

The Chemistry of 1,1-Dithiolates

1. Formation of Derivatives of 3-Nitrothiophene-2-thiol

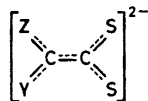
LARS HENRIKSEN and HERMAN AUTRUP

*Chemical Laboratory II (General and Organic Chemistry), University of Copenhagen,
The H. C. Ørsted Institute, DK-2100 Copenhagen, Denmark*

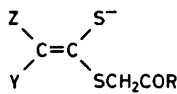
The reaction of dipotassium 2-nitroethylene-1,1-dithiolate (III) with α -halogeno aldehydes or ketones leads to derivatives of 3-nitrothiophene-2-thiols. These reactions proceed by an acid catalyzed cyclization of the initially formed 1-(acylmethylthio)-2-nitroethylene-1-thiolates (IV). The infrared and NMR spectra of the thiophene derivatives are discussed briefly.

The reaction of ethylene-1,1-dithiolates* (I) with α -halogeno aldehydes or ketones may lead to the formation of sulfur containing heterocycles by a cyclization reaction of the initially formed *S*-acylmethyl derivatives (II).

Two types of cyclization of II have previously been observed; firstly, the formation, under acidic conditions, of 2-alkylidene-1,3-dithiolan-4-ols¹⁻² by addition of the second thiolate group to the carbonyl group and, secondly, the formation of 2-acylthiophenes by the base catalyzed reaction between the active methylene group situated between the sulfur and the oxo group and one of the electron attracting 2-substituents in the original dithiolate.²⁻⁴



I



II

We now report a third cyclization mechanism for compounds of type II. Treatment of 2-nitroethylene-1,1-dithiolate (III) with α -halogeno aldehydes or ketones leads to the formation of derivatives of 3-nitrothiophene-2-thiol. These reactions must proceed by the formation of a bond between the carbonyl

* The term ethylene-1,1-dithiolate is used to designate the stable dianions of the dithio acids bearing either one or two strongly electron attracting substituents in the 2-position.

carbon atom and the carbon atom in the 2-position in the 2-nitromethylene-1,1-dithiolate. The parent thiols were not isolated, but transformed into 2,2'-bis(2-nitrothienyl)disulfides (VI) by oxidation with HNO_3 and into 2-methylthio-3-nitrothiophenes (VII) by methylation with methyl iodide. Analytical and some selected spectroscopic data on the compounds obtained are given in Tables 1 and 2, respectively.

Table 1. Derivatives of 3-nitrothiophene-2-thiol.

Compound	R	Formula	Melting point °C	Analyses	C	H	N	MW ^a
VIa	H	$\text{C}_8\text{H}_4\text{N}_2\text{O}_4\text{S}_4$	156–58 ^b	Found:	30.07	1.32	8.76	320
				Calc.:	30.49	1.49	8.69	320
VIIa	H	$\text{C}_8\text{H}_5\text{NO}_2\text{S}_2$	84–85 ^b	Found:	34.08	2.93	7.89	175
				Calc.:	34.29	2.88	8.00	175
VIb	Me	$\text{C}_{10}\text{H}_5\text{N}_2\text{O}_4\text{S}_4$	164–66 ^c	Found:	34.40	2.38	7.76	
				Calc.:	34.50	2.30	8.05	
VIIb	Me	$\text{C}_9\text{H}_7\text{NO}_2\text{S}_2$	110–11 ^b	Found:	38.17	3.82	7.38	
				Calc.:	38.10	3.73	7.41	
VIc	Ph	$\text{C}_{20}\text{H}_{13}\text{N}_2\text{O}_4\text{S}_4$	177–80 ^d	Found:	50.50	2.60	5.73	
				Calc.:	50.86	2.56	5.93	
VIIc	Ph	$\text{C}_{11}\text{H}_9\text{NO}_2\text{S}_2$	144–46 ^b	Found:	52.40	3.76	5.53	
				Calc.:	52.59	3.61	5.58	

^a From mass spectrum.

^b Recrystallization from ethanol.

^c , , dioxan/water.

^d , , chloroform.

In the IR-spectra the $\nu_{\text{as}}\text{-NO}_2$ vibration was assigned on the basis of its absorption intensity. It was not possible in this way to distinguish between the $\nu_{\text{s}}\text{-NO}_2$ and the lower band due to thiophene ring vibration,⁵ both occurring in the range 1340–1305 cm^{-1} . The assignment of the NMR-signals due to H(4) and H(5) in the 4-unsubstituted thiophenes, VIa and VIIa, is based upon deuteration experiments. These two compounds were obtained partially deuterated at C(5) from IVa partially deuterated at the CH_2 group. This was accomplished by carrying out the alkylation $\text{III} \rightarrow \text{IVa}$ in deuterium oxide.

The proposed transformations leading to nitrothiophenes VI and VII are outlined in Scheme 1.

