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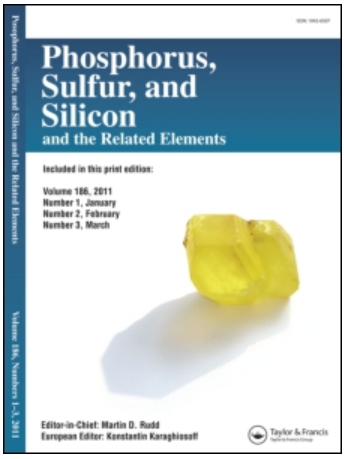

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A GENERAL SYNTHESIS OF NEW DITHIOLETHIONE DERIVATIVES: 5-(1-HYDROXYIMINO ALKYL)-1,2-DITHIOLE-3-THIONES AND 5-ACYL-I,2-DITHIOLE-3-THIONES

M. Abazid[a]; H. O. Bertrand[a]; M. O. Christen[b]; J. L. Burgot[a]
[a] Laboratoire de Chimie Analytique, UFR des Sciences Pharmaceutiques et Biologiques, Université de Rennes 1, Rennes cedex, France [b] Laboratoires de Thérapeutique Moderne (LTM - Solvay Pharma), Suresnes cedex, France

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A GENERAL SYNTHESIS OF NEW DITHIOLETHIONE DERIVATIVES: 5-(1-HYDROXYIMINO ALKYL)-1,2-DITHIOLE-3-THIONES AND 5-ACYL-1,2-DITHIOLE-3-THIONES

M. ABAZID,† H. O. BERTRAND,† M. O. CHRISTEN‡ and J. L. BURGOT†

†*Laboratoire de Chimie Analytique, UFR des Sciences Pharmaceutiques et Biologiques - Université de Rennes I - 35043 Rennes cedex, France*
‡*Laboratoires de Thérapeutique Moderne (LTM - Solvay Pharma) - 92151 Suresnes cedex, France*

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The synthesis of 5-(1-hydroxyiminoalkyl)-1,2-dithiole-3-thiones by allowing 5-alkyl-1,2-dithiole-3-thiones to react with an excess of sodium nitrite in acetic acid and by reducing highly insoluble intermediate disulfides by sodium sulfide in a DMSO-water mixture is described. 5-(1-hydroxyimino)-1,2-dithiole-3-thiones are easily transformed into 5-acyl-1,2-dithiole-3-thiones. All yields are quite satisfactory.

Key words: 5-alkyl-1,2-dithiole-3-thiones; disulfides; 5-(1-hydroxyiminoalkyl)-1,2-dithiole-3-thiones.

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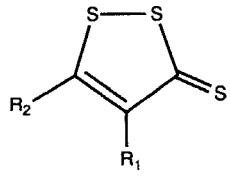
INTRODUCTION

1,2-dithiole-3-thiones **1** are compounds of pharmaceutical interest.[1,2,3,4,5,6 interalia] Few of the numerous compounds **1** previously described are functionalized in 5-position (or indeed in 4-position).[1]



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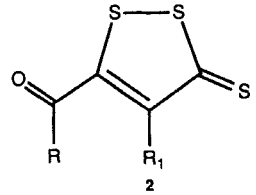
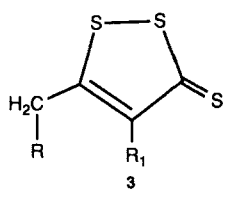


2

Due to the particular position of the carbonyl function among the other group and its great reactivity, we devoted our studies to the synthesis of 5-acyl-dithiolethiones **2**. To our knowledge, only three compounds of this type have been described. The first one is the one obtained by direct action of sulfur on isophorone.[7] Attempts to generalize this reaction to the synthesis of other compounds of type **2** performed by the same authors[8] and more recently by us (using different thionation reagents),[9] have failed. The two others have been identified as dyes in the

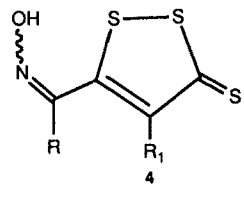
Ogston color test for chloral hydrate.[10] So, these respective preparations can, by no means, be generalized.

We report here an efficient method to synthesize 5-acyl-1,2-dithiole-3-thiones **2** via the corresponding 5-(1-hydroxyimino)-1,2-dithiole-3-thiones **4**. A preliminary communication concerning this method has been published elsewhere.[11] This synthesis is based on the 2- and 4-methyl (or methylene) pyridine-like reactivity of 5-methyl (or methylene) dithiolethiones **3**. The starting dithiolethiones **3** were chosen for the sake of studying the scope of the reaction.



3

3	R_1	R
a	H	H
b	H	Et
c	Me	H
d	$-(CH_2)-_3$	
e	Bz	H
f	Ph	H
g	Ph	Me
h	Ph	Ph
i	Cl	H
j	OMe	H



4

The pseudoacidic property of these groups allows the condensation of some electrophiles more often in basic media.[12-16] Corresponding 5-methyl dithiolylium ions are even more acidic.[17,18] Otherwise, nitrosation of organic compounds, with activated methyl or methylene groups is a well-known pathway to obtain the corresponding oximes, which in turn can be hydrolyzed into ketones or aldehydes.[19]

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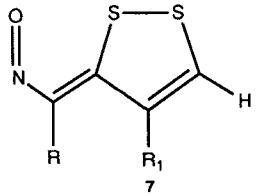
RESULTS

In the first step, addition of an excess of sodium nitrite to an acetic acid solution of starting dithiolethione **3** regularly gave the highly insoluble compound **5** (Scheme I) (Tables I, II and III).

