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

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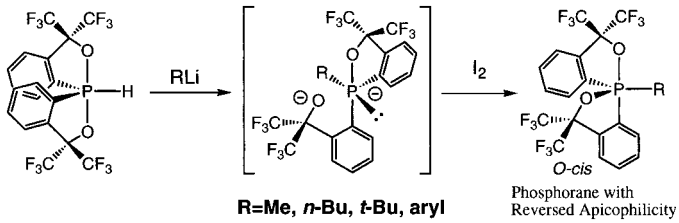
ABSTRACT



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-5[1] 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

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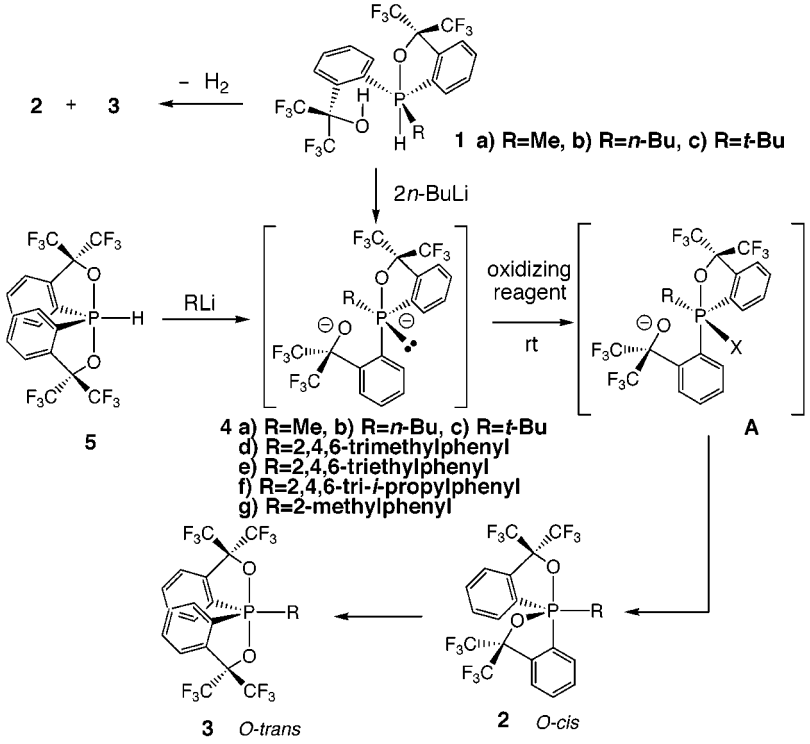
Scheme 1. Synthesis of Phosphorane with Reversed Apicophilicity *O-cis* **2**



P−H (apical) phosphorane **1b** with concomitant H_2 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 stereomutation[6] 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 (Et_2O) = −33.5], **4b** [δ_P (Et_2O) = −23.1], and **4c** [δ_P (Et_2O) = −10.1] were generated in situ by the reaction of **1a** [δ_P ($CDCl_3$) = −51.9], **1b** [δ_P ($CDCl_3$) = −33.4], and **1c** [δ_P ($CDCl_3$) = −14.7, −43.0][5] with 2 equiv of *n*-BuLi in Et_2O at −78 °C, respectively. Oxidation of the dianion **4** was carried out at room temperature (or at −78 °C) with 30% H_2O_2, *m*CPBA, and I_2. Formation of an isomer that exhibits reversed apicophilicity, *O-cis* **2**, was observed predominantly or exclusively by ^{31}P 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 ^{31}P NMR (Room Temperature after 30 min) in Et_2O

oxidizing reagent	**2a**:**3a**	**2b**:**3b**	**2c**:**3c**
30% H_2O_2	93:7	88:12	
*m*CPBA	92:8	>99:<1	88:12
I_2	96:4	>99:<1	>99:<1

The dianion **4c** was not oxidized by 30% H_2O_2, 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, ^{31}P 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 (Et_2O) = −9.8; **4e** (R=2,4,6-triethylphenyl): δ_P (Et_2O) = −10.8; **4f** (R=2,4,6-tri-*i*-propylphenyl): δ_P (Et_2O) = −10.8]. Thus, oxidative cyclization was attempted as a one-pot procedure by the addition of iodine (6 equiv) (Scheme 1). ^{31}P NMR observation of the mixtures directly after the addition of I_2 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

