Alkylation of P-containing zwitter-ions based on 2-cyanoacrylates

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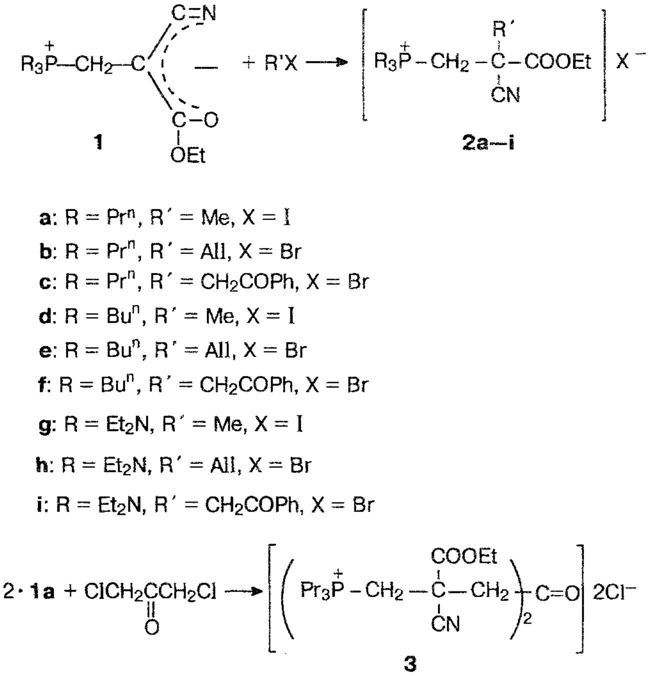
The interaction of P-containing zwitter-ions based on ethyl 2-cyanoacrylate with methyl iodide, allyl bromide, α-bromoacetophenone, and 1,3-dichloroacetone has been studied. Alkylation occurs at the central carbon atom of the pentade anion.

Key words: zwitter-ions, alkylation; phosphonium salts; alkyl halides; α-haloketones.

Earlier, it has been shown that, under certain conditions, compounds of tervalent phosphorus can interact with 2-cyanoacrylates without causing their polymerization.[1] With strong P-nucleophiles like Alk_3P and $(Et_2N)_3P$, stable zwitter-ions (**1**) are formed, which are the primary products of the polymerization of 2-cyanoacrylates under the action of P^{III}-containing compounds (see Ref. 2). In this communication, the reactions of zwitter-ions **1** with electrophiles containing mobile halogen atoms are considered.

Interaction of ethyl cyanoacetate salts with alkyl halides is known to afford *C*-alkylated products.[3] We have suggested that betains **1** containing the pentade anionic fragment $[\mathrm{N{\equiv}C{\cdots}C{\cdots}C{\cdots}O}]$,[4] like ethyl cyanoacetate salts, should also interact with alkylating reagents with the formation of a new C—C bond. In fact, methyl iodide, allyl bromide, α-bromoacetophenone, and 1,3-dichloroacetone alkylate betains **1** at the central carbon atom of the pentade anion to furnish phosphonium salts **2a—i** and **3** (Scheme 1).

Scheme 1



1

2a—i

$$R_3\overset{+}{P}-CH_2-C(R')(CN)-COOEt\ \ X^-$$

a: R = Pr^n, R′ = Me, X = I
b: R = Pr^n, R′ = All, X = Br
c: R = Pr^n, R′ = CH_2COPh, X = Br
d: R = Bu^n, R′ = Me, X = I
e: R = Bu^n, R′ = All, X = Br
f: R = Bu^n, R′ = CH_2COPh, X = Br
g: R = Et_2N, R′ = Me, X = I
h: R = Et_2N, R′ = All, X = Br
i: R = Et_2N, R′ = CH_2COPh, X = Br

$$2\cdot\mathbf{1a} + ClCH_2C(O)CH_2Cl \longrightarrow \left[\left(Pr_3\overset{+}{P}-CH_2-C(COOEt)(CN)-CH_2\right)_2C{=}O\right]\ 2Cl^-$$

3

The molar ratio of the alkylating reagent to betain **1** [R′X] : [**1**] was 1:1 or 1:2 for the preparation of salts **2a—i** or **3**, respectively. Reactions were monitored using ^{31}P NMR spectroscopy by following the appearance of new signals at 32—35 ppm or 52—53 ppm for compounds **2a—f** or **2g—i**, correspondingly ($\Delta(\delta P)$ = 2 to 3 ppm).

Salts **2** and **3**, which precipitated as oils, were purified by repricipitation. We were able to crystallize some of the oils by triturating with ether.

