Sulfur-Containing Heterocycles Derived by Reaction of ω-Keto Amides with *Lawesson*'s Reagent

by **Takehiko Nishio**

Department of Chemistry, University of Tsukuba, Tsukuba-shi, Ibaraki, 305-8571 Japan

The reaction of ω-keto amides with *Lawesson*'s reagent (**LR**: 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide) is described. Treatment of 3-keto amides (2-acylacetamides) **1** with **LR** gave the corresponding 3-keto thioamides **2**, along with 1,2-dithiole-3-thiones **3**. Treatment of 4-keto amides, 3-acyl propionamides **5**, with **LR** yielded five-membered heterocycles, pyrroles **6** and/or 2-aminothiophenes **7**. 5-Keto amides, 3-benzoyl butyramides **8**, reacted with **LR** to give dihydrothiopyran-2-thione **9** as the sole product, but in low yield. 2-Acylbenzamides **10** also reacted with **LR** to afford 3-mercaptoisoindolin-2-ones **11** or dihydroisobenzothiophene-1-thiones **12**.

1. Introduction. – One of the best known thionation reagents is 2,4-bis-(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide, known as *Lawesson*'s reagent (**LR**) [1]. Use of **LR** for the chemical conversion of carbonyl to thiocarbonyl compounds [1] and the synthesis of thiophenes from 1,4-dicarbonyl compounds [2] as well as thiazinones and thiazine-thiones from β-(acylamino)-α,β-unsaturated esters [3] have been well-investigated. Recently, we have reported on the direct conversion of alcohols into thiols [4] by treatment of alcohols with **LR** and novel routes to S-containing heterocycles such as tetrahydrothiophene-2-imines, tetrahydrothiophene-2-thione, tetrahydrothiopyran-2-thiones, dihydrothiazoles, and benzothiazines by the reaction of the substrates containing two functional groups, *e.g.*, ω-hydroxy amides [5] and ω-*N*-(acylamino) alcohols [6] with **LR**. To extend the use of **LR** to other bifunctional substrates, we have investigated the reaction of ω-keto amides **1**, **5**, **8**, and **10** with **LR**, and our results are described in this paper.

2. Results and Discussion. – 2.1. *Reaction of 3-Keto Amides* **1** *with* **LR**. The reaction of *N*-mono- and *N*,*N*-disubstituted 3-keto amides (2-acylacetamides) **1** with an equimolar amount of **LR** in toluene at reflux temperature under Ar for 30 min yielded 3-keto thioamides **2** as a mixture of keto and enol forms, along with 1,2-dithiole-3-thiones **3** (*Scheme 1* and *Table 1*). This result is in contrast to the reaction of the *N*-unsubstituted 3-keto amides yielding phosphorus heterocycles, reported by *Pedersen* and *Lawesson* [7]. The structures of 3-keto thioamides **2** were established on the basis of their spectral data, elemental analyses, and chemical evidence (see *Exper. Part*). The 3-keto thioamides **2a**, **b**, and **d** thus obtained were treated with MeI to give the (*Z*)-β-amino-β-(methylthio)-α,β-unsaturated ketones **4a**, **b**, and **d**, respectively, in excellent yields, for which in the ^{1}H-NMR spectrum a characteristic peak appeared as a broad *singlet* at lower field (12.20–13.52 ppm) due to the amino proton, indicating an intramolecular H-bonding between the CO and RNH groups.

Scheme 1

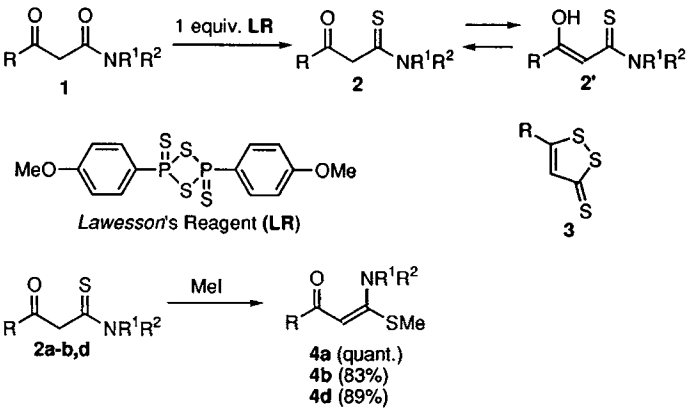


Table 1. *Yield of Products* **2** *and* **3**

	R	R^1	R^2	Yield [%][a])	
				2(**2**/**2'**)[b])	**3**
1a	Ph	Ph	H	65 (4:6)	20
1a[c])				63 (4:6)	23
1b	Ph	$PhCH_2$	H	59 (5:2)	3
1c	Ph	$PhCH_2$	$PhCH_2$	33 (1:1)	13
1d	Me	Ph	H	47 (6:4)	3
1d[c])				trace	51

[a]) Yield of the isolated product. [b]) Ratio of the keto/enol forms. [c]) In the presence of 2 equiv. of sulfur.

