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Reaction of Thioaldehydes with Amines

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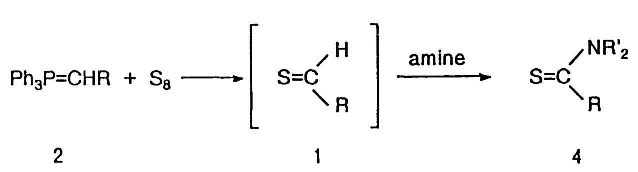
The reaction of phosphonium ylides with elemental sulfur gave thioaldehydes, which changed to the corresponding thioamides in good yields when treated with amines. When thioaldehydes containing α-hydrogens were treated with secondary amines, the corresponding enamines or reduction products were obtained.

The chemistry of thiocarbonyl compounds has been of current interest.1) Several authors have reported the formation of thioaldehydes (**1**). Kirby and Lochead reported the generation of thioaldehydes from S-esters of sodium hydrogenthiosulfate.1a) Generation of thioaldehydes also occurs from the Norrish cleavage of phenacyl sulfides.1b) Recently, we also showed that the reaction of phosphonium ylides (**2**) with elemental sulfur or thiiranes gave symmetrical olefins via thiocarbonyl compounds.2) Reactions of these relatively unstable thioaldehydes are of much interest. However, there are quite a few reports on the reaction of these thioaldehydes with amines. Okazaki has reported that the reaction of 2,4,6-tri-*t*-butylthiobenzaldehyde with primary amines afforded the corresponding imines.3) Recently, we reported the reaction of **1** with secondary amines (**3**) afforded the corresponding thioamides (**4**) in good yields.4) In this paper, we would like to give a detailed account on the reaction of thioaldehydes with amines.

Results and Discussion

We first tried the reaction of methoxycarbonylmethylenetriphenylphosphorane (**2a**) with sulfur in the presence of secondary amines, **3**. Treatment of **2a** with elemental sulfur and morpholine in toluene gave the corresponding thioamide (**4a**) in 75% yield. As shown in Table 1, other thioamides, **4**, were obtained in good yields. Since thioaldehyde (**1a**) could be also synthesized by the reaction of the corresponding sulfenyl chloride with triethylamine,1a) we also carried out the reaction of **1a** starting from methyl mercaptoacetate (methyl thioglycolate) (**5a**) with morpholine. The reaction of thioaldehydes derived from thiols with N-chlorosuccinimide (NCS) with secondary amines also gave the corresponding thioamides, **4**, in good yields. Other reactions were carried out in a similar manner. However, when phenylmethanethiol (**5d**) and methanethiol (**5e**) were used as starting thiols, only the corresponding sulfenamides (**6**) were obtained. Thus, electron-withdrawing groups were required to obtain thioamides in this reaction. (Table 2)



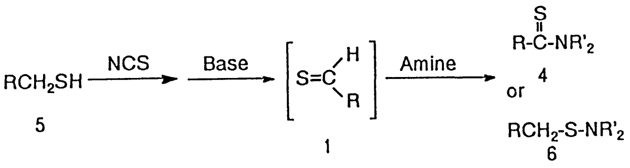
Scheme 1.

Table 1. Reaction of Thioaldehydes with Secondary Amines

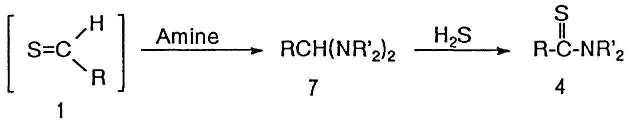
Thioaldehyde		Amine	Thioamide (yield/%)	
1	R	**3**	**4**	
a	COOMe	Morpholine	**4a**	75
a	COOMe	Dimethylamine	**4b**	76
a	COOMe	Piperidine	**4c**	60
a	COOMe	Pyrrolidine	**4d**	47
b	COOEt	Morpholine	**4e**	73
c	Ph	Morpholine	**4f**	56

Milligan and Swan reported that the reaction of *O*-carbamoylmethyl thiosulphate with primary and secondary amines afforded 2-amino-2-thiooxoacetoamides and disulfides. They suggested that these compounds might be formed in a complex manner from thioaldehyde intermediates.5) As to the formation of thioamides, **4**, the following mechanism is reasonable: Thioaldehydes, **1**, were converted to the corresponding bis(dialkylamino)alkanes, **7**, (aminal) by treatment with amines in a manner similar to the reaction of amines with aldehydes. The resulting **7** further reacted with the hydrogen sulfide produced to give thioamides, **4**.

