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Synthesis, structure, and thermolysis of pentacoordinate 1,3,2λ⁵-oxazaphosphetidines: the intermediates of aza-Wittig reactions

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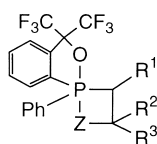
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Abstract

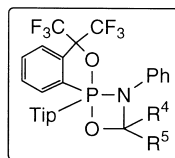
1,3,2λ⁵-Oxazaphosphetidines bearing the Martin ligand were synthesized by the reaction of the corresponding iminophosphorane and carbonyl compounds and characterized by X-ray crystallographic analysis. Thermolysis of the oxazaphosphetidine gave the cyclic phosphinate and the corresponding imine, indicating that the oxazaphosphetidine is an intermediate of the aza-Wittig reaction. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: oxazaphosphetidine; aza-Wittig reaction; iminophosphorane; X-ray analysis; thermolysis.

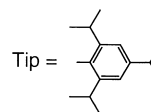
There is much interest in the chemistry of small-membered ring compounds with two or more main group elements in the ring in view of their characteristic structures and unique reactivities.¹ In the course of our study on heteracyclobutanes bearing a highly coordinate main group element at the position adjacent to the heteroatom,² we have achieved the synthesis of 1,2λ⁵-oxaphosphetanes **1**³ and 1,2λ⁵-azaphosphetidines **2**,⁴ i.e. the intermediates of Wittig reactions and Wittig-type reactions, respectively.



1: Z = O
2: Z = NPh



3



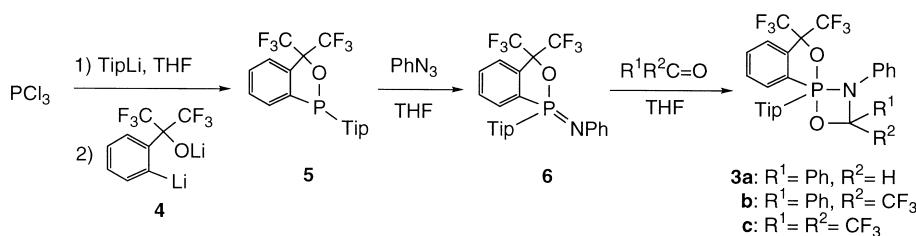
Tip =

On the other hand, a nitrogen version of the Wittig reaction, which is called the aza-Wittig reaction using iminophosphoranes in the place of phosphorus ylides, has also been utilized as an

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effective method for the synthesis of nitrogen-containing heterocycles.⁵ Pentacoordinate 1,3,2-oxazaphosphetidines, which are considered as the intermediates of aza-Wittig reactions,⁶ are anticipated to show the reactivities of both oxaphosphetanes and azaphosphetidines on their thermolysis. But there have been only few examples on the crystallographically characterized 1,3,2λ⁵-oxazaphosphetidines.^{7,8} Although an iminophosphorane that is synthesized from the corresponding phosphine and azide is used for the general aza-Wittig reaction, these previously reported oxazaphosphetidines were not derived from the corresponding phosphines. For the elucidation of the mechanism of aza-Wittig reactions, it is important to isolate their intermediates, although these isolations are ordinarily difficult because of their instability. Here, we describe the synthesis, crystal structure, and thermolysis of 1,3,2λ⁵-oxazaphosphetidines **3** bearing the Martin ligand⁹ and a bulky 2,4,6-triisopropylphenyl (denoted as Tip hereafter) group, which are the first examples of dioxyazaphosphorane [10-P-5(C2O2N)] with an oxazaphosphetidine framework.

Sequential treatment of PCl₃ with TipLi and dilithio derivative **4** of hexafluorocumyl alcohol gave cyclic phosphinite **5** ($\delta_P = 146.1$), which was allowed to react with phenyl azide at -78°C in THF to afford the corresponding iminophosphorane **6** ($\delta_P = 25.6$) (Scheme 1).⁹ As compounds **5** and **6** are an air and/or moisture-sensitive oil, they were used without isolation and purification.¹⁰ The reactions of iminophosphorane **6** with carbonyl compounds such as benzaldehyde and trifluoroacetophenone at 60 and 70°C , respectively, gave a diastereomeric mixture of the corresponding 1,3,2λ⁵-oxazaphosphetidines **3a** and **3b** which were hydrolyzed on silica gel. Treatment of **6** with hexafluoroacetone (denoted as HFA hereafter) at room temperature also gave **3c** in a pure form after chromatographic separation.¹¹ But no reaction took place upon heating a C₆D₆ solution of **6** and benzophenone in a sealed tube even at 120°C due to its low reactivity and steric congestion.



Scheme 1.

