Reactions of a Stable Phosphinyl Radical with Stable Aminoxyl Radicals

Shintaro Ishida,* Fumiya Hirakawa, and Takeaki Iwamoto*

Department of Chemistry, Graduate School of Science, Tohoku University, Aoba-ku, Sendai, Miyagi 980-8578

(E-mail: iwamoto@m.tohoku.ac.jp)

Reaction of stable phosphinyl radical **1a** with AZADO gave aminoxyphosphine **3** as the primary product by selective radical coupling at -40 °C. Compound **3** decomposed to phosphorane **4**, silyl phosphinate **5**, and aminophosphine **6** at room temperature. The molecular structures of **4–6** were determined by X-ray structural analysis. The homolytic N–O bond cleavage of **3** and the subsequent silyl migration of the resulting phosphinoyl radical **7** would be key steps in the reaction.

Phosphorus-centered dicoordinate radicals (phosphinyl radicals, R₂P•) have a bifunctionality owing to the lone pair and unpaired electron on the same phosphorus atom, whose reactivity deserves much attention.¹⁻³ Although reactions of phosphinyl radicals with alkenes, C-X bonds (X = halogen, hydrogen), tin hydride, oxygen, disulfides, and diselenide have been reported,³ selective radical coupling between phosphinyl radicals and other radicals to provide functionalized phosphines has not been investigated. We successfully synthesized stable dialkylphosphinyl radical $R^{H_2}P$ • (1a) $[R^{H_2} = 1, 1, 4, 4$ -tetrakis(trimethylsilyl)butane-1,4-diyl] that exists as a monomer both in solution and in the solid state (Chart 1).⁴ Recently, we have reported the synthesis of persistent heavier pnictogen-centered radicals $R^{H}_{2}Pn$ • [Pn = Sb (1b) and Bi (1c)] in solution by utilizing facile dissociation of the corresponding dimer and their reactions with 2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO) to afford **2b** and **2c** as selective radical coupling products.⁵ Thus, we anticipated selective radical coupling of **1a** with other stable radicals. We wish to report herein reactions of stable phosphinyl radical 1a with stable aminoxyl radicals AZADO (2-azaadamantane-N-oxyl)⁶ and TEMPO, which give unexpected oxidation products, cyclic phosphorane 4, silvl phosphinate 5, and aminophosphine 6. Product analysis and theoretical studies indicate that oxygen transfer from the aminoxyl radicals to 1a and subsequent silvl migration are key steps.



Chart 1. Stable dialkylphosphinyl radical 1a and related compounds.

Phosphinyl radical **1a** was treated with one equivalent of AZADO in a sealed NMR tube with toluene- d_8 at -40 °C, and the reaction was monitored by NMR spectroscopy (Scheme 1). The ³¹P{¹H} NMR spectrum of the resulting solution (Figure S5 in Supporting Information) showed one singlet signal, which

indicated formation of a sole diamagnetic product.^{7,8} The NMR data confirmed that the observed species at -40 °C was aminoxyphosphine 3; the observed NMR spectra are consistent with the existence of two kinds of trimethylsilyl groups, phosphacyclopentane ring, and 2-azaadamantyl moiety. Moreover, the singlet ³¹P signal observed at 186.1 ppm was well reproduced by the calculated ³¹P chemical shift (213.4 ppm) of the optimized structure of 3 (3_{opt}) by DFT calculations. With increasing temperature of the resulting solution, compound 3 decomposed to cyclic phosphorane 4, silyl phosphinate 5, and aminophosphine 6 in 82%, 7%, and 5% yields, respectively, with trace amounts of unidentified products. Interestingly, when a similar reaction was conducted at room temperature, the yields of the products were considerably changed (4, 28%; 5, 27%; 6, 35%). The reaction of **1a** with two equivalents of AZADO gave compound 5 in 61% yield. Products 4-6 did not undergo further reactions with AZADO at room temperature.



Scheme 1. Reaction of 1a with AZADO.

