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Mendeleev Commun., 2010, **20**, 44–46

Mendeleev
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An unusual cascade reaction of 4,5-dihydro-4,4-bis(trifluoromethyl)-2-phenyl-6,7-(4-chlorobenzo)[*e*]-1,3,2-dioxaphosphepin-5-one with chloral

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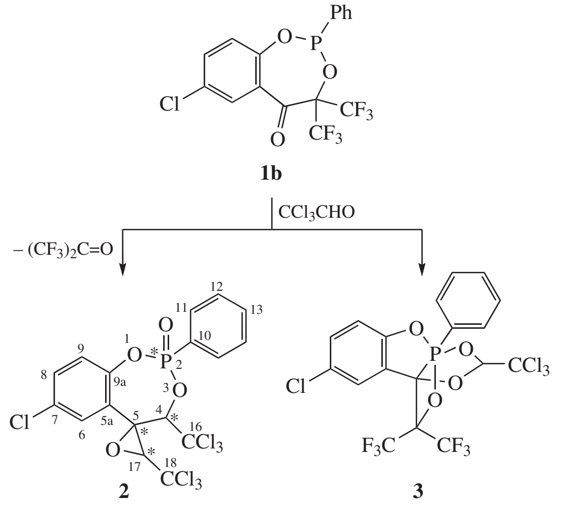
DOI: 10.1016/j.mencom.2010.01.017

The reaction of 4,5-dihydro-4,4-bis(trifluoromethyl)-2-phenyl-6,7-(4-chlorobenzo)[*e*]-1,3,2-dioxaphosphepin-5-one with chloral (1:2) proceeds with evolving hexafluoroacetone and gives spiro{2-oxo-4-trichloromethyl-4,5-dihydro-2-phenyl-6,7-(4-chlorobenzo)[*f*]-1,3,2-dioxaphosphepine-5,2′-(3′-trichloromethyl)oxirane} with a high stereoselectivity. Configuration of the four chiral centres ($P^2_S C^4_S C^5_S C^{3'}_S / P^2_R C^4_R C^5_R C^{3'}_R$) was determined by a single crystal X-ray diffraction.

The reactions of P^{III} derivatives with carbonyl compounds are important for the synthesis of compounds bearing pentacoordinated phosphorus, which are the intermediates in the nucleophilic displacement reaction at tetracoordinated phosphorus species.[1–6] Recently,[7,8] we found that the reaction of $\lambda^3\sigma^3$-1,3,2-dioxabenzophospholes having a γ- or δ-carbonyl group to the phosphorus atom in exocyclic substituent leads to the formation of ‘carcass’ phosphoranes. In spite of the formation of a few chiral centres, the process has a high regio- and stereoselectivity. The reaction was also applied to the P^{III} derivatives bearing γ-endocyclic carbonyl group relative to the phosphorus atom, such as 4,5-dihydro-4,4-bis(trifluoromethyl)-2-phenyl-6,7-benzo[*e*]- and 4,5-dihydro-4,4-bis(trifluoromethyl)-2-phenyl-6,7-(4-chlorobenzo)-[*e*]-1,3,2-dioxaphosphepin-5-ones **1a**,**b**. The 5-carbaphosphatrane derivatives with pentacoordinated phosphorus atom, containing three oxygen atoms in equatorial sets and two less apicophilic carbon ones in apical sets were unexpectedly obtained in the reaction of compounds **1a**,**b** with hexafluoroacetone.[9]

In this work, we attempted to use chloral as another reactive compound for the synthesis of 5-carbaphosphatranes. However, the interaction of chloral with dioxaphosphepine **1b** is more complex and proceeds by two main directions. The first direction leads to the formation of the unusual derivative with tetracoordinated phosphorus atom – spiro{2-oxo-4-trichloromethyl-4,5-dihydro-2-phenyl-6,7-(4-chlorobenzo)[*f*]-1,3,2-dioxaphosphepine-5,2′-(3′-trichloromethyl)oxirane} **2**. The evolving of hexafluoroacetone, detected owing to the characteristic odour, took place in the course of the reaction. The content of compound **2** in the reaction mixture is about 70%.[†] The second direction involves the formation of 5-carbaphosphatrane derivative **3** as a minor compound.

