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Syntheses of Unsymmetrical Sulfides and Bis(alkylthio)methanes from Diphenylphosphinodithioate Esters

Koshiro Goda, Fumito Hanafusa, and Naoki Inamoto

Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Tokyo 113

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Unsymmetrical sulfides were prepared by the reactions of diphenylphosphinodithioate esters with organolithiums in tetrahydrofuran (THF) at −78 °C or at room temperature in fairly good or excellent yields. Similarly, methylene bis(diphenylphosphinodithioate) gave bis(alkylthio)methanes by reactions with organolithiums in good yields. The use of bad-smelling thiols is avoided and the phosphorus part can be recycled after sulfurization and esterification. Allyl diphenylphosphinodithioate gave allylbenzene *via* $S_N2(C)$ reaction upon treatment with phenylmagnesium bromide in refluxing THF.

The reaction of alkyl diphenylphosphinodithioates (**1**) with butyllithium affords $[Ph_2PS]Li$ and butyl sulfides by $S_N2(S)$ mechanism.[1]

$$\underset{\mathbf{1}}{Ph_2P(S)SR} + R'Li \longrightarrow [Ph_2PS]Li + \underset{\mathbf{2}}{R\text{-}S\text{-}R'} \qquad (1)$$

This is utilized for the preparation of unsymmetrical sulfides (**2**).[2] This paper describes in detail the syntheses of unsymmetrical sulfides and bis(alkylthio)methanes from diphenylphosphinodithioate esters.

Preparation of Unsymmetrical Sulfides. The esters (**1**) were allowed to react with organolithiums in tetrahydrofuran (THF) at −78 °C or at room temperature for 0.5 h. After the reaction mixture had been quenched with water, the yields of sulfides (**2**) obtained were determined by gas chromatography (GLC) or by isolation with dry column chromatography (DCC). The results are summarized in Table 1.

In the case of the allyl ester, the yield of the corresponding sulfide is comparatively low, probably because of competitive Wittig type rearrangement.[1]

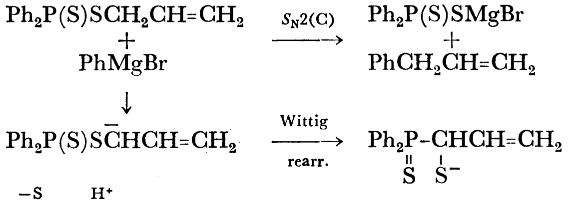
The reactions with Grignard reagents in refluxing THF, except for phenylmagnesium bromide, gave the corresponding sulfides (**2**) only in low yields accompanied by recovery of the starting esters (**1**).[1] The reaction of the allyl ester with phenylmagnesium bromide in THF at room temperature afforded allyldiphenylphosphine sulfide (**3**) (7%) and diphenylphosphinodithioic acid (19%) accompanied by 41% of unchanged ester and a small amount of allylbenzene. In refluxing THF, the reaction gave allylbenzene (70%) and diphenylphosphinodithioic acid (89%) together with a trace amount of triphenylphosphine sulfide ($S_N2(P)$ reaction).

Table 1. Reactions of **1** with organolithiums in THF

R	R′	Reaction temp (°C)	**2** (%)[a]
Me	Bu	−78	98
	Ph	r. t.	95
Et	Bu	−78	88
	Ph	r. t.	89
Ph	Bu	−78	95[b]
	Ph	r. t.	90
$PhCH_2$	Bu	−78	86
	Ph	−78	79[b]
	Ph	r. t.	60[b]
$CH_2{=}CHCH_2$	Bu	−78	63
	Ph	r. t.	72[b]

a) Determined by GLC unless noted otherwise. b) Isolated by DCC.

The formation of allylbenzene and **3** is illustrated as follows:



$$\begin{array}{ccc} Ph_2P(S)SCH_2CH{=}CH_2 & \xrightarrow{S_N2(C)} & Ph_2P(S)SMgBr \\ + & & + \\ PhMgBr & & PhCH_2CH{=}CH_2 \\ \downarrow & & \\ Ph_2P(S)S\overset{-}{C}HCH{=}CH_2 & \xrightarrow[\text{rearr.}]{\text{Wittig}} & Ph_2\underset{\underset{S}{\|}}{P}\text{-}\underset{\underset{S^-}{|}}{C}HCH{=}CH_2 \end{array}$$

$$\xrightarrow{-S}\ \xrightarrow{H^+}\ Ph_2P(S)CH_2CH{=}CH_2$$

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Namely, phenylmagnesium bromide attacks the α-carbon atom of the ester in $S_N2(C)$ manner at higher temperature to afford allylbenzene, while it abstracts the α-hydrogen atom in the ester at room temperature to form **3** through Wittig type rearrangement followed by desulfurization by a small amount of $[Ph_2PS]MgBr$ produced according to Eq. 1.