The initial formation of the 1-(acylmethylthio)-2-nitroethylene-1-thiolates (IV) probably proceeds rapidly (*cf.* the almost instantaneous formation² of the hydroxydithiolans *via* this type of intermediate). The presence of IV was demonstrated by the formation of 2-(1-methylthio-2-nitrovinyl)thio-1-phenylethanone (VIIIc) when the reaction mixture obtained from the reaction of III and phenacyl bromide was treated with methyl iodide.

Table 2. IR and NMR spectroscopic data for derivatives of 3-nitrothiophene-2-thiol.

Com- pound	NMR signals ^a			IR-absorption (cm ⁻¹) ^b	
	Chemical shift	Assignment	Solvent	$\nu_{\text{as-NO}_2}$	Thiophene ring and $\nu_{\text{s-NO}_2}$
VIa	2.34 d $J=5.8$ 1H 2.75 d $J=5.8$ 1H	H(4) H(5)	CDCl ₃	1485 s	1520 s 1315 s 1440 m 1325 s
VIIa	2.33 d $J=5.8$ 1H 2.41 d $J=5.8$ 1H 7.30 s 3H	H(4) H(5) -SCH ₃	(CD ₃) ₂ SO	1490 s	1515 s 1315 s 1435 m 1325 s
VIb	2.62 d $J=1.3$ 1H 7.62 d $J=1.3$ 3H	H(5) C(4)-CH ₃	(CD ₃) ₂ SO	1490 s	1550 s 1315 s 1450 m 1330 s
VIIb	3.26 d $J=1.3$ 1H 7.44 s 3H 7.53 d $J=1.3$ 3H	H(5) -SCH ₃ C(4)-CH ₃	CDCl ₃	1495 s	1545 s 1310 s 1445 m 1330 s
VIc	2.41 s 1H 2.69 s 5H	H(5) Ph	(CD ₃) ₂ SO	1510 s	1515 s 1310 s 1455 m 1340 s
VIIc	2.65 s 5H 3.01 s 1H 7.37 s 3H	Ph H(5) -SCH ₃	CDCl ₃	1490 s	1525 s 1305 s 1440 m 1330 s

^a Recorded on a Varian A 60 A instrument. Chemical shifts are given as τ -values, coupling constants in Hz; s=singlet, d=doublet.

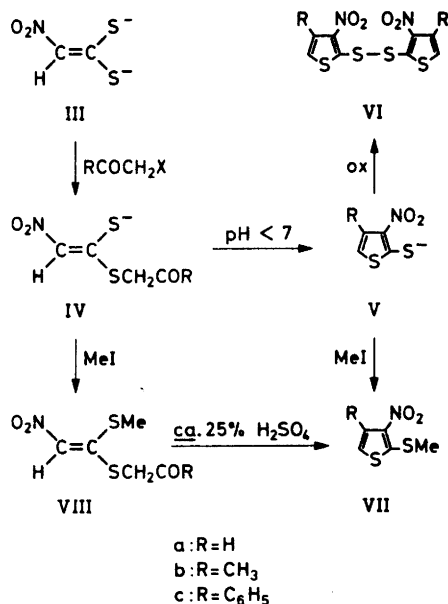
^b Recorded on a Perkin-Elmer Model 337 grating infrared spectrophotometer (KBr-discs); s=strong, m=medium.

Cyclization of IV, with the formation of 3-nitrothiophene-2-thiolates (V), is assumed to be the next step in the reaction. The observed products, VI and VII, are then formed by, respectively, oxidation and methylation of V.

An alternative route, not involving V, would be the oxidation or methylation of IV, followed by a relatively rapid cyclization, leading, respectively, to the products VI and VII. In the case of the formation of VII, this pathway, *i.e.* via VIII, can be ruled out. Although the cyclization of VIIIc could be accomplished in a strongly acidic medium this compound was stable under the reaction conditions leading to VIIc from III.

The formation of V is very slow in basic media (the pH in the solutions assumed to contain IV was usually *ca.* 9), but proceeds rapidly upon the addition of acid. The NMR spectrum of IVb (DMSO-*d*₆) showed signals at 4.57 τ (HCNO₂), 6.95 τ (SCH₂CO) and 8.45 τ (COCH₃). The spectrum of this solution recorded 5 min after the addition of a catalytic amount of CF₃COOH only showed signals due to Vb at 3.24 τ (HC(5)) and 7.67 τ (CH₃-C(4)). The

SCHEME 1



conversion of IV into V could not be reversed by the addition of excess base. Therefore, the effect of added acid can not be to shift an equilibrium between IV and V. This leaves the conclusion that the cyclization is acid catalyzed.

The cyclization can be visualized as an electrophilic attack of the carbonyl carbon atom on the C(2) atom in the nitroethylene-1,1-dithiolate, the latter atom serving as the nucleophilic center. The nucleophilic character of the C(2) atom in derivatives of 1,1-dithiolates has previously been shown by the electrophilic attack of NO_2^+ in this position.⁶ Thus, the acceleration of the reaction caused by the addition of acid is probably due to protonation of the carbonyl group. Protonation of the thiolate group, in analogy to the observed effect of *S*-methylation of IVc, would be expected to decrease the reactivity of IV.