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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]

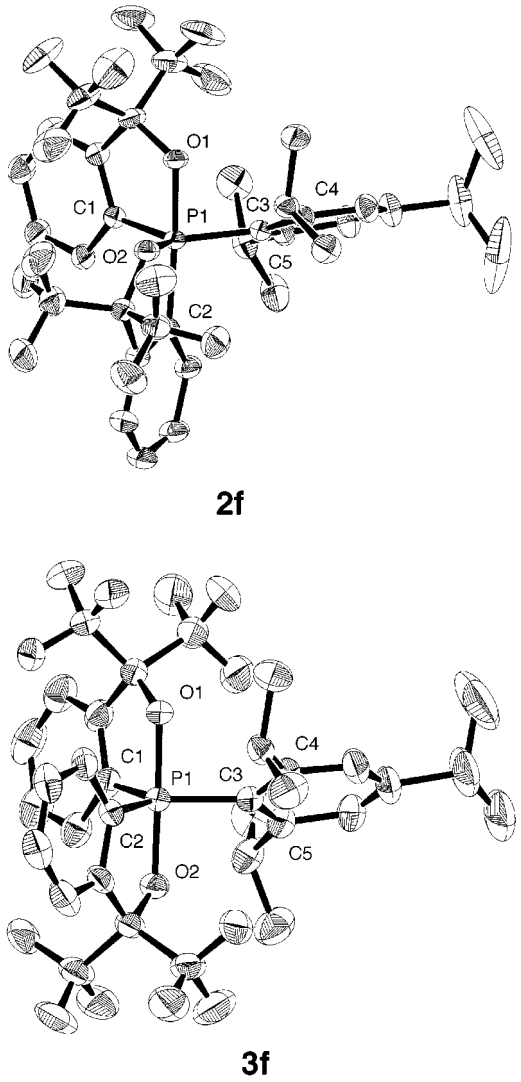

Figure 1. Crystal structures (30% thermal ellipsoids) of **2f** and **3f**.

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 ^{31}P NMR, and the same results were obtained as shown in Table 1 by I_2 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) phosphorane **5**. The optimum oxidizing reagent in our hands is I_2, 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) **Alkylspirophosphorane 2b.** To a solution of **5** (3.09 g, 5.99 mmol) in Et_2O (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 I_2 (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 $Na_2S_2O_3$ (50 mL ×2) and brine (50 mL ×2), and the organic layer was dried over anhydrous $MgSO_4$ 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. **Arylspirophosphorane 2f.** To a solution of 1-bromo-2,4,6-tri-*i*-propylbenzene (0.769 g, 2.72 mmol) in Et_2O (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) spirophosphorane **5** (200 mg, 0.388 mmol) in Et_2O (5 mL) at −78 °C, and stirring was continued at room temperature for 1 h followed by the addition of I_2 (591 mg, 2.33 mmol). After quenching with aqueous $Na_2S_2O_3$, the mixture was extracted with Et_2O (3 × 30 mL), and the collected organic layer was dried over $MgSO_4$. The solvent was evaporated in vacuo. Purification was carried out by TLC (silica gel, hexane/CH_2Cl_2 3:1) and recrystallization from hexane/CH_2Cl_2 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)1223-336-033; 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 (λ = 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 $P2_1/c$ (No. 14), a = 17.918(3) Å, b = 12.896(2) Å, c = 16.333(3) Å, β = 117.02(1)°, V = 3362.2(9) Å^3, Z = 4, ρ_{calc} = 1.419 g cm^{-3}. R = 0.0567 (R_w = 0.0958) for 4357 observed reflections (433 parameters) with $I > 3\sigma(I)$. Goodness of fit = 1.281. Crystal data for **3f**: monoclinic system, space group $C2/c$ (No. 15), a = 36.539(4) Å, b = 10.590(1) Å, c = 19.564(3) Å, β = 117.773(9)°, V = 6698(1) Å^3, Z = 8, ρ_{calc} = 1.425 g cm^{-3}. R = 0.0669 (R_w = 0.1009) for 3845 observed reflections (433 parameters) with $I > 3\sigma(I)$. 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 alkyllithiums give the best yield of **2**.