Thionation of *N*-(ω-Halogenoalkyl)-Substituted Amides with *Lawesson*'s Reagent: Facile Synthesis of 4,5-Dihydro-1,3-thiazoles and 5,6-Dihydro-4*H*-1,3-thiazines

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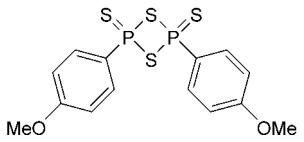
The thionation and cyclization of *N*-(ω-halogenoalkyl)-substituted amides (and related compounds) with *Lawesson*'s reagent (LR = 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide) has been investigated. Treatment of the amides **1** with LR gave the corresponding thioamides **2** in moderate to good yields (*Table*). The latter, upon treatment with base, afforded, either in a separate step or in a one-pot procedure, the cyclized title compounds, *i.e.*, the 4,5-dihydro-1,3-thiazoles **3** or the corresponding 5-6-dihydro-4*H*-thiazines **4** *via* dehydrohalogenation.

Introduction. – '1,3-Thiazolines' (=4,5-dihydro-1,3-thiazoles) and 1,3-thiazines are a class of heterocycles that have received considerable attention due to their interesting biological activities. Consequently, a number of methods for the synthesis of these compounds have been reported [1]. The well-known *Lawesson*'s reagent (LR = 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide), one of the best thionation reagents, converts a wide range of carbonyls to thiocarbonyl compounds [2].



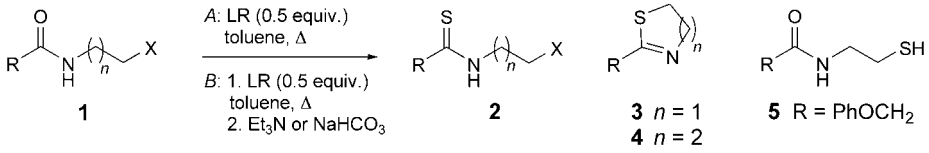
Lawesson's reagent (LR)

Several S- [3] and P-containing [4] heterocycles have been synthesized by reacting LR with the compounds possessing multiple funtional groups. We have reported that LR can be used for the direct conversion of alcohols to thiols [5], as well as for a novel synthesis of S-containing heterocycles by reaction of LR with substrates containing two functional groups, *e.g.*, hydroxy amides [3g,h], acylamino alcohols [3g,h,l,p], acylamino ketones [3n,q], and oxo amides [3m]. To extend the scope of such reactions with LR, we have now investigated *N*-(ω-halogenoalkyl)-substituted amides of type **1** as substrates (and related compounds) for the synthesis of S-containing 5- and 6-membered heterocycles.

Results and Discussion. – The reaction of the *N*-(ω-halogenoalkyl)amides **1a**–**1h**, **1j**, **1l**, and **1m** with 0.5 equiv. of LR in toluene at reflux temperature under Ar gas for 60 min yielded the corresponding halogenated thioamides **2a**–**2h**, **2j**, **2l**, and **2m** as the sole products in yields of 40–86% (*Table*). Treatment of compounds **2b** and **2e** with

Et_3N in toluene then afforded the cyclized products, *i.e.*, 4,5-dihydro-2-(phenoxymethyl)-1,3-thiazole (**3a**) and 5,6-dihydro-2-(phenoxymethyl)-4*H*-1,3-thiazine (**4d**) in quantitative yields, respectively. Analogously, the corresponding thiazoles **3a**, **g**, **h**, **j**, **l**, **n**, **p** and thiazines **4d**, **i**, **k**, **m**, **o**, **q** were produced, when the corresponding substrates **1a**–**1q** were exposed, in an one-pot procedure, to LR, followed by *in situ* treatment with base (Et_3N or $NaHCO_3$).

Table. *Specification of Substrates* **1** *and Yields of Products* **2**–**4**. For synthetic details, see the *Exper. Part*.



Entry	No.	R	*n*	X	Method	Isolated Yield [%]		
						2	**3**	**4**
1	**1a**	$PhOCH_2$	1	Cl	*A*	85	–	–
2	**1a**	$PhOCH_2$	1	Cl	*B*	–	77	–
3	**1a**	$PhOCH_2$	1	Cl	*B*[a])	–	42[b])	–
4	**1b**	$PhOCH_2$	1	Br	*A*	86	–	–
5	**1b**	$PhOCH_2$	1	Br	*B*	–	71	–
6	**1b**	$PhOCH_2$	1	Br	*A*[c])	54	–	–
7	**1b**	$PhOCH_2$	1	Br	*B*[a])	–	51[d])	–
8	**1c**	$PhOCH_2$	1	I	*A*	86	–	–
9	**1c**	$PhOCH_2$	1	I	*B*	–	60	–
10	**1d**	$PhOCH_2$	2	Cl	*A*	79	–	–
11	**1d**	$PhOCH_2$	2	Cl	*B*	–	–	85
12	**1d**	$PhOCH_2$	2	Cl	*B*[a])	–	–	44
13	**1e**	$PhOCH_2$	2	Br	*A*	81	–	–
14	**1e**	$PhOCH_2$	2	Br	*B*	–	–	78
15	**1e**	$PhOCH_2$	2	Br	*B*[a])	–	–	57
16	**1f**	$PhOCH_2$	2	I	*A*	77	–	–
17	**1f**	$PhOCH_2$	2	I	*B*	–	–	68
18	**1g**	$PhCH_2$	1	Cl	*A*	48	–	–
19	**1g**	$PhCH_2$	1	Cl	*B*	–	76	–
20	**1h**	Ph	1	Cl	*A*	40	–	–
21	**1h**	Ph	1	Cl	*B*	–	83	–
22	**1i**	Ph	2	Cl	*B*	–	–	84
23	**1j**	$4-Me-C_6H_4$	1	Cl	*A*	44	–	–
24	**1j**	$4-Me-C_6H_4$	1	Cl	*B*	–	76	–
25	**1k**	$4-Me-C_6H_4$	2	Cl	*B*	–	–	79
26	**1l**	$4-Cl-C_6H_4$	1	Cl	*A*	63	–	–
27	**1l**	$4-Cl-C_6H_4$	1	Cl	*B*	–	81	–
28	**1m**	$4-Cl-C_6H_4$	2	Cl	*A*	55	–	–
29	**1m**	$4-Cl-C_6H_4$	2	Cl	*B*	–	–	85
30	**1n**	2-Thienyl	1	Cl	*B*	–	84	–
31	**1o**	2-Thienyl	2	Cl	*B*	–	–	87
32	**1p**	2-Furyl	1	Cl	*B*	–	88	–
33	**1q**	2-Furyl	2	Cl	*B*	–	–	93

