CHEMISTRY LETTERS, pp. 1157-1158, 1981.

A NEW SYNTHESIS OF SULFIDES FROM THIOLS AND ALDEHYDES OR KETONES WITH PYRIDINE-BORANE IN TRIFLUOROACETIC ACID

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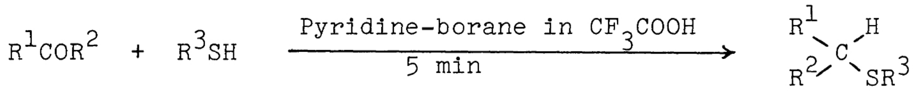
A mixture of thiols and aldehydes or ketones was converted into sulfides with pyridine-borane in trifluoroacetic acid.

The most widely-used method for the preparation of sulfides is based on the alkylation of thiolate anions with alkyl halides,1) and many other preparative methods have also been reported in the literatures.2) However, there has been no practical method for one-step preparation of sulfides starting from thiols and aldehydes or ketones.3)

The author wishes to report that symmetrical and unsymmetrical sulfides are obtained directly from thiols and aldehydes or ketones with pyridine-borane in trifluoroacetic acid.



$$R^1COR^2 + R^3SH \xrightarrow[\text{5 min}]{\text{Pyridine-borane in } CF_3COOH} R^1R^2CH(SR^3)$$

The reaction was simple and rapid, and was completed within a few minutes. A typical procedure is as follows: 1-Heptanethiol (3.8 mmol) in CH_2Cl_2 (2 ml) was added to a mixture of benzaldehyde (3.6 mmol) and trifluoroacetic acid (4 ml) with cooling. After 2-3 min stirring, pyridine-borane (0.36 ml) was added to the reaction mixture and it was stirred for 5 min. After evaporation of the solvent *in vacuo*, 10% NaOH (15-18 ml) was added to the residue and the solution was extracted with benzene (30 ml x 2), and the combined extracts were washed with saturated aq. NaCl (20 ml) and dried over anhydrous Na_2SO_4. After evaporation of benzene, the residue was purified by column chromatography [SiO_2, benzene-hexane (2:3) for elution] to give an oil (739 mg), which was distilled to give benzyl heptyl sulfide (555 mg, bp 128-130 °C/ 3 Torr, m/e 222 (M^+)) in 69% yield. When trifluoroacetic acid was not diluted with

Table Synthesis of Sulfides from Thiols and Aldehydes or Ketones

Aldehydes	Thiols	Sulfides	Sulfides distilled(%)[a)]	Bp, °C/Torr
C_6H_5CHO	$C_6H_5CH_2SH$	$(C_6H_5CH_2)_2S$	66	145/4
C_6H_5CHO	$CH_3(CH_2)_6SH$	$C_6H_5CH_2S(CH_2)_6CH_3$	69	128-130/3
$C_6H_5(CH_2)_2CHO$	$CH_3(CH_2)_3SH$	$C_6H_5(CH_2)_3S(CH_2)_3CH_3$	52(74)	118/4
$C_6H_5COCH_3$	$CH_3(CH_2)_3SH$	$C_6H_5CH(CH_3)S(CH_2)_3CH_3$	58(75)	111-112/8
$CH_3CH_2COCH_3$	$C_6H_5CH_2SH$	$CH_3CH_2CH(CH_3)SCH_2C_6H_5$	58	96-98/5

a) Figures in parenthesese indicate the isolated yield (%) by column chromatography.

dichloromethane in the case of aldehydes, the yield of the sulfide was slightly lowered probably due to the rapid decomposition of pyridine-borane in trifluoroacetic acid. Gas chromatographic analysis of the residue showed the presence of the considerable amount of the dithioacetal. On the other hand, in the case of ketones, the formation of hemithioketals is assumed to be more accelerated in trifluoroacetic acid than in diluted trifluoroacetic acid and better results were obtained by use of trifluoroacetic acid alone as solvent. The mode of the reaction will be explained as follows. Thiols add to the carbonyl double bond to form hemithioacetals which are immediately reduced to sulfides with pyridine-borane. Although dithioacetals prepared from another route are also reduced to sulfides in good yield under the same reaction conditions, it is not clear that a hydride attacks the dithioacetal directly or the hemithioacetal converted from the dithioacetal with equilibrium. Previously, we reported[4)] the synthesis of ethers from aldehydes and pyridine-borane, but in this case, the presence of ethers and alcohols was not detected in the reaction mixture, probably due to the higher affinity of thiols toward carbonyl compounds with those of hydroxy compounds.[5)] The procedure reported herein is a useful one in terms of direct functional group conversion, easy manipulation, and mild reaction conditions.

The author thanks Professor Shun-ichi Yamada of this university for encouragement.

REFERENCES

1) M. E. Peach, "The Chemistry of the Thiol Group," ed. by S. Patai, Interscience, New York, N. Y., 1974, p 725.

2) a) G. C. Barrett, "Organic Compounds of Sulphur, Selenium, and Tellurium," ed. by D. R. Hogg, Vol. 5, The Chemical Society , London, 1979, p 19; b) Idem, ibid., Vol. 4, 1977, p 16; c) B. Czech, S. Quici, and S. L. Regen, Synthesis, 1980, 113.

3) There is one case in which aldehydes were converted into sulfides, that is, aldehydes reacted with trimethylsilyl sulfides to give O-trimethylsilyl hemithioacetals, which were reduced to sulfides with $LiAlH_4$-$AlCl_3$ in ether. R. S. Glass, Synth. Commun., 6, 47 (1976).

4) Y. Kikugawa and Y. Ogawa, Chem. Pharm. Bull., 27, 2405 (1979).

5) Y. Ogata and A. Kawasaki, "The Chemistry of the Carbonyl Group," ed. by J. Zabicky, Vol. 2, Interscience, London, 1970, p 40.

(Received June 1, 1981)