Compounds 4-6 were characterized by NMR, MS, elemental analysis, and X-ray diffraction study; their molecular structures in the solid state are shown in Figures 1, 2, and S17 (in Supporting Information).⁹ Compound 4 has a siloxy(amino)phosphorane skeleton. The lengths of P1-O1 [1.6149(12) Å] and P1-N1 [1.6612(14) Å] bonds are within the standard range of P-O and P-N single bond lengths.10 The P1-C4 bond [1.6764(17)Å] is considerably shorter than the P1-C7 bond [1.8404(17) Å] and is similar to the reported ylide P=C bond of phosphorane $H_2C=P(NMe_2)_3$ [1.655(6)Å].¹¹ The C4 atom adopts planar trigonal geometry; the sum of the bond angles around C4 is $360.0(1)^\circ$. In the ¹³C{¹H} NMR spectrum of 4, two quaternary carbon nuclei resonate at 20.3 and 29.0 ppm as a doublet due to the ${}^{31}P$ nuclei, with ${}^{1}J_{PC}$ values of 146 and 75.4 Hz, respectively. Based on the large ${}^{1}J_{PC}$ value, the signal at 20.3 ppm is assignable to the ylide carbon (C4).

The P1–O1 and P1–O2 bond lengths of **5** being 1.4751(14) and 1.5889(14) Å indicate silyl phosphinate functionality. The C1–C2 bond length [1.340(3) Å] and planar geometry around C1 (the sum of the bond angles around C1 of $360.0(1)^\circ$) indicate that a double bond exists between the C1 and C2 atoms.



Figure 1. ORTEP drawing of **4**. Thermal ellipsoids are drawn at the 30% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths of **5** (Å): P1–O1 1.6149(12), P1–N1 1.6612(14), P1–C4 1.6764(17), P1–C7 1.8404(17), C4–C5 1.547(2), C5–C6 1.536(2), C6–C7 1.574(2).



Figure 2. ORTEP drawing of 5. Thermal ellipsoids are drawn at the 30% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): P1–O1 1.4751(14), P1–O2 1.5889(14), P1–C1 1.7971(18), P1–C4 1.8147(18), C1–C2 1.340(3), C2–C3 1.505(3), C3–C4 1.564(2).

Based on the experimental results, a proposed mechanism for the reaction of **1a** with AZADO is shown in Schemes 2 and 3. Homolytic N–O bond cleavage of **3** occurs to give phosphinoyl radical **7** and aminyl radicals **8**.^{12,13} The immediate 1,3-silyl migration of **7** forms radical **9** (Scheme 2). The following three kinds of radical couplings of (a) **8** and **9**, (b) **1a** and **8**, and (c) **9** and AZADO give **4**, **6**, and **10**, respectively.¹⁴ The second N–O bond cleavage of **10**, followed by hydrogen abstraction of **11**, affords **5** (Scheme 3). The observed temperature dependence of the product yields can be explained by the solvent cage effect of the radical coupling reactions; compounds **5** and **6** are formed by an out-of-cage process that is favorable at higher temperature.

The proposed key steps shown in Scheme 2 were supported by DFT calculations at the (U)M06-2X/6-31+G(d) level (Figure S19).^{15,16} While selective radical coupling of $1a_{opt}$ and



Scheme 2. A proposed formation mechanism of radical 9 ($Si = SiMe_3$, $NR_2 = 2$ -azaadamantyl).



Scheme 3. A proposed formation mechanism of 4-6.

AZADO_{opt} to provide $3a_{opt}$ is highly exothermic (-164.2 kJ mol⁻¹), homolytic cleavage of the N–O bond in $3a_{opt}$ to give a pair of phosphinoyl and aminyl radicals ($7_{opt} + 8_{opt}$) is moderately endothermic (+92.0 kJ mol⁻¹), which suggests that the oxygen transfer from AZADO_{opt} to $1a_{opt}$ to give 7_{opt} is energetically favorable.¹⁶ The subsequent silyl migration from carbon to oxygen is also exothermic; radical 9_{opt} is more stable than 7_{opt} by 60.1 kJ mol⁻¹.¹⁷

Reaction of **1a** with two equivalents of TEMPO in benzene at room temperature gave **5** and 2,2,6,6-tetramethylpiperidine (TMP) in 86% and 80% yields, respectively (eq 1). When one equivalent of TEMPO was used, **5**, TMP, and unreacted **1a** were obtained. Since structurally similar stibinyl and bismuthinyl radicals **1b** and **1c** react with TEMPO to form radical coupling products **2b** and **2c**,⁵ the reaction of **1a** with TEMPO would also give aminoxyphosphine **2a** as the primary intermediate. In the case of this reaction, radical coupling of **9** with TEMPO to give **5** is much faster than that with 2,2,6,6-tetramethylpiperidinyl radical **12**, probably due to steric repulsion.

