Studies on the Reaction of 2-Aminoacetophenone with Thiophosgene

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The reaction of 3- and 4-aminoacetophenone with thiophosgene in a chloroform-water-calcium carbonate mixture at room temperature results in good yields of the related, known isothiocyanates. At first, however, we failed in all our attempts to produce 2-isothiocyanatoacetophenones with this reaction. Closer inspection of the reaction showed, that the product distribution depends upon the concentration of hydrogen ions producted and on the reaction time. When the reaction was followed with thin-layer chromatography, it was observed that the isothiocyanates formed first. In the further course of the reaction, they were converted to the 4-methylene-2-oxo-3,1-benzothiazines by the action of protons. The final products of the reaction were the 4-(3,1-benzothiazin-4-yl)-methylene-3,1-benzothiazines, formed from the monomer in a dimerization process. Depending upon the time the protons were removed from the reaction mixture, different products could be isolated.

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Introduction.

In order to prepare 5-methyl-1,3,4-benzotriazepines [1], we wanted to obtain first the 2-isothiocyanatoacetophenones, **2a** and **2b**. We tried to produce these compounds by treating the 2-aminoacetophenones, **1a** and **1b** [2], with thiophosgene in a chloroform-water-calcium carbonate mixture (Scheme 1). Although the reaction of 3- and 4-aminoacetophenone with thiophosgene furnished good yields of the related isothiocyanates [3], under similar conditions, we failed at first in all of our attempts to isolate the desired compounds, **2a** and **2b**, in the usual way.

Scheme 1

1 R = a: H b: Cl 2

Depending upon the reaction conditions, several products without an isothiocyanate structure were isolated either as impure compounds or as mixtures of different compounds. It could be demonstrated that these products were formed from compounds **2a** and **b**, by treating the freshly prepared reaction solutions with methylhydrazine, which resulted in the expected thiosemicarbazide derivatives [1].

In this paper we are reporting the results of a detailed investigation of the reaction of 2-aminoacetophenone with thiophosgene.

Results and Discussion.

The reaction was first examined in the chloroform-

Table 1

Crystallographic Data for **5a**

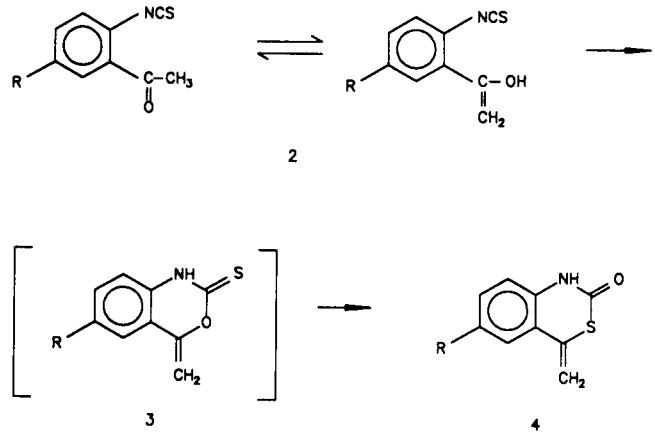
formula	$C_{18}H_{14}N_2O_2S_2 \cdot C_2H_6SO$
fw	432.60
cryst syst	monoclinic
space group	$P2_1/c$
a, Å	7.0880 (2)
b, Å	20.982 (5)
c, Å	14.450 (4)
β, deg	103.41 (2)
V, Å^3	2090.6 (9)
Z	4
D_{calcd}, g cm^{-3}	1.37
cryst dimens, mm	0.3 x 0.35 x 0.35
radiation	Mo Kα
monochromator	graphite
F(000)	904
μ, cm^{-1}	3.62
2θ limits, deg	4-55
no. of unique rflns	4797
no. of obsd data, I > 3σ(I)	2485
R [a]	0.0599
R_w [b]	0.0630

[a] $R = \Sigma||F_O|-|F_C||/\Sigma|F_O|$. [b] weight = $1/(\sigma^2(F)+0.001F^2)$.

water-calcium carbonate mixture. Immediately after the quickly occurring reaction ceased, the organic layer was separated and dried for a short time. The ir spectra, measured from the freshly prepared chloroform solution, showed strong absorption peaks at 2100 cm^{-1} and 2090 cm^{-1}, and this verified the formation of the isothiocyanates **2a** and **2b**, respectively.