The above mechanism was confirmed by the following two reactions. When the reaction of **2c** with sulfur in the presence of morpholine was carried out at 50 °C, **7** was isolated in 70% yield instead of **4f**. Additionally,



Scheme 2.



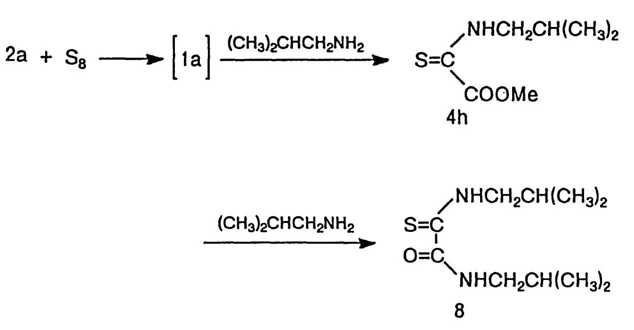
Scheme 3.

Table 2. Reaction of Thiols with NCS Followed by the Addition of Amines

Thiol 5	R	Conditions Base	Solvent	Temperature/°C	Amine	Products (Yield/%)	
5a	COOMe	DBU	CH_2Cl_2	Reflux	Morpholine	**4a**	55
		DBU	THF	Reflux	Morpholine	**4a**	65
		BuLi	THF	0	Morpholine	**4a**	75
		DBU	CH_2Cl_2	Reflux	Dimethylamine	**4b**	65
		BuLi	THF	0	Dimethylamine	**4b**	75
5b	COOEt	BuLi	THF	0	Morpholine	**4e**	70
5c	$4\text{-}NO_2C_6H_4$-	DBU	CH_2Cl_2	Reflux	Morpholine	**4g**	91
5d	Ph	DBU	CH_2Cl_2	Reflux	Morpholine	**6a**	55
		BuLi	THF	0	Morpholine	**6a**	70
5e	H-	BuLi	THF	0	Morpholine	**6b**	70

treatment of **7** with hydrogen sulfide afforded the corresponding thioamide, **4f**, 65% yield. It is well known that thioamides were formed by the reaction of sulfur with aryl alkyl ketones (Willgerodt–Kindler reaction).[6] In this case, the primary step might be the formation of aminals, **7**, resulting from the action of the amine on the ketones, which then changed to thioamides as shown in the present reaction.

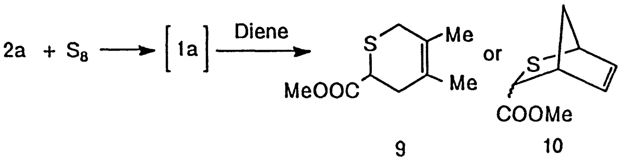
We further tried the reaction of **1a** with sulfur in the presence of primary amines. Treatment of **1a** with sulfur in the presence of isobutylamine also gave thioamides, **4h**. The resulting **4h** further reacted with isobutylamine to give *N*,*N'*-diisobutyl-2-amino-2-thiooxoacetamide (**8**) in 64% yield. However, when benzylidenetriphenylphosphorane, **2c**, was treated with elemental sulfur and isobutylamine, the observed products were benzylideneisobutylamine and triphenylphosphine sulfide. The corresponding thioamide could not be obtained. Electron-withdrawing groups on the phosphonium ylides might be necessary for thioamide synthesis.



