SYNTHESIS AND ANTIFUNGAL ACTIVITY OF NEW INDOLYLTHIAZINONE DERIVATIVES

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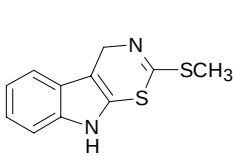
Dedicated to Professor Stefan Toma on the occasion of his 60th birthday.

New 6-(indol-3-yl)-5,6-dihydro-4*H*-1,3-thiazin-4-one derivatives were prepared by boron trifluoride catalyzed intramolecular cyclization of *N*′-substituted *N*-[3-(indol-3-yl)propenoyl]thioureas and by the reaction of 3-(indol-3-yl)propenoyl isothiocyanate with sodium hydrogensulfide. Antifungal activity of the prepared compounds was studied using the fungi *Alternaria brassicae* and *Alternaria brassicicola*.

Key words: Indoles; Thiazines; Thioureas; Isothiocyanates; Indolylthiazinones; Antifungal activity.

The fused ring systems containing indole and 1,3-thiazine moieties are a rare type of heterocyclic compounds with interesting biological properties. Among the phytoalexins isolated from cruciferous plants two thiazinoindole derivatives were identified, namely cyclobrassinin (**1**) (refs[1,2]) and cyclobrassinone (**2**) (ref.[3]), exhibiting antifungal[1–3] (**1**, **2**) and cancer chemopreventive[4] (**1**) activity. The 2-amino-1,3-thiazino[5,4-*b*]indol-4-ones (**3**), designed as potential inhibitors of human leukocyte elastase and related serine proteases, were recently prepared by cyclization of *N*′-alkyl(aryl)-*N*-[2-(ethoxycarbonyl)-indol-3-yl]thioureas[5].



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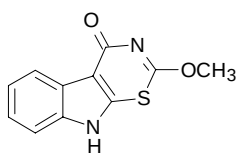

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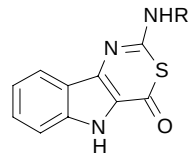

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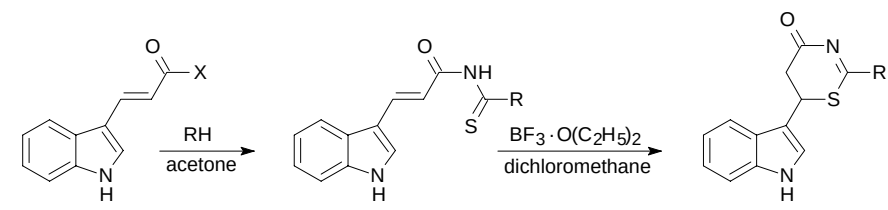
To our best knowledge, indolyl substituted 1,3-thiazines have not been investigated so far. In continuation of our previous work in the field of the synthesis of 1,3-thiazin-4-ones[6–8] from *N*-(α,β-unsaturated acyl)thiocarbamoyl compounds, we report here on the study of the synthesis and biological activity of 2-substituted 6-(indol-3-yl)-1,3-thiazin-4-one derivatives. The 3-(indol-3-yl)propenoic acid (**4**) was selected as the key starting compound. The preparation of this acid by the reaction of indole-3-carbaldehyde with malonic acid was reported to proceed with 50% yield[9]. However, in our hands the highest yield obtained was only 26%. Recently it was found that the acid **4** can be advantageously prepared in 85% yield by a modified Doebner reaction of indole-3-carbaldehyde with methylhydrogenmalonate in pyridine, under the catalytic effect of piperidine[10].

Treatment of the acid **4** with phosphorus trichloride in a mixture of dry benzene and acetonitrile afforded the unstable acid chloride **5**, which was transformed to 3-(indol-3-yl)propenoyl isothiocyanate (**6**) by the reaction with potassium thiocyanate in dry acetone at room temperature. Because of its high instability, isothiocyanate **6** could not be isolated as a pure compound and, therefore, the crude product was used in the nucleophilic addition reactions with primary and secondary amines and alcohols (Scheme 1). The resulting thioureas **7–9** were isolated by column chromatography, whereas thiourea **10** was obtained by crystallization from ethanol. Compared to the good yields (based on the acid **4**) of thioureas **7** (50%) and **8** (32%), the preparation of **9** and **10** was complicated by the formation of tars and the yields were only 16 and 8%, respectively. Intra-