Thin layer chromatography (tlc) showed that compounds **2a** and **2b**, formed in the first reaction step (Scheme 1), were obtained almost without any by-products. However, when the solution was stored at room temperature, the concentrations of **2a,b** decreased, and new compound **4a,b** possessing lower R_f values than **2a,b** were formed (Scheme 2). After some time, further new products, **5a** and **5b**, were detected that clearly originated from compounds **4a,b**, because the concentrations of compounds **4a,b** decreased simultaneously as the concentrations of **5a,b** increased (Scheme 3). Compounds **5a,b** were isolated consistently from the reaction mixtures as the final products of the reaction of 2-aminoacetophenones **1a,b** with thiophosgene; however, these substances were contaminated with compounds **4a,b**.

Scheme 2



It is of particular note that the formation of **4a,b** from **2a,b** occurred at a faster rate than the conversion of **4a,b**

Table 2

Atomic Coordinates (x10^4) and Isotropic Temperatue Factors ($Å^2$ x 10^3) for $C_{18}H_{14}N_2O_2S_2 \cdot (CH_3)_2SO$

	x	y	z	U
C(5')	3393 (6)	2583 (2)	2940 (3)	41 (2)
C(10')	2390 (7)	3119 (2)	3149 (3)	43 (2)
C(9')	781 (7)	3342 (2)	2476 (4)	51 (2)
C(8')	212 (8)	3058 (3)	1606 (4)	60 (2)
C(7')	1221(10)	2538 (3)	1392 (4)	65 (2)
C(6')	2777 (8)	2306 (2)	2059 (4)	52 (2)
N(1')	2959 (7)	3457 (2)	4009 (3)	55 (2)
C(2')	4113 (8)	3267 (2)	4830 (4)	57 (2)
O(2')	4385 (7)	3587 (2)	5570 (3)	81 (2)
S(3')	5253 (2)	2515 (1)	4879 (1)	63 (1)
C(4')	5231 (7)	2336 (2)	3624 (4)	47 (2)
C(41')	7005 (9)	2661 (3)	3369 (7)	74 (3)
C(11)	5455 (7)	1621 (2)	3594 (4)	47 (2)
C(4)	4158 (6)	1171 (2)	3647 (3)	41 (2)
S(3)	1817 (2)	1401 (1)	3786 (1)	48 (1)
C(2)	1062 (6)	744 (2)	4365 (3)	42 (2)
O(2)	-344 (5)	830 (2)	4717 (3)	63 (1)
N(1)	1991 (5)	180 (2)	4388 (3)	44 (1)
C(10)	3463 (6)	16 (2)	3941 (3)	39 (1)
C(5)	4506 (7)	480 (2)	3561 (3)	44 (2)
C(6)	5939 (10)	262 (3)	3117 (5)	73 (3)
C(7)	6370 (11)	-382 (3)	3080 (5)	81 (3)
C(8)	5369 (9)	-827 (3)	3473 (4)	63 (2)
C(9)	3916 (7)	-633 (2)	3897 (4)	49 (2)
S(1) *	125 (5)	4847 (2)	6637 (2)	84 (1)
S(2) *	-2503 (5)	4743 (1)	5788 (2)	67 (1)
O(1)	-1164 (6)	5334 (2)	6039 (3)	84 (2)
C(21)	-812 (11)	4085 (4)	6008 (5)	100 (2)
C(22) *	-3253 (19)	4729 (6)	4519 (9)	82 (4)
C(23) *	2438 (26)	4886 (8)	6278 (12)	118 (5)

Equivalent isotropic U defined as one-third of the trace of the orthogonalized U tensor.
* Population parmeter 0.5.

