

Highly Selective One-Pot Synthesis of Spirophosphoranes Exhibiting Reversed Apicophilicity by Oxidation of Dianions Generated from P–H Spirophosphorane

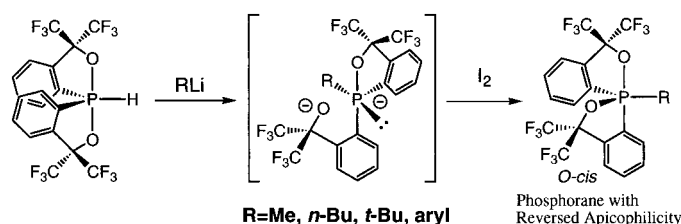
Kazumasa Kajiyama,[†] Miki Yoshimune, Masaaki Nakamoto, Shiro Matsukawa, Satoshi Kojima, and Kin-ya Akiba*

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

akiba@sci.hiroshima-u.ac.jp

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ABSTRACT



Mild and highly selective one-pot procedures for obtaining phosphoranes that exhibit reversed (*O-cis*) apicophilicity are described. On the basis of the procedures, *O-cis* phosphorane bearing an aryl group ($R = 2,4,6$ -tri-*i*-propylphenyl) could be isolated for the first time; the procedure is also applicable for alkyl derivatives. Particularly effective was the use of I_2 as an oxidizing reagent.

It is well established that trigonal bipyramidal 10-P-5¹ phosphoranes prefer to have the more electron-withdrawing groups of the five substituents at the apical positions on the basis of the concept of apicophilicity.² The only exceptions

to this generality had been the case where some sort of steric constraints disallowed such configurations.³ However, we have recently succeeded in the first isolation and full characterization of an phosphorane that exhibits reversed apicophilicity (*O-cis* **2b**) in which an oxygen atom occupies an equatorial position and a carbon atom an apical position in a five-membered ring without applying restrictions that would not permit the formation of the stereoisomer (*O-trans* **3b**).⁴ In the presence of pyridine, *O-cis* **2b** was formed as a major product via a unique thermal cyclization reaction of

* Present address: Advanced Research Center for Science and Engineering, Waseda University, 3-4-1 Ohkubo, Shinjuku-ku, Tokyo 169-8555, Japan. E-mail: akibaky@mn.waseda.ac.jp.

[†] Research Fellow of the Japan Society for the Promotion of Science. Address: Department of Chemistry, School of Science, Kitasato University, Kitasato, Sagami-hara, Kanagawa 228-8555, Japan.

(1) For *N-X-L* designation: Perkins, C. W.; Martin, J. C.; Arduengo, A. J., III; Lau, W.; Alegria, A.; Kochi, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 7753–7759.

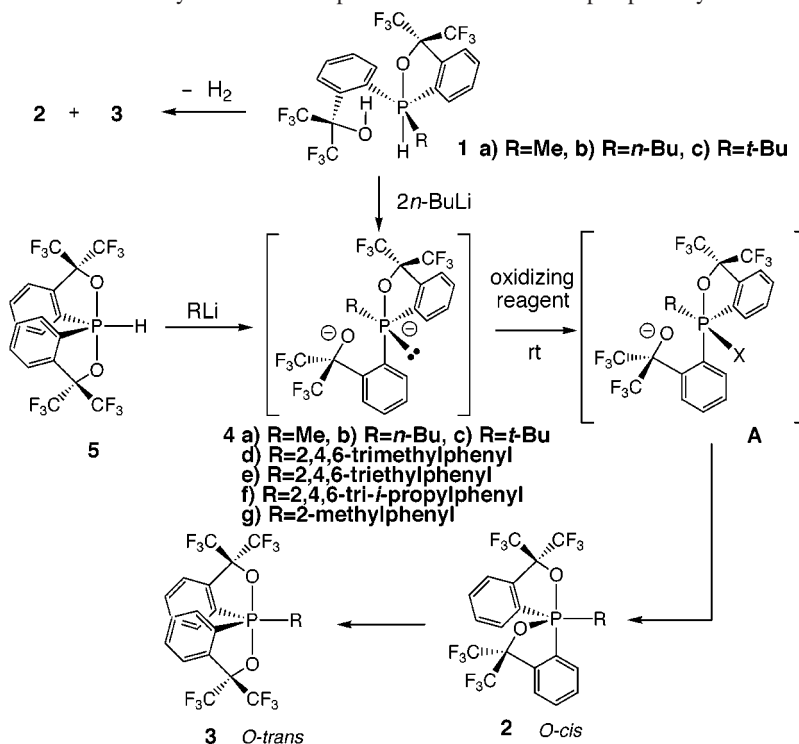
(2) Holmes, R. R. *Pentacoordinated Phosphorus—Structure and Spectroscopy*; ACS Monograph 175, 176; American Chemical Society: Washington, DC, 1980; Vol. I, II. Trippett, S. *Phosphorus Sulfur* **1976**, *1*, 89–98. Holmes, R. R. *J. Am. Chem. Soc.* **1978**, *100*, 433–446. Eisenhut, M.; Mitchell, H. L.; Traficante, D. D.; Kaufman, R. J.; Deutsch, J. M.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 5385–5397. Moreland, C. G.; Doak, G. O.; Littlefield, L. B.; Walker, N. S.; Gilje, J. W.; Braun, R. W.; Cowley, A. H. *J. Am. Chem. Soc.* **1976**, *98*, 2161–2165. Buono, G.; Llinas, J. R. *J. Am. Chem. Soc.* **1981**, *103*, 4532–4540. Griend, L. V.; Cavell, R. G. *Inorg. Chem.* **1983**, *22*, 1817–1820. McDowell, R. S.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 5849–5855. Wang, P.;

