Preparation of [4-*t*-Butyl-2,6-bis(*N*,*N*-dimethylaminomethyl)phenyl]-thioxophosphine Sulfide with Intramolecular Participation of Nitrogen Lone Pair in Stabilization

Masaaki YOSHIFUJI,* Akihiko OTOGURO, and Kozo TOYOTA
Department of Chemistry, Faculty of Science, Tohoku University, Aoba, Sendai 980-77
(Received December 9, 1993)

Synopsis. The 4-*t*-butyl-2,6-bis(*N*,*N*-dimethylaminomethyl)phenyl group was utilized to prepare [4-*t*-butyl-2,6-bis(*N*,*N*-dimethylaminomethyl)phenyl]thioxophosphine sulfide. A ^{31}P NMR chemical shift of the thioxophosphine sulfide shows a high field shift by 153 ppm compared with that of (2,4,6-tri-*t*-butylphenyl)thioxophosphine sulfide, suggesting a strong intramolecular participation with the lone-pair electrons of the nitrogen atom in stabilization of the $-P(=S)_2$ group.

Compounds with multiple-bonded heavier main-group elements, such as phosphorus, are currently of interest.[1] By utilizing an extremely bulky 2,4,6-tri-*t*-butylphenyl group (hereafter abbreviated as Ar) as a sterically protecting auxiliary, we and others have successfully prepared various types of multiple bonded phosphorus compounds, such as diphosphenes,[2] thioxophosphine sulfide (dithioxophosphorane, $R-P(=S)_2$),[3] and selenoxophosphine selenide (diselenoxophosphorane, $R-P(=Se)_2$).[4] We have also utilized 2,4-di-*t*-butyl-6-methylphenyl (Ar′ group),[5] 2,6-di-*t*-butylphenyl (Ax group),[6] and 2,4,6-tri-*t*-pentylphenyl (Aa group)[7] as sterically protecting groups in which bulky alkyl groups are substituted at the *o*-position. Very recently, we have reported the utilization of the 2,4-di-*t*-butyl-6-(dimethylamino)phenyl group (Mx group; Mx stands for octamethylxylidine)[8,9] as a novel protecting group, in which one of the *o*-*t*-butyl groups in the Ar is replaced by an electron-donating dimethylamino group. Utilizing the Mx group, we have prepared MxP=S[9] and MxP=Se[8] for the first time as well as $MxP(=S)_2$ and $MxP(=Se)_2$ as stable compounds. Since then, we have been interested in the role of the nitrogen lone pair of the Mx group and involved in modifying the Mx group with respect to the kind of element as well as the position of the heteroatom. During the course of this study, we prepared 2,4-di-*t*-butyl-6-methoxyphenyl (Mox group; Mox stands for methoxy-*m*-xylene derivative),[10] 2,4-di-*t*-butyl-6-(dimethylaminomethyl)phenyl (Mamx group; Mamx stands for dimethylaminomethyl-*m*-xylene derivative),[11] and 2,4-di-*t*-butyl-6-(methoxymethyl)phenyl (Momx group; Momx stands for methoxymethyl-*m*-xylene derivative).[12] Here, we report on the utilization of the 4-*t*-butyl-2,6-bis(*N*,*N*-dimethylaminomethyl)phenyl group (abbreviated to Mamt; Mamt stands for bis(dimethylaminomethyl)toluene derivative) as a novel protecting group in which such electronic effect as intramolecular coordination[13] seems to play a more important role than a steric effect in stabilization (Chart 1). The physicochemical properties of $MamtP(=S)_2$ (**6a**) were compared with those of $MxP(=S)_2$ (**6c**) or $ArP(=S)_2$ (**6f**) in order to obtain some insight into the stabilizing effect of the Mx group.

