Pergamon

Tetrahedron Letters 41 (2000) 5237–5241

TETRAHEDRON LETTERS

Synthesis, structure, and thermolysis of pentacoordinate 1,3,2λ^5-oxazaphosphetidines: the intermediates of aza-Wittig reactions

Naokazu Kano, Xing Jia Hua, Seiji Kawa and Takayuki Kawashima*

Department of Chemistry, Graduate School of Science, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

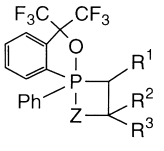
Received 17 April 2000; revised 18 May 2000; accepted 19 May 2000

Abstract

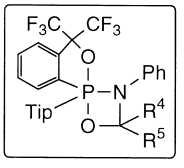
1,3,2λ^5-Oxazaphosphetidines bearing the Martin ligand were synthesized by the reaction of the corresponding iminophosphorane and carbonyl compounds and characterized by X-ray crystallographic analysis. Thermolysis of the oxazaphosphetidine gave the cyclic phosphinate and the corresponding imine, indicating that the oxazaphosphetidine is an intermediate of the aza-Wittig reaction.

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

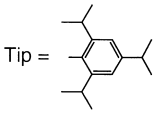
There is much interest in the chemistry of small-membered ring compounds with two or more main group elements in the ring in view of their characteristic structures and unique reactivities.[1] In the course of our study on heteracyclobutanes bearing a highly coordinate main group element at the position adjacent to the heteroatom,[2] we have achieved the synthesis of 1,2λ^5-oxaphosphetanes **1**[3] and 1,2λ^5-azaphosphetidines **2**,[4] i.e. the intermediates of Wittig reactions and Wittig-type reactions, respectively.



1: Z = O
2: Z = NPh



3



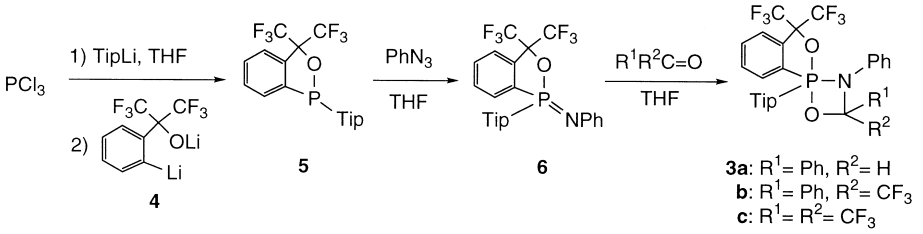
On the other hand, a nitrogen version of the Wittig reaction, which is called the aza-Wittig reaction using iminophosphoranes in the place of phosphorus ylides, has also been utilized as an

* Corresponding author. Fax: +81-3-5800-6899; e-mail: takayuki@chem.s.u-tokyo.ac.jp

0040-4039/00/$ - see front matter
PII: S0040-4039(00)00829-7

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 1,3,2λ^5-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 1,3,2λ^5-oxazaphosphetidines **3** bearing the Martin ligand[9] 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 PCl_3 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 1,3,2λ^5-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 C_6D_6 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 ^{1}H 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 ^{19}F 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 ^{31}P NMR spectra indicates that **3c** has a pentacoordinate phosphorane structure.[3] Oxazaphosphetidine **3c** did not dissociate into iminophosphorane **6** and HFA in $CDCl_3$ 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→SP[14] 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.

