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The reaction of 4-(1,3,2-benzodioxaphosphol-2-yloxy)-3-*tert*-butylpent-4-en-2-one with hexafluoroacetone

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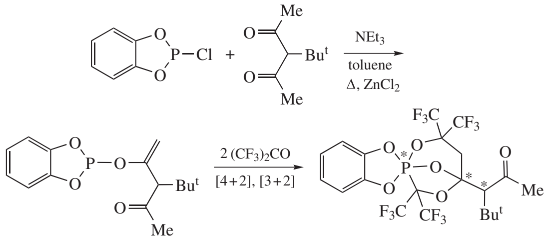
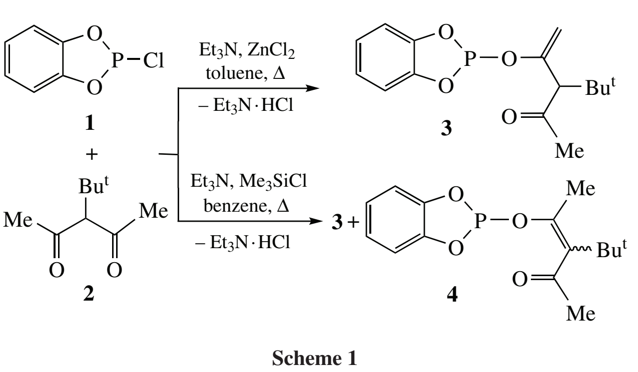
Catalytic ($ZnCl_2$, Et_3N) phosphorylation of *tert*-butylacetylacetone with 2-chloro-1,3,2-benzodioxaphosphole unexpectedly occurs with elimination of proton from the methyl group and leads to vinyloxyphosphole derivative, *viz.*, 4-(1,3,2-benzodioxaphosphol-2-yloxy)-3-*tert*-butylpent-4-en-2-one. Its reaction with hexafluoroacetone gives a cage phosphorane as a result of subsequent chemoselective [4+2]- and [3+2]-cycloadditions with stereoselectivity above 95%.



Pentacoordinated phosphorus derivatives are the intermediates in nucleophilic substitution reactions of the P^{IV} species,[1] in particular, phosphorylation and dephosphorylation reactions occurring in a living cell.[2] They are intermediates in olefination,[3] C–C cross-coupling,[4] hydrosilylation,[5] *etc*. Much attention is paid to the synthesis and reactivity of hypercoordinated phosphorus derivatives,[6] including quantum chemical calculations.[7]

We have previously obtained phosphoranes containing a rigid-cage structure,[8] which can serve as convenient models for studying structure–reactivity relationship among pentacoordinated phosphorus compounds.[9] This approach is based on cascade processes of intramolecular addition of P^{III} derivatives containing an exocyclic carbonyl group initiated by the activated compounds bearing homo- or heteroatom multiple bonds.

Here we used a new vinyl phosphite **3** containing a carbonyl group in the δ-position to the P^{III} atom (Scheme 1) as a starting compound for the synthesis of cage phosphoranes. Unlike acetylacetone,[10] the phosphorylation of *tert*-butylacetylacetone **2** with 2-chloro-1,3,2-benzodioxaphosphole **1** in the presence of triethylamine and chlorotrimethylsilane as a catalyst was very slow (64 h reflux in benzene, for details, see Online Supplementary Materials). In this case, an oxygen atom of compound **2** was subjected to phosphorylation and vinyl phosphite **3** was mainly (80%) resulted from prevailing elimination of the proton from the methyl group (see Scheme 1). Isomeric 4-(1,3,2-benzodioxaphosphol-2-yloxy)-3-*tert*-butylpent-3-en-2-one **4** (analogous to the product of phosphorylation of acetylacetone[10]) was obtained as a by-product in 20% yield after vacuum distillation. When phosphorylation of compound **2** with chlorophosphole **1** was performed in toluene (22 h reflux) in the presence of triethylamine and zinc chloride, single isomer **3** was obtained. Such an unusual course of phosphorylation (with the elimination of a proton from carbon C^1) in both cases is apparently connected with the steric effect of the *tert*-butyl group, interfering proton elimination from carbon C^3.



Scheme 1

Note that we did not find examples of the use of zinc chloride as a catalyst for phosphorylation of P^{III} derivatives. However, examples of the related silylation of carbonyl compounds with chlorotrimethylsilane in the presence of zinc chloride with the formation of trimethylsilylenols are known.[11] The structure of compound **3** was confirmed by ^1H, ^{13}C, $^{13}C\text{-}\{^1H\}$, ^{31}P NMR and IRS (see also Online Supplementary Materials).