Zhang, Y.; Glaser, R.; Reed, A. E.; Schleyer, P. v. R.; Streitwieser, A. *J. Am. Chem. Soc.* **1991**, *113*, 55–64. Wasada, H.; Hirao, K. *J. Am. Chem. Soc.* **1992**, *114*, 16–27. Thatcher, G. R. J.; Campbell, A. S. *J. Org. Chem.* **1993**, *58*, 2272–2281.

(3) Timosheva, N. V.; Prakasha, T. K.; Chandrasekaran, A.; Day, R. O.; Holmes, R. R. *Inorg. Chem.* **1995**, *34*, 4525–4526. Timosheva, N. V.; Chandrasekaran, A.; Prakasha, T. K.; Day, R. O.; Holmes, R. R. *Inorg. Chem.* **1996**, *35*, 6552–6560. Vollbrecht, S.; Vollbrecht, A.; Jeske, J.; Jones, P. G.; Schmutzler, R.; du Mont, W.-W. *Chem. Ber./Recl.* **1997**, *130*, 819–822.

(4) Kojima, S.; Kajiyama, K.; Nakamoto, M.; Akiba, K.-y. *J. Am. Chem. Soc.* **1996**, *118*, 12866–12867.

Scheme 1. Synthesis of Phosphorane with Reversed Apicophilicity *O-cis* **2**



P–H (apical) phosphorane **1b** with concomitant H₂ elimination,⁴ whereas **1a–c** gave *O-trans* **3a–c** in toluene and *o*-dichlorobenzene (Scheme 1).⁵ One disadvantage of this procedure is that it is not suitable for the preparation of phosphoranes that exhibit reversed apicophilicity and may undergo stereomutation⁶ around these temperatures. Herein we report on the mild and highly selective procedures for preparing phosphoranes that exhibit reversed apicophilicity *O-cis* **2** with two Martin ligands and one additional substituent, which proceeds through the oxidation of in situ generated dianion **4**.

First, for alkyl derivatives, dianions **4a** [δ_P (Et₂O) = –33.5], **4b** [δ_P (Et₂O) = –23.1], and **4c** [δ_P (Et₂O) = –10.1] were generated in situ by the reaction of **1a** [δ_P (CDCl₃) = –51.9], **1b** [δ_P (CDCl₃) = –33.4], and **1c** [δ_P (CDCl₃) = –14.7, –43.0]⁵ with 2 equiv of *n*-BuLi in Et₂O at –78 °C, respectively. Oxidation of the dianion **4** was carried out at room temperature (or at –78 °C) with 30% H₂O₂, *m*CPBA, and I₂. Formation of an isomer that exhibits reversed apicophilicity, *O-cis* **2**, was observed predominantly or exclusively by ³¹P NMR, and the ratio of *O-cis* **2** and *O-trans* **3** after 30 min in solution are shown in Table 1.

Table 1. Ratio of *O-cis* **2** and *O-trans* **3** in the Reaction Mixture Determined by ³¹P NMR (Room Temperature after 30 min) in Et₂O

oxidizing reagent	2a:3a	2b:3b	2c:3c
30% H ₂ O ₂	93:7	88:12	
<i>m</i> CPBA	92:8	>99:<1	88:12
I ₂	96:4	>99:<1	>99:<1

The dianion **4c** was not oxidized by 30% H₂O₂, and the starting material **1c** was recovered.