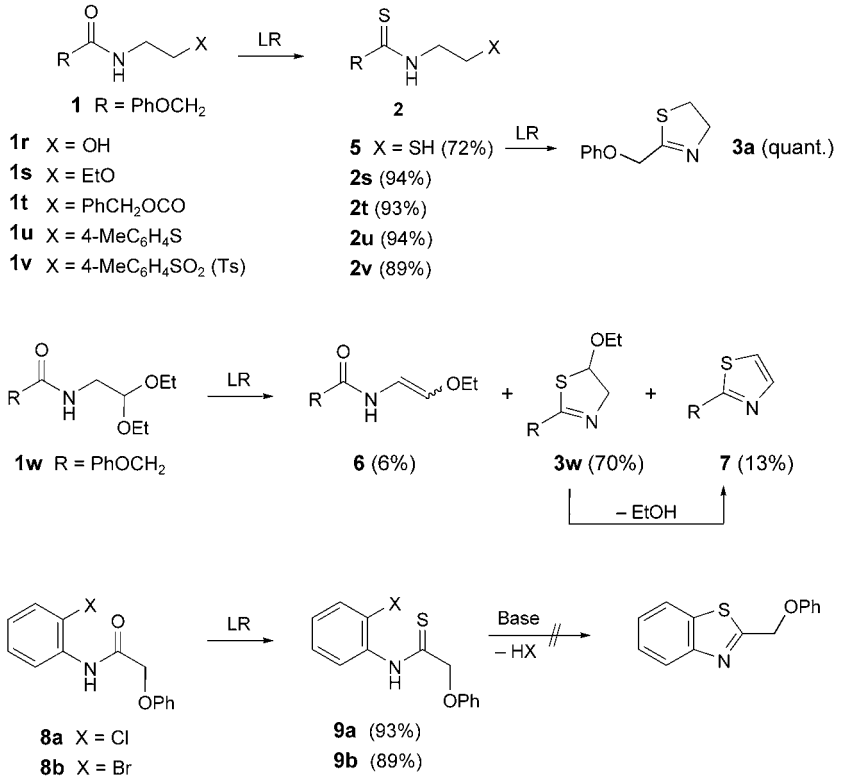
[a]) Treatment of **1** with P_2S_5 (0.5 equiv.) instead of LR, followed by addition of Et_3N (5 equiv.) *in situ*. [b]) Together with 16% of **5**. [c]) P_2S_5 (0.5 equiv.) was used instead of LR. [d]) Together with 15% of **5**.

Djerassi and *Scholz* have reported that treatment of *N*-(2-bromoethyl)-2-phenoxyacetamide (**1b**; $n=1$) and its homolog **1e** ($n=2$) with P_2S_5 in refluxing toluene gave the thiazole **3a** and the thiazine **4d** in 9 and 37% yield, respectively [6]. Therefore, we re-examined the reaction of **1b** with P_2S_5. In our hands, treatment of **1b** with P_2S_5 yielded the open-chain thio derivative **2b** as the sole product in 54% yield (*Entry 6* in the *Table*). However, the 4,5-dihydro-1,3-thiazole **3a** was obtained after the usual workup (extraction) of the reaction mixture. Compound **3a** was also produced in 51% yield when **1b** was treated with P_2S_5, followed by addition of base (one-pot procedure; *Entry 7*). In a similar manner, compounds **3a** and **4d**, derived from **1a** and from **1d** or **1e**, respectively, were obtained upon treatment with P_2S_5; however, in moderate yields only (*Entries 3*, *12*, and *15*). A small amount of the sulfanyl derivative **5**, which was probably formed by hydrolysis of **2a**, was produced in the reaction of compounds **1a**,**b** with P_2S_5 and base.

A reasonable mechanism for the formation of five- and six-membered heterocycles of type **3** and **4**, respectively, involves initial thionation of the *N*-(halogenoalkyl) amides **1** to the corresponding thioamides, followed by dehydrohalogenation and intramolecular cyclization upon treatment with base.