Pedersen and *Lawesson* have already reported that acetanilide **1d** and *N*,*N*-dimethylacetoacetamide reacted with **LR** in the presence of elemental sulfur to yield 1,2-dithiole-3-thiones **3** exclusively [7]. Therefore, the influence of elemental sulfur on the reaction of **1** with **LR** was investigated. The presence of elemental sulfur did not change the product distribution, when 3-keto amide **1a** was treated with **LR** in the presence of 2 equiv. of elemental sulfur. However, from the reaction of **1d** and **LR** in the presence of elemental sulfur, 5-methyl-3*H*-1,2-dithiole-3-thione **3d** was obtained as the sole product in 51% yield; this result is identical with published one [7].

2.2. *Reaction of 4- and 5-Keto Amides,* **5** *and* **8**, *Respectively, with* **LR**. 4-Keto amides (3-acylpropionamides) **5a**–**d** reacted with an equimolar amount of **LR** in toluene, under the same conditions as described above, to give the five-membered hererocycles, pyrroles **6a**–**d**, and 2-aminothiophenes **7a**–**d** (*Scheme 2* and *Table 2*). The yields of **7a**–**b** dropped to *ca.* one third, when 0.5 equiv. of **LR** was used in this reaction. Treatment of the 4-keto amide, 3-benzoyl-*N*-(toluene-4-yl)propionamide (**5b**), with **LR** in 1,2-dimethoxyethane (DME) at reflux temperature resulted in recovery of unchanged **5b**. Treatment of 3-benzoyl-*N*,*N*-dibenzylpropionamide (**5e**) with **LR** under the same conditions yielded 2-(dibenzylamino)-5-phenylthiophene (**7e**) exclusively. When a solution of 3-acetyl-*N*-anilinopropionamide (**5f**) and **LR** was refluxed in toluene or benzene, 2-methyl-

Scheme 2

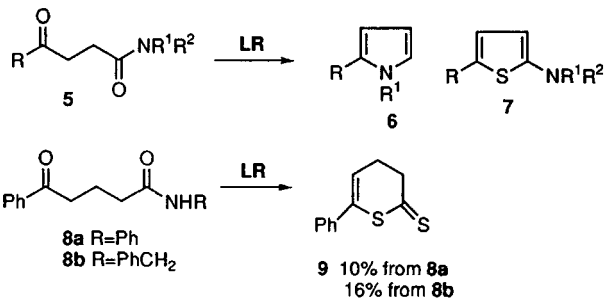


Table 2. *Yield of Products* **6** *and* **7**

	R	R^1	R^2	Solvent	Yield [%][a]) 6	7
5a	Ph	Ph	H	Toluene	48	51
5a[b])				Toluene	44	19
5b	Ph	4-CH_3–C_6H_4	H	Toluene	35	57
5b[b])				Toluene	40	18
5b				DME[c])	–[d])	–[d])
5c	Ph	4-Cl–C_6H_4	H	Toluene	36	32
5d	Ph	$PhCH_2$	H	Toluene	47	13
5e	Ph	$PhCH_2$	$PhCH_2$	Toluene		57
5f	Me	Ph	H	Toluene	25	–[e])
5f				Benzene	38	–[e])

[a]) Yield of isolated product. [b]) 0.5 equiv. of **LR** was used. [c]) 1,2-Dimethoxyethane was used as solvent. [d]) No reaction. [e]) Not isolated.

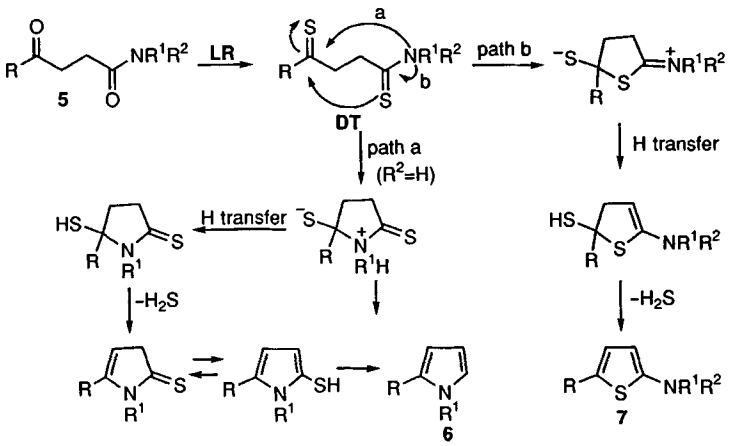
1-phenylpyrrole (**6f**) was obtained as the sole product in 25 and 38% yield, respectively. The structures of pyrroles **6** and 2-aminothiophenes **7** were elucidated on the basis of their spectral properties and elemental analyses.

A plausible mechanism for the formation of the five-membered heterocycles **6** and **7** involves initial thionation of **5** to the corresponding 4-thioxo thioamides **DT** followed by further changes shown in *Scheme 3*. A subsequent intramolecular nucleophilic attack of thioamide N-atom to thiocarbonyl group leads to cyclized product, which, after elimination of H_2S, suffers desulfurization of thioxo group [8] to pyrroles **6** (*Path a*). On the other hand, imidothiol form of **DT** undergoes a ring closure to give 2-aminothiophenes **7** (*Path b*).

