2,2-Dioxo-1*H*-thieno[3,4-*c*][1,2]thiazines. Synthesis and some Reactions of a New Heterocycle

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The first synthesis of substituted 2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*][1,2]thiazines **2** and some of their reactions are achieved. Compounds **2** were prepared from the 3,5-dimethyl-1,1-dioxo-1,2-thiazine-4-carbaldehydes **1** by reaction with sulfur and triethyl amine in dimethylformamide under mild conditions. They were characterized spectroscopically and by X-ray structure analysis. The formylation, chlorination and oxidation of **2** are reported.

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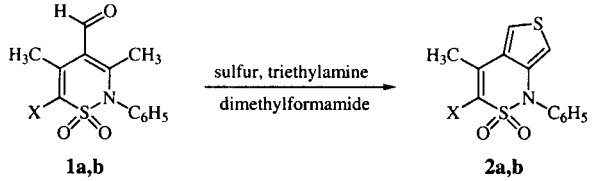
Recently different thieno[3,4-*e*]thiazines, thieno[3,2-*e*]-thiazines or thieno[2,3-*e*]thiazines were synthesized or patented [1-5]. Some derivatives are in use as drugs (Tilcotil®). These types of thienothiazines were formed by multistep reactions or under drastic reaction conditions. The synthesis of benzo[*c*]thiophenes [6] also (as the benzo analogues of the thieno[3,4-*c*][1,2]thiazines) is difficult. In this paper, we describe a simple synthesis of the 2,2-dioxo-1*H*-thieno[3,4-*c*][1,2]thiazines **2** by reaction of the 3,5-dimethyl-1,1-dioxo-1,2-thiazine-4-carbaldehydes **1** with sulfur and triethylamine in dimethylformamide at room temperature. A methyl thiol can be postulated as intermediate of a mild thiolation of the CH-acidic 3-methyl group in **1**. This intermediate is stabilized by formation of the aromatic thiophene system and not by further thiolation into a dithio carboxylic acid [7].

Scheme 1



1a,b **2a,b**

1,2 X

a SCH_3
b Cl

The colourless solids **2** were obtained in yields of 59% and 49%, respectively. Their ^1H nmr signals differ clearly from those of the unsubstituted thiophene. The C5-H signal appears downfield (δ = 8.2). The C7-H signal is observed at higher field (δ = 6.7-6.9) (thiophene: C2/5-H: δ = 7.2) [8]. The ^{13}C nmr signals are recorded at δ = 127-128 (C5) and at δ = 110-113 for C7, respectively (thiophene: δ = 125.6) [9].

The structure of **2a** has been established and characterized in detail by X-ray analysis.

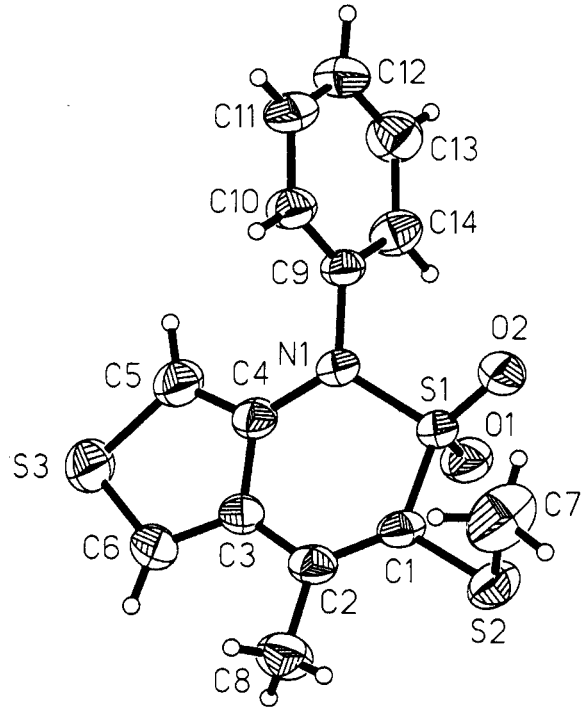


Figure 1 Molecular structure of **2a** with atom numbering. Displacement ellipsoids are drawn at the 50% probability level and H atoms as small circles of arbitrary size.

As far as we are aware, this is the first determination of a thieno- or benzo[*c*]-anellated 2,2-dioxo-1,2-thiazine; a search of the Cambridge Structural Database [10] found no other examples. The thiophene ring in **2a** is exactly planar and has the expected dimensions [11]. The thiazine ring is far from planar; bond lengths C2–C3 [1.449(4) Å] and C3–C4 [1.441(3) Å] are equal within 3σ and near the standard value for a $C(sp^2)$–$C(sp^2)$ single bond [1.466 Å [12]] whereas C1–C2 [1.346(4) Å] agrees well with the standard value for a $C(sp^2)$–$C(sp^2)$ double bond [1.335 Å [12]]. Furthermore, the geometry of the thiazine ring agrees well

with that of the closely related compound 2-(4-methoxyphenyl)-3,5-dimethyl-1,1-dioxo-1,2-thiazine (**3**) (Figure 2), which we have investigated for comparison.

