Synthesis of 3-Aminorhodanine Derivatives as Aldose Reductase Inhibitors

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A number of 5-condensated 3-acylaminorhodanines **3** was prepared as potential inhibitors of the aldose reductase by acylation of the amino group of 3-aminorhodanine **1** and subsequent condensation of the 5-methylene function with appropriate aldehydes. Some of these compounds displayed interesting activity.

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It is widely accepted that the enzyme aldose reductase has a key function in the development of certain diabetic complications such as neuro-, nephro- and retinopathy [1-5]. Therefore, there is a ongoing search for substances possessing an inhibitory effect on aldose reductase. Kador and Sharpless have published a model of the inhibitor binding site and certain structural requirements for inhibitor molecules [1,6]. One key feature is a suitably placed functional group capable of undergoing a nucleophilic attack.

We felt that the presence of more than one functional group which are accessible to a nucleophilic attack in one molecule might lead to another class of useful aldose reductase inhibitors.

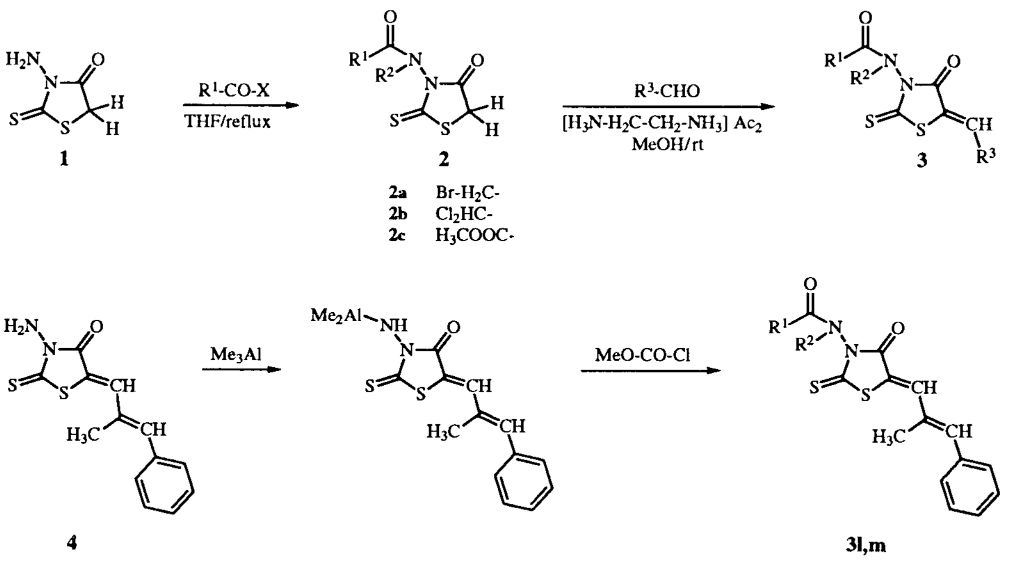
3-Aminorhodanine **1** seemed to be a suitable starting material for such compounds. The molecule itself possesses a carbonyl and a thiocarbonyl function. Acylation of the exocyclic amino group would yield another functionality susceptible to a nucleophilic attack. According to the model of Kador and Sharpless the additional presence of a lipophilic group is nessessary for tight binding of an inhibitor to the binding site of the enzyme. Such residues can be conveniently introduced by condensating the 5-methylene group of **1** with appropriate aldehydes leading to the target structure **3**.

The methodology for the synthesis of the compounds described here has already been published [7]. Usually, the acylation step was performed first simply by heating **1** with a carboxylic halide in an inert solvent. The acylation product **2** was used without further purification for the condensation step carried out in methanol with ethylenediammonium diacetate as a catalyst. Only the previously unknown acylaminorhodanines **2a-c** were isolated and characterized. The only exception to this scheme was the synthesis of **3l** and **m**. In this case 3-amino-5-cinnamylidenerhodanine **4** [7] was reacted with methyl chloroformate using trimethylaluminum as a catalyst to afford **3l** and **m** as a chromatographically separable mixture.

Compounds **3z** to **3ca** were synthesized from the haloacylrhodanines **3r,s** and **w** *via* a nucleophilic displacement reaction.

Most of 5-cinnamylidene substituted rhodanines show a double set of nmr signals in the proton as well as in the carbon nmr spectra. This is due to the existence of *s-cis* and *s-trans* isomers. In the experimental part only the signals of the major isomer (*s-trans*) are given.

Scheme 1



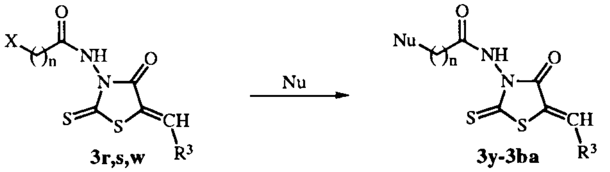
Table

3-Acylaminorhodanines 3

	R¹	R²	R³
3a	H	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3b	H	H	Z-CCl=CH-C$_6$H$_5$
3c	H	H	2-Benzothiazolyl
3d	H	H	5-Phenyl-1,3-thiazole-4-yl
3e	H	H	5-(3-Nitrophenyl)thiophene-2-yl
3f	H	H	1-(Phenylsulfonyl)indole-3-yl
3g	H	H	2-Naphthyl
3h	H$_3$C-	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3i	H$_3$C-	H	Biphenylyl
3j	H$_3$C-	H	4-Oxo-4*H*-benzopyrane-3-yl
3k	H$_3$C-	H	4-(2-Naphthalenesulfonyloxy)phenyl
3l	H$_3$CO	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3m	H$_3$CO	H$_3$COOC	Z-C(CH$_3$)=CH-C$_6$H$_5$
3n	H$_3$COOC	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3o	H$_3$COOC	H	4-Oxo-4*H*-benzopyrane-3-yl
3p	H$_5$C$_2$OOC-CH$_2$-	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3q	H$_3$COOC-(CH$_2$)$_2$-	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3r	Cl-H$_2$C-	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3s	Br-H$_2$C-	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3t	Br-H$_2$C-	H	2-Benzothiazolyl
3u	Br-H$_2$C-	H	5-Phenyl-1,3-thiazole-4-yl
3v	Cl$_2$HC-	H	Z-CCl=CH-C$_6$H$_5$
3w	Cl-H$_2$C-CH$_2$-	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3x	Cl-H$_2$C-CH$_2$-	H	3-Indolyl
3y	H$_5$C$_6$-CHCl-	H	6-Methyl-2-pyridyl
3z	I-H$_2$C-	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3aa	(1-Phenyltetrazol-5-yl)thiomethyl	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3ba	(1-Methyltetrazol-5-yl)thiomethyl	H	Z-C(CH$_3$)=CH-C$_6$H$_5$
3ca	2-(Benzothiazol-2-yl)thioethyl	H	Z-C(CH$_3$)=CH-C$_6$H$_5$

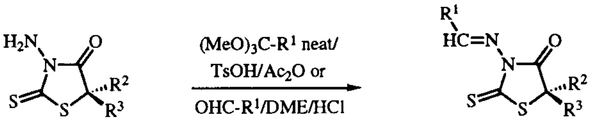
In addition to those 3-acylaminorhodanines **3** the 3-methyliminorhodanines **5** were prepared by condensing the free 3-amino function of **1** or **4** with an aldehyde or orthoester as described previously [7].