On treatment of 5-keto amides, 4-benzoyl-*N*-anilinobutyramide (**8a**) and 4-benzoyl-*N*-benzylbutyramide (**8b**), with an equimolar amount of **LR**, 6-phenyl-3,4-dihydro-2*H*-thiine-2-thione (**9**) was isolated as the only isolable product, but in low yield (*cf. Scheme 2*).

2.3. *Reaction of 2-Acylbenzamides* **10** *with* **LR**. Treatment of 2-acyl-*N*-(*tert*-butyl)benzamides **10a–c** with an equimolar amount of **LR** in toluene at reflux temper-

Scheme 3



ature gave 3-mercaptoisoindolin-1-ones **11a–c** in 19–66% yield (*Scheme 4* and *Table 3*). 3-Mercaptoisoindolin-1-one **11b** was also obtained in 26% yield when a mixture of **10b** and **LR** was refluxed in benzene. The formation of **11** could be explained in terms of thermal cyclization of **10**, followed by preferential thionation of hydroxy to thiol groups [4][9]. A similar treatment of *N*-adamantyl-2-(2-phenylacetyl)benzamide (**10d**) with **LR** in toluene yielded *N*-adamantyl-3-benzylideneisoindolin-1-one (**13**). The formation of **13** could be rationalized by elimination of H_2S from 2-mercaptoisoindolin-1-one, although

Scheme 4

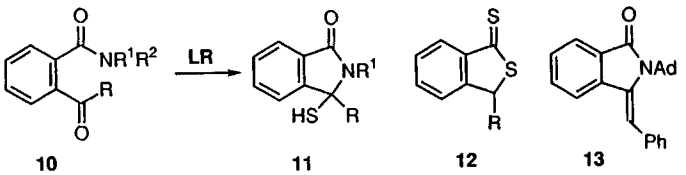


Table 3. *Yield of Products* **11–13**

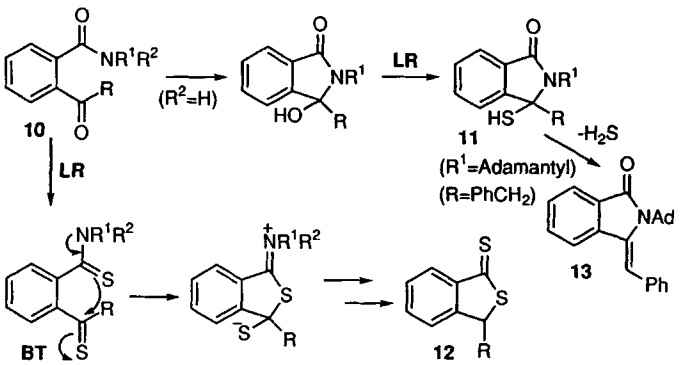
				Yield [%][a])		
	R	R^1	R^2	**11**	**12**	**13**
10a	Me	*t*-Bu	H	**11a** 53		
10b	$PhCH_2$	*t*-Bu	H	**11b** 19 (26)[b])		
10c	Ph	*t*-Bu	H	**11c** 66		
10d	$PhCH_2$	Adamantyl	H			22
10e	Ph	Et	Et		**12a** 31	
10f	$PhCH_2$	Et	Et		**12b** 22	
10g	$PhCH_2$	$PhCH_2$	$PhCH_2$		**12b** 52	

[a]) Yield of isolated product. [b]) In benzene.

this compound was not isolated. 2-Acyl-*N*,*N*-disubstituted benzamides **10e–g** were treated with **LR** in toluene at reflux temperature to yield dihydrobenzo[*c*]thiophene-1-thiones **12a, b**.

The formation of **12** could be explained in terms of the pathway depicted in *Scheme 5*. The 2-thioacyl-thiobenzamide **BT** was formed initially by thionation of **10**. The iminium thiolate form of **BT** undergoes a ring closure and then further thionation of imino to thiocarbonyl groups [1][5], leading to the dihydrobenzo[*c*]thiophene-1-thione **12**.

Scheme 5



Experimental Part

General. Chromatography: silica gel *Merck 60* and *Wakogel C-300* for flash chromatography (FC). M.p. and b.p.: *Yanaco* micro melting-point apparatus (*MP-J3*) and a *Shibata* glass tube oven distillation apparatus (*GTO-350RD*), respectively, and are uncorrected. IR Spectra: *Hitachi 260-30* spectrophotometer, in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *JEOL FX 90Q* (90 MHz) or *JEOL EX-270* (270 MHz) spectrometers; in $CDCl_3$ using Me_4Si as an internal standard; δ in ppm, J in Hz.

Reaction of ω-Keto Amides **1**, **5**, **8**, *and* **10** *with* **LR**: *General Procedure.* A soln. of ω-keto amides **1**, **5**, **8**, and **10** (2 mmol) and **LR** (2.1 mmol) in toluene (50 ml), unless otherwise noted, was heated to reflux under Ar for 15–30 min. After removal of the solvent, the residual oil was chromatographed on a silica-gel column with toluene/AcOEt 50:1–4:1 to give the products **2**, **3**, **6**, **7**, **9**, and **11–13**.