The stereoselectivity of the formation of product **2** is very high. In spite of three additional asymmetric centres, only one diastereoisomer was formed and isolated in view of crystals suitable for X-ray diffraction (as a solvate with one CH_2Cl_2 molecule).[‡] The molecular geometry of compound **2** is shown in Figure 1. The phosphorus atom has a distorted tetrahedral configuration, a seven-membered heterocycle has a distorted boat conformation and includes the planar four-atoms fragment C(5)C(5a)C(9a)O(1), the atoms P(2), O(3) and C(4) being situated on one side and at various distances of the latter. Phenyl and trichloromethyl substituents, as well as oxirane carbon atom [C(11)], are in pseudo-equatorial sets, the phosphoryl oxygen and the oxirane cycle



Scheme 1

[†] Solvents and commercial reagents were purified by conventional methods before use. All experiments were performed under an atmosphere of dry argon. Melting points are uncorrected. Measurements involved a Boetius melting point apparatus. NMR experiments were performed in $CDCl_3$ at 20 °C with Varian Unity-300 (^{31}P, ^{31}P-{^1H} at 121.42 MHz; ^{19}F at 282.4 MHz) and Bruker Avance-600 spectrometers with a 5 mm diameter inverse probe head with Z-active shielded gradients working at 600 MHz for ^1H and 150.864 MHz for ^{13}C. The δ_H and δ_P values were determined relative to internal (HMDS) or external (H_3PO_4) standard. The δ_F values were determined relative to internal standard (C_6F_6) and then re-calculated relative to $CFCl_3$. The δ_C values were determined relative to the deuterated solvent signal. IR spectra were recorded on a Specord M-80 instrument in Nujol. EI mass spectra were obtained with a TRACE MS Finnigan MAT instrument; the ionization energy was 70 eV and the ion source temperature was 200 °C. The samples were introduced into the ion source *via* a direct inlet system. The evaporating ampoule was heated from 35 to 150 °C at a rate of 35 K min^{-1}. The mass spectrometric data were processed using the Xcalibur system program.

oxygen are in pseudoaxial sets. The trichloromethyl substituent and the C(4)–C(5) bond are situated in *trans*-configuration.

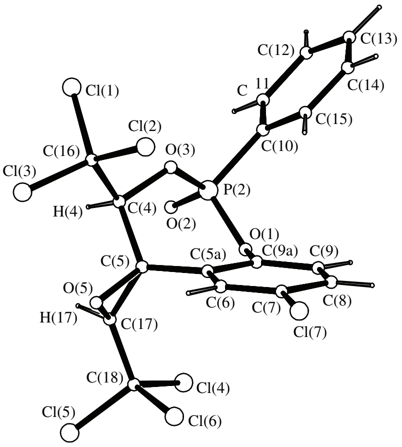
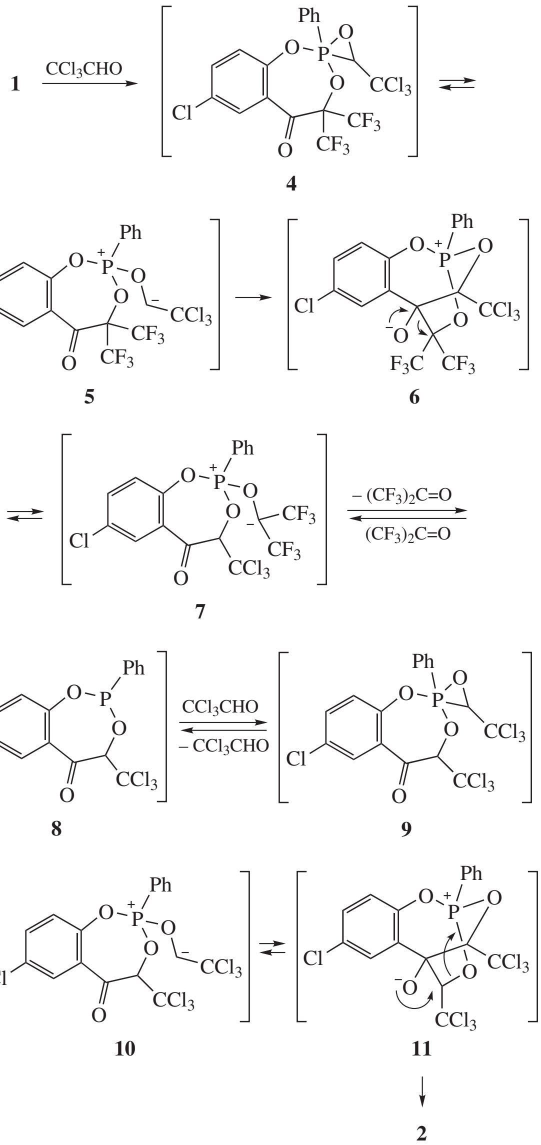


