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Sulfur-Containing Heterocycles Derived by the Reaction of Hydroxy-Amides and Lawesson's Reagent

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Abstract: A simple one-pot reaction between hydroxy-amides (**1**), located 1,3- or 1,4- to each other, and Lawesson's reagent (**LR**) gives sulfur-containg heterocycles such as tetrahydrothiophene-2-imines (**4**), tetrahydrothiophene-2-thione (**5**) and tetrahydrothiopyran-2-thione (**6**). Similar reaction of 3-N-acylamino-alcohols (**7**) affords thiazoline derivatives (**9**).

2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiaphosphetane-2,4-disulfide, commonly known as Lawesson's reagent (**LR**), has been developed as a powerful and versatile reagent for the conversion of a wide variety of carbonyls, including amide carbonyls, to thiocarbonyl compounds.[1] The **LR** also undergoes ring-closure reaction with substrates containing two functional groups such as 3-oxo-esters and -amides, α-hydroxy-ketones, 2-hydroxybenzoic acids, and 2-acylaminobenzoates to yield phosphorus[2-6] or sulfur-containing heterocycles.[7-8] Recently we reported a novel transformation of alcohols to thiols using LR, which allows the direct conversion of the hydroxy-group into a thiol-group.[9] These results suggest that in bifunctional systems having both hydroxy and amide groups, in which they are located 1,2-, 1,3-, or 1,4- to each other, the opportunity exists for ring-closure reactions to give 5- and 6-membered sulfur-containing heterocycles. We therefore investigated the reactions between hydroxy-amides and **LR** and here report simple new routes to sulfur-containing heterocycles.

3-Hydroxy amides **1a-c** reacted with an equimolar amount of **LR** in toluene at 110 °C under argon for 0.5 h giving thioenamides **2a-c** in high yields. The reaction efficiency dropped to half when 0.5 equiv. of **LR** was used in this reaction. The formation of thioenamides **2** can be explained in terms of thionation of the amide function and dehydration. The latter process probably involves initial conversion of the hydroxy to a thiol group, followed by loss of H_2S to give the final products **2**, since **LR** has dehydrating activity toward alcohols through thiols.[9] Treatment of 4-hydroxy amides **1d-f** with an equimolar amount of **LR** gave tetrahydro-thiophene-2-imines (**4**) and tetrahydrothiophene-2-thione (**5**). When 4-hydroxy amides **1e, f** were treated with 0.5 equiv. of **LR**, 4-mercapto amides **3e, f**[10] were isolated along with products **4e, f** and **5**. The reaction of 4-mercapto amide **3f** thus obtained with **LR** under the same conditions yielded imine **4f** and thione **5** in 33 and 39% yields, respectively. The imine **4f** also reacted with **LR** to form the thione **5**. A reasonable mechanism for these reactions is outlined in Scheme 2. Based on the above findings, the hydroxy amides **1** are apparently converted to the mercapto amides **3**, which then undergo thionation followed by cyclization yielding the imines **4**. The imines **4** subsequently undergo further thionation to form the thione **5**. Similarly, 5-hydroxy amide **1g** reacted with **LR** to afford tetrahydrothiopyran-2-thione **6**.