*2-Benzoyl-*N*-phenylthioacetamide* (**2a**; a 4:6 mixture of keto and enol form). M.p. 72–73°. IR (KBr): 3100, 1620, 1595, 1525, 1500, 1320, 770, 700. ^1H-NMR (for keto form **2a**): 4.63 (*s*, 2 H); 7.22–8.08 (*m*, 10 H); 10.97 (*s*, 1 H). ^1H-NMR (for enol form **2a′**): 6.26 (*s*, 1 H); 7.22–8.08 (*m*, 10 H); 8.44 (br. *s*, 1 H); 14.80 (br. *s*, 1 H). ^{13}C-NMR: 197.1 (*s*, C=S); 193.1 (*s*, C=O) for **2a**, and 191.1 (*s*, C=S) for **2a′**. Anal. calc. for $C_{15}H_{13}NOS$ (255.26): C 70.56, H 5.13, N 5.49; found: C 70.44, H 5.15, N 5.37.

*2-Benzoyl-*N*-benzylthioacetamide* (**2b**; a 5:2 mixture of keto and enol form). M.p. 83–84°. IR (KBr): 3240, 1610, 1535, 765, 740, 700. ^1H-NMR (for keto form **2b**): 4.53 (*s*, 2 H); 4.88 (*d*, J = 5.3, 2 H); 7.25–7.77 (*m*, 8 H); 8.02 (*d*, J = 7.3, 2 H); 9.42 (br. *s*, 1 H). ^1H-NMR (for enol form **2b′**): 4.83 (*d*, J = 5.3, 2 H); 5.97 (*s*, 1 H); 7.25–7.77 (*m*, 8 H); 8.02 (*d*, J = 7.3, 2 H); 14.51 (br. *s*, 1 H). ^{13}C-NMR: 196.5 (*s*, C=S); 194.4 (*s*, C=O) for **2b**, and 194.1 (*s*, C=S) for **2b′**. Anal. calc. for $C_{16}H_{15}NOS$ (269.29): C 71.34, H 5.61, N 5.20; found: C 71.11, H 5.60, N 5.15.

*2-Benzoyl-*N,N*-dibenzylthioacetamide* (**2c**; a 1:1 mixture of keto and enol form). M.p. 109–110°. IR (KBr): 1680, 1595, 1570, 1475, 765, 755, 700. ^1H-NMR (for keto form **2c**): 4.80 (*s*, 2 H); 5.37 (*d*, J = 30.5, 4 H); 7.16–7.61 (*m*, 14 H); 7.96 (*d*, J = 8.3, 1 H). ^1H-NMR (for enol form **2c′**): 4.75 (*s*, 4 H); 6.24 (*s*, 1 H); 7.16–7.61 (*m*, 14 H); 7.96 (*d*, J = 8.3, 1 H); 15.31 (br. *s*, 1 H). ^{13}C-NMR: 197.6 (*s*, C=S); 193.7 (*s*, C=O) for **2c**, and 191.2 (*s*, C=S) for **2c′**. Anal. calc. for $C_{23}H_{21}NOS$ (359.41): C 76.85, H 5.89, N 3.90; found: C 76.48, H 5.90, N 3.80.

3-Oxo-N-phenylbutanethioamide (**2d**; a 6:4 mixture of keto and enol form). M.p. 58–59°. IR (KBr): 3300, 1625, 1595, 1525, 1395, 1320, 780, 760, 730, 700. ^{1}H-NMR (for keto form **2d**): 2.33 (*s*, 3 H); 4.13 (*s*, 2 H); 7.15–7.44 (*m*, 4 H); 7.72–7.76 (*m*, 1 H); 10.85 (br. *s*, 1 H). ^{1}H-NMR (for enol form **2d'**): 1.99 (*s*, 3 H); 5.54 (*s*, 1 H); 7.15–7.44 (*m*, 4 H); 7.72–7.76 (*m*, 1 H); 8.08 (br. *s*, 1 H); 14.42 (br. *s*. 1 H). Anal. calc. for $C_{10}H_{11}NOS$ (193.20): C 62.15, H 5.75, N 7.25; found: C 61.95, H 5.7, N 7.15.

5-Phenyl-1,2-dithiole-3-thione (**3a**). M.p. 123–124° ([7]: 126°). IR (KBr): 1500, 1480, 1445, 1320, 1305, 1285, 1185, 1025, 1015, 840, 760, 960. ^{1}H-NMR: 7.35–7.69 (*m*, 6 H). ^{13}C-NMR: 126.9 (*d*); 129.6 (*d*); 131.6 (*s*); 132.2 (*d*); 136.0 (*d*); 172.9 (*s*); 215.6 (*s*).

5-Methyl-1,2-dithiole-3-thione (**3d**). M.p. ~32° ([7]: 33°). IR (KBr): 1510, 1420, 1315, 1180, 1145, 965. ^{1}H-NMR: 2.51 (*s*, 3 H); 7.01 (br. *s*, 1 H). ^{13}C-NMR: 18.3 (*q*); 139.2 (*d*); 172.2 (*s*); 216.3 (*s*).

