Regiochemistry of the reactions of phenylenedioxytrichlorophosphorane with phenylacetylene and propargyl chloride in the presence of benzyltrimethylammonium chloride

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NMR studies revealed that the reactions of phenylenedioxytrichlorophosphorane with phenylacetylene and propargyl chloride in the presence of benzyltrimethylammonium chloride predominantly yield derivatives of 2,7-dichloro-2-oxobenzo[*e*]-1,2-oxaphosphorinine, *i.e.*, the benzene ring is selectively chlorinated in the *meta*-position to the endocyclic O atom of the phosphorinine heterocycle.

Key words: acetylene derivatives, phosphorus(v) chlorides, regiochemistry of the reaction, benzo[*e*]-1,2-oxaphosphorinines, benzyltrimethylammonium chloride.

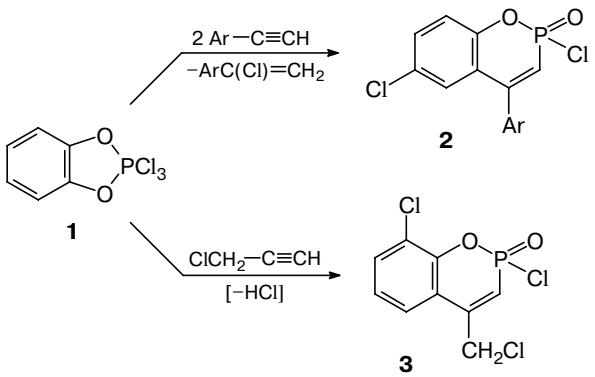
It is known[1] that the reactions of PCl_5 with aryl- and alkylacetylenes, which is an important method for the synthesis of unsaturated phosphonic acid derivatives, require a twofold excess of a P-containing reagent. In addition, the use of such reagents as SO_2, PR_3, $ROPCl_2$, P_4, *etc.* is necessary for the isolation of the target acids, since the reaction products are phosphonium salts with PCl_6^- as the counterion.

Recently,[2,3] we have found that easily available phenylenedioxytrichlorophosphorane (**1**) reacts with arylacetylenes in CH_2Cl_2 in the ratio of 1 : 2 (P^V derivative : acetylene) to give 4-aryl-2,6-dichloro-2-oxobenzo[*e*]-1,2-oxaphosphorinines (**2**). The formation of a P—C bond and *ipso*-substitution of a carbon atom for the phenylenedioxaphospholane O atom occurs together with selective introduction of the Cl atom into the *para*-position relative to the endocyclic O atom of the phosphorinine heterocycle. The evolved HCl molecule adds to the excess of arylacetylene to form chlorostyrenes.

The reaction of propargyl chloride with phosphorane **1** proceeds differently, predominantly yielding benzophosphorinine **3**, *viz.*, a product of *ortho*-chlorination of the phenylene substituent (Scheme 1).[4]

The goal of the present work was to study the effect of benzyltrimethylammonium chloride (**4**) on the reactions of phosphorane **1** with phenylacetylene and propargyl chloride.

Scheme 1



Results and Discussion

We found that the regiochemical outcome of chlorination in the reactions studied can be changed by using compound **4**. Upon mixing of ammonium salt **4** with phosphorane **1**, phosphate **5** is precipitated, which dissolves upon addition of an alkyne giving a transparent solution. It is known that similar derivatives of six-coordinate phosphorus are easily prepared (see, *e.g.*, Ref. 5). It turned out that the reactions of phosphate **5** with both phenylacetylene and propargyl chloride mainly yield benzophosphorinines (**6** and **7**) in which the Cl atom is in *meta*-position relative to the endocyclic O atom of the phosphorinine heterocycle (Scheme 2).