2-Bromo-5-*t*-butyl-1,3-bis(*N*,*N*-dimethylaminomethyl)benzene (**1**) was prepared by the reaction of 2-bromo-1,3-bis(bromomethyl)-5-*t*-butylbenzene[14] with dimethylamine in *N*,*N*-dimethylformamide (DMF) in 81% yield. Lithiation of the bromobenzene **1** with butyllithium in diethyl ether followed by quenching with water gave **3** in 93% yield, indicating the efficient formation of phenyllithium **2**. The thus-obtained phenyllithium **2** was allowed to react with phosphorus trichloride to give the corresponding phosphonous dichloride **4** [$\delta_P(CD_3CN)=134.0$]. The dichloride **4** was reduced to the corresponding phosphine **5a** with lithium aluminum hydride.[15] The phosphine **5a** was then allowed to react with elemental sulfur in benzene at room temperature for 20 min to give [4-*t*-butyl-2,6-bis(*N*,*N*-dimethylaminomethyl)phenyl]thioxophosphine sulfide (**6a**) in 45% yield (Scheme 1).

Table 1 shows ^{31}P NMR data of **5a** and **6a** together with those of some other related compounds. The ^{31}P NMR chemical shift of **5a** as well as other amino-group substituted phosphines **5b** and **5c** is very similar to that of $Ar'PH_2$ **5e**, indicating that the nitrogen does not strongly affect the environment of the phosphorus atom in these primary phosphines. However, **6a** shows a significantly high-field shift in ^{31}P NMR by ca 150 ppm compared with that of (2,4,6-tri-*t*-butylphenyl)thioxophosphine sulfide **6f** or (2,4-di-*t*-butyl-6-

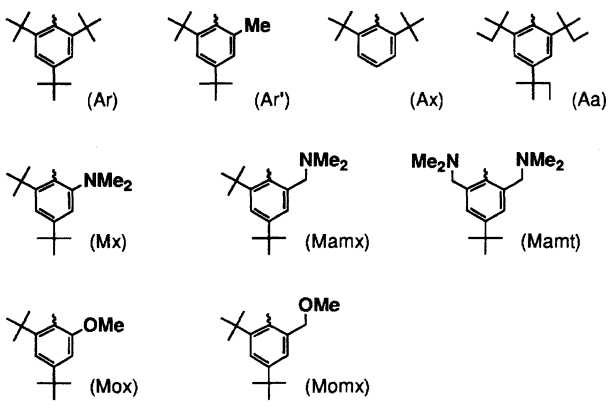
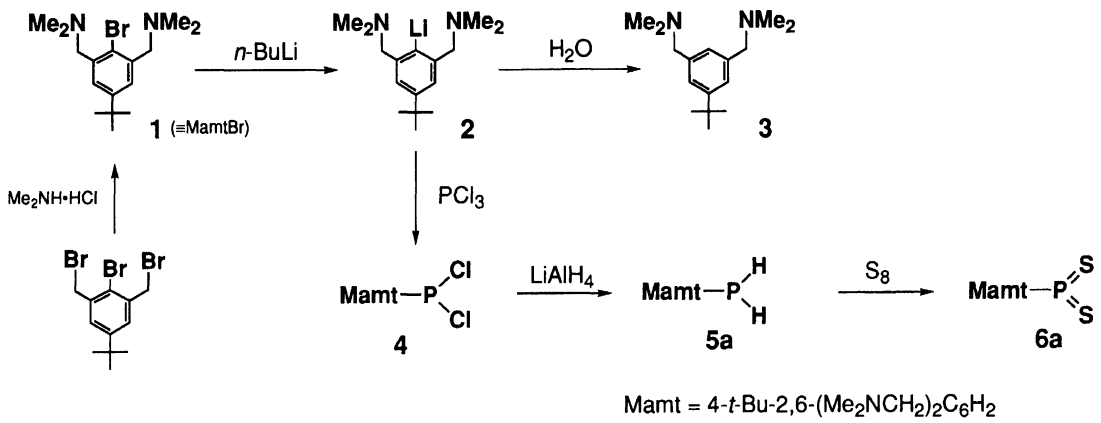
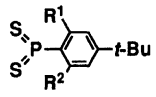
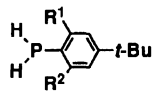


Chart 1.