Scheme 3

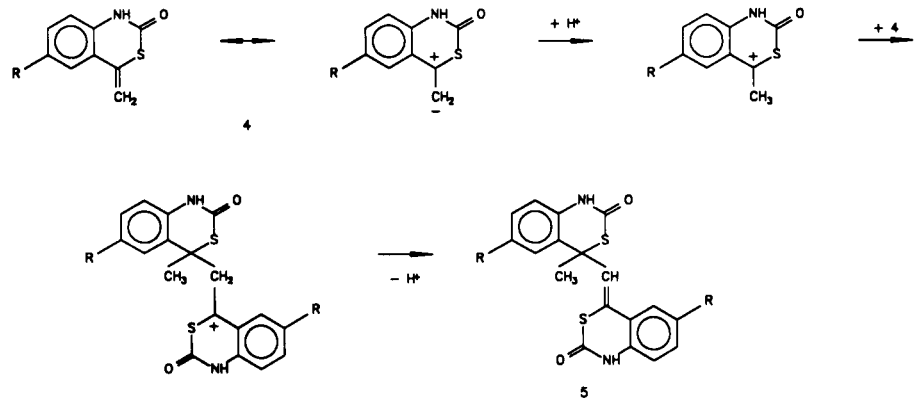


Table 3

Bond Lengths (pm) for $C_{18}H_{14}N_2O_2S_2 \cdot (CH_3)_2SO$

C(5')-C(10'')	139.9 (6)	C(5')-C(6')	137.4 (7)
C(5')-C(4')	153.2 (6)	C(10')-C(9')	139.7 (6)
C(10')-N(1')	140.6 (6)	C(9')-C(8')	136.5 (8)
C(8')-C(7')	137.8 (8)	C(7')-C(6')	137.5 (8)
N(1')-C(2')	133.6 (7)	C(2')-O(2')	123.9 (7)
C(2')-S(3')	176.6 (5)	S(3')-C(4')	184.9 (5)
C(4')-C(41')	154.9 (9)	C(4')-C11)	151.0 (6)
C(11)-C(4)	133.3 (6)	C(4)-S(3)	178.3 (5)
C(4)-C(5)	148.0 (6)	S(3)-C(2)	176.0 (5)
C(2)-O(2)	123.3 (6)	C(2)-N(1)	135.1 (6)
N(1)-C(10)	139.2 (7)	C(10)-C(5)	140.8 (6)
C(10)-C(9)	140.4 (6)	C(5)-C(6)	139.8 (9)
C(6)-C(7)	139.0 (8)	C(7)-C(8)	137.3 (9)
C(8)-C(9)	137.7 (9)		
S(1)-O(1)	150.2 (5)	S(1)-C(21)	188.3 (8)
S(1)-C(23)	183.3 (20)	S(2)-O(1)	155.2 (5)
S(2)-C(21)	180.8 (8)	S(2)-C(22)	178.7 (13)

Table 4

Bond Angles (deg) for $C_{18}H_{14}N_2O_2S_2 \cdot (CH_3)_2SO$

C(10')-C(5')-C(6')	118.1 (4)	C(10')-C(5')-C(4')	122.1 (4)
C(6')-C5')-C(4')	119.6 (4)	C(5')-C(10')-C(9')	119.6 (4)
C(5')-C(10')-N(1')	122.6 (4)	C(9')-C(10')-N1')	117.8 (4)
C(10')-C(9')-C(8')	120.9 (5)	C(9')-C(8')-C(7')	119.6 (5)
C(8')-C(7')-C(6')	119.7 (5)	C(5')-C(6')-C(7')	122.1 (5)
C(10')-N(1')-C(2')	128.8 (4)	N(1')-C(2')-O(2')	123.1 (5)
N(1')-C(2')-S(3')	118.8 (4)	O(2')-C(2')-S(3')	118.0 (4)
C(2')-S(3')-C(4')	104.0 (2)	C(5')-C(4')-S(3')	112.1 (3)
C(5')-C(4')-C(41')	108.2 (4)	S(3')-C(4')-C(41')	108.7 (4)
C(5')-C(4')-C(11)	113.4 (3)	S(3')-C(4')-C(11)	104.7 (3)
C(41')-C(4')-C(11)	109.5 (4)	C(4')-C(11)-C(4)	128.6 (5)
C(11)-C(4)-S(3)	119.1 (3)	C(11)-C(4)-C(5)	123.9 (4)
S(3)-C(4)-C(5)	116.9 (3)	C(4)-S(3)-C(2)	103.6 (2)
S(3)-C(2)-O(2)	116.4 (3)	S(3)-C(2)-N(1)	119.9 (4)
O(2)-C(2)-N(1)	123.7 (4)	C(2)-N(1)-C(10)	128.1 (4)
N(1)-C(10)-C(5)	121.9 (4)	N(1)-C(10)-C(9)	117.6 (4)
C(5)-C(10)-C(9)	120.4 (5)	C(4)-C(5)-C(10)	122.1 (4)
C(4)-C(5)-C(6)	120.8 (4)	C(10)-C(5)-C(6)	117.1 (4)
C(5)-C(6)-C(7)	121.7 (6)	C(6)-C(7)-C(8)	120.4 (7)
C(7)-C(8)-C(9)	119.6 (5)	C(10)-C(9)-C(8)	120.7 (5)
O(1)-S(1)-C(21)	101.5 (3)		
O(1)-S(1)-C(23)	105.8 (6)	C(21)-S(1)-C(23)	98.0 (6)
O(1)-S(2)-C(21)	103.0 (3)		
O(1)-S(2)-C(22)	105.9 (5)	C(21)-S(2)-C(22)	101.3 (5)

to **5a,b**. Depending upon the starting materials, **1a** or **1b**, the relative solubilities of compounds **4** and **5** in chloroform differed from each other. Compound **5a** crystallized quickly from the organic phase, whereas **4a** was more soluble in chloroform. With chloro compounds, **4b** and **5b**, more problems were encountered. Because **4b** was only sparingly soluble in chloroform, the final product, **5b**, contained considerable amounts of **4b**. However, both **5a** and **5b** could be purified successfully by repeated recrystallizations from acetone.

