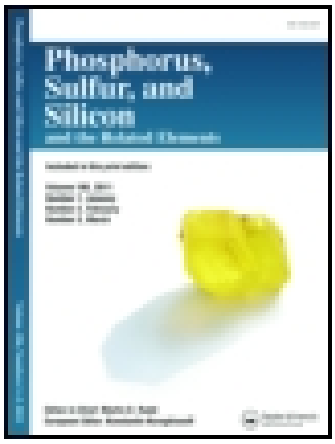

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Synthesis of 5-Formyl and 5-Acyl-1,2-dithiole-3-ones

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SYNTHESIS OF 5-FORMYL AND 5-ACYL-1,2-DITHIOLE-3-ONES

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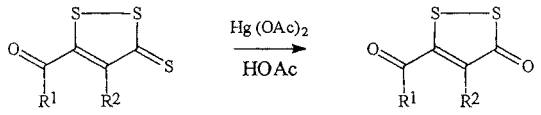
The preparation of new 5-formyl-, 5-acetyl- and 5-propionyl-1,2-dithiole-3-ones by oxidation of the corresponding 1,2-dithiole-3-thiones with mercuric acetate is described.

Keywords: 5-Formyl (or 5-acyl)-1,2-dithiole-3-ones; 5-formyl(or 5-acyl)-1,2-dithiole-3-thiones

1-(5-thioxo-5*H*-1,2-dithiole-3-yl)-ketones **1** together with the corresponding 1,2-dithiole-3-ones **2** are patented for their pharmacological properties, especially for their microbicidal ones.[1–3]

In the course of our studies devoted to the synthesis of new 1,2-dithiole-3-thiones[1,2] and to their physico-chemical properties,[4,5] we have determined water/n-octanol log P values of several 1,2-dithiole-3-thiones and 3-ones in order to establish quantitative structure activity relationships.[6] With this aim, we have prepared new 1,2-dithiole-3-ones



1a-n **2a-n**

	a	b	c	d	e	f	g	h	i	j	k	l	m	n
R¹	H	H	H	H	H	H	Me	Me	Me	Me	Et	Et	Et	$(CH_2)_3$
R²	H	Me	Et	Ph	OMe	Cl	H	Me	Et	Ph	H	Me	Et	

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2 by reaction of mercuric acetate with the corresponding 1,2-dithiole-3-thiones **1**, three of which were new and also are described herein. Mercuric acetate[7] was preferred to benzonitrile oxide[3] as the oxidant because it led to better yields.

EXPERIMENTAL SECTION

Infrared spectra were obtained with a diffuse reflectance infrared Fourier-transform 16-PC Perkin-Elmer. ^{1}H NMR spectra were measured at the CRMPO, Rennes, France, in $CDCl_3$ with a Bruker AM 300 MHz WB spectrometer and ^{13}C NMR spectra with a Bruker AM 75.5 MHz WB spectrometer. Mass spectra were recorded on a varian Mat 311 (Electronic impact 70 eV).

5 *H*-1,2-Dithiole-3-thiones

4-Ethyl-5-thioxo-5 H-*1,2-dithiole-3-carbaldehyde 1c*

Compound **1c** was obtained from 4-ethyl-5-methyl-1,2-dithiole-3-thione[8] according to the standard procedure using $NaNO_2$ in glacial acetic acid[1] with a yield of 17%. Red crystals; m.p. 76°C (heptane); IR:$\nu = 1674$ cm^{-1}; MS: *m/z*: 189.959 (calc. for $C_6H_6OS_3$: 189.9581), ^{1}H NMR $\delta = 1.26$ (t, 3H, $^3J = 7.5$ Hz, CH_3); 3.10 (q, 2H, $^3J = 7.5$ Hz,CH_2); 10.24(s, 1H, CHO); ^{13}C NMR $\delta = 14.7$ (qt, $^1J = 129$ Hz, $^2J = 5.4$ Hz, CH_3); 22.7 (td, $^1J = 131$ Hz, $^2J = 4.5$ Hz, CH_2); 155.1 (m, C-4); 159.6 (dt, $^2J = 3.4$ Hz, $^3J = 4.5$ Hz, C-5); 185.2 (d, $^1J = 189$ Hz, C=O); 217.2 (t, $^3J = 7$ Hz, C=S).

