), H...N 2.42 Å, angle C—H...O is 166°].

Experimental

The IR spectra were recorded on a Nicolet Magna IR-750 Fourier-transform spectrometer in KBr pellets. ^{1}H and ^{31}P NMR spectra were recorded on Bruker Avance$^{\text{TM}}$ 400 instrument (^{1}H, 400.13; ^{31}P, 161.98 MHz) in DMSO-d$_6$ using Me_4Si and 85% H_3PO_4 as the internal and the external standard, respectively. Reactions were carried out under dry argon. The solvents were used after purification and drying.

Preparation of P-zwitterions 2 (general procedure). To a solution of 3-aryl-2-cyanoethylacrylate (9 mmol) in MeCN (15 L) an equimolar amount of tributylphosphine was added dropwise with stirring at ~20 °C. After 1 h, the reaction mixture was cooled to –15 °C and kept at this temperature for 24 h. The crystals that formed were filtered off, washed with cold acetonitrile, dried *in vacuo*, and analysed.

(1-Cyano-1-ethoxycarbonyl)-2-phenyl-2-tributylphosphonioethanide (2a). The yield was 83%, m.p. 62—63 °C. Found (%): C, 71.52; H, 9.54; N, 3.41; P, 7.62. $C_{24}H_{38}NO_2P$. Calculated (%): C, 71.43; H, 9.49; N, 3.47; P, 7.68. IR, ν/cm^{-1}: 2133 (CN), 1601 (C=O). ^{1}H NMR, δ: 0.87 (t, 9 H, C$\underline{H}_3$CH$_2$, $J_{\text{H,H}}$ = 7 Hz); 1.09 (t, 3 H, Me, $J_{\text{H,H}}$ = 7 Hz); 1.32 (m, 12 H, CH$_2$); 2.23 (m, 6 H, CH$_2$P); 3.88 (dq, 2 H, CH$_2$O, $^1J_{\text{H,H}}$ = 9 Hz, $^2J_{\text{H,H}}$ = 7 Hz); 4.89 (d, 1 H, CHP, $J_{\text{H,H}}$ = 19 Hz); 7.12—7.27 (5 H, H arom.). ^{31}P NMR, δ: 36.4.

1-Cyano-1-ethoxycarbonyl-2-(4-hydroxyphenyl)-2-tributylphosphonioethanide (2b). The yield was 75%, m.p. 106—107 °C. Found (%): C, 68.64; H, 9.18; N, 3.42; P, 7.26. $C_{24}H_{38}NO_3P$. Calculated (%): C, 68.71; H, 9.13; N, 3.42; P, 7.26. IR, ν/cm^{-1}: 2138 (CN), 1598 (C=O). ^{1}H NMR, δ: 0.85 (t, 9 H, C$\underline{H}_3$CH$_2$, $J_{\text{H,H}}$ = 7 Hz); 1.09 (t, 3 H, Me, $J_{\text{H,H}}$ = 7 Hz); 1.34 (m, 12 H, CH$_2$); 2.21 (m, 6 H, CH$_2$P); 3.89 (dq, 2 H, CH$_2$O, $^1J_{\text{H,H}}$ = 9 Hz, $^2J_{\text{H,H}}$=7 Hz); 4.92 (d, 1 H, CHP, $J_{\text{H,H}}$ = 19 Hz); 7.61 (d, 2 H, H$_o$ arom., $J_{\text{H,H}}$ = 8 Hz); 8.09 (d, 2 H, H$_m$ arom., $J_{\text{H,H}}$ = 8 Hz); 8.91 (s, 1 H, OH). ^{31}P NMR, δ: 36.4.