1,2-Diphenylpyrrole (**6a**). M.p. 90–91° ([10]: 92°). IR (KBr): 1590, 1495, 1460, 760, 720, 700. ^{1}H-NMR: 6.31–6.47 (*m*, 2 H); 6.90–6.95 (*m*, 1 H); 7.01–7.41 (*m*, 10 H). ^{13}C-NMR: 109.3 (*d*); 110.7 (*d*); 124.4 (*d*); 125.7 (*d*); 126.2 (*d*); 126.5 (*d*); 128.0 (*d*); 128.2 (*d*); 128.9 (*d*); 133.0 (*s*); 133.8 (*s*); 140.5 (*s*).

2-Phenyl-5-(phenylamino)thiophene (**7a**). M.p. 113–114°. IR (KBr): 3390, 1600, 1535, 1500, 1465, 740, 690. ^{1}H-NMR: 5.61 (br. *s*, 1 H); 6.65 (*d*, *J* = 3.4, 1 H); 6.78–7.58 (*m*, 11 H). ^{13}C-NMR: 114.8 (*d*); 119.2 (*d*); 120.1 (*d*); 121.6 (*d*); 125.2 (*d*); 126.9 (*d*); 128.8 (*d*); 129.3 (*d*); 134.5 (*s*); 136.7 (*s*); 145.3 (*s*). Anal. calc. for $C_{16}H_{13}NS$ (251.29): C 76.46, H 5.21, N 5.57; found: C 76.14, H 5.21, N 5.51.

2-Phenyl-1-(toluene-4-yl)pyrrole (**6b**). B.p. 175°/3 Torr. IR (film): 1600, 1515, 1460, 1340, 820, 755, 705, 695. ^{1}H-NMR: 2.32 (*s*, 3 H); 6.29–6.45 (*m*, 2 H); 6.87–6.92 (*m*, 1 H); 6.97–7.28 (*m*, 9 H). ^{13}C-NMR: 20.9 (*q*); 109.0 (*d*); 110.4 (*d*); 124.4 (*d*); 125.5 (*d*); 126.1 (*d*); 127.9 (*d*); 128.2 (*d*); 129.5 (*d*); 133.1 (*s*); 133.7 (*s*); 136.3 (*s*); 138.1 (*s*). Anal. calc. for $C_{17}H_{15}N$ (233.30): C 87.52, H 6.48, N 6.00; found: C 87.44, H 6.58, N 6.05.

2-Phenyl-5-[(toluene-4-yl)amino]thiophene (**7b**). M.p. 128–129°. IR (KBr): 3390, 1615, 1595, 1535, 1500, 745, 685. ^{1}H-NMR: 2.27 (*s*, 3 H); 5.57 (br. *s*, 1 H); 6.60 (*d*, *J* = 3.9, 1 H); 6.81–7.57 (*m*, 10 H). ^{1}H-NMR: 20.5 (*q*); 115.3 (*d*); 117.6 (*d*); 121.6 (*d*); 125.1 (*d*); 126.8 (*d*); 128.8 (*d*); 129.8 (*d*); 134.6 (*s*); 135.7 (*s*); 142.7 (*s*); 146.3 (*s*). Anal. calc. for $C_{17}H_{15}NS$ (265.30): C 76.96, H 5.70, N 5.28; found: C 77.00, H 5.72, N 5.29.

1-(4-Chlorophenyl)-2-phenylpyrrole (**6c**). M.p. 72–73°. IR (KBr): 1590, 1490, 1460, 1415, 830, 760, 740, 720, 700. ^{1}H-NMR: 6.31–6.46 (*m*, 2 H); 6.89–6.91 (*m*, 1 H); 6.99–7.34 (*m*, 9 H). ^{13}C-NMR: 109.6 (*d*); 110.0 (*d*); 124.1 (*d*); 126.5 (*d*); 126.8 (*d*); 128.2 (*d*); 128.4 (*d*); 129.2 (*d*); 132.1 (*s*); 132.7 (*s*); 133.9 (*s*); 139.1 (*s*). Anal. calc. for $C_{16}H_{12}ClN$ (253.72): C 75.72, H 4.77, N 5.52; found: C 75.40, H 4.80, N 5.50.

2-[(4-Chlorophenyl)amino]-5-phenylthiophene (**7c**). M.p. 129–130°. IR (KBr): 3390, 1600, 1535, 1500, 815, 800, 750, 685. ^{1}H-NMR: 5.63 (br. *s*, 1 H); 6.67 (*d*, *J* = 3.9, 1 H); 6.75–6.91 (*m*, 2 H); 7.02–7.58 (*m*, 8 H). ^{13}C-NMR: 115.9 (*d*); 120.0 (*d*); 121.6 (*d*); 125.3 (*d*); 127.3 (*d*); 128.9 (*d*); 129.2 (*d*); 134.4 (*s*); 137.6 (*s*); 144.2 (*s*); 144.6 (*s*). Anal. calc. for $C_{16}H_{12}ClNS$ (285.77): C 67.24, H 4.23, N 4.90; found: C 67.21, H 4.25, N 4.90.