A possibility of $S_N2'(C)$ mechanism for the formation of allylbenzene can be excluded based on the results of the reactions of phenylmagnesium bromide with the 2-butenyl and 1-methylallyl esters, as shown below.

$$Ph_2P(S)SCH_2CH{=}CHCH_3 + PhMgBr \longrightarrow$$

$$PhCH_2CH{=}CHCH_3 + PhCH(CH_3)CH{=}CH_2 \quad (94 : 6)$$

$$+\ Ph_2P(S)SH$$

$$Ph_2P(S)SCH(CH_3)CH{=}CH_2 + Ph_2P(S)SCH_2CH{=}CHCH_3 \quad (54 : 46)$$

$$\xrightarrow{PhMgBr} PhCH(CH_3)CH{=}CH_2 + PhCH_2CH{=}CHCH_3 \quad (44 : 56)$$

$$+\ Ph_2P(S)SH$$

However, the $S_N2'(C)$ mechanism is not completely ruled out.

Thus, the Grignard reagents can not be used for the preparation of **2**, because of the low thiophilicity.[1]

Unsymmetrical sulfides are usually prepared by the reactions of alkali thiolates with alkyl halides,[3] alkyl phosphinates,[4] or dialkyl carbonates,[5] and by the reaction of 1-methyl-2-fluoropyridinium salt with alcohols and then thiols.[6] On the other hand, the present method can be carried out without the use of bad-smelling thiol, and $[Ph_2PS]Li$ produced in the reaction can be reconverted into diphenylphosphinodi-

Table 2. Reactions of **4** with RLi (at −78 °C in THF)

R	**5** (%)
Me	89[a]
Et	61[a]
Bu	99[b]
Ph	61[b]

a) By GLC. b) By isolation.

thioic acid, which is converted easily into the ester, by treatment with sulfur, indicating that the phosphorus part can be recycled.

Organosodiums can be used. For example, phenylsodium reacted with methyl and phenyl esters at room temperature to afford methyl phenyl sulfide and diphenyl sulfide in 67 and 82% yields, respectively.

Preparation of Bis(alkylthio)methanes. If methylene bis(diphenylphosphinodithioate) (**4**) is prepared from diphenylphosphinodithioic acid and dihalomethane, the preparation of bis(alkylthio)methanes (**5**) would be possible as follows.

$$2Ph_2P(S)SH + CH_2X_2 \longrightarrow$$

$$\underset{\mathbf{4}}{(Ph_2P(S)S)_2CH_2} \xrightarrow{2RLi} \underset{\mathbf{5}}{(RS)_2CH_2}$$

Compound **4** was prepared from dibromo- and diiodomethanes in 14 and 67% yields, respectively, but not from dichloromethane.

The reactions of **4** with organolithiums are summarized in Table 2. The yields of **5** are good or excellent.

When **4** is allowed to react with more than three moles of organolithium and the reaction mixture is treated with alkyl halides, 1,1-bis(alkylthio)alkanes can be prepared by one-pot reaction (see Experimental), which can be easily converted into the corresponding aldehydes.

It is interesting that the diphenylphosphinodithioates act as alkylthio-transfer reagent.

Experimental

Materials. Methyl-, ethyl-, and phenyllithiums were prepared by the method of Gilman *et al.*[7] Alkyl diphenylphosphinodithioates (**1**) were prepared by the methods described in the preceding paper.[1] 1-Phenyl-2-butene and 3-phenyl-1-butene were prepared by the reported method[8] and purified by fractional distillation.

The reactions were carried out under nitrogen or argon.

Preparation of Unsymmetrical Sulfides. General Procedure. Organolithium (*ca.* 3 mmol) was added to a solution of **1** (*ca.* 1.5 mmol) in THF (20 ml) cooled at −78 °C and the mixture was stirred for 0.5 h. After addition of water (0.5 ml) to a small amount of the reaction mixture was added an internal reference such as mesitylene, naphthalene, butyl ethyl sulfide, or phenanthrene. The yield of sulfide (**2**) was determined by GLC (H 523 on Diasolid at 100—150 °C). The sulfide was isolated from the residual part of the reaction mixture by DCC (SiO_2, CCl_4).

Reaction of [Ph_2PS]Li with Sulfur. To the reaction mixture from phenyl diphenylphosphinodithioate (0.99 g, 3.0 mmol) and butyllithium (3.0 mmol) in THF (100 ml) was added an excess amount of sulfur, and the mixture was allowed to stand overnight. After addition of 10% aq sodium hydroxide, the reaction mixture was washed with benzene in order to extract sulfide, and filtered for removal of excess sulfur. The filtrate was acidified with hydrochloric acid and extracted with benzene to give diphenylphosphinodithioic acid (0.635 g, 84%).

