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4-(1-Methyl-2-sulfamoylvinyl)pyrazoles by Ring Transformation of 1,1-Dioxo-2*H*-1,2-thiazine-4-carbaldehydes with Hydrazines

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Dedicated to Professor H. G. O. Becker on the Occasion of his 75th Birthday

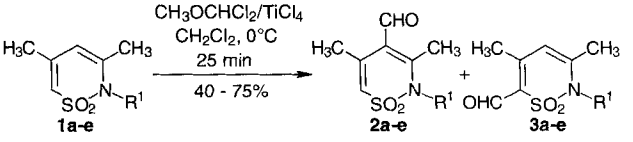
Abstract. As masked 1,3-dicarbonyl compounds, 1,1-dioxo-2*H*-1,2-thiazine-4-carbaldehydes (**2a–e**, **7**) undergo ring transformations with nucleophilic hydrazines to produce 4-[1-methyl-2-(arylsulfamoyl)vinyl]pyrazoles (**9a–i**). For **9h**, an X-ray structural analysis is reported. With less nucleophilic semicarbazide and *p*-nitrophenylhydrazine the hydrazones (**11a,b**) were isolated. The carbaldehydes **2a–e**, **7** and **8a,b** were synthesized by formylation of the 1,1-dioxo-2*H*-1,2-thiazines **1a–e**, **5** and **6a,b** with dichloromethyl methyl ether/$TiCl_4$. In the case of **1a–e** mixtures of 4- and 6-carbaldehydes (**2a–e/3a–e**) were obtained, which, however, could be used for the synthesis of pyrazoles.

Ring transformations are synthetic principles for the preparation and modification of heterocyclic systems [1–5]. For instance, several types of ring transformations are known for 2-aryl-3,5-dimethyl-1,1-dioxo-2*H*-1,2-thiazines [6–9]. Thus, 2,4-lutidine-5-sulfonanilide derivatives were obtained from 2-aryl-3,5-dimethyl-1,1-dioxo-2*H*-1,2-thiazine-6-carbaldehydes and nitrogen bases by making use of the masked 1,5-dicarbonyl structure of these carbaldehydes [10].

In this paper we describe preparations of 1,1-dioxo-2*H*-1,2-thiazine-4-carbaldehydes **2a–e**, **7** and **8a,b** and their reactions as masked 1,3-dicarbonyl compounds with hydrazines to produce pyrazoles **9**. The carbaldehydes are available by formylation of the 3,5-dimethyl-1,1-dioxo-2*H*-1,2-thiazines using dichloromethyl methyl ether (DCME) and $TiCl_4$ as catalyst.

In contrast, Vilsmeier–Haack formylation of **1** affords mainly 1,1-dioxo-2*H*-1,2-thiazine-6-carbaldehydes besides higher formylated products [11, 12]. With the more reactive formylation reagent DCME/$TiCl_4$ [13], both reactive centres of the 1,1-dioxo-2*H*-1,2-thiazine ring in position 4 and 6 are attacked. In the case of the *N*-aryl substituted derivatives **1a–d** approximately equal amounts of the 4-carbaldehydes **2a–d** and the 6-carbaldehydes **3a–d** are obtained. The ratios **2**:**3** were determined ^1H NMR spectroscopically. The CHO-signals of the 4-carbaldehydes **2a–d** appear at a lower field than the corresponding signals of the 6-carbaldehydes **3a–d**, which were used as reference substances [11]. For the formylation of the *N*-benzyl derivative **1e** a preference of position 4 (3.5:1) is observed (Table 1).

Changing the reaction conditions such as temperature, mole ratio of the reactants or the catalyst (e.g. substitution of $TiCl_4$ by $SnCl_4$ or $AlCl_3$) had little effect on the ratio **2**:**3**.



1,2,3	a	b	c	d	e
R^1	C_6H_5	C_6H_4-CH_3(p)	C_6H_4-OCH_3(p)	C_6H_4-Cl(p)	CH_2-C_6H_5

Scheme 1

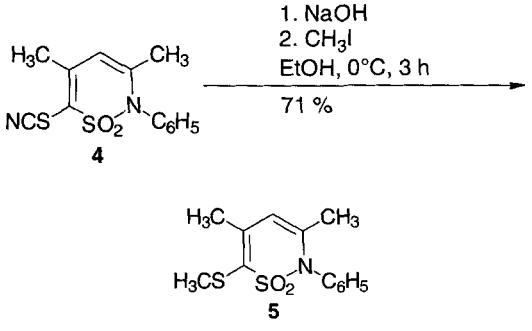
No formylation by DCME/$TiCl_4$ was achieved for 1,1-dioxo-2*H*-1,2-thiazines with weak acceptor substituents, e.g. for 3-chloromethyl-, 3-bromomethyl-5-methyl-1,1-dioxo-2-phenyl-2*H*-1,2-thiazine [14], or 6-

Table 1 Yields, product ratio and ^{1}H NMR data of the mixture of *N*-substituted (*R*) 3,5-dimethyl-1,1-dioxo-2*H*-1,2-thiazine-4-carbaldehydes (**2a–e**) and *N*-substituted (*R*) 3,5-dimethyl-1,1-dioxo-2*H*-1,2-thiazine-6-carbaldehydes (**3a–e**)