The reaction of vinyl phosphite **3** with hexafluoroacetone, unlike the case in our earlier work,[8] unexpectedly leads to cage phosphorane **5**, an addition product of the 1 : 2 composition (Scheme 2),[†] which is confirmed by high-resolution mass spectrometry (EI). The process, in our opinion, includes an unusual cascade of two consecutive [4+2]- and [3+2]-cycloaddition reactions (intermediates **A**–**C**). Taking into account that benzophospholes exhibit biphilic properties (*i.e.*, they can react as a nucleophile and an electrophile), the polar $P^{\delta+}$–O–C=$C^{\delta-}$ diheterosystem participates in a [4 + 2]-cycloaddition with hexafluoroacetone

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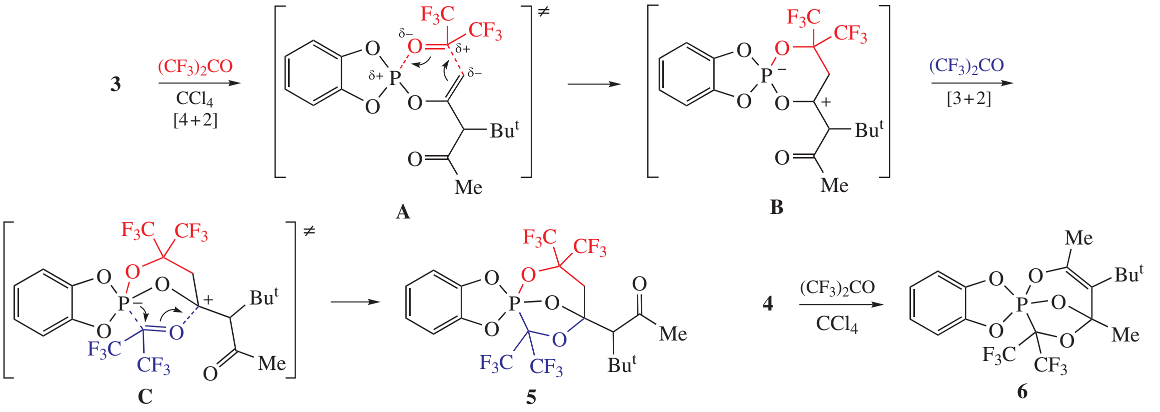
[†] *3,3,7,7-Tetrakis(trifluoromethyl)-1,1-*o*-phenylenedioxa-5-(1-*tert*-butyl-2-oxopropyl)-2,6,8-trioxa-1-phosphabicyclo[4.3.2^{1,5}]octane* **5**. Hexafluoroacetone (4.65 g, 28 mmol) was condensed into a solution of compound **3** (4.0 g, 14 mmol) in CCl_4 (20 ml), cooled under argon to –40 °C. The mixture was kept for 8 h until reaching 20 °C. The next day, a crystalline precipitate of compound **5** was formed, which was filtered and dried *in vacuo* (0.1 Torr), yield 5.7 g (67%), mp 107–109 °C. For characterization, see Online Supplementary Materials.



Scheme 2

instead of the classical diene and forms a further $P^{\delta-}$–O–$C^{\delta+}$ bipolar ion of the phosphoranide type *via* transition state **A**. The bipolar ion **B** then reacts with the second molecule of highly active hexafluoroacetone by a [3+2]-cycloaddition mode *via* transition state **C**. The process is stereoselective and leads to the formation of a single diastereoisomer of compound **5** (>95%) (phosphorus chirality does not affect the multiplicity of the signals in the spectra, apparently due to pseudo-rotation processes in a trigonal bipyramid in solution).

It is interesting to note that the reaction of the phosphole **3**, **4** mixture with hexafluoroacetone affords a mixture of compound **5** and 4-*tert*-butyl-2,5-dimethyl-7,7-bis(trifluoromethyl)-1,1-*o*-phenylenedioxa-2,6,8-trioxa-1-phosphabicyclo[4.3.2^{1,5}]octane **6** (*ca*. 20%) (see Scheme 2), from which only phosphorane **5** can be isolated in its pure form. Mass spectrum (see Online Supplementary Materials) of this mixture contains two peaks of molecular ions with exact mass values of 626.0727 (**5**) and 460.0875 (**6**). A broadened quartet (δ_P –28.3 ppm, $^3J_{FCCP}$ 6.7 Hz) in the ^{31}P-{^{1}H} NMR spectrum relates to the cage phosphorane **6**. There are two doublets of quartets (δ_F –66.31 ppm, $^4J_{FCCCF}$ 11.0 Hz, $^3J_{PCCF}$ 1.1 Hz and δ_F –67.68 ppm, $^4J_{FCCCF}$ 11.0 Hz, $^3J_{PCCF}$ 5.2 Hz) corresponding to the fluorine atoms of P–C(CF$_3$)$_2$ fragment in the ^{19}F NMR spectrum. The following signals belong to phosphorane **6** in the proton spectrum: singlets of Bu^t and C^3–Me groups (δ 1.19 and 2.24 ppm), doublet of C^4–Me group (δ 1.83 ppm, $^4J_{POCCH}$ 2.2 Hz).