The ^1H NMR and IR spectra of compounds **2a—i** and **3** differ substantially from those of the starting betains **1**. In the ^1H NMR spectra of compounds **2a—i** and **3**, the signals for the magnetically nonequivalent protons of the methylene group adjacent to the phosphorus atom appear as multiplets at 3.0—3.15 ppm and 3.6—3.75 ppm, which is typical of the $PCH_AH_BC^*$ spin system. In the IR spectra of the reaction products, the bands characteristic[2] of betains **1** disappear to give way to absorption bands at 1730—1750 and 2240 cm^{-1} caused by oscillations of the ester and nonconjugated nitrile moieties, respectively.

Experimental

^{31}P and ^1H NMR spectra were obtained on a Bruker WP 200 SY instrument operating at 71.01 and 200.13 MHz in $CHCl_3$ and $CDCl_3$ solutions relative to 85 % phosphoric acid and tetramethylsilane, respectively. IR spectra were recorded using a UR-20 spectrometer (Karl Zeiss).

Betains **1** were obtained according to the published procedure.[2] All of the reactions were carried out under Ar.

Synthesis of salts 2a—i and 3 (general procedure). A solution of an alkylating reagent (0.01 mol) in benzene (10 mL) was added dropwise at room temperature to a solution of

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Table 1. Spectral characteristics of phosphonium salts **2a—i**

