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The reaction of benzothiazolyl substituted α-phosphorylmethyl sulfoxides with several amines

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Abstract

We have examined the reactivities of α-phosphorylmethyl benzothiazolyl sulfoxides in the thermolyses and in the presence of several amines, such as aniline, benzylamine, piperidine, morpholine, and pyrrolidine. Thermolyses of the derivatives in the presence of 2,3-dimethyl-1,3-butadiene afforded 2-phosphoryl substituted 4,5-dimethyl-3,6-dihydro-2*H*-thiopyran *S*-oxide. In the reaction with amines, the complex product mixture, which contains α-phosphorylmethyl benzothiazolyl sulfides (**2** and **5**), α-phosphorylmethyl disulfides (**15** and **16**), and 2-amino substituted benzothiazole **14** was found to be formed besides the target phosphinecarbothioamides. Several mechanistic studies were performed to elucidate the formation mechanism, particularly for deoxygenated products from the starting sulfoxides, i.e., **2** and **5** from **3** and **6**, respectively.

Keywords: α-Phosphorylmethyl sulfoxide; Benzothiazole; Phosphinecarbothioamide; Hetero Diels–Alder reaction

1. Introduction

Previously, we reported that the thermolytic reaction of heteroaryl-substituted β-ketosulfoxides in the presence or absence of bases afforded the corresponding thioaldehyde or sulfines,[1] depending on the substituted heteroaryl groups. In the thermolyses of the sulfoxides bearing benzothiazolyl group, thioaldehydes are considered to be formed via the rearranged sulfenate ester intermediate.[1a] In contrast, 5-(1-phenyl)-1,2,3,4-tetrazolyl derivatives revealed to afford sulfines via the elimination of tetrazole by the E2 type elimination mechanisms.[1b]

Recently, we have extended the reaction of heteroaryl-substituted α-phosphorylmethyl sulfoxides under similar conditions, and reported novel phosphinecarbothioamide formations in the reaction of tetrazolyl α-phosphorylmethyl sulfoxides with several amines.[2,3]

In order to obtain the scope and limitations of the reactions, we further prepared several substituted α-phosphorylmethyl sulfoxides bearing benzothiazole group and studied their reactions with several amines. Herein, we report the results of the thermolysis in the presence of the diene and their reactions with amines with mechanistic studies.

2. Results and discussion

2.1. Thermolyses of α-phosphorylmethyl sulfoxides *3* and *6* in the presence of 1,3-dimethyl-2,3-butadiene

Benzothiazolyl substituted α-(diphenylphosphoryl)- and α-(diethoxyphosphoryl)methyl sulfoxides (**3** and **6**) were prepared following the procedure, which was reported previously.[3] The thermolysis of **3** in the presence of 2,3-dimethyl-1,3-butadiene was studied in 1,4-dioxane at several temperatures. The results are summarized in Table 1. The cycloadduct **8** or **10** was expectedly observed to be formed in moderate to high yields, via the hetero Diels–Alder reaction of diene with sulfine formed initially as similarly in the case of α-phosphorylmethyl tetrazolyl sulfoxides.[3] In these cases compound **9** or **11** were also formed by elimination of H_2O from **8** or **10**.[3]

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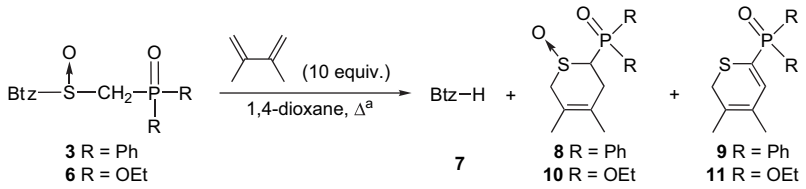
Table 1
Thermolyses of **3** and **6** in the presence of 2,3-dimethyl-1,3-butadiene



Entry	Sulfoxide	Conditions	Yields[b] (%)		
			7	**8/10**	**9/11**
1	**3**	140 °C, 5 h	36	61[c]	22[e]
2	**3**	140 °C, 2 h, Et_{3N} (1.5 equiv)	53	0	96[e]
3	**3**	160 °C, 1 h	39	0	68[e]
4	**6**	160 °C, 8 h	0	29[d]	57[f]

[a] In sealed tube.
[b] Isolated yields.
[c] Product is **8**.
[d] Product is **10**.
[e] Product is **9**.
[f] Product is **11**.

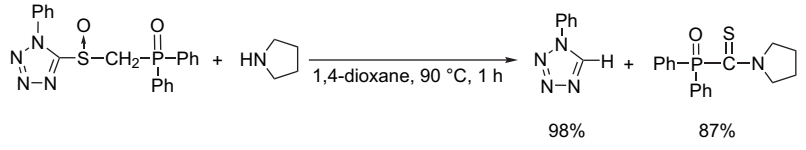
When the reaction of **3** was carried out at 140 °C for 5 h, the obtained products were 2-(diphenyl)phosphoryl-3,6-dihydro-4,5-dimethyl-2*H*-thiopyran *S*-oxide (**8**), 6-(diphenyl)phosphoryl-3,4-dimethyl-2*H*-thiopyran (**9**), and benzothiazole (**7**), in 36, 61, and 22% yields, respectively (entry 1). At higher temperature, 160 °C for 1 h, **8** disappeared and **9** was formed in 68% (entry 3). When the thermolysis was carried out in the presence of triethylamine at 140 °C, **9** was obtained quantitatively with 53% yield of **7** (entry 2).

In the thermolysis of **6** for 8 h at 160 °C, **10** and **11** were obtained in 29 and 57% yields, respectively (entry 4).

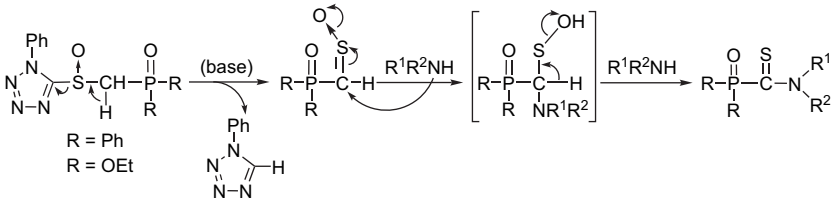
2.2. Reactions of benzothiazolyl sulfoxides *6* and *11* bearing α-(diphenylphosphoryl)- and α-(diethoxyphosphoryl)methyl groups with several amines

Since it is reported that the sulfines react with amines to afford the sulfinamide derivatives,[4] we studied the reaction of 5-(1-phenyl)-1*H*-tetrazolyl sulfoxide with several amines. In all cases, the expected corresponding sulfinamides were not obtained, but unexpected formation of phosphinecarbothioamide derivatives was seen as shown in Scheme 1 (the scheme is depicted using pyrrolidine as a base for the clarity).[2] The mechanism was considered as shown in Scheme 2.

In order to examine the effect of heteroaryl groups, we further extended the study of the reaction of **3** or **6** with amines under similar conditions. Contrary to the results in α-(dimethylphosphoryl)methyl 5-(1-phenyl)-1*H*-tetrazolyl sulfoxide (cf. Scheme 1),[3] the reactions afforded the complex product mixtures and their distributions were revealed to change greatly depending on the several amines used as summarized in Table 2. The great difference compared with the results in the case of α-phosphorylmethyl 5-(1-phenyl)-1*H*-tetrazolyl sulfoxides is as follows: (1) the formation of the unexpected deoxygenated compounds **2** and **5**, which were formally formed by the reduction of **3** and **6**, respectively,

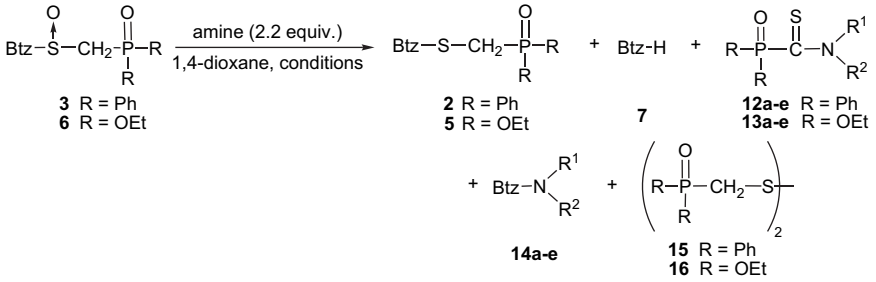


Scheme 1. The reaction of α-(diphenylphosphoryl)methyl tetrazolyl sulfoxide with pyrrolidine.