Reaction of Allyl Diphenylphosphinodithioate with Phenylmagnesium Bromide. 1) A mixture of the ester (1.12 g, 3.8 mmol) in THF (10 ml) and phenylmagnesium bromide (10.6 mmol) in THF (15 ml) was heated for several minutes and then stirred for 4 h at room temperature. The reaction mixture was acidified with dilute hydrochloric acid and extracted with benzene. The benzene extract was washed with aq sodium hydroxide. The aq alkaline extract gave diphenylphosphinodithioic acid (0.19 g, 19%) after acidification. The benzene solution was treated with DCC (SiO_2, AcOEt). The unchanged ester (0.45 g, 41%) was recovered and allyldiphenylphosphine sulfide (69 mg, 7%) was obtained as an oily substance. IR (neat): 1590 (C=C), 1430, 1110 (P–Ph), and 640 cm^{-1} (P=S); NMR (CCl_4): δ 3.30 (dd, $J_{PCH}=16$ Hz, $J_{HH}=6$ Hz, 2H, PCH_2), 4.85—5.15 (m, 1H, CH=C), 5.25 (d, $J_{HH}=5$ Hz, 1H, CH), 5.55—6.10 (m, 1H, –CH=), and 7.25—8.10 (m, 10H, 2P–Ph); MS: *m/e* 258 (M^+, 23%) and 217 (Ph_2PS^+, 100).

Found: C, 70.00; H, 6.12%. Calcd for $C_{15}H_{15}PS$: C, 69.74; H, 5.85%.

2) A mixture of the ester (0.345 g, 1.2 mmol) and phenylmagnesium bromide (2 mmol) in THF (12 ml) was refluxed for 2 h. The yield of allylbenzene was determined to be 70% by GLC using dibutyl ether as an internal reference. Ethyl acetate was added to the reaction mixture, and the mixture was washed with aq sodium hydroxide. The aq layer was acidified with hydrochloric acid and extracted with ethyl acetate to give diphenylphosphinodithioic acid (0.264 g, 89%). A trace amount of triphenylphosphine sulfide was isolated by DCC of the first ethyl acetate solution.

Preparation of 2-Butenyl Diphenylphosphinodithioate. A mixture of diphenylphosphinodithioic acid (25 g, 0.10 mol) and sodium hydroxide (4 g, 0.10 mol) in THF (50 ml) was stirred at room temperature for 1.5 h. 2-Butenyl chloride (9.3 g, 0.10 mol) was then added, and the mixture was refluxed for 2 h. After removal of THF, the residue was extracted with benzene to give crude ester (30.0 g, 98%) as oil, which was purified by means of DCC, because of the decomposition on vacuum distillation. IR (neat): 1420, 1100 (P–Ph), and 650 cm^{-1} (P=S); NMR ($CDCl_3$): δ 1.52 (d, $J=6$ Hz, 3H), 3.55 (dd, $J_{PSCH}=14$ Hz, $J=6$ Hz, 2H), 5.50 (m, 2H), and 7.3—8.3 (m, 10H).

Reaction of 2-Butenyl Diphenylphosphinodithioate with Phenylmagnesium Bromide. A mixture of the ester (1.16 g, 3.60 mmol) and phenylmagnesium bromide (5 mmol) in THF (30 ml) was refluxed for 4.5 h. After treatment with 0.2 M hydrochloric acid, the reaction mixture was extracted with carbon tetrachloride. The carbon tetrachloride extract was further extracted with aq sodium hydroxide. The aqueous layer afforded diphenylphosphinodithioic acid (0.21 g, 22%) after acidification and extraction with benzene. A mixture of 1-phenyl-2-butene and 3-phenyl-1-butene (94 : 6) was obtained from the carbon tetrachloride layer in 71% yield (by GLC).

Reaction of Sodium Diphenylphosphinodithioate with 1-Methylallyl Chloride Followed by Reaction with Phenylmagnesium Bromide. A mixture of diphenylphosphinodithioic acid (17.1 g, 68 mmol) and sodium hydroxide (3 g, 75 mmol) in THF (50 ml) was stirred at room temperature for 1.5 h. After addition of 1-methylallyl chloride (6.5 g, 72 mmol) the mixture was refluxed for 3 h. After removal of THF the residue was extracted with benzene and the dried benzene extract was evaporated to afford a mixture of 1-methylallyl and 2-butenyl diphenylphosphinodithioates (54 : 46 by NMR), yield 4.2 g (20%). NMR ($CDCl_3$; due to 1-methylallyl ester): δ 1.38 (d, $J=6$ Hz), 3.9—4.4 (m), 4.9—5.2 (m), 5.4—6.0 (m), and 7.3—8.3 (m). The ratio of both esters was determined on the basis of the peak areas at δ 3.55 (due to 2-butenyl ester, NMR data of which have been described already) and 3.9—4.4 (due to 1-methylallyl ester). Since separation of the two esters was unsuccessful, the mixture was used for the following reaction.