Compound **5** is the disulfide of the 5-mercapto-1-oxa-6,6a S^{IV} -dithio-2-azapentalene **6**, which is the tautomeric form of oxime dithiolethione **4** (Scheme II). Only the **5** Z isomer is formed.

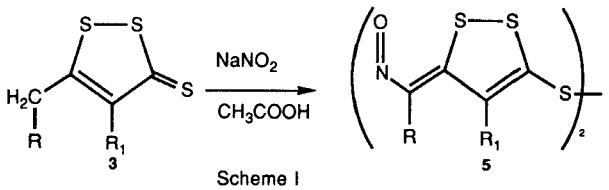
In some cases (R_1=CH_3, R=H; R_1=H, R=H), the 5-unsubstituted heteropentalenes **7** were isolated with poor yields. So, from a strictly synthetic standpoint, they can be considered as by-products.



7

The nomenclature in 1-oxa-6,6a S^{IV}-dithia-2-azapentalene for compounds **5**, **6** and **7** will be justified in the next section.

Disulfides **5** were reduced, later, into oxime dithiolethiones **4** by action of sodium sulfide in a D.M.S.O.-water mixture (Scheme III). Formation of disulfides **5** and their reduction into oximes **4** never failed, irrespective of the nature of the substituents.



Scheme I

TABLE I
Disulphides **5**

COMPOUNDS **5**			YIELDS [a]	M.P. [b,c]	Molecular	mass spectrometry [e]			starting dithiole thiones **3**
R_1	R		%	°C	formula	theo	exp	m·+	References
5 a	H	H	32	181	$C_8H_4O_2N_2S_6$		h		(32)
5 b	H	CH_2-CH_3	40	145	$C_{12}H_{12}O_2N_2S_6$		h		j
5 c	CH_3	H	68	206	$C_{10}H_8O_2N_2S_6$ [d]	379.8910	379,871 [f,i]		(34)
5 d	(-CH_2-)$_3$		62	104	$C_{14}H_{12}O_2N_2S_6$ [d]		h		(35)
5 e	$C_6H_5CH_2$	H	56	203	$C_{22}H_{16}O_2N_2S_6$	531,9536		532 g	(36)
5 f	C_6H_5	H	69	184	$C_{20}H_{12}O_2N_2S_6$	503,9223		504 g	(34)
5 g	C_6H_5	CH_3	72	243	$C_{22}H_{16}O_2N_2S_6$	531,9536	531,954 [f]		j
5 h	C_6H_5	C_6H_5	54	267	$C_{32}H_{20}O_2N_2S_6$	655,9849		656 g	(34)
5 i	Cl	H	50	205	$C_8H_2O_2N_2Cl_2S_6$	419,7817		420 g	(37)
5 j	OCH_3	H	70	214	$C_{10}H_8O_4N_2S_6$	411,8808	411,880 [f,i]		j

a) Yield of isolated product **5** based on **3**.
b) Uncorrected, measured on a Kofler apparatus.
c) Instantaneous (decomposition).
d) Microanalysis.
e) Mass spectra recorded in field desorption conditions.
f) High resolution spectroscopy.
g) Field desorption mass spectra, not in high resolution conditions.
h) Mass spectra Electronic impact 70 eV. In these conditions, only oxime dithiolethiones or their tautomeric forms are detected.
i) Presence of an unknown compound of molecular mass disulfide + 32
j) Original dithiolethione.

The transformation of oxime dithiolethiones **4** into 5-acyl-dithiolethiones **2** was straightforward. It was obtained by treatment of compounds **4** by an aqueous solution of formaldehyde in acidic solvolytic conditions and in the presence of a toluenic phase (Scheme IV). The only exception was oxime dithiolethione **4 h** ($R{=}C_6H_5$; $R_1{=}C_6H_5$). Whichever experimental conditions were adopted the preparation of its corresponding ketone failed. (Alternatively, the treatment of disulfides **5** in the same conditions gave directly the corresponding 5-acyl dithiolethiones **2**, probably as a result of the two consecutive reactions: reduction of **5** by formaldehyde followed by exchange of the hydroxyimino group between the oxime dithiolethione and formaldehyde).

For each step of the synthesis, yields were rather good. They were not significantly improved by direct treatment of disulfides **5** by formaldehyde.

It can be noted that, mixtures of E and Z oximes **4** (or alternatively E or Z isomers only according to the structures of the starting dithiolethiones **3**) were characterized by N.M.R. spectroscopy (Tables V and VI).