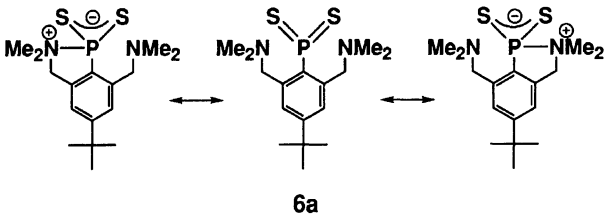


Scheme 1.

Table 1. ^{31}P NMR Data of Phosphine **5a**, Thioxophosphine Sulfide **6a**, and Some Other Related Compounds

Compound		R^1	R^2	δ_P in $CDCl_3$	$^1J_{PH}$/Hz
	**6a**	CH_2NMe_2	CH_2NMe_2	145.3	—
	6b	*t*-Bu	CH_2NMe_2[a]	149.6	—
	6c	*t*-Bu	NMe_2[b]	170.6	—
	6d	*t*-Bu	OMe[c]	277.6[h]	—
	6e	*t*-Bu	Me[d]	285.2[i]	—
	6f	*t*-Bu	*t*-Bu[e]	298.2	—
	**5a**	CH_2NMe_2	CH_2NMe_2	−148.7	207.4
	5b	*t*-Bu	CH_2NMe_2[a]	−143.6	203.6
	5c	*t*-Bu	NMe_2[b]	−141.6	213.7
	5d	*t*-Bu	OMe[c]	−155.4[h]	207.4[h]
	5e	*t*-Bu	Me[f]	−149.9[h]	201.1[h]
	5f	*t*-Bu	*t*-Bu[g]	−129.9	210.6

a) Data taken from Ref. 11. b) Data taken from Ref. 8a. c) Data taken from Ref. 10. d) Data taken from Ref. 16. e) Data taken from Ref. 3a. f) Data taken from Ref. 17. g) Data taken from Ref. 18a. h) Measured in C_6D_6. i) Measured in toluene.



Scheme 2.

methylphenyl)thioxophosphine sulfide **6e**. In ^{1}H NMR spectrum of **6a**, the twelve protons of the dimethylamino groups appeared equivalent as a doublet signal with J_{PH}=3.1 Hz. Such a high-field shift in ^{31}P NMR and spin-spin coupling of the NMe_2 protons through 6- and 5-bonds are also observed in the cases of **6b** and **6c**. These facts suggest that the phosphorus atom in **6a** is in a hypervalent pentacoordinate state[19] on the NMR time scale at 295 K, as shown in Scheme 2. Furthermore, the coordination of the nitrogen lone pair to the $-P(=S)_2$ group has recently been shown by X-ray crystallography in the case of **6b**.[11]

Similarly to the case of $MxP(=S)_2$ (**6c**), an attempted desulfurization reaction of **6a** with tris(dimethylamino)phosphine did not proceed, indicating that the P=S bond in **6a** is very much stabilized. These similar results may suggest that **6c**, as well as **6a** and **6b**, is stabilized mainly by through-space interaction between the phosphorus atom and the nitrogen lone pair.

Experimental

Instruments. Melting points were taken on a Yanagimoto MP-J3 micro melting points apparatus and were uncorrected. NMR spectra were recorded on a Bruker AC-200P or AM-600 spectrometer. UV spectra were measured on a Hitachi U-3210 spectrometer. IR spectra were obtained on a Horiba FT-300 spectrometer. MS spectra were taken on either a JEOL HX-110 or a Hitachi M-2500 spectrometer. The molecular weight was measured using a Corona Type-117 molecular weight apparatus. The reactions were performed under an argon atmosphere, unless otherwise specified.