In order to elucidate the reasons for the exceptional behavior of the isothiocyanates **2a,b**, the *p*H value of the stored chloroform solutions was controlled. Although the reaction mixtures were vigorously stirred and calcium carbonate added, acidic reactions occurred in all of the solutions; these were caused by hydrogen chloride. For this reason the action of protons in the conversion of **2a,b** to **4a,b** was postulated. To prove this, a more efficient auxiliary base, namely an excess of sodium bicarbonate, was used in place of calcium carbonate. In this case the formation of **4a,b** and **5a,b** was not observed. However, the isolation of **2a** failed when the reaction mixture was treated under the usual conditions. The desired compound **2a**, was obtained only by cautious handling and crystallization from *n*-hexane at temperatures about −20°. This 2-isothiocyanatoacetophenone was an unstable, low melting and colorless compound, possessing a typically penetrating odor. It is interesting to note that the related hexahydro derivative, 2-acetylcyclohexylisothiocyanate, prepared by Boiko *et al.* [4] from 1-acetylcyclohexene and potassium thiocyanate in the presence of sulfuric acid, is evidently much more stable.

Since we expected that compound **2b** would be more unstable than **2a**, due to the -I-effect of the chlorine atom to the carbonyl group, we did not try to isolate it.

When **2a,b** were dissolved in chloroform and a solution of dried hydrogen chloride in chloroform added, the formation of **4a** and **4b** took place with a variety of reaction times, depending upon the concentration of protons. Since

Table 5

Anisotropic Thermal Parameters (x10^3) for $C_{18}H_{14}N_2O_2S_2 \cdot (CH_3)_2SO$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(5')	43 (2)	29 (2)	56 (3)	12 (2)	21 (2)	2 (2)
C(10')	47 (3)	31 (2)	56 (3)	8 (2)	25 (2)	-1 (2)
C(9')	45 (3)	34 (2)	79 (4)	14 (3)	23 (3)	4 (2)
C(8')	53 (3)	45 (3)	77 (4)	16 (3)	3 (3)	-2 (3)
C(7')	95 (4)	44 (3)	53 (3)	7 (3)	8 (3)	-3 (3)
C(6')	72 (4)	35 (2)	54 (3)	8 (2)	21 (3)	6 (2)
N(1')	67 (3)	36 (2)	64 (3)	5 (2)	22 (2)	13 (2)
C(2')	77 (4)	42 (3)	57 (3)	4 (3)	27 (3)	-1 (3)
O(2')	129 (4)	59 (2)	60 (3)	1 (2)	29 (2)	4 (2)
S(3')	77 (1)	45 (1)	62 (1)	8 (1)	5 (1)	10 (1)
C(4')	45 (3)	35 (2)	65 (3)	11 (2)	23 (2)	3 (2)
C(41')	50 (3)	48 (4)	130 (7)	27 (4)	35 (4)	0 (3)
C(11)	41 (3)	33 (2)	76 (4)	15 (2)	30 (3)	12 (2)
C(4)	45 (3)	32 (2)	50 (3)	12 (2)	21 (2)	10 (2)
S (3)	43 (1)	32 (1)	76 (1)	13 (1)	26 (1)	9 (1)
C(2)	32 (2)	36 (2)	60 (3)	5 (2)	10 (2)	-2 (2)
O(2)	43 (2)	43 (2)	114 (3)	15 (2)	40 (2)	5 (1)
N(1)	38 (2)	32 (2)	67 (3)	10 (2)	22 (2)	-1 (2)
C(10)	43 (3)	29 (2)	44 (3)	-1 (2)	10 (2)	1 (2)
C(5)	54 (3)	29 (2)	52 (3)	5 (2)	21 (2)	10 (2)
C(6)	102 (5)	48 (3)	92 (4)	16 (3)	71 (4)	19 (3)
C(7)	117 (5)	54 (3)	95 (5)	6 (3)	69 (4)	35 (3)
C(8)	90 (4)	33 (3)	72 (4)	-4 (2)	30 (3)	17 (3)
C(9)	57 (3)	29 (2)	60 (3)	0 (2)	12 (3)	0 (2)
S(1) *	101 (3)	89 (2)	59 (2)	-8 (2)	14 (2)	37 (2)
S(2) *	85 (2)	47 (1)	72 (2)	-9 (1)	25 (2)	6 (1)
O(1)	94 (3)	58 (2)	94 (3)	-13 (2)	11 (2)	32 (2)

* Population parmeter 0.5.