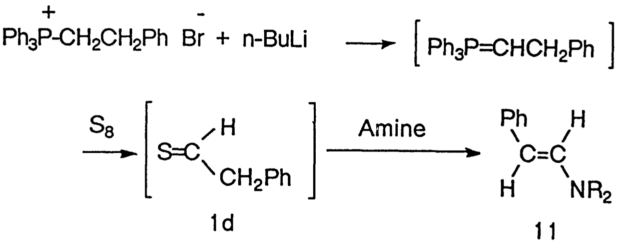
Scheme 4.

To confirm the formation of thioaldehydes, **1**, in this reaction, we tried the reaction of phosphonium ylides, **2**, with sulfur in the presence of dienes. Treatment of phosphonium ylide, **2a**, with elemental sulfur in the presence of 2,3-dimethyl-1,3-butadiene or cyclopentadiene afforded the corresponding Diels–Alder adduct, **9** or **10**, in 56% or 64% yield, respectively.

We then tried the reaction of thioaldehydes containing α-hydrogens with secondary amines. The results of these reactions were different from previous ones. First, we tried the reaction of phenethyltriphenylphosphonium bromide with elemental sulfur and secondary amines. The obtained products were the corresponding enamine (**11**) and triphenylphosphine



Scheme 5.



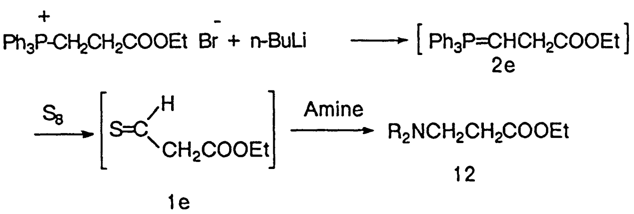
Scheme 6.

Table 3. Reaction of Thioaldehyde **1d** with Sulfur in the Presence of Secondary Amines

Compound 1	R	Amine	Conditions Solvent	Time/h	Products (yield%) 11	
d	CH_2Ph	Morpholine	Benzene	2	**11a**	10
d	CH_2Ph	Pyrrolidine	Benzene	2	**11b**	13
d	CH_2Ph	Dimethylamine	Benzene	2	**11c**	10

Table 4. Reaction of Thioaldehyde **1e** with Sulfur in the Presence of Amines

Compound		Secondary Amine	Conditions		Compounds (yield/%)	
1	R		Solvent	Time/h	**12**	
e	CH_2COOEt	Morpholine	Benzene	2	**12a**	60
e	CH_2COOEt	Dimethylamine	Benzene	2	**12b**	60
e	CH_2COOEt	Butylamine	Benzene	2	**12c**	57



Scheme 7.

sulfide. This result suggested that these reactions would proceed through thiobenzaldehyde intermediates, which further reacted with amines to give enamines. However, the yields of enamines were very low and other unidentifiable products were obtained. Meyer and Gewald reported that enamines were easily changed to the corresponding thioamides in good yields.[7] However, we could not isolate the corresponding thioamides in the present work. The difference in the reactivity might be due to the difference in the substituents.

We then tried the reaction of other types of thioaldehydes. Treatment of 2-ethoxycarbonylethylidenetriphenylphosphoran (**2e**) with elemental sulfur and morpholine afforded ethyl 3- morpholinopropionate (**12a**) and triphenylphosphine sulfide in 60 and 82% yields, respectively. Asinger et al. reported the reaction of alkyl aryl ketones with sulfur and NH_3.[6] They suggested that these ketones were converted to the corresponding thioketones, the thiocarbonyl group of which was reduced to the methylene group by treatment of hydrogen sulfide. The present reaction might proceed in a similar manner.

Thioamide syntheses from thioaldehydes were previously reported by only one group. Fischer and coworkers reported that the reaction of thioaldehyde-metal complexes with ynamines afforded thioamides by cycloaddition followed by extrusion of metals and the addition of carbon monooxide.[8]

In summary, we found that thioaldehydes show a different reactivity upon treatment with amines depending on whether the aldehydes have α-hydrogens or not. Thioaldehydes with the α-hydrogens gave the reduction products. On the other hand, thioaldehydes without the α-hydrogens afforded thioamides in good yields.

