Chlorination of 2,2,2,5-tetrachloro-6-methylbenzo[d]-1,3,2-dioxaphosphole

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An NMR investigation has shown that the reaction of 2,2,2,5-tetrachloro-6-methylbenzo[d]-1,3,2-dioxaphosphole 2 with an excess of molecular chlorine occurs stepwise with high stereoselectivity to give 2,3,4,5,6,6-hexachloro-3-dichlorophosphoryl-5-methyl-cyclohex-1-ene 4, which then undergoes stabilization *via* a 3,3-sigmatropic shift of the dichlorophosphonate fragment to give 1,2,4,4,5,6-hexachloro-3-dichlorophosphoryl-5-methylcyclohex-1-ene 5. The configuration of the hydrolysis product of the latter (1,2,4,4,5,6-hexachloro-5-methyl-3-phosphorylcyclohex-1-ene 6) was established by single crystal X-ray diffraction.

Selective incorporation of halogen atoms into organic molecules is a problem of current interest. In most cases, this is achieved using mild halogenating agents in various solvents;¹ the use of accessible halogens is restricted by the low selectivity of halogenation.¹ The reaction of chlorine with benzene derivatives such as phenols, anilines and pyrocatechols usually occurs as electrophilic substitution to give either mixtures of mono-, di- and trihalogen derivatives or a single product (exhaustive chlorination).² The reactions of methyl-substituted anilines and phenols can occur not only as ordinary substitution but also as a rare process of violation of benzene ring aromaticity resulting in mixtures of possible diastereomers of polychlorinated cyclohexen-3-ones.³ Aromaticity violation also occurs in the case of benzene chlorination under UV irradiation to give hexachlorocyclohexane.² We found previously⁴ that the reaction of chlorine with 2,2,2-trichloro-4-methyl- and 2,2,2-trichloro-5-methylbenzo[d]-1,3,2-dioxaphospholes in a 1:1 ratio results in 2,2,2,5-tetrachloro-4-methyl- and 2,2,2,5-tetrachloro-6-methylbenzo[d]-1,3,2-dioxaphospholes 1 and 2, respectively, in yields higher than 90%.

In this study, we found that, in the presence of an excess of chlorine, chlorination does not stop, and dioxaphosphole **2** can be further chlorinated with molecular chlorine under mild conditions; this involves aromaticity violation of the benzene fragment, that is, an addition reaction occurs.[†] We traced the reaction path by ³¹P NMR spectroscopy and showed that the reaction steps can be distinguished based on the kinetics. The structures of certain intermediates were found by ¹³C NMR spectroscopy.

Judging from the chemical shift $\delta_{\rm P}$ –31.5, the first step involves the formation of compound 3 containing a pentacoordinated phosphorus atom. The violation of the benzene ring aromaticity and the formation of a diastereoisomer containing four chiral centres [C(3a), C(4), C(5), C(7a)] was reliably established based on the ¹³C-{¹H} and ¹³C NMR spectra of this compound. In the molecule of phosphorane 3, five of the seven carbon atoms resonate in the high-field region typical of the sp3-hydridised carbon atom. The presence of two signals at δ 95–101 evidenced chlorine addition to the OC(3a)=C(7a)O bond and formation of a C-C(3a)(Cl)-C(7a)(Cl)-O fragment.⁵ The nuclei of the C(3a) and C(7a) ipso-carbon atoms are distinguishable owing to a difference in the electronic effects of the chloromethylene and alkenyl substituents [stronger deshielding of the C(3a) carbon atom]. The signal of the other sp^3 -hybridised nucleus [C(4)] is observed in the ¹³C-{¹H} NMR spectrum[‡] as a doublet with a characteristic *trans*-constant ${}^{3}J_{PCCC}$ (18.9 Hz). When the spectrum is recorded without decoupling from protons, this doublet is additionally split into a doublet of quartets, which is only possible if there is a methyl group at the C(5) atom. The multiplicity of the remaining signals for the C(6), C(7) and C(5) nuclei suggests that the location of the double bond is C(6)=C(7).