Table 6

H Atomic Coordinates (x 10^4) and Thermal Parameters (x10^3)

	x	y	z	U
H(1')	2446 (73)	3774 (25)	4023 (35)	58 (17)
H(9')	83 (63)	3715 (21)	2627 (29)	45 (12)
H(8')	-876 (73)	3229 (23)	1159 (34)	61 (15)
H(7')	995 (68)	2379 (22)	830 (34)	50 (15)
H(6')	3524 (68)	1978 (25)	1940 (33)	59 (15)
H(41A)	8309 (118)	2436 (34)	3804 (52)	136 (27)
H(41B)	7046 (94)	2471 (31)	2691 (49)	104 (25)
H(41C)	6787 (77)	3101 (30)	3393 (38)	80 (18)
H(11)	6645 (62)	1475 (19)	3520 (28)	37 (11)
H(1)	1575 (59)	-102 (19)	4715 (29)	32 (11)
H(6)	6687 (76)	541 (25)	2856 (38)	73 (17)
H(7)	7458 (82)	-477 (25)	2859 (39)	78 (18)
H(8)	5624 (63)	-1269 (23)	3490 (31)	51 (13)
H(9)	3220 (66)	-955 (22)	4247 (32)	56 (13)

the conversion of compounds **2** to **4** was catalyzed by protons, this led us to examine whether the same applied to the formation of compounds **5** from **4**. As a consequence, the reaction of **1a,b** with thiophosgene was carried out without an auxiliary base. Furthermore, the course of the reaction was followed by thin layer chromatography. When compounds **4a,b** reached their highest concentration and the solutions became turbid due to the beginning of crystallization, the 10 molecular amount of sodium bicarbonate and water was added; and the mixture shaken vigorously, until all the hydrogen chloride was extracted from the chloroform phase. According to our expectations, compounds **4a,b** could be isolated as crude products. While **4a** could be obtained as a relatively pure product after recrystallization from chloroform, the isolation of a sufficient amount of pure **4b**, needed for analytical purposes, was difficult. Hence, the exact determination of the elemental analysis of the composition of **4a,b** was carried out by mass spectrometry. By treating the chloroformic solutions of the isolated **4a,b** compounds with dry hydrogen chloride compounds **5a,b** were formed and the action of protons in the conversion of **4a,b** to **5a,b** was proved.

According to the mass spectrometric measurements, the molecular ion peaks of **4a** and **4b** appeared at m/z 177 and m/z 211, respectively. Because these agreed with the molecular weights of the related isothiocyanates **2a,b**, it was assumed, at first, that the formation of 4-methylene-2-

thioxo-3,1-benzoxazines, **3a,b**, had occurred by an intramolecular cyclization of **2a,b** (Scheme 2). The primary fragment ions, $[M\text{-}CO]^{+\cdot}$, $[M\text{-}NCO]^{+}$ and $[M\text{-}C_2HS]^{+}$, in the mass spectra were not, however, in accord with the postulated benzoxazine structure. Further evidence against this structure came from the infrared spectra of **4a,b**. The typical absorption bands for CONH groups, especially those for CO absorption, about 1650 cm^{-1}, hinted at a 4-methylene-2-oxo-3,1-benzothiazine structure for **4a,b**. These could only be formed from the intermediates, **3a,b**, in a ring opening-recyclization process. The results of the thin layer chromatography showed that the conversion of **3a,b** occurred very quickly. Thus, the only products obtained were **2a,b**, **4a,b** and **5a,b**. Similarly, Kricheldorf [5] has observed an analogous behavior in the intramolecular cyclization reaction of *cis*-2-isothiocyanatocyclohexane carbonic acid. The final assignments of the structures of **4a,b** were made by ^1H and ^{13}C nmr spectroscopy. In addition, the results concerning the further conversion of **4a,b** were in accordance with these structures.

The structure of **5**, 4-(3,1-benzothiazin-4-yl)methylene-3,1-benzothiazine (Scheme 3), was initially assigned on the basis of the spectral data presented in the experimental section. The molecular ion peaks at m/z 354 and 422 for **5a** and **5b**, respectively were verified by ammonia chemical ionization. The marked similarities between the ir and uv spectra of compounds **4a,b** and those of the related **5a,b** were evident. X-ray analysis provided the final proof for this structural determination.