Next, we investigated substrates with non-halogen leaving groups (X; see *Scheme*), namely the β-hydroxy (**1r**), β-ethoxy (**1s**), β-(benzyloxycarbonyl) (**1t**), β-[(4-methyl-

Scheme



phenyl)sulfanyl] (**1u**), β-[(4-methylphenyl)sulfonyl] (**1v**), and β,β-diethoxy (**1w**) analogs. Compound **1r** was treated with 0.5 equiv. of LR under the same condition as described above to give *N*-(2-mercaptoethyl)-2-phenoxyacetamide (**5**) in 72% yield. Further treatment of **5** with LR gave the cyclized dihydrothiazole **3a** in almost quantitative yield; this result is identical with those previously published [3o,p]. Treatment of **1s**–**1v** with LR afforded the corresponding thioacetamide derivatives **2s**–**2v** in good yields. However, these 'intermediates' could not be cyclized, not even upon treatment with base.

In the case of *N*-(2,2-diethoxyethyl)-2-phenoxyacetamide (**1w**), exposure to LR afforded a mixture of the thiazole **7** (13%), the 2-ethoxyvinyl derivative **6** (7%), and the 4,5-dihydro-5-ethoxy-1,3-thiazole **3w** (70%; *Scheme*). Thereby, the latter compound would be readily converted to **7** upon treatment with base (elimination of EtOH). In contrast, treatment of the *N*-(2-halogenophenyl)-2-phenoxyacetamides **8** with LR gave the corresponding thioacetamides **9** exclusively (*Scheme*).

Conclusions. – We have developed a one-pot procedure for the facile synthesis of 4,5-dihydro-1,3-thiazoles (**3**) and 5,6-dihydro-4*H*-1,3-thiazines (**4**). These compounds can be readily accessed by treatment of *N*-(ω-halogenoalkyl)-substituted amides with *Lawesson*'s reagent (LR), followed by addition of base.

Experimental Part

General. Flash-column chromatography (FC): *Wakogel C-300* and *Merck 60* silica gel. M.p.: *Yanaco MP-J3* micro-melting-point apparatus; uncorrected. B.p.: *Shibata GTO-350-RD* glass-tube-oven distillation apparatus. IR Spectra: *Jasco FT/IR-300* spectrophotometer; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Jeol JNM-EX-270* (270/67.5 MHz) or *Varian Gemini-200* (200/50 MHz); in $CDCl_3$, unless otherwise noted, with Me_4Si as internal standard; δ in ppm, *J* in Hz.

General Procedure (*Method A*) *for the Thionation of* N-*(ω-halogenoalkyl)acetamides*. A soln. of the substrate **1** (2 mmol) and *Lawessson*'s reagent (LR; 1 mmol)[1]) in toluene (20 ml) was heated to reflux under Ar gas for 1 h. After removal of the solvent, the residue was subjected to FC (SiO_2; toluene/AcOEt 2:1) or recrystallized (MeOH/AcOEt) to afford the thioamides **2** (see *Table*).

General Procedure (*Method B*) *for the One-Pot Cyclization of* N-*(ω-halogenoalkyl)acetamides*. A soln. of the substrate **1** (2 mmol) and LR (1 mmol) in toluene (20 ml) was heated to reflux under Ar gas for 1 h. After cooling down to r.t., Et_3N (5 ml) or a sat. aq. $NaHCO_3$ soln. (5 ml) was added, and this mixture was stirred for 30–60 min (TLC control). Usual workup (extraction) and purification by FC or recrystallization afforded the heterocyclic products **3** or **4** (see *Table*).

N-*(2-Chloroethyl)-2-phenoxyethanethioamide* (**2a**). M.p. 140–142°. ^1H-NMR (CD_3OD): 3.10–3.27 (*m*, 4 H); 4.89 (*s*, 2 H); 6.95–7.04 (*m*, 3 H); 7.25–7.35 (*m*, 2 H). ^{13}C-NMR (CD_3OD): 23.9; 38.4; 71.7; 113.9; 121.4; 128.8; 157.2; 197.6.

4,5-Dihydro-2-(phenoxymethyl)-1,3-thiazole (**3a**). B.p. 160°/3 Torr[2]). ^1H-NMR: 3.31 (*t*, *J* = 8.4, 2 H); 4.32 (*t*, *J* = 8.4); 4.89 (*s*, 2 H); 6.94–7.03 (*m*, 3 H); 7.25–7.34 (*m*, 2 H). ^{13}C-NMR: 32.8; 64.5; 67.4; 113.6; 121.5; 129.4; 157.8; 169.5.

N-*(2-Bromoethyl)-2-phenoxyethanethioamide* (**2b**). M.p. 147–148°. ^1H-NMR (CD_3OD): 3.88 (*t*, *J* = 9.2, 2 H); 4.51 (*t*, *J* = 9.2, 2 H); 5.37 (*s*, 2 H); 7.04–7.09 (*m*, 3 H); 7.32–7.38 (*m*, 2 H). ^{13}C-NMR (CD_3OD): 33.8; 56.0; 67.5; 116.8; 124.6; 131.7; 159.0; 196.3. Anal. calc. for $C_{10}H_{12}BrNOS$: C 43.80, H 4.41, N 5.11; found: C 43.58, H 4.60, N 4.98.

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[1]) Alternatively, P_2S_5 (1 mmol) can be used.

[2]) M.p. of the corresponding picrate: 177–179° [6].

