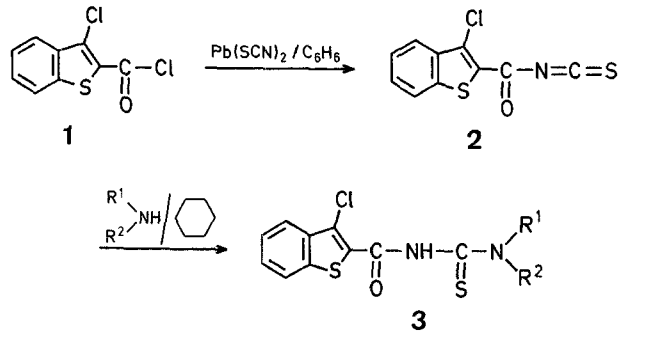
Convenient Photochemical Synthesis of 2-Substituted-4*H*-benzo[4,5]thieno[2,3-*e*]-1,3-thiazin-4-ones

Peter KUTSCHY*, Ján IMRICH, Juraj BERNÁT

Department of Organic Chemistry and Biochemistry, Faculty of Natural Sciences, P. J. Šafárik University, 04167 Košice, Czechoslovakia

A series of substituted 1,3-thiazines show antiradial[1,2], insecticidal, or fungicidal[3,4] activities and 1,3-thiazine moieties are constituents of cephalosporine antibiotics[5–8]. In continuation of our previous work on the preparation of 1,3-thiazines[9], it was intended to prepare the 2-substituted-4*H*-benzo[4,5]thieno[2,3-*e*]-1,3-thiazin-4-ones **(4)**.

We started the synthesis of the title compounds from 3-chloro-2-chlorocarbonylbenzo[*b*]thiophene **(1)**, which is readily available by the oxidation of 3-phenylpropenoic acid with thionyl chloride[10]. Treatment of **1** with lead(II) thiocyanate gives the 3-chloro-2-isothiocyanatocarbonylbenzo[*b*]thiophene **(2)**. This compound reacts with secondary amines affording the *N*-(3-chloro-2-benzo[*b*]thienocarbonyl)-*N'*,*N'*-disubstituted thioureas **3** (Table 1).



3,4	R^1	R^2
a	CH_3	CH_3
b	C_2H_5	C_2H_5
c	CH_3	
d		
e	$-(CH_2)_5-$	
f	$-(CH_2)_2-O-(CH_2)_2-$	

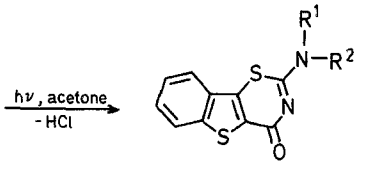


Table 1. Thiourea Derivatives **3** prepared

Product	Yield[a] [%]	m.p. [°C] (solvent)	Molecular formula[b]	I.R. $(CHCl_3)_3$ [cm^{-1}][c]		^{13}C-N.M.R. δ [ppm][d]	
				ν_{NH}	$\nu_{C=O}$	C=S	C=O
3a	65	148–149° (ethanol)	$C_{12}H_{11}ClN_2OS_2$ (298.8)	3370	1667	178.80	156.77
3b	72	139–141° (acetone)	$C_{14}H_{15}ClN_2OS_2$ (326.9)	3370	1673	177.83	157.15
3c	76	156–158° (ethanol)	$C_{17}H_{13}ClN_2OS_2$ (360.9)	3333	1670	180.19	157.42
3d	70	166–168° (acetone)	$C_{22}H_{15}ClN_2OS_2$ (423.0)	3333, 3373	1683	184.41	161.13
3e	71	147–149° (acetone)	$C_{15}H_{15}ClN_2OS_2$ (338.9)	3363	1663	176.78	156.40
3f	79	162–164° (ethanol)	$C_{14}H_{13}ClN_2O_2S_2$ (340.9)	3360	1663	178.33	158.69

[a] Yield of isolated product.
[b] Satisfactory microanalyses obtained: C ±0.26, H ±0.26, N ±0.19.
[c] Recorded on a Specord IR-75 (Zeiss Jena) instrument.
[d] Recorded on a TESLA BS 567 spectrometer (25.15 MHz) with tetramethylsilane as internal standard. Solvent: $CDCl_3$ for **3a**, **3b**, and **3e**; DMSO-d_6 for **3c**, **3d**, and **3f**.

