J|A|C|S
COMMUNICATIONS

Published on Web 06/11/2002

First Isolation and Characterization of an Anti-Apicophilic Spirophosphorane Bearing an Oxaphosphetane Ring: A Model for the Possible Reactive Intermediate in the Wittig Reaction

Satoshi Kojima, Masaya Sugino, Shiro Matsukawa, Masaaki Nakamoto, and Kin-ya Akiba*

Department of Chemistry, Graduate School of Science, Hiroshima University, 1-3-1 Kagamiyama, Higashi-Hiroshima 739-8526, Japan

Received September 6, 2001; Revised Manuscript Received March 12, 2002

The Wittig reaction is a well-established method for introducing double bonds in organic compounds.[1] In this reaction, two isomeric oxaphosphetane intermediates, **int-a** and **int-b**, are conceivable, and on the basis of the general belief that P−C bond dissociation is more advanced than that of P−O in the transition state, **int-b** bearing an apical carbon in the oxaphosphetane ring has been assumed by many to be the intermediate that gives the olefinic product (Scheme 1).[1,2] Skepticism about this hypothesis has arisen from the fact that species such as **int-b** could not be observed experimentally. Furthermore, a theoretical calculation on model phosphoranes (H in the place of Ph) showed that species such as **int-b** may only be semistable, thus adding to the controversy.[3]

In the pursuit of **int-b** type compounds, the greatest advance made thus far is the preparation of phosphorane **1a** (Chart 1),[4] which can be considered a model for an intermediate in the imino-Wittig reaction.[5] Here, **1a** has been *geared to be thermodynamically as stable* as isomer **1b**. For the oxygen series, even models for **int-a**-type isomers are scarce.[1f,g] Among these, especially noteworthy are the phosphoranes **2**, which were the first to be fully structurally characterized and which provided mechanistic insights into the olefin-forming step.[6] We have recently synthesized and isolated **3a**, the first anti-apicophilic spirophosphorane, via a thermal reaction[7] and more recently by oxidation.[8] By applying the latter methodology, we have succeeded in obtaining the anti-apicophilic analogue of spirophosphorane **2**, i.e., **5a**, *without altering the intrinsic apicophilic property of the substituents about the phosphorus atom*. Although the substitution pattern on the phosphorus atom slightly differs from that of phosphoranes in the typical Wittig reaction (**int-a**,**b**), **5a** can be considered to be the closest model for **int-b** reported to date.[9] Herein, we report on the preparation and characterization of this unique compound.

Compound **4**, the precursor to **5a**, was obtained as shown in Scheme 2. The use of the *t*-Bu group was based on our previous finding that it was extremely effective in stabilizing anti-apicophilic phosphoranes.[7] *t*-BuPCl$_2$ was first converted to sulfide **6**, which in a one-pot reaction was transformed into apical-H phosphorane **4** (47% yield from **6**).[10] Phosphorane **4** could not be obtained upon the use of the P oxide analogue of **6**. All attempts to isolate intermediates led to either decomposition or other undesirable reactions.

The cyclization reaction of **4** proved to be less facile than in the case of **3a**. Cyclization could be effected at the temperature of 150 °C (in DMSO), only to furnish **5b** and decomposition products of **5b**. However, the oxidation procedure using *n*-BuLi followed by iodine in ether (0 °C) gave **5a** as a 1:1 mixture with **5b** (Scheme 3).[10] Since the ratio could not be improved upon by changing reaction conditions, this probably reflects the kinetic selectivity in the ring-closing process. The desired anti-apicophilic **5a** fortunately crystallized out of the reaction mixture upon addition of hexane. Unlike **3a**, which could bear aqueous workup, **5a** was found to be labile to proton sources, resulting in facile stereomutation to **5b**. For instance, dissolution of **5a** in anhydrous $CDCl_3$ resulted in complete conversion to **5b** within minutes at room temperature, presumably due to residual acid in the solvent. On the other hand, in the presence of DBU (small excess) in diglyme, the half-life of **5a** was ca. 50 min at 70 °C. Since there was a propensity for the