There is no subsequent addition of chlorine to the double bond of compound **3**. During the storage of phosphorane **3** for 3–4 days at 20 °C, it is gradually converted into phosphate **4** $(\delta_{\rm p}$ –2.1) *via* a non-classical variant of the Arbuzov reaction. Phosphate **4** was obtained as a thick colourless oil. Its structure was established on the basis of the ¹³C and ¹³C-{¹H} NMR spectra.[†] Unlike compound **3**, the spectrum of phosphate **4** contains only one signal, which is characteristic of the O–C(Cl)–C environment and belongs to the C(3) nucleus (doublet, ²*J*_{POC} 15.2 Hz). In this case, the two low-field signals corresponding to the resonance of the carbon atoms at the double bond have the form of doublets due to the spin–spin coupling with the

Chlorination of 2,2,2,5-tetrachloro-6-methylbenzo[d]-1,3,2-dioxaphosphole. A chlorine solution (1.9 g in 20 ml of dichloromethane, -5 °C) was added to a stirred solution of phosphole **2** (6.5 g in 20 ml of dichloromethane) in an argon atmosphere at -50 °C. A mixture of compounds **2** (δ -23.2) and **3** in a ratio of 3:2 was obtained in three days. After six days, the ratio of compounds **2** and **3** was 1:6. Compound **3** was completely converted into phosphate **4** in two weeks (25 °C).

2,2,2,3*a*,4,5,6,7*a*-Octachloro-5-methyl-3*a*,7*a*,4,5-tetrahydrobenzo[d]-1,3,2-dioxaphosphole **3**. ¹³C NMR (hereinafter, the description of a signal in ¹³C-{¹H} NMR spectrum is given in parentheses) (CDCl₃) δ : 95.35 [ddd (d), C(7a), ³J_{HC(4)CC(7a)} 2.3 Hz, ²J_{POC(7a)} 1.2 Hz, ²J_{HC(7)C(7a)} 1.0-1.1 Hz], 122.94 [dd (s), C(7), ¹J_{HC(7)} 177.5 Hz, ⁴J_{HC(4)CC(7)} 1.4 Hz], 139.22 [dq (s), C(6), ²J_{HC(7)C(6)} 5.4 Hz, ³J_{HC(8)CC(6)} 4.3 Hz], 69.95 [m (s), C(5)], 69.12 [ddq (d), C(4), ¹J_{HC(4)} 156.1 Hz, ³J_{POC(24)} 18.9 Hz, ³J_{HC(8)CC(4)} 3.5 Hz], 100.77 [ddd (d), C(3a), ²J_{POC(3a)} 5.9 Hz, ³J_{HC(7)CC(3a)} 5.9 Hz, ²J_{HC(4)C(3a)} 2.5 Hz], 25.38 [qd (s), C(8)H₃, ¹J_{HC(8)} 132.7 Hz, ³J_{HC(4)CC(8)} 3.1 Hz]. ³¹P-{¹H} NMR (CDCl₃) δ_{P} : -31.5.

 $\begin{array}{l} 2,3,4,5,6,6-Hexachloro-3-dichlorophosphoryl-5-methylcyclohex-1-ene\\ \textbf{4}. \ ^{13}\text{C}\ \text{NMR}\ (\text{CDCl}_3)\ \delta:\ 132.30\ [dd\ (d),\ C(1),\ ^{1}J_{\text{HC}(1)}\ 180.4\ \text{Hz},\ ^{4}J_{\text{POCC}(1)}\\ 1.4\ \text{Hz}],\ 130.13\ [dd\ (d),\ C(2),\ ^{2}J_{\text{HC}(4)C(2)}\ 5.1\ \text{Hz},\ ^{3}J_{\text{POCC}(2)}\ 3.0\ \text{Hz}],\ 96.91\\ [ddd\ (d),\ C(3),\ ^{2}J_{\text{POC}(3)}\ 15.2\ \text{Hz},\ ^{3}J_{\text{HC}(4)C(2)}\ 11.3\ \text{Hz},\ ^{2}J_{\text{HC}(3)}\ 1.2\ \text{Hz}],\\ 71.16\ [ddq\ (d),\ C(4),\ ^{1}J_{\text{HC}(4)}\ 158.5\ \text{Hz},\ ^{3}J_{\text{POC}(4)}\ 3.5\ \text{Hz},\ ^{2}J_{\text{HC}(4)}\ 3.3\ \text{Hz}],\\ 75.37\ [ddq\ (s),\ C(5),\ ^{3}J_{\text{HC}(4)C(5)}\ 5.3\ \text{Hz},\ ^{2}J_{\text{HC}(5)}\ 5.3\ \text{Hz},\ ^{2}J_{\text{HC}(5)}\ 4.2\ \text{Hz}],\\ 87.97\ [m\ (s),\ C(6),\ ^{3}J_{\text{HC}(8)C(6)}\ 4.2\ \text{Hz},\ ^{3}J_{\text{HC}(2)}\ 2.7\ \text{Hz},\ ^{2}J_{\text{HC}(6)}\ 1.5\ \text{Hz}],\\ 23.00\ [q\ (s),\ C(7),\ ^{1}J_{\text{HC}(7)}\ 132.7\ \text{Hz},\ ^{3}J_{\text{HC}(4)C(7)}\ 4.4\ \text{Hz}].\ ^{31}\text{P-}^{1}\text{H}\}\ \text{NMR}\ (\text{CDCl}_3)\ \delta_{\text{P}}:-1.3.\end{array}$