Table 2. Conversion of Thiourea Derivatives **3** to Benzothienothiazinones **4**

Product	Irradiation time [h]	Yield[a] [%]	m.p. [°C] (solvent)	Molecular formula[b]	I.R. $(CHCl_3)$[c] $\nu_{C=O}$ [cm^{-1}]	^{13}C-N.M.R. δ [ppm][d]	
						C=N	C=O
4a	1	57	237–239° (ethanol)	$C_{12}H_{10}N_2OS_2$ (262.4)	1610	162.13	163.32
4b	1.5	55	169–170° (CCl_4)	$C_{14}H_{14}N_2OS_2$[e] (290.4)	1610	161.85	165.81
4c	1.25	80	263–265° (ethanol)	$C_{17}H_{12}N_2OS_2$ (324.4)	1610	162.47	163.12
4d	1.5	70	280–282° (ethanol)	$C_{22}H_{14}N_2OS_2$ (386.5)	1613	164.91	165.73
4e	1.5	65	258–260° (CCl_4)	$C_{15}H_{14}N_2OS_2$ (302.4)	1603	162.00	165.88
4f	1	70	273–275° (ethanol)	$C_{14}H_{12}N_2O_2S_2$ (304.4)	1610	162.13	163.77

[a] Yield of isolated product.
[b] Satisfactory microanalyses obtained: C ±0.24, H ±0.28, N ±0.26.
[c] Recorded on a Specord IR-75 (Zeiss, Jena) instrument.
[d] Measured on a TESLA BS 567 spectrometer (25.15 MHz) with tetramethylsilane as internal standard. Solvent: $CDCl_3$ for **4b**, **4d**, and **4e**; DMSO-d_6 for **4a**, **4c**, and **4f**.
[e] M.S.: $m/e = 290$ (M^+, 24%), 192 ($M - C_5H_{10}N_2$, 100%). Measured on a LKB 9000 spectrometer at 70 eV.

Recently nucleophilic substitution of a 3-chlorothiophene-1,1-dioxide derivative followed by cyclization has been reported[11]. This thermal reaction proceeds owing to the activating effect of the sulphonyl group.

By heating thioureas **3**, in solvents of different polarity or using the known methods employed for substitution reactions on halothiophenes[12–16], no benzothienothiazines are obtained. We found that the ring closure reaction occurs readily under the influence of ultraviolet light. Irradiation of thioureas **3** in acetone gives the 2-substituted-4*H*-benzo[4,5]thieno[2,3-*e*]-1,3-thiazin-4-ones **4** in good yields (Table 2).

The structure of benzothienothiazines **4** is corroborated by spectral methods. The I.R. spectra lack the characteristic NH stretching frequency, while the absorption bands of the carbonyl group appeared at lower frequencies as a result of conjugation with the C=N bond. In contrast to thioureas **3**, the ^{13}C-N.M.R. spectra of benzothienothiazines **4** did not contain signals of the thiocarbonyl group, but showed the signals of the carbon atoms of C=N endocyclic bond. The ^{1}H-N.M.R. spectra are also in accord with the proposed structure.

3-Chloro-2-isothiocyanatocarbonylbenzo[*b*]thiophene 2:
A mixture of 3-chloro-2-chlorocarbonylbenzo[*b*]thiophene (**1**; 20 g, 86 mmol) and lead(II) thiocyanate (20.7 g, 64 mmol) in benzene (200 ml) is refluxed with stirring for 3 h. After filtration and evaporation of the solvent, the residue is crystallized from hexane; yield: 14 g (64%); m.p. 92–93.5°C.

$C_{10}H_4ClNOS_2$	calc.	C 47.33	H 1.59	N 5.52
(253.7)	found	47.04	1.71	5.37

I.R. $(CHCl_3)$: $\nu = 1938$ (N=C=S), 1677 cm^{-1} (C=O).

***N*-(3-Chloro-2-benzo[*b*]thienocarbonyl)-*N'*,*N'*-disubstituted Thioureas 3; General Procedure:**
A stirred solution of 3-chloro-2-isothiocyanatocarbonylbenzo[*b*]thiophene (**2**; 3 g, 11.8 mmol) in cyclohexane (230 ml) is treated with the secondary amine (12 mmol) in cyclohexane (20 ml). The corresponding thiourea precipitates immediately. The product is filtered, washed with cyclohexane, dried, and crystallized from an appropriate solvent (Table 1).