The molecular structure of **5a** was formed by the unexpected dimerization of **4a** (Figure 1). The roughly planar benzothiazine moieties are perpendicular to each other, and the conformation of the heterocyclic rings is best described as an envelope, the deviations of the S3 and S3' atoms from the calculated, least-squares planes of the other ring atoms are 0.39 and 0.51 Å, respectively. This is understandable as ring A has a more "aromatic" character than ring B, due to the different hybridizations of the carbon atoms, C4 (sp^2) and C4' (sp^3). Thus the bond lengths, C4-C5 and C4-S3, in ring A are significantly shorter than the corresponding bond lengths in ring B (Figure 1).

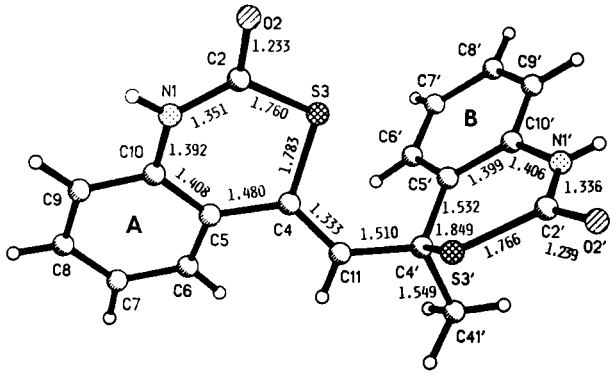


Figure 1. Molecular structure, atomic numbering scheme and selected bond lengths for **5a**.

After the structures of the isolated compounds were determined, it was possible to explain the course of the reaction when the chloroformic phases containing hydrogen chloride had been stored at room temperature (Scheme 2). In the last step, compounds **4a,b** dimerize to the final products by the action of protons. A possible mechanism for the formation of **5a,b** from **4a,b** is presented in Scheme 3. Since we did not find any publication describing dimerization reactions of other methylene heterocycles, although such compounds are able to undergo addition reactions with appropriate reactants [6], the formation of **5a,b** was unexpected. It is, however, noteworthy that all methylene-3,1-benzothiazines described in the literature possess a substituted methylene group [7,8]. No addition reactions are reported for these compounds that are synthesized by other methods than ours. Up to this time, 4-(3,1-benzothiazin-4-yl)methylene-3,1-benzothiazines have been unknown. Except for one report [8], compounds that contain two 3,1-benzothiazine ring systems, coupled through an sp^2 hybridized carbon atom possessing a methylene structure, have not previously been characterized.

EXPERIMENTAL

The yields are related to the isolated crude products. The melting points were determined by using either a Kofler-Boetius apparatus or Büchi capillary device; these are uncorrected. For the tlc analyses glass plates covered with Kieselgel G (Merck) were utilized, and a benzene-methanol mixture (9:1, Volume parts) was used as the mobile phase; iodine vapor was used for detection. The uv spectra were measured on a SPECORD UV/-VIS spectrophotometer, and the ir spectra performed on a SPECORD 71 IR spectrophotometer (both VEB Carl Zeiss Jena). Elemental analyses were made with a Carlo Erba CHN-S/O elemental analyzer 1106.

The mass spectra were recorded on a Jeol JMS-D300 mass spectrometer equipped with a data system JMA-2000H. Samples were introduced with a solid inlet probe. Exact mass measurements were carried out at a nominal resolving power of 5000. The nmr spectra were measured with a Bruker AM250/Aspect 3000 FT-NMR. The ^1H nmr assignments were based on the COSY spectra.

X-ray Crystallographic Analyses of **5a**.

Crystals of **5a** used for the X-ray crystal structural analyses were obtained from DMSO which was found as the solvate, too. Data were collected on a Nicolet R3m diffractometer using Mo Kα radiation (λ = .71073 Å), ω - scan mode with scan width 1° from K$\alpha_{1,2}$ and a variable scan speed of 2.44-29.3° min^{-1}. Accurate cell parameters were obtained from 25 automatically centered reflections, in the range $15° \leq 2\theta \leq 25°$. Other crystallographic data are presented in Table 1. Intensities were corrected for Lorentz and polarization factors. Empirical absorption corrections were made from ψ-scan data. The structure was solv-

ed by direct methods and refined by the full-matrix anisotropic least-squares techniques for non-hydrogen atoms, except for the carbon atoms of disordered DMSO, which were refined, isotropically, in a manner similar to the hydrogen atoms of the benzothiazine moieties. The SHELXTL program package was used for all calculations [9].