Figure 1 Molecular geometry of compound **2** in a crystal (a solvate with disordered CH_2Cl_2 molecule, the solvent is omitted for clarity). Selected bond lengths (Å) and bond angles (°): P(2)–O(2) 1.465(4), P(2)–O(3) 1.591(4), P(2)–O(1) 1.594(4), P(2)–C(10) 1.777(7), O(3)–C(4) 1.433(7), C(4)–C(5) 1.555(8), C(5)–C(5a) 1.503(8), C(5)–C(17) 1.482(8), O(5)–C(5) 1.430(7), O(5)–C(17) 1.431(8), O(2)–P(2)–O(3) 116.2(3), O(2)–P(2)–O(1) 109.9(3), O(3)–P(2)–O(1) 103.8(2), O(2)–P(2)–C(10) 115.8(3), O(1)–P(2)–C(10) 107.4(3), O(5)–C(5)–C(17) 58.8(4), O(5)–C(5)–C(5a) 116.8(5), C(17)–C(5)–C(5a) 123.1(5), O(5)–C(5)–C(4) 114.0(5), O(5)–C(17)–C(5) 58.8(4), O(5)–C(17)–C(18) 116.2(5).

The reaction of compound **1b** *with chloral.* The mixture of phosphonite **1b**[9] (7 mmol, 2.85 g), chloral (16 mmol, 2.52 g) and CH_2Cl_2 (20 ml) was kept during two months in an argon atmosphere (20 °C). Methylene chloride and chloral excesses were removed in a vacuum; the residue was dissolved in the CH_2Cl_2–pentane mixture (5:1) and was kept for six days. The precipitate was filtered off, washed with CH_2Cl_2–pentane mixture (5:1) and dried in a vacuum (0.1 Torr). Compound **2**, colourless crystals, mp 221–222 °C (decomp.), yield 58%. IR (Nujol, ν/cm^{-1}): 3005, 2948, 1901, 1740, 1592, 1481, 1440, 1414, 1305, 1272, 1205, 1132, 1114, 1070, 1013, 997, 927, 902, 887, 830, 803, 758, 745, 728, 703, 687, 670, 632, 623, 614, 603. ^{31}P-{^{1}H} NMR ([$^2H_6$]DMSO) δ_P: 14.8. ^{1}H NMR ([$^2H_6$]DMSO): 5.71 (s, H^{18}), 5.84 (s, H^4, $^3J_{PH}$ 3.0 Hz), 7.07 (d, H^9, $^3J_{HH}$ 8.9 Hz), 7.50 (dd, H^8, $^3J_{HH}$ 8.9 Hz, $^4J_{HH}$ 2.6 Hz), 7.58 (d, H^6, $^4J_{HH}$ 2.6 Hz), 7.61 (m, H^{12}, H^{14}), 7.73 (m, H^{11}, H^{15}, H^{13}). ^{13}C NMR ([$^2H_6$]DMSO) (a multiplicity of the signal in ^{13}C-{^{1}H} spectrum is given in parentheses): 81.45 [ddd (d), C^4, $^1J_{HC^4}$ 164.7 Hz, $^2J_{POC^4}$ 6.6 Hz, $^3J_{HC^{17}CC^4}$ 1.6 Hz], 63.91 [m (s), C^5, $^2J_{HCC^5}$ 2.0–2.3 Hz, $^2J_{HCC^5}$ 2.0–2.3 Hz, $^3J_{HC^6CC^5}$ 4.3–4.5 Hz], 123.61 [br. m (br. s), C^{5a}], 131.67 [dd (s), C^6, $^1J_{HC^6}$ 170.0 Hz, $^3J_{HC^8CC^6}$ 6.1 Hz], 129.34 [ddd (s), C^7, $^3J_{HC^9CC^7}$ 11.0 Hz, $^2J_{HCC^7}$ 3.6 Hz, $^2J_{HCC^7}$ 3.2 Hz], 130.81 [dd (s), C^8, $^1J_{HC^8}$ 170.1 Hz, $^3J_{HC^6CC^8}$ 5.1 Hz], 121.90 [dd (d), C^9, $^1J_{HC^9}$ 167.8 Hz, $^3J_{POCC^9}$ 5.5 Hz], 148.24 [dddd (d), C^{9a}, $^3J_{HC^6CC^{9a}}$ 9.5 Hz, $^3J_{HC^8CC^{9a}}$ 9.5 Hz, $^2J_{POC^{9a}}$ 9.4 Hz, $^2J_{HC^9C^{9a}}$ 4.2 Hz], 125.02 [dt (d), C^{10}, $^1J_{HC^{10}}$ 195.7 Hz, $^3J_{HC^{12,14}CC^{10}}$ 7.6 Hz], 130.99 [dddd (d), C^{11}, $^1J_{HC^{11}}$ 165.0 Hz, $^2J_{PCC^{11}}$ 10.5 Hz, $^3J_{HC^{13}CC^{11}}$ 7.4 Hz, $^3J_{HC^{15}CC^{11}}$ 7.4 Hz], 129.21 [ddd (d), C^{12}, $^1J_{HC^{12}}$ 167.4 Hz, $^3J_{PCCC^{12}}$ 16.0 Hz, $^3J_{HC^{14}CC^{12}}$ 8.3 Hz], 134.03 [br. dt (d), C^{13}, $^1J_{HC^{13}}$ 163.9 Hz, $^3J_{HC^{11}CC^{13}}$ 7.0 Hz, $^4J_{PCCCC^{13}}$ 2.1 Hz], 96.32 [d (d), C^{16}, $^3J_{POCC^{16}}$ 13.8 Hz], 69.83 [dd (s), C^{17}, $^1J_{HC^{17}}$ 193.2 Hz, $^3J_{HC^4CC^{17}}$ 4.4 Hz], 93.56 [d (s), C^{18}, $^2J_{HC^{17}C^{18}}$ 10.8 Hz]. MS, *m/z* (%): 554 (0.63) [M]$^{+\cdot}$ (calc. for $C_{17}H_{10}{}^{35}Cl_7O_4P$, 554), 519 (2.0) [M – Cl]$^+$, 483 (3.3) [M – HCl – Cl]$^+$, 437 (0.82) [M – CCl$_3$]$^+$, 389 (37.7) [$C_{15}H_9{}^{35}Cl_3O_4P$]$^+$, 366 (48.2) [$C_{16}H_9{}^{35}Cl_2O_4P$]$^+$, 294 (100.0) [$C_{14}H_{12}{}^{35}ClO_3P$]$^+$. Found (%): C, 33.43; H, 1.97; Cl, 49.57; P, 4.32. Calc. for $C_{17}H_{10}Cl_7O_4P\cdot CH_2Cl_2$ (%): C, 33.62; H, 1.87; Cl, 49.73; P, 4.82.