Scheme 2. Plausible mechanism for the formation of phosphinecarbothioamides.

Table 2
Reaction of **3** and **6** with several amines



Entry	Sulfoxide	Amine	Conditions	Yields[a] (%)				
				2/5	**7**	**12/13**	**14**	**15/16**
1	**3**	a, Ph–NH_2	90 °C, 64 h	11[b]	40	12 (**12a**)	15 (**14a**)	Trace[d]
2	**3**	b, 	90 °C, 3.5 h	42[b]	0	20 (**12b**)	51 (**14b**)	Trace[d]
3	**3**	c, 	90 °C, 1 h	20[b]	0	12 (**12c**)	67 (**14c**)	Trace[d]
4	**3**	d, 	90 °C, 0.75 h	28[b]	0	19 (**12d**)	72 (**14d**)	32[d]
5	**3**	e, 	90 °C, 0.5 h	24[b]	Trace[c]	6 (**12e**)	81 (**14e**)	Trace[d]
6	**6**	a, Ph–NH_2	100 °C, 6 h	Trace	0	Trace (**13a**)	76 (**14a**)	51[e]
7	**6**	b, 	100 °C, 3 h	18[c]	0	13 (**13b**)	39 (**14b**)	26[e]
8	**6**	c, 	100 °C, 0.25 h	27[c]	0	24 (**13c**)	35 (**14c**)	15[e]
9	**6**	d, 	100 °C, 1 h	20[c]	0	24 (**13d**)	53 (**14d**)	15[e]
10	**6**	e, 	100 °C, 0.25 h	26c	0	26 (**13e**)	27 (**14e**)	29[e]

[a] Isolated yields.
[b] Product is **2**.
[c] Product is **5**.
[d] Product is **15**.
[e] Product is **16**.

(2) the yield of **7** is almost 0%, (3) the formations of 2-amino substituted benzothiazole **14** were observed, (4) low yields of **12** and **13**, and (5) the formation of disulfides **15** and **16** were observed.

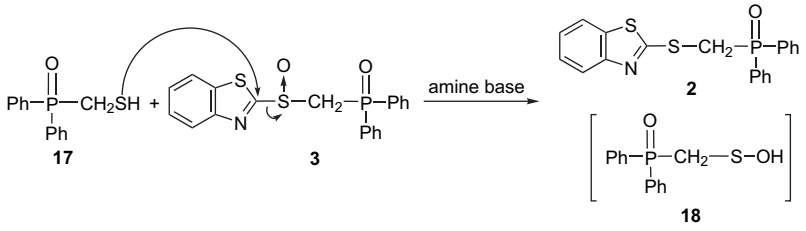
In the reactions of **3** the deoxygenated product **2** was formed in 11–42% yields together with the formation of phosphoryl substituted disulfide **15**. In addition, the yields for the corresponding phosphinecarbothioamide derivatives **12a–e** were reduced greatly, and particularly, benzothiazole (**7**) was not formed at all except entries 1 and 5.

The reactions of **6** with the same amines proceeded slowly compared with **3**. Therefore, the reactions of **6** were carried out at 100 °C. Similar results were obtained, however, the yields of the corresponding α-phosphorylmethyl derivatives **16** became higher compared with the case of **3**. This result seems to suggest that **16** is more stable than **15** under same conditions. The effect of the phosphoryl substituents and used amines on the yields and distribution of the products suggests that the amine used played crucial role, probably in the hydrogen abstraction and/or nucleophilic step in the reaction course, as mentioned later.

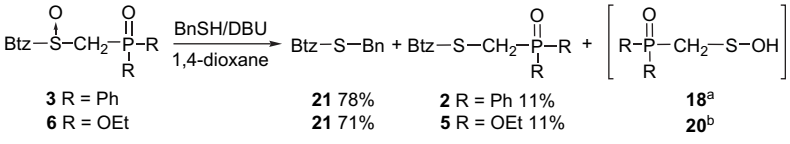
2.3. Mechanistic studies on the reaction of benzothiazolyl α-(phosphoryl)methyl sulfoxide with amines

As shown in Scheme 1, the reaction of α-(diphenylphosphoryl)methyl 5-(1-phenyl)-1*H*-tetrazolyl sulfoxide proceeded cleanly to give the corresponding phosphinecarbothioamide derivatives **12** and tetrazole in moderate and good yields, respectively. In the reaction of **3** and **6** under the same conditions, similar reaction pathway will be also conceivable. However, in the reaction pathway the formation of deoxygenated products **2** and **5**, the formation of 2-amino substituted benzothiazole **14** and the disulfides **15** and **16**, and the absence or very low yield of benzothiazole (**7**) could not be rationalized. Particularly, the formation of **14** in relatively high yield seems to suggest that the different mechanistic pathways, namely, direct displacement reaction of **3** or **6** with amines to form **14** are involved, as shown later in Scheme 8.

In order to elucidate the possible mechanism, we carried out the following model or controlled reactions. First, the formation of the reduction products **2** and **5** is unexpected and not conceivable easily, because no apparent redox conditions seem to exist



Scheme 3. Possible route to **2** by nucleophilic reactions of **3** with **17**.



[a]disulfide **15** was obtained in 17% yielded instead of sulfenic acid **18**
[b]disulfide **16** was obtained in 30% yielded instead of sulfenic acid **20**

Scheme 4. The reaction of **3** or **6** with benzylthiol in the presence of DBU.

in the reaction system. Probably, one of the possible routes to the deoxygenated product **2** will be via the nucleophilic displacement reaction of **3** with diphenylphosphorylmethyl thiol (**17**), in the presence of bases, producing the corresponding sulfenic acid **18**, as depicted in Scheme 3. Diethoxyphosphoryl substituted derivative **5** proceeded also in the same way, to produce the deoxygenated product **5** and sulfenic acid **20**.

Therefore, the controlled reactions of the same compound **3** or **6** with benzylthiol in the presence of DBU were carried out. In both cases, the displacement product benzothiazolyl benzyl sulfide **21** was expectedly formed in high yields together with the disulfides **15** or **16** and others as shown in Scheme 4.

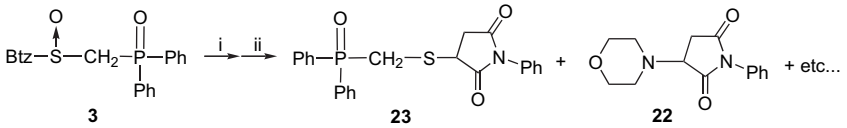
These experiments indicate clearly that the nucleophilic displacement reaction (addition–elimination mechanism) at C-2 position of benzothiazole ring with phosphorylmethyl thiols **17** or **19** is involved.

Further, in order to obtain the clue for the formation of the thiol **17** in the reaction sequence, we carried out the reaction of **3** with morpholine in the presence of *N*-phenylmaleimide as the Michael addition acceptor under the same conditions as shown in Scheme 5.