4 → **5** → **6** | **7-12** | **13**, **14**

	X
4	OH
5	Cl
6	NCS

	R
7, 13	NHC_6H_4-4-CH_3
8, 14	$NHCH_2C_6H_5$
9	$NHCH_3$

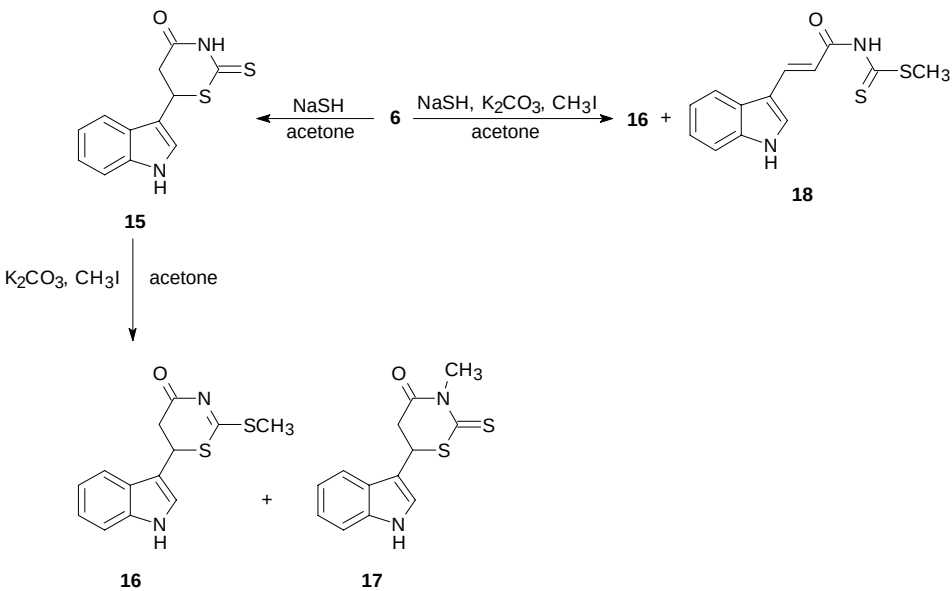
	R
10	$N(CH_2CH_2)_2O$
11	OC_2H_5
12	O-iC_3H_7

SCHEME 1

molecular cyclization of thioureas **7** and **8** in dichloromethane, catalyzed by boron trifluoride[7] afforded the 2-amino-6-(indol-3-yl)-5,6-dihydro-4*H*-1,3-thiazin-4-ones (**13** and **14**) in 46 and 67% yield, respectively. Similarly to the thioureas **7** and **8**, the reaction of isothiocyanate **6** with ethanol and propan-2-ol afforded the coresponding thiocarbamates **11** and **12** in low yields (16 and 19%, respectively) due to the formation of

tarry side products. The attempted boron trifluoride catalyzed cyclization of **11** and **12** in dichloroethane resulted in an intractable mixture of decomposition products.

Another approach to 1,3-thiazin-4-ones is the addition-cyclization reaction of α,β-unsaturated acyl isothiocyanates with sodium hydrogensulfide under mild reaction conditions[6,11,12]. Application of this reaction to the isothiocyanate **6** in a mixture of acetone and benzene as a solvent resulted in the formation of 6-(indol-3-yl)tetrahydro-2-thioxo-4*H*-1,3-thiazin-4-one (**15**) in 34% yield (Scheme 2). This reaction opens the way to the 2-methylsulfenyl derivative **16**, which was expected to possess interesting biological properties. Compound **16** was prepared by two methods. A good yield (66%) of the compound **16** together with the minor 3-methyl derivative **17** (16%) was obtained by methylation of the thiazine **15** with methyl iodide in the presence of potassium carbonate in acetone (method *A*). In method *B*, the reaction of the isothiocyanate **6** with sodium hydrogensulfide, performed in the presence of methyl iodide and potassium carbonate, afforded the desired compound **16** (18%) and the corresponding dithiocarbamate **18** (8%). In both methods, the products were separated by column chromatography on silica gel.