Compound	^{31}P NMR (in $CHCl_3$), δ	^1H NMR (in $CDCl_3$), δ (*J*/Hz)	IR, ν/cm^{-1}		
			COOEt	CN	Other bands
2a	31.84	1.10 (t, 9 H, $C\underline{H}_3CH_2CH_2P$); 1.35 (t, 3 H, $C\underline{H}_3CH_2O$); 1.69 (m, 6 H, $C\underline{H}_2CH_2P$); 2.51 (m, 6 H, $CH_2C\underline{H}_2P$); 1.89 (d, 3 H, CH_3, $J_{H,P} = 2.2$); 3.11 (dd, 1 H, $PC\underline{H}_AH_B$, $J_{H(A),H(B)} = 15.9$, $J_{H(A),P} = 12.9$); 3.75 (dd, 1 H, $PCH_A\underline{H}_B$, $J_{H(A),H(B)} = 15.9$, $J_{H(B),P} = 12.0$); 4.31 (q, 2 H, CH_2O)	1730	2245	—
2b	33.91	1.00 (t, 9 H, $C\underline{H}_3CH_2CH_2P$); 1.19 (t, 3 H, $C\underline{H}_3CH_2O$); 1.79 (m, 6 H, $C\underline{H}_2CH_2P$); 2.74 (m, 6 H, $CH_2C\underline{H}_2P$); 3.29 (m, 2 H, $C\underline{H}_2{-}CH{=}$); 3.80 (dd, 1 H, $PC\underline{H}_AH_B$, $J_{H(A),H(B)} = 15.9$, $J_{H(A)P} = 13.2$); 4.29 (q, 2 H, CH_2O); 4.45 (dd, 1 H, $PCH_A\underline{H}_B$, $J_{H(A),H(B)} = 15.9$, $J_{H(B),P} = 12.9$); 5.30 (m, 2 H, $C\underline{H}_2{=}CH$); 6.05 (m, 1 H, $C\underline{H}{=}CH_2$)	1740	2245	1650, 3085 (C=C)
2c	32.95	1.11 (t, 9 H, $C\underline{H}_3CH_2CH_2P$); 1.25 (t, 3 H, $C\underline{H}_3CH_2O$); 1.67 (m, 6 H, $C\underline{H}_2CH_2P$); 2.46 (m, 6 H, $CH_2C\underline{H}_2P$); 3.39 (t, 1 H, $PC\underline{H}_AH_B$, $J_{H(A),H(B)} = J_{H(A),P} = 15.5$); 4.14—4.47 (m, 5 H, CH_2O, $CH_2C{=}O$, $PCH_A\underline{H}_B$); 7.39—7.99 (m, 5 H, C_6H_5)	1745	2246	1680 (C=O, ketone)
2d	33.04	0.87 (t, 9 H, $C\underline{H}_3(CH_2)_2P$); 1.23 (t, 3 H, $C\underline{H}_3CH_2O$); 1.77 (d, 3 H, CH_3, $J_{H,P} = 2.3$); 3.05 (dd, 1 H, $PC\underline{H}_AH_B$, $J_{H(A),H(B)} = 15.8$, $J_{H(A),P} = 12.8$); 1.48 (m, 12 H, $(C\underline{H}_2)_2CH_2P$); 2.48 (m, 6 H, $(CH_2)_2C\underline{H}_2P$); 3.66 (dd, 1 H, $PCH_A\underline{H}_B$, $J_{H(A),H(B)} = 15.8$, $J_{H(B),P} = 12.0$); 4.31 (q, 2 H, CH_2O)	1747	2241	—
2e	35.30	1.10 (t, 9 H, $C\underline{H}_3(CH_2)_2P$); 1.13 (t, 3 H, $C\underline{H}_3CH_2O$); 1.80 (m, 12 H, $(C\underline{H}_2)_2CH_2P$); 2.88 (m, 6 H, $(CH_2)_2C\underline{H}_2P$); 3.30 (m, 2 H, $C\underline{H}_2CH{=}$); 3.75 (dd, 1 H, $PC\underline{H}_AH_B$, $J_{H(A),H(B)} = 15.7$, $J_{H(A),P} = 13.3$); 4.15 (m, 2 H, CH_2O); 4.61 (dd, 1 H, $PCH_A\underline{H}_B$, $J_{H(A),H(B)} = 15.7$, $J_{H(B),P} = 13.3$); 5.22—5.49 (m, 2 H, $C\underline{H}_2{=}CH$); 6.08 (m, 1 H, $C\underline{H}{=}CH_2$)	1740	2250	1645, 3090 (C=C)
2f	34.07	0.89 (t, 9 H, $C\underline{H}_3(CH_2)_2P$); 1.21 (t, 3 H, $C\underline{H}_3CH_2O$); 1.48 (m, 12 H, $(C\underline{H}_2)_2CH_2P$); 2.48 (m, 6 H, $CH_2C\underline{H}_2P$); 3.32 (dd, 1 H, $PC\underline{H}_AH_B$, $J_{H(A),H(B)} = 15.6$, $J_{H(A),P} = 13.2$); 4.10—4.39 (m, 5 H, $PCH_A\underline{H}_B$, $CH_2C{=}O$, CH_2O); 7.3—7.9 (m, 5 H, C_6H_5)	1745	2245	1685 (C=O, ketone)
2g	52.70	1.12 (t, 18 H, $C\underline{H}_3CH_2N$); 1.21 (t, 3 H, $C\underline{H}_3CH_2O$); 1.99 (d, 3 H, CH_3, $J_{H,P} = 2.8$); 3.09 (m, 13 H, CH_2N, $PC\underline{H}_AH_B$); 4.05 (dd, 1 H, $PCH_A\underline{H}_B$, $J_{H(A),H(B)} = 16.7$, $J_{H(B),P} = 12.8$); 4.18 (m, 2 H, CH_2O)	1742	2237	—
2h	52.92	1.14 (t, 18 H, $C\underline{H}_3CH_2N$); 1.26 (t, 3 H, $C\underline{H}_3CH_2O$); 2.34—3.31 (m, 15 H, CH_2N, $C\underline{H}_2{-}CH{=}C$, $PC\underline{H}_AH_B$); 4.22 (m, 2 H, CH_2O); 4.50 (dd, 1 H, $PCH_A\underline{H}_B$, $J_{H(A),H(B)} = 16.6$, $J_{H(B),P} = 13.9$); 5.18—5.35 (m, 2 H, $C\underline{H}_2{=}CH$); 5.82 (m, 1 H, $CH_2{=}C\underline{H}{-}$)	1747	2236	1649, 3086 (C=C)
2i	52.05	1.23 (t, 18 H, $C\underline{H}_3CH_2N$); 1.27 (t, 3 H, $C\underline{H}_3CH_2O$); 3.25 (m, 13 H, $\underline{CH}_2N, PC\underline{H}_AH_B$); 4.26 (m, 2 H, CH_2O); 4.44—4.77 (m, 3 H, $CH_{A'}H_{B'}C{=}O$, $PCH_A\underline{H}_B$, $J_{H(A),H(B)} = 16.6$, $J_{H(B),P} = 14.0$, $J_{H(A'),H(B')} = 17.3$); 7.40—7.57, 8.11—8.14 (all m, 5 H, C_6H_5)	1745	2265	1685 (C=O, ketone)

betain **1** (0.01 mol or 0.02 mol with 1,3-dichloroacetone) in benzene (20 mL) with stirring. Stirring was continued for additional 30—40 min. In the process, the reaction mixture grew turbid, and an oil precipitated. The benzene solution was then decanted, and the residue was washed successively with benzene and hexane and dried *in vacuo*. The yields were quantitative, according to ^{31}P NMR spectroscopy. The spectral characteristics of compounds **2a—i** are represented in Table 1.

