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The reaction of hex-1-yne with 2,2,2-trichlorobenzo[*d*]-1,3,2-dioxaphosphole

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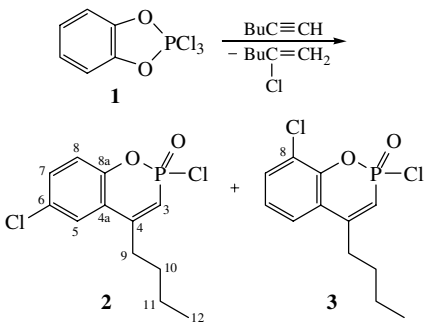
The title reaction gives 2,6-dichloro- and 2,8-dichloro-2-oxo-4-butylbenzo[*e*]-1,2-oxaphosphorinines in a ratio of 9:1.

It is well known that the reactions of 2,2,2-trihalobenzo[*d*]-1,3,2-dioxaphospholes with arylacetylenes differ from the reactions of the latter with phosphorus pentachloride: they give P-analogues of natural coumarin, *viz*., benzo[*e*]-1,2-oxaphosphorinines.[1,2] This reaction, which has a complex mechanism, along with the formation of a phosphoryl group and a P–C bond, also involves a process that is very rare in organic chemistry, namely, *ipso*-substitution of an oxygen atom in the phenylene fragment and regioselective halogenation of the latter under very mild conditions (10–20 °C). The rates and regiochemistry of these reactions are determined not only by the nature of the starting benzophosphole[3–5] but also, to a considerable extent, by the nature of the acetylene.[6] Phosphorus-containing derivatives of coumarin and chromene are of considerable interest as bioactive compounds.[7]

In this work, we found that alkylacetylenes such as hex-1-yne can also react with 2,2,2-trichlorobenzo[*d*]-1,3,2-dioxaphosphole **1**. Unlike propargyl chloride[6] (prolonged ageing or heating of the reaction mixture), hex-1-yne readily reacts with phosphole **1** at 10–20 °C with an exo effect to give two phosphorus-containing compounds, which manifest themselves as doublets in the ^{31}P NMR spectrum ($^2J_{PCH}$ 23.1–23.5 Hz) with an integral intensity ratio of 9:1. A study of the compounds obtained by ^{13}C and ^{13}C-{^{1}H} NMR methods showed† that they have a benzophosphorinine nature. This follows from the presence of the characteristic doublets of the C^3, C^8, C^{8a}, C^{4a} and C^9 nuclei in the ^{13}C-{^{1}H} spectra. The multiplicity of the signals in the ^{13}C NMR spectrum suggests that 4-butyl-2-oxo-6-chlorobenzo[*e*]-1,2-oxaphosphorinine **2** (the major reaction product) and 4-butyl-2-oxo-8-chlorobenzo[*e*]-1,2-oxaphosphorinine **3** are formed (Scheme 1). In particular, the presence of a chlorine atom at the 6-position in compound **2** follows from the multiplicity of the signal from the C^8 nucleus, which manifests itself in the ^{13}C NMR spectrum as a doublet of doublets ($^1J_{HC}$ 166.9, $^3J_{POCC^8}$ 8.2 Hz) due to the absence of spin–spin coupling with the proton at C^6.

