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FACILE CONVERSION OF THIOLESTERS INTO THIOLS USING CYSTEAMINE

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It has been found that thiols having functional groups susceptible to hydrolysis and reduction such as acylurea and nitro groups are readily prepared in high yields by simply treating the corresponding thiolesters with cysteamine in acetonitrile at 65°C for 10-40 min.

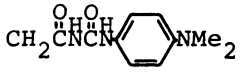
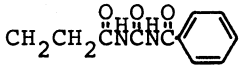
Thiols are generally prepared by alkylation of metallic hydrogensulfides or by hydrolysis of S-alkylthiouronium salts.[1] These methods, however, require rather basic conditions not to be applied to the preparation of thiols having functional groups susceptible to hydrolysis or aminolysis. In this connection, this paper describes a convenient and useful method for the preparation of thiols having functional groups such as acylurea (-$\overset{O}{\overset{\|}{C}}\overset{H}{N}\overset{O}{\overset{\|}{C}}\overset{H}{N}$-) or nitro groups by simply treating the corresponding thiolesters with cysteamine (2-aminoethanethiol).

Thiolesters could be converted into the corresponding thiols when treated with strong nucleophiles along with the acylation products. In view of high nucleophilicity of some thiols, nucleophilic substitution at the carbonyl carbon atom of thiolesters[2] (1) was investigated in detail in order to prepare the desired thiols. As a result, it was made clear that cysteamine (2) was the most effective as a nucleophile[3] in the above reaction (Table I). In a typical experiment, the thiolester (1a[4], 10 mmol) was mixed with 2 (11 mmol) in 40 ml of oxygen-free acetonitrile under argon at room temperature. The mixture was then kept at 65°C for 10 min with stirring. After the reaction mixture[5] was cooled to room temperature, precipitated pale yellow needles of the thiol (3a[4]) were collected by filtration. Concentration of the filtrate yielded additional needles of 3a. Anal. Calcd for $C_{11}H_{15}N_3O_2S$: C, 52.17; H, 5.97; N, 16.59; S, 12.64. Found: C, 52.45; H, 6.10; N, 16.64; S, 12.69. Concerning a reaction temperature, it was demonstrated that

$$\underset{\text{1a-d}}{CH_3\overset{O}{\overset{\|}{C}}SR} + \underset{\text{2}}{H_2NCH_2CH_2SH} \xrightarrow[CH_3CN]{} \underset{\text{3a-d}}{HSR} + \underset{\text{4}}{[CH_3\overset{O}{\overset{\|}{C}}SCH_2CH_2NH_2]}$$

the reaction was completed within 1 hr at room temperature in the case of 1a. In a similar manner, 2,4-dinitrobenzenethiol (3c) was isolated in 80% overall yield from 1-chloro-2,4-dinitrobenzene via S-2,4-dinitrophenyl thioacetate (1c), in contrast to the finding[6] that p-chloronitrobenzene, on treatment with sodium sul-

Table I. Conversion of Thiolesters (1) to Thiols (3) at 65°C in Acetonitrile[a)]

No.	Thiol R	Yield,%	Mp,°C (lit.)	Recrystallization Solvent
3a		97	167.0-167.5	Acetonitrile
3b		83	160-161(dec)	Ether
3c	$2,4\text{-}(NO_2)_2C_6H_3$	83	126-128 (128-130[b)])	Benzene-pet. ether
3d	$CH_2CH_2\overset{O}{\overset{\|}{C}}NH_2$	>45[c)]	98.5-99.5 (100[d)])	Ether

a) Reaction time (min): 1a, 10; 1b, 40; 1c, 10; 1d, 30.
b) N. Kharasch and A. J. Parker, J. Org. Chem., 24, 1029 (1959).
c) Lower yield of 3d is due to difficulty in isolation because of its high solubility in water or ether.
d) A. Luettringhaus and R. Schneider, Ann. Chem., 679, 123 (1964).

fide, is converted into p-aminobenzenethiol (69%) by the reduction of the nitro group.

In cases of 1a and 1c, it was confirmed by tlc that N-acetylcysteamine (5) was present in the reaction mixture. The formation of 5 is probably explained as an intramolecular acetyl transfer[7] from S→N in S-acetylcysteamine (4) initially produced.

REFERENCES

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1) R. B. Wagner and H. D. Zook, "Synthetic Organic Chemistry", John Wiley and Sons, Inc., New York, N. Y., 1953, p. 778.

2) All new compounds had satisfactory analytical and spectroscopic data to support the assignment. In general, the thiolesters 1 were easily prepared in high yields by alkylation of thioacetic acid with the corresponding chlorides in the presence of triethylamine at room temperature in acetonitrile.

3) In the case of 1a, o-aminobenzenethiol proved to be also effective only in the presence of a catalytic amount of triethylamine, however, elongation of the reaction time (1.5 hr) was required for the completion of the reaction.

4) The substituent R in 1a, 1b, 1c, or 1d is the same as in 3a, 3b, 3c, or 3d, respectively.

5) In the case of 1c, yellow solid of 3c precipitated readily on addition of water to this concentrated mixture.

6) H. Gilman and G. C. Gainer, J. Amer. Chem. Soc., 71, 1747 (1949).

7) T. Wieland and E. Bokelmann, Ann. Chem., 576, 20 (1952).

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