It is rationalized that, upon oxidation of the dianion **4**, phosphorane **A** is formed and then cyclization takes place to extrude X[–] by the oxide anion to give **2**.

To extend the validity of the oxidation protocol, the preparation of phosphoranes that exhibit reversed apicophilicity, **2d–g**, bearing aryl groups was attempted. To prepare **1**, aromatic lithium reagents (6 equiv, large excess) were reacted with P–H (equatorial) spirophosphorane **5** according to the procedure for alkyl derivatives.⁵ However, the expected phosphorane **1** was not obtained at all after usual treatment of the reaction mixture, giving only the cyclized *O-trans* **3** along with some decomposition products.

Fortunately, ³¹P NMR measurements of the reaction solution showed the formation of the corresponding dianion **4** at room temperature [**4d** (R=2,4,6-trimethylphenyl): δ_P (Et₂O) = –9.8; **4e** (R=2,4,6-triethylphenyl): δ_P (Et₂O) = –10.8; **4f** (R=2,4,6-tri-*i*-propylphenyl): δ_P (Et₂O) = –10.8]. Thus, oxidative cyclization was attempted as a one-pot procedure by the addition of iodine (6 equiv) (Scheme 1). ³¹P NMR observation of the mixtures directly after the addition of I₂ showed the quantitative formation of isomers that exhibit reversed apicophilicity, *O-cis* **2d–g**. After 30 min at room temperature, the ratio of *O-cis* **2** to *O-trans* **3** became 62:38 for **4d**, 63:37 for **4e**, 99:1 for **4f**, and 23:77 for **4g**. From the relative stability of **2d–g**, it is evident that steric effect is a major cause for stabilization against

(5) Kajiyama, K.; Kojima, S.; Akiba, K.-y. *Tetrahedron Lett.* **1996**, 37, 8409–8412.

(6) Berry, R. S. *J. Chem. Phys.* **1960**, 32, 933–938.

pseudorotation in the isomers that exhibit reversed apicophilicity. In the case of **2f**, pseudorotation was sufficiently slow to allow the isolation of pure product.⁷ The X-ray structures of **2f** and **3f** shown in Figure 1 verify their structure.⁸

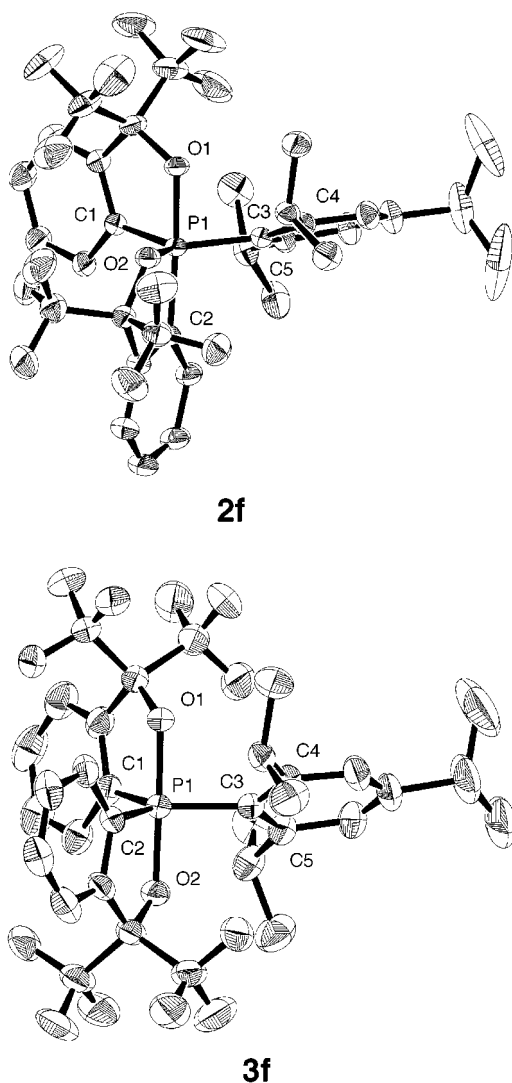


Figure 1. Crystal structures (30% thermal ellipsoids) of **2f** and **3f**.

On the basis of the success generating dianion **4** directly from **5** by excess (6 equiv) aryllithiums, the same procedure was applied with aliphatic lithiums (3 equiv). Formation of the dianion **4a–c** was observed by ³¹P NMR, and the same results were obtained as shown in Table 1 by I₂ oxidation.⁹

In summary, we have developed a mild and one-pot procedure for preparing phosphoranes that exhibit reversed apicophilicity, *O*-cis **2**, by using P–H (equatorial) phospho-

rane **5**. The optimum oxidizing reagent in our hands is I₂, since not only were the reaction temperatures mild but also the reaction conditions could be anhydrous. We believe that this method is applicable for the preparation of a wide range of phosphoranes that exhibit reversed apicophilicity, a novel class of pentacoordinate phosphorus compounds.