Experimental

General. Melting points are uncorrected. ^{1}H NMR spectra were determined with a JEOL PMX-60, a FX-90, or a GX-400 spectrometer. Mass spectra were recorded on a JEOL GS 270 spectrometer.

Materials. Stable phosphonium ylides were prepared by a method mentioned in the literature.[9] Methyl thioglycolate, *N*-chlorosuccinimide, 4-nitrobenzyl bromide were purchased from Wako Pure Chem. Compounds **12a** and **12b** were prepared by the reaction of ethyl acrylate with the corresponding amines.[10]

Reaction of 2a with Sulfur in the Presence of Secondary Amines. To a solution of **2a** (1.67 g, 10 mmol) and morpholine (1.74 g, 20 mmol) in toluene (25 ml) was added a solution of sulfur (0.64 g, 20 mmol) in toluene (20 ml). After refluxing for 12 h, the reaction mixture was washed with water and evaporated to give yellow oily crystals. This mixture was extracted with hexane (30 ml×3). The combined extracts were evaporated to give thioamide **4a**. Other reactions were carried out in a similar manner.

4a; 0.71 g (3.7 mmol, 75%), mp 77—79 °C, ^{1}H NMR ($CDCl_3$) δ=3.56—3.65 (m, 2H), 3.74—3.86 (m, 4H), 3.87 (s, 3H), 4.15—4.24 (m, 2H). Precise mass for $C_7H_{11}NO_3S$: 189.0459 (calcd), 189.0492 (found).

4b; 0.44 g (3.8 mmol, 76%), ^{1}H NMR($CDCl_3$) δ=3.17 (s, 3H), 3.30 (s, 3H), 3.83 (s, 3H). Precise mass for $C_5H_9NO_2S$: 147.0354 (calcd), 147.0419 (found).

4c; 0.58 g (2.8 mmol, 60%), ^{1}H NMR ($CDCl_3$) δ=1.88—2.20 (m, 4H), 3.49—3.78 (m, 4H), 3.86 (s, 3H). Precise mass for $C_8H_{13}NO_2S$: 187.0667 (calcd), 187.0631 (found).

4d; 0.41 g (2.4 mmol, 47%), ^{1}H NMR ($CDCl_3$) δ=1.58—1.85 (m, 4H), 3.40—3.86 (m, 2H), 3.86 (s, 3H), 3.96—4.23 (m, 2H). Precise mass for $C_7H_{11}NO_2S$: 173.0510 (calcd), 173.0473 (found).

4e; 0.68 g (3.6 mmol, 73%), ^{1}H NMR ($CDCl_3$) δ=1.32 (t, 3H), 3.53—4.11 (m, 8H), 4.29 (q, 2H). Precise mass for $C_8H_3NO_3S$: 203.0616 (calcd), 203.0562 (found).

Reaction of 2c with Sulfur in the Presence of Morpholine. To a solution of benzyltriphenylphosphonium bromide (2.25 g, 5 mmol) in benzene (30 ml) was added a solution of butyllithium (4.5 ml, 10% w/v, 7 mmol) in hexane at room temperature. After stirring for 1 h, morpholine (4.35 g, 50 mmol) and sulfur (0.32 g, 10 mmol) were added and refluxed for 2 h. The resulting mixture was washed with water (20 ml×2) and evaporated to give yellow oily crystals. This mixture was extracted with hexane (30 ml×3). The combined extracts were evaporated to give *N*-thiobenzoylmorpholine **4f** (0.58 g, 2.8 mmol, 56%), mp 134—134.5 °C, (lit,[11] mp 134.5—136 °C). ^{1}H NMR ($CDCl_3$) δ=3.62 (br s, 4H), 3.89 (m, 2H), 4.48 (m, 2H), 7.27 (m, 5H). Anal. Calcd for $C_{11}H_{13}NOS$: C, 63.74; H, 6.32; N, 6.76%. Found: C,63.95; H, 6.67; N, 6.90%.

Preparation of 4-Nitrophenylmethanethiol, (5c). To a solution of sodium thiosulfate (4.96 g, 20 mmol) in water (50 mL) was added a solution of 4-nitrobenzyl bromide (4.32 g, 20 mmol) in ethanol (20 mL). Afer stirring for 24 h, 5 mL of concd HCl was added to this solution and refluxed for 3 h.