1-(4-Methyl-5-thioxo-5 H-*1,2-dithiole-3-yl)-propan-1-one 1l*

Compound **1l** was obtained from 4-methyl-5-propyl-1,2-dithiole-3-thione[4] according to the standard procedure[1] with a yield of 20%. Red crystals; m.p. = 75°C (hexane); IR:$\nu = 1700$ cm^{-1}; MS: *m/z*: 203.9732 (calc. for $C_7H_8OS_3$: 203.9737); ^{1}H NMR $\delta = 1.27$ (t, 3H, $^3J = 7.2$ Hz, CH_2-CH_3); 2.46 (s, 3H, CH_3); 2.99 (q, 2H, $^3J = 7.2$ Hz, CH_2); ^{13}C NMR $\delta = 7.7$ (qt, $^1J = 129$ Hz, $^2J = 4$ Hz, CH_2-CH_3); 17.3 (q, $^1J = 131$ Hz, CH_3-4); 37.0 (tq ,$^1J = 129$Hz, $^2J = 4$Hz, CH_2); 145.9 (q, $^2J = 6.2$ Hz, C-4); 161.1 (q, $^3J = 5$ Hz, C-5); 195.7 (q, $^3J = 5.3$ Hz, C=O); 213.3 (q, $^3J = 5.5$ Hz, C=S).

1-(4-Ethyl-5-thioxo-5 H-*1,2-dithiole-3-yl)-propan-1-one 1m*

Compound **1m** was obtained from 4-ethyl-5-propyl-1,2-dithiole-3-thione[9] according to the standard procedure[1] with a yield of 11%. Red crystals; m.p. 45°C (hexane); IR: $\nu = 1702$ cm^{-1}; MS: *m/z*: 217.9891

(calc. for $C_8H_{10}OS_3$: 217.9894); ^1H $\delta = 1.09$ (t, 3H, $^3J = 7.3$ Hz, CH_3-4); 1.20 (t, 3H, $^3J = 7.0$ Hz, CH_3-5); 2.92 (q, 2H, $^3J = 7.3$ Hz, CH_2-4); 3.14 (q, 2H, $^3J = 7.0$ Hz, CH_2-5); ^{13}C $\delta = 7.9$ (qt, $^1J = 129$ Hz , $^2J = 4.5$ Hz, *C*H$_3$-5); 13.0 (qt, $^1J = 128$ Hz, $^2J = 4.5$ Hz, *C*H$_3$-4); 24.4 (tq, $^1J = 131$ Hz, $^2J = 4.5$ Hz, *C*H$_2$-4); 37.4 (tq, $^1J = 126$ Hz, $^2J = 4.5$ Hz, *C*H$_2$-5); 151.6 (m, C-4); 163.6 (t, $^3J = 5$ Hz, C-5); 196.2 (q, $^3J = 5.3$ Hz, C=O); 218.2 (t, $^3J = 7$ Hz, C=S).

5-Formyl and 5-Acyl-1,2-dithiole-3-ones (General Procedure)

Two equivalents of mercuric acetate in 70 ml of boiling acetic acid are added to 100 mL of a boiling solution containing one equivalent of the corresponding 1-(5-thioxo-5*H*-1,2-dithiole-3-yl)-ketone **1**. The mixture was stirred and heated for 3 h. The solution was then allowed to reach room temperature. After filtration and stripping off the solvent, the crude product was purified by silica gel chromatography with toluene to give the expected 5-acyl-1,2-dithiole-3-ones **2**.

5-Oxo-5 H-*1,2-dithiole-3-carbaldehyde 2a*

Compound **2a** was obtained from **1a**[1] with a yield of 30%. m.p. 83°C (ethylacetate); IR: $\nu = 1676$, 1647 cm^{-1}; MS: *m/z*: 145.9491 (calc. for $C_4H_2O_2S_2$: 145.9496); ^1H $\delta = 7.27$ (s, 1H, H-4); 10.04 (s, 1H, CHO); ^{13}C $\delta = 129.2$ (d, $^1J = 175$ Hz, C-4); 163.9 (m, C-5); 182.5 (dd, $^1J = 192$ Hz, $^3J = 5$ Hz, CHO); 193.8 (d, $^2J = 5.5$ Hz, C-3).