1-Cyano-1-ethoxycarbonyl-2-(4-methoxyphenyl)-2-tributylphosphonioethanide (2c). The yield was 87%, m.p. 69—70 °C. Found (%): C, 69.30; H, 9.21; N, 3.29; P, 6.94. $C_{25}H_{40}NO_3P$. Calculated (%): C, 69.26; H, 9.31; N, 3.23; P, 7.14. IR, ν/cm^{-1}: 2140 (CN), 1608 (C=O). ^{1}H NMR, δ: 0.81 (t, 9 H, C$\underline{H}_3$CH$_2$, $J_{\text{H,H}}$ = 7 Hz); 1.05 (t, 3 H, Me, $J_{\text{H,H}}$ = 7 Hz); 1.32 (m, 12 H, CH$_2$); 2.04 (s, 3 H, MeO); 2.18 (m, 6 H, CH$_2$P); 3.86 (dq, 2 H, CH$_2$O, $^1J_{\text{H,H}}$ = 9.5 Hz, $^2J_{\text{H,H}}$ = 7 Hz); 4.89 (d, 1 H, CHP, $J_{\text{H,H}}$ = 19 Hz); 7.80 (d, 2 H, H$_o$ arom., $J_{\text{H,H}}$ = 8 Hz); 8.23 (d, 2 H, H$_m$ arom., $J_{\text{H,H}}$ = 8 Hz). ^{31}P NMR, δ: 36.3.

2-(4-Bromophenyl)-1-cyano-1-ethoxycarbonyl-2-tributylphosphonioethanide (2d). The yield was 99%, m.p. 99—100 °C. Found (%): C, 59.80; H, 7.79; Br, 16.48; N, 3.01; P, 6.47. $C_{24}H_{37}BrNO_2P$. Calculated (%): C, 59.75; H, 7.73; Br, 16.56; N, 2.90; P, 6.42. IR, ν/cm^{-1}: 2140 (CN), 1597 (C=O). ^{1}H NMR, δ: 0.86 (t, 9 H, C$\underline{H}_3$CH$_2$, $J_{\text{H,H}}$ = 7 Hz); 1.09 (t, 3 H, Me, $J_{\text{H,H}}$ = 7 Hz); 1.34 (m, 12 H, CH$_2$); 2.16 (m, 6 H, CH$_2$P); 3.88 (dq, 2 H, CH$_2$O, $^1J_{\text{H,H}}$ = 9 Hz, $^2J_{\text{H,H}}$ = 7 Hz); 4.72 (d, 1 H, CHP, $J_{\text{H,H}}$ = 19 Hz); 7.52 (d, 2 H, H$_o$ arom., $J_{\text{H,H}}$ = 8 Hz); 7.59 (d, 2 H, H$_m$ arom., $J_{\text{H,H}}$ = 8 Hz). ^{31}P NMR, δ: 36.1.

1-Cyano-1-ethoxycarbonyl-2-(3-nitrophenyl)-2-tributylphosphonioethanide (2e). The yield was 94%, m.p. 124—126 °C. Found (%): C, 64.31; H, 8.39; N, 6.28; P, 6.85. $C_{24}H_{37}N_2O_4P$. Calculated (%): C, 64,27; H, 8,31; N, 6.25; P, 6,91. IR, ν/cm^{-1}: 2143 (CN), 1599 (C=O). ^{1}H NMR, δ: 0.86 (t, 9 H, C$\underline{H}_3$CH$_2$, $J_{\text{H,H}}$ = 7 Hz); 1.10 (t, 3 H, Me, $J_{\text{H,H}}$ = 7 Hz); 1.34 (m, 12 H, CH$_2$); 2.23 (m, 6 H, CH$_2$P); 3.90 (dq, 2 H, CH$_2$O, $^1J_{\text{H,H}}$ = 9 Hz, $^2J_{\text{H,H}}$ = 7 Hz); 4.96 (d, 1 H, CHP, $J_{\text{H,H}}$ = 19 Hz); 7.71 (t, 1 H, H$_m$ arom., $J_{\text{H,H}}$ = 8 Hz); 8.03 (d, 1 H, H$_o$ arom., $J_{\text{H,H}}$ = 8 Hz); 8.21 (d, 1 H, H$_p$ arom., $J_{\text{H,H}}$ = 8 Hz); 8.50 (s, 1 H, H$_o$ arom.). ^{31}P NMR, δ: 36.9.