1,2,4,4,5,6-Hexachloro-3-dichlorophosphoryl-5-methylcyclohex-1-ene 5 was obtained by heating (180 °C, 5 min) of phosphate 4, as the yellow viscous oil with 90% content (3.5 g), bp 145–148 °C (1 Torr). ¹H NMR (400 MHz, CDCl₃) δ : 5.94 [br. d, 1H, H(3), ³J_{POCH} 12.0 Hz], 5.03 [br. s, 1H, H(6)], 2.13 [br. s, 3H, Me]. ¹³C NMR (CDCl₃) δ : 126.62 [br. s (br. s), C(1)], 132.00 [br. s (br. s), C(2)], 84.26 [dd (d), C(3), ¹J_{HC(3)} 162.3 Hz, ²J_{POC(3)} 7.8 Hz], 89.83 [br. m (d), C(4), ³J_{POCC(4)} 2.5 Hz], 73.95 [br. s (s), C(5)], 65.39 [br. d (br. s), C(6), ¹J_{HC(6)} 163.4 Hz], 25.63 [br. q (br. s), C(7)H₃, ¹J_{HC(7)} 132.8 Hz]. ³¹P NMR (CDCl₃) δ _P: 13.2 (d, ³J_{POCH} 12.0 Hz).

1,2,4,4,5,6-Hexachloro-5-methyl-3-phosphorylcyclohex-1-ene **6**. Colourless crystals of compound **6** (mp 211 °C) were obtained by hydrolysis of phosphate **5** in aqueous acetone. ¹H NMR (400 MHz, [²H₆]DMSO) δ : 2.08 (br. s, 3H, Me), 5.60 [d, 1H, H(6), ³J_{POCH} 11.7 Hz], 5.69 [d, 1H, H(3), ⁶J_{POCCCCH} 1.1 Hz]. ³¹P NMR ([²H₆]DMSO) δ_{P} : -2.7 (d, ³J_{POCH} 11.6 Hz).

[†] *General Procedures.* Solvents and commercial reagents were purified by conventional methods. All experiments were performed under an atmosphere of dry argon. Melting points are uncorrected. Measurements involved a Boetius melting point apparatus. NMR spectra were recorded on Bruker MSL-400 (¹H, 400 MHz; ¹³C, 100.6 MHz), Bruker WM-250 (¹H, 250 MHz) and Bruker CXP-100 (³¹P, 36.48 MHz) spectrometers. The $\delta_{\rm P}$ values were determined relative to an external standard (H₃PO₄). The $\delta_{\rm C}$ and $\delta_{\rm H}$ values were determined relative to an internal standard (HMDS).



phosphorus atom. Moreover, the C(4), C(5) and C(6) nuclei that have a spin-spin coupling with the methyl-group protons resonate at strong fields characteristic of sp^3 -hybridised carbon atoms. At this step (the conversion of phosphorane **3** to phosphate **4**), the allylic rearrangement is accompanied by the regioselective cleavage of the C(7a)–O bond and the formation of a phosphoryl group. The regiochemistry of the process is probably more consistent with a higher stability of the intermediate allylic carbocation with a positive charge at the C(7a) atom than at the C(3a) atom.