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TABLE II

Disulphides **5**. ^{1}H N.M.R. Spectra

COMPOUNDS	R_1	R	300 MHz [a] $CDCl_3$ δ p.p.m./T.M.S. s : singulet , d : doublet , t : triplet , q : quadruplet .
5 a	H	H	3'-H , s , 8.87 ; 4'-H , s , 8.12
5 b	H	CH_2-CH_3	3'-CH_2 , q , 3.0 ; 3"-CH_3 , t , 1.35 ; 4'-H , s , 8.05
5 c	CH_3	H	3'-H , s , 8.8 ; 4'-CH_3 , s , 2.75
5 d	(-CH_2-)$_3$		3'-CH_2 , t , 3.04 ; 4'-CH_2 , t , 3.15 ; -CH_2- , t , 2.23
5 e	C_6H_5-CH_2	H	3'H , s , 8.85 ; 4'-CH_2 ; s , 4.55 ; C_6H_5 , m , 7.3
5 f	C_6H_5	H	3'-H , s , 8.41 ; C_6H_5 , m , 7.48 - 7.62
5 g	C_6H_5	CH_3	3'-CH_3 , s , 1.88 ; C_6H_5 , m , 7.44 - 7.58
5 h	C_6H_5	C_6H_5	3'-C_6H_5 and 4'-C_6H_5 , m , 6.99 - 7.15
5 i	Cl	H	3'-H , s , 9.23
5 j	OCH_3	H	3'-H , s , 8.8 ; OCH_3 , s , 4.1

a) BRUKER AM 300 WB Spectrometer. (Centre Régional des Mesures Physiques de l'Ouest : C.R.M.P.O.).

TABLE III

Disulphides **5**. ^{13}C N.M.R. Spectra

COMPOUNDS	R_1	R	75.5 MHz [a,b] $CDCl_3$ δ p.p.m./T.M.S. s : singulet , d : doublet , t : triplet , q : quadruplet , m : multiplet.
5 a	H	H	3-C , d , 144.5 ; 3a-C , s , 167.5 ; 4-C , d , 120.9 ; 5-C , s , 182.4
5 b	H	CH_2-CH_3	3-C , s , 157.5 , 3'-CH_2 , t , 22.3 ; 3"-CH_3 , q , 11.7 ; 3a-C , s , 167.5 ; 4-C , d , 120.1 ; 5-C , s , 183.3
5 c	CH_3	H	3-C , d , 143.8 ; 3a-C , s , 165.5 ; 4-C , s , 131.3 ; 5-C , s , 180.1 ; 4'-CH_3 , q , 15.9
5 d	(-CH_2-)$_3$		3-C , s , 154.5 ; 3a-C , s , 162.8 ; 4-C , s , 134.6 ; 5-C , s , 177.2 ; 3'-C , t , 26.5 ; 4'-C , t , 25.0 ; -CH2- , t , 22.0
5 e	C_6H_5-CH_2	H	3-C , d , 144.0 ; 3a-C , s , 166.5 ; 4-C , s , 136.3 ; 5-C , s , 178.7 ; 4'-CH_2 , t , 35.9 ; C_6H_5 , m , 127.5 - 129.2
5 f	C_6H_5	H	3-C , d , 141.9 ; 3a-C , s , 166.5 ; 4-C , s , 136.8 ; 5-C , s , 180.8 ; C_6H_5 , m , 129.9 - 132.9
5 g	C_6H_5	CH_3	3-C , s , 152.8 ; 3'-CH_3 , q , 16.1 ; 3a-C , s , 165.1 ; 4-C , s , 136.4 ; 5-C , s , 183.0 ; C_6H_5 , m , 129.2 - 133.5
5 h	C_6H_5	C_6H_5	3-C , s , 157.3 ; 3'-C_6H_5 , m , 127.7 - 130.7 ; 3a-C , s , 163.9 ; 4-C , s , 137.5 ; 4'-C_6H_5 , m 128.6 - 132.5 ; 5-C , s , 182.5
5 i	Cl	H	3-C , d , 146.2 ; 3a-C , s , 167.5 ; 4-C , s , 117.0 ; 5-C , s , 177.6
5 j	OCH_3	H	3-C , d , 142.5 ; 3a-C , s , 167.2 ; 4-C , s , 158.1 ; 5-C , s , 182.9 ; OCH_3 , q , 62.7

a) BRUKER AM 300 WB Spectrometer. (C.R.M.P.O.).
b) are considered only $^1J_{C-H}$ coupling constants.

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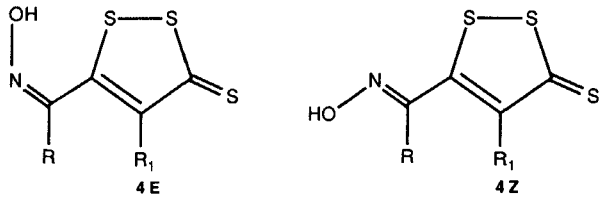

4 E 4 Z

However, it should be mentioned that the data given in the tables are those obtained by recording spectra as soon as oximes were dissolved in D.M.S.O. at 25°C. In fact, the ratio E/Z can vary according to different parameters (the separation of the two isomers and the conditions of the conversion Z – E will be reported later).[20] It is also worth noting that we could not characterize, in the preceding experimental conditions the tautomeric forms of oximes **4**: the 5-mercapto-heteropentalenes **6** by N.M.R. spectroscopy. Neither have preliminary records in other solvents (acetone-d_6, $CDCl_3$, pyridine) exhibited the presence of these forms.[20]

