BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 2559—2562 (1973)

Reactions of Diphenylphosphinothioyl Isothiocyanate and Related Compounds with Some Nucleophiles and Carbodiimides

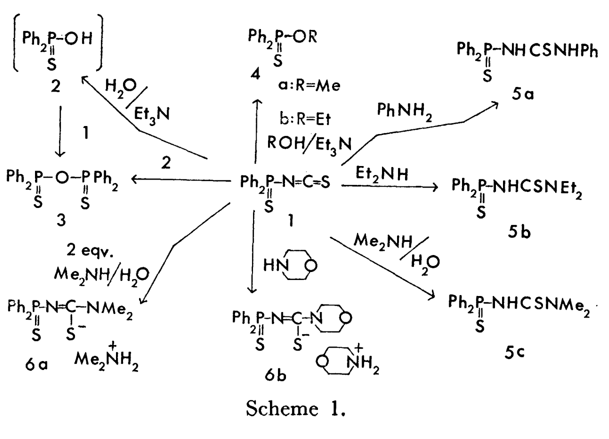
Iwao Ojima,* Kin-ya Akiba, and Naoki Inamoto
Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Tokyo 113

(Received March 23, 1973)

Diphenylphosphinothioyl isothiocyanate (**1**) reacted with alcohols, water and diphenylphosphinothioic acid to give the esters and anhydride of diphenylphosphinothioic acid by substitution reaction on the phosphorus atom, but reacted with amines by addition to the isothiocyanate group to afford diphenylphosphinothioylthioureas or their ammonium salts. Diphenylphosphine and *p*-toluenethiol, however, did not react with **1**. On the contrary, diphenylphosphinothioyl isocyanate underwent only addition reaction with water, amine and thiol. Isothiocyanate (**1**) and *p*-toluenesulfonyl isothiocyanate were found to undergo 1,2-cycloaddition reaction with carbodiimides across the C=S bond to produce 1,3-thiazetidine derivatives.

Diphenylphosphinothioyl isothiocyanate (**1**) is an ambident substrate and has two reaction sites on phosphorus and carbon atoms.

This paper describes the reaction sites of **1** in the reactions with some nucleophiles and carbodiimides. Nucleophiles used were water, alcohols diphenylphosphinothioic acid (**2**), amines, diphenylphosphine and *p*-toluenethiol. Reactions of **1** with **2**[1)] and diethylamine[2)] have been reported. The results of these reactions are summarized in Scheme 1.



Scheme 1.

---

* Present address: Sagami Chemical Research Center, Nishi-onuma, Sagamihara, Kanagawa 229.

1) I. Ojima, K. Akiba, and N. Inamoto, This Bulletin, **42**, 2975 (1969).

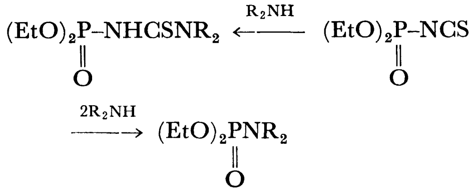
2) I. Ojima, T. Onishi, T. Iwamoto, N. Inamoto, and K. Tamaru, *ibid.*, **44**, 2150 (1971).

It is remarkable that nucleophiles, the center of which is oxygen, attack selectively the phosphorus atom of **1** in the presence of triethylamine. This is attributable to formation of strong P–O bond in the substitution reaction.

The amines added to the carbon atom of the isothiocyanate group to give diphenylphosphinothioylthioureas (**5**) in quantitative yields, whereas diphenylamine did not react with **1** even when reaction temperature was raised up to 120 °C, because of its low nucleophilicity. Thioureas (**5**) can act as bidentate ligands.[2)]

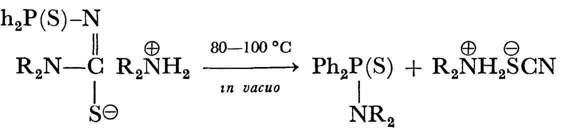
The reaction with 40% aqueous dimethylamine shows that the addition reaction with the amine predominates over the substitution reaction with water.