2-Bromo-5-*t*-butyl-1,3-bis(*N*,*N*-dimethylaminomethyl)benzene (1). A mixture of 2-bromo-1,3-bis-

(bromomethyl)-5-*t*-butylbenzene[14] (818.4 mg, 2.05 mmol), dimethylamine hydrochloride (5.01 g, 61.4 mmol), and triethylamine (14 g) in DMF (70 ml) was stirred at room temperature for 30 min. After being added to aqueous NaOH (120 ml), the reaction mixture was extracted with hexane (200 ml twice). The hexane extract was concentrated under reduced pressure and the product was recrystallized from hexane to give 542.7 g (81%) of **1**: Colorless plates, mp 80—80.5 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.32 (9H, s, *t*-Bu), 2.30 (12H, s, NMe), 3.53 (4H, s, CH_2), and 7.33 (2H, s, arom.); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$) δ=31.2 ($C\underline{Me}_3$), 34.4 ($\underline{C}Me_3$), 45.6 (NMe), 64.2 (CH_2), 123.9 (arom., C2), 126.7 (arom., C4 and C6), 137.8 (arom., C1 and C3), and 149.5 (arom., C5); UV (hexane) 235 (sh, log ε 3.65) and 270 nm (2.25); IR (KBr) 1462, 1356, and 1045 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 327 (M^++1; 2), 325 (M^+−1; 2), 283 (M^+-NMe_2+1; 19), 238 (M^+-2NMe_2; 9), and 58 ($CH_2NMe_2^+$; 100). Found: C, 58.52; H, 8.03; N, 8.41%. Calcd for $C_{16}H_{27}BrN_2$: C, 58.71; H, 8.31; N, 8.56%.

1,3-Bis(*N,N*-dimethylaminomethyl)-5-*t*-butylbenzene (3). To a solution of the bromobenzene **1** (138.8 mg, 0.424 mmol) in diethyl ether (10 ml) was added 0.65 mmol of butyllithium (1.63 M in hexane, 1 M=1 mol dm^{-3}) at room temperature. The resulting solution was stirred for 5 min and quenched with a small amount of water. The reaction mixture was extracted with diethyl ether and dried ($MgSO_4$). Evaporation of the solvent in vacuo gave 98.1 mg (93%) of **3**: Colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.32 (9H, s, *t*-Bu), 2.23 (12H, s, NMe), 3.40 (4H, s, CH_2), 7.04 (1H, broad s, arom.), and 7.20 (2H, d, ^4J=1.5 Hz, arom.); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$) δ=31.4 ($C\underline{Me}_3$), 34.5 ($\underline{C}Me_3$), 45.3 (NMe), 64.6 (CH_2), 124.8 (arom., C4 and C6), 127.1 (arom., C2), 138.2 (arom., C1 and C3), and 150.9 (arom., C5); UV (hexane) 220 (sh, log ε 4.03) and 262 nm (2.58); IR (neat) 1466, 1456, 1363, and 1041 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 248 (M^+; 16), 205 (M^+-NMe_2+1; 64), 160 (M^+-2NMe_2; 95), and 58 ($CH_2NMe_2^+$; 100). Found: *m/z* 248.2233. Calcd for $C_{16}H_{28}N_2$: M, 248.2253.

[4-*t*-Butyl-2,6-bis(*N,N*-dimethylaminomethyl)-phenyl]phosphine (5a). To a solution of the bromobenzene **1** (1.05 g, 2.63 mmol) in diethyl ether (30 ml) was added 4.9 mmol of butyllithium (1.64 M in hexane) at room temperature; the solution was then stirred for 5 min. The resulting solution was added to a solution of phosphorus trichloride (4.6 mmol) in diethyl ether (30 ml) at −78 °C. The solution was then warmed up to room temperature and the solvent was removed in vacuo to give the phosphonous dichloride **4**. The dichloride **4** was dissolved in diethyl ether (10 ml) and the solution was then added to $LiAlH_4$ (5.08 mmol) in ether (10 ml) at 0 °C and stirred for 30 min. The solution was warmed up to room temperature and the solvent was removed in vacuo. Hexane (ca. 40 ml) was added to the residue and the resulting suspension was allowed to pass through Celite (Wako 531-16855) to remove inorganic materials. Then the solvent was removed in vacuo to give 440 mg (60%) of **5a**: ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.31 (9H, s, *t*-Bu), 2.20 (12H, s, NMe), 3.45 (4H, s, CH_2), 3.73 (2H, d, $^1J_{PH}$=207.4 Hz, PH_2), and 7.18 (2H, d, $^4J_{PH}$=2.0 Hz, arom.); ^{31}P NMR (81 MHz, $CDCl_3$) δ=−148.7 (t, $^1J_{PH}$=207.4 Hz); IR (KBr) 2283 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 280 (M^+; 20), 235 (M^+-NMe_2-1; 68), and 220 (M^+-NMe_2-Me-1; 100). Found: *m/z* 280.2064. Calcd for $C_{16}H_{29}N_2P$: M, 280.2068.