The resulting solution was condensed to 40 mL and extracted with dichloromethane (15 mL) for three times. The combined extract was dried over MgSO$_4$ and evaporated to give the corresponding thiol, **5c** (2.21 g, 65%), mp 56—57 °C, (lit,[132] mp 58 °C).

Reaction of Methyl Thioglycolate with *N*-Chlorosuccinimide Followed by the Addition of DBU and Elemental Sulfur. To a solution of *N*-chlorosuccinimide (0.81 g, 6.0 mmol) in 20 mL of dichloromethane was added a solution of methyl thioglycolate (0.53 g, 5.0 mmmol) in dichloromethane (10 mL). After stirring for 2 h, the resulting suspension was filtered. The yellow filtrate was added to a solution of DBU (1.17 g, 7.0 mml) and morpholine (0.52 g, 6.0 mmol) in dichloromethane (30 mL) After refluxing for 3 h, the reaction mixture was washed with water and extracted with ether (15 mL×3). The combined extracts were dried over sodium sulfate and evaporated to give a pale yellow oil. The resulting oil was chromatographed over silica gel by elution with dichloromethane–ethyl acetate to afford **4a** in 65% yield. Mp 77—79 °C. Thioamides **4b** and **4e** were also prepared in a similar manner.

Reaction of 4-Nitrophenylmethanethiol, (5c), with NCS Followed by the Addition of DBU and Morpholine. To a solution of NCS (0.67 g, 5 mmol) in dichloromethane (20 mL) was added a solution of 4-nitrophenylmethanethiol (0.68 g, 4 mmol) in dichloromethane (10 mL) at room temperature. After stirring for 2 h, the resulting suspension was filtered. The filtrate was added a solution of morpholine (0.35 g, 4 mmol) and DBU (0.76 g, 5 mmol) in dichloromethane (30 mL) and refluxed for 3 h. The reaction mixture was washed with water, dried over MgSO$_4$, and evaporated to give pale yellow crystals. Recrystallization from methanol afforded colorless crystals of thioamide, **4g** (yield 91%). Mp 193—194 °C; Anal. Calcd for $C_{11}H_{12}N_2O_3S$: C, 52.37; H, 4.79; N, 11.10%. Found: C, 52.02; H, 4.86; N, 11.07%.

Reaction of Methanesulfenyl Chloride with Morpholine. To a solution of morpholine (0.87 g, 10 mmol) in 30 ml of THF was added a solution of methanesulfenyl chloride (0.28 g, 3 mmol) in THF at −15 °C. Immediately, white crystals of morpholinium chloride were precipitated. The suspension was stirred for 3 h, washed with water, and extracted with hexane (15 mL×3). The combined extracts were dried over MgSO$_4$ and evaporated to give a pale brown oil, which was subjected to bulb-to-bulb distillation to give a pale yellow oil of methylsulfenylmorpholide (mp 40—50 °C/0.5 mmHg; lit,[13] 48—49 °C/5 mmHg, 1mmHg=133.322 Pa). *N*-benzylsulfenylmorpholine, (**6a**), was obtained in a similar manner. Mp 73—74 °C, (lit,[13]) mp 73.5—74.5 °C.

Reaction of 2c with Morpholine in the Presence of Sulfur at 50 °C (Preparation of 7). To a suspension of benzyltriphenylphosphonium chloride (1.94 g, 5 mmol) in benzene (25 mL) was added butyllithium (10% w/v, 4 mL, 6 mmol) in hexane. To this suspension, morpholine (1.74 g, 20 mmol) and sulfur (0.32 g, 10 mmol) were added portionwise at room temperature. After stirring for 1 h at 50 °C, the reaction mixture was evaporated to give pale yellow oily crystals. Recrystallization from ethanol gave colorless crystals of aminal **7** (0.71 g, 3.25 mmol), mp 100—101 °C, (lit,[14] 100—101.5 °C).