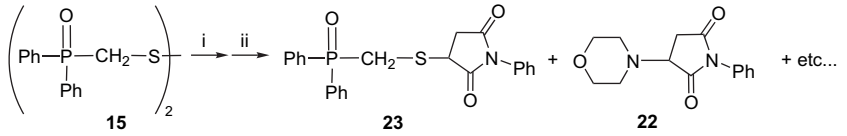
The formation of the thiol **17**-trapped product **23** was observed expectedly, however, the yield was very low, together with the major formation of morpholine Michael adduct **22** and other complex products derived from the further reaction with thiol **17** formed initially.

In order to make sure the formation of thiol **17** (or the corresponding thiolate anion) by the reaction of disulfide **15** with the amines used, **15** was prepared authentically and the reaction with morpholine was carried out in the presence of *N*-phenylmaleimide. The similar product distribution was obtained as in the case of the reaction of **3** under similar conditions as shown in Scheme 6. This result clearly indicated that thiol **17** (or the corresponding thiolate) is formed by the nucleophilic attacking with morpholine toward **15**. Usually, the common disulfide is hard to cleave with amines, however, similar nucleophilic cleavage of the S–S bond by amines was reported in the case of the disulfides bearing electron withdrawing substituents, such as di-*o*-dinitrophenyl disulfide.[5]

Further, in order to study more clearly the behavior of the disulfide in the course of reaction, **15** was subjected to the controlled reaction under several conditions. First, the reaction of

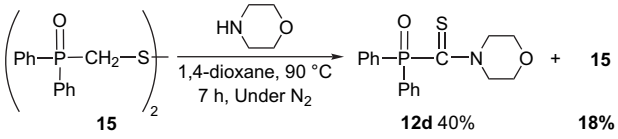


Scheme 5. The reaction of **3** with morpholine in the presence of *N*-phenylmaleimide. (i) Morpholine, 1,4-dioxane, 90 °C, 15 min; (ii) *N*-phenylmaleimide, 7.5 h.



Scheme 6. The reaction of **15** with morpholine in the presence of *N*-phenylmaleimide. (i) Morpholine, 1,4-dioxane, 90 °C, 30 min; (ii) *N*-phenylmaleimide, 1,4-dioxane, 90 °C, 3 h.

15 with benzothiazole in 1,4-dioxane at 90 °C was carried out, however, the formation of the deoxygenated product **2** was not observed even after prolonged reaction time. Therefore, the direct displacement reaction of **15** with benzothiazole seems not to be involved. Second, the reactions of disulfide **15** with morpholine were carried out under several conditions. The results seem to indicate that **12d** was formed directly through disulfide **15**, as shown in Scheme 7. The formations of the corresponding derivatives were reported in the reaction of phenacyl disulfides with morpholine under similar conditions.[6]



Scheme 7. Reaction of **15** with morpholine.

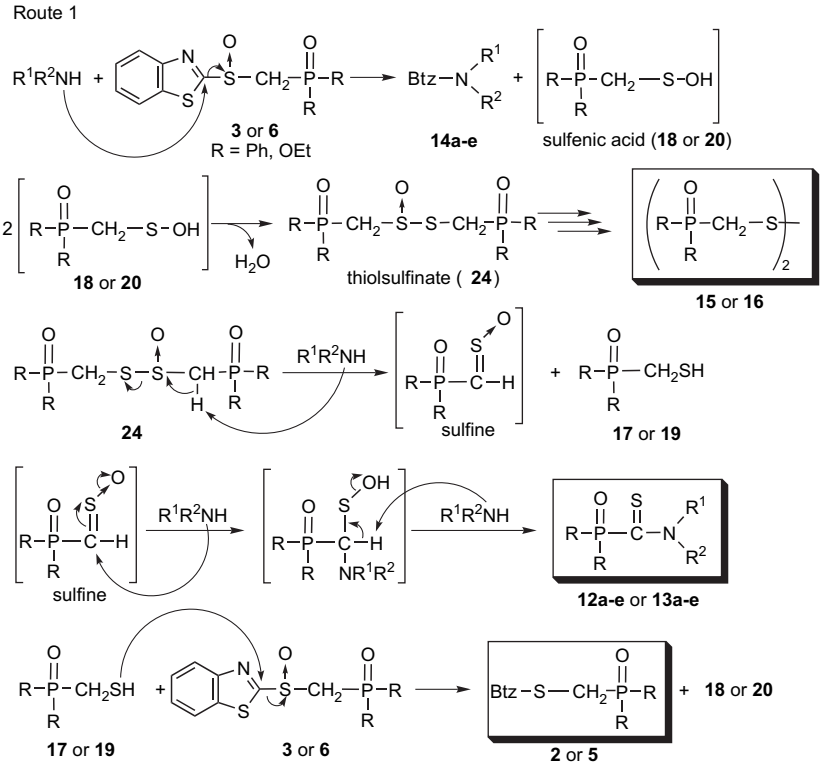
From all the model and controlled experiments, we propose two mechanistic pathways. Namely, the possible mechanism for the formation of anomalous product **12d** or **13d** is as follows: route 1: via the reaction of thiolsulfinate **24** formed initially with amines, and route 2: via the reaction of disulfide **15** or **16** formed initially with amines.

Route 1 is depicted in Scheme 8. First, the displacement reaction of **3** or **6** with amines proceeded to afford **14** and sufenic acid **18** or **21**, which was immediately converted to thiolsulfinate **24** by self-condensation. Successively, the elimination reaction of **24** proceeded to afford the sulfines in the presence of amine base. The addition reaction of the sulfines thus formed with amines led to phosphinecarbothioamide **12** or **13**. Then, the nucleophilic attacking with the eliminated thiol **17** and **19** toward **3** or **6** took place to afford the deoxygenated product **2** or **5** in the presence of amine base, respectively. Meanwhile, the formation of disulfide **15** or **16** occurred consecutively by the cascade reaction of thiolsulfinate **24**. Consequently, this route 1 seems to explain the formation of all the products in the reaction of **3** or **6** with amines.

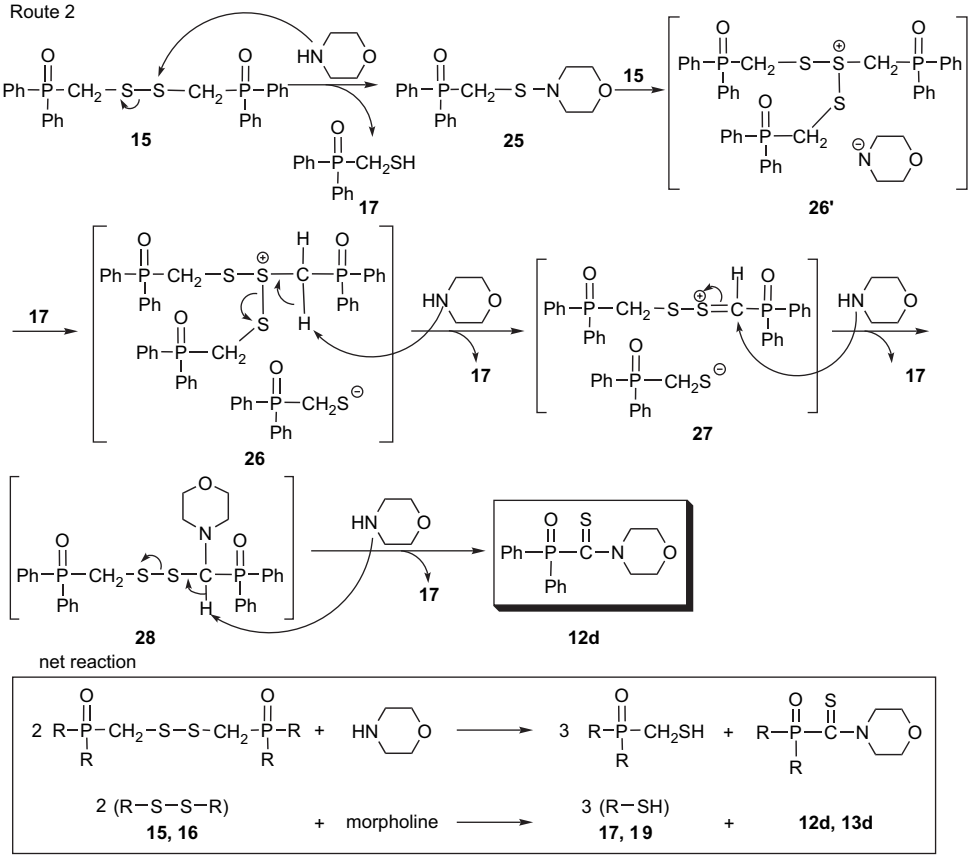
The route 2 to the product **12** or **13** by the reaction of **15** or **16** with amines, respectively, seems also to be involved, as shown in Scheme 9 (the mechanistic pathway is depicted in the case of the reaction **15** with morpholine for clarity).