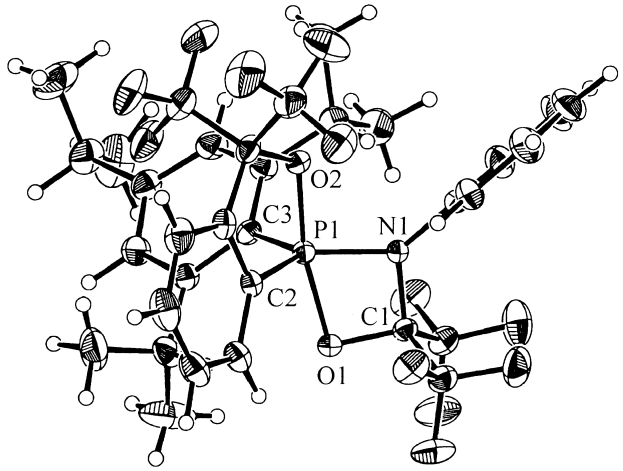
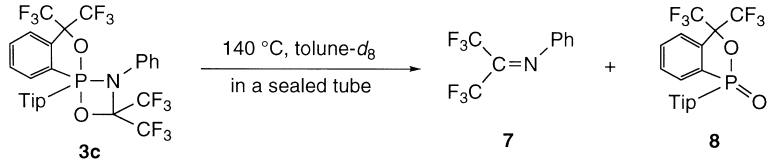


Figure 1. ORTEP drawing of **3c** with thermal ellipsoid plot (30% probability). Selected bond lengths (Å), angles (deg), and torsion angles (deg): P1–O1, 1.786(1); P1–O2, 1.719(1); P1–C2, 1.815(2); P1–C3, 1.844(2); P1–N1, 1.688(2); N1–C1, 1.443(2); O1–C1, 1.379(2); O1–P1–O2, 167.29(7); O1–P1–N1, 74.84(7); 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, 1,3,2λ^5-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 1,3,2λ^5-oxazaphosphetidine bearing the Martin ligand. It was found by its thermolysis that oxazaphosphetidine has two reactivities, respectively, as an oxaphosphetane and an azaphosphetidine.

Acknowledgements

This work was partially supported by Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan. We thank Professor T. Asano, Oita University, for his generous gift of an authentic sample of hexafluoroisopropylideneaniline. We also thank Central Glass and Tosoh Akzo Co. Ltd., for the gifts of organofluorine compounds and alkyllithiums, respectively.

References

1. (a) Lukevics, E.; Pudova, O. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Pergamon: Oxford, U.K., 1996; Vol. 1B, pp. 1189–1213. (b) Kawashima, T.; Okazaki, R. In *Advances in Strained and Interesting Organic Molecules*; Halton, B., Ed.; JAI Press: Stamford, Connecticut, 1999; Vol. 7, pp. 1–41.
2. (a) Kawashima, T.; Okazaki, R. *Synlett* **1996**, 600–608, and references cited therein. (b) Ohno, F.; Kawashima, T.; Okazaki, R. *J. Am. Chem. Soc.* **1996**, *118*, 697–698. (c) Ohno, F.; Kawashima, T.; Okazaki, R. *Chem. Commun.* **1997**, 1671–1672.
3. (a) Kawashima, T.; Kato, K.; Okazaki, R. *J. Am. Chem. Soc.* **1992**, *114*, 4008–4010. (b) Kawashima, T.; Kato, K.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 869–870. (c) Kawashima, T.; Kato, K.; Okazaki, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 1606–1606. (d) Kawashima, T.; Kato, K.; Okazaki, R. *J. Am. Chem. Soc.* **1998**, *120*, 6848–6848.
4. Kawashima, T.; Soda, T.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1096–1098.
5. For recent reviews on the aza-Wittig reaction, see: (a) Gololobov, Y. G.; Kasukhin, L. F. *Tetrahedron* **1992**, *48*, 1353–1406. (b) Molina, P.; Vilaplana, M. J. *Synthesis* **1994**, 1197–1218.
6. (a) Koketsu, J.; Ninomiya, Y.; Suzuki, Y.; Koga, N. *Inorg. Chem.* **1997**, *36*, 694–702. (b) Lu, W. C.; Liu, C. B.; Sun, C. C. *J. Phys. Chem. A.* **1999**, *103*, 1078–1083.
7. Sheldrick, W. S.; Schomburg, D.; Schmidpeter, A.; von Criegern, T. *Chem. Ber.* **1980**, *113*, 55–69.
8. (a) Storzer, W.; Röschenthaler, G.-V.; Schmutzler, R.; Sheldrick, W. S. *Chem. Ber.* **1981**, *114*, 3609–3624. (b) Francke, R.; Dakternieks, D.; Gable, R. W.; Hoskins, B. F.; Röschenthaler, G.-V. *Chem. Ber.* **1985**, *118*, 922–930.
9. $LiC_6H_4C(CF_3)_2OLi$, which can be prepared by directed lithiation of hexafluorocumyl alcohol, is usually used for the introduction of this ligand, see: Perozzi, E. F.; Michalak, R. S.; Figuly, G. D.; Stevenson III, W. H.; Dess, D. B.; Ross, M. R.; Martin, J. C. *J. Org. Chem.* **1981**, *46*, 1049–1053.