N-*(2-Iodoethyl)-2-phenoxyethanethioamide* (**2c**). M.p. 190–192°. ^{1}H-NMR (CD_3OD): 3.86 (*t*, *J* = 9.4, 2 H); 4.50 (*t*, *J* = 9.4, 2 H); 4.50 (*t*, *J* = 9.4, 2 H); 5.38 (*s*, 2 H); 6.98–7.11 (*m*, 3 H); 7.31–7.42 (*m*, 2 H). ^{13}C-NMR (CD_3OD): 33.0; 55.5; 66.8; 116.1; 123.8; 131.0; 158.3; 184.2. Anal. calc. for $C_{10}H_{12}INOS$: C 37.39, H 3.37, N 4.36; found: C 37.47, H 3,60, N 4.19.

N-*(3-Chloropropyl)-2-phenoxyethanethioamide* (**2d**). M.p. 137–139°. ^{1}H-NMR (CD_3OD): 2.19–2.29 (*m*, 2 H); 3.36 (*t*, *J* = 5.8, 2 H); 3.76 (*t*, *J* = 5.1, 2 H); 5.14 (*s*, 2 H); 6.89–7.07 (*m*, 3 H); 7.28–7.36 (*m*, 2 H). ^{13}C-NMR (CD_3OD): 17.6; 25.7; 41.9; 67.6; 114.2; 122.0; 129.0; 154.2; 188.8.

*5,6-Dihydro-2-(phenoxymethyl)-4*H*-1,3-thiazine* (**4d**). B.p. 145°/3 Torr[2]). ^{1}H-NMR: 1.78–1.91 (*m*, 2 H); 3.02 (*t*, *J* = 5.9, 2 H); 3.73 (*t*, *J* = 5.9, 2 H); 4.63 (*s*, 2 H); 6.89–7.02 (*m*, 3 H); 7.26–7.36 (*m*, 2 H). ^{13}C-NMR: 18.7; 25.1; 46.6; 72.2; 114.3; 120.8; 128.9; 157.6; 158.7.

N-*(3-Bromopropyl)-2-phenoxyethanethioamide* (**2e**). M.p. 136–137°. ^{1}H-NMR (CD_3OD): 2.24–2.36 (*m*, 2 H); 3.41 (*t*, *J* = 6.0, 2 H); 3.82 (*t*, *J* = 5.5, 2 H); 5.19 (*s*, 2 H); 6.93–7.10 (*m*, 3 H); 7.30–7.40 (*m*, 2 H). ^{13}C-NMR (CD_3OD): 18.3; 26.5; 42.2; 68.0; 114.9; 122.8; 156.4; 185.3. Anal. calc. for $C_{11}H_{14}BrNOS$: C 45.84, H 4.90, N 4.86; found: C 45.73, H 4.96, N 4.86.

N-*(3-Iodopropyl)-2-phenoxyethanethioamide* (**2f**). M.p. 138–140°. ^{1}H-NMR (CD_3OD): 2.25–2.38 (*m*, 2 H); 3.43 (*t*, *J* = 5.6, 2 H); 3.83 (*t*, *J* = 5.6, 2 H); 5.19 (*s*, 2 H); 7.03–7.10 (*m*, 3 H); 7.31–7.41 (*m*, 2 H). ^{13}C-NMR (CD_3OD): 19.8; 28.0; 44.1; 69.9; 116.4; 124.1; 131.1; 158.4; 183.4. Anal. calc. for $C_{11}H_{14}INOS$: C 37.39, H 3.77, N 4.36; found: C 37.47, H 3.75, N 4.19.

N-*(2-Chloroethyl)-2-phenylethanethioamide* (**2g**). M.p. 107–109°. ^{1}H-NMR (CD_3OD): 3.68 (*t*, *J* = 9.3, 2 H); 4.41 (*s*, 2 H); 4.55 (*t*, *J* = 9.3, 2 H); 7.25–7.38 (*m*, 5 H). ^{13}C-NMR (CD_3OD): 31.6; 37.8; 54.3; 128.8; 129.4; 132.3; 195.4.

4,5-Dihydro-2-(phenylmethyl)-1,3-thiazole (**3g**). B.p. 115°/3 Torr ([7]: 137–139°/6 Torr). ^{1}H-NMR: 3.26 (*t*, *J* = 8.4, 2 H); 3.82 (*s*, 2 H); 4.24 (*t*, *J* = 8.4, 2 H); 7.21–7.38 (*m*, 5 H). ^{13}C-NMR: 33.5; 40.1; 64.0; 126.5; 128.0; 128.5; 135.5; 170.0.

N-*(2-Chloroethyl)benzenecarbothioamide* (**2h**). M.p. 118–120°. ^{1}H-NMR: 3.83 (*t*, *J* = 8.9, 2 H); 4.72 (*t*, *J* = 8.9, 2 H); 6.18 (br. *s*, 1 H); 7.55–7.63 (*m*, 2 H); 7.71–7.85 (*m*, 1 H); 8.24–8.29 (*m*, 2 H). ^{13}C-NMR (CD_3OD): 31.1; 55.3; 125.5; 129.8; 130.6; 136.5; 185.8.

4,5-Dihydro-2-phenyl-1,3-thiazole (**3h**). B.p. 110°/3 Torr (lit. b.p. 105–107°/2 Torr [7]). ^{1}H-NMR: 3.42 (*t*, *J* = 8.4, 2 H); 4.46 (*t*, *J* = 8.4, 2 H); 7.36–7.51 (*m*, 3 H); 7.82–7.88 (*m*, 2 H). ^{13}C-NMR: 33.6; 65.2; 128.5; 131.2; 133.3; 157.4; 168.6.