Compound **3** was obtained by removing the solvent from filtrate (after filtration of compound **2**) and crystallization of a residue under a layer of pentane. Yield 17%, colourless crystals, mp 118–119 °C (decomp.). IR (Nujol, ν/cm^{-1}): 1614, 1592, 1476, 1462, 1441, 1355, 1323, 1293, 1223, 1168, 1127, 1109, 1069, 1041, 1018, 1003, 973, 935, 893, 867, 853, 839, 825, 794, 774, 764, 746, 728, 693, 645, 630. ^{31}P-{^{1}H} NMR (CDCl$_3$) δ_P: 6.0 (s). ^{19}F NMR (CDCl$_3$) δ_F: –72.8 (q, CF$_3$, $^4J_{FF}$ 10.7 Hz), –73.9 (q, CF$_3$, $^4J_{FF}$ 10.7 Hz). MS, *m/z*: 562 [M]$^{+\cdot}$ (calc. for $C_{17}H_9{}^{35}Cl_4F_6O_4P$, 562). Found (%): C, 36.09; H, 2.01; P, 5.61. Calc. for $C_{17}H_9Cl_4F_6O_4P$ (%): C, 36.17; H, 1.60; P, 5.50.



Scheme 2

The mechanism of the cascade formation of spirane **2** is rather complex and unclear. Nevertheless, we may propose the following reaction scheme, which can be conditionally divided into two parts (Scheme 2). The first part is an unusual reaction

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[‡] *X-ray diffraction data for* **2**: $C_{17}H_{10}Cl_7O_4P\cdot CH_2Cl_2$, M = 642.30, monoclinic, space group $P2_1/n$, a = 11.804(3), b = 11.430(5) and c = 18.364(5) Å, β = 95.59(3)°, V = 2465.9(14) Å^3, Z = 4, d_{calc} = 1.73 g cm^{-3}. Cell parameters and intensities of 4947 independent reflections (3247 with $I \geq 2\sigma$) were measured on an Enraf-Nonius CAD-4 diffractometer in the ω-scan mode, $\theta \leq 74.00°$, using CuKα radiation with graphite monochromator. The intensity falling was not observed at three control measurements. An empirical absorption correction based on ψ-scans was applied [μ(CuKα) = = 10.2 cm^{-1}]. The structure was solved by direct method using the SIR program[13] and refined by the full matrix least-squares using SHELX-97[14] program package. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were calculated and refined as riding atoms. The final divergence factors are R = 0.079, Rw = 0.194 based on 3247 reflections with $F^2 \geq 2\sigma^2$. All calculations were performed on PC using WinGX[15] program. Cell parameters, data collection and data reduction were performed on Alpha Station 200 computer using MoLEN.[16] In the methylene chloride molecule Cl^{4A} (Cl^{4B}) and H atoms are disordered in a crystal and were refined with occupancy of 0.701(8) [0.299(8)]. Figures were made using the program PLATON.[17]