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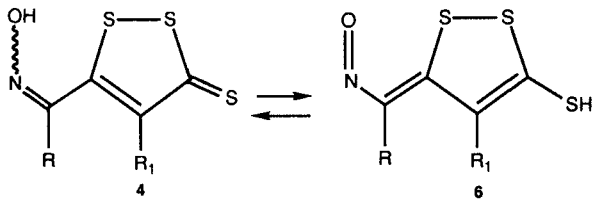
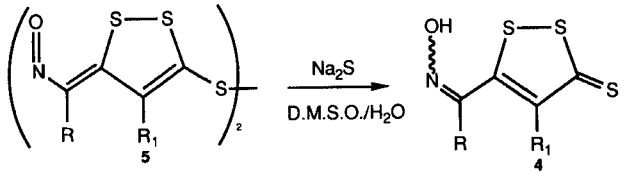
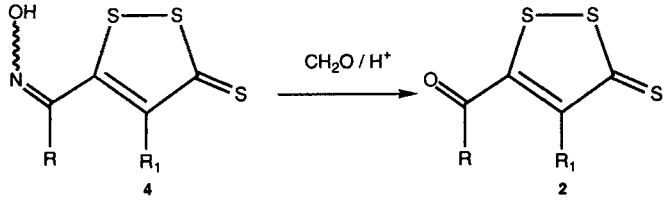


Scheme II



Scheme III



Scheme IV

DISCUSSION

Analytical data of oxime dithiolethiones **4** and aldehyde (or ketone) dithiolethiones **2** are consistent with the claimed structures (Tables IV–IX).

Concerning the isomery E/Z of compounds **4**, the assignation of structures **4E**

TABLE IV

5-(1-hydroxyiminoalkyl)-1,2-dithiole-3-thiones **4**

COMPOUNDS 4			YIELDS [a] %	RATIO [b] E/Z	M.P. [c] °C	Molecular formula	H.R.M.S. [e] exp	H.R.M.S. [e] theo	ν_{OH} [f] cm^{-1}
	R_1	R							
4 a	H	H	60	65/35	142	$C_4H_3NOS_3$	176,937	176,9376	2200-3500
4 b	H	CH_2-CH_3	63	75/25	126	$C_6H_7NOS_3$	204,969	204,9689	2350-3550
4 c	CH_3	H	75	70/30	174	$C_5H_5NOS_3$ [d]	190,354	190,9533	2100-3500
4 d	$(-CH_2-)_3$		75	100 Z	195	$C_7H_7NOS_3$ [d]	216,969	216,9698	1900-3500
4 e	$C_6H_5CH_2$	H	90	95/5	143	$C_{11}H_9NOS_3$	266,984	266,9846	2500-3500
4 f	C_6H_5	H	75	100 E	164	$C_{10}H_7NOS_3$	252,969	252,9689	2600-3600
4 g	C_6H_5	CH_3	75	100 E	162	$C_{11}H_9NOS_3$	266,984	266,9846	2400-3600
4 h	C_6H_5	C_6H_5	65	100 E	171	$C_{17}H_{13}NOS_3$	343,013	343,0159	2600-3700
4 i	Cl	H	80	95/5	230	$C_4H_2NOS_3{}^{35}Cl$	210,897	210,8987	2400-3600
4 j	OCH_3	H	90	80/20	107	$C_5H_5NO_2S_3$ [d]	206,948	206,9480	2400-3600

a) Total yield (E + Z when mixture occurs) based on disulphides **5** .
b) See text.
c) Melting point of the mixture (if it occurs) ; EtOH/H_2O mixture
d) Microanalysis.
e) Spectra recorded on Varian Mat 311 (Electronic impact 70 eV) (C.R.M.P.O.).
f) Diffuse reflectance infrared Fourier-transform 16-PC Perkin Elmer.

TABLE V

5-(1-hydroxyiminoalkyl)-1,2-dithiole-3-thiones **4**. ^1H N.M.R. Spectra

COMPOUNDS 4			300 MHz [a] D.M.S.O.-d_6 δ p.p.m./T.M.S. s : singulet , t : triplet, m : multiplet.
	R_1	R	
4 a	H	H	E : 4-H , s , 7.46 ; 5'-H , s , 8.42 ; OH , s , 12.72. Z : 4-H , s , 7.54 ; 5'-H , s , 8.09 ; OH , s , 13.85.
4 b	H	CH_2-CH_3	E : 4-H , s , 7.6 ; 5'-CH_2 , m , 2.71 ; 5"-CH_3 , t , 1.1 ; OH , s , 12.70 Z : 4-H , s , 7.5 ; 5'-CH_2 , m , 2.75 ; 5"-CH_3 , t , 1.3 ; OH , s , 13.67
4 c	CH_3	H	E : 4-CH_3 , s , 2.23 ; 5'-H , s , 8.59 ; OH , s , 12.70. Z : 4-CH_3 , s , 2.33 ; 5'-H , s, 8.19 ; OH , s , 13.80.
4 d	$(-CH_2-)_3$		Z : $(-CH_2-)_3$, m , 1.87 - 2.66 ; OH , s , 13.40.
4 e	$C_6H_5CH_2$	H	E : 4-CH_2- , s , 4.22 ; C_6H_5- , m , 7.16 - 7.26 ; 5'-H , s , 8.57 ; OH , s , 12.82. Z : 4-CH_2- , s , 4.35 ; C_6H_5- , m , 7.16 - 7.26 ; 5'-H , s , 8.20 ; OH , s , 14.00.
4 f	C_6H_5	H	E : C_6H_5 , m , 7.29 - 7.49 ; 5'-H , s , 7.69 ; OH , s , 12.80.
4 g	C_6H_5	CH_3	E : C_6H_5 , m , 7.22 - 7.45 ; 5'-CH_3 , s , 1.41 ; OH undetermined
4 h	C_6H_5	C_6H_5	E : 4-C_6H_5 , m , 7.18 - 7.32 ; 5'-C_6H_5 , m , 7.25 - 7.42 ; OH , s , 12.55.
4 i	Cl	H	E : 5'-H , s , 8.25 ; OH undetermined Z : 5'-H , s , 8.10 ; OH undetermined
4 j	OCH_3	H	E : OCH_3 , s , 3.89 ; 5'-H , s , 8.28 ; OH , s , 12.74. Z : OCH_3 , s , 3.91 ; 5'-H , s , 7.94 ; OH undetermined

a) BRUKER AM 300 WB Spectrometer (C.R.M.P.O.).