Reaction of 2c with Sulfur in the Presence of Primary Amines. To a solution of benzyltriphenylphosphonium bromide (2.25 g, 5 mmol) in benzene was added a solution of butyllithium (4.5 ml, 10% w/v, 7 mmol) at room temperature. After stirring for 1 h, butylamine (3.60 g, 50 mmol) and sulfur (0.32 g, 10 mmol) were added and refluxed for 2 h. The resulting mixture was washed with water and evaporated to give yellow oily crystals. The mixture was extracted with hexane (30 ml×3). The combined extracts were evaporated to give a yellow oil, which was distilled under reduced pressure (bulb-to-bulb distillation) to give a colorless oil of benzylidenebutylamine. Other reaction was carried out in a similar manner. Benzylidenebutylamine: 0.41g (2.6 mmol, 51%), 50—60 °C/4 mmHg, (lit,[15] 128—131 °C/25 mmHg), ^{1}H NMR (CDCl$_3$) δ=0.70—2.00 (m, 7H), 3.72—3.87 (m, 2H), 7.10—7.93 (m, 5H), 8.17 (s, 1H). Benzylideneisobutylamine; 0.56 g (3.5 mmol, 70%), 50—60 °C/4 mmHg, ^{1}H NMR (CDCl$_3$) δ=0.99 (d, 2CH$_2$ J=6.8 Hz), 1.78—2.30 (m, 1H), 3.43 (d, CH$_2$, J=6.8 Hz), 7.20—7.72 (m, 5H), 8.06 (s, 1H).

Reaction of 2a with Sulfur in the Presence of Diene. To a solution of **2a** (1.68 g, 5.0 mmol) and 2, 3-dimethyl-1,3-butadiene (2 ml, 20 mmol) in toluene (40 ml) was added elemental sulfur (0.64 g, 20 mmol). After refluxing for 20 h, the resulting mixture was evaporated to give reddish-brown oily crystals. This mixture was extracted with methanol(30 ml×2). The combined extracts were evaporated to give a reddish-brown oil, which was chromatographed over silica gel by elution with hexane–dichloromethane (3:1) to give adduct **9** (0.52 g, 2.8 mmol, 56%).[2,16] Adduct **10** was prepared in a similar manner.

10;[2] 0.54 g (3.2 mmol, 64%), ^{1}H NMR (CDCl$_3$) (*Endo*) δ=1.66 (br s, CH$_2$), 3.56 (s, Me), 3.75 (br s, CH), 4.18 (br CH), 4.44 (d, CH, J=3.0 and 5.1 Hz); (*Exo*) δ=1.84 (br s, CH$_2$), 3.29 (s, CH), 3.54 (br, CH), 3.86 (s, Me), 4.07 (br, CH), 5.91 (dd, =CH, J=3.2 and 6.2 Hz), 6.36 (dd, =CH, J=3.2 and 4.8 Hz).

Reaction of 2a with Sulfur in the Presence of Primary Amines, To a solution of **2a** (1.67 g, 5 mmol) and isobutylamine (1.82 g, 25 mmol) in benzene (50 mL) was added a solution of sulfur (0.32 g, 10 mmol) in benzene. After refluxing for 5 h, the reaction mixture was washed with water and evaporated to give yellow oily crystals. This mixture was extracted with hexane (30 ml×3). The combined extracts were evaporated to give a yellow oil, which was distilled under reduced pressure (bulb-to-bulb distillation) to give a colorless oil of **8**.

8; 0.66 g (3.1 mmol, 61%), mp 90—100 °C/2.5 mmHg. ^{1}H NMR (CDCl$_3$) δ=0.94 (d, 2 CH$_3$, J=3.2 Hz), 1.01 (d, 2 CH$_3$ J=3.4 Hz), 1.65—2.33 (m, 2 H), 3.16 (t, CH$_2$, J=6.6 Hz), 3.44—3.60 (m, CH$_2$), 8.59 (br, NH), 10.00 (br, NH). ^{13}C NMR (CDCl$_3$) δ=20.02 (CH$_3$), 20.28 (CH$_3$), 27.39 (CH), 28.43 (CH), 48.02 (CH$_2$), 53.39 (CH$_2$), 158.71 (C=O), 186.53 (C=S). Precise mass for $C_{11}H_2N_2ON_2OS$: 216.1296 (calcd) , 216.1273 (found).