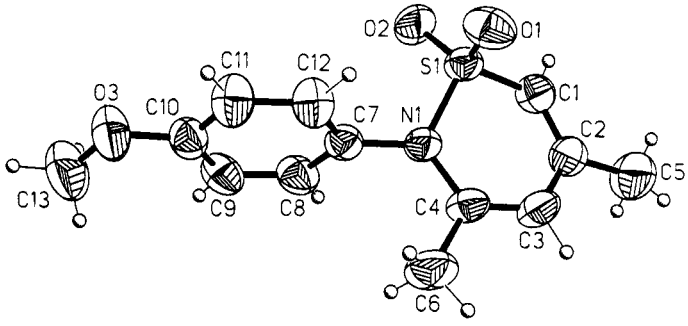
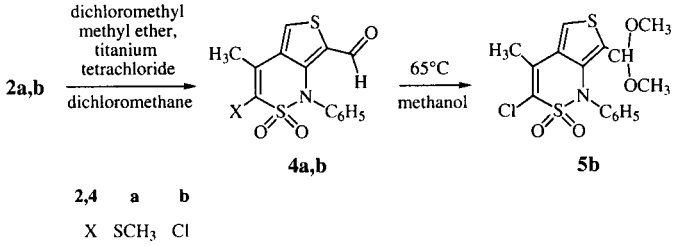


Figure 2 Molecular structure of **3** with atom numbering. Displacement ellipsoids are drawn at the 50% probability level and H atoms as small circles of arbitrary size.

With dichloromethyl methyl ether/titanium tetrachloride [13,14] the thieno[3,4-*c*]thiazines **2** obtained are formylated regioselectively in the 7-position. In contrast to that, no reaction was observed with phosphoryl chloride/dimethylformamide as the formylation agent under comparable reaction conditions.

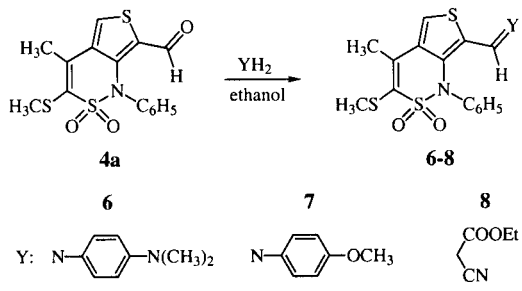
Scheme 2



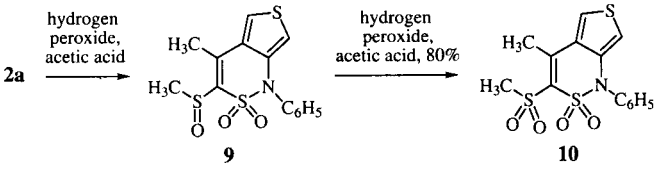
In the carbaldehyde **4b** the formyl group is strongly electrophilic by the influence of the electron withdrawing fused ring system and the chloro substituent. Therefore the carbaldehyde reacts spontaneously in hot methanol to the corresponding dimethyl acetal **5b**. Furthermore, the carbaldehydes **4** react in a usual way with anilines and undergo Knoevenagel reactions with C-H-acidic compounds. Therefore, the carbaldehydes **4** are interesting synthons for diverse reaction types. Compound **6** is currently evaluated for its nonlinear optical properties as a donor-acceptor chromophore.

The thienothiazine **2a** reacts with hydrogen peroxide in acetic acid at room temperature to the sulfoxide **9**, which has lost its ability to be formylated by dichloromethyl methyl ether/titanium tetrachloride. At higher temperature and with an excess of hydrogen peroxide the corresponding sulfone **10** is available. An oxidation of the thiophene system is not observed for **2a,b** under these conditions. That is also in accordance with the acceptor properties of the anellated 1,1-dioxo-1,2-thiazine ring.

Scheme 3

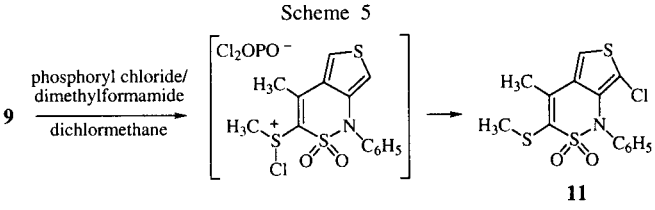


Scheme 4



By reaction of compound **9** with phosphoryl chloride/dimethylformamide a colourless, crystalline solid was obtained in a yield of 70%. Due to the spectroscopic data structure **11** was assigned to it. We assume that **11** is formed from **9** *via* an intermediate chloro sulfonium salt [15] which chlorinates the electron rich α-position of the thiophene ring. This reaction corresponds to the halogenation of enamines by halogen sulfonium salts [16]. By chlorination of **2a** with sulfuryl chloride in chloroform the identical product **11** was synthesized.