Scheme 2



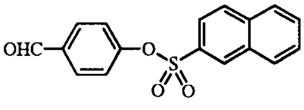
3r,s,w **3y-3ba**

n = 1, 2 Nu: I⁻, 1-Ph-tetrazol-5-yl-S⁻, 1-Me-tetrazol-5-yl-S⁻
X = Cl, Br Benzothiazol-2-yl-S⁻

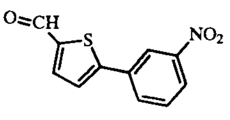


1, 4 **5**

	R¹	R²	R³
5a	H$_3$CO-	=CH-(CH$_3$)C=CH-C$_6$H$_5$	
5b	Z-C(CH$_3$)=CH-C$_6$H$_5$	H	H
5c	Z-CCl=CH-C$_6$H$_5$	H	H
5d	1-Phenylsufonylindol-3-yl	H	H



6a



6b

Most of the aldehydes used are commercially available or were prepared by literature methods [8-10]. The preparation of the new aldehydes **6a,b** is detailed in the Experimental.

Representative examples of the compounds described here have been tested against rat lens aldose reductase [11]. Some of them displayed interesting inhibitory activity. These results will be published elsewere.

EXPERIMENTAL

Melting points were determined on a Leitz HM Lux apparatus. They are uncorrected. Microanalyses were obtained on a Hewlett Packard CHN-Autoanalyser (N only) and a Labormatic CH-Analyser. Mass spectra were recorded on a Vacuum Generators Spectrometer 7070H with El (70 eV). The infrared spectra were run using a Perkin Elmer PE 398 instrument. The ^{1}H and ^{13}C nmr spectra were recorded on a Jeol JNM-GX 400 instrument.

General Procedure for the Preparation of 3-Acylaminorhodanines 2.

To a solution of 3-aminorhodanine **1** in THF were added 1-3 equivalents of the carboxylic halide. This mixture was refluxed for 3 hours. The residue obtained after removal of the solvent was generally used without further purification.

3-(2-Bromoacetylamino)-2-thioxothiazolidin-4-one (**2a**).

The crude product was dissolved in toluene from which the compound crystallized as pale yellow crystals, yield 59%, mp 106°; uv/vis (methanol): λ (log ε) = 270 (4.34) nm; ir (potassium bromide): ν 3150, 1750, 1670 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.40 (s, 1H), 4.43 (m, 1H), 4.40 (m, 1H), 4.09 (s, 2H); ^{13}C nmr ([D$_6$]-DMSO): δ 199.4, 169.9, 164.6, 33.4, 26.0; ms: m/z 270 (35), 268 (34, M$^+$).

Anal. Calcd. for $C_5H_5BrN_2O_2S_2$ (269.13): C, 22.31; H, 1.87; Br, 29.69; N, 10.41; S, 23.82. Found: C, 22.42; H, 1.88; Br, 29.53; N, 10.38; S, 23.45.

3-(2,2-Dichloroacetylamino)-2-thioxothiazolidin-4-one (**2b**).

This compound was chromatographically purified (dichloromethane) and recrystallized from toluene, yellow crystals, yield 35%, mp 118°; ir (potassium bromide): ν 3170, 3000, 1760, 1700 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.85 (s, 1H), 6.78 (s, 1H), 4.50 (m, 1H), 4.43 (m, 1H); ^{13}C nmr ([D$_6$]-DMSO): δ 198.9, 169.6, 162.2, 60.4, 33.5; ms: m/z 262 (16), 260 (69), 258 (93, M$^+$).

Anal. Calcd. for $C_5H_4Cl_2N_2O_2S_2$ (259.13): C, 23.18; H, 1.56; Cl, 27.36; N, 10.81; S, 24.75. Found: C, 23.13; H, 1.54; Cl, 27.19; N, 10.92; S, 24.47.

3-[(2-Methoxyoxalyl)amino]-2-thioxothiazolidin-4-one (**2c**).

This compound was chromatographically purified (ethyl acetate), oil, yield 68%; ir (potassium bromide): ν 3260, 1760, 1720 cm^{-1}; ^1H nmr (deuteriochloroform): δ 9.61 (s, 1H), 4.11 (s, 2H), 3.99 (s, 3H); ^{13}C nmr (deuteriochloroform): δ 195.2, 168.3, 158.6, 153.5, 54.2, 32.9; ms: m/z 234 (69, M^+), 175 (100); hrms Calcd. for $C_6H_6N_2O_4S_2$: 233.9769. Found: 233.9778.

General Procedure for the Preparation of 5-Condensed 3-Acylaminorhodanines **3**.

The crude product from the acylation step was dissolved in a sufficient amount of methanol. After addition of the aldehyde (1 equivalent) and ethylenediammonium diacetate (0.1-1 equivalents) the resulting mixture was stirred at rt for 12-18 hours. The precipitated product was collected and purified by column chromatography and/or recrystallization.

3-Formylamino-5-*Z*-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3a**).

This compound was recrystallized from toluene/dioxane, yield 74%, orange crystals, mp 186°; uv/vis (dichloromethane): λ (log ε) = 394 (4.67), 296 (3.93) nm; ir (potassium bromide): ν 3220, 1730, 1675, 1560 cm^{-1}; ^1H nmr ([D_6]-DMSO): δ 11.26 (s, 1H), 8.40 (s, 1H), 7.67 (s, 1H), 7.48-7.45 (m, 4H), 7.41-7.37 (m, 2H), 2.23 (s, 3H); ^{13}C nmr ([D_6]-DMSO): δ 190.0, 163.0, 159.2, 144.9, 140.8, 135.7, 133.0, 129.6, 128.8, 128.6, 117.6, 15.8; ms: m/z 304 (36, M^+), 141 (100).

Anal. Calcd. for $C_{14}H_{12}N_2O_2S_2$ (304.38): C, 55.24; H, 3.97; N, 9.20; S, 21.07. Found: C, 55.23; H, 3.92; N, 9.16; S, 21.00.

5-*Z*-[(2*E*)-2-Chloro-3-phenylpropenylidene]-3-(formylamino)-2-thioxothiazolidin-4-one (**3b**).

