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A Novel Method for the Preparation of Thioformates and Thiols by using Thioformimidates

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Several new S-alkylated thioformimidates were synthesized and their applications to the synthesis of thiolformates and thiols were investigated.

Keywords——thioformimidates; thiols; thiolformates; thioformanilide; Michael-type addition

Although there have been several studies on the synthesis and reactions of formyl amine derivatives, little information has been reported on the thioformyl analogs.[1] This manuscript deals with the synthesis of several new S-alkylated thioformimidates **1** and their use for the synthesis of thiolformates and thiols.

Two methods to prepare **1** were tried: one was the S-alkylation of thioformanilide **2** with alkyl halides and the other was the Michael-type addition of **2** to methyl methacrylate in the presence of sodium methoxide. The former reaction was found to give **1** in good yields, while the latter did not yield thioformimidate but thiol **3f** and formimidate. In the latter case, the thiol was considered to be produced *via* an addition–elimination reaction of methoxide anion with thioformimidate formed initially.

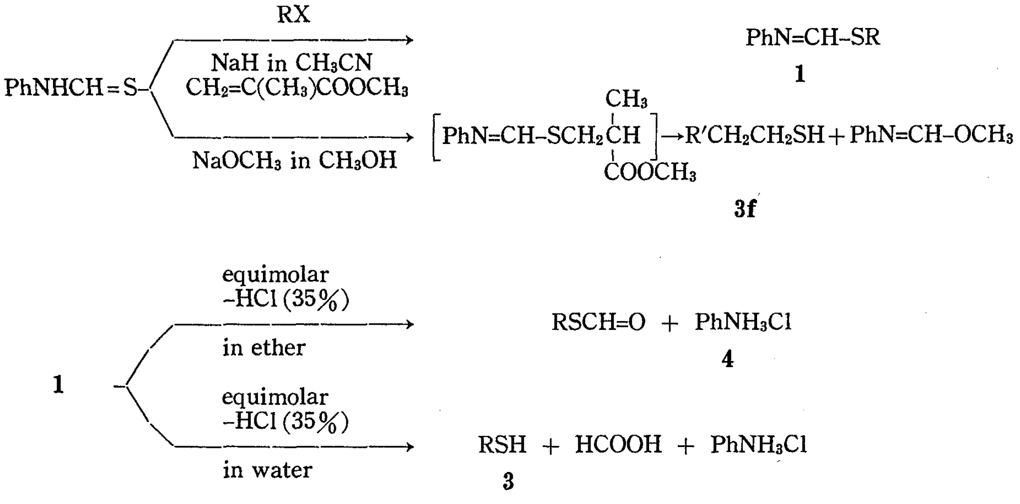

Chart 1

The reaction of **1** with an equimolar amount of concentrated HCl (35%) in ether at room temperature for 10 min gave almost pure thiolformates **4**, simply by filtration of the reaction mixture.

On the other hand, when compounds **1** were treated with an equimolar amount of HCl in water at room temperature overnight, the corresponding thiols **3** were obtained in nearlty quantitative yields.

Table I. Thioformimidate Compounds **1**

	RX	Yield of **1** (%)	bp °C/Torr		^{1}H-NMR ($CDCl_3$, 60 MHz) δ –CH= (ppm)
			Found	Reported[2]	
1a	C_2H_5I	81	65—66/1	94—95/7	8.41
1b	C_4H_9I	85	140—141/15	151—152/20	8.38(92), 8.30(8)[a]
1c	$C_8H_{17}Cl$	67	135—136/3		8.43(98), 8.36(2)[a]
1d	CH_3OCOCH_2Cl	93	—[b]		8.43
1e	$PhCH_2Cl$	88	168—170/2		8.50

a) *E*(%) and *Z*(%) forms are given in parentheses.
b) Decomposition of the product took place. Purified by TLC.

Table II. Thioformidate Compounds **4**

	RX	Yield of **4**[a] (%)	bp °C/Torr		^{1}H-NMR ($CDCl_3$, 60 MHz) δ –CH=O (ppm)
			Found	Reported[3]	
4a	C_2H_5	63(85)	94—95/760	94—95/760	10.10
4b	C_4H_9	76(90)	77—78/8	146—148/760	10.10
4c	C_8H_{17}	71(88)	96—98/10	96—98/10	10.10
4d	$PhCH_2$	83(93)	94—96/10		10.11

a) Isolated yields. GLC yield are given in parentheses and all the products were characterized by comparison with the reported bp values[3] and by means of ^{1}H-NMR.

Table III. Thiol Compounds **3**

	R	Yield of **3**[a] (%)
3a	C_2H_5	82
3b	C_4H_9	90
3c	C_8H_{17}	59
3d	CH_3OCOCH_2	93[b]
3e	$PhCH_2$	92
3f	$CH_3OCOCH(CH_3)CH_2$	69[b]

a) Isolated yields. All the products were characterized by comparison with authentic samples.
b) Thioglycolic acid (3 %) and 2-methyl-3-thiolpropionic acid (9%) were also formed.

Experimental

^{1}H nuclear magnetic resonance (NMR) spectra were taken with a Hitachi 24B (60 MHz) spectrometer. Gas liquid chromatography (GLC) was run on a Hitachi 163 unit with a flame ionization detector using a glass column (3 mm × 2.0 m) packed with SE-30.

Thioformimidates 1——General Procedures: An alkyl halide (10 mmol) was added to a mixture of **2** (10 mmol) and sodium hydride (10 mmol; 50% oil dispersion, washed with acetonitrile to remove mineral oil) in acetonitrile (2 ml) under a nitrogen atmosphere and the mixture was stirred for 1 h at room temperature. The solvent was evaporated off *in vacuo* and then the residue was extracted three times with ether. The ether extract was concentrated *in vacuo* to give the thioformimidates **1** in almost pure form. The properties and yields of **1** prepared in this way are summarized in Table I.

The Michael-type Addition of Thioformanilide to Methyl Methacrylate——A solution of thioformanilide (**2**, 10 mmol), methyl methacrylate (10 mmol) and sodium methoxide (10 mmol) in methanol (5 ml) was stirred overnight at room temperature. Then, methanol was evaporated off and the residue was neutralized with 1 N hydrochloric acid. The reaction mixture was extracted three times with ether. The ether extract was dried over anhydrous magnesium sulfate and distilled *in vacuo* to give methyl 3-mercapto-2-methylpropionate. (Table III-f).

Thiolformates 4——General Procedures: An equimolar amount of concentrated hydrochloric acid (35%) was added dropwise to a stirred mixture of **1** (10 mmol) and ether (5 ml) at room temperature. Anilinum salt precipitated with in a few minutes. The mixture was stirred for 10 min and then the precipitate was filtered off and the filtrate was concentrated *in vacuo* to give **4** in almost pure form. The properties and yields of **4** prepared in this way are summarized in Table II.

Thiols 3——General Procedure: An equimolar amount of concentrated hydrochloric acid (35%) was added to a mixture of 1 (10 mmol) and water (10 ml) and the mixture was stirred overnight at room temperature. Then, the reaction mixture was extracted three times with ether and the extract was dried over anhydrous magnesium sulfate and distilled to give **3**. The yields of **3** prepared in this way are summarized in Table III(a—e).

References

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