Scheme 5



EXPERIMENTAL

The nmr spectra were obtained on a Varian Gemini 300 spectrometer (^{1}H nmr 300 MHz; ^{13}C nmr 75 MHz) by using tetramethylsilane as the internal standard. The ir spectra were recorded on a Philips PU 9426 FTIR. The uv/vis spectra were obtained on a Shimadzu 3101 PC. Mass spectra (EI) were recorded on a AMD 402. Microanalyses were done on a Leco CHNS-932 analyser.

The 3,5-dimethyl-6-methylthio-1,1-dioxo-2-phenyl-1,2-thiazine-4-carbaldehyde (**1a**) [14] and the 2-(4-methoxyphenyl)-3,5-dimethyl-1,1-dioxo-1,2-thiazine (**3**) [17] were prepared according to a literature procedure.

Table 1

Single Crystal X-Ray Crystallographic Analyses of **2a** and **3**

		2a	**3**
A. Crystal Parameters			
formula		$C_{14}H_{13}NO_2S_3$	$C_{13}H_{15}NO_3S$
crystallization medium		diethyl ether/pentane	methanol
crystal size, mm		0.68 x 0.35 x 0.11	0.23 x 0.29 x 0.42
cell dimensions	a, Å	11.938(2)	7.5184(9)
	b, Å	8.589(2)	18.043(2)
	c, Å	14.762(2)	10.165(2)
	α, °	90.0	90.0
	β, °	105.414(9)	101.043(7)
	γ, °	90.0	90.0
	V, Å^3	1459.1(5)	1353.4(3)
space group		$P2_1/n$	$P2_1/c$
molecules/unit cell		4	4
density calcd, g/cm^3		1.472	1.302
linear absorption coefficient, mm^{-1}		0.507	0.239
B. Refinement Parameters			
number of reflections		4237	3930
nonzero reflections (I>2σ)		2720	2380
R-index [a], %		4.83	4.07
Rw-index [b], %		14.27	11.64
GOF [c]		1.129	1.008
weighting scheme parameters r, s [d]		0.0559, 0.3348	0.0638, 0.0409
secondary extinction factor χ [e]		-	0.009(2)

[a] R-index = $\Sigma||Fo|-|Fc||/(|Fo|$, [b] Rw-index = $\{\Sigma[w(Fo^2-Fc^2)^2]/\Sigma[w(Fo^2)^2]\}^{1/2}$, [c] GOF = $\{\Sigma[w(Fo^2-Fc^2)^2]/(n-p)\}^2$ where p ... number of parameters refined; n ... number of reflections used [d] $w = 1/[\sigma^2(Fo^2)+(rP)^2+sP]$ where $P = (Fo^2+2Fc^2)/3$, [e] Fc,corr = $kFc[1+0.001\chi Fc^2\lambda^3/\sin(2\theta)]^{-1/4}$

Table 2a

Bond Lengths (Å) and Bond Angles (°) for **2a**

S1-O2	1.423(2)	C2-C3	1.449(4)
S1-O1	1.434(2)	C2-C8	1.502(4)
S1-N1	1.658(2)	C3-C6	1.371(4)
S1-C1	1.759(3)	C3-C4	1.441(3)
S2-C1	1.758(3)	C4-C5	1.357(4)
S2-C7	1.793(4)	C9-C14	1.375(4)
S3-C6	1.696(3)	C9-C10	1.383(3)
S3-C5	1.714(3)	C10-C11	1.384(4)
N1-C4	1.403(3)	C11-C12	1.367(5)
N1-C9	1.447(3)	C12-C13	1.368(5)
C1-C2	1.346(4)	C13-C14	1.387(4)
O2-S1-O1	117.2(1)	C6-C3-C4	110.7(2)
O2-S1-N1	106.8(1)	C6-C3-C2	126.4(2)
O1-S1-N1	111.0(1)	C4-C3-C2	122.9(2)
O2-S1-C1	111.2(1)	C5-C4-N1	126.0(2)
O1-S1-C1	107.8(1)	C5-C4-C3	113.3(2)
N1-S1-C1	101.7(1)	N1-C4-C3	120.6(2)
C1-S2-C7	102.0(2)	C4-C5-S3	111.0(2)
C6-S3-C5	92.5(2)	C3-C6-S3	112.5(2)
C4-N1-C9	119.1(2)	C14-C9-C10	120.4(2)
C4-N1-S1	116.9(2)	C14-C9-N1	121.7(2)
C9-N1-S1	119.1(2)	C10-C9-N1	117.9(2)
C2-C1-S2	124.9(2)	C11-C10-C9	119.2(3)
C2-C1-S1	121.3(2)	C12-C11-C10	120.5(3)
S2-C1-S1	113.0(1)	C11-C12-C13	120.1(3)
C1-C2-C3	120.1(2)	C12-C13-C14	120.4(3)
C1-C2-C8	121.6(3)	C9-C14-C13	119.3(3)
C3-C2-C8	118.3(3)		