First, sulfenamide **25** was formed by the nucleophilic cleavage of disulfide **15** with amines as mentioned previously. Successively, sulfonium salt **26′** was formed by sulfenylation of disulfide **15** with sulfenamide. The formation of the similar sulfonium salt intermediate **26** was also reported.[7] Finally, phosphinecarbothioamide **12d** was formed via the sequence of the reaction of **27** to **28** as depicted in Scheme 9. In this route, the deoxygenated product **2** is also formed by the reaction of **3** with the thiol **17**. As a result, this reaction seems to provide the redox system involving reduction of disulfide **15** to thiol **17** and oxidation of disulfide **15** to **12d**. However, whether route 1 or 2 is mainly involving or not is still controversial.

Finally, in order to make clear the formation of thiol **17** or **19** in the course of the reaction, α-(diphenylphosphoryl)-methyl 2-(5-chlorobenzothiazolyl)sulfoxide (**30**) was prepared



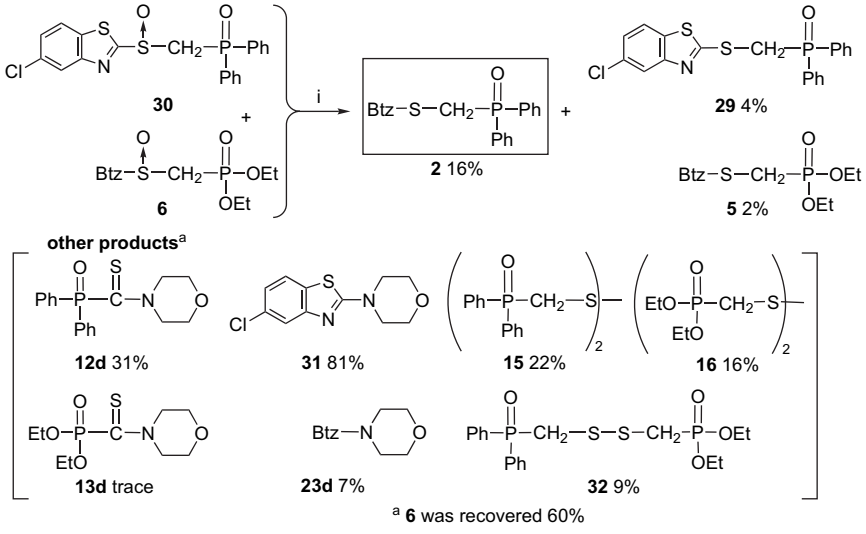
Scheme 8. Routes 1 (possible route to **12a–e** or **13a–e**, **15** or **16**, and **2** or **5**, respectively).



Scheme 9. Route 2 (possible route to **12d**).

and the cross-over reaction between **6** and **30** with morpholine under similar conditions were carried out. The results are summarized in Scheme 10. The formation of the cross-over product **2** and the distribution of other products clearly suggest that the involvement of the route via the reaction of **6** with thiol **17** derived from **30**.

The observation of the difference of the reactivities between **6** and **17** will be explained by the difference of the electronic nature of C-2 carbon. The greater electrophilicity at C-2 carbon of **30** by the electronic effect at 5-chloro substituent accelerated the displacement reaction than that toward **6**, which resulted in the 60% recovery of **6**. It is interesting to note that disulfides **15** and **16** seems to be rather stable and obtained in 22 and 16% yield, respectively, despite the formation of **12d** in 31% yield. These results may indicate that the route 1 (Scheme 8) proceeded more predominantly than route 2 (Scheme 9).



Scheme 10. Cross-over reaction of **30** and **6** with morpholine. (i) Morpholine 5.0 equiv, 1,4-dioxane, rt, 2 days.

3. Conclusion

Several heteroaryl phosphoryl substituted methyl sulfoxides **3** and **6** were prepared, and their thermolysis and their reaction with amines were examined. In the thermolysis, in the presence of 2,3-dimethyl-1,3-butadiene, the hetero Diels–Alder reaction adducts were formed and converted to 3,6-dihydro-thiopyrane derivatives **8–11** as similarly in the case of the heteroaryl β-ketosulfoxides.[1b] In the reaction of tetrazolyl sulfoxide, the formation of phosphinecarbothioamides **12** and **13** was considered to be via sulfine, which was formed initially by the base catalyzed elimination of tetrazole due to the high leaving ability. In the reaction of benzothiazolyl sulfoxides **3** and **6** with amines, the formation of phosphinecarbothioamide derivatives was poor with complex product distribution when compared with tetrazolyl substituted phosphoryl sulfoxides, and the formation of deoxygenated products **2** and **5** was observed. In view of the results of the intensive mechanistic studies, it is suggested that the reaction proceed via thiol **17** or **19**, which was formed in the course of the reaction.

4. Experimental section

4.1. General

All the melting points were uncorrected using micro melting point apparatus. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ using TMS as an internal standard. The elemental analyses were performed at Micro analytical Laboratory of the Department of Material Systems Engineering and Life Science, University of Toyama. All the reactions were monitored with TLC and the products were separated by column chromatography using silica gel 60 and also by preparative layer chromatography using silica gel 60 PF_{254} with UV detection. All the reagents were the highest quality and further purified by distillation or recrystallization. The solvents were further purified by general method.

4.2. General procedure for the preparation of sulfides *2* and *29*

To a stirred solution of diphenylphosphinomethyl tosylate **1** (1.0 equiv) and 2-mercaptobenzothiazole (1.2 equiv) in THF was added K_2CO_3 (3.0 equiv) at rt and stirred for about 2 h. After the starting materials were consumed, THF was evaporated off, residue was dissolved in $CHCl_3$, and then the precipitate was filtered off. The organic layer was washed with H_2O and dried over anhydrous $MgSO_4$. Then, the removal of solvent afforded crude sulfides **2** and **29**, which were purified by flash chromatography.

4.2.1. α-(Diphenylphosphoryl)methyl 2-benzothiazolyl sulfide (*2*)

Yield 81%; mp: 125–126 °C (CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 4.36 (d, J=7.6 Hz, 2H), 7.27–7.31 (m, 1H), 7.39–7.52 (m, 7H), 7.68–7.71 (m, 1H), 7.81–7.86 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 31.0 (d, $^1J_{C-P}$=67.7 Hz), 121.0, 121.4, 124.5, 126.0, 128.6 (d, $^2J_{C-P}$=12.3 Hz), 130.9 (d, $^1J_{C-P}$=103.2 Hz), 131.2 (d, $^3J_{C-P}$=9.9 Hz), 132.3 (d, $^4J_{C-P}$= 2.3 Hz), 135.6, 152.3, 164.8 (d, $^3J_{C-P}$=5.6 Hz); IR (KBr): 3054, 2959, 2908, 1190 cm^{-1}. Anal. Calcd for $C_{20}H_{16}NOPS_2$: C, 62.97; H, 4.23; N, 3.67. Found: C, 63.02; H, 4.25; N, 3.67.