R	Yield (%)	Ratio **2** : **3**	Prod.	^{1}H NMR (DMSO-d_6/TMS) d, *J* (Hz)	Prod.	^{1}H NMR (DMSO-d_6/TMS) d, *J* (Hz)
C_6H_5	55	1.2 : 1	**2a**	2.31, 2.42 (s, 3H, CH_3), 6.94 (s, 1H, C6-H), 7.37 (m, 2H, Ar-H), 7.45 (m, 3H, Ar-H), 10.04 (s, 1H, CHO)	**3a**	2.01, 2.56 (s, 3H, CH_3), 6.16 (s, 1H, C4-H), 7.45 (m, 2H, Ar-H), 7.61 (m, 3H, Ar-H), 9.86 (s, 1H, CHO)
C_6H_4–CH_3 (*p*)	60	1.2 : 1	**2b**	2.31, 2.41, 2.54 (s, 3H, CH_3), 6.92 (s, 1H, C6-H), 7.35 (d, 2H, *J* = 8.2, Ar-H), 7.39 (d, 2H, *J* = 8.3, Ar-H), 10.02 (s, 1H, CHO)	**3b**	1.96, 2.38, 2.51 (s, 3H, CH_3), 6.09 (s, 1H, C4-H), 7.27 (d, 2H, *J* = 8.2, Ar-H), 7.36 (d, 2H, *J* = 8.2, Ar-H), 9.81 (s, 1H, CHO)
C_6H_4–OCH_3 (*p*)	40	0.7 : 1	**2c**	2.27, 2.37 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.87 (s, 1H, C6-H), 7.10 (d, 2H, *J* = 8.8, Ar-H), 7.33 (d, 2H, *J* = 8.9, Ar-H), 9.98 (s, 1H, CHO)	**3c**	1.97, 2.50 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 6.07 (s, 1H, C4-H), 7.08 (d, 2H, *J* = 8.9, Ar-H), 7.32 (d, 2H, *J* = 8.9, Ar-H), 9.81(s, 1H, CHO)
C_6H_4–Cl (*p*)	75	0.8 : 1	**2d**	2.28, 2.37 (s, 3H, CH_3), 6.94 (s, 1H, C6-H), 7.35 (d, 2H, *J* = 8.6, Ar-H), 7.58 (d, 2H, *J* = 8.5, Ar-H), 10.00 (s, 1H, CHO)	**3d**	1.98, 2.51 (s, 3H, CH_3), 6.12 (s, 1H, C4-H), 7.45 (d, 2H, *J* = 8.5, Ar-H), 7.64 (d, 2H, *J* = 8.5, Ar-H), 9.83 (s, 1H, CHO)
CH_2–C_6H_5	60	3.5 : 1	**2e**	2.48, 2.66 (s, 3H, CH_3), 5.39 (s, 2H, CH_2), 7.02 (s, 1H, C6-H), 7.42 (m, 3H, Ar-H), 7.53 (m, 2H, Ar-H), 10.09 (s, 1H, CHO)	**3e**	2.36, 2.61 (s, 3H, CH_3), 5.34 (s, 2H, CH_2), 6.17 (s, 1H, C4-H), 7.35 (m, 3H, Ar-H), 7.45 (m, 2H, Ar-H), 9.99 (s, 1H, CHO)

iodo-3,5-dimethyl-1,1-dioxo-2-phenyl-2*H*-1,2-thiazine [15]. The starting materials were recovered unchanged. These results indicate that formylation of the 1,1-dioxo-2*H*-1,2-thiazine ring is strongly influenced by electronic effects of the substituents.

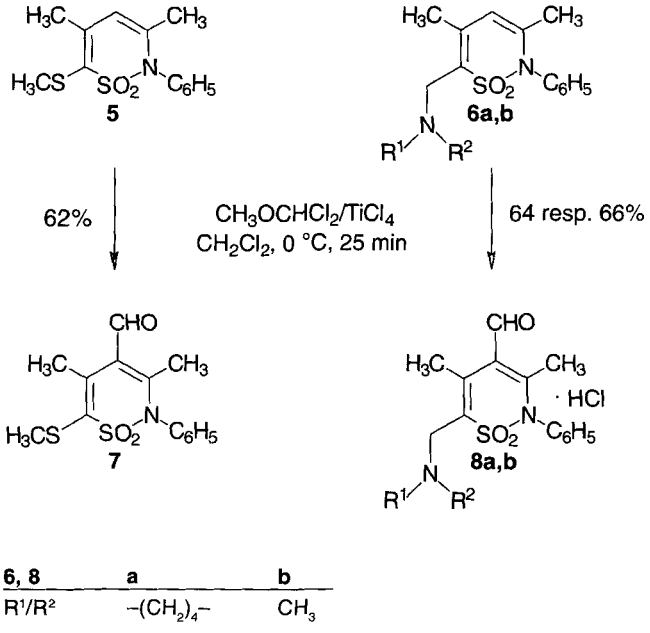
In order to enable site selective formylation of the 1,1-dioxo-2*H*-1,2-thiazine ring in position 4 a donor substituent such as the dialkylaminomethyl [16] or the methylmercapto group was introduced into the 6-position. The methylthio group was prepared by alkaline hydrolysis of the 6-thiocyanate [17] and methylation of the formed thiolate.



Scheme 2

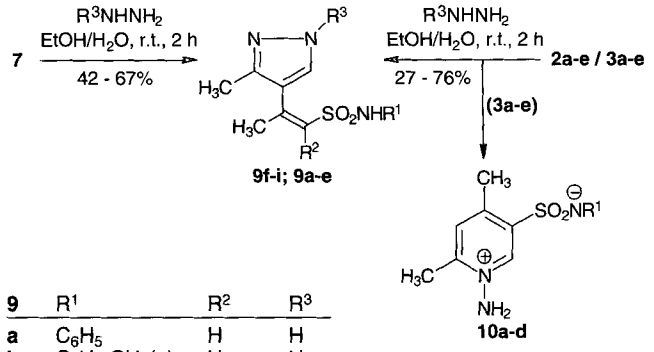
Formylation of the 6-methylthio derivative **5** and the 6-dialkylaminomethyl derivatives **6a,b** afforded the 4-carbaldehydes **7** and **8a,b** in moderate yields (62 to 66%) (Scheme 3).