Table 2b

Bond Lengths (Å) and Bond Angles (°) for **3**

S1 - O1	1.423(1)	C2 - C5	1.504(3)
S1 - O2	1.427(1)	C3 - C4	1.340(2)
S1 - N1	1.666(1)	C4 - C6	1.500(3)
S1 - C1	1.707(2)	C7 - C8	1.371(3)
O3 - C10	1.367(2)	C7 - C12	1.386(2)
O3 - C13	1.400(3)	C8 - C9	1.383(3)
N1 - C4	1.400(2)	C9 - C10	1.374(3)
N1 - C7	1.441(2)	C10 - C11	1.372(3)
C1 - C2	1.338(2)	C11 - C12	1.373(3)
C2 - C3	1.432(3)		
O1 - S1 - O2	116.7(1)	C4 - C3 - C2	123.8(2)
O1 - S1 - N1	108.4(1)	C3 - C4 - N1	120.5(1)
O2 - S1 - N1	107.7(1)	C3 - C4 - C6	122.8(2)
O1 - S1 - C1	110.6(1)	N1 - C4 - C6	116.7(2)
O2 - S1 - C1	111.3(1)	C8 - C7 - C12	119.7(2)
N1 - S1 - C1	100.8(1)	C8 - C7 - N1	120.5(2)
C10 - O3 - C13	118.9(2)	C12 - C7 - N1	119.8(2)
C4 - N1 - C7	122.6(1)	C7 - C8 - C9	120.3(2)
C4 - N1 - S1	118.6(1)	C10 - C9 - C8	119.8(2)
C7 - N1 - S1	116.3(1)	O3 - C10 - C11	115.7(2)
C2 - C1 - S1	120.2(1)	O3 - C10 - C9	124.4(2)
C1 - C2 - C3	121.1(2)	C11 - C10 - C9	119.9(2)
C1 - C2 - C5	120.3(2)	C10 - C11 - C12	120.6(2)
C3 - C2 - C5	118.6(2)	C11 - C12 - C7	119.7(2)

Table 3a

Atomic Coordinates and Equivalent Isotropic Displacement Coefficients (Å) for **2a**

	x	y	z	U_{eq}
S1	0.3983(1)	0.0613(1)	0.1981(1)	0.042(1)
S2	0.3611(1)	0.3558(1)	0.0937(1)	0.057(1)
S3	0.7623(1)	-0.1991(1)	0.1568(1)	0.071(1)
O1	0.3246(2)	-0.0458(3)	0.1348(1)	0.056(1)
O2	0.3500(2)	0.1388(3)	0.2642(1)	0.060(1)
N1	0.5187(2)	-0.258(3)	0.2591(1)	0.043(1)
C1	0.4533(2)	0.1952(3)	0.1306(2)	0.041(1)
C2	0.5471(2)	0.1617(3)	0.0999(2)	0.041(1)
C3	0.6141(2)	0.0223(3)	0.1323(2)	0.041(1)
C4	0.5987(2)	-0.0704(3)	0.2095(2)	0.042(1)
C5	0.6724(3)	-0.1936(4)	0.2300(2)	0.056(1)
C6	0.7007(2)	-0.0379(4)	0.0977(2)	0.055(1)
C7	0.4025(5)	0.4824(6)	0.1936(4)	0.090(2)
C8	0.5861(4)	0.2667(5)	0.0329(3)	0.061(1)
C9	0.5177(2)	-0.1076(3)	0.3445(2)	0.038(1)
C10	0.6065(2)	-0.772(4)	0.4242(2)	0.047(1)
C11	0.6110(3)	-0.1589(4)	0.5059(2)	0.056(1)
C12	0.5278(3)	-0.2670(4)	0.5083(2)	0.059(1)
C13	0.4383(3)	-0.2936(4)	0.4301(2)	0.060(1)
C14	0.4321(3)	-0.2133(3)	0.3474(2)	0.049(1)

6-Chloro-3,5-dimethyl-1,1-dioxo-2-phenyl-1,2-thiazine-4-carbaldehyde (**1b**). (See also [14,18]).

Titanium tetrachloride (1.29 ml, 11.7 mmoles) and dichloromethyl methyl ether (0.63 ml, 7.1 mmoles) were added at 0° to a stirred solution of 6-chloro-3,5-dimethyl-1,1-dioxo-2*H*-1,2-thiazine [18] (940 mg, 3.5 mmoles) in dried dichloromethane (5 ml). After stirring for 25 minutes at 0° the solution obtained was hydrolyzed by adding chopped ice. The organic phase was