4.2.2. α-(Diphenylphosphoryl)methyl 2-(5-chlorobenzothiazolyl)sulfide (*29*)

Yield 93%; mp 160–161 °C (white crystal from CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 4.34 (d, J=8.4 Hz, 2H), 7.25–7.28 (m, 1H), 7.42–7.53 (m, 6H), 7.59 (d, J=8.4 Hz, 1H), 7.80–7.87 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 31.0 (d, $^1J_{C-P}$= 67.8 Hz), 121.2, 121.6, 124.8, 128.6 (d, $^2J_{C-P}$=12.3 Hz), 130.8 (d, $^1J_{C-P}$=103.2 Hz), 131.1 (d, $^3J_{C-P}$=9.1 Hz), 132.1, 132.3 (d, $^4J_{C-P}$=2.5 Hz), 133.7, 153.0, 167.1 (d, $^3J_{C-P}$=5.7 Hz); IR (KBr): 1431, 1198, 999 cm^{-1}. Anal. Calcd for $C_{20}H_{15}NOPS_2Cl$: C, 57.76; H, 3.64; N, 3.37. Found: C, 57.73; H, 3.63; N, 3.13.

4.3. α-(Diethoxyphosphoryl)methyl 2-benzothiazolyl sulfide (*5*)

To a stirred solution of tosylate **4** (1.0 equiv) and 2-mercaptobenzothiazole (1.2 equiv) in DMF was added K_2CO_3 (3.0 equiv) at rt. This reaction mixture was stirred for about 8 h at 80 °C. After the starting materials were consumed, DMF was evaporated off, residue was dissolved in $CHCl_3$, and then the precipitate was filtered off. The organic layer was washed with H_2O and dried over anhydrous $MgSO_4$. Then, the removal of solvent afforded to crude sulfide **5**, which was purified by flash chromatography. Yield 83%; colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.30 (t, J=7.1 Hz, 6H), 3.81 (d, J=7.1 Hz, 2H), 4.15–4.22 (m, 4H), 7.29–7.33 (m, 1H), 7.40–7.44 (m, 1H), 7.75–7.77 (m, 1H), 7.85–7.87 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 16.3 (d, $^3J_{C-P}$=6.0 Hz), 25.9 (d, $^1J_{C-P}$= 148.7 Hz), 63.0 (d, $^2J_{C-P}$=6.4 Hz), 121.1, 121.5, 124.5, 126.1, 135.5, 152.6, 164.9; IR (NaCl disc): 2360, 1252, 1049, 1022, 970 cm^{-1}; HRMS (EI) m/z calcd for $C_{12}H_{16}NO_3PS_2$: 317.0309. Found: 317.0316.

4.4. General procedure for the preparation of sulfoxides *3*, *6*, and *30*

To a stirred solution of sulfide (1 mmol) in $CHCl_3$ (20 mL) was added *m*-CPBA (1.2 mmol) in $CHCl_3$ (20 mL) at rt. After stirring for 1 h, the reaction mixture was washed with saturated solution of $NaHCO_3$ three times. The aqueous layer was extracted with $CHCl_3$.The combined organic layer was washed with water and dried over anhydrous $MgSO_4$. After removal of the solvent, the residue was purified by flash column chromatography on silica gel.

4.4.1. α-(Diphenylphosphoryl)methyl 2-benzothiazolyl sulfoxide (*3*)

Yield 81%; mp 170–171 °C (CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 4.23 (dd, J=14.4, 14.4 Hz, 1H), 4.35 (dd, J=14.4, 14.4 Hz, 1H), 7.45–7.60 (m, 8H), 7.81–7.88 (m,

4H), 7.96 (d, J=8.4 Hz, 1H), 8.03 (d, J=8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 58.2 (d, $^1J_{C-P}$=60.2 Hz), 122.2, 124.2, 126.4, 127.0, 128.8 (d, $^2J_{C-P}$=12.1 Hz), 128.9 (d, $^2J_{C-P}$=13.2 Hz), 130.8 (d, $^1J_{C-P}$=100.8 Hz), 131.0 (d, $^1J_{C-P}$=105.8 Hz), 131.2 (d, $^3J_{C-P}$= 9.8 Hz), 131.4 (d, $^3J_{C-P}$=10.7 Hz), 132.6 (d, $^4J_{C-P}$=2.5 Hz), 132.7 (d, $^4J_{C-P}$=2.4 Hz), 136.4, 153.4, 169.7 (d, $^3J_{C-P}$= 10.3 Hz); IR (KBr): 1055 cm^{-1}. Anal. Calcd for $C_{20}H_{16}NO_2PS_2$: C, 60.44; H, 4.06; N, 3.52. Found: C, 60.48; H, 4.11; N, 3.50.

4.4.2. α-(Diethoxyphosphoryl)methyl 2-benzothiazolyl sulfoxide (**6**)

Yield 68%; colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.34 (t, J=7.1 Hz, 3H), 1.37 (t, J=7.1 Hz, 3H), 3.65 (dd, J=12.9, 12.9 Hz, 1H), 3.86 (dd, J=14.8, 14.8 Hz, 1H), 4.18–4.29 (m, 4H), 7.49–7.53 (m, 1H), 7.56–7.61 (m, 1H), 8.00–8.03 (m, 1H), 8.07–8.10 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 16.2 (d, $^3J_{C-P}$=6.0 Hz), 16.3 (d, $^3J_{C-P}$=4.5 Hz), 53.4 (d, $^1J_{C-P}$=139.8 Hz), 63.20 (d, $^2J_{C-P}$=6.2 Hz), 63.22 (d, $^2J_{C-P}$=6.2 Hz), 122.3, 124.1, 126.5, 127.1, 136.2, 153.5, 176.8 (d, $^3J_{C-P}$=13.4 Hz); IR (NaCl disc): 1473, 1255, 1045, 1020, 974, 822, 798, 764 cm^{-1}; HRMS (EI) m/z calcd for $C_{12}H_{16}NO_4PS_2$: 333.0258. Found: 333.0260.

4.4.3. α-(Diphenylphosphoryl)methyl 2-(5-chlorobenzothiazolyl)sulfoxide (**30**)

Yield 89%; mp 172–174 °C (CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 4.22 (dd, J=14.4, 14.4 Hz, 1H), 4.34 (dd, J=14.4, 14.4 Hz, 1H), 7.45–7.61 (m, 7H), 7.80–7.89 (m, 5H), 8.00 (d, J=2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 58.0 (d, $^1J_{C-P}$= 60.3 Hz), 122.9, 123.9, 127.0, 128.8 (d, $^2J_{C-P}$=12.4 Hz), 128.9 (d, $^2J_{C-P}$=13.2 Hz), 130.9 (d, $^1J_{C-P}$=104.9 Hz), 130.8 (d, $^1J_{C-P}$=104.9 Hz), 131.1 (d, $^3J_{C-P}$=10.7 Hz), 131.4 (d, $^3J_{C-P}$= 10.6 Hz), 132.6 (d, $^4J_{C-P}$=3.3 Hz), 132.7 (d, $^4J_{C-P}$=3.3 Hz), 133.1, 134.7, 154.1, 179.0 (d, $^3J_{C-P}$=10.7 Hz); IR (KBr): 1435, 1196, 1057, 903, 746, 694 cm^{-1}. Anal. Calcd for $C_{20}H_{15}NO_2PS_2Cl$: C, 55.62; H, 3.50; N, 3.24. Found: C, 55.56; H, 3.61; N, 3.11.