[4-*t*-Butyl-2,6-bis(*N,N*-dimethylaminomethyl)-phenyl]thioxophosphine Sulfide (6a). A solution of 29.3 mg (0.10 mmol) of the phosphine **5a** and 14.9 mg (0.46 mg-atom) of elemental sulfur in benzene (5 ml) was stirred for 20 min. The solvent was evaporated under reduced pressure and the residue was washed with hexane to remove the unreacted sulfur by decantation. Column chromatography (Al_2O_3/AcOEt) of the residue afforded 16.1 mg (45%) of **6a**: Colorless crystals, mp 196.5—198.0 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.31 (9H, s, *t*-Bu), 2.63 (12H, d, $^6J_{PH}$=3.1 Hz, NMe), 4.06 (4H, s, CH_2), and 7.24 (2H, d, $^4J_{PH}$=4.8 Hz, arom.); $^{31}P\{^1H\}$ NMR (81 MHz, $CDCl_3$) δ=145.3; $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ=31.1 (s, $C\underline{Me}_3$), 34.9 ($\underline{C}Me_3$), 45.1 (s, NMe), 61.0 (d, $^3J_{PC}$=5.7 Hz, CH_2), 123.3 (d, $^3J_{PC}$=11.6 Hz, arom., C3 and C5), 133.4 (d, $^1J_{PC}$=100.7 Hz, arom., C1), 137.6 (d, $^2J_{PC}$=10.6 Hz, arom., C2 and C6), and 154.8 (d, $^4J_{PC}$=2.7 Hz, arom., C4); UV (hexane) 220 (log ε 3.92), 261 (sh, 3.37), and 296 nm (sh, 3.14); IR (KBr) 714 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 342 (M^+; 90), 327 (M^+−Me; 12), 309 (M^+-S-1; 38), 297 (M^+-NMe_2-1; 32), and 264 ($M^+-2S-Me+1$; 100); MW (C_6H_6) 363. Found: *m/z* 342.1353. Calcd for $C_{16}H_{27}N_2PS_2$: M, 342.1353.

Attempted Reaction of 6a with Tris(dimethylamino)phosphine. To a solution of the thioxophosphine sulfide **6a** (35.6 mg, 0.104 mmol) in toluene (10 ml) was added tris(dimethylamino)phosphine (20 μl, 0.11 mmol); the resulting solution was refluxed for 1 h. The ^{31}P NMR spectrum of the solution showed only peaks due to the starting **6a** and the aminophosphine. A further addition of tris(dimethylamino)phosphine (0.17 mmol) with refluxing for an additional 2 h did not make any difference in the ^{31}P NMR, and 30.4 mg (85%) of the starting **6a** was recovered after column chromatography (Al_2O_3/AcOEt).

This work was supported in part by the Grants-in-Aid for Scientific Research Nos. 03233105 and 02403008 from the Ministry of Education, Science and Culture. The authors also thank Shin-Etsu Chemical Co., Ltd. for donating organosilicon compounds and Tosoh Akzo Co., Ltd. for organolithium reagents.

Note added in proof. Compound **1** was independently prepared by Akiba et al.: 67th National Meeting of the Chemical Society of Japan, Tokyo, April, 1984, No.4H138.

References

1) "Multiple Bonds and Low Coordination in Phosphorus Chemistry," ed by M. Regitz and O. J. Scherer, Georg Thieme Verlag, Stuttgart (1990).

2) M. Yoshifuji, I. Shima, N. Inamoto, K. Hirotsu, and T. Higuchi, *J. Am. Chem. Soc.*, **103**, 4587 (1981); **104**, 6167 (1982).