Table 3b

Atomic Coordinates and Equivalent Isotropic Displacement Coefficients (Å) for **3**

	x	y	z	U_{eq}
S1	0.25637(5)	0.29835(2)	0.43865(4)	0.0487(1)
O1	0.2495(2)	0.2285(1)	0.5023(1)	0.0704(5)
O2	0.4272(2)	0.3200(1)	0.4095(1)	0.0714(5)
O3	0.7348(2)	0.4795(1)	0.9319(1)	0.0798(6)
N1	0.1922(2)	0.3636(1)	0.5357(1)	0.0498(4)
C1	0.0884(2)	0.3049(1)	0.3000(2)	0.0534(5)
C2	-0.0804(2)	0.3226(1)	0.3125(2)	0.0570(6)
C3	-0.1191(2)	0.3472(1)	0.4379(2)	0.0594(6)
C4	0.0081(2)	0.3694(1)	0.5414(2)	0.0533(5)
C5	-0.2327(4)	0.3198(2)	0.1927(3)	0.091(1)
C6	-0.0367(4)	0.4031(2)	0.6661(3)	0.082(1)
C7	0.3330(2)	0.3952(1)	0.6363(1)	0.0467(5)
C8	0.3773(3)	0.4687(1)	0.6314(2)	0.0608(7)
C9	0.5103(3)	0.4991(1)	0.7295(2)	0.0644(7)
C10	0.6005(2)	0.4551(1)	0.8310(2)	0.0557(6)
C11	0.5600(3)	0.3811(1)	0.8337(2)	0.0643(7)
C12	0.4266(3)	0.3507(1)	0.7375(2)	0.0582(6)
C13	0.7788(6)	0.5550(2)	0.9386(4)	0.101(1)

separated and polar side products were removed by adding about 100 mg of silica gel. After filtration the solution was evaporated under vacuum. Ethanol (3 ml) was added to the viscous residue and the solution was cooled to -28°. Thereafter the formed solid was separated by suction and washed with cold ethanol, yield 552 mg (53%), mp 89-90°; ir (potassium bromide): δ 1681, 1344, 1172 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): δ 2.28, 2.11 (s, 3 H, CH_3), 7.42 (m, 2 H, aromatic protons), 7.59 (m, 3 H, aromatic protons), 10.00 (s, 1 H, CHO); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 17.6, 18.3, (CH_3), 108.9, 117.7, 129.6, 130.1, 130.5, 133.3, 140.8, 154.4, 188.9; ms: (70 eV) m/z 297 (M^+), 232 (M^+ - HSO_2).

Anal. Calcd. for $C_{13}H_{12}ClNO_3S$: C, 52.44; H, 4.06; N, 4.70; S, 10.77. Found: C, 52.84; H, 4.40; N, 4.72; S, 11.09.

General Procedure for the Preparation of the 1*H*-Thieno[3,4-*c*]-1,2-thiazines **2a,b**. (See also [19]).

To a solution of **1a,b** (0.323 mmole) dissolved in 1 ml of dimethylformamide, sulfur (11 mg, 0.345 mmole) and triethylamine (0.045 ml 0.32 mmole) were added. The mixture was stirred at room temperature for 2 (**2a**) and 5 h (**2b**), respectively. After adding of 5-10 ml of 6 *N* hydrochloric acid, the solution was extracted with ether (4 x 25 ml). The organic layer was dried (sodium sulfate) and concentrated. The residue was recrystallized from acetic acid.

4-Methyl-3-methylthio-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*]-[1,2]thiazine (**2a**).

This compound was obtained as colorless crystals, yield 62 mg (59%), mp 136°; ir (potassium bromide): ν 1326, 1149 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): δ 2.39, 2.61 (s, 3 H, CH_3), 6.66 (d, 1 H, J = 2.7 Hz, C7-H), 7.35 (d, 2 H, J = 7.0 Hz, aromatic protons), 7.50 (m, 3 H, aromatic protons), 8.20 (d, 1 H, J = 2.7 Hz, C5-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 18.3, 19.2 (CH_3), 110.1 (C7), 127.4, 127.8 (C5), 127.9, 128.7, 129.1, 130.1, 137.4, 138.7, 144.8; ms: (70 eV) m/z 323 (M^+), 259 (M^+ - SO_2), 244 (M^+- SO_2CH_3).

Anal. Calcd. for $C_{14}H_{13}NO_2S_3$: C, 51.99; H, 4.05; N, 4.33; S, 29.74. Found: C, 52.06; H, 3.97; N, 4.30; S, 30.12.

3-Chloro-4-methyl-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*][1,2]-thiazine (**2b**).

This compound was obtained as colorless crystals, yield 50 mg (49%), mp 171°; ir (potassium bromide): ν 3102, 1488, 1353, 1164 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): δ 2.46 (s, 3 H, CH_3), 6.91 (d, 1 H, J = 2.8 Hz, C7-H), 7.33 (d, 2 H, J = 6.8 Hz, aromatic protons), 7.51 (m, 3 H, aromatic protons), 8.21 (d, 1 H, J = 2.8 Hz, C5-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 17.2 (CH_3), 113.1 (C7), 127.1 (C5), 127.8, 128.6, 129.6, 130.4, 136.8, 137.3, 137.7; ms: (70 eV) m/z 311 [M^+], 246 [M^+ - HSO_2].

Anal. Calcd. for $C_{13}H_{10}ClNO_2S_2$: C, 50.08; H, 3.23; N, 4.49; S, 20.56. Found: C, 50.41; H, 3.56; N, 4.36; S, 20.25.

General Procedure for the Preparation of the 7-Formyl-1*H*-thieno[3,4-*c*][1,2]thiazines **4a,b**.