1-Benzyl-2-phenylpyrrole (**6d**). B.p. 175°/3 Torr. M.p. ~25°. IR (KBr): 1600, 1495, 1465, 1450, 1300, 1070, 770, 755, 720, 705, 700. ^{1}H-NMR: 5.12 (*s*, 2 H); 6.27 (*d*, *J* = 2.4, 2 H); 6.73 (*t*, *J* = 2.4, 1 H); 6.93–7.05 (*m*, 2 H); 7.17–7.36 (*m*, 8 H). ^{13}C-NMR: 50.6 (*t*); 108.5 (*d*); 108.9 (*d*); 122.9 (*d*); 126.4 (*d*); 126.9 (*d*); 127.2 (*d*); 128.3 (*d*); 128.6 (*d*); 128.8 (*d*); 133.3 (*s*); 134.9 (*s*); 138.8 (*s*). Anal. calc. for $C_{17}H_{15}N$ (223.30): C 87.52, H 6.48, N 6.00; found: C 87.21, H 6.56, N 6.11.

2-(Benzylamino)-5-phenylthiophene (**7d**). M.p. ~35°. IR (KBr): 3350, 1590, 1545, 1500, 1450, 1360, 745, 725, 695. ^{1}H-NMR: 4.04 (br. *s*, 1 H); 4.27 (*s*, 2 H); 5.96 (*d*, *J* = 3.4, 1 H); 6.93 (*d*, *J* = 3.4, 1 H); 7.02–7.49 (*m*, 10 H). ^{13}C-NMR: 51.9 (*t*); 105.0 (*d*); 122.3 (*d*); 124.5 (*d*); 125.9 (*d*); 127.6 (*d*); 127.8 (*d*); 128.7 (*d*); 135.0 (*s*); 138.5 (*s*); 154.4 (*s*). Anal. calc. for $C_{17}H_{15}NS$ (265.30): C 76.94, H 5.70, N 5.28; found: C 76.58, H 5.51, N 5.21.

2-(Dibenzylamino)-5-phenylthiophene (**7e**). M.p. 86–87°. IR (KBr): 1590, 1545, 1505, 1435, 1360, 760, 745, 735, 695. ^{1}H-NMR: 4.48 (*s*, 4 H); 5.90 (*d*, *J* = 3.9, 1 H); 6.95 (*d*, *J* = 3.9, 1 H); 7.08–7.75 (*m*, 15 H). ^{13}C-NMR: 56.8 (*t*); 104.4 (*d*); 122.7 (*d*); 124.2 (*d*); 125.6 (*d*); 127.3 (*d*); 127.5 (*d*); 127.9 (*s*); 128.5 (*d*); 128.3 (*d*); 128.6 (*d*); 135.0 (*s*); 137.3 (*s*); 157.5 (*s*). Anal. calc. for $C_{24}H_{21}NS$ (355.42): C 81.09, H 5.95, N 3.94; found: C 81.29, H 6.01, N 3.95.

2-Methyl-1-phenylpyrrole (**6f**). B.p. 140°/3 Torr ([11]: 100°/4 Torr). IR (film): 1595, 1500, 1410, 1325, 760, 695. ^{1}H-NMR: 2.20 (*s*, 3 H); 5.98–6.18 (*m*, 1 H); 6.19 (*t*, *J* = 2.9, 1 H); 6.69–6.78 (*m*, 1 H); 7.18–7.53 (*m*, 5 H). ^{13}C-NMR: 12.9 (*q*); 108.0 (*d*); 108.1 (*d*); 121.3 (*d*); 125.7 (*d*); 126.8 (*d*); 129.0 (*d*); 140.4 (*s*).

6-Phenyl-3,4-dihydrothiine-2-thione (**9**). B.p. > 200°/2 Torr (dec.). IR (film): 1680, 1615, 1595, 1485, 1445, 1240, 1160, 805, 750, 695. ^{1}H-NMR: 2.48–2.68 (*m*, 2 H); 3.02–3.18 (*m*, 2 H); 6.61 (*t*, *J* = 5.4, 1 H); 7.21–7.52 (*m*, 5 H). ^{13}C-NMR: 24.5 (*t*); 47.2 (*t*); 122.1 (*d*); 126.0 (*d*); 128.8 (*d*); 136.2 (*s*); 236.7 (*s*). MS: 206 (M^+); 173 ($[M - SH]^+$), 147, 121, 115.

2-(tert-Butyl)-3-mercapto-3-methylisoindolin-1-one (**11a**). M.p. 51–52°. IR (KBr): 2540, 1670, 1465, 1345, 1320, 1215, 765, 740, 700. ^{1}H-NMR: 1.78 (*s*, 9 H); 2.07 (*s*, 3 H); 2.58 (*s*, 1 H); 7.37–7.57 (*m*, 3 H); 7.71 (*d*, *J* = 7.6,

1 H). ^{13}C-NMR: 29.2 (*q*); 31.4 (*q*); 57.9 (*s*); 70.4 (*s*); 121.1 (*d*); 122.9 (*d*); 128.5 (*d*); 129.5 (*s*); 132.3 (*d*); 141.9 (*s*); 152.7 (*s*). Anal. calc. for $C_{13}H_{17}NOS$ (235.27): C 66.35, H 7.28, N 5.95; found: C 66.21, H 7.31, N 5.84.