*5,6-Dihydro-2-phenyl-4*H*-1,3-thiazine* (**4i**). B.p. 125°/3 Torr (lit. b.p. 124°/1.5 Torr [8]). ^{1}H-NMR: 1.86–1.98 (*m*, 2 H); 3.16 (*t*, *J* = 6.0, 2 H); 3.92 (*t*, *J* = 5.4, 2 H); 7.32–7.46 (*m*, 3 H); 7.71–7.81 (*m*, 2 H). ^{13}C-NMR: 19.1; 26.5; 48.0; 126.3; 128.3; 130.4; 139.6; 158.3.

N-*(2-Chloroethyl)-4-methylbenzenecarbothioamide* (**2j**). M.p. 115–117°. ^{1}H-NMR: 2.46 (*s*, 3 H); 3.82 (*t*, *J* = 8.8, 2 H); 4.69 (*t*, *J* = 8.6, 2 H); 7.38 (*d*, *J* = 8.1, 2 H); 8.17 (*d*, *J* = 8.1, 2 H). ^{13}C-NMR: 22.1; 30.9; 54.6; 122.7; 130.5; 130.8; 148.7; 185.9.

4,5-Dihydro-2-(4-methylphenyl)-1,3-thiazole (**3j**). M.p. 39.5–40.5° (lit. m.p. 41.5–42.5° [9]). ^{1}H-NMR: 2.38 (*s*, 3 H); 3.39 (*t*, *J* = 8.3, 2 H); 4.44 (*t*, *J* = 8.3, 2 H); 7.20 (*d*, *J* = 8.1, 2 H); 7.72 (*d*, *J* = 8.1, 2 H). ^{13}C-NMR: 21.4; 33.6; 65.2; 128.4; 129.2; 130.7; 141.6; 168.4.

*5,6-Dihydro-2-(4-methylphenyl)-4*H*-1,3-thiazine* (**4k**). M.p. 44–45°. ^{1}H-NMR: 1.84–1.93 (*m*, 2 H); 2.36 (*s*, 3 H); 3.14 (*t*, *J* = 6.1, 2 H); 3.90 (*t*, *J* = 6.1, 2 H); 6.17 (*d*, *J* = 8.1, 2 H); 7.67 (*d*, *J* = 8.1, 2 H). ^{13}C-NMR: 19.2; 21.3; 26.5; 47.9; 126.2; 129.0; 136.8; 140.8; 158.4. Anal. calc. for $C_{11}H_{13}NS$: C 69.09, H 6.85, N 7.33; found: C 68.97, H 6.58, N 7.11.

4-Chloro-N-*(2-chloroethyl)benzenecarbothioamide* (**2l**). M.p. 101–102°. ^{1}H-NMR: 3.89 (*t*, *J* = 9.0, 2 H); 4.70 (*t*, *J* = 9.0, 2 H); 7.58 (*d*, *J* = 8.8, 2 H); 8.17 (*d*, *J* = 8.8, 2 H). ^{13}C-NMR: 31.4; 54.9; 123.8; 130.2; 131.7; 143.6; 185.6.

2-(4-Chlorophenyl)-4,5-dihydro-1,3-thiazole (**3l**). M.p. 50–51° ([9]: 53.5–55°). ^{1}H-NMR: 3.42 (*t*, *J* = 8.4, 2 H); 4.45 (*t*, *J* = 8.4, 2 H); 7.38 (*d*, *J* = 8.6, 2 H); 7.76 (*d*, *J* = 8.6, 2 H). ^{13}C-NMR: 33.9; 65.2; 128.4; 128.7; 129.6; 131.7; 137.1; 167.2.

4-Chloro-N-*(3-chloropropyl)benzenecarbothioamide* (**2m**). M.p. 135–137°. ^{1}H-NMR: 2.27–2.39 (*m*, 2 H); 3.44 (*t*, *J* = 5.8, 2 H); 4.04 (*t*, *J* = 5.8, 2 H); 7.52 (*d*, *J* = 8.6, 2 H); 8.03 (*d*, *J* = 8.6, 2 H). ^{13}C-NMR: 18.6; 28.0; 43.2; 129.3; 129.5; 129.9; 141.9, 178.9.

*2-(4-Chlorophenyl)-5,6-dihydro-4*H*-1,3-thiazine* (**4m**). B.p. 140°/3 Torr. ^{1}H-NMR: 1.84–1.97 (*m*, 2 H); 3.15 (*t*, *J* = 5.8, 2 H); 3.90 (*t*, *J* = 5.8, 2 H); 7.34 (*d*, *J* = 8.6, 2 H); 7.72 (*d*, *J* = 8.6, 2 H). ^{13}C-NMR: 19.0; 26.5; 48.0; 127.5; 128.4; 136.2; 137.9; 156.8. Anal. calc. for $C_{10}H_{10}ClNS$: C 56.73, H 4.67, N 6.67; found: C 56.76, H 4.92, N 6.33.

