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The Optically Active Phosphinodithioates. Synthesis and Conversion to the Optically Active Phosphine Sulfides

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The optically active phosphinodithioates were prepared by the reaction of the corresponding phosphinothioates with Lawesson's reagent in high chemical and optical yields, and were allowed to react with n-BuLi, followed by treatment with the electrophiles to give the corresponding optically active secondary or tertiary phosphine sulfides.

It has been known that Lawesson's reagent, 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (LR), is one of the powerful reagents for sulfurization of carbonyl compounds such as ketones, esters, and amides.[1] The phosphine oxides can also be sulfurized by LR to give the corresponding sulfides.[2] However, there is no report on the stereochemistry of the sulfurization. If the reaction could be applied to the optically active phosphinothioates, the resulting phosphinodithioates would be chiral and give the optically active lithium phosphinothioites by the method reported previously.[3] Here, we wish to report on the preparation of the optically active phosphinodithioates and conversion to the optically active secondary or tertiary phosphine sulfides.

The reactions of (-)-S-methyl t-butylphenylphosphinothioate (**2a**) and (-)-S-methyl 1-naphthylphenylphosphinothioates(**2b**), which were readily prepared from (-)-t-butylphenylphosphinothioic (**1a**) and (-)-1-naphthylphenylphosphinothioic acids (**1b**) respectively,[4] with LR in refluxing toluene gave the optically active phosphinodithioates (-)-**3a** and (+)-**3b** in yields of 90 and 76%, respectively. The optically active (-)-**3a** was allowed to react with n-BuLi in tetrahydrofuran at -78°C, followed by treatment with water or iodomethane to afford the corresponding

secondary (**4a**) (83%) or tertiary phosphine sulfides (**5a**) (92%) in optically active forms, together with butyl methyl sulfide.[5] Similarly (+)-**3b** gave (+)-**4b** (89%) or (+)-**5b** (55%).

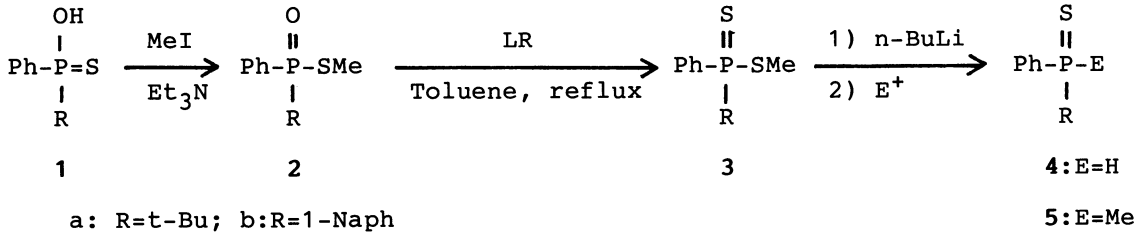


Table 1. The Optical Rotations of Compounds **1**, **2**, **3**, **4**, and **5**.

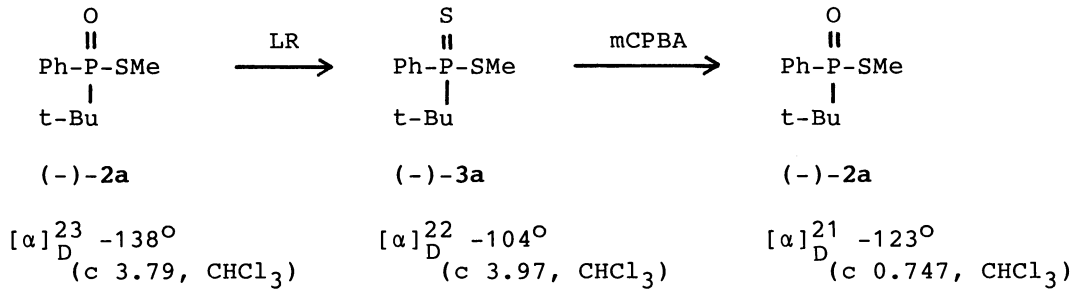
	$[\alpha]_D^T$					$[\alpha]_D^T$			
	α/°	T/°C	c/g dl^{-1}	Solvent		α/°	T/°C	c/g dl^{-1}	Solvent
1a	-26.3[a]	22	0.608	MeOH	**4a**[c]	+82.9	23	0.62	PhH
1b	-60.4[b]	25	0.770	$CHCl_3$	**4b**	+104	22	0.73	PhH
2a	-138	23	3.79	$CHCl_3$	**5a**	+51.5	20	0.770	$CHCl_3$
2b	-43.3	24	1.06	$CHCl_3$	**5b**[d]	+129	21	0.445	$CHCl_3$
3a	-104	22	3.97	$CHCl_3$	**5a**[e]	+52.1	25	0.53	$CHCl_3$
3b	+58.6	22	0.916	$CHCl_3$	**5b**[e]	+84.2	25	0.60	$CHCl_3$