In summary, the reaction of stable phosphinyl radical 1a with stable aminoxyl radical AZADO afforded the corresponding aminoxyphosphine 3 as the primary intermediate. The homolytic N–O bond cleavage of 3 and the subsequent silyl migration of the resulting phosphinoyl radical 7 provided compounds 4-6 as the final products. The reaction of 1a with TEMPO would proceed in a similar manner.

This work was supported in part by JSPS KAKENHI Grant Number 25708004 (S. I.), MEXT KAKENHI (Grant-in-Aid for Scientific Research on Innovative Areas "Stimuli-responsive Chemical Species") Grant Number 24109004 (T. I.), Grant-in-Aid for JSPS Fellows (F. H.). We deeply appreciate Professor Dr. Yoshiharu Iwabuchi and Dr. Yusuke Sasano (Graduate School of Pharmaceutical Sciences, Tohoku University) for the gift of AZADO.

Supporting Information is available electronically on J-STAGE.

References and Notes

- For a recent review of phosphine-centered radicals in organic synthesis, see: D. Leca, L. Fensterbank, E. Lacôte, M. Malacria, *Chem. Soc. Rev.* 2005, 34, 858.
- 2 For recent reviews of persistent and stable phosphinyl radicals and related heavier main group elements radicals, see: a) M. Geoffroy, *Recent Res. Dev. Phys. Chem.* 1998, 2, 311. b) P. P. Power, *Chem. Rev.* 2003, 103, 789. c) S. Marque, P. Tordo, in *Topics in Current Chemistry*, Springer, 2005, Vol. 250, p. 43. doi:10.1007/b100981. d) A. Armstrong, T. Chivers, R. T. Boeré, *ACS Symp. Ser.* 2005, 917, 66. e) J. Konu, T. Chivers, in *Stable Radicals: Fundamentals and Applied Aspects of Odd-Electron Compounds*, ed. by R. Hicks, Wiley, Chichester, 2010, p. 395. doi:10.1002/9780470666975.ch10.
- 3 Selected reports on the reactivity of phosphinyl radicals: a) J. Pellon, J. Am. Chem. Soc. 1961, 83, 1915. b) G. M. Burch, H. Goldwhite, R. N. Haszeldine, J. Chem. Soc. 1963, 1083. c) H. Fritzsche, U. Hasserodt, F. Korte, Angew. Chem., Int. Ed. Engl. 1964, 3, 64. d) H. Low, P. Tavs, Tetrahedron Lett. 1966, 7, 1357. e) R. Fields, H. Goldwhite, R. N. Haszeldine, J. Kirman, J. Chem. Soc. C 1966, 2075. f) R. Fields, R. N. Haszeldine, J. Kirman, J. Chem. Soc. C 1970, 197. g) R. Fields, R. N. Haszeldine, N. F. Wood, J. Chem. Soc. C 1970, 744. h) R. Fields, R. N. Haszeldine, N. F. Wood, J. Chem. Soc. C 1970, 1370. i) S. K. Wong, W. Sytnyk, J. K. S. Wan, Can. J. Chem. 1971, 49, 994. j) P. Agarwal, N. A. Piro, K. Meyer, P. Müller, C. C. Cummins, Angew. Chem., Int. Ed. 2007, 46, 3111. k) O. Back, M. A. Celik, G. Frenking, M. Melaimi, B. Donnadieu, G. Bertrand, J. Am. Chem. Soc. 2010, 132, 10262. 1) N. A. Giffin, A. D. Hendsbee, T. L. Roemmele, M. D. Lumsden, C. C. Pye, J. D. Masuda, Inorg. Chem. 2012, 51, 11837. See also ref 4.
- 4 S. Ishida, F. Hirakawa, T. Iwamoto, J. Am. Chem. Soc. 2011, 133, 12968; Radical 1a serves as a ligand for transition metal. See also: T. Iwamoto, F. Hirakawa, S. Ishida, Angew. Chem., Int. Ed. 2012, 51, 12111.
- 5 S. Ishida, F. Hirakawa, K. Furukawa, K. Yoza, T. Iwamoto, *Angew. Chem., Int. Ed.* **2014**, *53*, 11172.
- 6 M. Shibuya, M. Tomizawa, I. Suzuki, Y. Iwabuchi, J. Am. Chem. Soc. 2006, 128, 8412.
- 7 NMR data of **3**: ¹H NMR (400 MHz, C_7D_8 , -40 °C): δ 0.37 (s, 9H, CH₃), 0.42 (s, 9H, CH₃), 1.29–1.36 (br, 2H), 1.49–2.14 (m, 12H), 2.45–2.54 (br, 2H), 3.69–3.80 (br, 2H); ¹³C{¹H} NMR (100 MHz, C_7D_8 , -40 °C): δ 2.2 (d, ³J_{PC} = 12.0 Hz, CH₃), 4.1 (s, CH₃), 26.1 (s, CH), 26.5 (s, CH), 27.1 (d, ¹J_{PC} = 67.4 Hz, C), 30.1 (s, CH₂), 33.5 (s, CH₂), 36.4 (d, ²J_{PC} = 17.1 Hz), 36.5 (s, CH₂), 54.3 (s, CH); ²⁹Si{¹H} NMR (79 MHz, C_7D_8 , -40 °C): δ 2.5, 4.5 (d, ²J_{PSi} = 41.3 Hz); ³¹P{¹H} NMR (162 MHz, C_7D_8 , -40 °C): δ 186.1. For