4,5-Dihydro-2-(2-thienyl)-1,3-thiazole (**3n**). M.p. 41–42° ([9]: 40.5–41.5°). ^{1}H-NMR: 3.15 (*t*, *J* = 8.2, 2 H); 4.39 (*t*, *J* = 8.2, 2 H); 7.06 (*dd*, *J* = 3.8, 5.6, 1 H); 7.42–7.46 (*m*, 2 H). ^{13}C-NMR: 34.4; 64.7; 127.6; 129.7; 130.8; 137.1; 161.7.

*5,6-Dihydro-2-(2-thienyl)-4*H*-1,3-thiazine* (**4o**). M.p. 60.5–62.5°. ^{1}H-NMR: 1.86–1.98 (*m*, 2 H); 3.14 (*t*, *J* = 6.0, 2 H); 3.86 (*t*, *J* = 6.0, 2 H); 7.01 (*dd*, *J* = 3.6, 5.0, 2 H); 7.33–7.37 (*m*, 2 H); 7.43–7.46 (*m*, 1 H). ^{13}C-NMR: 19.1; 25.8; 47.2; 125.7; 126.7; 127.5; 143.5; 151.5. Anal. calc. for $C_8H_9NS_2$: C 52.46, H 4.95, N 7.65; found: C 52.12, H 4.91, N 7.47.

2-(2-Furyl)-4,5-dihydro-1,3-thiazole (**3p**) [10]. Oil. ^{1}H-NMR: 3.40 (*t*, *J* = 8.2, 2 H); 4.42 (*t*, *J* = 8.2, 2 H); 6.49 (*dd*, *J* = 1.6, 3.6, 1 H); 6.91 (*d*, *J* = 3.6, 1 H); 7.53 (*d*, *J* = 1.6, 1 H). ^{13}C-NMR: 33.0; 64.3; 111.4; 113.4; 147.7; 157.7.

*2-(2-Furyl)-5,6-dihydro-4*H*-1,3-thiazine* (**4q**) [10]. Oil. ^{1}H-NMR: 1.87–1.99 (*m*, 2 H); 3.17 (*t*, *J* = 4.8, 2 H); 3.90 (*t*, *J* = 4.8, 2 H); 6.43 (*dd*, *J* = 1.8, 3.4, 1 H); 6.81 (*d*, *J* = 3.4, 1 H); 7.47 (*d*, *J* = 1.8, 1 H). ^{13}C-NMR: 19.0; 25.4; 46.9; 109.9; 110.8; 143.4; 143.5; 151.0.

Reaction of the 2-Phenoxyacetamides **1r**–**v** *Containing Non-Halogen Substituents.* A soln. of the substrate **1** (2 mmol) and LR (1 mmol) in toluene (20 ml) was heated to reflux under Ar gas for 0.5–5 h. After removal of the solvent, the residue was subjected to FC (SiO_2; toluene/AcOEt 4:1 → 2:1) to give the products **5**, **3a**, **2s**–**w**, **6**, and **7**.

N-*(2-Mercaptoethyl)-2-phenoxyethanethioamide* (**5**). B.p. 155°/3 Torr. IR (film): 3316, 2560, 1668. ^{1}H-NMR: 1.34 (*t*, *J* = 8.6, 1 H); 2.64–2.75 (*m*, 2 H); 3.49–3.59 (*m*, 2 H); 4.52 (*s*, 2 H); 6.91–7.07 (*m*, 3 H); 7.22–7.38 (*m*, 2 H). ^{13}C-NMR: 24.5; 41.8; 67.3; 114.7; 122.3; 129.9; 157.2; 168.5.

N-*(2-Ethoxyethyl)-2-phenoxyethanethioamide* (**2s**). M.p. 58–59°. ^{1}H-NMR: 1.14 (*t*, *J* = 7.0, 3 H); 3.46 (*q*, *J* = 7.0, 2 H); 3.62 (*t*, *J* = 5.2, 2 H); 4.91 (*s*, 2 H); 3.90–3.99 (*m*, 2 H); 6.88–7.07 (*m*, 3 H); 7.22–7.38 (*m*, 2 H). ^{13}C-NMR: 14.5; 44.0; 66.1; 66.8; 73.3; 114.1; 121.9; 129.4; 156.5; 196.3. Anal. calc. for $C_{12}H_{17}NO_2S$: C 60.22, H 7.16, N 5.85; found: C 60.32, H 7.33, N 6.01.

2-[(2-Phenoxyethanethioyl)amino]ethyl Phenylacetate (**2t**). B.p. 150°/3 Torr. IR (film): 3325, 1757, 1250, 1204. ^{1}H-NMR: 3.86–4.07 (*m*, 2 H); 4.46 (*t*, *J* = 5.2, 2 H); 4.91 (*s*, 2 H); 4.54 (*s*, 2 H); 4.86 (*s*, 2 H); 6.82–7.05 (*m*, 5 H); 7.22–7.36 (*m*, 5 H); 8.58 (br. *s*, 1 H). ^{13}C-NMR: 43.3; 61.9; 64.6; 73.3; 114.1; 114.4; 121.5; 122.0; 127.9; 129.5; 156.7; 168.8; 197.6.

N-*{2-[(4-Methylphenyl)sulfanyl]ethyl}-2-phenoxyethanethioamide* (**2u**). M.p. 94.5–96°. ^{1}H-NMR: 2.28 (*t*, 3 H); 3.15 (*t*, *J* = 6.1, 3 H); 3.93 (*m*, 2 H); 4.83 (*s*, 2 H); 6.88–6.94 (*m*, 2 H); 7.04–7.09 (*m*, 2 H); 7.21–7.36 (*m*, 5 H); 8.70 (br. *s*, 1 H). ^{13}C-NMR: 20.5; 32.2; 42.7; 73.3; 114.5; 121.9; 129.5; 129.6; 131.0; 137.1; 156.4; 197.4. Anal. calc. for $C_{17}H_{19}NOS_2$: C 64.31, H 6.03, N 4.41; found: C 64.18, H 6.22, N 4.52.