2-Substituted-4*H*-benzo[4,5]thieno[2,3-*e*]-1,3-thiazin-4-ones 4; General Procedure:
A solution of thiourea **3** (3 mmol) in acetone (230 ml) is irradiated with 150 W high pressure mercury lamp (TQ 150, Original Hanau) for 1–1.5 h under a nitrogen atmosphere. After evaporation of the solvent the residue is chromatographed on silica gel (100 g; eluent: benzene/acetone 5/2).

Received: March 21, 1983

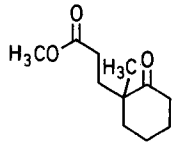
* Address for correspondence.

1 E. Campaigne, P. K. Nargung, *J. Org. Chem.* **29**, 224 (1964).
2 V. Wolf, W. Braun, *Arzneim.-Forsch.* **10**, 304 (1960).
3 J. L. Garraway, *Chem. Ind. (London)* **1965**, 1880.
4 R. A. Mathes, F. D. Stewart, *U. S. Patent* 514004; *C. A.* **44**, 8381 (1950).
5 E. P. Abraham, G. G. F. Newton, *Biochem. J.* **79**, 337 (1961).
6 G. C. Barret, *J. Chem. Soc.* **1964**, 783.
7 J. L. Spencer et al., *J. Org. Chem.* **32**, 500 (1967).
8 R. B. Woodward et al., *J. Am. Chem. Soc.* **88**, 852 (1966).
9 J. Imrich, P. Kristian, *Collect. Czech. Chem. Commun.* **47**, 3268 (1982).
10 T. Higa, A. J. Krubsack, *J. Org. Chem.* **40**, 3037 (1975).
11 W. Ried, B. J. Mavunkar, H. Knorr, *Chem. Ber.* **110**, 1356 (1977).

[12] H. D. Hartough, *Thiophene and its Derivatives*, Interscience Publishers, Inc., New York, 1952, chap. 5, pp. 143-159.
[13] S. Gronowitz, *Arkiv Kemi* **12,** 239 (1958).
[14] R. Adams, A. Ferrotti, *J. Am. Chem. Soc.* **81,** 4927 (1959).
[15] D. E. Ames, O. Ribeiro, *J. Chem. Soc. Perkin Trans. 1* **1975,** 1390.
[16] S. Conde et al., *Synthesis* **1976,** 412.

J. K. Whitesell, M. A. Whitesell, *Synthesis* **1983** (7), 517–536:

Compound **14** (p. 521) should be named 3-methoxycarbonylmethyl-8a-methyl-5-methylene-2-oxo-6-(2,2-dimethylpropanoyloxy)-*trans*-decalin. The structure of compound **25** (p. 522) should be:



25

T. Kolasa, *Synthesis* **1983** (7), 539:

The heading for the 6th column in the Table should be (*Z*/*E*)-Ratio.

S. Kano, Y. Yuasa, T. Yokomatsu, S. Shibuya, *Synthesis* **1983** (7), 585–587:

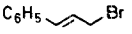
Compounds **5** should be named 3-oxo-2,3,4,5-tetrahydro-1*H*-azepino[4,3-*b*][1]benzothiophenes.

M. Sawada, Y. Furukawa, Y. Takai, T. Hanafusa, *Synthesis* **1983** (7), 593–595:

Compounds **4** and **5** should be named 2,4-dialkyl-1,3,6-trioxo-2,3,4,4a,5,6-hexahydro-1*H*-[1,3,5]triazino[1,2-*a*]quinolines and 1,3-dimethyl-2,4,8-trioxo-1,2,3,4,7,8-hexahydro-8a*H*-pyrido[1,2-*a*][1,3,5]triazine, respectively.

R. B. Cheikh, R. Chaabouni, A. Laurent, P. Mison, A. Nafti, *Synthesis* **1983** (9), 685–700:

The first substrate in Table 3 (p. 689) should be:



Y. Imai, A. Mochizuki, K. Kakimoto, *Synthesis* **1983** (10), 851:

The title compounds **4** should be named 4*H*-1,2,4-benzothiadiazine 1,1-dioxides.

R. Rastogi, S. Sharma, *Synthesis* **1983** (11); 861–882:

Compound **109** (p. 870) should be named: 7,12-dioxo-6,7-dihydro-12*H*-benzimidazo[1,2-*b*][2,4]benzodiazepine.

P. Kutschy, J. Imrich, J. Bernát, *Synthesis* **1983** (11), 929–931:

The title compounds **4** should be named 2-amino-4-oxo-4*H*-[1]benzothieno[2,3-*e*]-1,3-thiazines.