Reaction of 2d with Sulfur in the Presence of Secondary Amines (Preparation of Enamines). To a solution of phenethyltriphenylphosphonium bromide (2.24 g, 5 mmol) in the benzene was added a solution of butyllithium (4.5 ml, 10% w/v, 7 mmol) in hexane at room temperature. After stirring for 1 h, morpholine (2.18 g, 25 mmol) and sulfur (0.32 g, 10 mmol) were added and stirred for 2 h. The resulting mixture was washed with water and evaporated to give brown oily crystals. This mixture was extracted with hexane (15 mL×3). The combined extracts were evaporated to give a yellow oil, which was distilled under reduced pressure (bulb-to-bulb distillation) to give a colorless oil of **11a**.

11a; 0.095 g (0.5 mmol, 10%), mp 100—110 °C/1.0 mmHg. ^{1}H NMR (CDCl$_3$) δ=2.98 (t, 4H, J=4.63 and 5.13 Hz), 3.73 (t, 4H,J= 4.88 Hz), 5.41 (d, =CH, J=14.16 Hz), 6.59, (d, =CH, J=14.16 Hz), 7.18 (m, 5H). ^{13}C NMR ($CDCl_3$) δ= 49.03 (CH_2), 66.36 (CH_2), 101.47 (=CH), 124.28, 124.38, 128.50, 138.74 (Ar), 139.66 (=CH). Precise mass for $C_{12}H_{15}NO$: 189.1154 (calcd), 189.1167 (found).

11b; 0.11 g (0.065 mmol, 13%), mp 140—150 °C/1.5 mmHg.[17] ^{1}H NMR ($CDCl_3$ δ=1.90 (m, 4H), 3.21 (m, 4H), 5.08 (d, =CH, J=13.92 Hz), 6.96—7.18 (m, Ar and =CH). ^{13}C NMR ($CDCl_3$) δ=25.25 (CH_2), 48.97 (CH_2, 97.62 (=CH), 122.92, 123.36, 128.50, 140.20 (Ar), 135.82 (=CH).

11c; 0.08 g (0.05 mmol, 10%), mp 90—100 °C/1.0 mmHg. ^{1}H NMR ($CDCl_3$ δ=2.77 (S, 2 CH_3), 5.17 (d, =CH), 6.76 (d, =CH), 7.20 (m, 5 H).

Reaction of 2e with Sulfur in the Presence of Amines. To a suspension of (2-ethoxycarbonylethyl)triphenylphosphonium bromide (2.22 g, 5 mmol) in benzene was added a solution of butyllithium (4.5 ml, 10% w/v, 7.0 mmol) in hexane at room temperature. After stirring for 1 h, morpholine (4.35 g, 50 mmol) and sulfur (0.32 g, 10 mmol) were added and the solution was refluxed for 2 h. The resulting mixture was washed with water and evaporated to give yellow oily crystals. This mixture was extracted with hexane(30 ml×3). The combined extracts were evaporated to give a yellow oil, which was distilled under reduced pressure (bulb-to-bulb distillation) to give a colorless oil of **12a**. Other reactions were carried out in a similar manner.

12a; 0.56 g (3.0 mmol, 60%), mp 80—90 °C/2.0 mmHg. ^{1}H NMR ($CDCl_3$) δ= 1.27 (t, CH_3), 2.32—2.72 (m, 8H), 3.57 (m, 4H), 4.14 (q, 2H). ^{13}C NMR ($CDCl_3$) δ=14.30 (CH_3), 32.29 (CH_2), 53,52 (CH_2), 54.07 (CH_2), 60.35 (CH_2), 66.96 (CH_2).