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TABLE VI

5-(1-hydroxyiminoalkyl)-1,2-dithiole-3-thiones **4**. ^{13}C N.M.R. Spectra

COMPOUNDS 4			75,5 MHz [a] D.M.S.O.-d6 δ p.p.m./T.M.S.
	R_1	R	s : singulet , d : doublet , t : triplet , q : quadruplet , m : multiplet[b].
4a	H	H	E : 3-C , s , 215.6 ; 4-C , d , 139.3 ; 5-C , s , 165.3 ; 5'-C , d , 143.7. Z : 3-C, s , 213.6 ; 4-C , d , 141.7 ; 5-C , s , 157.1 ; 5'-C , d , 139.8.
4b	H	CH_2-CH_3	E : 3-C, s , 216.4 ; 4-C , d , 136.4 ; 5-C , s , 168.6 ; 5'-C , s , 156.0 ; CH_2 , t , 18.8 ; CH_3 , q , 10.5 Z : 3-C , s , 213.3 ; 4-C , d , 139.4 ; 5-C , s , 157.9 ; 5'-C , s , 148.9 ; CH_2 , t , 26.1 ; CH_3 , q , 11.6
4c	CH_3	H	E : 3-C , s , 215.6 ; 4-C , s , 143.2 ; 4-CH_3 , q , 15.0 ; 5-C , s , 159.8 ; 5'-C , d , 145.1 Z : 3-C , s , 212.9 ; 4-C , s , 139.7 ; 4-CH_3 , q , 15.65 ; 5-C , s , 151.6 ; 5'-C , d, 144.9
4d	(-CH_2-)3		Z : 3-C , s , 211.1 ; 4-C , s , 147.6 ; (-CH_2-)3 , 3 x t , 20.7 - 27.9 - 28.4 ; 5 - C , s , 151.0 ; 5'-C , s , 147.8
4e	C_6H_5-CH_2	H	E : 3-C , s , 215.4 ; 4-C , s , 145.6 ; 4'-CH_2 , t , 33.2 ; 5-C , s , 161.7 ; 5'-C , d , 144.7 ; C_6H_5- , m , (i) 138.3 , (o) 127.7 , (m) 128.4 , (p) 126.2. Z : 3-C , s , 213.0 ; 4-C , s , 147.3 ; 4'-CH_2 , t , 33.5 ; 5-C , s , 153.2 ; 5'-C , d , 139.3 ; C_6H_5- , m , (i) 138.4 , (o) 127.7 , (m) 128.4 , (p) 126.2.
4f	C_6H_5	H	E : 3-C , s , 214.8 ; 4-C , s , 147.3 ; 5-C , s , 161.5 ; 5'-C , d , 144.7 ; C_6H_5- , m , (i) 132.6 ; (o) 130.2, (m) 128.4 , (p) 128.8.
4g	C_6H_5	CH_3	E : 3-C , s , 215.1 ; 4-C , s , 145.4 ; 5-C , s , 166.5 ; 5'-C , s , 151.9 ; 5'-CH_3 , q , 12.9 ; C_6H_5 , m , (i) 136.1 , (o) 129.2 ; (m) 128.2 , (p) 128.6
4h	C_6H_5	C_6H_5	E : 3-C , s , 214.1 ; 4-C , s , 147.0 ; 5-C , s , 163.0 ; 5'-C , s , 147.4 ; 4-C_6H_5 , m , (i) 130.3 , (o) 129.1 , (m) 128.7 , (p) 129.7 ; 5'-C_6H_5 , m , (i) 132.6 , (o) 125.8 , (m) 127.9 , (p) 128.6.
4i	Cl	H	E : 3-C , s , 207.3 ; 4-C , s , 133.7 ; 5-C , s , 158.8 ; 5'-C , 144.0 Z : 3-C , s , 207.3 ; 4-C , s , 128.3 ; 5-C , s , 150.0 ; 5'-C , 139.1
4j	OCH_3	H	E : 3-C , s , 206.4 ; 4-C , s , 157.3 ; OCH_3 , q , 60.8 ; 5-C , s , 151.7 ; 5'-C , d , 142.9. Z : 3-C , s , 204.0 ; 4-C , s , 158.8 ; OCH_3 , q , 60.5 ; 5-C , s , 143.7 ; 5'-C , d , 137.8

a) BRUKER AM 300 WB Spectrometer (C.R.M.P.O.) b) are considered only $^1J_{C-H}$ coupling constants