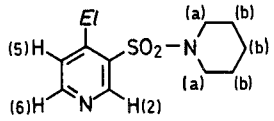
P. Breant, M. Marsais, G. Quéguiner, *Synthesis* **1983** (10), 822–824:

The following data should be added to the ^{1}H-N.M.R. spectra of compounds **3a–c** (p. 824):

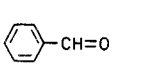
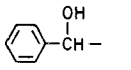
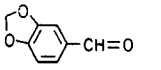
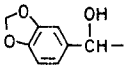
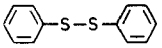
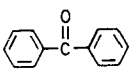
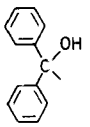
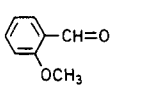
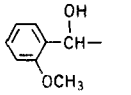
For compounds **3a–c**, $J_{H\text{-}4,H\text{-}5}$ = 8 Hz; $J_{H\text{-}5,H\text{-}6}$ = 5 Hz; $J_{H\text{-}4,H\text{-}6}$ = 2 Hz; $J_{H\text{-}4,H\text{-}2}$ = 2 Hz.

Tables 1 and 2 (p. 823) should be read as follows:

Table 1. 4-Substituted 3-Piperidinosulfonylpyridines prepared



5a, 7a-10a

Electrophile	*El*	Product	Yield [%]	m.p. [°C]	Molecular formula[a]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm][b]
		**5a**	80	127°	$C_{17}H_{18}N_2O_3S$ (330.4)	1.5 [m, 6 H(b)]; 3.1 [m, 4 H(a)]; 4.0 (m, OH); 5.3 (m, 1 H); 6.7 (m, 5 H); 7.53 (d, H-5); 8.63 (d, H-6); 8.93 (s, H-2)
		**7a**	60	80° (dec)	$C_{18}H_{18}N_2O_5S$ (374.4)	1.6 [m, 6 H(b)]; 3.2 [m, 4 H(a)]; 5.96 (s, 2 H); 6.63 (s, 1 H); 6.9 (m, 3 H); 7.50 (d, H-5); 8.86 (d, H-6); 8.93 (s, H-2)
$(H_3C)_3Si-Cl$	$(H_3C)_3Si-$	**8a**	42	<50°	$C_{13}H_{20}N_2O_2SSi$ (296.5)	0.50 (s, 9 H); 1.7 [m, 6 H(b)]; 3.2 [m, 4 H(a)]; 7.70 (d, H-5); 8.70 (d, H-6); 8.95 (s, H-2)
		**9a**	80	82°	$C_{16}H_{16}N_2O_2S_2$ (332.4)	1.7 [m, 6 H(b)]; 3.2 [m, 4 H(a)]; 6.70 (d, H-5); 7.56 (s, 5 H); 8.30 (d, H-6); 8.93 (s, H-2)
		**6a**	95	195°	$C_{23}H_{22}N_2O_3S$ (406.5)	1.5 [m, 6 H(b)]; 3.2 [m, 4 H(a)]; 6.70 (s, OH); 6.75 (d, H-5); 7.30 (s, 10 H); 8.51 (d, H-6); 9.06 (s, H-2)
		**10a**	53	164°	$C_{18}H_{20}N_2O_4S$ (360.4)	1.7 [m, 6 H(b)]; 3.2 [m, 4 H(a)]; 3.70 (s, 3 H); 4.2 (m, OH); 6.70 (s, 1 H); 7.15 (d, H-5); 7.5 (m, 4 H); 8.80 (d, H-6); 9.06 (s, H-2)
–	–	**12**	–	–	–[c]	1.7 [m, 6 H(b)]; 3.3 [m, 4 H(a)]; 4.6 (m, OH); 5.96 (d, 1 H, J = 3 Hz); 7.85 (d, H-5); 8.86 (d, H-6); 9.00 (s, H-2)
–	–	**13**	–	–	–[c]	1.7 [m, 6 H(b)]; 3.3 [m, 4 H(a)]; 5.83 (d, 1 H, J = 3 Hz); 7.60 (d, H-5); 8.83 (d, H-6); 9.13 (s, H-2)

[a] Satisfactory microanalyses obtained: C ±0.38, H ±0.32, N ±0.14; exception: **7**: C −0.70%.

[b] $J_{H\text{-}5,H\text{-}6}$ = 5 Hz for all products.

[c] See text.