3) a) M. Yoshifuji, K. Toyota, K. Ando, and N. Inamoto, *Chem. Lett.*, **1984**, 317; b) M. Yoshifuji, K. Shibayama, K. Toyota, and N. Inamoto, *Tetrahedron Lett.*, **24**, 4227 (1983); c) R. Appel, F. Knoch, and H. Kunze, *Angew. Chem., Int. Ed. Engl.*, **22**, 1004 (1983); d) J. Navech, J. P. Majoral, and R. Kraemer, *Tetrahedron Lett.*, **24**, 5885 (1983).

4) M. Yoshifuji, K. Shibayama, and N. Inamoto, *Chem. Lett.*, **1984**, 603.
5) M. Yoshifuji, K. Shibayama, N. Inamoto, T. Matsushita, and K. Nishimoto, *J. Am. Chem. Soc.*, **105**, 2495 (1983).
6) M. Yoshifuji, T. Niitsu, D. Shiomi, and N. Inamoto, *Tetrahedron Lett.*, **30**, 5433 (1989).
7) M. Yoshifuji, S. Sasaki, and N. Inamoto, *J. Chem. Soc., Chem. Commun.*, **1989**, 1732; M. Yoshifuji, K. Toyota, M. Murayama, S. Sasaki, and N. Inamoto, *Science Reports, Tohoku University, Ser. 1*, **72**, 26 (1989).
8) a) M. Yoshifuji, M. Hirano, and K. Toyota, *Tetrahedron Lett.*, **34**, 1043 (1993); b) M. Yoshifuji, M. Hirano, S. Sangu, and K. Toyota, *Science Reports, Tohoku University, Ser. 1*, **75**, 1 (1992).
9) M. Yoshifuji, S. Sangu, M. Hirano, and K. Toyota, *Chem. Lett.*, **1993**, 1715.
10) M. Yoshifuji, D.-L. An, K. Toyota, and M. Yasunami, *Chem. Lett.*, **1993**, 2069.
11) M. Yoshifuji, K. Kamijo, and K. Toyota, *Tetrahedron Lett.*, in press.
12) M. Yoshifuji, K. Kamijo, and K. Toyota, *Bull. Chem. Soc. Jpn.*, **66**, 3440 (1993).
13) G. van Koten, J. T. B. H. Jastrzebski, J. G. Noltes, A. L. Spek, and J. C. Schoone, *J. Organomet. Chem.*, **148**, 233 (1978); G. van Koten, *Pure Appl. Chem.*, **61**, 1681 (1989); P. Arya, J. Boyer, F. Carré, R. Corriu, G. Lanneau, J. Lapasset, M. Perrot, and C. Priou, *Angew. Chem., Int. Ed. Engl.*, **28**, 1016 (1989).
14) M. Tashiro and T. Yamato, *J. Org. Chem.*, **50**, 2939 (1985).
15) Recently, a similar phosphine, 2,6-bis(dimethylaminomethyl)phenylphosphine, was reported: D. A. Atwood, A. H. Cowley, and J. Ruiz, *Inorg. Chim. Acta*, **198—200**, 271 (1992).
16) A. S. Ionkin, V. M. Nekhoroshkov, and Yu. Ya. Efremov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1991**, 1654.
17) M. Baudler and J. Simon, *Chem. Ber.*, **121**, 281 (1988).
18) a) M. Yoshifuji, K. Toyota, K. Shibayama, and N. Inamoto, *Chem. Lett.*, **1983**, 1653; b) K. Issleib, H. Schmidt, and Chr. Wirkner, *Z. Anorg. Allg. Chem.*, **488**, 75 (1982).
19) I. Granoth and J. C. Martin, *J. Am. Chem. Soc.*, **103**, 2711 (1981); T. Kawashima, K. Kato, and R. Okazaki, *J. Am. Chem. Soc.*, **114**, 4008 (1992); Y. Yamamoto, X. Chen, and K.-y. Akiba, *J. Am. Chem. Soc.*, **114**, 7906 (1992); H. Fujihara, N. Oi, T. Erata, and N. Furukawa, *Tetrahedron Lett.*, **31**, 1019 (1990).