The structures of **3a–c** were strongly supported by their NMR spectra.¹¹ Data for **3c** are shown below as a typical example. In the ¹H NMR spectrum of **3c**, the ortho proton of the Martin ligand resonated at low field ($\delta = 8.52$), which is a typical feature of compounds with a trigonal-bipyramidal (TBP) structure bearing a polar apical bond.¹² In the ¹⁹F NMR spectrum of **3c**, four quartets for the trifluoromethyl groups of HFA and the Martin ligand units were observed due to their nonequivalence emerging from the ring formation. An upfield shift (from $\delta = 25.6$ for **6** to $\delta = -18.6$ for **3c**) observed in the ³¹P NMR spectra indicates that **3c** has a pentacoordinate phosphorane structure.³ Oxazaphosphetidine **3c** did not dissociate into iminophosphorane **6** and HFA in CDCl₃ solution at room temperature in contrast to Schmidpeter's oxazaphosphetidines.⁷ The *N*-apical pseudorotamer of **3c** was not detected by variable temperature NMR spectra between 27°C and 107°C , although *N*-apical pseudorotamers were observed at room temperature for azaphosphetidines **2**.⁴

The X-ray crystallographic analysis of **3c**¹³ (Fig. 1) indicated its distorted trigonal-bipyramidal structure at the phosphorus atom with two oxygen atoms at the apical positions and two carbon and nitrogen atoms at the equatorial positions (TBP→SP¹⁴ 22.2%). The structural feature of **3c** is very similar to those of **1** and **2**.^{3,4} While the O1–C1 bond length [1.379(2) Å] is somewhat shorter than those of previously reported oxazaphosphetidines [between 1.406(5) and 1.426(7) Å],^{7,8} the other bond lengths of the four-membered ring are similar to those of other 1,3,2-oxazaphosphetidines and those of the theoretically optimized intermediate of the aza-Wittig reaction.^{6b} The bond angle between two apical bonds deviates from 180° by 12.71(7)° probably due to the ring strain. The phosphorus atom is placed on the equatorial plane and the torsion angle P1–N1–C1–O1 is 1.1(1)°, indicating that the four-membered ring is almost planar. The nitrogen atom has almost trigonal-planar coordination and the plane of the benzene ring on the nitrogen atom lies perpendicular to the plane of the four-membered ring, probably emerging from steric repulsion.

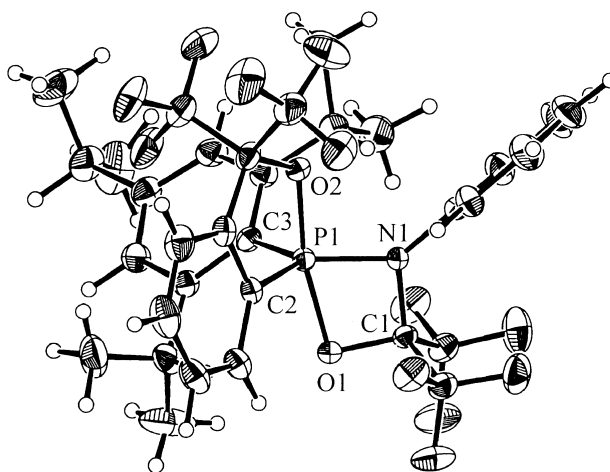
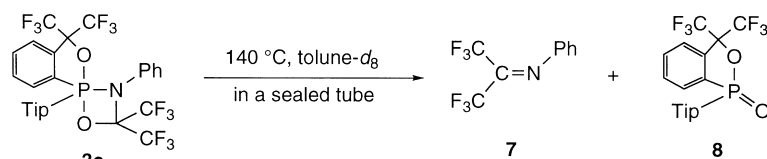


Figure 1. ORTEP drawing of **3c** with thermal ellipsoid plot (30% probability). Selected bond lengths (Å), angles (deg), and torsion angles (deg): P1–O1, 1.786(1); P1–O2, 1.719(1); P1–C2, 1.815(2); P1–C3, 1.844(2); P1–N1, 1.688(2); N1–C1, 1.443(2); O1–C1, 1.379(2); O1–P1–O2, 167.29(7); O1–P1–N1, 74.84(7); N1–P1–C2, 121.50(9); N1–P1–C3, 122.31(9); C2–P1–C3, 115.87(10); N1–C1–O1, 96.9(2); P1–O1–C1, 93.2(1); P1–N1–C1, 95.1(1); P1–N1–C1–O1, 1.1(1)