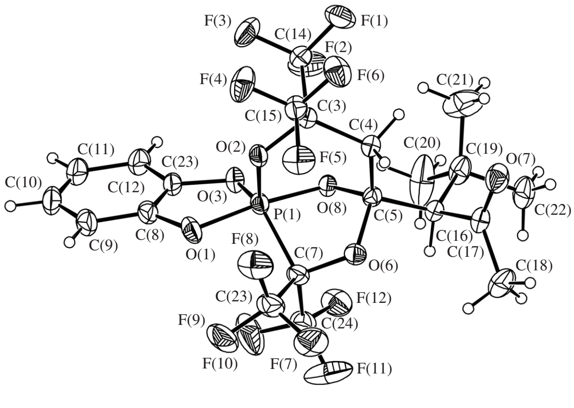


Figure 1 Geometry of molecule **5** in the crystal [P(1)$_S$C(5)$_S$C(16)$_R$/P(1)$_R$C(5)$_R$C(16)$_S$ diastereoisomer, P(1)$_R$C(5)$_R$C(16)$_S$ enantiomer is shown]. Non-hydrogen atoms are shown as thermal ellipsoids with a probability of 30%. Selected bond lengths (Å) and bond and torsion angles (°): P(1)–O(1) 1.676(3), P(1)–O(2) 1.603(3), P(1)–O(3) 1.618(3), P(1)–O(8) 1.668(2), P(1)–C(7) 1.899(4), O(1)–P(1)–O(2) 91.5(1), O(1)–P(1)–O(3) 91.7(1), O(1)–P(1)–O(8) 171.2(1), O(1)–P(1)–C(7) 91.7(1), O(2)–P(1)–O(3) 116.6(1), O(2)–P(1)–O(8) 97.3(1), O(2)–P(1)–C(7) 107.5(1), O(3)–P(1)–O(8) 85.2(1), O(3)–P(1)–C(7) 135.6(1), O(8)–P(1)–C(7) 84.8(1), O(2)–P(1)–O(1)–C(8) 107.7(2), O(3)–P(1)–O(1)–C(8) –9.0(2).

The structure of compound **5** was proved by ^{1}H, ^{13}C, ^{13}C-{^{1}H}, ^{19}F, ^{31}P, ^{31}P-{^{1}H} NMR, IRS, interpretation of ^{13}C NMR spectrum was made taking into account our earlier work.[14] The spatial configuration of molecule **5** was established by the single crystal XRD method[‡] (Figure 1). The geometry of the phosphorus atom in molecule **5** corresponds to a slightly distorted trigonal bipyramid with a flat base within ±0.0367(8) Å, where the atoms P(1), C(2), O(3), C(7) are lying. The atoms O(1) and O(8) located in the apical positions deviate from this plane by distances 1.712(2) and –1.611(2) Å.

It is worth pointing out that the O(1)···O(8) distance [3.337(4) Å] is practically the same as the sum of P(1)–O(1) and P(1)–O(8) bond lengths [3.344(3) Å] and is consistent with the almost regular trigonal-bipyramidal configuration of the phosphorus; this is also indicated by the bond angle O(1)–P(1)–O(8) [171.2(1)°]. The equatorial P(1)–O(3) and P(1)–O(2) bond lengths are slightly shorter than the corresponding apical O–P bond lengths. The sum of the bond angles at the trigonal bipyramid base [359.7(1)°] is close to the ideal value of 360°. The dioxaphospholane hetero-

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[‡] *Crystal data for* **5**. The X-ray diffraction (XRD) data for the single crystals of **5** were collected on a Bruker Smart Apex II CCD diffractometer (ω-scan mode) using graphite-monochromated MoKα (λ = 0.71073 Å) radiation at 293(2) K. The performance mode of the sealed X-ray tube was 50 kV, 30 mA. A suitable crystal of appropriate dimensions was mounted on a glass fiber in a random orientation. Data collection: images were indexed and integrated using the APEX3 data reduction package (v2018.7-2, Bruker AXS). Final cell constants were determined by global refinement of reflections from the complete data set. Data were corrected for systematic errors and absorption using SADABS-2016/2. XPREP-2014/2 and the Assign Spacegroup routine of WinGX-2018.3 were used for analysis of systematic absences and space group determination.