Prolonged storage of phosphate 4 at 20 °C or with heating results in an unusual 3,3-sigmatropic shift of the dichlorophosphate group; however, it may be regarded as a variant of the Claisen 3,3-rearrangement.⁶ According to NMR spectra, phosphate 5 is formed as a single diastereomer, in which the P-O bond is hydrolysis-resistant. X-ray diffraction data for hydrolysis product 6 (Figure 1) suggest that a single crystal contains two enantiomers 6A and 6B in a 1:1 ratio, in which the configurations of the C(3), C(5) and C(6) atoms are R, S, S and S, R, R, respectively.^{\ddagger} Compound 6 forms crystals as a salt with DMSO and a solvate with water. The carbon ring in the molecule of 6A has a *semichair* conformation: the four-atom fragment C(6A)C(1A)C(2A)C(3A) is planar [to within 0.08(1) Å], and the C(4A) and C(5A) atoms deviate by -0.31(1) and 0.31(1) Å on both sides of the plane; in the molecule of 6B, this is a semichair approaching a sofa: the four-atom fragment C(6B)-

[‡] X-ray crystallography of compound **6**: 2C₇H₆Cl₆O₄P·2C₂H₇OS·2H₂O, M = 494.95, triclinic, space group $P\overline{1}$, a = 8.756(8), b = 10.472(8)and c = 21.64(2) Å, $\alpha = 102.04(7)^{\circ}$, $\beta = 99.18(7)^{\circ}$, $\gamma = 94.24(7)^{\circ}$, $V = 100.04(7)^{\circ}$ = 1904(3) Å³, Z = 2, d_{calc} = 1.727 g cm⁻³. Cell parameters and intensities of 4449 independent reflections (2077 with $I \ge 2\sigma$) were measured on an Enraf-Nonius CAD-4 diffractometer in the $\omega/2\theta$ -scan mode, $\theta \leq 57.3^{\circ}$, using CuKa radiation with a graphite monochromator. Data corrections were not applied (μ_{Mo} 10.3 cm⁻¹). The structure was solved by a direct method using the SIR program⁷ and refined by the full matrix leastsquares using the SHELXL97 program.8 All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included in the calculated positions with thermal parameters 30% larger than those of the atoms to which they were attached. The final residuals were R = 0.1351 and $R_w = 0.4048$. All calculations were performed on a PC using the WinGX program.9 Determination of cell parameters, data collection and data reduction were performed on an Alpha Station 200 computer using the MoLEN program.¹⁰ All the figures were made using the PLATON program.11

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/ conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 274794. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2005.