Titanium tetrachloride (1.29 ml, 11.7 mmoles) and dichloromethyl methyl ether (0.63 ml, 7.1 mmoles) were added at 0° to a stirred solution of **2a** and **2b**, respectively (3.5 mmoles) in dried dichloromethane (5 ml). After stirring for 1 hour at 0° the solution obtained was hydrolyzed by adding chopped ice. The organic phase was separated, dried and evaporated *in vacuo*. The residue was washed with methanol.

7-Formyl-4-methyl-3-methylthio-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*][1,2]thiazine (**4a**).

This compound was obtained as a colorless solid, yield 80 mg (73%), mp 153-156°; ir (potassium bromide): ν 1654, 1351, 1168, 1151 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): δ 2.37, 2.66 (s, 3 H, CH_3), 7.35 (d, 2 H, J = 6.7 Hz, aromatic protons), 7.48 (m, 3 H, aromatic protons), 8.78 (s, 1 H, C5-H), 9.15 (s, 1 H, CHO); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 18.9, 19.2 (CH_3), 127.8, 128.3, 128.5, 129.4, 130.4, 130.5, 136.3 (C5), 140.3, 142.9, 144.8, 181.4 (CHO); ms: (70 eV) m/z 351 [M^+], 287 [M^+ - SO_2], 272 [M^+- SO_2CH_3].

Anal. Calcd. for $C_{15}H_{13}NO_3S_3$: C, 51.26; H, 3.73; N, 3.99; S, 27.37. Found: C, 51.11; H, 3.97; N, 4.09; S, 27.09.

3-Chloro-7-formyl-4-methyl-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*]-[1,2]thiazine (**4b**).

This compound was obtained as a colorless solid, yield 59 mg (55%), mp 150-153°; ir (potassium bromide): ν 3097, 1656, 1531, 1405, 1357, 1174, 1149 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): δ 2.51 (s, 3 H, CH_3), 7.34 (d, 2 H, J = 6.1 Hz, aromatic protons), 7.46 (m, 3 H, aromatic protons), 8.77 (s, 1 H, C5-H), 9.35 (s, 1 H, CHO); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 17.5 (CH_3), 122.6, 127.6, 129.4, 130.1, 130.3, 130.4, 135.2 (C5), 136.9, 140.4, 141.3, 181.4 (CHO); ms: (70 eV) m/z 339 [M^+], 274 [M^+ - HSO_2].

Anal. Calcd. for $C_{14}H_{10}ClNO_3S_2$: C, 49.48; H, 2.97; N, 4.12; S, 18.87. Found: C, 49.43; H, 3.22; N, 3.90; S, 18.89.

3-Chloro-4-methyl-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*][1,2]-thiazine-7-dimethylacetal (**5b**).

A suspension of 100 mg of the carbaldehyde **4b** was refluxed in methanol, until all solid was solved. The pecipitated crystals were separated after cooling, yield 100 mg (88%), mp 165-169°; ir (potassium bromide): ν 3095, 1361, 1172, 1147, 1097, 1058 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): δ 2.46 (s, 3 H, CH_3), 3.03 (s, 6 H, OCH_3), 5.06 (s, 1 H, CH), 7.06 (d, 2 H, J = 6.9 Hz, aromatic protons), 7.38 (m, 3 H, aromatic protons), 8.27 (s, 1 H, C5-H), 9.35 (s, 1 H, CHO); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 17.2 (CH_3), 52.9, 97.5, 122.4, 126.0, 127.1, 128.5, 129.6, 130.3, 132.9, 133.0, 137.4, 139.8; ms: (70 eV) m/z 385 [M^+], 354, 322.

Anal. Calcd. for $C_{16}H_{16}ClNO_4S_2$: C, 49.80; H, 4.18; N, 3.63; S, 16.62. Found: C, 49.84; H, 4.22; N, 3.48; S, 16.88.

4-Methyl-3-methylthio-7-(4-*N,N*-dimethylaminoanilinomethylidene)-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*][1,2]thiazine (**6**).

In a solution of 4-*N,N*-dimethylaminoanilinium dihydrochloride (60 mg, 0.28 mmole) in 2 ml of ethanol, the free base was liberated by adding 32 mg of potassium hydroxide (0.56 mmole). After filtration, the solution was added to 100 mg of the aldehyd **4a** (0.28 mmole) suspended in 2 ml of ethanol. After stirring for 4 hours, the solid obtained was separated and recrystallized from toluene, yield 124 mg (92%), mp 256-259°; ir (potassium bromide): ν 1610, 1513, 1349, 1166, 1157 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): δ 2.32, 2.63 (s, 3 H, CH_3), 2.89 (s, 6 H, NCH_3), 6.64 (d, 2 H, J = 8.8 Hz, aromatic protons), 6.94 (d, 2 H, J = 6.1 Hz, aromatic protons), 7.25 (d, 2 H, J = 7.4 Hz, aromatic protons), 7.35 (t, 1 H, J = 7.1 Hz, aromatic protons), 7.43 (t, 2 H, J = 7.4 Hz, aromatic protons), 8.16 (s, 1 H), 8.38 (s, 1 H); ^{13}C nmr (deuteriochloroform): δ 18.8, 19.0, 40.5 (CH_3), 112.5, 122.5, 126.6, 126.8, 128.0, 129.6, 131.3, 132.4, 137.4, 139.2, 140.9, 142.7, 144.4, 149.8; ms: (70 eV) m/z 469 [M^+], 405 [M^+ - SO_2], 390 [M^+ - SO_2CH_3], 372; uv/vis (dichloromethane): λ_{max} (lg ε) = 422 (4.29), 315 (4.30), 266 (4.37) nm.