This compound was chromatographically purified (dichloromethane:ethyl acetate 4:1) and recrystallized from toluene/dioxane, yield 81%, orange crystals, mp 244°; uv/vis (methanol): λ (log ε) = 396 (4.59), 264 (4.66) nm; ir (potassium bromide): ν 3220, 1725, 1670, 1570 cm^{-1}; ^1H nmr ([D_6]-DMSO): δ 11.25 (s, 1H), 8.39 (s, 1H,), 7.90 (s, 1H), 7.86-7.82 (m, 2H), 7.81 (s, 1H), 7.53-7.47 (m, 3H); ^{13}C nmr ([D_6]-DMSO): δ 190.6, 162.9, 159.1, 141.7, 133.5, 133.3, 130.5, 130.0, 128.7, 126.1, 120.6; ms: m/z 324 (10, M^+), 115 (100).

Anal. Calcd. for $C_{13}H_9ClN_2O_2S_2$ (324.80): C, 48.07; H, 2.79; Cl, 10.91; N, 8.62; S, 19.75. Found: C, 48.28; H, 2.86; Cl, 11.08; N, 8.68; S, 19.44.

5-(Benzothiazol-2-yl-methylene)-3-formylamino-2-thioxothiazolidin-4-one (**3c**).

This compound was recrystallized from toluene/dioxane, yield 51%, yellow crystals, mp >255°; ir (potassium bromide): ν 3230, 3030, 1730, 1675, 1635 cm^{-1}; ^1H nmr ([D_6]-DMSO): δ 11.32 (s, 1H), 8.43 (s, 1H), 8.22 (m, 1H), 8.20 (m, 1H), 8.21 (s, 1H), 7.63 (m, 1H), 7.55 (m, 1H); ^{13}C nmr ([D_6]-DMSO): δ 194.1, 162.5, 160.8, 159.9, 152.9, 136.1, 127.5, 126.7, 126.6, 123.6, 122.8, 122.4; ms: m/z 321 (44, M^+), 191 (100).

Anal. Calcd. for $C_{12}H_7N_3O_2S_3$ (321.39): C, 44.86; H, 2.20; N, 13.09; S, 29.88. Found: C, 44.92; H, 2.28; N, 12.95; S, 29.78.

3-Formylamino-5-[(2-phenyl-1,3-thiazol-4-yl)methylene]-2-thio xothiazolidin-4-one (**3d**).

This compound was recrystallized from dioxane, yield 58%, yellow crystals, mp >250°; ir (potassium bromide): ν 3190, 3080, 1730, 1670, 1600 cm^{-1}; ^1H nmr ([D_6]-DMSO): δ 11.25 (s, 1H), 8.46 (s, 1H), 8.43 (s, 1H), 8.04-8.00 (m, 2H), 7.91 (s, 1H), 7.62-7.55 (m, 3H); ^{13}C nmr ([D_6]-DMSO): δ 194.0, 168.4, 163.1, 159.2, 150.0, 131.8, 131.1, 129.4, 128.9, 126.4, 125.2, 121.2; ms: m/z 347 (28, M^+), 217 (100).

Anal. Calcd. for $C_{14}H_9N_3O_2S_3$ (347.43): C, 48.40; H, 2.61; N, 12.09; S, 27.69. Found: C, 48.24; H, 2.69; N, 12.21; S, 27.46.

3-Formylamino-5-[5-(3-nitrophenyl)thiophen-2-ylmethylene]-2-thioxothiazolidin-4-one (**3e**).

This compound was chromatographically purified (ethyl acetate:*n*-hexane 3:1 → ethyl acetate) and recrystallized from toluene/dioxane/pentane, yield 43%, orange crystals; ir (potassium bromide): ν 3150, 3090, 3070, 1720, 1685, 1580, 1530, 1515, 1350 cm^{-1}; ^1H nmr ([D_6]-DMSO): δ 11.30 (s, 1H), 8.53 (t, 1H), 8.41 (s, 1H), 8.25-8.21 (m, 2H), 8.19 (s, 1H), 7.98 (d, 1H), 7.85 (d, 1H), 7.76 (t, 1H); ^{13}C nmr ([D_6]-DMSO): δ 188.6, 162.5, 159.1, 148.8, 148.5, 137.8, 137.3, 133.8, 132.0, 130.8, 127.6, 127.1, 123.3, 119.9, 117.1; ms: m/z 391 (3, M^+), 261 (100).

Anal. Calcd. for $C_{15}H_9N_3O_4S_3$ (391.43): C, 46.03; H, 2.32; N, 10.73; S, 24.57. Found: C, 45.74; H, 2.60; N, 10.44; S, 24.21.

3-Formylamino-5-[(1-phenylsulfonylindol-3-yl)methylene]-2-thioxothiazolidin-4-one (**3f**).

This compound was recrystallized from dioxane/pentane, yield 64%, yellow crystals, mp >260°; ir (potassium bromide): ν 3240, 1720, 1690, 1600, 1370, 1140 cm^{-1}; ^1H nmr ([D_6]-DMSO): δ 8.44 (s, 1H), 8.17 (m, 2H), 8.10 (s, 1H), 8.08 (s, 1H), 8.03 (s, 1H), 8.01 (m, 1H), 7.75 (m, 1H) 7.64 (m, 2H), 7.50 (m, 1H), 7.42 (m, 1H); ^{13}C nmr ([D_6]-DMSO): δ 189.2, 162.6, 159.5, 136.4, 135.5, 134.0, 130.2, 128.7, 128.2, 127.3, 126.6, 124.7, 124.4, 120.5, 120.0, 116.6, 113.4; ms: m/z 443 (6, M^+), 172 (100).

Anal. Calcd. for $C_{19}H_{13}N_3O_4S_3$ (443.51): C, 51.46; H, 2.95; N, 9.47. Found: C, 51.45; H, 3.18; N, 9.22.

3-Formylamino-5-(2-naphthylmethylene)-2-thioxothiazolidin-4-one (**3g**).

This compound was chromatographically purified (ethyl acetate:*n*-hexane 2:3) and recrystallized from toluene/dioxane, yield 93%, yellow crystals, mp 252°; ir (potassium bromide): ν 3180, 1735, 1700, 1600 cm^{-1}; ^1H nmr ([D_6]-DMSO): δ = 11.30 (s, 1H), 8.43 (s, 1H), 8.28 (s, 1H), 8.10-7.74 (2m, 5H), 7.68-7.62 (m, 2H); ^{13}C nmr ([D_6]-DMSO): δ 190.0, 162.9, 159.2, 134.7, 133.6, 132.7, 132.1, 130.2, 129.1, 128.9, 128.5, 127.7, 127.2, 126.2, 119.4; ms: m/z 314 (2, M^+), 184 (100).