a) Optical purity (o.p.) was 94%.[4] b) Diethylamine salt of **1b** (93% o.p.).[4] c) (-)-**3a** ($[\alpha]_D^{27}$ -100° (c 0.84, $CHCl_3$)) was used. d) This value was obtained when MeI was added after 15 min. After 1 h, $[\alpha]_D^{21}$ +99.6° (c 0.247, $CHCl_3$) was observed. e) Obtained from **4a,b**.

To our knowledge, this is the first example for simple optically active secondary phosphine sulfide.[6] The secondary phosphine sulfides **4a,b** were quite stable under ordinary atmospheric conditions in hours, but deteriorated upon prolonged exposure into many oxidized species which could not be characterized. In the case of reaction of **3b**, S-methylation occurred competitively to give S-methyl 1-naphthylphenylphosphinothioite on quenching with iodomethane. The value of the optical rotation depends on the reaction time before the addition of iodomethane for **5b**, but not for **5a**, indicating that lithium phosphinothioite from **3a** is optically more stable than that from **3b**. The optically active **5a,b** could be obtained by the

deprotonation of **4a,b** with n-BuLi and subsequent treatment with iodomethane in yields of 68 and 43%, respectively.

In order to clarify the stereochemistry of the sulfurization, (-)-**3a** was converted to (-)-**2a** by the reaction with m-chloroperbenzoic acid (mCPBA) in CH_2Cl_2 at 0 °C, which is known to proceed with retention of configuration.[7] Considering



(-)-**2a** (-)-**3a** (-)-**2a**

$[\alpha]_D^{23}$ -138° (c 3.79, $CHCl_3$) $[\alpha]_D^{22}$ -104° (c 3.97, $CHCl_3$) $[\alpha]_D^{21}$ -123° (c 0.747, $CHCl_3$)

that (-)-**3a** was prepared from (-)-**2a** and that the optical rotation of **2a** retains 89% after the conversion cycle, it is reasonably concluded that both the sulfurization by LR and the oxidation with mCPBA proceed at least with 89% retention. Attempts to determine the optical purity of **5a** were unsuccessful, but it can be estimated to be high from the following results: 1) The optical rotation is independent of the reaction time (see before). 2) t-Butyl(hydroxymethyl)phenylphosphine sulfide (**6a**), which was obtained by the similar alkylation of lithium phosphinothioite from **3a** with methoxymethyl bromide and the subsequent hydrolysis, is optically pure by NMR spectrometry.[8]

t-Butylphenylphosphinothioic acid (**1a**) ($[\alpha]_D^{22}$ +23.0° (c 0.572, MeOH)) was obtained by oxidation of lithium phosphinothioite from (-)-**3a** with oxygen, indicating 87% net inversion from (-)-**1a** via four steps. The positions occupied by oxygen and sulfur atoms are switched each other before and after the reaction cycle. Therefore, net inversion means that all reaction steps involved proceed with retention of configuration on the phosphorus atom.

References

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4) **1a:** M. J. P. Harger, J. Chem. Soc., Perkin Trans. 2, 1980, 1505; **1b:** V. A. Chausov and I. F. Lutsenko, Zh. Obshch. Khim., 43, 69 (1973).