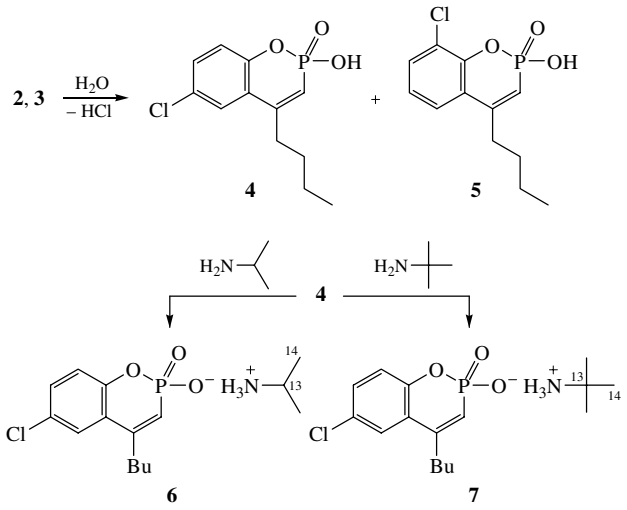


Scheme 1

The chemical shift and multiplicity of the signal of the same carbon (C^8) (absence of a direct $^1J_{HC^8}$ constant) for minor phosphorinine **3** is evidence for chlorination at the *ortho* position with respect to the endocyclic oxygen atom. The elemental composition of the isomeric benzophosphorinines was also confirmed by mass spectrometry: the EI mass spectrum contains 294, 292 and 290 molecular ion peaks corresponding to the molecular formula $C_{12}H_{14}Cl_2O_2P$.

Chlorophosphorinines **2** and **3** readily undergo hydrolysis to give stable cyclic phosphonic acids **4** and **5**. Phosphonic acid **4**‡ isolated in a pure state was treated with amines to give isopropylammonium salt **6** and *tert*-butylammonium salt **7** (Scheme 2).§

Thus, hex-1-yne (an alkylacetylene) reacts with 2,2,2-trichlorobenzo[*d*]-1,3,2-dioxaphosphole to give benzophosphorinines in an almost quantitative yield, thus expanding considerably the synthetic capabilities of the method described previously[1,2] for arylacetylenes. Unusual features of this reaction include the high rate (in comparison with the reaction with propargyl chloride[6]) and preferential chlorination at the 6-position of the phosphorinine heterocycle.



Scheme 2

† The melting points are uncorrected; measurements involved a Boetius melting point apparatus. NMR spectra were recorded on Bruker MSL-400 (400 MHz, ^{1}H; 100.6 MHz, ^{13}C) and Bruker CXP-100 (36.48 MHz, ^{31}P) spectrometers. The δ_H and δ_P values were determined relative to an internal (HMDS) or external (H_3PO_4) standard. The δ_C values were determined relative to the signal of the deuterated solvent. IR spectra were recorded on a Bruker Vector-22 instrument in Nujol. The EI mass spectra were obtained on a TRACE MS Finnigan MAT instrument; the ionization energy was 70 eV; the temperature of the ion source was 200 °C. The samples were introduced into the ion source *via* a direct inlet system. The heating of the evaporator tube was programmed from 35 to 150 °C at a rate of 35 K min^{-1}. Mass-spectrometric data were processed using the Xcalibur program.