Attack of amines on the phosphorus atom has been reported in the case of diethoxyphosphoryl isothiocyanate.[3)]



$$(EtO)_2\underset{\substack{\|\\O}}{P}\text{-NHCSNR}_2 \xleftarrow{R_2NH} (EtO)_2\underset{\substack{\|\\O}}{P}\text{-NCS} \xrightarrow{2R_2NH} (EtO)_2\underset{\substack{\|\\O}}{P}NR_2$$

In the case of **1**, however, the reactions with two equivalents of dimethylamine or morpholine provided ammonium salts (**6**), no substitution being observed under the present reaction conditions, though a formation of P–N bond by decomposition of **6** is possible.[4)]

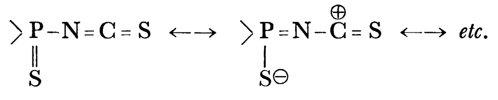


$$\underset{\substack{|\\S^{\ominus}}}{\overset{\substack{Ph_2P(S)\text{-}N\\ \|}}{R_2N\text{—}C}}\ \overset{\oplus}{R_2NH_2} \xrightarrow[\mathit{in\ vacuo}]{80\text{—}100\,^{\circ}C} \underset{\substack{|\\NR_2}}{Ph_2P(S)} + R_2\overset{\oplus}{N}H_2\overset{\ominus}{S}CN$$

6

It is curious that diphenylphosphine and *p*-toluenethiol, strong nucleophiles, react not with **1** but with ordinary isothiocyanates.[1,5)]

The IR spectrum of **1** displays a strong band at 1960 cm^{-1} (–N=C=S). The value is considerably low as compared with that of ordinary isothiocyanates (2020—2100 cm^{-1}). This phenomenon would be interpreted by a large contribution of a canonical structure (**1′**).

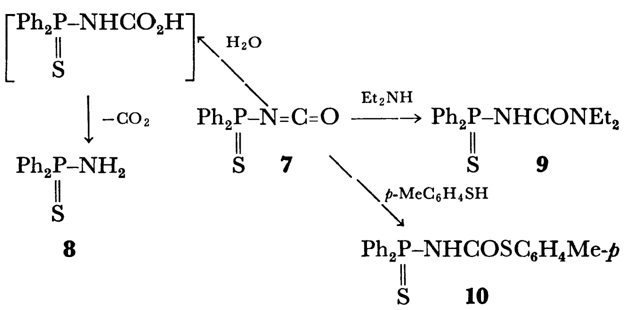


$$\rangle\underset{\substack{\|\\S}}{P}\text{-N=C=S} \longleftrightarrow \rangle P\text{=N-}\underset{\substack{|\\S^{\ominus}}}{\overset{\oplus}{C}}\text{=S} \longleftrightarrow \mathit{etc.}$$

1 **1′**

The large contribution of **1′** increases the reactivity of the carbon atom of **1** toward nucleophiles, and also the hardness[6)] of the carbon atom. The reaction with soft bases, diphenylphosphine and *p*-toluenethiol, may therefore become difficult.

In contrast with the reactions of **1**, diphenylphosphinothioyl isocyanate (**7**) reacted with water and diethylamine to give aminodiphenylphosphine sulfide (**8**) and 1,1-diethyl-3-diphenylphosphinothioylurea (**9**), respectively, no nucleophilic attack on the phosphorus atom being observed. Addition of *p*-toluenethiol to **7** produced a monothiocarbamate (**10**). This is attributable to a higher reactivity of the isocyanate group.