2-Isothiocyanatoacetopheneone **2a**.

A solution of **1a** (0.006 mole) in chloroform (8 ml) was added dropwise, within 15 minutes, to the well-stirred mixture of thiophosgene (0.006 mole), chloroform (6 ml), water (4 ml) and calcium carbonate (0.006 mole), cooled in an ice-water bath. Sodium bicarbonate (0.008 mole) was added to this mixture, and the stirring was continued for a further 15 minutes. The solid was removed, and the separated organic phase was dried over sodium sulphate for a short time. The solvent was evaporated at room temperature on a rotary evaporator. The resulting oil was treated with *n*-hexane six times (10 ml each time) at room temperature, and the combined extracts were evaporated to half of the original volume. The solution was stored at −20° for some hours; the formed, colorless crystals were separated very quickly, washed with cold *n*-hexane and dried, colorless crystals from *n*-hexane, 70%, mp 19-21°; ir (chloroform): 2100 cm^{-1} (N=C=S); ms: (EI) m/z 177 ($M^{+\cdot}$).

Anal. Calcd. for C_9H_7NOS: N, 7.90. Found: N, 8.06.

General Procedure for the Preparation of 4-Methylene-2-oxo-1,4-dihydro-2*H*-3,1-benzothiazines (**4**).

A solution of the related **1** (0.035 mole) in chloroform (50 ml) was added dropwise, within 15 minutes to the well-stirred mixture of thiophosgene (0.035 mole), chloroform (35 ml) and water (25 ml) cooled in an ice-water bath. After stirring for a further 5 minutes, the organic layer was separated and stored over sodium sulphate at room temperature. Using samples of this solution, the course of reaction was followed by thin layer chromatography. When **5** (the compound with lowest R_f value) was formed in a clearly observable concentration, the reaction was stopped by the addition of sodium bicarbonate (0.35 mole) and water (30 ml). The reaction mixture was shaken until the organic phase showed a neutral reaction. After filtration the chloroformic layer was separated, dried over sodium sulphate, and the solvent was evaporated to dryness. The residue was treated with small amounts of acetone; the formed crystals were collected, washed with acetone and dried.

4-Methylene-2-oxo-1,4-dihydro-2*H*-3,1-benzothiazine (**4a**).

This compound was obtained as colorless crystals from chloroform, 35%, mp 137-138°; ir (potassium bromide): cm^{-1} 3200 (NH), 1645 (CO), 1575, 1505; uv: λ max (log ε) 238 (3.81), 327 (2.93); ms: (EI) m/z 177 ($M^{\cdot}$, 60), 149 (177-CO, 50), 135 (177-NCO, 75), 120 (177-C_2HS, 100), 60 (COS, 59).

Anal. Calcd. for C_9H_7NOS: C, 61.00; H, 3.98; N, 7.90; $M^{+\cdot}$ 177.0249. Found: C, 58.65; H, 4.43; N, 7.57; $M^{+\cdot}$ 177.0254 [10].

6-Chloro-4-methylene-2-oxo-1,4-dihydro-2*H*-3,1-benzothiazine (**4b**).

This compound was obtained as colorless crystals from chloroform, 40%, mp 159-163°; ir (potassium bromide): cm^{-1} 3155 (NH), 1665 (CO), 1555, 1500; uv: λ max (log ε) 247 (4.00), 357 (2.65); ms: (EI) m/z 211 ($M^{+\cdot}$, 49), 183 (211-CO, 27), 169 (211-NCO, 84), 154 (211-C_2HS, 100), 60 (COS, 85); ^1H nmr (DMSO-d_6): δ 5.29 (d), 5.99 (d), (2H $=CH_2$), 7.13 (s), 7.38 (d), 7.77 (d), (1H, 1H, 1H, arom), 11.21 (bs, N—H).

Anal. Calcd. for C_9H_6ClNOS: C, 51.07; H, 2.86; N, 6.62; $M^{+\cdot}$ 210.9858. Found: C, 45.03; H, 2.74; N, 6.55; $M^{+\cdot}$ 210.9843 [10].

General Procedure (Method A) for the Preparation of 4-(3,1-Benzothiazin-4-yl)methylene-3,1-benzothiazines **5**.

A solution of the related **1** (0.006 mole) in chloroform (8 ml) was added dropwise, within 15 minutes, to the well-stirred mixture of thiophosgene (0.006 mole), chloroform (6 ml) and water (4 ml) cooled in an ice-water bath. The organic layer was separated, dried over sodium sulphate, filtered and stored overnight. The formed crystals were collected, washed with chloroform and dried.