*Reaction of 2,2,2-trichlorobenzo[*d*]-1,2,3-dioxaphosphole* **1** *with hex-1-yne*. A solution of hex-1-yne (8.4 ml, 0.073 mol) in 10 ml of CH_2Cl_2 was added to a mixture of phosphole **1** (9 g, 0.037 mol) and 15 ml of CH_2Cl_2 (20 °C) with intense bubbling of argon. Simultaneously, the evolution of HCl was observed. The reaction mixture was then evacuated (12 Torr, 130 °C) to give a light brown glassy oil, which was a mixture of compounds **2** and **3**. ^{31}P NMR (36.48 MHz, CH_2Cl_2): δ_P 18.5 (d, $^2J_{PCH}$ 23.1 Hz), compound **2**; δ_P 18.9 (d, $^2J_{PCH}$ 23.1 Hz), compound **3**. ^{13}C NMR ($CDCl_3$) of compound **2** (here and below, the multiplicity of the signal in the ^{13}C-{^{1}H} spectrum is given in parentheses): 112.92 [ddt (d), C^3, $^1J_{PC^3}$ 156.3 Hz, $^1J_{HC^3}$ 169.1 Hz, $^3J_{HC^9CC^3}$ 5.3 Hz], 155.51 [m (s), C^4], 121.79 [m (d), C^{4a}, $^3J_{PCCC^{4a}}$ 19.2 Hz], 125.79 [dd (s), C^5, $^1J_{HC^5}$ 165.6 Hz, $^3J_{HC^7CC^5}$ 4.6 Hz], 129.90 [ddd (s), C^6, $^3J_{HC^8CC^6}$ 10.3 Hz, $^2J_{HC^7C^6}$ 3.6 Hz, $^2J_{HC^5C^6}$ 3.6 Hz], 131.27 [dd (s), C^7, $^1J_{HC^7}$ 169.0 Hz, $^3J_{HC^5CC^7}$ 5.2 Hz], 120.56 [dd (d), C^8, $^1J_{HC^8}$ 166.9 Hz, $^3J_{POCC^8}$ 8.2 Hz], 146.70 [dddd (d), C^{8a}, $^3J_{HC^7CC^{8a}}$ 10.1–10.4 Hz, $^3J_{HC^5CC^{8a}}$ 10.1–10.4 Hz, $^2J_{POC^{8a}}$ 9.4 Hz, $^2J_{HC^8C^{8a}}$ 3.3 Hz], 33.62 [tdm (d), C^9, $^3J_{PCCC^9}$ 19.2 Hz, $^1J_{HC^9}$ 127.1 Hz], 29.46 [br. tm (s), C^{10}, $^1J_{HC^{10}}$ 123.0 Hz], 21.70 [br. tm (s), C^{11}, $^1J_{HC^{11}}$ 122.0 Hz], 13.29 [qm (s), C^{12}, $^1J_{HC^{12}}$ 125.2 Hz, $^2J_{HC^{11}C^{12}}$ 3.2 Hz]. ^{1}H NMR ($CDCl_3$) for **2**: 0.06 (t, Me, 3H, $^3J_{H^{11}CCH^{12}}$ 7.3 Hz), 0.54 (m, C^{11}H$_2$, 2H, $^3J_{HCCH}$ 7.2–7.4 Hz), 0.71 (m, C^{10}H$_2$, 2H, $^3J_{HCCH}$ 7.4 Hz, $^3J_{HCCH}$ 7.2 Hz), 1.79 (m, C^{9}H$_2$, 2H, $^3J_{HCCH}$ 7.2 Hz), 5.42 (br. d, H^3, 1H, $^2J_{PCH}$ 23.2 Hz), 6.28 (d, H^8, 1H, $^3J_{H^7CCH^8}$ 8.7 Hz), 6.49 (ddd, H^7, 1H, $^3J_{H^8CCH^7}$ 8.7 Hz, $^4J_{H^5CCCH^7}$ 2.4 Hz, $^5J_{POCCCH^7}$ 1.7 Hz), 6.66 (d, H^5, 1H, $^4J_{H^7CCCH^5}$ 2.4 Hz). ^{13}C NMR ($CDCl_3$) for **3**: 112.85 [ddt (d), C^3, $^1J_{PC^3}$ 156.4 Hz, $^1J_{HC^3}$ 169.5 Hz, $^3J_{HC^9CC^3}$ 5.6 Hz], 156.44 [m (s), C^4], 121.98 [m (d), C^{4a}, $^3J_{PCCC^{4a}}$ 19.7 Hz], 125.79 [dd (s), C^5, $^1J_{HC^5}$ 165.6 Hz, $^3J_{HC^7CC^5}$ 4.6 Hz], 124.65 [d (s), C^6, $^1J_{HC^6}$ 166.1 Hz], 132.02 [dd (s), C^7, $^1J_{HC^7}$ 167.7 Hz, $^3J_{HC^5CC^7}$ 8.6 Hz], 124.10 [m (d), C^8, $^3J_{POCC^8}$ 7.8 Hz], 146.11 [dddd (d), C^{8a}, $^3J_{HC^7CC^{8a}}$ 8.5–8.7 Hz, $^3J_{HC^5CC^{8a}}$ 8.5–8.7 Hz, $^2J_{POC^{8a}}$ 9.8 Hz, $^4J_{HC^6CCC^{8a}}$ 1.6 Hz], 34.08 [tdm (d), C^9, $^3J_{PCCC^9}$ 19.7 Hz], 29.46 [tm (s), C^{10}, $^1J_{HC^{10}}$ 123.0 Hz], 21.70 [tm (s), C^{11}, $^1J_{HC^{11}}$ 122.0 Hz], 13.29 [qm (s), C^{12}, $^1J_{HC^{12}}$ 125.2 Hz, $^2J_{HC^{11}C^{12}}$ 3.2 Hz]. ^{1}H NMR ($CDCl_3$) for **3**: 0.04 (m, Me, 3H, $^3J_{H^{11}CCH^{12}}$ 7.4 Hz), 0.54 (m, C^{11}H$_2$, 2H, $^3J_{HCCH}$ 7.2–7.4 Hz), 0.71 (m, C^{10}H$_2$, 2H, $^3J_{HCCH}$ 7.2–7.4 Hz), 1.81 (m, C^{9}H$_2$, 2H, $^3J_{HCCH}$ 7.2 Hz), 5.42 (br. d, H^3, 1H, $^2J_{PCH}$ 23.2 Hz), 6.34 (dd, H^6, 1H, $^3J_{H^5CCH^6}$ 7.9–8.0 Hz, $^3J_{H^7CCH^6}$ 7.9–8.0 Hz), 6.60 (ddd, H^7, 1H, $^3J_{H^6CCH^7}$ 8.0 Hz, $^4J_{H^5CCCH^7}$ 2.2 Hz, $^5J_{POCCCH^7}$ 1.6 Hz), 6.65 (br. dd, H^5, 1H, $^3J_{H^6CCH^5}$ 7.9 Hz, $^4J_{H^7CCCH^5}$ 2.4 Hz). MS, *m/z* (the values of *m/z* are given for ions containing the most abundant isotopes): 294, 292, 290 [M]$^{+\cdot}$, 261, 255, 253 [M$^{+\cdot}$ – C_3H_7], 250, 248, 216, 214, 212, 183, 165, 149, 131, 115, 102, 75, 41.