A solution of the ester mixture (0.72 g, 2.40 mmol) and phenylmagnesium bromide (3.5 mmol) in THF (30 ml) was refluxed for 4 h and the reaction mixture was subjected to the treatment similar to that in the reaction of 2-butenyl ester. Diphenylphosphinodithioic acid and a mixture of 1-phenyl-2-butene and 3-phenyl-1-butene (56 : 44 by GLC) were obtained in 57 and 51% yields, respectively.

*Preparation of **4**.* *1) From Dibromomethane*: Dibromomethane (25 g, 0.14 mol) was added to a mixture of diphenylphosphinodithioic acid (30 g, 0.12 mol) and sodium hydroxide (5 g, 0.13 mol) in ethanol (200 ml), and the mixture was refluxed for 3 h. The reaction mixture was washed with water and extracted with benzene. After evaporation of benzene from the benzene extract, a small amount of ethanol was added to the residual oil and the mixture was allowed to stand at 0 °C. The resulting crystals were collected and recrystallized from acetonitrile, mp 90—91 °C, yield 4.4 g (14%). IR (KBr): 1425, 1095 (P–Ph), 650 (P=S), and 520 cm^{-1} (P–S); ^1H-NMR ($CDCl_3$): δ 4.56 (t, $J_{PSCH}=16$ Hz, 2H, CH_2) and 7.10—8.10 (m, 20H, 4Ph); ^{31}P-NMR (THF): δ_P −63.8 ppm.

Found: C, 58,32; H. 4.33; S, 24.86%. Calcd for $C_{25}H_{22}P_2S_4$: C, 58.57; H, 4.33; S, 25.02%.

2) From Diiodomethane: Diiodomethane (25 g, 0.09 mmol) was added to a mixture of diphenylphosphinodithioic acid (45 g, 0.18 mol) and sodium hydroxide (7.4 g, 0.19 mol) in THF (200 ml), and the mixture was refluxed for 16 h under stirring. A similar treatment of the reaction mixture gave 32 g (67%) of **4**, mp 90—91 °C.

*Reaction of **4** with Butyllithium.* A typical procedure is as follows.

Butyllithium (3.0 mmol) in hexane (2 ml) was added to a solution of **4** (0.425 g, 0.83 mmol) in THF (15 ml) at —78 °C, and the mixture was stirred for 15 min. After addition of methyl iodide (1 ml), the reaction mixture was subjected to DCC (SiO_2, CCl_4) to give methyl diphenylphosphinodithioate (0.36 g, 85%) and bis(butylthio)methane (0.16 g, 99%); NMR (CCl_4): δ 0.91 (t, $J_{HH}=6$ Hz, 6H, 2Me), 1.53 (m, 8H, $4CH_2$), 2.63 (t, $J_{HH}=7$ Hz, 4H, $2SCH_2$), and 3.68 (s, 2H, S–CH_2–S).

*One-Pot Synthesis of 1,1-Bis(phenylthio)ethane from **4**.* To a solution of **4** (1.14 g, 2.2 mmol) in THF (20 ml) was added phenyllithium (10 mmol) in ether (10 ml) at −78 °C and the mixture was stirred at this temperature for 30 min. After addition of methyl iodide (0.7 ml, 10 mmol) at 0 °C, the mixture was stirred for 20 min and subjected to DCC (SiO_2, CCl_4) to give 1,1-bis(phenylthio)ethane (0.21 g, 41%); NMR (CCl_4): δ 1.68 (d, $J=7$ Hz, 3H, $CHC\underline{H}_3$), 4.62 (q, $J=7$ Hz, 1H, $C\underline{H}Me$), and 7.20—7.60 (m, 10$\underline{H}$, 2Ph), and methyl phenyl sulfide (50 mg).

Reactions of Phenylsodium. *1) With Methyl Diphenylphosphinoditioate*: Phenylsodium (8 mmol) in THF (3 ml) was added to a solution of the ester (0.54 g, 2.0 mmol) in THF (15 ml) and the mixture was stirred at room temperature for 1 h. After addition of methanol, the reaction mixture was evaporated and analyzed by GLC. The yield of methyl phenyl sulfide was 67%.

2) With Phenyl Diphenylphosphinoditioate: Phenylsodium (8 mmol) in THF (3 ml) was added to a solution of the ester (0.49 g, 1.5 mmol) in THF (15 ml) and the mixture was stirred at room temperature for 1 h. After addition of methanol, diphenyl sulfide (0.23 g, 82%) was isolated from the reaction mixture by DCC (SiO_2, $CHCl_3$, and then SiO_2, CCl_4).

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