SCHEME 2

The structures of the prepared compounds were confirmed by spectral methods. Two doublets with a coupling constant of about 16 Hz in the ^{1}H NMR spectra of compounds **7–12** and **18** evidence the presence of CH=CH double bond in *E*-configuration, whereas two multiplets of the ABX-system of the CH–CH_2 grouping present in the spectra of products **13–17** confirm their thiazinone structure. These data, as well as infrared spec-

tra of the synthesized compounds, are in accord with previously published data for analogous thioureas, monothiocarbamates and 4*H*-1,3-thiazin-4-ones[6,7].

The observed *m/z* values as well as fragmentation patterns in the mass spectra of the compounds **14** and **15** are also in accord with the proposed structures[6,7].

Antifungal activity of the thiazine derivatives **13–16** was studied by using the fungi *Alternaria brassicae* and *Alternaria brassicicola* and compared to the activity of indole phytodexin camalexin, 3-(thiazol-2-yl)indole, which exhibits[13] a significant antifungal activity against *Cladosporium Sp*.. The activity was determined at different concentrations ranging from 1 to 100 μg ml^{-1}, and at incubation periods of 2, 10 and 20 h. The minimum inhibitory concentration (MIC) for complete inhibition of germination of *Alternaria brassicae* spores was 20 μg ml^{-1} for camalexin. For the compounds **13–16** the MIC was higher than 100 μg ml^{-1} (Table I). Similarly, the MIC for *Alternaria brassicicola* was 20 μg ml^{-1} for camalexin and higher than 100 μg ml^{-1} for all other compounds (Table II). The germination inhibition rates (%) of *Alternaria brassicae* spores subjected to different concentrations of the five compounds were significantly different after 2, 10 and 20 h (Table III). This was also true for *Alternaria brassicicola* spores except for the compounds **14** and **16** (Table IV). For the both species, the germination inhibition rates decreased with increasing incubation time, camalexin having the highest germination inhibition rates among all the tested compounds after any particular incubation time.

EXPERIMENTAL

The infrared absorption spectra were recorded on an IR-75 spectrometer (Zeiss, Jena) in chloroform; the wavenumbers are given in cm^{-1}. ^{1}H NMR spectra were measured on a Tesla BS 487A (80 MHz) spectrometer in deuteriochloroform (compounds **11**, **13** and **16–18**), hexadeuterioacetone (compounds

TABLE I
Multigroup comparison of germination inhibition rates (%) of *Alternaria brassicae* spores at different concentrations of compounds **13–16**

Compound	Concentration[a], μg ml^{-1}								
	2	4	6	10	20	40	60	80	100
Camalexin	35.40	50.10	66.40	74.40	99.70	99.90	100.00	100.00	100.00
13	1.69	6.30	8.30	15.00	15.30	15.90	16.00	16.00	18.50
14	20.20	21.15	21.75	22.30	23.20	23.59	25.10	25.50	26.90
15	18.67	19.78	21.15	25.97	35.89	41.57	45.11	58.79	70.79
16	4.50	6.00	10.50	15.80	25.40	35.00	36.70	37.00	38.40

[a] Means of all the inhibition rates (%) after 2, 10, and 20 h.

7, **9** and **14**) and in a mixture of hexadeuteriodimethyl sulfoxide and deuteriochloroform (compounds **8**, **10**, **12** and **15**) with tetramethylsilane as an internal standard. Chemical shifts are given in ppm (δ scale), coupling constants (*J*) in Hz. The mass spectra of compounds **14** and **15** were recorded on a JMS 100D spectrometer (Jeol) at ionization energy 70 eV. The reaction course was monitored by thin-layer chromatography (TLC) on Silufol plates (Kavalier, Czech Republic).