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‡ *4-Butyl-6-chloro-2-hydroxy-2-oxobenzo[*e*]-1,2-oxaphosphorinine* **4**. The light brown glassy residue obtained was hydrolysed in humid ether. In 30–40 min, a white precipitate of phosphorinine **4** was formed, which was washed with diethyl ether and dried *in vacuo*. Yield 8 g (85%), mp 132 °C. IR (ν/cm^{-1}): 404, 438, 459, 504, 550, 594, 668, 736, 776, 821, 840, 879, 904, 945, 1014, 1084, 1136, 1182, 1236, 1248, 1268, 1312, 1352, 1377, 1420, 1464, 1555, 1601, 1894, 2338, 2360, 2725, 2853, 3047, 3415. ^{13}C NMR ([$^2H_6$]DMSO, 45 °C) δ_C: 114.40 [ddt (d), C^3, $^1J_{PC^3}$ 170.8 Hz, $^1J_{HC^3}$ 161.8 Hz, $^3J_{HC^9CC^3}$ 5.7 Hz], 150.76 [m (s), C^4], 123.21 [m (d), C^{4a}, $^3J_{PCCC^{4a}}$ 17.7 Hz], 125.64 [dd (s), C^5, $^1J_{HC^5}$ 165.4 Hz, $^2J_{HC^7CC^5}$ 4.9 Hz], 127.38 [ddd (s), C^6, $^3J_{HC^8CC^6}$ 11.3 Hz, $^2J_{HC^7C^6}$ 4.5 Hz, $^2J_{HC^5C^6}$ 4.5 Hz], 130.15 [dm (s), C^7, $^1J_{HC^7}$ 168.8 Hz, $^3J_{HC^5CC^7}$ 5.8 Hz, $^3J_{HC^8C^7}$ 4.5 Hz], 120.88 [dd (d), C^8, $^1J_{HC^8}$ 167.4 Hz, $^3J_{POCC^8}$ 6.8 Hz], 149.89 [ddd (d), C^{8a}, $^3J_{HC^7CC^{8a}}$ 9.0–10.0 Hz, $^3J_{HC^5CC^{8a}}$ 9.0–10.0 Hz, $^2J_{POC^{8a}}$ 6.9 Hz], 33.23 [ddm (d), C^9, $^3J_{PCCC^9}$ 17.4 Hz, $^1J_{HC^9}$ 129.5 Hz, $^3J_{HC^3CC^9}$ 6.2 Hz, $^2J_{HC^{10}C^9}$ 3.9 Hz], 29.67 [tm (s), C^{10}, $^1J_{HC^{10}}$ 126.8 Hz], 21.70 [br. tm (s), C^{11}, $^1J_{HC^{11}}$ 124.8 Hz, $^2J_{HCC^{11}}$ 4.2 Hz, $^2J_{HCC^{11}}$ 3.3 Hz], 13.68 [qm (s), C^{12}, $^1J_{HC^{12}}$ 124.8 Hz, $^2J_{HCC^{12}}$ 4.7 Hz, $^2J_{HCC^{12}}$ 3.9 Hz). ^{31}P NMR ([$^2H_6$]DMSO, 45 °C) δ_P: 12.9 (d, $^2J_{PCH}$ 17.1 Hz). Found (%): C, 53.02; H, 5.27; Cl, 12.89; P, 11.51. Calc. for $C_{12}H_{14}ClO_3P$ (%): C, 52.84; H, 5.14; Cl, 13.02; P, 11.38.