Anal. Calcd. for $C_{15}H_{10}N_2O_2S_2$ (314.38): C, 57.31; H, 3.21; N, 8.91; S, 20.40. Found: C, 57.17; H, 3.33; N, 8.56; S, 20.10.

3-Acetylamino-5-[(2*E*)-2-methyl-3-phenylpropylidene]-2-thioxothiazolidin-4-one (**3h**).

This compound was chromatographically purified (dichloromethane:ethyl acetate 4:1) and recrystallized from toluene, yield 75%, yellow crystals, mp 249°; uv/vis (methanol): λ (log ε) = 391 (4.58), 293 (3.95), 238 (4.02) nm; ir (potassium bromide): ν = 3230, 1730, 1690 cm^{-1}; ^1H nmr ([D_6]-DMSO): δ 11.12 (s, 1H), 7.63 (s, 1H), 7.48-7.42 (m, 4H), 7.40-7.36 (m, 2H), 2.23 (s, 3H), 2.08 (s, 3H); ^{13}C nmr ([D_6]-DMSO): δ 190.5, 167.5, 163.3, 144.7, 140.5, 135.7, 133.0, 129.5, 128.7, 128.5, 117.7, 20.2, 15.8; ms: m/z 318 (24, M$^+$), 276 (100).

Anal. Calcd. for $C_{15}H_{14}N_2O_2S_2$ (318.41): C, 56.58; H, 4.43; N, 8.80; S, 20.14. Found: C, 56.61; H, 4.42; N, 9.00; S, 20.17.

3-Acetylamino-5-(4-phenylbenzylidene)-2-thioxothiazolidin-4-one (**3i**).

This compound was chromatographically purified (dichloromethane:ethyl acetate 4:1) and recrystallized from toluene/dioxane, yield 19%, yellow crystals, mp 238°; ir (potassium bromide): ν 3180, 1725, 1670, 1590 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.18 (s, 1H), 7.96 (s, 1H), 7.90-7.86 (m, 2H), 7.79-7.74 (m, 4H), 7.53-7.48 (m, 2H), 7.45-7.40 (m, 1H), 2.10 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 190.3, 167.6, 163.2, 142.5, 138.6, 134.1, 131.7, 131.5, 129.0, 128.3 127.5, 126.8, 119.1, 20.2; ms: m/z 354 (53, M$^+$), 210 (100).

Anal. Calcd. for $C_{18}H_{14}N_2O_2S_2$ (354.44): C, 61.00; H, 3.98; N, 7.90; S, 18.09. Found: C, 60.95; H, 3.98; N, 7.82; S, 18.09.

3-Acetylamino-5-*Z*-[(4-oxo-4*H*-benzopyran-3-yl)methylene]-2-thioxothiazolidin-4-one (**3j**).

This compound was recrystallized from dioxane, yield 45%, yellow crystals, mp >260°; ir (potassium bromide): ν 3180, 1715, 1675, 1640, 1610, 1590 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.13 (s, 1H), 9.08 (s, 1H), 8.17 (m, 1H), 7.91 (zm, 1H), 7.87 (m, 1H), 7.65 (s, 1H), 7.60 (m, 1H), 2.07 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 194.0, 174.6, 167.4, 163.7, 163.6, 155.2, 135.0, 127.9, 126.4, 125.4, 122.8, 120.9, 118.4, 117.8, 20.1; ms: m/z 346 (38, M$^+$), 202 (100).

Anal. Calcd. for $C_{15}H_{10}N_2O_4S_2$ (346.37): C, 52.02; H, 2.91; N, 8.09; S 18.52. Found: C, 51.89; H, 3.02; N, 8.03; S, 18.53.

3-Acetylamino-5-[4-(2-naphthalenesulfonyloxy)benzylidene]-2-thioxothiazolidin-4-one (**3k**).

This compound was recrystallized from THF/methanol/pentane, yield 65%, yellow crystals, mp 185°; ir (potassium bromide): ν 3350, 1730, 1710 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.16 (s, 1H), 8.62 (m, 1H), 8.24 (m, 1H), 8.23 (m, 1H), 8.12 (m, 1H), 7.91 (m, 1H), 7.86 (s, 1H), 7.81 (m, 1H), 7.72 (m, 1H), 7.70-7.66 (m, 2H), 7.29-7.25 (m, 2H), 2.08 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 190.2, 167.7, 163.1, 150.3, 135.1, 132.8, 132.5, 131.8, 131.4, 131.2, 130.3, 130.1, 130.0, 129.6, 128.1, 128.0, 123.1, 122.3, 120.4, 20.2; ms: m/z 484 (35, M$^+$), 127 (100).

Anal. Calcd. for $C_{22}H_{16}N_2O_5S_3$ (484 55): C, 54.53; H, 3.33; N, 5.78; S, 19.85. Found: C, 54.51; H, 3.30; N, 5.88; S, 19.50.

Reaction of 3-Amino-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**4**) with Methyl Chloroformate.

To a solution of **4** (554 mg, 2 mmoles) in dry dioxane (50 ml) under nitrogen was added trimethylaluminium (2 ml of a 2*M* solution in toluene, 4 mmoles). After 15 minutes, methyl chloroformate (0.5 ml, 6.46 mmoles) was added. The resulting mixture was kept at 50° for 2 days. After removal of the solvent the residue was dissolved in dichloromethane (50 ml) and washed with dilute hydrochloric acid (2 x 25 ml) and water (2 x 25 ml). Chromatography (dichloromethane:ethyl acetate 9:1) of the oily residue afforded **3l** and **m**.

3-Methoxycarbonylamino-(5-*Z*)[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3l**).

This compound was recrystallized from methanol, yield 46%, orange crystals, mp 166°; uv/vis (dichloromethane): λ (log ε) = 396 (4.54), 296 (3.93) nm; ir (potassium bromide): ν 3230, 1715 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 7.61 (s, 1H), 7.44-7.35 (m, 5H), 7.11 (s, 1H), 3.83 (s, 3H), 2.26 (s, 3H); ^{13}C nmr (deuteriochloroform): δ 190.1, 164.0, 154.4, 144.8, 141.2, 136.1, 133.2, 129.6, 128.8, 128.6, 118.1, 53.9, 16.3; ms: m/z 334 (76, M$^+$), 141 (100).

Anal. Calcd. for $C_{15}H_{14}N_2O_3S_2$ (334.30): C, 53.88; H, 4.22; N, 8.38; S, 19.18. Found: C, 53.69; H, 4.22; N, 8.43; S, 18.99.

3-[*N,N*-Bis(methoxycarbonyl)amino]-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3m**).

This compound was recrystallized from dioxane/methanol, yield 20%, orange crystals, mp 157°; ir (potassium bromide): ν 1810, 1720, 1580 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 7.62 (s, 1H), 7.43-7.36 (m, 5H), 7.12 (s, 1H), 3.89 (s, 6H), 2.28 (s, 3H); ms: m/z 392 (52, M$^+$), 141 (100).