details, see Supporting Information.

- 8 No EPR signals except for **1a** was observed during the reaction.
- 9 Synthetic details, characterization, and molecular structures obtained by X-ray structural analysis of compounds 4–6 are described in Supporting Information. CCDC 1016228 (4), 1016229 (5), 1016227 (6) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.
- 10 a) A. Bondi, *J. Phys. Chem.* **1964**, *68*, 441. b) F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, R. Taylor, *J. Chem. Soc., Perkin Trans. 2* **1987**, S1.
- 11 N. W. Mitzel, B. A. Smart, K.-H. Dreihäupl, D. W. H. Rankin, H. Schmidbaur, J. Am. Chem. Soc. 1996, 118, 12673.
- 12 Decomposition of aminoxyphosphines by N–O bond cleavage has been reported, see: a) M. R. Banks, R. F. Hudson, *J. Chem. Soc., Perkin Trans.* 2 1989, 463. b) C. A. D. Sousa, M. L. C. Vale, J. E. Rodríguez-Borges, X. García-Mera, *New J. Chem.* 2010, 34, 2546.
- 13 Homolytic N–O bond cleavage has been postulated in the reaction of phosphinidene tungsten complex with TEMPO: V. Nesterov, S. Schwieger, G. Schnakenburg, S. Grimme, R. Streubel, *Organometallics* 2012, *31*, 3457; Very recently Streubel et al. reported in situ generated tungsten coordinated phosphinyl radical with TEMPO forms aminoxyphosphine–tungstem complex and its thermal decomposition. See: V. Nesterov, Z.-W. Qu, G. Schnakenburg, S. Grimme, R. Streubel, *Chem. Commun.* 2014, *50*, 12508.
- 14 Reactions of phosphinoyl radical (Ph₂PO•) with aminoxyl radicals to form (aminoxy)phosphine oxides have been reported: W. K. Busfield, I. D. Grice, I. D. Jenkins, *Aust. J. Chem.* 1995, 48, 625.
- 15 All calculations were carried out at the (U)M06-2X/ 6-31+G(d) level using Gaussian 09 program package. No imaginary frequency numbers were found in the optimized structures. Relative energies were estimated with zero-point correction. Details and full citation of Gaussian 09 were described in the Supporting Information.
- 16 The formation of radical **11** from **1a** and aminoxyl radicals are energetically downhill processes. Energy diagrams of the proposed mechanism of the reactions of **1a** with AZADO and TEMPO are described in Figure S19. Reaction of $\mathbf{8}_{opt} + \mathbf{9}_{opt} \rightarrow \mathbf{4}_{opt}$ is also calculated to be exothermic by $-253.6 \text{ kJ mol}^{-1}$.
- 17 Large spin density on phosphorus atom in $\mathbf{9}_{opt}$ (ρ (C) = 0.39, ρ (P) = 0.46) would be responsible for P–O bond formation by radical coupling of $\mathbf{9}$ and aminoxyl radical. See also a plot of SOMO of $\mathbf{9}_{opt}$ (Figure S20).