EXPERIMENTAL

3-Nitro-2-methylthiophene (VIIa). Chloroacetaldehyde (10 mmol; 2.6 ml 30 % aqueous solution) was added to an aqueous solution of dipotassium 2-nitroethylene-1,1-dithiolate (III) (10 mmol; 2.31 g). The solution was stirred for 3 h at room temperature. Methyl iodide (10 mmol; 1.41 g) and hydrochloric acid (10 mmol) were added and the stirring continued for 30 min. The mixture was extracted with chloroform, the dried extracts evaporated *in vacuo*, and the oily residue dissolved in ethanol; VIIa precipitated from the cooled solution as a yellow crystalline material (1.09 g; 62 %). The compounds VIIb (0.62 g; 33 %) and VIIc (0.67 g; 25 %) were prepared in a similar manner by substituting chloroacetone and phenacyl bromide for chloroacetaldehyde. The reaction of III with phenacyl bromide in aqueous DMF was studied by the following method. Methyl iodide was added to samples of the reaction mixture. These were extracted with chloro-

form and the product mixture investigated by TLC. (Silicagel PF₂₅₄₊₃₆₆; solvent: benzene/petroleum ether/acetone 3:3:1). With hydrochloric acid added to the reaction mixture, VIIc was present in the sample taken immediately after the addition of acid. Without this addition VIIIc was the only defined product observed for a length of 3 h when a trace amount of VIIc was detected. Addition of an excess of NaOH 5 min after the addition of the hydrochloric acid did not affect the composition of the subsequent samples, *i.e.* VIIc was present but not VIIIc.

2,2'-Bis(3-nitrothienyl)disulfide (VIa). Chloroacetaldehyde (10 mmol; 2.6 ml 30 % aqueous solution) was added to an aqueous solution of III (10 mmol; 2.31 g). The solution was stirred for 3 h and nitric acid (10 mmol) was added. A yellow-brown substance precipitated. Recrystallization from dioxan/water (1:1) gave VIa (1.02 g; 65 %). When a non-oxidating acid was used a poor yield of VIa was obtained unless oxygen was led through the reaction mixture. *2,2'-Bis(4-methyl-3-nitrothienyl)disulfide (VIb)* (1.29 g; 75 %) and *2,2'-bis(3-nitro-4-phenylthienyl)disulfide (VIc)* (1.89 g; 81 %) were prepared in an analogous way.

2-(1-Methylthio-2-nitrovinyl)thio-1-phenylethanone (VIIIc). Methyl iodide (2 mmol; 0.28 g) was added to a solution of III (2 mmol; 0.462 g) in 50 % aqueous DMF. The solution was stirred for 15 min. Phenacyl bromide (2 mmol; 0.40 g) was added and the stirring continued for 2 h. A crystalline material was isolated by filtration and washed with water. Recrystallization from ethanol gave VIIIc (0.22 g; 41 %), m.p. 167–169°C. (Found: C 49.15; H 4.09; N 5.16. Calc. for C₁₁H₁₁NO₃S₂: C 49.05; H 4.09; N 5.16).

Conversion of VIIIc to VIIc. VIIIc (1 mmol; 0.27 g) was dissolved in 25 % ethanolic sulfuric acid (5 ml). The solution was kept at room temperature for 15 min and then poured into ice-water. A yellow material precipitated. Recrystallization from ethanol gave VIIc (0.10 g; 38 %).

VIIb was prepared in a similar manner *via* VIIIb (0.06 g; 34 %).

1-(1-Methylthio-2-nitrovinyl)thio-2-propanone (VIIIb). Methyl iodide (10 mmol; 1.42 g) was added to an aqueous solution of III (10 mmol; 2.36 g). The solution was stirred for 15 min. Chloroacetone (10 mmol; 0.92 g) was added and the stirring continued for 2 h. The mixture was extracted with ether and the dried extracts evaporated *in vacuo* yielding VIIIb (0.56 g; 27 %), m.p. 87–89°C. (Found: C 34.62; H 4.33; N 6.71. Calc. for C₈H₉NO₃S₂: C 34.80; H 4.31; N 6.78).

REFERENCES

1. Campaigne, E. and Haaf, F. J. *J. Org. Chem.* **30** (1965) 732.
2. Jensen, K. A. and Henriksen, L. *Acta Chem. Scand.* **22** (1968) 1107.
3. Gompper, R., Kutter, E. and Töfl, W. *Ann.* **659** (1962) 90.
4. Smutny, E. J. *J. Am. Chem. Soc.* **91** (1969) 208.
5. Katritzky, A. R. and Boulton, A. J. *J. Chem. Soc.* **1959** 3500.
6. Henriksen, L. *13. Nordiske Kemikermøde (Abstracts, Copenhagen 1968)* 200.

Received November 11, 1969.