Anal. Calcd. for $C_{17}H_{16}N_2O_5S_2$ (392.43): C, 52.03; H, 4.11; N, 7.14; S, 16.35. Found: C, 51.77; H, 4.17; N, 7.51; S, 16.29.

3-[(2-Methoxyoxalyl)amino]-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3n**).

The crude reaction product was washed with methanol and ethyl ether, yield 47%, yellow powder, mp 194°; ir (potassium bromide): ν 3320, 3130, 1725, 1685, 1625, 1560 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 12.36 (s, 1H), 7.69 (s, 1H), 7.49-7.38 (m, 6H), 3.92 (s, 3H), 2.24 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 189.2, 162.6, 158.7, 154.7, 145.2, 141.1, 135.6, 132.9, 129.5, 128.8, 128.5, 117.1, 53.5, 15.7; ms: m/z 362 (52, M$^+$), 141 (100).

Anal. Calcd. for $C_{16}H_{14}N_2O_4S_2$ (362.41): C, 53.03; H, 3.89; N, 7.73; S, 17.70. Found: C, 53.09; H, 4.14; N, 8.11; S, 17.33.

3-[(2-Methoxyoxalyl)-amino]-5-[(4-oxo-(4*H*)-benzopyran-3-yl)-methylene]-2-thioxothiazolidin-4-one (**3o**).

The crude reaction product was washed with methanol and ethyl ether, yield 79%, yellow powder, mp 205°; uv/vis (methanol): λ (log ε) = 389 (4.44), 262 (4.57) nm; ir (potassium bromide): ν 3410, 1760, 1730, 1710, 1650, 1610, 1590 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 12.33 (s, 1H), 9.07 (s, 1H), 8.15 (m, 1H), 7.89 (m, 1H), 7.74 (m, 1H), 7.66 (s, 1H), 7.59 (m, 1H), 3.93 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 192.8, 174.9, 164.4, 163.2, 158.7, 155.3, 154.7, 135.3, 129.2, 126.6, 125.5, 122.9, 120.3, 118.6, 117.8, 53.6; ms: m/z 390 (19, M$^+$), 202 (100); hrms: Calcd. for $C_{16}H_{10}N_2O_6S_2$: 389.9980. Found: 389.9981.

3-[(2-Ethoxycarbonylacetyl)amino]-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3p**).

This compound was chromatographically purified (dichloromethane:ethyl acetate 4:1) and recrystallized from toluene, yield 50%, orange crystals, mp 163°; ir (potassium bromide): ν 3220, 1740, 1720, 1680 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.40 (s, 1H), 7.63 (s, 1H), 7.49-7.44 (m, 4H), 7.43-7.40 (m, 2H), 4.13 (q, 2H), 3.54 (d, 1H), 3.51 (d, 1H), 2.23 (s, 3H), 1.22 (t, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 190.0, 166.2, 163.6, 163.1, 144.8, 140.6, 135.7, 133.0, 129.6, 128.6, 128.5, 117.7, 60.8, 40.3, 15.8, 13.9; ms: m/z 390 (31, M$^+$), 174 (100).

Anal. Calcd. for $C_{18}H_{18}N_2O_4S_2$ (390.46): C, 55.37; H, 4.65; N, 7.17; S, 16.42. Found: C, 55.24; H, 4.59; N, 7.14; S 16.36.

3-[(3-Methoxycarbonylpropionyl)amino]-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3q**).

This compound was recrystallized from toluene, yield 87%, yellow crystals, mp 183°; ir (potassium bromide): ν 3220, 3200, 3000, 2940, 2900, 1720, 1680 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ

11.15 (s, 1H), 7.61 (s, 1H), 7.49-7.30 (2m, 6H), 3.16 (s, 3H), 2.69-2.58 (2m, 4H), 2.23 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 190.2, 171.9, 169.3, 163.1, 144.4, 140.4, 135.6, 132.9, 129.4, 128.5, 128.4, 117.7, 51.2, 28.2, 27.9, 15.7; ms: m/z 391 (3, M$^+$+1), 141 (100).

Anal. Calcd. for $C_{18}H_{18}N_2O_4S_2$ (390.47): C, 55.37; H, 4.65; N, 7.18; S, 16.39. Found: C, 54.99; H, 4.68; N, 7.24; S, 16.50.

3-(2-Chloroacetylamino)-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3r**).

This compound was recrystallized from toluene, yield 78%, yellow crystals, mp 182°; ir (potassium bromide): ν 3200, 3020, 1725, 1705, 1560, 1530 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.54 (s, 1H), 7.64 (s, 1H), 7.49-7.43 (m, 4H), 7.40-7.36 (m, 2H), 4.39 (s, 2H), 2.24 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 189.9, 164.7, 163.0, 144.8, 140.8, 135.7, 133.0, 129.6, 128.7, 128.5, 117.5, 40.4, 15.8; ms: m/z (%) = 354 (21), 352 (48, M$^+$), 141 (100).

Anal. Calcd. for $C_{15}H_{13}ClN_2O_2S_2$ (352.85): C, 51.06; H, 3.71; Cl, 10.05; N, 7.94; S, 18.18. Found: C, 51.07; H, 3.73; Cl, 10.24; N, 7.91; S, 18.17.

3-(2-Bromoacetylamino)-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3s**).

This compound was recrystallized from toluene, yield 40%, orange needles; ir (potassium bromide): ν 3190, 3010, 1725, 1700 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.58 (s, 1H), 7.65 (s, 1H), 7.49-7.43 (m, 4H), 7.40-7.38 (m, 2H), 4.15 (s, 2H), 2.23 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 189.8, 164.6, 162.9, 144.7, 140.7, 135.6, 132.9, 129.5, 128.7, 128.6, 117.6, 25.9, 15.8; ms: m/z 398 (28), 396 (26, M$^+$), 141 (100).

Anal. Calcd. for $C_{15}H_{13}BrN_2O_2S_2$ (397.30): C, 45.35; H, 3.30; Br, 20.11; N, 7.05; S, 16.14. Found: C, 45.37; H, 3.28; Br, 20.31; N, 7.16; S, 16.07.

5-(Benzothiazol-2-yl-methylene)-3-(2-bromoacetylamino)-2-thioxothiazolidin-4-one (**3t**).

This compound was recrystallized from toluene/dioxane, yield 76%, yellow crystals, mp 261°; ir (potassium bromide): ν 3220, 3020, 2980, 1730, 1670 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.64 (s, 1H), 8.25 (m, 1H), 8.22 (m, 2H), 8.24 (s, 1H), 7.65 (m, 1H), 7.58 (m, 1H), 4.17 (s, 2H); ^{13}C nmr ([D$_6$]-DMSO): δ 194.0, 164.8, 162.5, 160.9, 152.9, 136.1, 127.5, 126.7, 126.5, 123.6, 122.8, 122.5, 25.9; ms: m/z 415 (0.8), 413 (0.7, M$^+$), 293 (100).