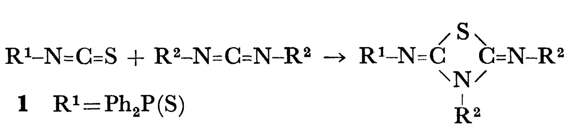


$$\underset{\mathbf{7}}{\underset{\substack{\|\\S}}{Ph_2P}\text{-N=C=O}} \xrightarrow{H_2O} \left[\underset{\substack{\|\\S}}{Ph_2P}\text{-NHCO}_2H\right] \xrightarrow{-CO_2} \underset{\mathbf{8}}{\underset{\substack{\|\\S}}{Ph_2P}\text{-NH}_2}$$

$$\mathbf{7} \xrightarrow{Et_2NH} \underset{\mathbf{9}}{\underset{\substack{\|\\S}}{Ph_2P}\text{-NHCONEt}_2} \qquad \mathbf{7} \xrightarrow{p\text{-}MeC_6H_4SH} \underset{\mathbf{10}}{\underset{\substack{\|\\S}}{Ph_2P}\text{-NHCOSC}_6H_4Me\text{-}p}$$

If the contribution of **1′** is large, **1** should undergo 1,4-cycloaddition like thioacyl isothiocyanate.[7)] Reactions of **1** with carbodiimides were performed from this standpoint.[8)]

When an equimolar mixture of **1** and dicyclohexylcarbodiimide was heated, the adduct (**11a**) was obtained in a nearly quantitative yield. The IR spectrum showed a very strong band at 1640 cm^{-1} (C=N), and the UV spectrum displayed absorption maxima at 223 (log ε 4.81) and 260 nm (sh., log ε 4.23).



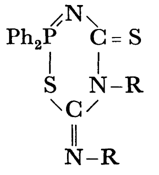
$R^1\text{-N=C=S} + R^2\text{-N=C=N-}R^2 \rightarrow$ **11**

1 $R^1 = Ph_2P(S)$

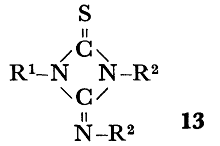
14 $R^1 = p\text{-}MeC_6H_4SO_2$

11

a : $R^1 = Ph_2P(S)$, $R^2 = c\text{-}C_6H_{11}$
b : $R^1 = Ph_2P(S)$, $R^2 = i\text{-}Pr$
c : $R^1 = p\text{-}MeC_6H_4SO_2$, $R^2 = c\text{-}C_6H_{11}$



12



13

a : $R^1 = Ph_2P(S)$, $R^2 = c\text{-}C_6H_{11}$
b : $R^1 = p\text{-}NO_2C_6H_4$, $R^2 = c\text{-}C_6H_{11}$
c : $R^1 = p\text{-}MeC_6H_4SO_2$, $R^2 = o\text{-}MeC_6H_4$
d : $R^1 = p\text{-}NO_2C_6H_4$, $R^2 = i\text{-}Pr$
e : $R^1 = MeSO_2$, $R^2 = Ph$

The spectral data confirm that **11a** is a new 1,3-thiazetidine derivative, and not a 1,3-diazetidine derivative (**13a**) or a 1,4-cycloadduct (**12**), because the strong absorption band at 223 nm is too short to be assigned to the π–π* transition of a C=S bond[9)] and no absorption band caused by *n*–π* transition could be detected. Furthermore, **11a** did not catalyse the

---

3) A. Schmidpeter and K. Stoll, *Angew. Chem.*, **79**, 242 (1967).

4) A. Schmidpeter and H. Groeger, *Chem. Ber.*, **100**, 3052 (1967).

5) For example, K. Issleib and G. Harzfeld, *Chem. Ber.*, **97**, 3430 (1964).

6) R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, **89**, 1827 (1967).

7) J. Goerdeler and H. Schenk, *Chem. Ber.*, **98**, 3831 (1965).

8) Preliminary report: I. Ojima and N. Inamoto, *Chem. Commun.*, **1970**, 1629.

9) K. Hirayama, "Handbook of Ultraviolet and Visible Spectra of Organic Compounds," Plenum Press, New York, (1967), p. 87.

decomposition of sodium azide by iodine (Feigl test),[10] indicating the absence of a C=S group.

The reaction of **1** with diisopropylcarbodiimide gave a similar adduct (**11b**).