Scheme 1

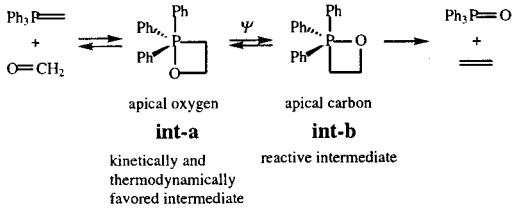
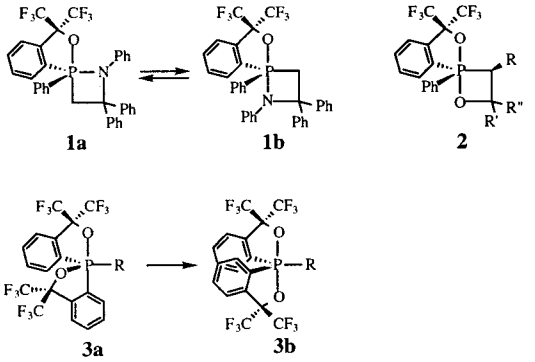
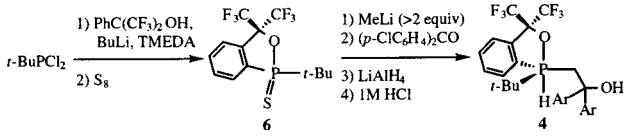


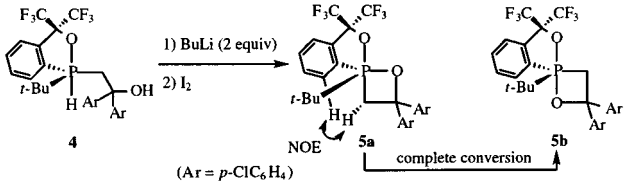
Chart 1



Scheme 2



Scheme 3



* Address correspondence to this author. Present address: Advanced Research Center for Science and Engineering, Waseda University, 3-4-1 Ohkubo, Shinjuku-ku, Tokyo 169-8555, Japan.

10.1021/ja0170145 CCC: $22.00

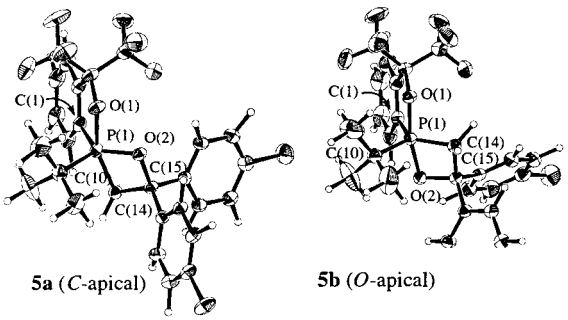


Figure 1. ORTEP drawing of **5a** and **5b** showing the thermal ellipsoids at the 30% probability level.

stereomutation of **5a** to accelerate in the presence of acids and deteriorate in the presence of DBU, it is very likely that the isomerization pathway involves P−O bond dissociation−recombination. A ^{31}P NMR measurement (detection limit assumed at 1%) of **5b** at 120 °C (*p*-xylene) did not show the presence of **5a** in equilibrium, implying that the lower limit in energy difference is $\Delta G_{393\,K} = 3.6$ kcal mol^{-1}. Thus, it is evident that **5a** is thermodynamically much less favorable than **5b**.

The NMR spectra of **5a** (acetone-d_6) were found to be very characteristic of its supposed trigonal bipyramidal structure in solution and were similar to those reported for **1a**.[10] The coupling constants between the phosphorus and the apical bound carbon nuclei ($^1J_{PC} = 29.4$ Hz), and between the phosphorus nucleus and the protons ($^2J_{PH} = 6.8$, 11.2 Hz) on this carbon, were small compared to their counterparts in **5b** ($^1J_{PC} = 106.7$ Hz; $^2J_{PH} = 20.0$, 23.0 Hz), as expected from the involvement of the weak hypervalent bond.[11] The proton ortho to P on the aryl ring ($\delta_H = 7.76$) of the Martin ligand was not shifted downfield as much as for **5b** ($\delta_H = 8.30$), which has a more polar apical bond. An NOE of 11% was observed between the ortho proton mentioned above and the proton on the oxaphosphetane ring facing this hydrogen (Scheme 3). The observed lower field ^{31}P chemical shift for **5a** ($\delta_P = -6.3$) compared to that for **5b** ($\delta_P = -10.9$) could be attributed to the σ-acceptor property of the equatorial oxygen substituent, which should be more influential than that occupying the apical position.

Indisputable evidence for the structure of the anti-apicophilic spirophosphorane **5a** was obtained from X-ray structural analysis, as shown in comparison with that of **5b** in Figure 1.[10] Both the group of three equatorial elements and phosphorus, and the group of four atoms in the oxaphosphetane ring, were found to form planes, respectively for both **5a** and **5b**, implying that both compounds are essentially of trigonal bipyramid nature. As expected, the apical P−C bond was found to be much longer (**5a**, 1.914 Å) than the corresponding P−C bond in **5b** (1.820 Å), while the opposite trend was observed for the four-membered ring P−O bond (**5a**, 1.663 Å; **5b**, 1.745 Å). The apical bond was also distorted more in **5a** than in **5b**.