Anal. Calcd. for $C_{13}H_8BrN_3O_2S_3$ (414.31): C, 37.78; H, 1.95; Br, 19.10; N, 10.17; S, 23.23. Found: C, 37.69; H, 2.21; Br, 19.16; N, 10.46; S, 22.95.

3-(2-Bromoacetylamino)-5-[(2-phenyl-1,3-thiazol-4-yl)-methylene]-2-thioxothiazolidin-4-one (**3u**).

This compound was recrystallized from dioxane, yield 57%, yellow crystals, mp 247°; uv/vis (methanol): λ (log ε) = 389 (4.40), 278 (4.31), 262 (4.33) nm; ir (potassium bromide): ν 3270, 3100, 3040, 3020, 1730, 1685, 1600 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.66 (s, 1H), 8.48 (s, 1H), 8.05-8.02 (m, 2H), 7.92 (s, 1H), 7.62-7.57 (m, 3H), 4.18 (s, 2H); ^{13}C nmr ([D$_6$]-DMSO): δ 193.9, 168.4, 164.8, 163.1, 150.0, 131.7, 131.1, 129.4, 129.0, 126.4, 125.2, 121.1, 25.9; ms: m/z 441 (13), 439 (12), 217 (100).

Anal. Calcd. for $C_{15}H_{10}BrN_3O_2S_3$ (440.35): C, 40.91; H, 2.29; Br, 18.15; N, 9.52; S; 21.84. Found: C, 40.99; H, 2.38; Br, 18.54; N, 9.45; S, 21.55.

5-[(2*E*)-2-Chloro-3-phenylpropenylidene]-3-(2,2-dichloroacetylamino)-2-thioxothiazolidin-4-one (**3v**).

This compound was chromatographically purified (dichloromethane), yield 54%, orange crystals, mp 207°; ir (potassium bromide): ν 3240, 1720, 1570, 1560 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 12.12 (s, 1H), 7.86 (s, 1H), 7.89-7.84 (m, 2H), 7.83 (s, 1H), 7.55-7.48 (m 3H), 6.86 (s, 1H); ^{13}C nmr ([D$_6$]-DMSO): δ 190.1, 162.6, 162.4, 142.2, 134.0, 133.4, 130.7, 130.2, 128.9, 126.1, 120.3, 64.4; ms: m/z 410 (13), 408 (34), 406 (32, M$^+$), 115 (100).

Anal. Calcd. for $C_{14}H_9Cl_3N_2O_2S_2$ (407.72): C, 41.24; H, 2.22; Cl, 26.09; N, 6.87; S, 15.73. Found: C, 41.34; H, 2.33; Cl, 26.08; N, 6.70; S, 15.74.

3-(3-Chloropropionylamino)-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3w**).

This compound was recrystallized from toluene, yield 47%, orange crystals mp 166°; ir (potassium bromide): ν 3240, 1720, 1685, 1560 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.32 (s, 1H), 7.63 (s, 1H), 7.48-7.43 (m, 4H), 7.40-7.36 (m, 2H), 3.84 (t, 2H), 2.90 (td, 2H), 2.23 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 190.2, 167.6, 163.1, 144.7, 140.6, 135.7, 133.0, 129.5, 128.7, 128.5, 117.7, 39.5, 36.8, 15.8; ms: m/z 366 (6, M$^+$), 141 (100).

Anal. Calcd. for $C_{16}H_{15}ClN_2O_2S_2$ (366.88): C, 52.38; H, 4.12; Cl, 9.66; N, 7.64; S, 17.48. Found: C, 52.37; H, 4.09; Cl, 9.92; N, 7.58; S, 17.44.

3-(3-Chloropropionylamino)-5-(indol-3-yl-methylene)-2-thioxothiazolidin-4-one (**3x**).

This compound was recrystallized from dioxane/pentane, yield 92%, yellow-orange crystals, mp 212°; ir (potassium bromide): ν 3370, 3220, 3000, 1680, 1590 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 12.43 (s, 1H), 11.27 (s, 1H), 8.16 (s, 1H), 7.97-7.95 (m, 1H), 7.95 (s, 1H), 7.53-7.51 (m, 1H), 7.28-7.23 (m, 2H), 3.84 (t, 2H), 2.88 (td, 2H); ^{13}C nmr ([D$_6$]-DMSO): δ 189.5, 167.6, 162.9, 136.4, 131.0, 127.6, 126.7, 123.4, 121.6, 118.5, 112.6, 111.2, 110.9, 39.6, 36.1; ms: m/z 365 (15, M$^+$), 173 (100).

Anal. Calcd. for $C_{15}H_{12}ClN_3O_2S_2$ (365.85): C, 49.25; H, 3.31; Cl, 9.69; N, 11.49; S, 17.53. Found: C, 49.39; H, 3.39; Cl, 9.53; N, 11.62; S, 17.16.

3-(2-Chloro-2-phenylacetylamino)-5-[(6-methylpyridin-2-yl)-methylene]-2-thioxothiazolidin-4-one (**3y**).

This compound was chromatographically purified (ethyl acetate:*n*-hexane 2:3) and recrystallized from toluene/dioxane/pentane, yield 58%, yellow crystals, mp 232°; ir (potassium bromide): ν 3210, 1725, 1690 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.84 (s, 1H), 7.89-7.83 (m, 2H), 7.77-7.73 (m, 1H), 7.64-7.61 (m, 2H), 7.46-7.32 (m, 3H), 5.98 (s, 1H), 2.60 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 196.8, 165.6, 163.2, 158.2, 150.1, 137.9, 136.1, 130.1, 129.1, 128.6, 128.5, 128.2, 128.1, 125.8, 124.1, 123.53, 57.6, 23.4; ms: m/z 405 (5), 403 (12, M$^+$), 235 (100).

Anal. Calcd. for $C_{18}H_{14}ClN_3O_2S_2$ (403.90): C, 53.53; H, 3.49; Cl, 8.78; N, 10.40; S, 15.88. Found: C, 53.49; H, 3.47; Cl, 8.92; N, 10.49; S, 15.89.

3-(2-Iodoacetylamino)-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3z**).