Ulrich and Sayigh[11] reported that the 1,2-cycloaddition of carbodiimide and isothiocyanate having electron-withdrawing group always gives 1,3-diazetidine derivative (**13**). *p*-Toluenesulfonyl isothiocyanate (**14**) ($\nu_{N=C=S}$ 1890 cm^{-1}) was allowed to react with dicyclohexylcarbodiimide under conditions similar to those used by Ulrich *et al.* Adduct (**11c**), which also gave a negative Feigl test, was obtained in a nearly quantitative yield.

Comparison of the C=N stretching vibrations (1620—1640 cm^{-1}) of 1,3-thiazetidines (**11**) with those of **13** reported by Ulrich and Sayigh[11] also suggests that the adducts (**13**) are 1,3-thiazetidines (see Table 1). Recent work by Ulrich *et al.*[12] supports our results.[8]

TABLE 1. C=N STRETCHING VIBRATIONS OF 1,3-THIAZETIDINES (**11**) AND "1,3-DIAZETIDINES (**13**)" REPORTED BY ULRICH *et al.*[11]

	R^1	R^2	$\nu_{C=N}$ (cm^{-1})
11a	$Ph_2P(S)$	*c*-C_6H_{11}	1640
11b	$Ph_2P(S)$	*i*-Pr	1630
11c	*p*-$MeC_6H_4SO_2$	*c*-C_6H_{11}	1620
"**13b**"	*p*-$NO_2C_6H_4$	*c*-C_6H_{11}	1655
"**13c**"	*p*-$MeC_6H_4SO_2$	*o*-MeC_6H_4	1600
"**13d**"	*p*-$NO_2C_6H_4$	*i*-Pr	1655
"**13e**"	$MeSO_2$	Ph	1615

These results show that the cycloaddition of the isothiocyanates having electron-withdrawing group and carbodiimides occurs across the C=S bond of the isothiocyanate to give 1,3-thiazetidines, and not across the C=N bond to give 1,3-diazetidines.

Experimental

All melting and boiling points are uncorrected. IR, UV, NMR and Mass spectra were measured with Hitachi Model EPI-G2, Hitachi Model EPS-3, JEOL-C-60H, and Hitachi Model RMU-6D spectrometers, respectively.

Materials. Diphenylphosphinothioyl isothiocyanate (**1**) was prepared from diphenylphosphinothioyl chloride and ammonium thiocyanate, mp 48—49 °C (lit,[4] 48 °C). *p*-Toluenesulfonyl isothiocyanate (**14**) was prepared from potassium *N*-(*p*-toluenesulfonyl)dithiocarbamate[13] and thionyl chloride, bp 114—118 °C/0.5 mmHg (lit,[14] 115—125 °C/0.65 mmHg).

*Preparation of Diphenylphosphinothioyl Isocyanate (**7**).* A mixture of potassium cyanate (10.0 g, 0.12 mol) and diphenylphosphinothioyl chloride (25.3 g, 0.10 mol) in 400 ml of acetonitrile was stirred at room temperature for 24 hr, and filtered. The filtrate was evaporated and the residue was treated with petroleum ether to give colorless crystals of **7** in an almost quantitative yield. Mp 42—43 °C, IR (Nujol): 2240 cm^{-1} (-N=C=O).

Found: C, 59.97; H, 4.08; N, 5.33; S, 12.62%. Calcd for $C_{13}H_{10}NOPS$: C, 60.23; H, 3.89; N, 5.40; S, 12.37%.

*Reaction of **1** with Water.* A solution of **1** (0.5 g, 1.8 mmol) and water (1 g, 55 mmol) in 100 ml of acetone was heated in the presence of a few drops of triethylamine under reflux for 5 hr. After the solvent was removed, the residue was recrystallized from benzene to give diphenylphosphinothioic anhydride (**3**) in a quantitative yield, mp 197—198 °C (lit,[15] 197—198 °C).

*Reaction of **1** with Ethanol and Methanol.* A solution of **1** (0.75 g, 2.6 mmol) in 100 ml of ethanol was heated under reflux in the presence of a few drops of triethylamine for 2 hr. After the solvent was removed, the residue was dissolved in petroleum ether and recrystallized to give ethyl diphenylphosphinothioate (**4b**) in a quantitative yield, mp 38—39 °C (lit,[16] 42—43 °C). The IR spectrum is identical with that of an authentic sample.