4.5. General procedure for the thermal reaction of sulfoxides **3** and **6** in the presence of 2,3-dimethyl-1,3-butadiene

Sulfoxide **3** or **6** (1.0 equiv) and 2,3-dimethyl-1,3-butadiene (10 equiv) were dissolved in 1,4-dioxane (2.0 mL). The solution was placed and sealed in a Pyrex tube under nitrogen. The reaction was carried out for appropriate reaction time at the applied temperature. The separation and purification of the products were made by preparative thin layer chromatography on silica gel with AcOEt/hexane/$CHCl_3$ mixture.

4.5.1. 2-(Diphenyl)phosphoryl-3,6-dihydro-4,5-dimethyl-2H-thiopyran S-oxide (**8**)

Mp 162–164 °C (CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 1.66 (s, 3H), 1.74 (s, 3H), 2.32–2.41 (m, 1H), 2.74–2.83 (m, 1H), 3.49 (dd, J=15.8, 15.6 Hz, 2H), 3.77 (q, J=6.8 Hz, 1H), 7.50–7.60 (m, 6H), 7.81–7.91 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 19.4, 20.1, 27.5 (d, $^3J_{C-P}$=1.6 Hz), 53.4 (d, $^2J_{C-P}$=3.3 Hz), 58.1 (d, $^1J_{C-P}$=64.5 Hz), 118.5, 127.3 (d, $^3J_{C-P}$=6.6 Hz), 128.7 (d, $^3J_{C-P}$=6.6 Hz), 128.8 (d, $^3J_{C-P}$=6.6 Hz), 130.3 (d, $^1J_{C-P}$= 100.8 Hz), 130.9 (d, $^1J_{C-P}$=101.6 Hz), 131.2 (d, $^2J_{C-P}$= 9.1 Hz), 131.5 (d, $^2J_{C-P}$=9.1 Hz), 132.3 (d, $^4J_{C-P}$=3.3 Hz), 132.5 (d, $^4J_{C-P}$=3.3 Hz); IR (KBr): 1198, 1049 cm^{-1}. Anal. Calcd for $C_{19}H_{21}O_2PS$: C, 66.26; H, 6.15. Found: C, 66.57; H, 6.44.

4.5.2. 6-(Diphenyl)phosphoryl-3,4-dimethyl-2H-thiopyran (**9**)

Unstably brown crude compound; ^{1}H NMR ($CDCl_3$) δ 1.85 (s, 3H), 1.90 (s, 3H), 3.19 (s, 2H), 6.98 (d, J=16.2 Hz, 1H), 7.45–7.58 (m, 6H), 7.79–7.83 (m, 4H); HRMS (EI) m/z calcd for $C_{19}H_{19}OPS$: 326.0894. Found: 326.0875.

4.5.3. 2-(Diethoxy)phosphoryl-5,6-dihydro-3,4-dimethyl-2H-thiopyran S-oxide (**10**)

Colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J=7.07 Hz, 3H), 1.36 (t, J=7.03 Hz, 3H), 1.75 (s, 3H), 1.78 (s, 3H), 1.95–2.05 (m, 1H), 2.60–2.71 (m, 1H), 3.38 (d, J=16.1 Hz, 1H), 3.66 (d, J=16.1 Hz, 1H), 3.87 (dt, J=6.79, 6.79 Hz, 1H), 4.11–4.26 (m, 4H); IR (KBr): 3600–3100, 1246, 1022, 970, 773 cm^{-1}; HRMS (EI) m/z calcd for $C_{11}H_{21}O_4PS$: 280.0898. Found: 280.0912.

4.5.4. 6-(Diethoxy)phosphoryl-3,4-dimethyl-2H-thiopyran (**11**)

Unstably compound; ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J=6.79 Hz, 6H), 1.76 (s, 3H), 1.84 (s, 3H), 3.13 (s, 2H), 4.00–4.12 (m, 4H), 6.89 (d, J=18.4 Hz, 1H); IR (NaCl disc): 1246, 1022, 970, 773 cm^{-1}; HRMS (EI) m/z calcd for $C_{11}H_{19}O_3PS$: 262.0793. Found: 262.0815.

4.6. General procedure for the reaction of sulfoxides **3** and **6** with amines

The solution of sulfoxide **3** or **6** (1.0 equiv) and amine (2.2 equiv) in 1,4-dioxane (3.0 mL) was stirred for appropriate reaction time at the applied temperatures under nitrogen. The separation and purification of the products were made by preparative thin layer chromatography on silica gel eluting with AcOEt/hexane/$CHCl_3$ mixture.

4.6.1. Diphenylphosphorylthioformic acid anilide (**12a**)

Mp 161–162 °C (yellow crystal from CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 7.30 (t, J=6.7 Hz, 1H), 7.43 (t, J=8.0 Hz, 2H), 7.47–7.52 (m, 4H), 7.60 (t, J=7.4 Hz, 2H), 7.99–8.04 (m, 4H), 8.09 (d, J=8.4 Hz, 2H), 11.18 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 121.6, 127.4, 128.4 (d, $^2J_{C-P}$=13.3 Hz), 129.0 (d, $^1J_{C-P}$=108.1 Hz), 129.1, 132.7 (d, $^4J_{C-P}$=3.3 Hz), 132.9 (d, $^3J_{C-P}$=9.9 Hz), 138.4 (d, $^2J_{C-P}$=11.5 Hz), 194.0 (d, $^1J_{C-P}$=89.2 Hz); IR (KBr): 3300–2800, 1172, 1116 cm^{-1}. Anal. Calcd for $C_{19}H_{16}NOPS$: C, 67.64; H, 4.78; N, 4.15. Found: C, 67.81; H, 5.09; N, 4.28.

4.6.2. Diphenylphosphorylthioformic acid benzylamide (**12b**)

Mp 164–166 °C (pale yellow crystal from CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 4.91–4.93 (m, 2H), 7.26–7.38 (m, 5H), 7.46–7.51 (m, 4H), 7.57–7.60 (m, 2H), 7.96–8.01 (m, 4H), 9.82 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 49.5 (d,

$^3J_{C-P}$=5.8 Hz), 128.29, 128.30, 128.4 (d, $^3J_{C-P}$=5.8 Hz), 129.0, 129.2 (d, $^1J_{C-P}$=108.1 Hz), 132.6, 132.7 (d, $^2J_{C-P}$=9.9 Hz), 135.1, 197.1 (d, $^1J_{C-P}$=86.7 Hz); IR (KBr): 3500–2900, 1168, 1123 cm^{-1}. Anal. Calcd for $C_{20}H_{18}NOPS$: C, 68.36; H, 5.16; N, 3.99. Found: C, 68.35; H, 5.18; N, 3.89.

*4.6.3. Diphenylphosphorylthioformic acid piperidide (**12c**)*

Mp 153–154 °C (yellow crystal from CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 1.40–1.43 (m, 2H), 1.67–1.71 (m, 4H), 4.21 (t, J=5.6 Hz, 2H), 4.36 (t, J=5.6 Hz, 2H), 7.45–7.57 (m, 6H), 7.81–7.86 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 24.1, 25.6, 26.7, 51.8 (d, $^3J_{C-P}$=2.9 Hz), 53.7 (d, $^3J_{C-P}$=4.2 Hz), 128.2 (d, $^2J_{C-P}$=12.3 Hz), 131.88 (d, $^1J_{C-P}$=109.8 Hz), 131.95 (d, $^3J_{C-P}$=9.0 Hz), 131.97, 194.5 (d, $^1J_{C-P}$=91.8 Hz); IR (KBr): 1186, 1117 cm^{-1}. Anal. Calcd for $C_{18}H_{20}NOPS$: C, 65.63; H, 6.12; N, 4.25. Found: C, 65.47; H, 6.14; N, 4.03.