4-[(4-Methyl-2-oxo-1,4-dihydro-2*H*-3,1-benzothiazin-4-yl)methylene]-2-oxo-1,4-dihydro-2*H*-3,1-benzothiazine (**5a**).

This compound was obtained as colorless crystals from acetone, 80%, mp 255-256°; ir (potassium bromide): cm^{-1} 3160 (NH), 1650 (CO), 1640 (CO), 1575; uv λ max (log ε) 258 (infl, 4.17), 316 (3.74); ms: (EI) m/z 354 ($M^{+\cdot}$, 8), 294 (354-COS, 40), 234 (40), 233 (55), 219 (41), 177 (C_9H_7NOS, 100), 162 (34), 149 (58), 148 (23), 131 (54), 117 (35), 116 (28), 60 (CHS, 34); ^1H nmr (DMSO-d_6): δ 1.89 (s, H41'), 6.60 (s, H11), 7.04 (d, H9, J = 8 Hz), 7.06 (d, H9', J = 8 Hz), 7.37 (t, H8, J = 8 Hz), 7.26 (t, H8', J = 8 Hz), 7.15 (t, H7, J = 7.5 Hz), 7.06 (t, H7', J = 7.5 Hz), 7.79 (d, H6, J = 8 Hz), 7.24 (d, H6', J = 8 Hz), 10.98-11.15 (2s, H1 and H1'); ^{13}C nmr (DMSO-d_6): δ 34.3 (q, C41'), 51.1 (s, C4'), 118.0 (d), 118.2 (d), 118.4 (d), 124.0 (d), 124.14 (d), 125.13 (s), 125.3 (d), 125.7 (d). 128.2 (d), 128.8 (d), 130.6 (d), 132.3 (s), 136.4 (s), 136.9 (s), 161.8 (s, C=O), 165.8 (s, C=O).

Anal. Calcd. for $C_{18}H_{14}N_2O_2S_2$: C, 61.00; H, 3.98; N, 7.90; $M^{+\cdot}$ 354.0497. Found: C, 61.06; H, 3.92; N, 7.92; $M^{+\cdot}$ 354.0487.

6-Chloro-4-[(6-chloro-4-methyl-2-oxo-1,4-dihydro-2*H*-3,1-benzothiazin-4-yl)methylene]-2-oxo-1,4-dihydro-2*H*-3,1-benzothiazine (**5b**).

This compound was obtained as colorless crystals from acetone, 70%, mp 259° dec; ir (potassium bromide): cm^{-1} 3160 (NH), 1640 (CO), 1570; uv: λ max (log ε) 263 (4.29), 333 (3.64); ms: (EI) m/z 421 ($M^{+\cdot}$-1), 211 (100), 183 (43), 148 (73), 83 (26); ^1H nmr (DMSO-d_6): δ 1.91 (s, H41'), 6.68 (s, H11), 7.06 (d, H9, J = 8 Hz), 7.10 (d, H9', J = 8 Hz), 7.44 (d, H8, J = 8.5 Hz), 7.35 (d, H8', J = 8.5 Hz), 7.95 (s, H6), 7.29 (s, H6'), 11.44 (s, H1), 11.25 (s, H1'). The two-dimensional NOESY spectrum showed clearly an intramolecular interaction between H6 and H11; ^{13}C nmr (DMSO-d_6): δ 34.0 (C41'), 50.8 (C4'), 119.6, 119.8, 119.9, 124.9, 125.5, 126.7, 127.7, 128.2, 128.8, 129.7, 130.3, 130.9, 135.3, 135.8, 161.3 (C=O), 165.3 (C=O).

Anal. Calcd. for $C_{18}H_{12}Cl_2N_2O_2S_2$: C, 51.07; H, 2.86; N, 6.62. Found: C, 51.22; H, 2.84; N, 6.64.

Method B for **5a**.

To the solution of **2a** (0.001 mole) in chloroform (5 ml) was added a solution (5 ml) of hydrogen chloride in chloroform (1%). After storage for one day at room temperature, the solvent was evaporated until half of the original volume was left. The crystals were collected, washed with chloroform and dried, yield 90%.

Method C.

Into the solution of **4** (0.003 mole) in chloroform (30 ml) was bubbled dry hydrogen chloride, for a short time. After storage for several hours at room temperature, the formed crystals were collected and dried, yield almost quantitative.

Supplementary Materials.

Tables of observed and calculated structure factors are available from the authors.

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[10] Better analysis was not obtainable because the isolation of the completely pure compound was not possible, *cf.* discussion.