In a similar reaction with methanol, **4a** was obtained in a quantitative yield, mp 83—85 °C (lit,[16] 84.5—85.5 °C).

*Reaction of **1** with Aniline.* Aniline (0.53 g, 5.7 mmol) and **1** (1.5 g, 5.6 mmol) were mixed without solvent and an exothermic reaction occurred. The mixture was then heated at 80—90 °C for a few minutes. White crystals thus obtained were recrystallized from dichloromethane or ethanol to give 3-diphenylphosphinothioyl-1-phenylthiourea (**5a**) in a nearly quantitative yield, mp 143—145 °C.

Found: C, 61.85; H, 4.62; N, 7.38; S, 16.90%. Calcd for $C_{19}H_{17}N_2PS_2$: C, 61.96; H, 4.62; N, 7.62; S, 17.39%.

*Reaction of **1** with Aqueous Dimethylamine.* 40% aqueous dimethylamine (1.0 g, 8.9 mmol) and **1** (3.0 g, 10.9 mmol) were mixed. After an exothermic reaction subsided, the solvent was removed under reduced pressure. The residue was washed with ether to give 1,1-dimethyl-3-diphenylphosphinothioylthiourea (**5c**) in an almost quantitative yield, mp 94—96 °C (lit,[4] 95.5—96 °C).

Use of two equivalents of 40% aqueous dimethylamine gave the corresponding dimethylammonium salt (**6a**).[2]

*Reaction of **1** with Morpholine.* A mixture of morpholine (1.8 g, 20.7 mmol) and **1** (2.8 g, 10.1 mmol) in 50 ml of ether was stirred at room temperature. An exothermic reaction occurred to give ammonium salt (**6b**) in a quantitative yield, mp 135—138 °C (from ethanol).

Found: C, 56.06; H, 6.03; N, 9.41; S, 14.51%. Calcd for $C_{21}H_{28}N_3O_2PS_2$: C, 56.12; H, 6.24; N, 9.35; S, 14.25%.

Equimolar mixture of morpholine and **1** also produced **6b**. No free thiourea derivative could be obtained.

*Reaction of **7** with Water.* A solution of **7** (0.50 g, 1.93 mmol) and 2 ml of water in 50 ml of acetone was heated under reflux for 2 hr. The mixture was allowed to stand overnight at room temperature to afford aminodiphenylphosphine sulfide (**8**) in an almost quantitative yield, mp 99—101 °C (lit,[17] 102—104 °C).

---

[10] F. Feigl, "Spot Tests in Organic Analysis," Fifth Eng. Ed., Elsevier Pub. Co., Amsterdam, (1956), pp. 228—233.

[11] H. Ulrich and A. A. R. Sayigh, *Angew. Chem.*, **77**, 545 (1965); H. Ulrich, "Cycloaddition Reactions of Heterocumulenes," Academic Press, New York, (1967), pp. 233—235.

[12] H. Ulrich, B. Tucker, and A. A. R. Sayigh, *J. Amer. Chem. Soc.*, **94**, 3484 (1972).

[13] K. Hartke, *Arch. Pharm.*, **299**, 174 (1966); *Chem. Abstr.*, **64**, 15783e (1966).

[14] Farbenfabriken Bayer A. -G. (by K. Dickore and E. Kuehle), Ger. 1,183,492, Dec. 17, 1964; *Chem. Abstr.*, **62**, 7691c (1965).

[15] T. R. Hopkins and P. W. Vogel, *J. Amer. Chem. Soc.*, **78**, 4447 (1956).

[16] T. A. Mastryukova, T. A. Melent'eva, and M. I. Kabachnik, *Zh. Obshch. Khim.*, **35**, 1197 (1965); *Chem. Abstr.*, **63**, 11605f (1965).