Cultures of *Alternaria brassicae* (BERK) SACC. and *Alternaria brassicicola* (SCHW.) WILTSHIRE were grown in Petri dished on V8 juice agar, supplemented with Rose Bengal[14] for 7 days in the dark at room temperature (about 22 °C). Spores were collected by flooding the cultures with sterile distilled water and washing twice by low speed centrifugation. Stock solutions of various compounds (5 mg ml^{-1} in methanol) were appropriately diluted to get concentrations of 1, 2, 4, 6, 10, 20, 40, 60, 80, and 100 μg ml^{-1} of the compounds in 2% aqueous methanol. One μg ml^{-1} concentration was not included

TABLE II
Multigroup comparison of germination inhibition rates (%) of *Alternaria brassicicola* spores at different concentrations of compounds **13–16**

Compound	Concentration[a], μg ml^{-1}									
	1	2	4	6	10	20	40	60	80	100
Camalexin	23.60	34.40	43.90	63.90	76.10	99.40	99.20	99.90	99.60	99.30
13	4.10	4.00	4.90	6.70	7.10	7.40	7.80	7.40	9.30	10.10
14	8.60	8.70	9.00	9.40	9.30	9.70	10.60	12.50	14.50	16.61
15	9.80	11.20	14.20	17.96	19.80	22.50	27.80	30.70	33.96	41.50
16	1.30	5.10	4.30	13.50	14.20	21.20	31.70	32.10	31.80	32.10

[a] Means of all the inhibition rates (%) after 2, 10, and 20 h.

TABLE III
Multigroup comparison of germination inhibition rates (%) of *Alternaria brassicae* spores at different incubation periods

Compound	Incubation period[a], h		
	2	10	20
Camalexin	93.50	81.20	67.50
13	32.30	3.20	2.20
14	29.00	21.60	3.30
15	60.90	28.60	23.00
16	60.70	5.30	3.80

[a] Means of the inhibition rates (%) at concentrations of 2, 4, 6, 10, 20, 40, 60, 80, and 100 μg ml^{-1}.

in experiments with *Alternaria brassicae*. The final spore concentration in these solution was $1 . 10^5$ spores per ml. Control treatments were similar but without the compounds. Three 20 μl droplets with each compound concentration were placed on a sterile glass slide which was kept in a humid chamber in the dark at room temperature. A drop of Lactophenol Cotton Blue was added after 2, 10, and 20 h and spore germination monitored by observing at least 100 spores in each of the three droplets. The experiment was repeated twice, so that there were nine counts for spore germination in each treatment. These nine counts were averaged, adjusted relative to control, and the germination inhibition rate (in %) calculated.

3-(Indol-3-yl)propenoyl Isothiocyanate (**6**)

To a suspension of acid **4** (356 mg, 2 mmol) in a mixture of dry benzene (20 ml) and dry acetonitrile (3 ml) phosphorus trichloride (247 mg, 174 μl, 2 mmol) was added and the reaction mixture was stirred for 15 min at room temperature. The resulting solution was decanted from the phosphoric acid deposited on the flask walls, the flask washed with dry benzene (5 ml) and the solution concentrated to approximately 1/5 of its original volume to remove the excess of phosphorus trichloride. The obtained solution of acyl chloride **5** was diluted with dry acetone (5 ml) and added dropwise during 2–3 min to a solution of potassium thiocyanate (194 mg, 2 mmol) in dry acetone (25 ml). The mixture was stirred for 20 min at room temperature, filtered with the aid of charcoal and the flask was washed with dry acetone (5 ml). The obtained solution of crude isothiocyanate **6** was directly used in the subsequent reactions.

N′-Substituted *N*-[3-Indol-3-yl)propenoyl]thioureas (**7–10**)

The corresponding amine (2 mmol) was added to a stirred acetone solution of crude isothiocyanate **6**, prepared from 2 mmol of acid **4** and stirring was continued for 20 min at room temperature. The solvent was evaporated and the residue chromatographed on silica gel (50 g, cyclohexane–acetone, 2 : 2) (compounds **7–9**) or crystallized from ethanol (compound **10**).

N′*-(4-Methylphenyl)-N-[3-(indol-3-yl)propenoyl]thiourea* (**7**). Yield 335 mg (50%), m.p. 200–202 °C (acetone–cyclohexane). For $C_{19}H_{17}N_3OS$ (335.4) calculated: 68.04% C, 5.11% H, 12.53% N; found:

TABLE IV
Multigroup comparison of germination inhibition rates (%) of *Alternaria brassicicola* spores at different incubation periods

Compound	Incubation period[a], h		
	2	10	20
Camalexin	91.40	73.60	56.80
13	18.30	1.80	0.60
14	18.20	0.30	0.20
15	52.30	9.50	0.02
16	54.50	0.70	1.00

[a] Means of all the inhibition rates (%) at 1, 2, 4, 6, 10, 20, 40, 60, 80, and 100 μg ml^{-1}.