Heating a solid sample of **5a** at the melting point temperature (ca. 120 °C) for 5 min gave only **5b** as a consequence of pseudorotation. Only after prolonged heating of **5b** at the melting point (140 °C) could olefin formation (quantitative) be observed. Thus, for compound **5a** it is apparent that the bond strength of the apical P−C bond of the oxaphosphetane ring makes the bond cleavage process (Wittig reaction) much higher in energy than stereomutation.

In summary, the preparation and characterization of **5a** have been accomplished. This success implies that the previously hypothesized Wittig reaction intermediate with an apical carbon may actually exist as a thermodynamically stable species. A question unanswered here, whether the less stable isomer is actually the direct precursor to the olefin product, may be clarified by modification of the substituents upon the oxaphosphetane ring in **5a**.[12]

Acknowledgment. The authors are grateful to Central Glass Co. Ltd. for a generous gift of hexafluorocumyl alcohol. Partial support of this work through a Grant-in-Aid for Scientific Research (No. 11304044) provided by the Ministry of Education, Science, Culture, and Sports of the Japanese Government is heartily acknowledged.

Supporting Information Available: Experimental procedures for the syntheses of **4**, **5a**, **5b**, **6, 4′**, **5b′**, and **6′** and their NMR data, and crystallographic data for **4**, **5a**, **5b**, **4′**, and **5b′**, where primes stand for 2,4,6-mesityl compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For leading reviews, see: (a) Wadsworth, W. S., Jr. *Org. React.* **1977**, *25*, 73−253. (b) Cadogan, J. I. G. *Organophosphorus Reagents in Organic Synthesis*; Academic Press: New York, 1979. (c) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863−927. (d) Kelly, S. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 1, pp 730−817. (e) Johnson, A. W. *Ylides and Imines of Phosphorus*; Wiley-Interscience: New York, 1993. (f) Vedejs, E.; Peterson, M. J. *Top. Stereochem.* **1994**, *21*, 1−157. (g) Vedejs, E.; Peterson, M. J. *Adv. Carbanion Chem.* **1996**, *2*, 1−85.

(2) Bestmann, H. J.; Roth, K.; Wilhelm, E.; Böhme, R.; Burzlaff, H. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 876−877.

(3) Naito, T.; Nagase, S.; Yamataka, H. *J. Am. Chem. Soc.* **1994**, *116*, 10080−10088.

(4) (a) Kawashima, T.; Soda, T.; Kato, K.; Okazaki, R. *Phosphorus, Sulfur Silicon* **1996**, *109*−*110*, 489−492. (b) Kawashima, T.; Soda, T.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1096−1098.

(5) For examples on phosphorane stabilization using the Martin ligand, see: (a) Martin, J. C. *Science* **1983**, *221*, 509−514. (b) Moon, C. D.; Chopra, S. K.; Martin, J. C. In *Phosphorus Chemistry, Developments in American Science*; Walsh, E. N., Griffiths, E. J., Parry, R. W., Quin, L. D., Eds.; ACS Symposium Series 486; American Chemical Society: Washington, DC, 1992; pp 128−136.

(6) (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.; Okazaki, R. *Synlett* **1996**, 600−608 and references therein.

(7) (a) Kajiyama, K.; Kojima, S.; Akiba, K.-y. *Tetrahedron Lett.* **1996**, *37*, 8409−8412. (b) Kojima, S.; Kajiyama, K.; Nakamoto, M.; Akiba, K.-y. *J. Am. Chem. Soc.* **1996**, *118*, 12866−12867.

(8) Kajiyama, K.; Yoshimune, M.; Nakamoto, M.; Matsukawa, S.; Kojima, S.; Akiba, K.-y. *Org. Lett.* **2001**, *3*, 1873−1875.

(9) For a phosphorane bearing an oxaphosphetane ring with an apically fixed carbon atom, see: Vollbrecht, S.; Vollbrecht, A.; Jeske, J.; Jones, P. G.; Schmutzler, R.; du Mont, W.-W. *Chem. Ber.* **1997**, *130*, 819−822.

(10) See Supporting Information for details.

(11) Cavell, R. G. In *Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis*; Verkade, J. G., Quin, L. D., Eds.; VCH Publishers: Deerfield Beach, FL, 1987; pp 231−254.

(12) Following the suggestion of a reviewer, a phosphorane (**4′**) bearing a bulky aromatic 2,4,6-trimethylphenyl group in the place of the *tert*-butyl group in **4** was prepared and subjected to the cyclization conditions. NMR signals corresponding to the C-apical isomer (**5a′**) could not be observed in the reaction mixture (see Supporting Information).

JA0170145