Figure 1 Molecular geometry 6A and 6B in a crystal. Selected bond lengths (d, Å): Cl(2A)-C(2A) 1.67(1), Cl(1A)-C(1A) 1.68(1), Cl(6A)-C(6A) 1.78(1), Cl(5A)-C(5A) 1.84(1), Cl(3A)-C(4A) 1.77(1), Cl(4A)- $\begin{array}{c} C(4A) & 1.76(1), & Cl(2B) - C(2B) & 1.70(1), & Cl(6B) - C(6B) & 1.86(2), & P(1A) - O(1A) & 1.56(1), & P(1A) - O(2A) & 1.52(1), & P(1A) - O(2A) & 1.54(1), & P(1A) - O(2A) & P(1A$ O(4A) 1.50(1), P(1B)–O(1B) 1.58(1), P(1B)–O(2B) 1.46(1), P(1B)–O(4B) 1.58(1), P(1B)-O(3B) 1.49(1), O(1A)-C(3A) 1.47(1), O(1B)-C(3B) 1.46(1), C(1A)-C(2A) 1.31(2), C(1B)-C(2B) 1.34(2), C(2A)-C(3A) 1.55(2), C(2B)-C(3B) 1.50(2), C(1A)-C(6A) 1.51(1), C(5A)-C(6A) 1.65(2), C(5B)-C(6B) 1.50(2), C(5A)-C(7A) 1.64(2), C(5B)-C(7B) 1.57(2). Selected bond angles (\u03c6/\u03c6): O(1A)-P(1A)-O(3A) 103.6(6), O(2A)-P(1A)-O(3A) 111.4(7), O(1A)–P(1A)–O(4A) 107.8(6), O(1A)–P(1A)–O(2A) 110.6(6), O(3A)–P(1A)–O(4A) 106.4(7), O(2A)–P(1A)–O(4A) 116.2(7), O(1B)–P(1B)–O(4B) 102.4(6), O(2B)–P(1B)–O(3B) 117.6(7), O(3B)– P(1B)-O(4B) 107.8(6), O(1B)-P(1B)-O(3B) 107.2(6), P(1B)-O(1B)-C(3B) 123.2(8). Selected torsion angles (τ /°): O(4A)–P(1A)–O(1A)–C(3A) 113(1), O(4B)–P(1B)–O(1B)–C(3B) 119.2(9), P(1A)–O(1A)–C(3A)–C(2A) -112(1), P(1B)-O(1B)-C(3B)-C(2B) 114(1), C(3A)-C(2A)-C(1A)-C(6A)10(2), Cl(2A)-C(2A)-C(3A)-O(1A) 43(1), Cl(5A)-C(5A)-C(6A)-Cl(6A) 158.4(6), C(1A)-C(6A)-C(5A)-Cl(5A) -78.(1), Cl(1B)-C(1B)-C(6B)-C(5B) -173(1), C(3A)-C(4A)-C(5A)-C(6A) -54(1), C(2B)-C(1B)-C(6B)-Cl(6B) -115(1), C(2B)-C(1B)-C(6B)-C(5B) 12(2), C(1A)-C(2A)-C(3A)-C(4A) -24(2), C(1A)-C(2A)-C(3A)-O(1A) -147(1), Cl(6B)-C(6B)-C(5B)-C(4B) 88(1), C(1B)-C(6B)-C(5B)-C(4B) -37(2), Cl(1A)-C(1A)-C(6A)-Cl(6A) -73(1), C(1B)-C(6B)-C(5B)-Cl(5B) 78(1), C(3B)-C(4B)-C(5B)-C(6B) 54(2), C(6B)-C(5B)-C(4B)-Cl(4B) -66(1), C(2A)-C(3A)-C(4A)-C(5A) 46(1), C(2A)-C(1A)-C(6A)-Cl(6A) 107(1), C(2A)-C(1A)-C(6A)C(5A) -16(2), Cl(3A)-C(4A)-C(3A)-C(2A) -75(1), Cl(4A)-C(4A)-C(3A)-O(1A) -68(1), Cl(3A)-C(4A)-C(3A)-O(1A) 48(1), Cl(5B)-C(5B)-C(4B)-C(3B) -57(1), Cl(6A)-C(6A)-C(5A)-C(4A) -83(1), C(5A)-C(4A)-C(3A)-O(1A) 169(1), Cl(2B)-C(2B)-C(3B)-C(4B) -160(1), C(1B)-C(2B)-C(3B)-C(4B) 146(1), C(1B)-C(2B)-C(3B)-C(4B) 26(2)

C(1B)C(2B)C(3B) is planar [to within 0.02(1) Å], and the C(5B)and C(4B) atoms deviate by -0.50(2) and 0.17(1) Å, respectively, from the plane. The deviation of these atoms on different sides allows one to consider this conformation as a semichair. However, the very small deviation of the C(4B) atom [0.17(1) Å]from the C(6B)C(1B)C(2B)C(3B) plane also allows us to consider that the five-atom fragment C(6B)C(1B)C(2B)C(3B)C(4B) is approximately planar and the ring conformation is a *sofa*. The lengths of the C-Cl bonds at the C=C double bond are shortened due to the effect of the phosphorus-containing substituents at the C(1) carbon atom [Cl(1A)-C(1A) 1.67(1) Å, Cl(2A)–C(2A) 1.68(1) Å, Cl(1B)–C(1B) 1.71(1) Å, Cl(2B)–C(2B) 1.65(1) Å]. Since the crystal structure incorporates four solvatetype solvent molecules (2DMSO and 2H₂O), the crystal contains multiple classical hydrogen bonds of the O-H-O type, which result in the formation of infinite layers along one of the crystallographic axes.

Thus, the reaction of 2,2,2,5-tetrachloro-6-methylbenzo[d]-1,3,2-dioxaphosphole **2** with chlorine is the first example of chlorination of an annelated 1,3,2-diheterocyclane at an aromatic fragment, which occurs under mild conditions without additional stimulation by catalysis or irradiation. Apart from the unusually facile aromaticity violation and allylic rearrangement, the previously unknown 3,3-sigmatropic shift of the phosphoryl group also occurs. This reaction is a convenient method for the stereoselective synthesis of hardly accessible polyfunctional cyclohexene derivatives.

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