The ^{31}P NMR spectra of compounds **6** and **7** contain doublets at δ 16.9 and 16.6, respectively ($^2J_{PCH}$ = 23—26 Hz). More detailed ^1H and ^{13}C NMR study of the heterocycles was performed for compounds subjected to hydrolysis to give stable phosphonic acids (**8** and **9**). The ^1H NMR spectra of **8** and **9** (see Experimental) contain low-field signals for the trisubstituted phenylene fragment, thus confirming the presence of the Cl atom in the ring. Its position was determined by ^{13}C and ^{13}C-{^1H} NMR spectroscopy (Table 1). The ^{13}C-{^1H} spectra of phosphorinines **8** and **9** contain a

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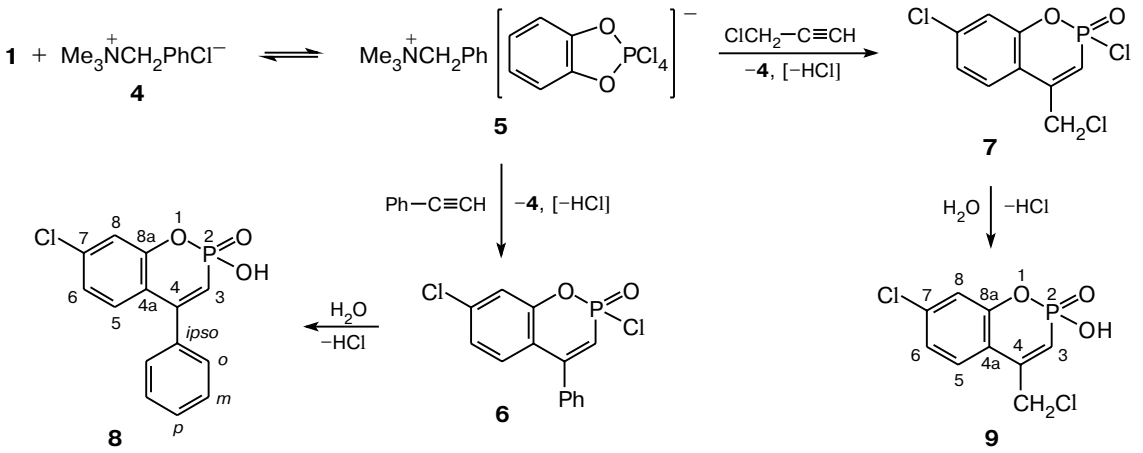
Scheme 2



low-field (δ 134.8) singlet for the C(7) atom (see Table 1). The low-field value and the shape of this signal in the ^{13}C NMR spectrum (ddd) indicate that the Cl atom is in *para*-position relative to the C(4a) atom. If the Cl atom were in *para*-position relative to the O(1) atom, a signal for the C(6) atom would be shifted upfield (δ ~127.0) owing to the *para*-shielding effect of the O(1) atom, in conformity with the known data.[2,3] For the *ortho*-position of the Cl atom (*i.e.*, at the C(8) atom), the $\delta_{C(8)}$ value would be even higher-field (δ ~125.4), with a noticeable constant $^2J_{POC}$ = 8.1 Hz (*cf.* Ref. 4). The presence of the Cl atom at position 7 of the benzophosphorinine system is also evidenced by the multiplicity of a signal for the C(4a) atom (dddd) in compound **8**, which suggests the presence of the H(6) and H(8) protons (spin-spin coupling constant across three bonds is 6—12 Hz in benzene derivatives[6]).

It should be noted that a traditional isomer (**2a**, Ar = Ph), in which the Cl atom is in *para*-position relative to the endocyclic O atom, is also formed in the reaction with phenylacetylene, though in small amounts (~18%). Its hydrolysis gave 6-chloro-2-hydroxy-2-oxo-4-phenylbenzo[*e*]-1,2-oxaphosphorinine (**10**). This compound was obtained in small amounts and was not isolated; however, its structure was reliably determined based on the ^{13}C NMR spectrum of a fraction of a precipitate enriched with this compound. The complete ^{13}C NMR spectrum of phosphorinine **10** in DMF-d_7 was described by us earlier.[3]

Thus, based on the ^{13}C NMR data, one can state that this version of the reaction affords 7-chlorobenzophosphorinines. Such a strong effect of salt **4** on the reaction outcome can indicate the ionic character of chlorination of the phenylene fragment.