5) Physical and spectral data of (-)-**2a**, (-)-**3a**, (+)-**4a**, and (+)-**5a** are shown as typical examples: (-)-**2a**: bp 110 °C/0.15-0.2 Torr. ^{1}H-NMR($CDCl_3$): δ 1.19 (d, $^{3}J_{H,P}$=16.8 Hz, 9H, C(C$\underline{H}_3$)$_3$), 2.14 (d, $^{3}J_{H,P}$=10.5 Hz, 3H, SC$\underline{H}_3$), 7.36-7.64 (m, 3H, m- and p-protons of Ph), and 7.73-8.06 (m, 2H, o-protons of Ph). ^{31}P-NMR ($CDCl_3$): δ_P 67.78. (-)-**3a**: mp 73.5-74.5 °C (hexane-CH_2Cl_2). ^{1}H-NMR ($CDCl_3$): δ 1.23 (d, $^{3}J_{H,P}$=18.3 Hz, 9H, C(C$\underline{H}_3$)$_3$), 2.24 (d, $^{3}J_{H,P}$=13.2 Hz, 3H, SC$\underline{H}_3$), 7.40-7.57 (m, 3H, m- and p-protons of Ph), and 7.91-8.22 (m, 2H, o-protons of Ph). ^{31}P-NMR ($CDCl_3$): δ_P 94.30. High resolution mass spectrometry (HRMS)(70 eV): m/z Found: 244.0507. Calcd for $C_{11}H_{17}PS_2$: 244.0507. (+)-**4a**: mp 72-76 °C. ^{1}H-NMR ($CDCl_3$): δ 1.18 (d, $^{3}J_{H,P}$=18.2 Hz, 9H, C(C$\underline{H}_3$)$_3$), 6.89 (d, $^{1}J_{H,P}$=442 Hz, 1H, P$\underline{H}$), and 7.40-7.90 (m, 5H, $C_6\underline{H}_5$). ^{31}P-NMR ($CDCl_3$): δ_P 52.70. HRMS (70 eV): m/z Found: 198.0632. Calcd for $C_{10}H_{15}PS$: 198.0632.
(+)-**5a**: mp 78.0-79.0 °C. ^{1}H-NMR ($CDCl_3$): δ 1.17 (d, $^{3}J_{H,P}$=16.6 Hz, 9H, C(C$\underline{H}_3$)$_3$), 2.00 (d, $^{2}J_{H,P}$=12.5 Hz, PC$\underline{H}_3$), 7.40-7.56(m, 3H, m- and p-protons of Ph), and 7.75-8.03 (m, 2H, o-protons of Ph). ^{31}P-NMR ($CDCl_3$): δ_P 55.93. HRMS (70 eV): m/z Found: 212.0779. Calcd for $C_{11}H_{17}PS$: 212.0787.

6) Cf. PhP(S)HO(-)Men was reported by J. Michalski; Tsukuba Post-Conference on Heteroatom Chemistry, Tsukuba, July 1987, Abstr., p. 13.

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8) (+)-**6a**: mp 85.0-88.0 °C. $[\alpha]_D^{24}$ +15.58° (c 0.410, $CHCl_3$). ^{1}H-NMR($CDCl_3$): δ 1.20 (d, $^{3}J_{H,P}$=16.4 Hz, 9H, C(C$\underline{H}_3$)$_3$), 3.09 (bs, 1H, O$\underline{H}$), 4.12 (dd, $^{2}J_{H,H}$=12.7 Hz, $^{2}J_{H,P}$=1.2 Hz, 1H, PC$\underline{H}$H'), 4.42 (d, $^{2}J_{H,H}$=12.7 Hz, 1H, PCH$\underline{H}$'), 7.42-7.59 (m, 3H, m- and p-protons of Ph), and 7.66-7.80 (m, 2H, o-protons of Ph). ^{31}P-NMR ($CDCl_3$): δ_P 63.88. HRMS (70 eV): m/z Found: 228.0740. Calcd for $C_{11}H_{17}OPS$: 228.0738. Only signals due to a single enantiomer were observed in ^{1}H-, ^{13}C-, and ^{31}P-NMR spectra on adding chiral shift reagent, Eu(tfc)$_3$.

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