(2-Cyano-2-ethoxycarbonylpropyl)tripropylphosphonium iodide (2a) was isolated as a viscous colorless oil.

(2-Cyano-2-ethoxycarbonyl-4-pentenyl)tripropylphosphonium bromide (2b) was isolated as a yellow-green oil.

(2-Cyano-2-ethoxycarbonyl-2-phenacylethyl)tripropylphosphonium bromide (2c) was isolated as a yellow powder, m.p. 38.5—39.5 °C. Found (%): C, 57.04; H, 6.67; Br, 16.65; P, 6.34. $C_{23}H_{35}BrNO_3P$. Calculated (%): C, 57.26; H, 6.89; Br, 16.56; P, 6.42.

(2-Cyano-2-ethoxycarbonylpropyl)tributylphosphonium iodide (2d) was isolated as a pink powder, m.p. 83—84 °C. Found (%): C, 48.9; H, 7.95; I, 27.18; P, 6.67. $C_{19}H_{37}INO_2P$. Calculated (%): C, 48.61; H, 7.88; I, 27.07; P, 6.70.

(2-Cyano-2-ethoxycarbonyl-4-pentenyl)tributylphosphonium bromide (2e) was isolated as a yellow oil. Found (%): C, 56.79; H, 8.75; Br, 18.03; P, 6.63. $C_{21}H_{39}BrNO_2P$. Calculated (%): C, 56.25; H, 8.70; Br, 17.85; P, 7.02.

(2-Cyano-2-ethoxycarbonyl-2-phenacylethyl)tributylphosphonium bromide (2f) was isolated as a yellow powder, m.p. 42.5—43.5 °C.

(2-Cyano-2-ethoxycarbonylpropyl)tris(diethylamino)phosphonium iodide (2g) was isolated as a yellow powder, m.p. 108.5—109.5 °C. Found (%): C, 44.04; H, 7.59; I, 25.12; N, 10.62; P, 5.95. $C_{19}H_{25}IN_4O_2P$. Calculated (%): C, 44.35; H, 7.56; I, 24.70; N, 10.87; P, 6.02.

(2-Cyano-2-ethoxycarbonyl-4-pentenyl)tris(diethylamino)phosphonium bromide (2h), m.p. 152.5—153.5 °C (from toluene—acetonitrile). Found (%): C, 51.10; H, 8.42; Br, 15.92; P, 6.12. $C_{21}H_{27}BrN_4O_2P$. Calculated (%): C, 51.11; H, 8.51; Br, 16.22; P, 6.28.

(2-Cyano-2-ethoxycarbonyl-2-phenacylethyl)tris(diethylamino)phosphonium bromide (2i) was isolated as a white powder, m.p. 92.5—93.5 °C (from benzene—acetonitrile). Found (%): C, 54.80; H, 7.74; Br, 13.58; P, 5.40. $C_{26}H_{29}BrN_4O_3P$. Calculated (%): C, 54.65; H, 7.70; Br, 14.01; P, 5.43.

3,3′-Carbonylbis[(2-cyano-2-ethoxycarbonylpropyl)tripropylphosphonio] dichloride (3) was isolated as a yellow powder, m.p. 77.5—78.5 °C. Found (%): C, 56.44; H, 8.68; Cl, 10.11; P, 8.75. $C_{33}H_{60}Cl_2N_2O_5P_2$. Calculated (%): C, 56.81; H, 8.60; Cl, 10.18; P, 8.89. ^{31}P NMR, δ: 32.7. ^{1}H NMR, δ: 1.10 (t, 9 H, $C\underline{H}_3CH_2CH_2P$); 1.27 (t, 3 H, $C\underline{H}_3CH_2O$); 1.65 (m, 6 H, $C\underline{H}_2CH_2P$); 2.45 (m, 6 H, $CH_2C\underline{H}_2P$); 3.37 (t, 1 H, $PC\underline{H}_AH_B$, $J_{H(B),H(A)} = J_{H(A),P} =$ 14.8 Hz); 3.86—4.05 (m, 3 H, $CH_2C{=}O$, $PCH_A\underline{H}_B$); 4.28 (q, 2 H, CH_2O). IR, ν/cm^{-1}: 1730 (C=O, ketone); 1760 (C=O, ester); 2255 (CN).

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