Scheme 1

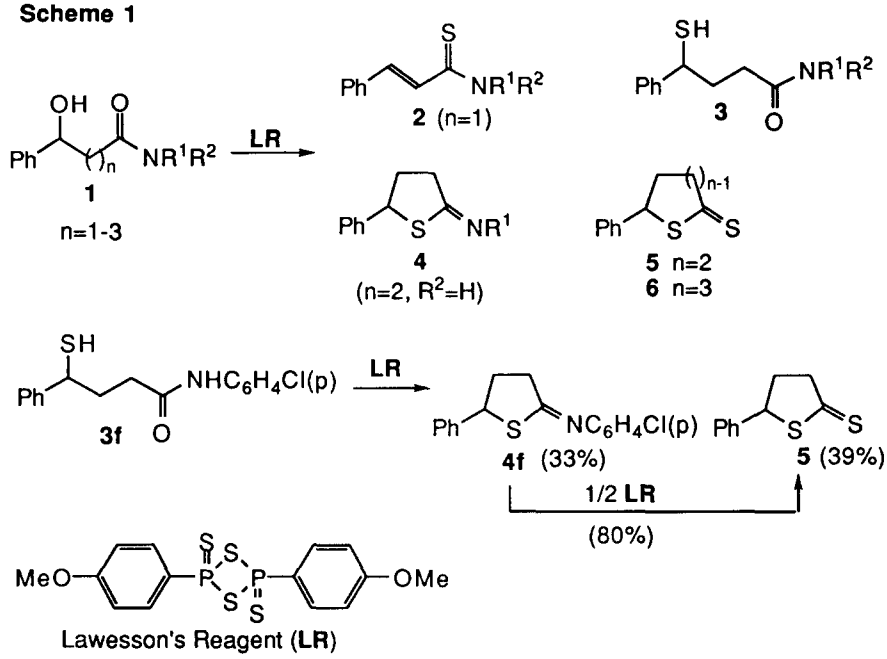
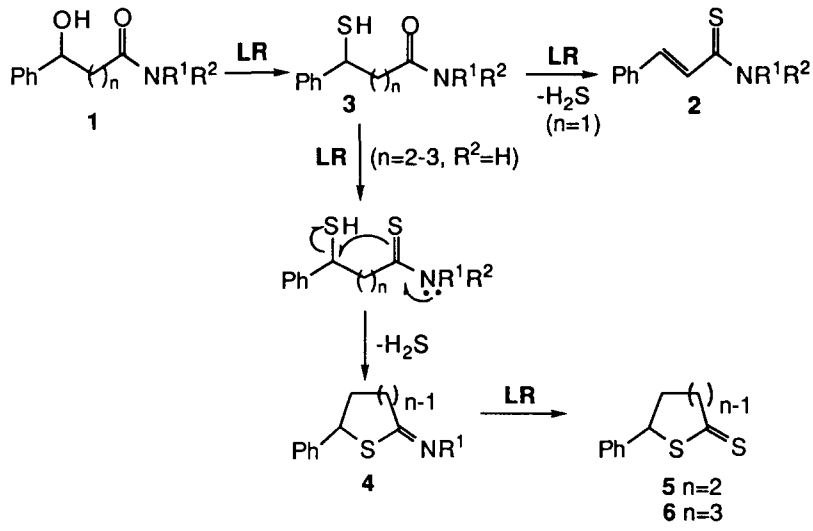


Table 1. Yields of Products **2**-**6** from **1** and **LR**.

Compd.				Molar ratio	Yields (%)				
No.	n	R^1	R^2	**LR**/**1**	**2**	**3**	**4**	**5**	**6**
1a	1	Ph	H	1	94	-	-	-	-
1a				0.5	48	-	-	-	-
1b	1	$PhCH_2$	H	1	97	-	-	-	-
1c	1	$PhCH_2$	$PhCH_2$	1	58	-	-	-	-
1d	2	Ph	H	1	-	-	51	33	-
1e	2	*p*-Tol	H	1	-	-	49	48	-
1e				0.5	-	9	35	5	-
1f	2	*p*-ClC_6H_4	H	1	-	-	45	52	-
1f				0.5	-	8	37	5	-
1g	3	Ph	H	1	-	-	-	-	48

Scheme 2



Treatment of N-acylamino alcohols **7a-d** with an equimolar amount of **LR** in toluene at reflux temperature yielded thiazoline derivatives **9a-d**. However, treatment of N-acylamino alcohol **7d** with 0.5 equiv. of **LR** gave N-acylamino thiol **8d** (63 %)[10] as the main product accompanied by a small amount of thiazoline **9d** (4 %). N-Acylamino thiol **8d** thus obtained was converted into thiazoline **9d** when treated with **LR**.