4-Methyl-5-oxo-5 H-*1,2-dithiole-3-carbaldehyde 2b*

Compound **2b** was obtained from **1b**[1] with an overall yield of 36%. m.p. 79°C (ethylacetate); IR: $\nu = 1670$, 1647 cm^{-1}; MS: *m/z*: 159.9652 (calc. for $C_5H_4O_2S_2$: 159.9653); ^1H $\delta = 2.41$(s, 3H, CH_3); 10.26 (s, 1H, CHO); ^{13}C $\delta = 12.8$ (q, CH_3); 138.4 (m, C-4); 155.2 (m, C-5); 183.7 (d, $^1J = 190$ Hz, CHO); 196.1 (q, C-3).

4-Ethyl-5-oxo-5 H-*1,2-dithiole-3-carbaldehyde 2c*

Compound **2c** was obtained from **1c** with a yield of 80%. m.p. 48°C (ethylacetate); IR: $\nu = 1670$, 1645 cm^{-1}; MS: *m/z*: 173.9809 (calc. for $C_6H_6O_2S_2$: 173.9809); ^1H $\delta = 1.26$ (t, 3H, $^3J = 7.5$ Hz, CH_3); 2.88 (q, 2H, $^3J = 7.5$ Hz, CH_2); 10.24 (s, 1H, CHO); ^{13}C NMR $\delta = 14.6$ (qt, $^1J = 128.5$ Hz, $^2J = 5$ Hz, CH_3); 20.8 (tq, $^1J = 131.5$ Hz, $^2J = 4$ Hz, CH_2); 144.1 (m, C-4); 155.6 (dt, $^2J = 35$ Hz, $^3J = 4$ Hz, C-5); 183.7 (d, $^1J = 189$ Hz, CHO); 195.9 (t, $^3J = 6$ Hz, C-3).

5-Oxo-4-phenyl-5 H-*1,2-dithiole-3-carbaldehyde 2d*

Compound **2d** was obtained from **1d**[1] with a yield of 75%. m.p. 153°C (heptane); IR: $\nu = 1670$, 1640 cm^{-1}; MS: *m/z*: 221.9800 (calc. for $C_{10}H_6O_2S_2$: 221.9809); ^1H $\delta = 7.41$ (m, 2H, C_6H_5-*m*); 7.51 (m, 3H, C_6H_5-*o*, *p*); 9.82 (s, 1H, CHO); ^{13}C NMR $\delta = 128.9$ (d, $^1J = 161$ Hz, C_6H_5-*m*); 129.4 (t, $^3J = 6.5$ Hz, C_6H_5-4); 130.2 (d, $^1J = 160$ Hz, C_6H_5-*p*); 130.3 (dm, $^1J = 161$ Hz, C_6H_5-*o*); 141.0 (t, $^3J = 4$ Hz, C-4); 157.9 (d, $^2J = 35$ Hz, C-5); 185.4 (d, $^1J = 194$ Hz, CHO); 194.4 (s, C-3).

4-Methoxy-5-oxo-5 H-*1,2-dithiole-3-carbaldehyde 2e*

Compound **2e** was obtained from **1e**[1] with a yield of 80%. m.p. 54°C (hexane); IR: $\nu = 1670$, 1632 cm^{-1}; MS: *m/z*: 175.9599 (calc. for $C_5H_4O_3S_2$: 175.9602); ^1H $\delta = 4.19$ (s, 3H, CH_3); 10.11 (s, 1H, CHO); ^{13}C NMR $\delta = 60.3$ (q, $^1J = 148$ Hz, CH_3); 141.4 (d, $^2J = 34$ Hz, C-5); 154.0 (q, $^3J = 4$ Hz, C-4); 183.8 (d, $^1J = 194$ Hz, CHO); 189.0 (s, C-3).