Compound **3s** (1.2 g, 3 mmoles) was dissolved in hot toluene. After addition of a solution of potassium iodide (1.5 g) and tetrabutylammonium iodide (200 mg) in water (50 ml) the mixture was refluxed for 2 hours. The aqueous phase was separated and the organic phase washed with hot water (2 x 100 ml). The solution was dried over sodium sulfate. The sodium sulfate was extracted with dioxane and the toluene-solution and the combined extracts were evaporated. The resulting residue was chromatographically (ethyl acetate:*n*-hexane 2:3) purified and recrystallized from toluene, yield 52%, orange crystals, mp 182°; ir (potassium bromide): ν 3200, 1685, 1555 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.51, 7.63 (s, 1H), 7.50-7.43 (m, 4H), 7.41-7.36 (m, 2H), 3.88 (s, 2H), 2.24 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 190.0, 166.5, 163.1, 144.8, 140.6, 135.7, 133.0, 129.5, 128.7, 128.5, 117.6, 15.8, -4.5; ms: m/z 444 (2, M$^+$), 141 (100).

Anal. Calcd. for $C_{15}H_{13}IN_2O_2S_2$ (444.30): C, 40.55; H, 2.95; N, 6.30; S, 14.43. Found: C, 40.23; H, 3.05; N, 6.08; S, 14.24.

5-[(2*E*)-2-Methyl-3-phenylpropenylidene]-3-{2-[(1-phenyltetrazol-5-yl)thio]acetylamino}2-thioxothiazolidin-4-one (**3aa**).

To a solution of **3s** (850 mg, 2.14 mmoles) in hot toluene (150 ml) was added 5-mercapto-1-phenyltetrazole (540 mg, 3 mmoles) and TEA (0.5 ml). The mixture was refluxed for 4 hours, diluted with toluene (100 ml) and washed with water (2 x 75 ml). The organic phase was dried over sodium sulfate and evaporated. The residue was chromatographed (dichloromethane: ethyl acetate 9:1) and recrystallized from toluene/dioxane, yield 87%, yellow crystals, mp 201°; uv/vis (methanol): λ (log ε) = 389 (4.11), 261 (4.67) nm; ir (potassium bromide): ν 3250, 1730, 1700, 1570, 1500 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.63 (s, 1H), 7.71-7.67 (m, 6H), 7.65-7.62 (m, 1H), 7.50-7.38 (m, 5H), 4.46 (m, 2H), 2.22 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 189.9, 165.1, 163.0, 153.2, 144.9, 140.8, 135.7, 133.0, 132.9, 130.6, 130.0, 129.6, 128.8, 128.6, 124.4, 117.6, 34.6, 15.8; ms: m/z 174 (12), 118 (100).

Anal. Calcd. for $C_{22}H_{18}N_6O_2S_3$ (494.61): C, 53.42; H, 3.67; N, 16.99; S, 19.45. Found: C, 53.33; H, 3.77; N, 16.93; S, 19.32.

3-{2-[(1-Methyltetrazol-5-yl)thio]acetylamino}-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3ba**).

To a suspension of **3r** (1050 mg, 3 mmoles) in methanol (40 ml) was added dioxane until a clear solution occured. To this solution was added 5-mercapto-1-methyltetrazole sodium salt (590 mg, 3.4 mmoles). After 8 hours reflux the solvent was evaporated. The residue was chromatographed (dichloromethane:ethyl acetate 4:1) and recrystallized from dioxane/toluene/methanol, yield 75%, yellow crystals, mp 208°; ir (potassium bromide): ν 3320, 2970, 1725, 1715, 1570 cm^{-1}; ^{1}H nmr ([D$_6$l]-DMSO): δ 11.57 (s, 1H), 7.62 (s, 1H), 7.48-7.43 (m, 4H), 7.40-7.38 (2m, 2H), 4.30 (m, 2H), 3.99 (s, 3H), 2.22 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 189.8, 165.3, 163.0, 152.4, 144.9, 140.6, 135.7, 133.0, 129.5, 128.6, 128.5, 117.6, 34.8, 33.7, 15.8; ms: m/z 432 (21, M$^+$), 116 (100).

Anal. Calcd. for $C_{17}H_{16}N_6O_2S_3$ (432.54): C, 47.21; H, 3.73; N, 19.43; S, 22.24. Found: C, 46.96; H, 3.77; N, 19.06; S, 21.86.

3-{3-[(Benzothiazol-2-yl)thio]propionylamino}-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**3ca**).

2-Mercaptobenzothiazole (334 mg, 2 mmoles) was dissolved in dry dioxane (40 ml) under nitrogen. Sodium hydride (80 mg, 2 mmoles) was added and the mixture was refluxed for 30 minutes. Then **3w** (732 mg, 2 mmoles) was added and the mixture was refluxed for further 4 hours. After evaporation of the solvent the residue was chromatographed (dichloromethane) and recrystallized from toluene, yield 35%, yellow crystals, mp 196°; ir (potassium bromide): ν 3170, 3000, 1720, 1675, 1560 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 11.35 (s, 1H), 7.79 (s, 1H), 7.81-7.76 (m, 1H), 7.66-7.57 (m, 1H), 7.52-7.43 (m, 5H), 7.41-7.35 (m, 3H), 4.69 (m, 2H), 2.95 (m, 2H), 2.23 (s, 3H); ^{13}C nmr ([D$_6$]-DMSO): δ 190.0, 188.0, 167.9, 163.1, 144.8, 141.0, 140.6, 135.7, 133.0, 129.6, 128.7, 128.5, 127.1, 126.5, 124.8, 121.7, 117.7, 113.6, 41.8, 30.0, 15.8; ms: m/z 497 (6, M$^+$), 167 (100).

Anal. Calcd. for $C_{23}H_{19}N_3O_2S_4$ (497.68): C, 55.51; H, 3.85; N, 8.44. Found: C, 55.45; H, 3.86; N, 8.15.

3-(Methoxymethyleneamino)-5-[(2*E*)-2-methyl-3-phenylpropenylidene]-2-thioxothiazolidin-4-one (**5a**).

To trimethyl orthoformate (25 ml) was added **4** (550 mg, 2 mmoles), acetic anhydride (0.5 ml) and *p*-toluenesulfonic acid (25 mg). The mixture was refluxed for 6 hours. Then the solvent was evaporated *in vacuo* and the residue chromatographed (ethyl acetate:*n*-hexane 2:3) and recrystallized from ethyl acetate, yield 63%, red crystals, mp 162°; ir (potassium bromide): ν 3010, 3000, 1700, 1615, 1575 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 8.08 (s, 1H), 7.54 (s, 1H) 7.48-7.31 (m, 5H), 7.08 (s, 1H), 4.09 (s, 3H), 2.25 (s, 3H); ^{13}C nmr (deuteriochloroform): δ 187.6, 167.9, 164.1, 144.1, 140.0, 136.0, 133.4, 129.5, 128.7, 128.6, 119.6, 56.0, 16.2; ms: m/z 318 (30, M$^+$), 141 (100).

Anal. Calcd. for $C_{15}H_{14}N_2O_2S_2$ (318.41): C, 56.58; H, 4.43; N, 8.80; S, 20.14. Found: C, 56.53; H, 4.43; N, 8.54; S, 20.17.