With hydrazines the masked 1,3-dicarbonyl compound **7** furnishes the pyrazoles **9f–i**. Correspondingly, from mixtures of the 4- and 6-carbaldehydes **2a–e**/**3a–e**, which are difficult to separate, compounds **9a–e** can be prepared successfully, because the sulfonamidates **10** [10] arising from the 6-carbaldehydes are of low solubility in nonpolar solvents and can be removed by filtration (Scheme 4).



Scheme 3

For the 4-carbaldehydes **8a,b** no ring transformation could be induced with hydrazines under alkaline conditions. Apparently, the electron releasing dialkylaminomethyl group stabilizes the thiazine ring and prevents nucleophilic ring opening to a 1,3-dicarbonyl compound.



9	R^1	R^2	R^3
a	C_6H_5	H	H
b	C_6H_4-CH_3(p)	H	H
c	C_6H_4-OCH_3(p)	H	H
d	C_6H_4-Cl(p)	H	H
e	CH_2-C_6H_5	H	H
f	C_6H_5	SCH_3	H
g	C_6H_5	SCH_3	C_6H_5
h	C_6H_5	SCH_3	$C(CH_3)_3$
i	C_6H_5	SCH_3	$(CH_2)_2OH$

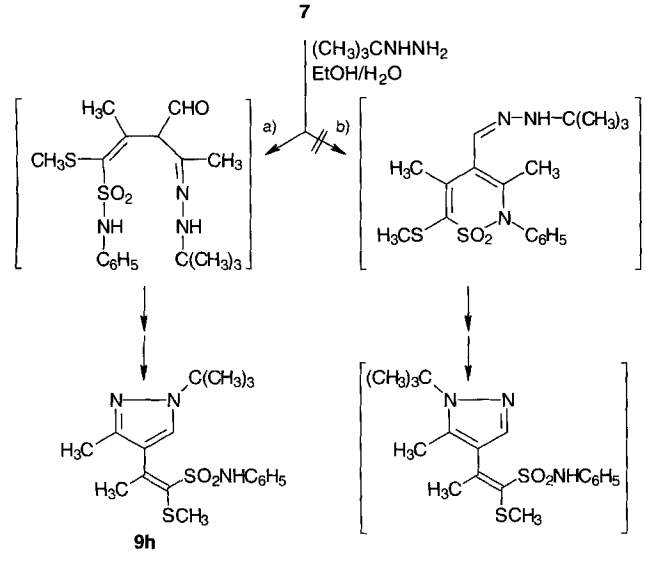
10	R^1
a	C_6H_5
b	C_6H_4-CH_3(p)
c	C_6H_4-OCH_3(p)
d	C_6H_4-Cl(p)

Scheme 4

The structural assignments of the pyrazoles are based on ^{13}C NMR spectroscopic data. The shifts of the pyrazole and the *N*-phenyl ring carbon atoms are comparable with literature data [18–20].

For compounds **9a–f** line broadening in the NMR spectra indicates prototropic equilibria. Only sharp signals are observed after protonation with D_2SO_4 (Table 3).

While the mass spectra of 1,1-dioxo-2*H*-1,2-thiazines are characterized by elimination of SO_2, for pyrazoles **9** the *N*-aryl(benzyl)sulfonamide fragment is observed.



Scheme 5

Conceivably, pyrazoles can be formed by ring opening attack of the hydrazine on position 3 of the thiazines followed by ring closure to a 3-methyl pyrazole (route a), Scheme 5). Alternatively, the aldehyde hydrazone is formed. Subsequent base induced ring opening and ring closure leads to 5-methyl pyrazoles (route b), Scheme 5).

In order to discriminate between these alternatives, X-ray crystal structure analysis was carried out for the product **9h** obtained from **7** with *tert*-butyl hydrazine. Compound **9h** proved to be a 3-methyl pyrazole, which could only have been formed via route a) [21].

The exocyclic double bond of **9h** has (*Z*)-configuration. The C=C bond length (134.8(3) pm) indicates scarcely single bond character and thus a high barrier to geometrical isomerization.

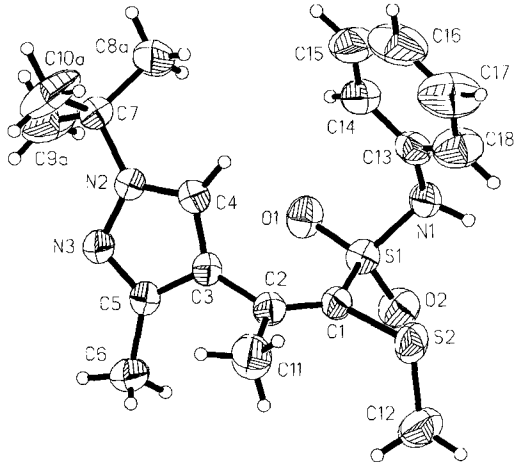
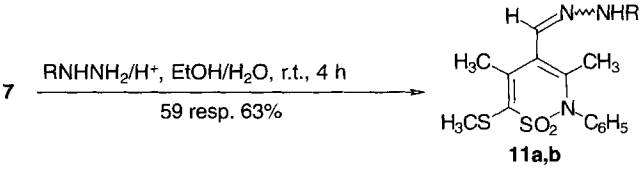


Fig. 1 Molecular structure of 1-*tert*-butyl-3-methyl-4-[1-methyl-2-methylthio-2-(*N*-phenylsulfamoyl)vinyl]pyrazole (**9h**)

With less nucleophilic hydrazines, e.g. *p*-nitrophenylhydrazine or semicarbazide, the ring transformation of **7** failed. No reaction was observed in alkaline medium. However, under acidic conditions the hydrazones **11a** and **11b** could be isolated (^{13}C NMR, MS).