The crystals of compound **5**, $C_{21}H_{19}F_{12}O_6P$, are monoclinic, space group *Pn*, a = 7.377(5), b = 9.960(6) and c = 16.925(10) Å, β = 92.832(7)°, V = 1242.1(13) Å^3, Z = 2, Z' = 1, d_{calc} = 1.675 g cm^{-3}, μ(MoKα) = = 0.238 mm^{-1}, F(000) = 632, 2.045 ⩽ θ ⩽ 29.697°, R_{int} = 0.0176, R_σ = = 0.0266, 11250 reflections were measured, 5847 of which were independent; completeness to θ of 25.242° was 99.6%. The structure was solved by the direct method using SHELXT-2018/2[16] and refined by the full-matrix least-squares on F^2 using SHELXL-2018/3.[17] Calculations were mainly performed using the WinGX-2018.3 suite of programs.[18] Non-hydrogen atoms were refined anisotropically. The hydrogen atoms were inserted at the calculated positions and refined as riding atoms. The absolute structure of crystal was determined on the basis of the Flack parameter [0.14(5)].[19] The refinement of 365 parameters with 2 restraints converged to R_1 = 0.0362, wR_2 = 0.0924 for 5254 reflections with $I > 2\sigma(I)$ and R_1 = = 0.0414, wR_2 = 0.0965 for all data with S = 1.026 and residual electron density, $\rho_{max/min}$ = 0.229 and –0.222 e Å^{-3}.

CCDC 1904287 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

cycle is flat within ±0.054(2) Å; O(2), O(8) and C(7) atoms deviate from the O(1)C(8)C(13)O(3)P(1) plane by 1.529(2), –0.083(2) and –1.172(3) Å, respectively. The conformation of the six-membered heterocycle of the rigid molecular bicyclooctane core is a *distorted boat* [the C(4)C(5)O(2)P(1) fragment is planar within ±0.038(3) Å, the remaining atoms of the six-membered heterocycle, O(8) and C(3), deviate from this plane to one side by –0.769(2) and –0.320(3) Å]. The C(7), C(14), O(3) and O(6) atoms deviate from the C(4)C(5)O(2)P(1) plane by 1.517(4), –1.809(4), –1.388(2) and 1.432(2) Å and occupy the axial positions. The C(15), C(16) and O(1) atoms deviate from this plane by 0.580(4), –0.214(3) and –0.718(3) Å and occupy the equatorial positions. The conformation of five-membered heterocycle of the bicyclooctane scaffold is slightly distorted envelope, where O(8)C(5)O(6)C(7) atoms are lying in a plane [within 0.037(2) Å], and the P(1) atom deviates from it by –0.8615(7) Å. The O(3), C(16) and C(23) atoms deviate from the above plane by –0.424(2), 1.219(3) and –0.791(4) Å and occupy the equatorial positions. The C(4), C(24), O(1) and O(2) atoms deviate from O(8)C(5)O(6)C(7) plane by –1.401(3), 1.399(4), –1.523(2) and –2.294(2) Å and are located in axial positions. The dihedral angles between C(4)C(3)O(2)/ C(5)C(4)P(1)O(2), C(5)O(8)P(1)/C(5)C(4)P(1)O(2) and O(8)P(1)C(7)/ O(6)C(5)O(8)C(7) planes are 23.7(3), 64.6(2) and 41.4(2)°, respectively. The PLATON program[15] indicates a short intramolecular F(5)···F(8) contact of 2.686(4) Å, which explains the presence of a long-range spin–spin coupling constant between the fluorine atoms of the groups C(15)F(3) and C(23)F(3) ($^7J_{\mathrm{FF}}$ 11.5–12.0 Hz).

In conclusion, the unusual direction of the *tert*-butylacetylacetone phosphorylation, namely, with elimination of proton from a methyl group and the formation of 4-(1,3,2-benzodioxaphosphol-2-yloxy)-3-*tert*-butylpent-4-en-2-one **3**, was revealed in this work. Compound **3** reacts with hexafluoroacetone *via* a two-stage cascade process involving the Diels–Alder and Huisgen [4+2]- and [3+2]-cycloadditions to form the cage phosphorane **5** with a high stereoselectivity without participation of the δ-carbonyl group of the starting phosphole **3**. The process is promising for the involvement of other types of $\mathrm{P^{III}}$ derivatives bearing the oxyvinyl fragment and activated carbonyl compounds.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2019.09.009.

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