*3-Benzyl-2-(*tert*-butyl)-3-mercaptoisoindolin-1-one* (**11b**). M.p. 46–47°. IR (KBr): 2540, 1665, 1460, 1445, 1345, 1325, 1205, 740, 735, 695. ^{1}H-NMR: 1.69 (*s*, 9 H); 2.72 (*s*, 1 H); 3.68 (*d*, *J* = 5.2, 1 H); 3.92 (*d*, *J* = 5.2, 1 H); 6.66 (*d*, *J* = 6.3, 2 H); 7.02–7.12 (*m*, 3 H); 7.26–7.69 (*m*, 4 H). ^{13}C-NMR: 28.7 (*q*); 47.4 (*t*); 58.0 (*s*); 73.7 (*s*); 121.9 (*d*); 123.0 (*d*); 127.2 (*d*); 128.1 (*d*); 128.7 (*d*); 129.3 (*d*); 130.4 (*s*); 132.1 (*d*); 135.1 (*d*); 151.0 (*s*); 168.5 (*s*). Anal. calc. for $C_{19}H_{21}NOS$ (311.37): C 73.29, H 6.80, N 4.50; found: C 73.38, H 6.85, N 4.48.

*2-(*tert*-Butyl)-3-mercapto-3-phenylisoindolin-1-one* (**11c**). M.p. 139–140°. IR (KBr): 2570, 1685, 1605, 1464, 1445, 1340, 1320, 1215, 760, 750, 700. ^{1}H-NMR: 1.54 (*s*, 9 H); 2.69 (*s*, 1 H); 7.02–7.06 (*m*, 1 H); 7.25–7.59 (*m*, 7 H); 7.73–7.89 (*m*, 1 H). ^{13}C-NMR: 28.7 (*q*); 58.0 (*s*); 76.2 (*s*); 121.8 (*d*); 123.0 (*d*); 126.0 (*s*); 128.2 (*d*); 128.3 (*d*); 128.7 (*d*); 132.5 (*d*); 141.2 (*s*); 153.7 (*s*); 168.7 (*s*). Anal. calc. for $C_{18}H_{19}NOS$ (297.34): C 72.72, H 6.44, N 4.71; found: C 72.63, H 6.43, N 4.83.

*3-Phenyl-1*H,*3*H-*benzo[*c*]thiophene-1-thione* (**12a**). M.p. 96–97°. IR (KBr): 1590, 1570, 1465, 1450, 1270, 1125, 1045, 900, 765, 750, 720, 700. ^{1}H-NMR: 5.97 (*s*, 1 H); 7.23–7.61 (*m*, 8 H); 8.10 (*d*, *J* = 7.8, 1 H). ^{13}C-NMR: 60.6 (*d*); 124.5 (*d*); 126.0 (*d*); 128.3 (*d*); 128.5 (*d*); 128.6 (*d*); 129.1 (*d*); 133.0 (*d*); 137.4 (*s*); 143.5 (*s*); 151.2 (*s*); 227.7 (*s*). Anal. calc. for $C_{14}H_{10}S_2$ (242.22): C 69.42, H 4.13; found: C 69.22, H 4.16.

*3-Benzyl-1*H,*3*H-*benzo[*c*]thiophene-1-thione* (**12b**). M.p. 82–83°. IR (KBr): 1595, 1570, 1490, 1465, 1260, 1125, 1045, 900, 770, 750, 700. ^{1}H-NMR: 3.04 (*A* of *ABX*, *J* = 9.9, 13.8, 1 H); 3.53 (*B* of *ABX*, *J* = 5.3, 13.8, 1 H); 5.09 (*X* of *ABX*, *J* = 5.3, 9.9, 1 H); 7.21–7.50 (*m*, 7 H); 7.57–7.64 (*m*, 1 H); 8.00–8.04 (*m*, 1 H). ^{13}C-NMR: 41.6 (*t*); 58.5 (*d*); 124.6 (*d*); 124.8 (*d*); 127.2 (*d*); 128.7 (*d*); 129.1 (*d*); 132.6 (*d*); 137.6 (*s*); 143.9 (*s*); 150.0 (*s*); 227.5 (*s*). Anal. calc. for $C_{15}H_{12}S_2$ (256.25): C 70.27, H 4.72; found: C 70.06, H 4.71.

2-Adamantyl-3-benzylideneisoindolin-1-one (**13**). M.p. 72–73°. IR (KBr): 1700, 1630, 1475, 1445, 1315, 1300, 835, 770, 725, 695. ^{1}H-NMR: 1.65–1.85 (*m*, 6 H); 2.22 (br. *s*, 3 H); 2.70 (br. *s*, 5 H); 6.76 (*d*, *J* = 7.9, 1 H); 7.10–7.47 (*m*, 8 H); 7.71 (*d*, *J* = 7.6, 1 H). ^{13}C-NMR: 30.2 (*d*); 36.4 (*t*) 41.2 (*t*); 60.8 (*s*); 115.2 (*d*); 122.6 (*d*); 123.1 (*d*); 127.6 (*d*); 128.5 (*d*); 128.8 (*d*); 129.5 (*d*); 130.9 (*d*); 135.6 (*s*); 136.5 (*s*); 136.9 (*s*); 168.3 (*s*). Anal. calc. for $C_{25}H_{25}NO$ (355.46): C 84.47, H 7.09, N 3.94; found: C 84.11, H 7.12, N 3.95.