*4.6.4. Diphenylphosphorylthioformic acid morpholide (**12d**)*

Mp 165–167 °C (yellow crystal from CH_2Cl_2/AcOEt/hexane), lit. mp 150–151 °C;[8] ^{1}H NMR ($CDCl_3$) δ 3.55 (t, J=4.8 Hz, 2H), 3.79 (t, J=4.8 Hz, 2H), 4.30 (t, J=4.8 Hz, 2H), 4.48 (t, J=4.8 Hz, 2H), 7.26–7.51 (m, 4H), 7.55–7.59 (m, 2H), 7.81–7.86 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 50.4 (d, $^3J_{C-P}$=2.9 Hz), 52.9 (d, $^3J_{C-P}$=3.9 Hz), 66.5, 66.9, 128.3 (d, $^2J_{C-P}$=12.4 Hz), 131.3 (d, $^1J_{C-P}$=110.1 Hz), 132.0 (d, $^3J_{C-P}$=9.0 Hz), 132.2 (d, $^4J_{C-P}$=3.3 Hz), 196.3 (d, $^1J_{C-P}$=88.8 Hz); IR (KBr): 1183, 1173, 1109 cm^{-1}. Anal. Calcd for $C_{17}H_{18}NO_2PS$: C, 61.62; H, 5.47; N, 4.23. Found: C, 61.57; H, 5.49; N, 4.05.

*4.6.5. Diphenylphosphorylthioformic acid pyrrolidide (**12e**)*

Mp 153–155 °C (yellow crystal from CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 1.91–2.03 (m, 4H), 3.84–3.91(m, 2H), 4.12–4.15 (m, 2H), 7.45–7.49 (m, 4H), 7.53–7.57 (m, 2H), 7.83–7.89 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 22.9, 26.6, 52.7 (d, $^3J_{C-P}$=2.5 Hz), 55.4 (d, $^3J_{C-P}$=3.3 Hz), 128.2 (d, $^2J_{C-P}$=12.3 Hz), 131.1(d, $^1J_{C-P}$=109.0 Hz), 132.1 (d, $^4J_{C-P}$=2.4 Hz), 132.2 (d, $^3J_{C-P}$=9.0 Hz), 192.1 (d, $^1J_{C-P}$=88.5 Hz); IR (KBr): 1193, 1182, 1115, 1101 cm^{-1}. Anal. Calcd for $C_{17}H_{18}NOPS$: C, 64.75; H, 5.75; N, 4.44. Found: C, 64.85; H, 5.78; N, 4.32.

*4.6.6. Diethoxyphosphorylthioformic acid anilide (**13a**)*

Yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.40 (dt, J=0.8, 7.2 Hz, 6H), 4.22–4.34 (m, 4H), 7.29–7.32 (m, 1H), 7.44 (t, J=8.0 Hz, 2H), 7.98 (d, J=8.1 Hz, 2H), 10.57 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 16.1 (d, $^3J_{C-P}$=6.6 Hz), 65.3 (d, $^2J_{C-P}$=7.4 Hz), 122.0, 127.4, 129.0, 138.0 (d, $^3J_{C-P}$=14.9 Hz), 190.6 (d, $^1J_{C-P}$=181.7 Hz); IR (NaCl disc): 3400–2900, 1360, 1230 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{11}H_{16}NO_3PS$: 273.0589. Found: 273.0618.

*4.6.7. Diethoxyphosphorylthioformic acid benzylamide (**13b**)*

Mp 75–77 °C (pale yellow crystal from CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 1.37 (t, J=7.2 Hz, 6H), 4.17–4.33 (m, 4H), 4.85 (dd, J=2.0, 5.6 Hz, 2H), 7.31–7.39 (m, 5H), 9.19 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 16.2 (d, $^3J_{C-P}$=6.6 Hz), 49.3 (d, $^3J_{C-P}$=8.2 Hz), 65.1 (d, $^2J_{C-P}$=7.4 Hz), 128.3, 128.4, 129.0, 135.0, 193.2 (d, $^1J_{C-P}$=180.2 Hz); IR (KBr): 3340–2850, 1520, 1500, 1394, 1250, 1050 cm^{-1}. Anal. Calcd for $C_{12}H_{18}NO_3PS$: C, 50.16; H, 6.31; N, 4.87. Found: C, 50.31; H, 6.18; N, 4.85.

*4.6.8. Diethoxyphosphorylthioformic acid piperidide (**13c**)*

Yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.38 (t, J=7.2 Hz, 6H), 1.75 (br s, 6H), 4.16–4.37 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 16.2 (d, $^3J_{C-P}$=6.5 Hz), 24.2, 25.4, 26.9, 50.6 (d, $^3J_{C-P}$=6.6 Hz), 54.6 (d, $^3J_{C-P}$=4.1 Hz), 64.2 (d, $^2J_{C-P}$=8.2 Hz), 190.3 (d, $^1J_{C-P}$=188.3 Hz); IR (NaCl disc): 3700–3200, 3100–2800, 1438, 1240, 1086 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{11}H_{20}NO_3PS$: 265.0902. Found: 265.0882.

*4.6.9. Diethoxyphosphorylthioformic acid morpholide (**13d**)*

Yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.39 (dt, J=0.8, 7.2 Hz, 6H), 3.78–3.82 (m, 4H), 4.23–4.35 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 16.2 (d, $^3J_{C-P}$=6.6 Hz), 49.3 (d, $^3J_{C-P}$=6.5 Hz), 53.8 (d, $^3J_{C-P}$=3.3 Hz), 64.5 (d, $^2J_{C-P}$=7.4 Hz), 66.4, 66.9, 191.9 (d, $^1J_{C-P}$=187.6 Hz); IR (NaCl disc): 3700–2800, 1478, 1437, 1253, 1120, 1065, 1030 cm^{-1}; HRMS (EI) *m/z* calcd for $C_9H_{18}NO_4PS$: 267.0694. Found: 267.0705.

*4.6.10. Diethoxyphosphorylthioformic acid pyrrolidide (**13e**)*

Yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.37 (dt, J=0.8, 7.2 Hz, 6H), 1.97–2.12 (m, 4H), 3.81–3.85 (m, 2H), 4.07–4.11 (m, 2H), 4.23–4.37 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 16.2 (d, $^3J_{C-P}$=6.6 Hz), 23.4, 26.5, 53.2 (d, $^3J_{C-P}$=1.6 Hz), 54.3 (d, $^3J_{C-P}$=6.6 Hz), 64.3 (d, $^2J_{C-P}$=7.4 Hz), 191.9 (d, $^1J_{C-P}$=187.6 Hz); IR (NaCl disc): 3700–2700, 1450, 1250, 1168, 1062, 1030, 980 cm^{-1}; HRMS (EI) *m/z* calcd for $C_9H_{18}NO_3PS$: 251.0745. Found: 251.0744.

*4.7. General procedure for the preparation of disulfides **15** and **16***

To a stirred solution of Na_2S (1.0 equiv) in EtOH (15 mL) was added S_8 (1.05 equiv). The solution was refluxed for 30 min under stirring. Tosylate **1** or **4** (1.0 equiv) solution in EtOH (15 mL) was added dropwise into the Na_2S_2 solution. The solution was refluxed for 7–12 h. After removal of EtOH, the residue was treated with $CHCl_3$ and the precipitate was filtered off. The organic layer was separated and dried over anhydrous $MgSO_4$. After the removal of solvent, the residue was separated and purified by preparative thin layer chromatography on silica gel to give disulfide **15** or **16**.