Anal. Calcd. for $C_{23}H_{23}N_3O_2S_3$: C, 58.82; H, 4.94; N, 8.95; S, 20.48. Found: C, 58.77; H, 5.15; N, 8.76; S, 20.66.

4-Methyl-3-methylthio-7-(4-methoxyanilinomethyliden)-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*][1,2]thiazine (**7**).

A solution of 36 mg of 4-methoxyaniline (0.28 mmole) was added to a suspension of 100 mg of the carbaldehyde **4a** (100 mg, 0.28 mmole) in 2 ml of ethanol. The mixture was heated under reflux for 2 hours. The precipitated pure solid was separated and dried, yield 100 mg (77%), mp 165-166°; ir (potassium bromide): ν 1608, 1504, 1349, 1249, 1168, 1157 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): δ 2.33, 2.63 (s, 3 H, CH_3), 3.72 (s, 3 H, OCH_3), 6.86 (d, 2 H, J = 8.8 Hz, aromatic protons), 6.95 (d, 2 H, J = 8.8 Hz, aromatic protons), 7.25 (d, 2 H, J = 7.4 Hz, aromatic protons), 7.43 (m, 3 H, aromatic protons), 8.13 (s, 1 H), 8.43 (s, 1 H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 18.8, 19.0, 55.6 (CH_3), 114.9, 122.7, 127.7, 128.5, 128.8, 130.2, 130.5, 131.0, 131.2, 139.1, 141.1, 143.0, 145.1, 147.2, 158.9; ms: (70 eV) m/z 456 [M^+], 392 [M^+- SO_2], 377 [M^+- SO_2CH_3], 359; uv/vis (dichloromethane) λ_{max} (lg ε) = 366 (4.28), 307 (4.17) nm.

Anal. Calcd. for $C_{22}H_{20}N_2O_3S_3$: C, 57.87; H, 4.42; N, 6.14; S, 21.06. Found: C, 57.85; H, 4.29 N, 5.88; S, 20.88.

7-(2-Ethyloxycarbonyl-2-cyanovinyl)-4-methyl-3-methylthio-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*][1,2]thiazine (**8**).

A solution of 0.032 ml of cyanoacetic acid ethyl ester (0.28 mmole), triethylamine (0.04 ml, 0.28 mmole) and acetic acid (0.5 ml) in 1 ml of ethanol was added to a solution of 100 mg of **4a** (0.28 mmole) in 2 ml of ethanol. After stirring for 4 hours, one half of the solvent was evaporated and the pure product was separated, yield 120 mg (95%), mp 172-174°; ir (potassium bromide): ν 3085, 2220, 1725, 1587, 1486, 1392, 1357, 1255, 1224, 1174, 1157, 1103 cm^{-1}; ^1H nmr (dimethyl-d_6 sulfoxide): δ 1.21 (t, 3 H, J = 7.1 Hz, CH_3), 2.33, 2.66 (s, 3 H, CH_3), 4.15 (q, 2 H, J = 7.1 Hz, CH_2), 7.17 (d, 2 H, J = 7.1 Hz, aromatic protons), 7.42 (m, 3 H, aromatic protons), 8.00 (s, 1 H), 8.83 (s, 1 H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 14.0, 18.8, 19.0, 62.5 (CH_3), 99.4, 115.4, 123.9, 127.2, 128.9, 129.2, 130.1, 130.9, 135.7, 140.3, 141.3, 143.9, 144.3, 161.3; ms: (70 eV) m/z 446 [M^+], 382 [M^+ - SO_2], 354 [M^+ - $SO_2C_2H_4$]; uv/vis (dichloromethane) λ_{max} (lg ε) = 372 (3.87), 328 (3.87), 271 (3.91) nm.

Anal. Calcd. for $C_{20}H_{18}N_2O_4S_3$: C, 53.79; H, 4.06; N, 6.27; S, 21.54. Found: C, 53.81; H, 4.34; N, 6.25; S, 21.94.

4-Methyl-3-methylsulfinyl-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*]-[1,2]thiazine (**9**).