Scheme 3

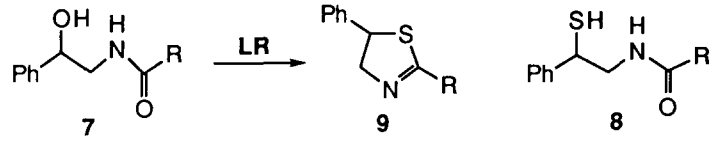


Table 2. Yields of Products **8**-**9** from **7**.

		Molar ratio	Yield (%)	
Compd. No.	R	**LR/7**	**8**	**9**
7 a	Ph	1	-	56
7 a		0.5	-	31
7 b	*p*-Tol	1	-	60
7 c	$PhCH_2$	1	-	36
7 d	Adamantyl	1	-	22
7 d		0.5	63	4

This result indicates that the formation of thiazolines **9** can be interpreted to be a ring closure of the initially produced N-acylamino thiols followed by a loss of hydrogen sulfide.

References

1 Cava, M. P.; Levinson, M. I. *Tetrahedron*, **1985**, *41*, 5061-5087.

2 Pederson, B. S.; Lawesson, S.-O. *Tetrahedron*, **1979**, *35*, 2433-2437.

3 Scheibye, S.; Shabana, R.; Lawesson, S-O. *Tetrahedron*, **1982**, *38*, 993-1001.

4 El-Barbary, A. A.; Clausen, K.; Lawesson, S-O. *Tetrahedron*, **1980**, *36*, 3309-3315.

5 El-Barbary, A. A.; Lawesson, S-O. *Tetrahedron*, **1981**, *37*, 2641-2646.

6 Shabana, R.; Osman, F. H.; Atress, S. S. *Tetrahedron*, **1994**, *50*, 6975-6988.

7 Clausen, K.; Lawesson, S-O. *Bull. Soc. Chim. Belg.*, **1979**, *88*, 305-311.

8 Clausen, K.; Lawesson, S-O. *Nouv. J. Chim.*, **1980**, *4*, 43-46.

9 Nishio, T. *J. Chem. Soc., Chem. Commun.*, **1989**, 205-206; *J. Chem. Soc., Perkin Trans. 1*, **1993**, 1113-1117.

10 4-Mercapto amide **3e**: oil; IR(film) 3300, 2540, and 1655 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 1.88 (1H, d, J=5.9 Hz), 2.27 (3H, s), 2.05-2.18 (4H, m), 3.80-4.08 (1H, m), 6.95-7.40 (9H, m), and 8.05 (1H, br s); ^{13}C-NMR($CDCl_3$) δ 20.7 (q), 35.2 (t), 43.2 (d), 120.1 (d), 126.7 (d), 127.3 (d), 128.6 (d), 129.2 (d), 133.7 (s), 135.2 (s), 143.8 (s), and 170.4 (s).

4-Mercapto amide **3f**: m.p. 87-89 °C; IR(KBr) 3270, 3200, 2550, and 1665 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 1.93 (1H, d, J=5.8 Hz), 2.20-2.42 (4H, m), 3.90-4.11 (1H, m), and 7.18-7.46 (10H, m); ^{13}C-NMR($CDCl_3$) δ 35.0 (t), 35.3 (t), 43.2 (d), 121.2 (d), 126.8 (d), 127.5 (d), 128.8 (d), 128.9 (d), 136.3 (s), 143.7 (s), and 170.3 (s).

N-Acylamino thiol **8d**: m.p. 130-131 °C; IR(KBr) 3380, 2520, and 1625 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 1.60-2.10 (16H, m), 3.54-3.69 (2H, m), 4.07-4.29 (1H, m), 5.87 (1H, br s), and 7.22-7.32 (5H, m); ^{13}C-NMR($CDCl_3$) δ 28.0 (d), 36.4 (t), 39.1 (t), 40.6 (s), 43.2 (d), 47.2 (t), 127.2 (d), 127.7 (d), 128.8 (d), 141.3 (s), and 177.9 (s).

Satisfactory elemental analyses were obtained on all products.

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