68.32% C, 5.23% H, 12.67% N. IR spectrum: 3 470 and 3 410 (NH), 1 666 (C=O), 1 607 (C=C). ^{1}H NMR spectrum: 2.34 s, 3 H (CH_3); 7.09 d, 1 H and 8.13 d, 1 H, *J* = 15.5 (CH=CH); 7.16–8.15 m, 9 H (H-arom.); 9.23 s, 1 H, 10.37 s, 1 H and 11.01 s, 1 H (NH).

N′-Benzyl-N-[3-(indol-3-yl)propenoyl]thiourea (**8**). Yield 220 mg (33%), m.p. 157–159 °C (acetone–cyclohexane). For $C_{19}H_{17}N_3OS$ (335.4) calculated: 68.04% C, 5.11% H, 12.53% N; found: 68.53% C, 5.27% H, 12.58% N. IR spectrum: 3 477 and 3 416 (NH), 1 683 (C=O), 1 610 (C=C). ^{1}H NMR spectrum: 4.93 d, 2 H (CH_2); 6.83 d, 1 H and 7.97 d, 1 H, *J* = 15 (CH=CH); 7.36–8.23 m, 10 H (H-arom.); 10.48 s, 1 H, 10.66 s, 1 H and 11.45 s, 1 H (NH).

N′-Methyl-N-[3-(indol-3-yl)propenoyl]thiourea (**9**). Yield 83 mg (16%), m.p. 230–231 °C (acetone–cyclohexane). For $C_{13}H_{13}N_3OS$ (259.3) calculated: 61.21% C, 5.05% H, 16.20% N; found: 61.54% C, 5.17% H, 16.43% N. IR spectrum: 3 473 and 3 412 (NH), 1 666 (C=O), 1 600 (C=C). ^{1}H NMR spectrum: 3.16 d, 3 H (CH_3); 7.06 d, 1 H and 7.97 d, 1 H, *J* = 15.7 (CH=CH); 7.23–8.18 m, 5 H (H-arom.); 10.39 s, 1 H, 10.54 s, 1 H and 11.03 s, 1 H (NH).

4-{N-[3-(Indol-3-yl)propenoyl]thiocarbamoyl}morpholine (**10**). Yield 50 mg (8%), m.p. 184–186 °C (ethanol). For $C_{16}H_{17}N_3O_2S$ (315.4) calculated: 60.93% C, 5.43% H, 13.33% N; found: 61.39% C, 5.59% H, 13.58% N. IR spectrum: 3 470 and 3 410 (NH), 1 646 (C=O), 1 693 (C=C). ^{1}H NMR spectrum: 3.71 s, 8 H (CH_2); 6.88 d, 1 H and 7.80 d, 1 H, *J* = 15.5 (CH=CH); 7.26–8.05 m, 5 H (indolyl); 10.52 s, 1 H and 11.85 s, 1 H (NH).

2-Substituted 6-(Indol-3-yl)-5,6-dihydro-4*H*-1,3-thiazin-4-ones (**13**, **14**)

To a stirred suspension of the thiourea **7** or **8** (0.31 mmol) in dichloromethane (10 ml), a solution of boron trifluoride etherate (88 mg, 70 µl, 0.63 mmol) in dichloromethane (3 ml) was slowly added. After standing for 24 h at room temperature, the thiourea gradually dissolved. The obtained solution was washed with a 4% solution of sodium hydrogencarbonate (3.5 ml), the dichloromethane layer was separated and dried with magnesium sulfate. The solvent was evaporated and the residue crystallized from a suitable solvent.

6-(Indol-3-yl)-2-[(4-methylphenyl)amino]-5,6-dihydro-4H-1,3-thiazin-4-one (**13**). Yield 45 mg (43%), m.p. 112–114 °C (chloroform–cyclohexane). For $C_{19}H_{17}N_3OS$ (335.4) calculated: 68.04% C, 5.11% H, 12.53% N; found: 68.31% C, 5.24% H, 12.72% N. IR spectrum: 3 487 and 3 336 (NH), 1 690 (C=O), 1 612 (C=C). ^{1}H NMR spectrum: 2.28 s, 3 H (CH_3); 3.35 m, 2 H (CH_2); 4.94 m, 1 H (CH); 6.90–7.72 m, 9 H (H-arom.); 8.42 s, 1 H and 9.89 s, 1 H (NH).