4-Chloro-5-oxo-5 H-*1,2-dithiole-3-carbaldehyde 2f*

Compound **2f** was obtained from **1f** [1] with a yield of 70%. m.p. 89°C (hexane); IR: $\nu = 1676$, 1604 cm^{-1}; MS: *m/z*: 181.9070 (calc. for $C_4HClO_2S_2$: 181.9077); ^1H $\delta = 10.26$ (s, 1H, CHO); ^{13}C NMR $\delta = 130.9$ (s, C-4); 153.1 (d, $^2J = 34$ Hz, C-5); 182.9 (d, $^1J = 197$ Hz, CHO); 187.7 (s, C-3).

5-Acetyl-1,2-dithiole-3-one 2g

Compound **2g** was obtained from **1g**[2] with a yield of 50%. m.p. 119°C (methanol); IR: $\nu = 1684$, 1642 cm^{-1}; MS: *m/z*: 159.9652 (calc. for $C_5H_4O_2S_2$: 159.9653); ^1H $\delta = 2.65$ (s, 3H, CH_3); 7.18 (s, 1H, H-4); ^{13}C NMR $\delta = 27.6$ (q, $^1J = 129$ Hz, CH_3); 125.2 (d, $^1J = 175$ Hz, C-4); 165.4 (d, $^2J = 7$ Hz, C-5); 190.6 (m, CH_3C=O); 194.7 (d, $^2J = 5.4$ Hz, C-3).

5-Acetyl-4-methyl-1,2-dithiole-3-one 2h

Compound **2h** was obtained from **1h**[2] with a yield of 40%. m.p. 44°C (methanol); IR: $\nu = 1671$, 1646 cm^{-1}; MS: *m/z*: 173.9809 (calc. for $C_6H_6O_2S_2$: 173.9809); ^1H $\delta = 2.31$ (s, 3H, CH_3-4); 2.65 (s, 3H, COCH_3); ^{13}C NMR $\delta = 14.7$ (q, CH_3-4); 30.0 (q, $^1J = 129$ Hz, CH_3CO); 134 (q, C-4); 157.3 (m, C-5); 192.0 (m, CH_3C=O); 195.9 (q, C-3).

5-Acetyl-4-ethyl-1,2-dithiole-3-one 2i

Compound **2i** was obtained from **1i**[2] with a yield of 63%. m.p. 38°C (methanol); IR: $\nu = 1704$, 1652 cm^{-1}; MS: *m/z*: 187.9956 (calc. for $C_7H_8O_2S_2$: 187.9956); ^1H $\delta = 1.14$ (t, 3H, CH_2CH_3); 2.64 (s, 3H, COCH_3); 2.76 (q, 2H, CH_2); ^{13}C NMR $\delta = 13.2$ (qt, $^1J = 128$ Hz, $^2J = 6.5$ Hz,

CH_2CH_3); 22.1 (tq, $^1J = 132$ Hz, $^2J = 4.5$ Hz, CH_2); 29.6 (q , $^1J = 129$ Hz, $COCH_3$); 139.6 (m, C-4); 157.1 (q, $^3J = 4.4$ Hz, C-5); 191.9 (q, , $^2J = 6.5$ Hz, $COCH_3$); 195.6 (t, $^3J = 6$ Hz, C-3).

5-Acetyl-4-phenyl-1,2-dithiole-3-one 2j

Compound **2j** was obtained from **1j**[1] with a yield of 70%. m.p. 69°C (hexane); IR: $\nu = 1664$, 1646 cm^{-1}; MS: *m/z*: 235.9954 (calc. for $C_{11}H_8O_2S_2$: 235.9966); ^1H $\delta = 2.02$ (s, 3H, CH_3); 7.29 (m, 2H, C_6H_5-*m*); 7.48 (m, 3H, C_6H_5-*o*, *p*); ^{13}C NMR $\delta = 29.5$ (q, $^1J = 130$ Hz, CH_3); 129.1 (d, $^1J = 160$ Hz, C_6H_5-*m*); 129.7 (d, $^1J = 161$ Hz, C_6H_5-*o*); 129.9 (m, C_6H_5-*p*); 131.8 (m, C_6H_5-4); 136.1 (t, $^3J = 3.5$ Hz, C-4); 161.8 (s, C-5); 194.1 (s, C-3); 194.4 (q, $^2J = 6.5$ Hz, $COCH_3$).