Methylation of 3-Keto Thioamides **2a**, **b**, *and* **d** *with MeI.* To a soln. of 3-keto thioamides **2a**, **b**, and **d** (1 mmol) in acetone (15 ml) in the presence of K_2CO_3 (1.1 mmol), a soln. of MeI (2 mmol) in acetone (5 ml) was added, and then the mixture was stirred at r.t. for 2 h. The usual workup gave *β*-amino-*β*-(methylthio)-*α*,*β*-unsaturated ketones **4a**, **b**, and **d**.

3-(Methylthio)-1-phenyl-3-(phenylamino)prop-2-en-1-one (**4a**). M.p. 55–56° ([12]: 56–57°). IR (KBr): 1590, 1550, 1475, 1430, 1275, 740, 715, 700. ^{1}H-NMR: 2.41 (*s*, 3 H); 5.88 (*s*, 1 H); 7.19–7.47 (*m*, 8 H); 7.88–7.93 (*m*, 2 H); 13.52 (br. *s*, 1 H). ^{13}C-NMR: 14.8 (*q*); 88.7 (*d*); 125.2 (*d*); 126.4 (*d*); 127.0 (*d*); 128.3 (*d*); 129.0 (*d*); 130.9 (*d*); 138.2 (*s*); 140.2 (*s*); 167.6 (*s*); 186.1 (*s*).

3-(Benzylamino)-3-(methylthio)-1-phenylprop-2-en-1-one (**4b**). M.p. 65–66°. IR (KBr): 1585, 1550, 1465, 1430, 1270, 765, 740, 695. ^{1}H-NMR: 2.34 (*s*, 3 H); 4.53 (*d*, *J* = 5.9, 2 H); 5.68 (*s*, 1 H); 7.18–7.38 (*m*, 8 H); 7.83–7.88 (*m*, 2 H); 12.20 (br. *s*, 1 H). ^{13}C-NMR: 14.3 (*q*); 47.7 (*t*); 86.7 (*d*); 126.9 (*d*); 127.2 (*d*); 127.5 (*d*); 128.2 (*d*); 128.5 (*d*); 130.5 (*d*); 137.1 (*s*); 140.5 (*s*); 169.5 (*s*); 185.3 (*s*). Anal. calc. for $C_{17}H_{17}NOS$ (283.32): C 72.05, H 6.05, N 4.94; found: 71.74, H 5.91, N 4.80.

4-(Methylthio)-4-(phenylamino)but-3-en-2-one (**4d**). B.p. 250°/3 Torr. IR (film): 3450, 1585, 1465, 1630, 1270, 765, 740, 695. ^{1}H-NMR: 2.13 (*s*, 3 H); 2.29 (*s*, 3 H); 5.18 (*s*, 1 H); 7.16–7.36 (*m*, 5 H); 12.94 (br. *s*, 1 H). ^{13}C-NMR: 14.5 (*q*); 29.2 (*q*); 91.6 (*d*); 125.2 (*d*); 126.2 (*d*); 128.9 (*d*); 138.2 (*s*); 165.9 (*s*); 193.0 (*s*). Anal. calc. for $C_{11}H_{13}NOS$ (207.22): C 63.74, H 6.32, N 6.76; found: C 63.46, H 6.25, N 6.69.

REFERENCES

[1] M. P. Cava, M. I. Levinson, *Tetrahedron* **1985**, *41*, 5061.

[2] D. R. Schridhar, M. Jogibhukta, P. S. Rao, V. K. Handa, *Synthesis* **1982**, 1061; *Indian J. Chem.* **1983**, 1187; T. Nishio, N. Okuda, C. Kashima, *J. Heterocycl. Chem.* **1988**, *25*, 1437.

[3] R. Shabana, J. B. Rasmussen, S.-O. Lawesson, *Tetrahedron* **1981**, *37*, 1819; K. Clausen, S.-O. Lawesson, *Bull. Soc. Chim. Belg.* **1979**, *88*, 305; *Nouv. J. Chem.* **1980**, *4*, 43.

[4] T. Nishio, *J. Chem. Soc., Chem. Commun.* **1989**, 205; *J. Chem. Soc., Perkin Trans. 1* **1993**, 1113.

[5] T. Nishio, *Tetrahedron Lett.* **1995**, *36*, 6113.

[6] T. Nishio, *J. Org. Chem.* **1997**, *62*, 1106.

[7] B. S. Pedersen, S.-O. Lawesson, *Tetrahedron* **1979**, *35*, 2433.

[8] T. Nishio, N. Okuda, C. Kashima, *J. Chem. Soc., Perkin Trans. 1* **1992**, 899.
[9] T. Nishio, N. Okuda, Y. Mori, C. Kashima, *Synthesis* **1989**, 396.
[10] K. E. Schulte, J. Reisch, H. Walker, *Chem. Ber.* **1965**, *98*, 98.
[11] T. Tsuchiya, H. Arai, H. Igeta, *Chem. Pharm. Bull.* **1973**, *21*, 1516.
[12] A. Kumar, V. Aggarwal, H. Ila, H. Juniappa, *Synthesis* **1980**, 748.

Received March 30, 1998