Thermolysis of **3c** at 140°C in toluene-*d*₈ gave the corresponding imine **7** (90%) and cyclic phosphinate **8** (100%) (Scheme 2).¹⁵ Furthermore, the oxazaphosphetidine is anticipated to show other reactivity on the thermolysis, i.e. the formation of the iminophosphorane as in the cases of azaphosphetidines **2**. This process, however, must be reversible. Therefore, thermolysis in the presence of water was considered to offer evidence for its existence, because product **6** can be irreversibly removed from its system by its hydrolysis. In fact, thermolysis of **3c** with an excess amount (20 equiv.) of water (140°C, 3 h) gave HFA (96%), **8** (100%) and aniline (89%) as main products with a small amount of imine **7** (4%). Aniline derived not from imine **7** but from iminophosphorane **6**, because **7** does not react with water under the same reaction conditions. Since aniline and **8** are hydrolysis products of **6**, the thermolysis process of **3c** giving **6** and HFA was evidenced by their formation. These results indicate two reaction pathways for the thermolysis of **3c**. One path is the aza-Wittig reaction giving imine **7** and cyclic phosphinate **8**. Thus, 1,3,2λ⁵-oxazaphosphetidines **3c** can be regarded as an intermediate of the aza-Wittig reaction.



Scheme 2.

The other path is regeneration of iminophosphorane **6** and HFA. The formation of the iminophosphorane is considered as a characteristic reaction of not only azaphosphetidines but also oxazaphosphetidines.

In summary, we have succeeded in the synthesis and X-ray structural analysis of 1,3,2λ⁵-oxazaphosphetidine bearing the Martin ligand. It was found by its thermolysis that oxazaphosphetidine has two reactivities, respectively, as an oxaphosphetane and an azaphosphetidine.

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10. Cyclic phosphinite **5** gave the corresponding phosphinate **8** on exposure to air. Iminophosphorane **6** also gave readily **8** in the presence of water.
11. Selected spectroscopic and analytical data for **3c**: colorless crystals; mp 178–181°C (dec.); ^1H NMR (500 MHz, CDCl_3) δ 0.27 (d, $^3J_{\text{HH}} = 6.6$ Hz, 3H), 1.06 (d, $^3J_{\text{HH}} = 6.6$ Hz, 3H), 1.11 (d, $^3J_{\text{HH}} = 6.6$ Hz, 3H), 1.13 (d, $^3J_{\text{HH}} = 6.9$ Hz, 6H), 1.33 (d, $^3J_{\text{HH}} = 6.6$ Hz, 3H), 2.76 (sept, $^3J_{\text{HH}} = 6.9$ Hz, 1H), 3.54 (sept, $^3J_{\text{HH}} = 6.6$ Hz, 1H), 3.72 (sept, $^3J_{\text{HH}} = 6.6$ Hz, 1H), 6.77 (d, $^4J_{\text{PH}} = 7.2$ Hz, 1H), 7.03 (d, $^4J_{\text{PH}} = 7.2$ Hz, 1H), 7.12 (d, $^3J_{\text{HH}} = 7.6$ Hz, 2H), 7.22–7.29 (m, 3H), 7.58 (brs, 1H), 7.67 (t, $^3J_{\text{HH}} = 7.6$ Hz, 1H), 7.73 (dd, $^3J_{\text{HH}} = 7.6$ Hz, $^4J_{\text{HP}} = 9.4$ Hz, 1H), 8.52 (dd, $^3J_{\text{HH}} = 7.6$ Hz, $^3J_{\text{HP}} = 11.4$ Hz, 1H); ^{19}F NMR (254 MHz, CDCl_3) δ -76.53 (q, $^4J_{\text{FF}} = 9.8$ Hz), -74.99 (q, $^4J_{\text{FF}} = 9.8$ Hz), -72.71 (q, $^4J_{\text{FF}} = 9.8$ Hz), -72.35 (q, $^4J_{\text{FF}} = 9.8$ Hz); ^{31}P NMR (109 MHz, CDCl_3) δ -18.6 (s); MS(FAB): m/z 734 ($[\text{M}+\text{H}]^+$, 8.7%). Anal. calcd for $\text{C}_{33}\text{H}_{32}\text{NF}_{12}\text{O}_2\text{P}$: C, 53.80; H, 4.46; N, 2.09. Found: C, 54.03; H, 4.40; N, 1.91.
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13. Crystal data for **3c** at 296 K with Mo $\text{K}\alpha$ radiation ($\lambda = 0.71070$ Å): $\text{C}_{33}\text{H}_{32}\text{F}_{12}\text{NO}_2\text{P}$; $MW = 733.58$; monoclinic; space group $P2_1/c$; $a = 10.437(2)$ Å, $b = 18.668(3)$ Å, $c = 17.753(3)$ Å; $\beta = 105.29(1)^\circ$; $V = 3336.5(9)$ Å³; $Z = 4$; $D_c = 1.460$ g cm⁻³; $\mu(\text{Mo K}\alpha) = 1.81$ cm⁻¹; R (R_w) = 0.043 (0.023).
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15. The ratio of these products was determined based on the integral of ^{19}F NMR spectra of the reaction solution.