11	a	b
R	C_6H_4-NO_2(p)	$CONH_2$

Scheme 6

This work was supported by the Hermann-Schlosser-Foundation of the DEGUSSA and by the Deutsche Forschungsgemeinschaft.

Experimental

NMR-spectra were measured using a Varian Gemini 300 spectrometer (^{1}H NMR 300 MHz; ^{13}C NMR 75 MHz). IR spectra were recorded on a Philips PU 9426 FTIR spectrometer as KBr pellets. Mass spectra (EI) were obtained using an AMD 402 spectrometer. Microanalyses were performed on a Leco CHNS-932 analyser. Satisfactory microanalyses were obtained for all new substances (C, H, N, S ± 0.5%). The 2-aryl-3,5-dimethyl-1,1-dioxo-2*H*-1,2-thiazines (**1a–d**) [22], the 3-chloromethyl- and 3-bromomethyl-5-methyl-1,1-dioxo-2-phenyl-2*H*-1,2-thiazines [14], the 6-iodo-3,5-dimethyl-1,1-dioxo-2-phenyl-2*H*-1,2-thiazine [15] and the 3,5-dimethyl-1,1-dioxo-2*H*-1,2-thiazine-6-carbaldehydes (**3a–e**) [11] were synthesized as described in the literature.

2-Benzyl-3,5-dimethyl-1,1-dioxo-2H-1,2-thiazine (**1e**)

2,4-Dimethyl-2,2-dioxo-1,2-oxthiine [23] (2.00 g, 12.5 mmol) and benzylamine (14 ml, 0.125 mol) were suspended in anisole (20 ml) and stirred under reflux for 6 h. After cooling the reaction mixture was filtered and the solvent of the filtrate evaporated to dryness. The residue was washed with 2M HCl and then with water. The product was dried and crystallized from MeOH. Yield 1.49 g (48%); *m.p.* 144–146 °C (MeOH). – ^{1}H NMR ($CDCl_3$): δ 2.03, 2.04 (s, 3H, CH_3), 5.00 (s, 2H, CH_2), 5.52 (s, 1H, C4-H), 6.20 (s, 1H, C6-H), 7.16–7.33 (m, 5H, Ar-H). – ^{13}C NMR ($CDCl_3$): δ 20.6, 21.6 (CH_3), 46.8 (CH_2), 107.7 (C4), 110.9 (C6), 126.4, 127.5, 128.7, 136.3 (Ar), 145.0 (C3), 148.8 (C5).

3,5-Dimethyl-6-methylthio-1,1-dioxo-2-phenyl-2H-1,2-thiazine (**5**)

A solution of NaOH (137 mg, 3.4 mmol) in EtOH (7 ml) was added to a suspension of the rhodanide **4** [17] (1 g, 3.4 mmol) in EtOH (10 ml) and stirred for 2 min. Then CH_3I (320 µl, 5.1 mmol) was added to the yellow solution at 0 – 5 °C. After stirring for 3 h, the solvent was removed under reduced pressure. The remained solid was dissolved in Et_2O and the residue was filtered off. After the evaporation of the solvent the obtained product was dried and recrystallized from MeOH. Yield 679 mg (71%); *m.p.* 102 °C (MeOH). – ^{1}H NMR ($CDCl_3$): δ 1.87, 2.30, 2.42 (s, 3H, CH_3), 5.71 (s,1H, C4-H), 7.28 (m, 2H, Ar-H), 7.41 (m, 3H, Ar-H). – ^{13}C NMR (DMSO-d_6/TMS): δ 19.9, 20.9, 21.0 (CH_3), 108.3 (C4), 119.4 (C6), 129.88, 129.90, 129.93, 134.7 (Ar), 144.3 (C3), 149.9 (C5). – EI-MS: *m/z*(%) 281 (M^+, 92%), 217 (39%), 202 (100%), 187 (96%). – IR (KBr): ν = 1157, 1267, 1326, 1373, 1488, 1513, 1591, 1604 cm^{-1}

Synthesis of Mixtures of Carbaldehydes 2a–e/3a–e and 7, 8a,b (General Procedure)

$TiCl_4$ (1.29 ml, 11.7 mmol) and dichloromethyl methyl ether (0.63 ml, 7.1 mmol) were added at 0 °C to a stirred solution of the corresponding 1,1-dioxo-2*H*-1,2-thiazine **1, 5** or **6** [16, 22] (3.5 mmol) in dried CH_2Cl_2 (5 ml). After stirring for 25 min at 0 °C the solution obtained was hydrolyzed by adding chopped ice. The organic phase was separated and polar impurities were removed by adding about 100 mg silica gel. After filtration the solution was evaporated under vacuum and reprocessed as follows.