[17] I. N. Zhmurova, I. Yu. Voitsekhovskaya, and A. V. Kirsanov, *Zh. Obshch. Khim.*, **29**, 2083 (1959); *Chem. Abstr.*, **54**, 8681h (1960).

*Reaction of **7** with Diethylamine.* Diethylamine (0.40 g, 5.5 mmol) was added to **7** (1.1 g, 4.25 mmol) without solvent and heated at 50—60 °C for 5 min. Crystals thus produced were recrystallized from cyclohexane to give 1,1-diethyl-3-diphenylphosphinothioylurea (**9**) in a nearly quantitative yield, mp 128—130 °C. IR (Nujol): 3150 (NH) and 1625 cm^{-1} (C=O).

Found: C, 61.41; H, 6.15; N, 8.39; S, 9.51%. Calcd for $C_{17}H_{21}N_2OPS$: C, 61.44; H, 6.33; N, 8.44; S, 9.64%.

*Reaction of **7** with* p*-Toluenethiol.* A mixture of **7** (0.5 g, 1.9 mmol) and *p*-toluenethiol (0.25 g, 2.0 mmol) was heated at 50 °C for one hour without solvent. The resulting solid was recrystallized from benzene-petroleum ether to give *S*-*p*-tolyl *N*-(diphenylphosphinothioyl)monothiocarbamate (**10**) in a nearly quantitative yield, mp 94—96 °C (dec); IR (Nujol): 3350 sh, 3180 (NH), and 1695 cm^{-1} (C=O).

Found: C, 62.86; H, 4.69; N, 3.51; S, 16.93%. Calcd for $C_{20}H_{18}NOPS_2$: C, 62.64; H, 4.73; N, 3.65; S, 16.72%.

*Reaction of **1** with Dicyclohexylcarbodiimide.* A solution of **1** (0.55 g, 2.0 mmol) and carbodiimide (0.414 g, 2.01 mmol) in 100 ml of dry cyclohexane was heated under reflux for 30 min. After the solvent had been removed, the residue was recrystallized from petroleum ether to give the adduct (**11a**) in a quantitative yield, mp 120—122 °C. IR (Nujol): 1640 cm^{-1} (C=N); $\lambda_{\max}^{c\text{-}C_6H_{12}}$: 223 (log ε 4.81) and 260 sh nm (log ε 4.23); MS: *m/e* 481 (M$^+$, 9%) and 217 (Ph_2PS^+, 100).

Found: C, 64.52; H, 6.41; N, 8.05; S, 13.61%. Calcd for $C_{26}H_{32}N_3PS_2$: C, 64.86; H, 6.65; N, 8.73; S, 13.31%.

When a mixture of **1** and the carbodiimide was heated at 90—95 °C for a few minutes, the adduct (**11a**) was also obtained in a quantitative yield.

*Reaction of **1** with Diisopropylcarbodiimide.* A mixture of **1** (0.577 g, 2.02 mmol) and carbodiimide (0.279 g, 2.21 mmol) was heated without solvent for 2 hr. An oily product was obtained in a nearly quantitative yield. Since the distillation resulted in decomposition, column chromatography on silica gel using petroleum ether was performed to obtain colorless oil (**11b**). IR (neat): 1630 cm^{-1} (C=N).

Found: C, 59.65; H, 5.98; N, 10.63; S, 16.12%. Calcd for $C_{20}H_{24}N_3PS_2$: C, 59.83; H, 6.02; N, 10.46; S, 15.97%.

Reaction of p*-Toluenesulfonyl Isothiocyanate (**14**) with Dicyclohexylcarbodiimide.* A mixture of **14** (1.0 g, 4.72 mmol) and carbodiimide (1.0 g, 4.86 mmol) was heated at 80 °C for 30 min. The resulting solid was recrystallized from petroleum ether to give the adduct (**11c**) in a quantitative yield, mp 144—146 °C. IR (Nujol): 1620 cm^{-1} (C=N); $\lambda_{\max}^{c\text{-}C_6H_{12}}$: 229 sh (log ε 4.43), 235 sh (4.50), 248 (4.55), and 262 sh nm (4.46).