12b; 0.44 g (3.0 mmol, 60%), 100—110 °C/3.0 mmHg. ^{1}H NMR ($CDCl_3$) δ=1.26 (t, CH_2, J=7.08 Hz), 2.25 (s, 2CH_3), 2.55 (m, 4H), 4.15 (q, 2H, J=7.33 and 7.08 Hz). ^{13}H NMR ($CDCl_3$) δ=14.25 (CH_2), 33.05 (CH_2), 45.24 (2CH_3), 54.93 (CH_2), 60.35 (CH_2), 172.49 (C=O).

Ethyl 3-Butylaminopropionate (12c); 0. 50 g (2.9 mmol, 57%), mp 90—100 °C/2.5 mmHg. ^{1}H NMR ($CDCl_3$) δ= 0.69—1.58 (m, 7H), 1.25 (t, CH_3), 2.25—1.96 (m, 6H), 4.06 (q, 2H). Precise mass for $C_9H_{19}NO_2$; 173.1415 (cald), 173.1396 (found).

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References

1) a) G. W. Kirby and A. W. Lochead, *J. Chem. Soc., Chem. Commun.*, **1983**, 1325; b) G. W. Kirby, A. W. Lochead, G. Baldwin, and R. C. Gerald Kopez, *J. Chem. Soc., Chem. Commun.*, **1983**, 1029; *Tetrahedron*, **39**, 1487 (1983); c) E. Block and S. Ahmad, *J. Am. Chem. Soc.*, **106**, 8295 (1984); d) G. A Krafft and P. T. Meinke, *Tetrahedron Lett.*, **26**, 1947 (1985).

2) K. Okuma, Y. Tachibana, J. Sakata, T. Komiya, I. Kaneko, Y. Komiya, S. Yamamoto, and H. Ohta, *Bull. Chem. Soc. Jpn.*, **61**, 4323 (1988). K. Okuma, Y. Yamasaki, T. Komiya, Y. Komiya, Y. Kodera, and H. Ohta, *Chem. Lett.*, **1987**, 357.

3) R. Okazaki, *Nippon Kagaku Kaishi.*, **1987**, 1142.

4) K. Okuma, Y. Komiya, and H. Ohta, *Chem. Lett.*, **1988**, 1145.

5) B. Milligan and J. M. Swan, *J. Am. Chem. Soc.*, **81**, 2969 (1959)

6) F. Asinger, W. Schäfer, K. Halcour, A. Saus, and H. Triem, *Angew. Chem., Int. Ed. Engl.*, **3**, 19 (1964), and references cited therein.

7) R. Meyer and K. Gewald, *Angew. Chem., Int. Ed. Engl.*, **6**, 294 (1967).

8) H. Fischer, A. Tiriliomis, U. Gerbing, B. Huber, and G. Müller, *J. Chem. Soc., Chem. Commun.*, **1987**, 559.

9) G. Wittig and U. Schollkopf, *Chem. Ber.*, **78**,1318 (1954).; For reviews, see J. Emsley and D. Hall,"The Chemistry of Phosphorus," Harper & Row Ltd., London (1976), pp. 274—278; A. Maecker, *Org. React., N. Y.*, **14**, 270 (1965).

10) R. W. Holley and A. D. Holley, *J. Am. Chem. Soc.*, **71**, 2124 (1949).

11) F. H. McMillan and J. A. King, *J. Am. Chem. Soc.*, **70**, 4143 (1948).

12) W. J. Horn, *J. Am. Chem. Soc.*, **43**, 2603 (1921).

13) H. Minato, K. Okuma, and M. Kobayashi, *J. Org. Chem.*, **43**, 652 (1978).

14) M. Zief and J. P. Mason, *J. Am. Chem. Soc.*, **64**, 1 (1942).

15) K. N. Campbell, C. H. Helbing, M. P. Flokowski, and B. K. Campbell, *J. Am. Chem. Soc.*, **70**, 3868 (1948).

16) C. M. Bladen, I. E. G. Fergguson, G. W. Kirby, A. W. Lochead, and D. C. McDougall, *J. Chem. Soc., Chem. Commun.*, **1983**, 423.

17) H. Böhme and G. Berg, *Chem. Ber.*, **99**, 2127 (1966).