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.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.27 (d, $^{3}J_{HH}$ = 6.6 Hz, 3H), 1.06 (d, $^{3}J_{HH}$ = 6.6 Hz, 3H), 1.11 (d, $^{3}J_{HH}$ = 6.6 Hz, 3H), 1.13 (d, $^{3}J_{HH}$ = 6.9 Hz, 6H), 1.33 (d, $^{3}J_{HH}$ = 6.6 Hz, 3H), 2.76 (sept, $^{3}J_{HH}$ = 6.9 Hz, 1H), 3.54 (sept, $^{3}J_{HH}$ = 6.6 Hz, 1H), 3.72 (sept, $^{3}J_{HH}$ = 6.6 Hz, 1H), 6.77 (d, $^{4}J_{PH}$ = 7.2 Hz, 1H), 7.03 (d, $^{4}J_{PH}$ = 7.2 Hz, 1H), 7.12 (d, $^{3}J_{HH}$ = 7.6 Hz, 2H), 7.22–7.29 (m, 3H), 7.58 (brs, 1H), 7.67 (t, $^{3}J_{HH}$ = 7.6 Hz, 1H), 7.73 (dd, $^{3}J_{HH}$ = 7.6 Hz, $^{4}J_{HP}$ = 9.4 Hz, 1H), 8.52 (dd, $^{3}J_{HH}$ = 7.6 Hz, $^{3}J_{HP}$ = 11.4 Hz, 1H); ^{19}F NMR (254 MHz, $CDCl_3$) δ –76.53 (q, $^{4}J_{FF}$ = 9.8 Hz), –74.99 (q, $^{4}J_{FF}$ = 9.8 Hz), –72.71 (q, $^{4}J_{FF}$ = 9.8 Hz), –72.35 (q, $^{4}J_{FF}$ = 9.8 Hz); ^{31}P NMR (109 MHz, $CDCl_3$) δ –18.6 (s); MS(FAB): *m*/*z* 734 ([M+H]$^{+}$, 8.7%). Anal. calcd for $C_{33}H_{32}NF_{12}O_2P$: C, 53.80; H, 4.46; N, 2.09. Found: C, 54.03; H, 4.40; N, 1.91.
12. Granoth, I.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 4618–4621.
13. Crystal data for **3c** at 296 K with Mo Kα radiation (λ = 0.71070 Å): $C_{33}H_{32}F_{12}NO_2P$; *MW* = 733.58; monoclinic; space group $P2_1/c$; a = 10.437(2) Å, b = 18.668(3) Å, c = 17.753(3) Å; β = 105.29(1)°; V = 3336.5(9) Å^3; Z = 4; D_c = 1.460 g cm^{-3}; μ(Mo Kα) = 1.81 cm^{-1}; R (R_w) = 0.043 (0.023).
14. Holmes, R. R.; Deiters, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 3318–3326.
15. The ratio of these products was determined based on the integral of ^{19}F NMR spectra of the reaction solution.