An aqueous solution of hydrogen peroxide (33%, 0.063 ml, 0.62 mmole) was added to a solution of 100 mg of **2a** (0.31 mmole) in a mixture of 3 ml acetic acid/ 0.3 ml chloroform and stirred for 24 hours. After adding of 10 ml of water, the mixture was extracted 4 times with dichloromethane. The organic layer was washed with an aqueous sodium bicarbonate solution and with water and dried. The solvent was evaporated. The residue was recrystallized from ethanol, yield 87 mg (83%), mp 180-183°; ir (potassium bromide): ν 1560, 1346, 1166, 1060 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.70 (s, 3 H, CH_3), 3.17 (s, 3 H, $SOCH_3$), 6.52 (d, 1 H, J = 3.2 Hz, C7-H), 7.36 (m, 2 H, aromatic protons), 7.42 (m, 3 H, aromatic protons), 7.78 (d, 1 H, J = 3.2 Hz, C5-H); ^{13}C nmr (deuteriochloroform): δ = 13.4, 39.7 (CH_3), 110.5, 127.7, 128.0, 128.5, 129.2, 129.8, 134.0, 136.6, 139.2, 144.0; ms: (70 eV) m/z 339 [M^+], 260, 242, 228, 212.

Anal. Calcd. for $C_{14}H_{13}NO_3S_3$: C, 49.54; H, 3.83; N, 4.13; S, 28.33. Found: C, 49.39; H, 4.02; N, 4.14; S, 28.14.

4-Methyl-3-methylsulfonyl-2,2-dioxo-1-phenyl-1*H*-thieno[3,4-*c*]-[1,2]thiazine (**10**).

An aqueous solution of hydrogen peroxide (33%, 0.4 ml, 4 mmoles) was added to a solution of 100 mg of **2a** (0.31 mmole) in a mixture of 3 ml acetic acid/ 0.3 ml chloroform and refluxed for 8 hours. After adding of 10 ml of water, the precipitated solid was separated, yield 50 mg (45%); ir (potassium bromide): ν 1560, 1488, 1359, 1324, 1162, 1141 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.87 (s, 3 H, CH_3), 3.28 (s, 3 H, SO_2CH_3), 6.57 (d, 1 H, J = 2.9 Hz, C7-H), 7.37 (m, 2 H, aromatic protons), 7.44 (m, 3 H, aromatic protons), 7.94 (d, 1 H, J = 2.9 Hz, C5-H).

7-Chloro-4-methyl-3-methylthio-2,2-dioxo-1-phenyl-1*H*-thieno-[3,4-*c*]-1,2-thiazine (**11**). (Route A).

To a solution of 100 mg of **9** (0.3 mmole) in 2.5 ml of dimethylformamide phosphoryl chloride (0.07 ml, 7.6 mmoles) was added at 0°. The solution was stirred for 30 minutes. Thereafter, 3.5 ml of 1,2-dichloroethane was added. The mixture was allowed to react at room temperature for 2 hours. The solvent was evaporated *in vacuo*. The residue obtained was hydrolyzed by adding chopped ice. The mixture was extracted with ether (6 x 20 ml). The organic phase was dried and the solvent removed *in vacuo*. The solid obtained was recrystallized from ethanol, yield 77 mg (70%), mp 172-174°.

(Route B).

Sulfuryl chloride (0.025 ml, 0.31 mmole) was added to a solution of **2a** (100 mg, 0.31 mmole) in 2 ml of chloroform and stirred for 1 hour. The solvent was evaporated. The obtained residue was recrystallized from ethanol, yield 96 mg (87%), mp 172-174°; ir (potassium bromide): ν 3093, 1560, 1456, 1344, 1180, 1170, 1157 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.40, 2.56 (s, 3 H, CH_3), 7.08 (d, 2 H, J = 7.3 Hz, aromatic protons), 7.28 (m, 3 H, aromatic protons), 7.39 (s, 1 H, C5-H); ^{13}C nmr (deuteriochloroform): δ 18.4, 18.8 (CH_3), 120.8, 121.3, 126.8, 127.7, 129.0, 130.4, 130.7, 134.0, 138.7, 142.1; ms: (70 eV) m/z 357 [M^+], 293 [M^+- SO_2], 278 [M^+- SO_2CH_3].

Anal. Calcd. for $C_{14}H_{12}ClNO_2S_3$: C, 46.99; H, 3.38; N, 3.91; S, 26.87. Found: C, 46.93; H, 3.74; N, 3.89; S, 26.44.

X-Ray Structure Determinations of **2a** and **3** [20].

The X-ray data were measured on a Stoe Stadi4 diffractometer using graphite monochromatized Mo-K_α radiation (λ = 0.71073 Å) at T = 298(2) K (**2a**) and 293 K (**3**), respectively. No absorption corrections have been applied. The structures were solved by direct methods of phase determination and refined by full-matrix least squares methods on F^2. Non-H atoms were refined with anisotropic displacement parameters, H atoms were located in a difference Fourier map and refined with isotropic displacement parameters.

Computation and drawings were performed using SHELXS-86 (Sheldrick, 1990), SHELXL-93 (Sheldrick, 1993) and Siemens XP/PC (1990) [21].

(Table 1) (Table 2a) (Table 2b) (Table 3a) (Table 3b)

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[20] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-101150. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

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