Table 1. ^{13}C and ^{13}C-{^1H} NMR data for benzophosphorinines **8** and **9**

Carbon atom	δ (*J*/Hz)[a]	
	8[b]	**9**[c]
C(3)	116.3 d (dd, J_{PC} = 169, J_{HC} = 163)	117.6 d (ddt, J_{PC} = 169, J_{HC} = 164, J_{HCCC} = 5)
C(4)	150.9 d (m, J_{PCC} = 2)	145.1 d (m, J_{PCC} = 2)
C(4a)	121.1 d (dddd, J_{PCCC} = 17, $J_{HC(3)CC}$ = 8, $J_{HC(6)CC}$ = 8, $J_{HC(8)CC}$ = 5)	118.6 d (m, J_{PCCC} = 16.2, $J_{HC(3)CC}$ = 8, $J_{HC(6)CC}$ = 6—7, $J_{HC(8)CC}$ = 5, J_{CH2CC} = 3)
C(5)	129.8 d (br.dd, J_{HC} = 164, $J_{PC(3)C(4)C(4a)C}$ = 1)	127.7 d (br.d, J_{HC} = 164)
C(6)	123.4 s (dd, J_{HC} = 170, $J_{HC(8)CC}$ = 5)	123.2 s (dd, J_{HC} = 170, $J_{HC(8)CC}$ = 5)
C(7)	134.8 s (ddd, $J_{HC(5)CC}$ = 13, J_{HCC} = 4, J_{HCC} = 3)	134.8 s (ddd, $J_{HC(5)CC}$ = 13, J_{HCC} = 4, J_{HCC} = 3)
C(8)	119.3 d (dddd, J_{HC} = 169, $J_{POC(8a)C}$ = 7, $J_{HC(6)CC}$ = 5, $J_{HC(5)CCC}$ = 2)	119.0 d (dddd, J_{HC} = 169, $J_{POC(8a)C}$ = 7, $J_{HC(6)CC}$ = 5, $J_{HC(5)CCC}$ = 1)
C(8a)	152.0 d (dddd, J_{POC} = 7, $J_{HC(5)C(4a)C}$ = 9, $J_{HC(8)C}$ = 4, $J_{HC(6)CCC}$ = 1)	151.9 d (m, J_{POC} = 7)

[a] The multiplicities of ^{13}C-{^1H} and ^{13}C NMR signals (in parentheses) are indicated.
[b] Other signals, δ: 138.3 d (br.ddt, C_i, J_{PCCC_i} = 19 Hz, $J_{HC(3)CC_i}$ = 7 Hz, J_{HCmCC_i} = 6 Hz); 128.3 s (br.ddd, C_o, J_{HC_o} = 161 Hz, $J_{HC_pCC_{po}}$ = 7 Hz, $J_{HC_{o'}CC_o}$ = 7 Hz); 128.7 s (ddd, C_m, J_{HCm} = 162 Hz, $J_{HCm'CCm}$ = 7 Hz, J_{HCCm} = 2 Hz); 128.9 s (dt, C_p, J_{HC_p} = 162 Hz, $J_{HC_oCC_p}$ = 7 Hz).
[c] The spectrum also contains a signal at δ 44.4 d (tdd, CH_2Cl, J_{HC} = 154 Hz, J_{PCCC} = 22 Hz, $J_{HC(3)CC}$ = 8 Hz).

Experimental

^1H, ^{13}C, ^{13}C-{^1H}, ^{31}P, and ^{31}P-{^1H} NMR spectra were recorded on Bruker WM-250 (^1H, 250 MHz) and Bruker MSL-400 instruments (^{31}P, 162.0 MHz and ^{13}C, 100.6 MHz) in DMSO-d_6 at 45 °C or in ethanol-d_6 at 40 °C. The signals were referred to Me_4Si with the residual protons (^1H) or carbon nuclei of DMSO or ethanol (^{13}C) as the internal standards and with H_3PO_4 as the external standard (^{31}P). IR spectra were recorded on a UR-20 instrument (suspensions in Vaseline oil).