*4.7.1. Bis-(diphenyl)phosphorylmethyl disulfide (**15**)*

Yield 80%; mp 174–176 °C (CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 3.77 (d, J=7.2 Hz, 4H), 7.43–7.54 (m, 12H), 7.74–7.79 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 40.2 (d, $^1J_{C-P}$=65.3 Hz), 128.7 (d, $^2J_{C-P}$=11.6 Hz), 131.2 (d, $^3J_{C-P}$=9.0 Hz), 131.6 (d, $^1J_{C-P}$=101.6 Hz), 132.1 (d, $^4J_{C-P}$=3.3 Hz); IR (KBr): 3432 (br), 1437, 1190, 1120 cm^{-1}. Anal. Calcd for

$C_{26}H_{24}O_2P_2S_2$: C, 63.14; H, 4.89. Found: C, 63.06; H, 4.95; HRMS (EI) *m/z* calcd for $C_{26}H_{24}O_2P_2S_2$: 494.0693. Found: 494.0694.

*4.7.2. Bis-(diethoxy)phosphorylmethyl disulfide (**16**)*

Yield 89%; colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.34 (t, J=7.1 Hz, 12H), 3.22 (d, J=13.0 Hz, 4H), 4.13–4.23 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 16.4 (d, $^3J_{C-P}$=5.7 Hz), 34.1 (d, $^1J_{C-P}$=145.4 Hz), 62.7 (d, $^2J_{C-P}$=6.6 Hz); IR (NaCl disc): 3600–3300, 2982, 2909, 2360, 2341, 1249, 1049, 1023, 968, 822, 804 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{10}H_{24}O_6P_2S_2$: 366.0490. Found: 366.0453.

*4.8. General procedure for the reaction of sulfoxides **3** and **6** with benzylthiol in the presence of DBU*

The solution of sulfoxide **3** or **6** (1.0 equiv) and DBU (2.0 equiv) in 3.0 mL of 1,4-dioxane was stirred for 5 min at rt. To the solution was added benzylthiol (2.0 equiv) and reaction proceeded in a short time. The separation and purification of the products were made by preparative thin layer chromatography on silica gel eluting with AcOEt/hexane/$CHCl_3$ mixture.

4.9. General procedure for the thiol trapping reaction

The solution of sulfoxide **3** or disulfide **15** (1.0 equiv) and morpholine (4.0 equiv) in 1,4-dioxane (3.0 mL) was stirred for appropriate reaction time at 90 °C under nitrogen. Then, *N*-phenylmaleimide (1.0 equiv) was added to the reaction mixture. After 7.5 h, reaction mixture was reduced in vacuo. The separation and purification of the products were made by preparative thin layer chromatography on silica gel eluting with AcOEt/hexane/$CHCl_3$ mixture.

*4.9.1. 3-(Morpholin-4-yl)-1-phenylpyrrolidine-2,5-dione (**22**)*

Mp 155–157 °C (colorless crystal from CH_2Cl_2/hexane), lit. mp 175 °C;[9] ^{1}H NMR ($CDCl_3$) δ 2.61–2.66 (m, 2H), 2.83 (dd, J=24.6, 18.8 Hz, 1H), 2.90–2.95 (m, 2H), 3.03 (dd, J=18.6, 18.8 Hz, 1H), 3.76 (t, J=4.40 Hz, 4H), 3.90 (dd, J=8.99, 8.79 Hz, 1H), 7.25–7.28 (m, 2H), 7.38–7.42 (m, 1H), 7.45–7.50 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 31.8, 49.6, 62.6, 66.8, 126.4, 128.8, 129.2, 131.4, 173.9, 174.7; IR (KBr): 1711, 1498, 1387, 1198, 1171, 1115 cm^{-1}. Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.42; H, 6.26; N, 10.60.

*4.9.2. 3-(Diphenyl-phosphinoylmethylsulfanyl)-1-phenyl-pyrrolidine-2,5-dione (**23**)*

Mp 178–182 °C (CH_2Cl_2/AcOEt/hexane); ^{1}H NMR ($CDCl_3$) δ 2.58 (dd, J=18.8, 18.8 Hz, 1H), 3.27 (dd, J=20.6, 25.9 Hz, 1H), 3.43 (dd, J=15.0, 15.6 Hz, 1H), 4.13 (dd, J=15.2, 15.2 Hz, 1H), 4.49 (ddd, J=9.59, 4.00, 1.20 Hz, 1H), 7.26–7.28 (m, 2H), 7.38–7.42 (m, 1H), 7.45–7.59 (m, 8H), 7.75–7.83 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 29.0 (d, $^1J_{C-P}$=69.4 Hz), 35.4, 38.5, 126.4, 128.7 (d, $^3J_{C-P}$=3.5 Hz), 128.80, 128.84 (d, $^3J_{C-P}$=3.3 Hz), 129.2, 130.8 (d, $^1J_{C-P}$=105.7 Hz), 130.9 (d, $^2J_{C-P}$=9.9 Hz), 131.3 (d, $^2J_{C-P}$=9.1 Hz), 131.4, 132.2 (d, $^1J_{C-P}$=100.1 Hz), 132.3 (d, $^4J_{C-P}$=2.41 Hz), 173.3, 175.8; IR (KBr): 1712, 1385, 1188, 750, 696 cm^{-1}. Anal. Calcd for $C_{23}H_{20}NO_3PS$: C, 65.55; H, 4.78; N, 3.32. Found: C, 65.10; H, 4.92; N, 3.18.

*4.10. General procedure for the reaction of disulfide **15** with morpholine*

The solution of disulfide **15** (1.0 equiv) and amine (5.0 equiv) in 1,4-dioxane (3.0 mL) was stirred for appropriate reaction time at 90 °C under nitrogen at 7 h. The separation and purification of the products were made by preparative thin layer chromatography on silica gel eluting with AcOEt/hexane/$CHCl_3$ mixture.

*4.11. General procedure for the cross-over reaction of sulfoxides **6** and **30** with morpholine*

The solution of sulfoxides **6** and **30** (1.0 equiv) and amine (5.0 equiv) in 1,4-dioxane (5.0 mL) was stirred for 2 days at rt under nitrogen. The separation and purification of the products were made by preparative thin layer chromatography on silica gel eluting with AcOEt/hexane/$CHCl_3$ mixture.

*4.11.1. 2-N-Morpholino-(5-chlorobenzothiazole) (**31**)*

Mp 108–110 °C (CH_2Cl_2/hexane), lit. mp 115 °C;[10] ^{1}H NMR ($CDCl_3$) δ 3.62 (t, J=4.80 Hz, 4H), 3.83 (t, J=4.80 Hz, 4H), 7.06 (dd, J=2.10, 0.50 Hz, 1H), 7.50 (d, J=8.39 Hz, 1H), 7.54 (d, J=2.00 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 48.4, 66.2, 119.3, 121.3, 121.7, 128.8, 131.9, 153.6, 170.0; IR (KBr): 1533, 1446, 1377, 1342, 1284, 1227, 1114, 883 cm^{-1}. Anal. Calcd for $C_{11}H_{11}N_2OSCl$: C, 51.86; H, 4.35; N, 11.00. Found: C, 51.84; H, 4.35; N, 10.88; HRMS (EI) *m/z* calcd for $C_{11}H_{11}ClN_2OS$: 254.0281. Found: 254.0264.

*4.11.2. (Diphenylphosphinoylmethyldisulfanylmethyl)-phosphonic acid diethyl ester (**32**)*

Oily product; ^{1}H NMR ($CDCl_3$) δ 1.31 (t, J=7.07 Hz, 6H), 3.14 (d, J=12.8 Hz, 2H), 3.83 (d, J=7.51 Hz, 2H), 4.09–4.16 (m, 4H), 7.48–7.58 (m, 6H), 7.76–7.81 (m, 4H); HRMS (EI) *m/z* calcd for $C_{18}H_{24}O_4P_2S_2$: 430.0591. Found: 430.0596.

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