§ *Isopropylammonium 4-butyl-6-chloro-2-oxobenzo[*e*]-1,2-oxaphosphorinin-2-oate* **6**. A solution of isopropylamine (0.5 ml, 0.0055 mol) in 5 ml of diethyl ether was added to a suspension of phosphorinine **4** (1.5 g, 0.0055 mol) in 10 ml of diethyl ether (20 °C). The resulting mixture was stirred for 2 h and left overnight. The precipitate of compound **6** was filtered off and dried *in vacuo*. Yield 0.9 g (46%), mp 125 °C. IR (ν/cm^{-1}): 420, 429, 449, 478, 510, 519, 542, 587, 649, 664, 724, 733, 757, 813, 836, 888, 900, 938, 952, 1002, 1033, 1073, 1097, 1111, 1131, 1199, 1229, 1238, 1252, 1265, 1321, 1348, 1378, 1395, 1468, 1543, 1604, 1618, 1640, 1760, 1834, 1901, 2029, 2144, 2259, 2365, 2474, 2568, 2757, 2920, 3449. ^{1}H NMR ($CDCl_3$) δ: 0.93 (t, C^{12}H$_3$, 3H, $^3J_{H^{11}CCH^{12}}$ 7.3 Hz), 1.17 (d, 2C^{14}H$_3$, 6H, $^3J_{H^{13}CCH^{14}}$ 6.5 Hz), 1.40 (tq, C^{11}H$_2$, 2H, $^3J_{HCCH}$ 7.1 Hz, $^3J_{HCCH}$ 7.1 Hz), 1.55 (tt, C^{10}H$_2$, 2H, $^3J_{HCCH}$ 8.4 Hz, $^3J_{HCCH}$ 8.4 Hz), 2.53 (t, C^{9}H$_2$, 2H, $^3J_{HCCH}$ 7.2 Hz), 3.18 (m, C^{13}H, 1H, $^3J_{H^{14}CCH^{13}}$ 5.6 Hz), 6.14 (d, H^3, 1H, $^2J_{PCH}$ 17.6 Hz), 7.06 (d, H^8, 1H, $^3J_{H^7CCH^8}$ 8.6 Hz), 7.16 (dd, H^7, 1H, $^3J_{H^6CCH^7}$ 8.6 Hz, $^4J_{H^5CCCH^7}$ 2.5 Hz), 7.38 (d, H^5, 1H, $^4J_{H^7CCCH^5}$ 2.5 Hz), 8.59 (m, NH_3, 3H). ^{31}P NMR ([$^2H_6$]DMSO, 45 °C) δ_P: –0.1 (d, $^2J_{PCH}$ 15.7 Hz). Found (%): C, 55.60; H, 7.3; Cl, 11.70; N, 4.24; P, 9.87. Calc. for $C_{15}H_{23}ClNO_3P$ (%): C, 54.29; H, 6.94; Cl, 10.71; N, 4.22; P, 9.35.