Reaction of trichlorophosphorane (1) with propargyl chloride in the presence of benzyltrimethylammonium chloride (4). Dry salt **4** (1.36 g, 7.3 mmol) was added to a solution of phosphorane **1** (1.8 g, 7.3 mmol) in 10 mL of CH_2Cl_2 to give a voluminous bright yellow precipitate of phosphate **5** (δ_P −97), and then propargyl chloride (1.08 g, 15 mmol, 2 equiv.) was added. The reaction was completed over two weeks at 20 °C (^{31}P NMR (CH_2Cl_2) of **7**, δ: 16.6; no signals for compounds **1** and **5**), the reaction mixture becoming transparent. Water (4 mL) was added with stirring and cooling to 10—20 °C to the resulting solution. The organic layer was separated, and the products were extracted from the aqueous layer with $CHCl_3$ (10 mL). The organic extracts were combined, and the white crystals that precipitated within 2—3 h were filtered off the next day. The yield of 7-chloro-4-chloromethyl-2-hydroxy-2-oxobenzo[*e*]-1,2-oxaphosphorinine (**9**) was 0.8 g (~41%), m.p. 205—207 °C. Found (%): C, 40.67; H, 2.89; Cl, 26.32; P, 11.77. $C_9H_7Cl_2O_3P$. Calculated (%): C, 40.75; H, 2.64; Cl, 26.79; P, 11.69. IR, ν/cm^{-1}: 405, 415, 461, 510, 525, 574, 612, 656, 700, 713, 820, 860, 880, 950, 968, 1008, 1022, 1090, 1160, 1176, 1210, 1233, 1270 sh, 1380, 1400, 1548, 1600, 1630—1640 (δ(OH)), 2170—2180 vs (br), 2250—2300 vs (br), 2550—2650 vs (br), 3350—3400 vs (br). ^1H NMR (DMSO-d_6), δ: 4.84 (br.s, 2 H, $ClCH_2$); 6.63 (d, 1 H, H(3), $^2J_{PCH}$ = 16.6 Hz); 7.31 (dd, 1 H, H(6), ^3J = 8.4 Hz, ^4J = 2.0 Hz); 7.35 (d, 1 H, H(8), ^4J = 2.0 Hz); 7.70 (d, 1 H, H(5), ^3J = 8.4 Hz). ^{31}P NMR (DMSO-d_6), δ: 3.3 (d, $^2J_{PCH}$ = 16.5 Hz).

Reaction of trichlorophosphorane (1) with phenylacetylene in the presence of benzyltrimethylammonium chloride (4). Phenylacetylene (2.3 g, 22 mmol) in 5 mL of CH_2Cl_2 (0 °C) was added dropwise to a bright yellow precipitate of phosphate **5** prepared from trichlorophosphorane **1** (3.46 g, 14 mmol) and salt **4** (2.6 g, 14 mmol) in 20 mL of CH_2Cl_2. The precipitate dissolved approximately one day later to give a transparent light yellow solution. According to the ^{31}P NMR data, the reaction gave a mixture of phosphorinines **2a** and **6** in a ratio of 2 : 9 (δ 16.5 and 16.9, respectively). The reaction mixture was treated with water (4 mL), and the organic layer was separated. The solvent was removed, and the residue was recrystallized from benzene—ether. The yield of 2-hydroxy-2-oxo-4-phenyl-7-chlorobenzo[*e*]-1,2-oxaphosphorinine (**8**) was 0.6 g, m.p. 192—195 °C. Found (%): C, 54.22; H, 3.77; Cl, 12.09; P, 11.02. $C_{14}H_{10}ClO_3P$. Calculated (%): C, 54.43; H, 3.42; Cl, 12.13; P, 10.59. IR, ν/cm^{-1}: 642, 670, 704, 720, 745, 760, 830, 870, 972, 1018, 1165, 1204, 1260, 1345, 1595, 1605, 2255, 2550. ^1H NMR (ethanol-d_6), δ: 6.25 (d, PCH, $^2J_{PCH}$ = 16.2 Hz); 7.44 (d, H(8), $^4J_{HCCCH}$ = 2.0 Hz); 7.64 and 7.78 (both m, H(5), H(6), C_6H_5). ^{31}P NMR (ethanol-d_6), δ: 5.3 (d, $^2J_{PCH}$ = 15.9 Hz).

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