TABLE VII

5-acyl-1,2-dithiole-3-thiones **2**

COMPOUNDS						H.R.M.S. [d]		VCO [e]
	R_2	R	YIELDS [a] %	M.P. [b] °C	Molecular formula	exp	theo	cm^{-1}
2a	H	H	55	99	$C_4H_3OS_3$	161,926	161,9267	1670
2b	H	CH_2-CH_3	50	117	$C_6H_6OS_3$	189,958	189,9580	1682
2c	CH_3	H	85	105	$C_5H_4OS_3$ [c]	175,942	175,9424	1660
2d	(-CH_2-)3		55	95	$C_7H_6OS_3$	201,956	201,9580	1670
2e	$C_6H_5CH_2$	H	70	127	$C_{11}H_8OS_3$	251,974	251,9737	1681
2f	C_6H_5	H	80	131	$C_{10}H_6OS_3$	237,959	237,9581	1640
2g	C_6H_5	CH_3	80	85	$C_{11}H_8OS_3$	251,973	251,9737	1666
2i	Cl	H	65	136	$C_4H_1OS_3$ ^{35}Cl	195,889	195,8878	1680
2j	OCH_3	H	90	102	$C_5H_4O_2S_3$	191,937	191,9373	1663

a) Yields of isolated product **2** based on **4**.
b) Uncorrected, measured on a Reichert apparatus ; Cyclohexane.
c) Microanalysis.
d) High resolution mas spectrometry Varian Mat 311 Electronic impact 70 eV (C.R.M.P.O.).
e) Diffuse reflectance infrared Fourier-transform 16-PC Perkin Elmer.

and **4Z** was based on homonuclear Overhauser effects (N.O.Es.) in DMSO-d_6. In ^{13} C N.M.R., the $^3J_{C-H}$ coupling constants of 10 Hz between the aldehydic carbon and the hydroxyl proton in the E isomer only was particularly noticeable. Moreover, the $^1J_{C-H}$ between the aldehydic carbon and the proton associated is about 174.4 Hz for the E isomer and about 185.5 Hz for the Z[21,22] isomer. Otherwise, with

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TABLE VIII

5-acyl-1,2-dithiole-3-thiones **2**. ^{1}H N.M.R. Spectra

COMPOUNDS			300 MHZ [a] $CDCl_3$ δ p.p.m./T.M.S.
	R_1	R	s : singulet , d : doublet , t : triplet , q : quadruplet , m : multiplet.
2 a	H	H	4-H , s , 7.55 ; 5'-H , s , 10.00
2 b	H	CH_2-CH_3	4-H , s , 7.69 ; 5'-CH_2 , q , 2.89 ; 5"-CH_3 , t , 1.54
2 c	CH_3	H	4-CH_3 , s , 2.62 ; 5'-H , s , 8.31
2 d	(-CH_2-)$_3$		(-CH_2-)$_3$, m , 2.23 , 2.71 , 2.81
2 e	C_6H_5-CH_2	H	-CH_2- , s , 4.43 ; C_6H_5- , m , 7.20 - 7.28 ; 5'-H , s , 10.16
2 f	C_6H_5	H	C_6H_5- , m , 7;57 ; 5'-H , s , 9.76
2 g	C_6H_5	CH_3	C_6H_5- , m , 7.24 - 7.52 ; 5'-CH_3 , s , 1.92
2 i	Cl	H	5'-H , s , 10.2
2 j	OCH3	H	-OCH_3 , s , 4.20 ; 5'-H , s , 10.10

a) BRUKER AM 300 WB Spectrometer (C.R.M.P.O.).

TABLE IX

5-acyl-1,2-dithiole-3-thiones **2**. ^{13}C N.M.R. Spectra

COMPOUNDS			75.5 MHz [a,b] $CDCl_3$ δ p.p.m./T.M.S.
	R_1	R	s : singulet , d : doublet , t : triplet , q : quadruplet , m : multiplet.
2 a	H	H	3-C , s , 215.7 ; 4-C , d , 144.6 ; 5-C , s , 165.0 ; 5'-C , d , 183.5
2 b	H	CH_2-CH_3	3-C , s , 217.1 ; 4-C , d , 140.2 ; 5-C , s , 166.7 ; 5'-C , s , 194.6 ; CH_2 , t , 33.7 ; CH_3 , q , 7.7
2 c	CH_3	H	3-C , s , 217.0 ; 4-C , d , 149.3 ; 5-C , s , 159.4 ; 4-CH_3 , q , 15.6 ; 5'-C , d , 185.4
2 d	(-CH_2-)$_3$		3-C , s , 216.2 ; 4-C , s , 153.5 ; (-CH_2-)$_3$, 23.0 - 27.3 - 37.9 ; 5-C , s , 159.9 ; 5'-C , s , 194.6
2 e	C_6H_5-CH_2	H	3-C , s , 217.1 ; 4-C , s , 151.4 ; 4-CH_2- , t , 34.4 ; C_6H_5 , (i) 137.5 - (o) 128.0 - (m) 129.0 - (p) 127.2 ; 5-C , s , 161.3 ; 5'-C , d , 185.4
2 f	C_6H_5	H	3-C , s , 218.6 ; 4-C , s , 153.5 ; C_6H_5 , (i) 132.46 , (o) 131.82 , (m) 130.6 , (p) 129.3 ; 5-C , s , 163.7 ; 5'-C , d , 188.2
2 g	C_6H_5	CH_3	3-C , s , 219.6 ; 4-C , s , 148.6 ; C_6H_5- , (i) 133.7 - (o) 129.1 - (m) 130.1 - (p) 129.9 ; 5-C , s , 165.8 ; 5'-C , s , 194.5 ; 5'-CH_3 , q , 29.4
2 i	Cl	H	3-C , s , 207.5 ; 4-C , s , 141.0 ; 5-C , s , 156.9 ; 5'-C , d , 185.5
2 j	OCH_3	H	3-C , s , 207.9 ; 4-C , s , 162.7 ; -OCH_3 , q , 62.1 ; 5-C , s , 149.9 ; 5'-C , d , 182.2

a) BRUKER AM 300 WB Spectrometer (C.R.M.P.O.).
b) are considered only $^1J_{C-H}$ coupling constants

ketoximes **4** the carbonyl of which bears an alkylgroup, the assignation is based on the value of the shift of the adjacent linked alkyl carbon. According to Buchanan *et al.*, they are the more deshielded.[23] For other substituents or when only one isomer was obtained, its structure is only tentatively assigned.