Mixture of 2-Aryl-3,5-dimethyl-1,1-dioxo-2H-1,2-thiazine-4-carbaldehydes (**2a–e**) *and 2-Aryl-3,5-dimethyl-1,1-dioxo-2H-1,2-thiazine-6-carbaldehydes* (**3a–e**)

The viscose residue was dried and analysed by ^{1}H NMR spectroscopy in order to determine the ratio between the thiazine-4-carbaldehyde **2** and the thiazine-6-carbaldehyde **3** and used for the synthesis of **9a–e** (Table 1) [24].

3,5-Dimethyl-6-methylthio-1,1-dioxo-2-phenyl-2H-1,2-thiazine-4-carbaldehyde (**7**)

MeOH (3 ml) was added to the viscose residue and the solution was cooled down to –28 °C. Thereafter the formed solid was separated by suction and washed with cold MeOH (3 ml) (Table 2).

6-Dialkylaminomethyl-3,5-dimethyl-1,1-dioxo-2-phenyl-2H-1,2-thiazine-4-carbaldehyde-hydrochlorides (**8a,b**)

Et_2O (10 ml) was added to the viscose residue and the formed residue was separated by suction and washed several times with Et_2O (Table 2).

Table 2 Yields, melting points and spectroscopic data of the 3,5-dimethyl-6-methylthio-1,1-dioxo-2-phenyl-2*H*-1,2-thiazine-4-carbaldehyde (**7**) and the 6-dialkylaminomethyl-3,5-dimethyl-1,1-dioxo-2-phenyl-2*H*-1,2-thiazine-4-carbaldehyde-hydrochlorides (**8a,b**)

Prod.	Yield (%)	*m.p.* (°C)	MS (70 eV) *m/z* (%)	IR (KBr) ν (cm^{-1})	^{13}C NMR (DMSO-d_6 / TMS) δ (ppm)	^{1}H NMR (DMSO-d_6/ TMS) δ (ppm)
7	62	125	309 (M^+, 3) 245 (1) 229 (3) 150 (10)	1168, 1348, 1677	18.2, 19.5, 19.7 (CH_3), 117.3 (C4), 122.1 (C6), 129.7, 130.1, 130.4, 133.7 (Ar), 150.6 (C3), 156.8 (C5), 189.3 (CHO)	2.31, 2.42, 2.67 (s, 3H, CH_3), 7.30 (m, 2H, Ar-H), 7.49 (m, 3H, Ar-H), 10.04 (s, 1H, CHO)
8a	66	172	346 (13) 276 (100) 212 (41) 184 (32)	1155, 1340, 1351, 1488, 1672	18.3, 19.4 (CH_3), 22.6, 48.0, 53.6 (CH_2), 117.7 (C4), 118.7 (C6), 129.7, 130.2, 130.6, 133.5 (Ar), 151.0 (C3), 157.4 (C5), 189.3 (CHO)	1.95 (s, 4H, CH_2), 2.33, 2.60 (s, 3H, CH_3), 3.09, 3.53, 4.40 (s, 2H, CH_2), 7.46 (m, 2H, Ar-H), 7.59 (m, 3H, Ar-H), 10.05 (s, 1H, CHO), 11.17 (s, 1H, NH^+)
8b	64	189	320 (15) 276 (100) 212 (25) 184 (19)	1155, 1338, 1351, 1488, 1673	18.3, 19.4, 42.4 (CH_3), 51.0 (CH_2), 117.0 (C4), 118.7 (C6), 129.7, 130.2, 130.7, 133.4 (Ar), 151.7 (C3), 157.6 (C5), 189.3 (CHO)	2.35, 2.58 (s, 3H, CH_3), 2.81 (s, 6H, CH_3), 4.36 (s, 2H, CH_2), 7.43 (m, 2H, Ar-H), 7.59 (m, 3H, Ar-H), 10.05 (s, 1H CHO), 10.61 (s, 1H, NH^+)

3(5)-Methyl-4-[1-methyl-2-(*N*-arylsulfamoyl)vinyl]pyrazoles (9a–e) [25] (General Procedure)

The mixture of the aldehydes **2a–e** and **3a–e** (0.5 mmol) and $N_2H_4 \cdot H_2O$ (30 µl, 0.62 mmol) were added to a mixture of EtOH (15 ml) and water (0.6 ml). After stirring for 2 h the solvent was removed under vacuum. Then Et_2O (30 ml) was added to the obtained viscose residue. The precipitated solid was separated by suction, washed with Et_2O (20 ml) and reprocessed as follows.

3(5)-Methyl-4-[1-methyl-2-(N-phenylsulfamoyl)vinyl]pyrazole (**9a**)

The precipitated solid is the lutidine derivative **10a** [10]. The Et_2O solutions were evaporated and the obtained viscose residue was solved in cyclohexane/ethyl acetate (3 ml, 1:1). After some time the pyrazole **9a** precipitated from the solution, was separated by suction and dried.

3(5)-Methyl-4-[1-methyl-2-(N-(4-methylphenyl)sulfamoyl)vinyl]pyrazole (**9b**)

The precipitated solid was dissolved in $CHCl_3$ (3 ml). At 0 °C the *N*-aminopyridiniumsulfonamidate **10b** [10] was precipitated by gradually adding Et_2O and separated by suction. At a temperature of 0 °C, the remaining solution was evaporated under vacuum to dryness and the pyrazole **9b** was obtained analytically pure as residue.