2-Benzylamino-6-(indol-3-yl)-5,6-dihydro-4H-1,3-thiazin-4-one (**14**). Yield 70 mg (67%), m.p. 157–159 °C (chloroform–light petroleum). For $C_{19}H_{17}N_3OS$ (335.4) calculated: 68.04% C, 5.11% H, 12.53% N; found: 68.29% C, 5.28% H, 12.69% N. IR spectrum: 3 477 and 3 360 (NH), 1 720 (C=O), 1 610 (C=C). ^{1}H NMR spectrum: 3.08 m, 2 H (CH_2); 4.62 d, 2 H (CH_2); 4.98 m, 1 H (CH); 7.07–7.74 m, 10 H (H-arom.); 8.75 s, 1 H and 10.47 s, 1 H (NH). Mass spectrum, *m/z* (%): 335 (M^+, 21), 230 (16), 170 (100), 171 (24), 115 (27), 116 (7), 143 (21) and 91 (19).

Alkyl *N*-[3-(Indol-3-yl)propenoyl]thiocarbamates (**11**, **12**)

To an acetone solution of crude isothiocyanate **6** prepared from 1 mmol of acid **4**, the corresponding alcohol (5 ml) was added and the reaction mixture was stirred at 70 °C for 10 min. After cooling to room temperature, the mixture was diluted with benzene (15 ml) and washed with water (50 ml). The benzene layer was separated, dried with anhydrous sodium sulfate and the solvent was evaporated.

Ethyl N-[3-(indol-3-yl)propenoyl]thiocarbamate (**11**). Yield 44 mg (16%), m.p. 100–102 °C (acetone–water). For $C_{14}H_{14}N_2O_2S$ (274.4) calculated: 61.28% C, 5.14% H, 10.21% N; found: 61.78% C, 5.24% H, 10.72% N. IR spectrum: 3 477 and 3 330 (NH), 1 690 (C=O), 1 623 (C=C). ^{1}H NMR

spectrum: 1.35 t, 3 H (CH_3); 4.28 q, 2 H (CH_2); 6.45 d, 1 H and 7.92 d, 1 H, J = 16 (CH=CH); 7.13–8.02 m, 6 H (H-arom.); 8.90 s, 1 H (NH).

Isopropyl N-[3-(indol-3-yl)propenoyl]thiocarbamate (**12**). Yield 55 mg (19%), oil. For $C_{15}H_{16}N_2O_2S$ (288.4) calculated: 62.47% C, 5.59% H, 9.72% N; found: 62.73% C, 5.70% H, 9.97% N. IR spectrum: 3 488 and 3 335 (NH), 1 702 (C=O), 1 628 (C=C). ^{1}H NMR spectrum: 1.28 d, 6 H (CH_3); 5.08 m, 1 H (CH); 6.39 d, 1 H and 7.92 d, 1 H, J = 15.7 (CH=CH); 7.20–8.03 m, 6 H (H-arom.); 8.98 s, 1 H (NH).

6-(Indol-3-yl)-2-thioxotetrahydro-4*H*-1,3-thiazin-4-one (**15**)

The acetone solution of crude isothiocyanate **6** prepared from 1 mmol of acid **4** was diluted with benzene (10 ml). A freshly prepared solution of sodium hydrogensulfide (171 mg, 2 mmol) in methanol (15 ml) was added dropwise into this solution during 15 min with stirring and water cooling. The reaction mixture was then washed with water (30 ml), the benzene layer was separated and the water layer extracted with dichloromethane (2 × 15 ml). The combined extracts were dried with anhydrous sodium sulfate, filtered with charcoal and the solvent evaporated. Yield 89 mg (34%), m.p. 178–180 °C (dichloromethane–hexane). For $C_{12}H_{10}N_2OS_2$ (262.4) calculated: 54.93% C, 3.84% H, 10.68% N; found: 55.23% C, 3.97% H, 10.86% N. IR spectrum: 3 483 and 3 347 (NH), 1 713 (C=O), 1 423 (C=C). ^{1}H NMR spectrum: 3.37 m, 2 H (CH_2); 5.07 m, 1 H (CH), 7.02–7.99 m, 5 H (H-arom.); 10.14 s, 1 H and 11.57 s, 1 H (NH). Mass spectrum, *m/z* (%): 262 (M^+, 61), 170 (100), 171 (16), 143 (21), 160 (12), 130 (40), 115 (40) and 59 (7).