N-*{2-[(4-Methylphenyl)sulfonyl]ethyl}-2-phenoxyethanethioamide* (**2v**). M.p. 128–130°. ^{1}H-NMR: 2.40 (*s*, 3 H); 3.42–3.47 (*m*, 2 H); 4.13–4.19 (*m*, 2 H); 4.81 (*s*, 2 H); 6.93–7.08 (*m*, 3 H); 7.24–7.36 (*m*, 4 H); 7.71 (*d*, *J* = 8.3, 2 H); 9.12 (br. *s*, 1 H). ^{13}C-NMR: 21.6; 38.3; 53.6; 73.5; 114.9; 122.3; 127.9; 129.8; 130.2; 135.4; 145.4; 156.7; 197.5. Anal. calc. for $C_{17}H_{10}NOS_2$: C 64.31, H 6.03, N 4.41; found: C 64.18, H 6.22, N 4.52.

N-*(2-Ethoxyethenyl)-2-phenoxyethanamide* (**6**). Oil. IR (film): 3422, 1685. ^{1}H-NMR: 1.28 (*t*, *J* = 7.0, 3 H); 3.86 (*q*, *J* = 7.0, 2 H); 4.55 (*s*, 2 H); 5.73 (*d*, *J* = 4.9, 1 H); 6.19 (*dd*, *J* = 4.9, 10.6, 1 H); 6.93–7.06 (*m*, 3 H); 7.23–7.39 (*m*, 2 H); 8.26 (br. *s*, 1 H). ^{13}C-NMR: 14.6; 66.6; 67.8; 101.9; 114.2; 121.6; 129.2; 132.6; 156.6; 164.1.

2-(Phenoxymethyl)-1,3-thiazole (**7**). B.p. 125°/3 Torr[3]). ^{1}H-NMR: 5.39 (*s*, 2 H); 6.98–7.04 (*m*, 3 H); 7.21–7.31 (*m*, 2 H); 7.36 (*d*, *J* = 3.4, 1 H); 7.80 (*d*, *J* = 3.4, 1 H). ^{13}C-NMR: 66.8; 114.5; 119.5; 121.3; 129.3; 142.1; 157.5, 166.9.

5-Ethoxy-4,5-dihydro-2-(phenoxymethyl)-1,3-thiazole (**3w**). This compound easily decomposed to **7**. ^{1}H-NMR: 1.16 (*t*, *J* = 6.9, 3 H); 3.26–3.40 (*m*, 1 H); 3.47–3.59 (*m*, 1 H); 4.12–4.23 (*m*, 1 H); 4.53 (*d*, *J* = 14.3, 1 H); 4.94 (*s*, 2 H); 5.61 (*d*, *J* = 5.3, 1 H); 6.93–7.02 (*m*, 3 H); 7,23–7.37 (*m*, 2 H). ^{13}C-NMR: 13.2; 63.8; 67.4; 70,8; 90.3; 113.3; 121.2; 129.1; 157.6; 167.0.

Thionation of N-*(2-Halogenophenyl)-2-phenoxyethanamides* **8**. A soln. of **8** (2 mmol) and LR (1 mmol) in toluene (20 ml) was heated at reflux under Ar gas for 0.5–5 h (TLC control). After removal of the solvent, the residue was subjected to FC (SiO_2; toluene/AcOEt 4:1 → 2:1) to afford the corresponding thioamides **9**. The latter could *not* be cyclized in the presence of base (see *Scheme*).

N-*(2-Chlorophenyl)-2-phenoxyethanethioamide* (**9a**). M.p. 89–90°. ^{1}H-NMR: 5.00 (*s*, 2 H); 6.99–7.06 (*m*, 3 H); 7.09–7.47 (*m*, 5 H); 8.89–8.95 (*m*, 1 H); 10.33 (br. *s*, 1 H). ^{13}C-NMR: 75.0; 115.1; 122.7; 124.0; 126.5;

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[3]) M.p. of the picrate: 154–156° [11].

127.3; 127.6; 129.6; 130.0; 134.5; 156.8; 195.1. Anal. calc. for $C_{14}H_{12}ClNOS$: C 60.53, H 4.35, N 5.04; found: C 60.30, H 4.48, N 4.95.

N-*(2-Bromophenyl)-2-phenoxyethanethioamide* (**9b**). M.p. 94.5–95.5°. ^{1}H-NMR: 5.01 (*s*, 2 H); 7.07–7.19 (*m*, 4 H); 7.25–7.43 (*m*, 3 H); 7.60–7.65 (*m*, 1 H); 8.84–8.90 (*m*, 1 H); 10.30 (br. *s*, 1 H). ^{13}C-NMR: 75.0; 115.1; 116.9; 122.6; 124.5; 127.9; 128.1; 130.0; 132.9; 135.6; 156.9; 195.1. Anal. calc. for $C_{14}H_{12}BrNOS$: C 52.18, H 3.75, N 4.35; found: C 52.02, H 3.98, N 4.24.