Table 3 Yields, melting points and spectroscopic data of the substituted 4-[1-methyl-2-(arylsulfamoyl)vinyl]pyrazoles (**9a–i**)

Prod.	Yield [a] (%)	*m.p.* (°C)	MS (70 eV) *m/z* (%)	IR (KBr) ν (cm^{-1})	^{13}C NMR (DMSO-d_6 / TMS) [b] δ (ppm)	^{1}H NMR (DMSO-d_6 / TMS) δ (ppm), *J* (Hz)
9a	47	137	277 (M^+, 13) 213 (46) 198 (100) 185 (19)	1126, 1147, 1307, 3363	(10.0), 26.3, (25.9), 115.2, (117.3), 119.0, (119.8), 123.2, (124.0), 124.4, (128.7), 129.1, (129.3), (133.1), (137.6), 138.4, (141.1), (142.0), 144.8	2.03, 2.08 (s, 3H, CH_3), 6.38 (s, 1H), 7.02 (m, 3H, Ar-H), 7.25 (m, 2H, Ar-H), 7.49 (s, 1H, Py-H), 9.50 (s, 1H, NH), 12.60 (s, 1H, Py-NH)
9b	56	166	291 (M^+, 64) 226 (38) 212 (100) 121 (20) 107 (58)	1126, 1294, 1512, 3363	(10.3), 20.5, (20.9), 26.3, (26.3), 115.2, (117.9), 119.6, (121.1), 124.3, (129.3), 129.5, (130.3), 132.5, (133.6), (134.0), 135.7, (135.5), (141.3), (142.6), 144.7	2.02, 2.10, 2.23 (s, 3H, CH_3), 6.32 (s, 1H), 6.92 (d, 2H, *J* = 8.1, Ar-H), 7.06 (d, 2H, *J* = 8.1, Ar-H), 7.46 (s, 1H, Py-H), 9.51 (s, 1H, NH), 12.60 (s, 1H, Py-NH)
9c	27	161	307 (M^+, 58) 122 (100)	1128, 1295, 1510, 3353	(10.3), 26.3, (26.4), 55.4, (55.9), 114.4, (114.9), 115.2, (117.9), 122.6, (124.0), 124.2, (129.1), 130.9, (130.5), (133.3), (140.8), 144.0, (142.5), 156.2, (157.1)	2.02, 2.10 (s, 3H, CH_3), 3.71 (s, 3H, OCH_3), 6.29 (s, 1H), 6.85 (d, 2H, *J* = 8.6, Ar-H), 6.98 (d, 2H, *J* = 8.6, Ar-H), 7.42 (s, 1H, Py-H), 9.34 (s, 1H, NH), 12.58 (s, 1H, Py-NH)
9d	76	204	311 (M^+, 25) 231 (61) 184 (51)120 (100) 94 (30)	1130, 1315, 1495, 3357	(10.4), 26.3, (26.4), 115.1, (117.6), , 120.4 (121.5), 124.1, (128.3), 127.1, (128.7), 129.0, (129.6), (133.5), 137.4, (137.1), (142.1), (142.4), 145.3	2.04, 2.08 (s, 3H, CH_3), 6.39 (s, 1H), 6.99 (d, 2H, *J* = 8.6, Ar-H), 7.31 (d, 2H, *J* = 8.6, Ar-H), 7.50 (s, 1H, Py-H), 9.85 (s, 1H, NH), 12.62 (s, 1H, Py-NH)
9e	64	125	291 (M^+, 9) 122 (100) 106 (60) 91 (23)	1128, 1151, 1296, 3375	(10.3), 26.5, (26.1), 46.0, (45.8), 115.4, (117.7), 125.6, 127.3, (127.4), 127.8, (127.8), 128.4, (128.5), (129.4), (133.2), (138.1), 138.4, (138.4), 142.1, (142.1)	2.02, 2.19 (s, 3H, CH_3), 3.98 (d, 2H, *J* = 6.3, CH_2), 6.27 (s, 1H), 7.27 (m, 5H, Ar-H), 7.47 (t, 1H, *J* = 6.3, NH), 7.54 (s, 1H, Py-H), 12.57 (s, 1H, Py-NH)
9f	67	146	323 (M^+, 66) 167 (81) 119 (100)	946, 1128, 1294, 1332, 1415, 1496, 1598, 3367	10.9, (10.1), 19.2, (19.6), 27.2, (27.3), 117.8, (119.3), 118.1, (119.9), 122.1, (123.9), 128.7, (129.5), 132.8, (132.7), (137.3), (137.9), 138.9, (141.6), 151.7 (148.4)	2.05, 2.30, 2.31 (s, 3H , CH_3), 6.92 (m, 3H, Ar-H), 7.18 (m, 2H, Ar-H), 7.33 (s, 1H, Py-H), 9.84 (s, 1H, NH), 12.54 (s, 1H, Py-NH)
9g	42	182	399 (M^+, 92) 243 (100) 227 (20) 195 (100)	1149, 1332, 1351, 1411, 1500, 1598, 3139, 3239	12.5, 19.5, 27.6, 117.9, 118.7, 119.7, 123.2, 126.4, 126.5, 129.4, 129.5, 134.5, 138.3, 139.6, 147.4, 151.1	2.07, 2.35, 2.38 (s, 3H, CH_3), 6.99 (m, 3H, Ar-H), 7.25 (m, 3H, Ar-H), 7.45 (m, 2H, Ar-H), 7.75 (m, 2H, Ar-H), 8.26 (s, 1H, Py-H), 10.06 (s, 1H, NH)
9h	67	136	379 (M^+, 24) 223 (24) 167 (51) 119 (41)	1149, 1199, 1305, 1334, 1369, 1409, 1496, 3211	12.7, 19.5, 27.4, 29.6, 57.8, 118.1, 118.5, 122.9, 126.0, 129.0, 132.8, 138.4, 144.0, 152.3	1.47 (s, 9H, CH_3), 2.00, 2.30, 2.32 (s, 3H, CH_3), 6.96 (m, 3H, Ar-H), 7.21 (m, 2H, Ar-H), 7.49 (s, 1H, Py-H), 9.89 (s, 1H, NH)
9i	52	88	367(M^+,100) 211 (71) 163 (53)	924, 1062, 1142, 1170, 1320, 1336, 1352, 1416, 1486, 3220,	12.4, 19.4, 27.1, 53.8, 60.1, 118.2, 118.5, 122.9, 129.1, 130.3, 133.1, 138.2, 144.9, 151.6	1.88, 2.30, 2.31 (s, 3H, CH_3), 3.69 (t, 2H, *J* = 4.6, CH_2), 4.02 (t, 2H, *J* = 4.7, CH_2), 4.99 (OH), 6.89 (d, 2H, *J* = 7.2, Ar-H), 6.96 (t, 1H, *J* = 7.2, Ar-H), 7.21 (t, 2H, *J* = 7.2, Ar-H), 7.47 (s, 1H, py-H), 9.61 (s, 1H, NH)