The structure of 1-oxa-6,6a S^{IV}-dithia-2-azapentalene for the products **7** was essentially established because product **7a** obtained with the starting dithiolethione **3a** had physical data identical with those of the compound obtained and described as such by Reid *et al.*[18,24]

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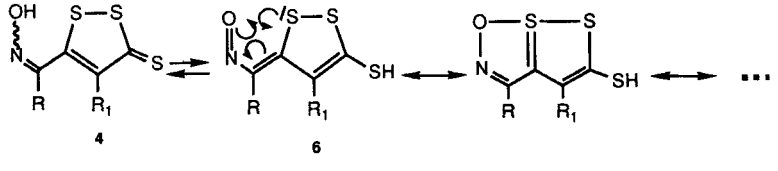
The structure of disulfides **5** was based on the following arguments: 1) IR spectra of compounds **5** and of **7** exhibited neither the characteristic group frequency of an N=O moiety nor those of a C=N group and of an SH group. They looked very similar except for two relatively strong bands in the regions 980 cm^{-1}, 1080 cm^{-1} and 1300 cm^{-1}, 1400 cm^{-1} and allowed us to conclude that compounds **5** and **7** belong to the same structural class. We must note that in normal conditions of ionization (electronic impact 70 eV) in mass spectrometry the molecular ions of disulfides **5** are not observed. Only the peak corresponding to the molecular ion of oxime **4** (or to the tautomeric form **6**) is observed. However mass spectra in field desorption conditions were recorded for seven compounds (Table I). Spectra exhibited the molecular ions of molecular mass of disulfide + 32 (Up to now, we have not succeeded in separating these compounds from disulfide by chromatography, due to the great insolubility of these compounds and due to their probably similar structures).

2) NMR data agree with the structure of disulfides **5** (Tables II and III).

3) Otherwise, oximes **4** were easily oxidised into disulfides **5** by iodine in alcoholic solution at room temperature. So, when performing the synthesis, disulfides **5** were probably the oxydation products, by excess of nitrous acid, of oxime dithiolethiones **4** which had been formed in a first step. This is suggested by the easy oxidation of oximes **4** by nitrous acid in the experimental conditions of the reaction. (Interestingly, however, when no excess of sodium nitrite was added, only disulfide **5** could be isolated). Oxidation of oximes **4** into disulfides **5**, strongly suggests the existence of the tautomeric equilibrium between oxime dithiolethione **4** and its tautomeric form: the 5-mercapto-heteropentalene **6** (Scheme II) despite the fact that it was never detected by N.M.R. spectroscopy as mentioned above. It can be inferred that the equilibrium **4** ⇄ **6** is strongly displaced towards oximes **4**. This is an interesting finding because 1-oxa- 6,6a S^{IV}-dithia-2-azapentalenes **7** (as well as those, from a more general point of view, substituted on 5-carbon) are considered as bicyclic aromatic compounds with considerable Π-electron delocalisation[24,25 interalia] (Scheme V). Therefore, oximes **4**, must also be considered as compounds with considerable Π-electron delocalisation.

The mechanism of the formation of oxime dithiolethione **4** remains conjectural. However, as it is indicated by our first semi-empirical calculations, it probably looks like the mechanism invoked in the nitrosation of ketone in acidic medium.[26] In anhydrous acetic acid, a medium of high protic activity,[27] the thione group can be protonated and by a prototropic process can give the conjugated enethiol which can undergo an electrophilic attack by the nitrosonium ion[28] followed by a new prototropic process to give compound **6** (Scheme VI). The possibility of protonation of the thione group of a dithiolethione supports this hypothesis.[29]



Scheme V

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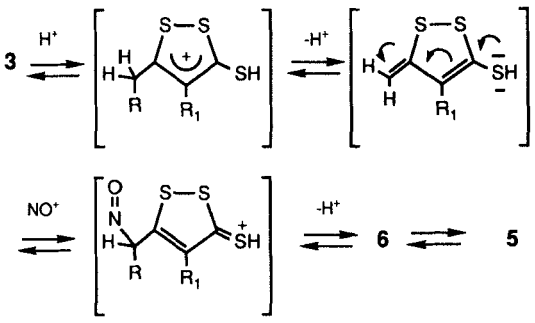

Scheme VI

The mechanism of formation of heteropentalenes **7** remains conjectural too. We only note, that some reactions with extrusion of sulfur in oxidising media are reported in literature.[30,31] These two mechanisms are being studied.

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EXPERIMENTAL

All the starting dithiolethiones are described in literature (Table I) except 5-ethyl 4-phenyl, 4-methoxy 5-methyl and 5-propyl dithiolethiones.