CCDC 748834 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2010.

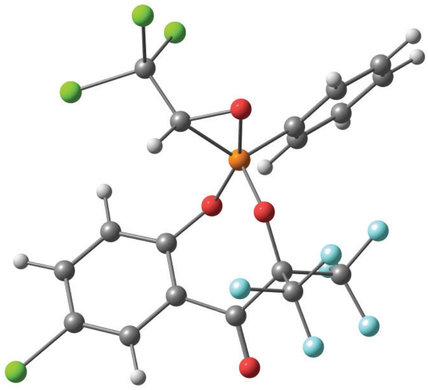
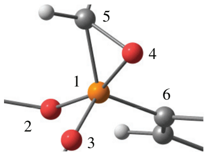


Figure 2 Calculated geometry of pentacoordinated phosphorus intermediate **4**.

Table 1 Selected bond lengths and bond angles of intermediate **4** in twist-boat conformation.



Bond	*d*/Å	Angle	*φ*/°
1–2	1.720	2–1–3	97.2
1–3	1.667	2–1–4	159.7
1–4	1.713	2–1–5	110.7
1–5	1.802	2–1–6	94.7
1–6	1.819	3–1–4	90.6
		3–1–5	107.7
		3–1–6	115.4

of replacement of a hexafluoroacetone fragment by chloral, which leads to the formation of dioxaphosphepine **8** *via* a range of intermediates **4**–**7**. The first stage of this process is likely the symmetry-allowed [1 + 2]-cycloaddition or the cheletropic reaction, which yields spirophosphorane **4**, bearing a three-membered cycle. The recent quantum-chemical calculations for the related reaction of chloral with 2-methoxy-5,6-benzo[*d*]-1,3,2-dioxaphosphorin-4-one give a relatively stable intermediate spirophosphorane structurally similar to the intermediate **4**.[10] The structure of **5** may be a transition state in passing to bipolar intermediate **6**, which converts further to bipolar species **7**. This bipolar ion is an unstable intermediate of the reversible reaction of P$^{\text{III}}$ derivative **8** with hexafluoroacetone. Chloral and hexafluoroacetone have a closely related reactivity, but a quite different volatility, that leads to the fast removal of hexafluoroacetone from the reaction sphere.

The second part of the reaction scheme, starting from the interaction of chloral with intermediate phosphepine **8**, is analogous to the first one in some general features. It involves a cascade formation of intermediates **9**–**11**. Distinct from bipolar ion **6**, the intermediate **11** turns into epoxide **2** as a result of the alkoxide anion intramolecular attack on the carbon atom bound to trichloromethyl group with simultaneous P=O bond formation.

We made an attempt to study the mechanism of the reaction by the quantum chemical calculations. First, the structures of compound **1b** and intermediate **4** were investigated by the density functional theory (DFT) method with the PBE functional and Triple *z* basis, using the Priroda program.[11,12] A few conformations of seven-membered heterocycle of compound **1b**, namely, boat and twist-boat ones were optimized, in which a phenyl substituent is located in the equatorial and axial sets. Among them a twist-boat form with an equatorial orientation of phenyl substituent is most favourable. The selected bond lengths and bond angles of intermediate **4** in twist-boat conformation are given in Table 1, and the molecular geometry is shown in Figure 2. The configuration of the phosphorus atom in spirophosphorane **4** is more likely a distorted square pyramid rather than a trigonal bipyramid. The full energies of chloral, compound **1b** and intermediate **4**, calculated by DFT/PBE/TZ2P method are –1532.01034, –2239.54278 and –3771.54913, respectively; that is, the formation of intermediate **4** demands very slight expenditure of energy (2.6 kcal mol^{-1}).

This work was supported by the Russian Foundation for Basic Research (grant no. 07-03-00180).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2010.01.017.

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Received: 5th October 2009; Com. 09/3399