[a] Yields of **9a–e** related to the amount of **2a–e** in the mixture of **2/3** [b] values given in parentheses: after addition of D_2SO_4

Table 4 Yields, melting points and spectroscopic data of the 3,5-dimethyl-6-methylthio-1,1-dioxo-2-phenyl-2*H*-1,2-thiazine-4-carbaldehyde-*p*-nitrophenylhydrazone (**11a**) and the 3,5-dimethyl-6-methylthio-1,1-dioxo-2-phenyl-2*H*-1,2-thiazine-4-carbaldehyde-semicarbazone (**11b**)

Prod.	Yield (%)	*m.p.* (°C)	MS (70 eV) *m/z* (%)	IR (KBr) ν (cm^{-1})	^{13}C NMR (DMSO-d_6 / TMS) δ (ppm)	^{1}H NMR (DMSO-d_6 / TMS) δ (ppm), *J* (Hz)
11a	63	146	444 (M^+, 39) 380 (100) 289 (68)	1108, 1270, 1309, 1319, 1488, 1504, 1596, 3278	18.9, 19.4, 20.5, 111.3, 116.7, 123.8, 126.4, 129.2, 129.6, 129.8, 135.0, 138.5, 139.6, 143.4, 149.0, 150.6	2.08, 2.36, 2.56 (s, 3H, CH_3), 7.06 (d, 2H, *J* = 8.7, Ar-H), 7.29 (m, 2H, Ar-H), 7.51 (m, 3H, Ar-H), 8.09 (m, 2H, Ar-H), 8.12 (s, 1H, CHN), 11.22 (s, 1H, NH)
11b	59	95	366 (M^+, 3) 302 (68) 212 (25) 168 (83)	1151, 1344 1427, 1454, 1488, 1571, 1683, 3343, 3480	18.7, 19.6, 20.4, 116.7, 123.4, 129.5, 129.9, 130.1, 135.2, 137.4, 143.8, 149.8, 157.0	1.97 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 6.30 (s, 2H, NH_2), 7.25 (m, 2H, Ar-H), 7.49 (m, 3H, Ar-H), 7.90 (s, 1H, CHN), 10.08 (s, 1H, NH)

3(5)-Methyl-4-[1-methyl-2-(N-(4-methoxyphenyl)sulfamoyl)-vinyl]pyrazole (**9c**) and *3(5)-Methyl-4-[1-methyl-2-(N-(4-chlorophenyl)sulfamoyl)vinyl]pyrazole* (**9d**) analogous **9b**

After the separation of **10c,d** (see **9b**) [10] the obtained residue was dissolved in cyclohexane/ethyl acetate (3 ml, 1:1). After some time the pyrazoles **9c**, resp. **9d**, started to precipitate from the solution, were separated by suction and dried.

3(5)-Methyl-4-[1-methyl-2-(N-benzylsulfamoyl)vinyl]pyrazole (**9e**)

The precipitated solid was dissolved in cyclohexane/ethyl acetate (3 ml, 1:1). After some time the product **9e** started to precipitate from this solution, was separated by suction and dried.

3-Methyl-4-[1-methyl-2-methylthio-2-(*N*-phenylsulfamoyl)vinyl]pyrazoles (9f–i) (General Procedure)

The carbaldehyde **7** (100 mg, 0.323 mmol) was suspended in a mixture of EtOH (7 ml) and H_2O (0.2 ml). Then the corresponding hydrazine (0.646 mmol) was added. For synthesizing **9h** a mixture of *tert*-butylhydrazinium hydrochloride and the equivalent of Na_2CO_3 was added, solved in EtOH/H_2O (2 ml). The reaction mixture was stirred at room temperature for 2 h. After evaporation the viscose residue was grinded with some Et_2O. The white solid was isolated and recrystallized from EtOH/H_2O (Table 3).

X-ray investigation of 9h [26]

$C_{18}H_{25}N_3O_2S_2$, M_w=379.53, orthorhombic, space group $P2_12_12_1$, a = 9.919(1), b = 11.173(2), c = 18.100(2) Å, V= 2006.0(4) Å^3, Z=4, $F(000)$=808, MoK_α radiation (λ= 0.71073 Å). The structure was solved by direct methods of phase determination and refined by full-matrix least-squares on F^2. wR_2 = 0.1266 (5795 unique reflections), Diffractometer: Stoe STADI4. The computation and drawings were performed by using SHELXS-86 (Sheldrick, 1986), SHELXL-93 (Sheldrick, 1993) and Siemens XP/PC (1990) [27].