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Supporting Information Available: Preparation, spectral details, and elemental analyses for **2a–g** and **3a–g**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(7) **Alkylspiroposphorane 2b.** To a solution of **5** (3.09 g, 5.99 mmol) in Et₂O (50 mL) was added *n*-BuLi (1.52 M hexane solution, 11.7 mL, 18.0 mmol) at 0 °C, and then the solution was stirred for 3 h at room temperature. The solution was allowed to cool to –78 °C, and then I₂ (4.60 g, 18.1 mmol) was added. The mixture was stirred for 1 h at –78 °C. The resulting solution was washed with aqueous Na₂S₂O₃ (50 mL × 2) and brine (50 mL × 2), and the organic layer was dried over anhydrous MgSO₄ and concentrated in vacuo. Resulting crude product was washed with *n*-hexane to afford a white solid of **2b** (3.12 g, 5.45 mmol, 91.1%). Preparation by hydrogen elimination and the spectral data of **2b** were already reported.⁴ The properties of **2a** are similar to those of **2b** and **2f** and will be reported in due course. **Arylspiroposphorane 2f.** To a solution of 1-bromo-2,4,6-tri-*i*-propylbenzene (0.769 g, 2.72 mmol) in Et₂O (5 mL) was added *n*-BuLi (1.46 mL, 2.33 mmol, *c* 1.62 M in hexane) at –78 °C. The mixture was allowed to warm to room temperature and was stirred for 4 h. To the mixture was added a solution of P–H (equatorial) spiroposphorane **5** (200 mg, 0.388 mmol) in Et₂O (5 mL) at –78 °C, and stirring was continued at room temperature for 1 h followed by the addition of I₂ (591 mg, 2.33 mmol). After quenching with aqueous Na₂S₂O₃, the mixture was extracted with Et₂O (3 × 30 mL), and the collected organic layer was dried over MgSO₄. The solvent was evaporated in vacuo. Purification was carried out by TLC (silica gel, hexane/CH₂Cl₂ 3:1) and recrystallization from hexane/CH₂Cl₂ to give **2f** (197 mg, 0.275 mmol, 71%).

(8) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-154409 and 154410. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax: (+44)1223-336-0033; e-mail: deposit@ccdc.cam.ac.uk). Crystals suitable for X-ray structure determination were mounted on a MacScience MXC3 diffractometer and irradiated with graphite-monochromated Cu Kα radiation ($\lambda = 1.54178$ Å) for data collection. The structure was solved using the teXsan (Rigaku) system and refined by full-matrix least-squares. Crystal data for **2f**: monoclinic system, space group *P*2₁/*c* (No. 14), *a* = 17.918(3) Å, *b* = 12.896(2) Å, *c* = 16.333(3) Å, $\beta = 117.02(1)^\circ$, *V* = 3362.2(9) Å³, *Z* = 4, $\rho_{\text{calc}} = 1.419$ g cm^{–3}. *R* = 0.0567 (*R*_w = 0.0958) for 4357 observed reflections (433 parameters) with *I* > 3σ(*I*). Goodness of fit = 1.281. Crystal data for **3f**: monoclinic system, space group *C*2/*c* (No. 15), *a* = 36.539(4) Å, *b* = 10.590(1) Å, *c* = 19.564(3) Å, $\beta = 117.773(9)^\circ$, *V* = 6698(1) Å³, *Z* = 8, $\rho_{\text{calc}} = 1.425$ g cm^{–3}. *R* = 0.0669 (*R*_w = 0.1009) for 3845 observed reflections (433 parameters) with *I* > 3σ(*I*). Goodness of fit = 1.011. The apical bonds of **2f** are longer than the corresponding equatorial bonds; O1–P1(ap) 1.778(2) > O2–P1(eq) 1.677(2) Å, and C2–P1(ap) 1.887(3) > C1–P1(eq) 1.824(3) Å, whereas the pairs of bonds of **3f** are almost equal; O–P(ap) 1.755(2), 1.763(2) Å, and C–P(eq) 1.824(4), 1.830(4) Å.

(9) It is not clear at present why 6 equiv of aryllithiums and 3 equiv of alkylolithiums give the best yield of **2**.