6-(Indol-3-yl)-4-methylsulfenyltetrahydro-4*H*-1,3-thiazin-4-one (**16**)

Method A. To a solution of thiazine **15** (1 mmol) in acetone (20 ml) methyl iodide (426 mg, 187 µl, 3 mmol) and potassium carbonate (166 mg, 1.2 mmol) were added and the reaction mixture was stirred at room temperature for 17 h. The insoluble material was filtered off, the filtrate evaporated and the residue chromatographed on silica gel (50 g, ethyl acetate–cyclohexane 1 : 2), to yield 171 mg (62%) of the title compound **16** and 44 mg (16%) of the isomeric 3-methyl derivative **17** as a minor product.

Method B. To a stirred acetone solution of the isothiocyanate **6** prepared from 1 mmol of the acid **4**, a freshly prepared solution of sodium hydrogensulfide (214 mg, 2.5 mmol) in methanol (22 ml) was added at room temperature, followed by methyl iodide (426 mg, 187 µl, 3 mmol) and potassium carbonate (276 mg, 2 mmol). After stirring at room temperature for 2.5 h, the mixture was poured into 50 ml of water and the product was extracted with chloroform (2 × 15 ml). After drying with anhydrous sodium sulfate and evaporation of the solvent, the residue was chromatographed on silica gel (50 g, cyclohexane–acetone 2 : 1) to yield 50 mg (18%) of the titled compound **16** and 22 mg (8%) of the dithiocarbamate **18**.

6-(Indol-3-yl)-2-methylsulfenyltetrahydro-4H-1,3-thiazin-4-one (**16**). M.p. 123–125 °C (ethanol–water). For $C_{13}H_{12}N_2OS_2$ (276.4) calculated: 56.49% C, 4.38% H, 10.14% N; found: 56.79% C, 4.54% H, 10.29% N. IR spectrum: 3 447 (NH), 1 683 (C=O), 1 600 (C=C). ^{1}H NMR spectrum: 2.59 s, 3 H (CH_3); 3.21 m, 2 H (CH_2); 5.12 m, 1 H (CH); 7.13–7.70 m, 5 H (H-arom.); 8.37 s, 1 H (NH).

6-(Indol-3-yl)-3-methyltetrahydro-4H-1,3-thiazin-4-one (**17**). M.p. 117–118 °C (ethanol–water). For $C_{13}H_{12}N_2OS_2$ (276.4) calculated: 56.49% C, 4.38% H, 10.14% N; found: 56.84% C, 4.38% H, 10.14% N. IR spectrum: 3 483 (NH), 1 700 (C=O), 1 604 (C=C). ^{1}H NMR spectrum: 3.54 m, 2 H (CH_2); 3.73 s, 3 H (CH_3); 4.96 m, 1 H (CH); 7.16–7.75 m, 5 H (H-arom.); 8.25 s, 1 H (NH).

Methyl N-[3-(indol-3-yl)propenoyl]dithiocarbamate (**18**). M.p. 164–168 °C (acetone–cyclohexane). For $C_{13}H_{12}N_2OS_2$ (276.4) calculated: 56.49% C, 4.38% H, 10.14% N; found: 56.81% C, 4.52% H, 10.33% N. IR spectrum: 3 473 and 3 683 (NH), 1 700 (C=O), 1 643 (C=C). ^{1}H NMR spectrum: 2.44 s,

3 H (CH_3); 6.80 d, 1 H and 7.88 d, 1 H, J = 15.8 (CH=CH); 7.21–7.87 m, 5 H (H-arom.); 8.69 s, 1 H and 8.92 s, 1 H (NH).

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