1-Cyano-1-ethoxycarbonyl-2-(4-nitrophenyl)-2-tributylphosphonioethanide (2f). The yield was 99%, m.p. 127—128 °C. Found (%): C, 64.21; H, 8.42; N, 6.32; P, 6.74. $C_{24}H_{37}N_2O_4P$. Calculated (%): C, 64,27; H, 8,31; N, 6.25; P, 6,91. IR, ν/cm^{-1}: 2135 (CN), 1601 (C=O). ^{1}H NMR, δ: 0.85 (t, 9 H, C$\underline{H}_3$CH$_2$, $J_{\text{H,H}}$ = 7 Hz); 1.09 (t, 3 H, Me, $J_{\text{H,H}}$ = 7 Hz); 1.34 (m, 12 H, CH$_2$); 2.21 (m, 6 H, CH$_2$P); 3.89 (dq, 2 H, MeO, $^1J_{\text{H,H}}$ = 9 Hz, $^2J_{\text{H,H}}$ = 7 Hz); 4.92 (d, 1 H, CHP, $J_{\text{H,H}}$ = 19 Hz); 7.83 (d, 2 H, H$_o$ arom., $J_{\text{H,H}}$ = 8 Hz); 8.26 (d, 2 H, H$_m$ arom., $J_{\text{H,H}}$ = 8 Hz). ^{31}P NMR, δ: 37.0.

X-ray diffraction analysis of compound 2f. Orange crystals of **2f** • 0.5MeCN ($C_{25}H_{38.5}N_{2.5}O_4P$, M = 469.05) are triclinic, space group $P\bar{1}$; at T = 100 K: a = 11.6960(4) Å, b = 12.7335(5) Å, c = 18.7338(7) Å, α = 79.265(1)°, β = 87.532(1)°, γ = 74.366(1)°, V = 2639.72(17) Å^3, Z = 4, d_{calc} = 1.180 g cm^{-3}, F(000) = 1012, μ = 0.136 mm^{-1}. The unit cell parameters and intensities of 48441 reflections were measured on an automated Bruker SMART APEX II CCD diffractometer (T = 100 K, λ-Mo-Kα radiation, graphite monochromator, ϕ and ω scanning technique, $2\theta \le 61°$). The structure was solved by the direct method and refined using the full-matrix least-squares method in the anisotropic approximation for nonhydrogen atoms. The crystal of compound **2f** contains the solvation molecule of acetonitrile. The positions of the hydrogen atoms of acetonitrile solvation molecule were located objectively from difference Fourier syntheses and refined in the isotropic approximation with fixed positional and thermal parameters ($U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$). The positions of the remaining hydrogen atoms were calculated geometrically and refined in the isotropic approximation with fixed positional (the riding model) and thermal ($U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ for the methyl groups and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ for all remaining groups) parameters. The final divergence factors were as follows: R_1 = 0.039 based on 13311 independent reflections with $I > 2\sigma(I)$ and wR_2 = 0.109 based on all 16282 independent reflections, S = 1.002. All calculations were carried out using the SHELXTL software.^{4}

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References

1. F. Ramirez, J. F. Pilot, C. P. Smith, *Tetrahedron*, 1968, **24**, 3735.
2. Yu. G. Gololobov, G. D. Kolomnikova, N. O. Krilova, *Tetrahedron Lett.*, 1994, **35**, 1751.
3. F. Texier-Boullet, A. Foucaud, *Tetrahedron Lett.*, 1982, **23**, 4927.
4. G. M. Sheldrick, *Acta Crystallogr.*, 2008, **A64**, 112.

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