REFERENCES

[1] A. Dondoni, P. Merino, in 'Comprehensive Heterocyclic Chemistry II', Eds. A. R. Katritzky, C. W. Rees, E. F. V. Scriven, Pergamon Press, Oxford, 1996, Vol. 3, p. 373; H. Quiniou, O. Guillton, in 'Advances in Heterocyclic Chemistry', Ed. A. R. Katritzky, Academic Press, San Diego, California, 1990, Vol. 50, p. 85; J. Liebscher, in 'Houben-Weyl', 4th ed., Ed. E. Schaumann, Thieme, Stuttgart, 1994, Vol. E8b, p. 1; M. Sainsbury, in 'Comprehensive Heterocyclic Chemistry II', Eds. A. R. Katritzky, C. W. Rees, E. F. V. Scriven, Pergamon Press, Oxford, 1996, Vol. 6, p. 301, 383.

[2] M. P. Cava, M. L. Levinson, *Tetrahedron* **1985**, *41*, 5061; R. A. Cherkasov, G. A. Kutyrev, A. N. Pudovik, *Tetrahedron* **1985**, *41*, 5061; D. Brillon, *Sulfur Rep.* **1992**, 297.

[3] a) K. Clausen, S.-O. Lawesson, *Bull. Soc. Chim. Belg.* **1979**, *88*, 305; b) K. Clausen, S.-O. Lawesson, *Nouv. J. Chim.* **1980**, *4*, 43; c) A. Ishii, J. Nakayama, M.-X. Ding, N. Kotaka, M. Hoshino, *J. Org. Chem.* **1990**, *55*, 2421; d) J. Nakayama, H. Motoyama, H. Machida, M. Shimomura, M. Hoshino, *Heterocycles* **1984**, *22*, 1527; e) A Ishii, T. Omata, K. Umezawa, J. Nakayama, *Bull. Chem. Soc. Jpn.* **2000**, *73*, 729; f) P. N. Nugara, N.-Z. Huang, M. V. Lakshmikanthan, M. P. Cava, *Heterocycles* **1991**, *32*, 1559; g) T. Nishio, *Tetrahedron Lett.* **1995**, *36*, 6113; h) T. Nishio, H. Sekiguchi, *Tetrahedron* **1999**, *55*, 5017; i) K. Kang, H. S. U, *Synth. Commun.* **1995**, *25*, 2647; j) T. Ozturk, *Tetrahedron Lett.* **1996**, *37*, 2821; k) C. W. Ong, C. M. Chen, L. F. Wang, P. C. Shieh, *Tetrahedron Lett.* **1998**, *39*, 9191; l) T. Nishio, *J. Org. Chem.* **1997**, *62*, 1106; m) T. Nishio, *Helv. Chim. Acta* **1998**, *81*, 1207; n) M. Ori, T. Nishio, *Heterocycles* **2000**, *52*, 111; o) M. Ori, T. Nishio, *Heterocycles* **2001**, *54*, 201; p) T. Nishio, Y. Konno, M. Ori, M. Sakamoto, *Eur. J. Org. Chem.* **2001**, 3553; q) T. Nishio, M. Ori, *Helv. Chim. Acta* **2001**, *84*, 2347; r) A. A. Kiryanov, P. Sampson, A. J. Seed, *J. Org. Chem.* **2001**, *66*, 7925.

[4] B. S. Pederson, S.-O. Lawesson, *Tetrahedron* **1979**, *35*, 2433; A. A. El-Barbary, K. Clausen, S.-O. Lawesson, *Tetrahedron* **1980**, *36*, 3309; A. A. El-Barbary, S.-O. Lawesson, *Tetrahedron* **1981**, *37*, 2641; S. Sheibye, S.-O. Lawesson, C. Romming, *Acta Chem. Scand., Ser. B* **1981**, *35*, 239; S. Sheibye, R. Shabana, S.-O. Lawesson, *Tetrahedron* **1982**, *38*, 993; R. Shabana, F. Osman, S. S. Atres, *Tetrahedron* **1994**, *50*, 6975; N. Duban-Assibat, A. Baceiredo, G. Betrand, *J. Org. Chem.* **1995**, *60*, 3904; R. N. Butler, E. C. Makenna, D. Grogen, *Chem. Commun.* **1997**, 2149; Y. A. Ibrahim, A. M. Kadry, M. R. Ibrahim, J. N. Lisgarten, B. S. Potter, R. A. Palmer, *Tetrahedron* **1999**, *55*, 13457; S.-L. Deng, D.-Z. Liu, *Synthesis* **2001**, 2445.

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

[6] C. Djerassi, C. T. Scholz, *J. Org. Chem.* **1950**, *15*, 694.

[7] R. Kuhn, F. Heidelberg, *Liebigs Ann. Chem.* **1954**, *590*, 55.

[8] P. A. S. Smith, J. M. Sullivan, *J. Org. Chem.* **1961**, *26*, 1132.

[9] A. K. Bose, M. S. Manhas, J. S. Chib, H. P. S. Chawanda, B. Dayal, *J. Org. Chem.* **1974**, *39*, 2877.

[10] B. George, E. P. Papadopoulos, *J. Org. Chem.* **1977**, *42*, 441.

[11] R. Vivadi, H. J. M. Dou, G. Vernin, J. Metzger, *Bull. Soc. Chim. Fr.* **1969**, *11*, 4041.

Received October 5, 2004