5-ethyl-4-phenyl-1,2-dithiole-3-thione **3g**. It was obtained from 1-phenyl 2-butanone which is a commercial product (Aldrich: purity > 98%) via the 1,1-bis(methylthio)-2-phenyl 1-pentene 3-one prepared by condensation of carbon disulfide on ethyl-benzyl-ketone, in the presence of sodium t-amylate followed by a methylation according the synthesis of A. Thuillier and J. Vialle.[32]

*1,1-bis (methylthio)-2-phenyl-1-pentene-3-one

Yellow liq. Yield %: 80. ^{1}H N.M.R. [$CDCl_3$, δ p.p.m./T.M.S.]: 1,35 [t, 3H]: 2,55 to 2,85 [m, 8H]: 7.65 [s, 5H].

*5-ethyl 4-phenyl 1,2-dithiole 3-thione **3g**

Orange-yellow crystals (benzene) F = 64° yield %: 70

^{1}H N.M.R. [$CDCl_3$, δ p.p.m./T.M.S.]: 1.35 [t, 3H]; 2.65 [q, 2H]; 7.25–7.65 [m, 5H] satisfactory microanalysis: C, H, S: ± 0,25

4-methoxy-5-methyl-1,2-dithiole-3-thione **3j**. It was prepared in the same manner as the previous one starting with commercial methoxyacetone (Janssen, purity > 99%).

Yellow crystal (ligroin) F = 51°C overall yield %: 40.

^{1}H N.M.R. [$CDCl_3$, δ p.p.m./T.M.S]: 2,48 [s, 3H]: 3,90 [s, 3H]

satisfactory microanalysis: C, H, S, O: ±0,25

5-propyl-1,2-dithiole-3-thione **3b**. It was prepared by direct sulfuration of ethyl butyrylacetate (Aldrich, purity > 98%) according to the synthesis of L. Legrand and N. Lozac'h.[33]

Dark red liq., yield %: 70

^{1}H N.M.R.[$CDCl_3$, δ p.p.m./T.M.S.]: 1,10 [t, 3H]: 1,87 [m, 2H]; 2,83 [t, 2H]; 7,23 [s, 1H].

5-mercapto-1-oxa-6,6a S^{IV}-dithia-2-azapentalene-disulfides **5**. General procedure: To a stirred solution prepared by dissolving 1 g of starting dithiolethione **3** in 70 cm^3 anhydrous acetic acid, was added a strong excess of anhydrous sodium nitrite till a precipitate appeared. This occurred generally within around ten minutes. The addition, gave a red colour while nitrous fumes developed. At the beginning of the precipitation the solution turned safran-yellow. The mixture was then allowed to stand for one night. The disulfide was collected by filtration, washed with water and ethanol and dried in vacuum (Tables I–III).

Remark: From a synthetic standpoint, we have found that better yields in disulfides **5** are obtained by treating, at room temperature, starting dithiolethiones **3** by an excess of nitrous acid. In these conditions, disulfides **5** are systematically isolated. Due to their great insolubility, these products precipitate quantitatively and the yields obtained are good by displacement of the equilibrium. Moreover, this pathway is a convenient mean of purification because the starting dithiolethiones **3** and possibly by-products **7** (when they exist) stay in the acetic acid solution.

5-(1-hydroxyiminoalkyl)-1,2-dithiole-3-thiones **4**. General procedure: An excess of nonahydrated sodium sulfide was added at room temperature to a suspension of disulfides **5** into a mixture of D.M.S.O./ water (50%) till the blood-red coloration of the sodium salt of oxime **4** appeared. The medium was acidified by a solution of diluted hydrochloric acid. The orange precipitate formed was extracted by diethylether. The ethereal solution was washed, dried on anhydrous sodium sulfate and then filtered and concentrated. Oximes **4** were systematically crystallised in ethanaol-water mixtures. (Oximes **4** can be purified by chromatography on silicagel 0,060–0,200 mm. They are eluted by n-heptane and diethylether mixtures) (Tables IV–VI).

5-acyl-1,2-dithiole-3-thiones **2**: General procedure: Oximes **4** were reacted with an aqueous solution of formaldehyde (37%) in acidic condition (pH = 0) in the presence of a toluenic phase for two hours at 60°C. The obtained dark-red toluene phase was then washed with water, dried on anhydrous sulfate, filtered and concentrated. The crude products were crystallized in cyclohexane (5-acyl-dithiolethiones can be chromatographied. They are eluted by ligroin - toluene mixtures) (Tables VII–IX).

Heteropentalenes **7a**, **7c**. The reaction of nitrosation of the corresponding starting dithiolethione **3** was performed as before but at 70°C. The acetic filtrate (from the isolation of disulfide **5**) was diluted with water and extracted with toluene. Toluenic solution was treated as usually. Heteropentalene **7** was eluted after traces of starting dithiolethione and oxime dithiolethione **4**.

1-oxa-6,6a S^{IV}-dithia-2-azapentalene **7a** molecular formula $C_4H_3NOS_2$
F = 83°C, orange crystals (benzene) (litt[24] F = 83°C – 85°C)

4-methyl-1-oxa-6,6a S^{IV}-*dithia-2-azapentalene* **7c**
molecular formula $C_5H_5NOS_2$

F = 116°C, orange crystals (methanol) C.N.S ± 0,30

^{1}H N.M.R. [$CDCl_3$, δ p.p.m./T.M.S.] [3H, s, 2.70]; [1H, s, 9.00]; [1H, s, 9.10] MS: m/z = 159.

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