tert-*Butylammonium 4-butyl-6-chloro-2-oxobenzo[*e*]-1,2-oxaphosphorinin-2-oate* **7**. A solution of *tert*-butylamine (1.2 ml, 0.011 mol) in 5 ml of diethyl ether was added to a suspension of phosphorinine **4** (3.0 g, 0.011 mol) in 10 ml of diethyl ether (20 °C). The resulting mixture was stirred for 4 h and left overnight. The mixture was then evacuated until half of its volume remained. The precipitate of compound **7** was filtered off and dried *in vacuo*. Yield 2.7 g (67%), mp 183 °C. IR (ν/cm^{-1}): 415, 463, 515, 538, 576, 587, 646, 657, 669, 722, 732, 781, 817, 880, 907, 939, 1036, 1079, 1130, 1188, 1207, 1264, 1310, 1349, 1377, 1401, 1464, 1553, 1606, 1626, 1644, 1874, 2007, 2177, 2361, 2546, 2633, 2734, 2853, 2923, 3364, 3451. ^{13}C NMR ([$^2H_6$]DMSO, 45 °C) δ_C: 122.34 [ddt (d), C^3, $^1J_{PC^3}$ 165.6 Hz, $^1J_{HC^3}$ 156.8 Hz, $^3J_{HC^9CC^3}$ 5.5 Hz], 142.70 [m (s), C^4], 124.92 [m (d), C^{4a}, $^3J_{PCCC^{4a}}$ 15.8 Hz], 124.36 [dd (s), C^5, $^1J_{HC^5}$ 162.7 Hz, $^3J_{HC^7CC^5}$ 4.9 Hz], 124.70 [ddd (s), C^6, $^3J_{HC^8CC^6}$ 11.3 Hz, $^2J_{HC^7C^6}$ 2.3 Hz, $^2J_{HC^5C^6}$ 2.3 Hz], 127.88 [dd (s), C^7, $^1J_{HC^7}$ 165.7 Hz, $^3J_{HC^5CC^7}$ 4.6 Hz], 120.43 [dd (d), C^8, $^1J_{HC^8}$ 162.0 Hz, $^3J_{POCC^8}$ 5.0 Hz], 152.08 [m (d), C^{8a}, $^2J_{POC^{8a}}$ 7.2 Hz], 33.02 [tdm (d), C^9, $^3J_{PCCC^9}$ 15.6 Hz, $^1J_{HC^9}$ 127.1 Hz], 29.66 [tm (s), C^{10}, $^1J_{HC^{10}}$ 129.2 Hz], 21.57 [tm (s), C^{11}, $^1J_{HC^{11}}$ 127.1 Hz], 13.46 [qm (s), C^{12}, $^1J_{HC^{12}}$ 124.0 Hz]. ^{31}P NMR ([$^2H_6$]DMSO, 45 °C) δ_P: –1.2 (d, $^2J_{PCH}$ 18.9 Hz). Found (%): C, 57.01; H, 8.24; Cl, 9.68; N, 4.16; P, 9.11. Calc. for $C_{16}H_{25}ClNO_3P$ (%): C, 55.57; H, 7.24; Cl, 10.27; N, 4.05; P, 8.97.

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