General Procedure for the Preparation of 3-Condensated Aminorhodanines **5b-d**.

To a solution of **1** (1 equivalent) and the aldehyde (1 equivalent) in DME (10 ml/mmole) was added concentrated hydrochloric acid (1.0 ml) and the mixture was refluxed for 2 hours. The residue obtained after evaporation of the solvent was purified as stated below.

3-[(2*E*)-2-Methyl-3-phenylpropenylideneamino]-2-thioxothiazolidin-4-one (**5b**).

The compound was chromatographically purified (ethyl acetate:*n*-hexane) and recrystallized from toluene, yield 80%, yellow crystals, mp 133°; ir (potassium bromide): ν 3080, 1730, 1575 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 8.30 (s, 1H), 7.49-7.41 (m, 4H), 7.38-7.36 (m, 1H), 7.03 (s, 1H), 4.07 (s, 2H), 2.31 (s, 3H); ^{13}C nmr (deuteriochloroform): δ 194.8, 174.1, 169.1, 145.3, 135.5, 133.4, 129.8, 128.9, 128.6, 33.7, 12.7; ms: m/z 276 (0.5, M$^+$), 143 (100).

Anal. Calcd. for $C_{13}H_{12}N_2OS_2$ (276.38): C, 56.50; H, 4.38; N, 10.14; S, 23.20. Found: C, 56.49; H, 4.40; N, 10.11; S, 23.18.

3-[(2*E*)-2-Chloro-3-phenylpropenylidenamino]-2-thioxothiazolidin-4-one (**5c**).

The compound was chromatographically purified (ethyl acetate:*n*-hexane 2:3) and recrystallized from toluene, yield 34%, yellow crystals, mp 160°; ir (potassium bromide): ν 1720, 1700, 1675 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 8.61 (s, 1H), 7.90-7.87 (m, 2H), 7.48-7.42 (m, 3H), 7.26 (s, 1H), 4.08 (s, 2H); ^{13}C nmr (deuteriochloroform): δ 194.3, 168.9, 166.1, 141.7, 133.1, 130.8, 130.7, 128.7, 126.4, 33.6; ms: m/z 298 (1), 296 (3, M$^+$), 261 (100).

Anal. Calcd. for $C_{12}H_9ClN_2OS_2$ (296.79): C, 48.64; H, 3.06; Cl, 11.81; N, 9.46; S, 21.60. Found: C, 48.47; H, 3.02; Cl, 11.90; N, 9.50; S, 21.67.

3-[(1-Phenylsulfonylindol-3-yl)-methyleneamino]-2-thioxothiazolidin-4-one (**5d**).

This compound was recrystallized from toluene/dioxane, yield 49%, yellow crystals, mp 211°; ir (potassium bromide): ν 1725, 1600 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 8.88 (s, 1H), 8.41 (m, 1H), 8.05 (s, 1H), 7.98 (m, 1H), 7.95 (m, 2H), 7.60 (m, 1H), 7.50 (m, 2H), 7.42 (dt, 1H), 7.38 (td, 1H), 409 (s, 2H); ^{13}C nmr ([D$_6$]-DMSO): δ 197.1, 169.8, 163.3, 136.4, 135.2, 134.9, 134.6, 130.1, 127.0, 126.3, 126.1, 124.8, 123.3, 116.0, 113.2, 34.6; ms: m/z 415 (40, M$^+$), 141 (100).

Anal. Calcd. for $C_{18}H_{13}N_3O_3S_3$ (415.50): C, 52.03; H, 3.15; N, 10.11; S, 23.15. Found: C, 51.97; H, 3.26; N, 10.22; S, 22.78.

4-(2-Naphthalenesulfonyloxy)benzaldehyde (**6a**).

A solution of 4-hydroxybenzaldehyde (1.22 g, 10 mmoles) and 2-naphthalenesulfonyl chloride (2.26 g, 10 mmoles) in pyridine (70 ml) was stirred 30 minutes at 0° and an additional hour at rt. The mixture was poured on a mixture of ice (200 ml) and concentrated hydrochloric acid. The resulting suspension was extracted with dichloromethane (3 x 100 ml) and the combined extracts were washed with dilute hydrochloric acid (2 x 75 ml) and dried (sodium sulfate). The oily residue obtained after evaporation of the solvent was filtered over silica gel (dichloromethane) yielding an oil that crystallized upon standing. The solid was recrystallized from *n*-hexane/chloroform, yield 1.3 g (42%), colorless crystals, mp 86°; ir (potassium bromide): ν 3060, 2820, 2730, 1695, 1585 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 9.95 (s, 1H), 8.40 (m, 1H), 8.10-7.60 (m, 8H), 7.30-7.10 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 190.4, 153.6, 135.3, 134.7, 131.7, 131.6, 131.1, 130.3, 129.7, 129.6, 129.3, 127.9, 122.8, 122.4; ms: m/z 312 (22, M$^+$), 127 (100).

Anal. Calcd. for $C_{17}H_{12}O_4S$ (312.32): C, 65.38; H, 3.87; S, 10.27. Found: C, 65.40; H, 3.88; S, 10.19.

5-(3-Nitrophenyl)thiophene-2-carboxaldehyde (**6b**).

To a suspension of 5-bromo-thiophene-2-carboxaldehyde (1.15 g, 6 mmoles) and 3-nitrophenylboronic acid (1.2 g, 7.2 mmoles) in toluene (30 ml) under nitrogen was added $Pd(PPh_3)_4$ (346 mg, 0.3 mmole), sodium carbonate solution (2*M*, 30 ml) and ethanol (12 ml). After 5.5 hours under reflux the mixture was poured in dichloromethane (150 ml) and water (100 ml). The aqueous phase was extracted with dichloromethane (2 x 50 ml) and the combined organic phases were dried (sodium sulfate) and concentrated to 5 ml. Chromatography (dichloromethane) yielded a solid which was recrystallized from *n*-hexane/chloroform, yield 1.17 g (84%), beige crystals, mp 147°; ir (potassium bromide): ν 3090, 3080, 1725, 1665, 1520 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 9.94 (s, 1H), 8.52 (t, 1H), 8.24 (ddd, 1H), 7.98 (ddd, 1H), 7.80 (d, 1H), 7.64 (t, 1H), 7.54 (d, 1H); ^{13}C nmr (deuteriochloroform): δ 182.7, 150.5, 148.8, 143.9, 137.1, 134.8, 132.1, 130.4, 125.7, 123.7, 121.1; ms: m/z 233 (100, M$^+$).

Anal. Calcd. for $C_{11}H_7NO_3S$ (233.24): C, 56.65; H, 3.03; N, 6.01; S, 13.75. Found: C, 56.64; H, 3.13; N, 6.33; S, 13.70.

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