5-Propionyl-1,2-dithiole-3-one 2k

Compound **2k** was obtained from **1k**[1] with a yield of 80%. m.p. 99–100°C (methanol); IR: $\nu = 1686$, 1630 cm^{-1}; MS: *m/z*: 173.9809 (calc. for $C_6H_6O_2S_2$: 173.9809); ^1H $\delta = 1.24$ (t, 3H, CH_3); 2.98 (q, 2H, CH_2); 7.16 (s, 1H, H-4); ^{13}C NMR $\delta = 7.6$ (qt, $^1J = 129$ Hz, $^2J = 4.5$ Hz, CH_3); 38.7 (tq, $^1J = 126$ Hz, $^2J = 4.5$ Hz, CH_2); 124.3 (d, $^1J = 175$ Hz, C-4); 165.3 (d, $^2J = 8$ Hz, C-5); 193.7 (m, *C*OEt); 194.9 (d, $^2J = 5.4$ Hz, C-3).

4-Methyl-5-propionyl-1,2-dithiole-3-one 2l

Compound **2l** was obtained from **1l** with a yield of 82%. m.p. 98–99°C (methanol); IR: $\nu = 1668$, 1630 cm^{-1}; MS: *m/z*: 187.9975 (calc. for $C_7H_8O_2S_2$: 187.9966); ^1H $\delta = 1.24$ (t, 3H, CH_3-CH_2); 2.29 (s, 3H, CH_3-4); 2.93 (q, 2H, CH_2); ^{13}C NMR $\delta = 7.6$ (qt, $^1J = 129$ Hz, $^2J = 4.4$ Hz, CH_3-CH_2); 14.6 (q, $^1J = 131$ Hz, CH_3-4); 35.9 (tq, $^1J = 126$ Hz, $^2J = 4.4$ Hz, CH_2); 133.7 (q, $^2J = 6.5$ Hz, C-4); 157.2 (m, C-5); 195.2 (m, *C*OEt); 195.9 (m, C-3).

4-Ethyl-5-propionyl-1,2-dithiole-3-one 2m

Compound **2m** was obtained from **1m** with a yield of 40%. m.p. 49–50°C (methanol); IR: $\nu = 1666$, 1625 cm^{-1}; MS: *m/z*: 202.0132 (calc. for $C_8H_{10}O_2S_2$: 202.0122); ^1H $\delta = 1.14$ (t, 3H, CH_3CH_2-4); 1.24 (t, 3H, CH_3CH_2CO); 2.76 (q, 2H, CH_2-4); 2.95 (q, 2H, CH_2-CO); ^{13}C NMR $\delta =$ 7.6 (qt, $^1J = 129$ Hz, $^2J = 4.5$ Hz, CH_3CH_2CO); 13.2 (qt, $^1J = 128$ Hz, $^2J = 5$ Hz, CH_3CH_2-4); 22.1 (tq, $^1J = 131$ Hz,$^2J = 4.5$ Hz, CH_2-4); 35.6 (tq, $^1J = 125$ Hz, $^2J = 4.5$ Hz,CH_2CO); 139.3 (q, $^3J = 5.5$ Hz, C-4); 157.0 (t, $^3J = 5$ Hz, C-5); 195.2 (q, $^3J = 5.5$ Hz, *C*OEt); 195.9 (t, $^3J = 6$ Hz, C-3).

4,5,6,7-Tetrahydro-4 H-*benzo–1,2-dithiole-3,7-dione 2n*

Compound **2n** was obtained from **1n**[1] with a yield of 45%. m.p. 52–53°C (hexane); IR: $\nu = 1684$, 1654 cm^{-1}; MS: *m/z*: 185.9805 (calc.

for $C_7H_6O_2S_2$: 185.9809); ^1H $\delta = 2.22$ (m, 2H, CH_2-CH_2-CH_2); 2.69 (t, 2H, CH_2-4); 2.74 (t, 2H, CH_2CO); ^{13}C NMR $\delta = 22.9$ (t, $^1J = 131$ Hz, CH_2-CH_2-CH_2); 24.8 (t, $^1J = 132$ Hz, CH_2-4); 38.8 (t, $^1J = 130$ Hz, CH_2CO); 141.9 (m, C-4); 154.8 (t, $^3J = 4.5$ Hz, C-5); 193.1 (m, CH_2CO); 195.1 (s, C-3).

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