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A FACILE SYNTHESIS OF UNSYMMETRICAL DISULFIDES

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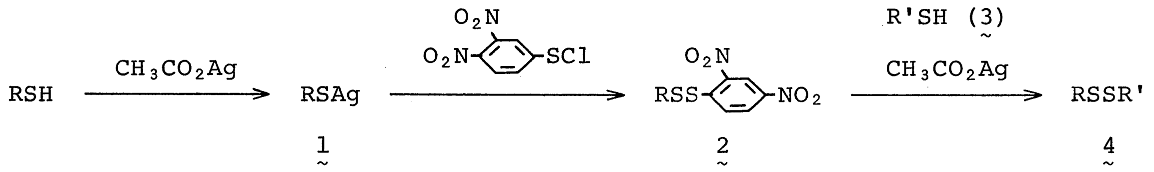
Unsymmetrical disulfides were readily prepared in high yields by successive treatment of silver thiolates initially with 2,4-dinitrobenzenesulfenyl chloride in acetonitrile at 0 °C and then with the second thiols and silver acetate in DMF at room temperature.

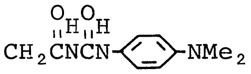
The general and attractive routes to the unsymmetrical disulfides are to utilize nucleophilic displacement reactions of sulfenyl compounds with thiols.[1] Several sulfenyl compounds are available for this purpose. However, there has not been described the formation of the corresponding two symmetrical disulfides which is generally observed in the preparation of unsymmetrical disulfides. This paper is concerned with a convenient and useful method for the preparation of unsymmetrical disulfides by use of silver thiolates and 2,4-dinitrobenzenesulfenyl chloride under mild conditions.

This procedure involves initial conversion of silver thiolates (**1**) (readily prepared from thiols and silver acetate quantitatively) to an intermediary alkyl 2,4-dinitrophenyl disulfides (**2**)[2] and subsequent displacement with the second thiols (**3**).



In a typical experiment, 2-(*N*-acetyl)aminoethanethiol (4 mmol) was converted to the corresponding silver thiolate (**1**, R=$CH_3CONHCH_2CH_2$) quantitatively in dry oxygen-free pyridine (15 ml) at room temperature by treatment with silver acetate (4 mmol). The yellow solid of **1** was collected by filtration, washed with hot water, and dried *in vacuo*. Silver thiolate **1** was used in the next step without further purification. Dry 2,4-dinitrobenzenesulfenyl chloride[3] (2 mmol) was mixed with **1** (2 mmol) in 20 ml of anhydrous acetonitrile and the suspension was stirred for 2 h at 0 °C[4] under nitrogen. The reaction mixture was filtered off to remove resulting silver chloride, and the filtrate was concentrated under reduced pressure. The residue was subjected to preparative tlc (CH_2Cl_2) to give the pure disulfide (**2**, R=$CH_3CONHCH_2CH_2$) as yellow crystals in 91% yield.[5] When the mixture of silver acetate (1 mmol), **2** (1 mmol), and α-toluenethiol (1 mmol) in dry oxygen-free DMF (10 ml) was stirred for 2 h at room temperature, orange silver 2,4-dinitrobenzenethiolate (**5**)[6] was formed. Work-up of the reaction mixture in the standard manner

Table I.

R	R'	Yield, %[a]			Mp [n_D^{25}]
		$(RS)_2$	RSSR'	$(SR')_2$	of RSSR', °C
$C_6H_5CH_2$	$CH_2CO_2C_2H_5$	4	78	1>	[1.5631]
$C_6H_5CH_2$	$CH(CH_3)_2$	1	87	b	[1.5698]
$C_6H_5CH_2$	$CH_2CH_2\overset{H}{N}\overset{O}{C}CH_3$	3	81	1>	43.5-44.0
CH_3CH_2	$CH_2C_6H_5$	b	73	6	[1.5843]
$CH_3\overset{O}{C}\overset{H}{N}CH_2CH_2$	$CH_2C_6H_5$	1>	94	6	43.5-44.0
$Me_2CHCH_2CH_2\overset{O}{C}\overset{H}{N}\overset{O}{C}\overset{H}{N}CH_2CH_2$	 $CH_2\overset{O}{C}\overset{H}{N}\overset{O}{C}\overset{H}{N}$-$NMe_2$	b	92[c]	b	174.5-175.5

[a] Isolated yields after purification by preparative tlc on silica gel.
[b] Undetermined. [c] Yield based on quantitative analysis by tlc on silica gel by the procedure of S. J. Purdy and E. V. Truter, Chem. Ind. (London), 506 (1962).

gave the pure unsymmetrical disulfide (4, R=$CH_3CONHCH_2CH_2$, R'=$CH_2C_6H_5$) in 94% yield,[2] together with a small amount of bis[2-(N-acetyl)aminoethyl] disulfide (<1%) and dibenzyl disulfide (6%). As shown in Table I, the method described above proved to afford a wide variety of unsymmetrical disulfides selectively. Further, the present method could also be applied to the synthesis of unsymmetrical disulfides from thiols capable of forming hydrogen bonding[7] by their acylurea moieties (-CONHCONH-).

In conclusion, the observed remarkable selectivity in this reaction seems to be mainly based upon the high stability of 2,4-dinitrobenzenesulfenyl group as both the corresponding sulfenium cation and thiolate anion.

NOTES AND REFERENCES

1) S. J. Brois, J. F. Pilot, and H. W. Barnum, J. Am. Chem. Soc., 92, 7629 (1970), and references cited therein.
2) The analytical and spectral data for all new compounds were fully consonant with the proposed structures.
3) N. Kharasch and R. B. Langford, "Organic Syntheses", Collect. Vol. V, Wiley, New York, N.Y., 1973, p 474.
4) The reactions at room temperature gave 2 in lower yields, together with a small amount of the two corresponding symmetrical disulfides.
5) The yields of 2 were ca. 90% in most cases.
6) The structure of 5 was established by its essentially quantitative conversion into 2,4,2',4'-tetranitrodiphenyl sulfide (6) on treatment with 2,4-dinitrochlorobenzene in pyridine. The identity of 6 was confirmed by its melting point and nmr, ir, and mass spectra: H. H. Hodgson and D. P. Dodgson, J. Chem. Soc., 1002 (1948).
7) T. Mukaiyama, T. Endo, and S. Noguchi, Tetrahedron Lett., 2291 (1971).

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