3,5-Dimethyl-6-methylthio-1,1-dioxo-2-phenyl-2H-1,2-thiazine-4-carbaldehyde-p-nitrophenylhydrazone (**11a**)

A solution consisting of *p*-nitrophenylhydrazine (50 mg, 0.326 mmol), concentrated H_2SO_4 (50 µl), water (1.5 ml), EtOH (3 ml) and the carbaldehyde **7** (100 mg, 0.323 mmol) was stirred for 4 h, the obtained solid was separated by suction and washed with Et_2O (Table 4).

3,5-Dimethyl-6-methylthio-1,1-dioxo-2-phenyl-2H-1,2-thiazine-4-carbaldehyde-semicarbazone (**11b**)

Semicarbazide hydrochloride (120 mg, 1.07 mmol) and anhydrous sodium acetate (120 mg, 1.46 mmol) were powdered together. After adding absolute alcohol (6 ml), the mixture was shortly heated under reflux. The carbaldehyde **7** (100 mg, 0.323 mmol) was added to the hot filtered solution and stirred for a few hours. Then the solution was evaporated to half of it's volume and the product precipitated by the adding of water (Table 4).

References

[1] H. C. van der Plas, Ring Transformations of Heterocycles. Academic Press, New York 1973, Vols. 1 and 2
[2] A. Rottmann, J. Liebscher, J. Prakt. Chem. **338** (1996) 397
[3] M. Vivona, S. Buscemi, V. Frenna, G. Gusmano, Adv. Heterocycl. Chem. **56** (1993) 49
[4] K. Sakai, H. Suemune, Stud. Nat. Prod. Chem. **10** (1992) 303
[5] T. Zimmermann, J. Heterocycl. Chem. **32** (1995) 991
[6] E. Fanghänel, E. A. Do Nascimento, R. Radeglia, G. Lutze, B. Bode, J. Prakt. Chem. **321** (1979) 946
[7] E. Fanghänel, A. Hucke, H. Hasan, A. Ullrich, R. Radeglia, O. Simonsen, J. Prakt. Chem. **337** (1995) 104
[8] B. Helferich, R. Dhein, K. Geist, H. Jünger, D. Wiehle, Liebigs Ann. Chem. **646** (1961) 45
[9] J. Rocek, Collect. Czech. Chem. Commun. **19** (1954) 275
[10] E. Fanghänel, A. Hucke, Th. Lochter, U. Baumeister, H. Hartung, Org. Synth. (1996) Synthesis **1996**, 1375
[11] E. Fanghänel, H. Mohammed, A. M. Richter, R. Radeglia, Z. Chem. **24** (1984) 403
[12] H. Hasan, R. Radeglia, E. Fanghänel, J. Prakt. Chem. **332** (1990) 666
[13] H. Groß, A. Rieche, E. Höft, E. Beyer, Org. Synth. Coll. Vol. V (1973) 365
[14] H. Hasan, R. Radeglia, E. Fanghänel, J. Prakt. Chem. **333** (1991) 25

[15] E. Fanghänel, H. Mohammed, A. M. Richter, R. Radeglia, J. Prakt. Chem. **327** (1985) 428
[16] E. Fanghänel, H. Hasan, J. Prakt. Chem. **330** (1988) 323
[17] E. Fanghänel, H. Hasan, K. Voigt, K. Mielke, A. Ullrich, R. Radeglia, J. Prakt. Chem. **330** (1988) 142
[18] J. Elguero, Comprehensive Heterocyclic Chemistry. Pergamon Press, Oxford, New York 1984, Vol. 5, 167
[19] E. Pretsch, Th. Clerc, J. Seibl, W. Simon, Strukturaufklärung organischer Verbindungen. Springer Verlag, Berlin 1986, 3. Auflage
[20] R. Radeglia, E. Fanghänel, J. Prakt. Chem. **320** (1978) 339
[21] In the light of these results it can be supposed that the ring transformation of the thiazine-6-carbaldehydes to substituted lutidine-5-sulfonanilides which were described in an earlier publication [10] can be performed by nucleophilic ring opening as the first reaction step, as well.
[22] B. Helferich, R. Dhein, K. Geist, H. Jünger, D. Wiehle, Liebigs Ann. Chem. **646** (1961) 32
[23] Th. Morel, P. E. Verkade, Rec. Trav. Chim. Pays Bas **68** (1949) 619
[24] The separation of the mixture of **2a–d/3a–d** into the pure carbaldehydes **2** and **3** is difficult and results in a yield of **3** equal to their synthesis via Vilsmeier Haack reaction [11]. No pure carbaldehyde **2a–d** could be isolated.
[25] The *N*-Aminopyridiniumsulfamidates **10a–e** formed from the carbaldehydes **3a–e** [10] were separated as by-products.
[26] Further details of the crystal structure determination are available on request from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, on quoting the depository number CSD-405837
[27] G.M. Sheldrick, SHELXS-86, Program for the solution of crystal structures, Univ. Göttingen (1986); G. M. Sheldrick, SHELXL-93, Program for the refinement of crystal structures, Univ. Göttingen (1993)
XP/PC, Molecular graphics program for the display and analysis of stereochemical data, V. 4.2 for MS-DOS, Siemens Analytical X-ray Instruments, Inc., Madison, Wisconsin, U.S.A. (1990)

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