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A new method for the preparation of 5-acylidene and 5-imino substituted rhodanine derivatives and their antioxidant and antimicrobial activities

Şevket Hakan Üngören [a,*], Sevil Albayrak [b], Ahmet Günay [a], Lutfiye Yurtseven [b], Nurgül Yurttaş [a]

[a] Department of Chemistry, Faculty of Arts and Sciences, Bozok University, Yozgat, Turkey
[b] Department of Biology, Faculty of Sciences, Erciyes University, Kayseri, Turkey

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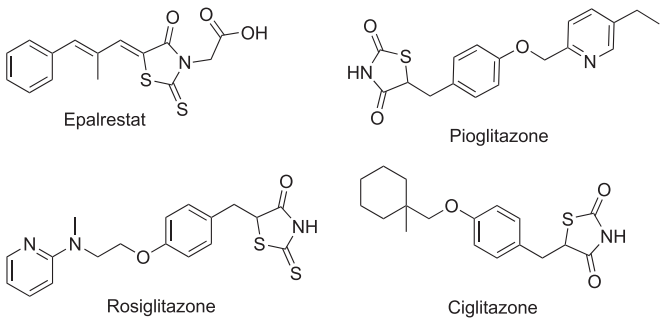
ABSTRACT

Versatile syntheses of 5-imino or 5-acylidene substituted 1,3-thiazolidin-4-one derivatives are reported from α-dioxothiazole systems and phosphoranes via Wittig reactions. Antimicrobial and antioxidant activity of the compounds were evaluated. 5-Carbonylmethylene substituted 2-thioxo-1,3-thiazolidines have better antioxidant properties than the 5-arylimino substituted ones. The % inhibition value of the compound **3** (90.8%) was near to that of standard BHT (93.6%) at the same concentration. Compounds **5** and **15**, which have the alkyliden-amide group at the C-5 position of the 1,3-thiazolidine ring showed the highest antimicrobial activities among the synthesized compounds.

1. Introduction

2-Thioxo-1,3-thiazolidin-4-one, commonly named as rhodanine,[1] is privileged scaffold[2] that shows multiple biological activities[3] by means of selective affinity towards various enzymes such as aldose reductase,[4] β-lactamase,[5] HCV NS3 protease,[6] histidine decarboxylase,[7] *N*-acetyltransferase[8] and histone acetyltransferase.[9] The 1,3-thioazolidin-4-one skeleton is also a pharmacophore for treatment of type 2 diabetes and is found in the structure of some drugs like Epalrestat, Pioglitazone, Rosiglitazone, Ciglitazone.[3]



Moreover, there is an important application of 5-acylidene substituted rhodanines as dye sensitizer,[10] and also 5-arylimino substituted derivatives of rhodanine framework are very interesting structures as optical materials.[11] Thus, rhodanine structures have become useful for the development of not only bioactive, but also optoelectronic materials.

A short time ago, the synthesis of some 5-imino substituted rhodanines was revealed from the reaction of the corresponding thiazolidines and aryl nitroso compounds.[11] On the other hand, only two methods are known about the preparation of 5-acylidene rhodanines. The first one is well known and it based on the Knoevenagel reaction of 2-thioxo/oxo/imino substituted rhodanine derivatives with aldehydes.[1,12] The second method is the cyclization of thioureas or dithiocarbamic acids with dialkylacetylene dicarboxylates (DAADs).[13] The second method is not used commonly because of the limited availability of DAADs.

Considering the importance of thiazolidine compounds, we can report that a new generalized protocol about the preparation of 5-

* Corresponding author. Tel.: +90 354 242 1021; fax: +90 354 242 1022; e-mail address: hungoren@erciyes.edu.tr (Ş.H. Üngören).

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0040-4020/

acylidene and 5-arylimino substituted rhodanine derivatives is able to provide rich sources of valuable chemical materials.

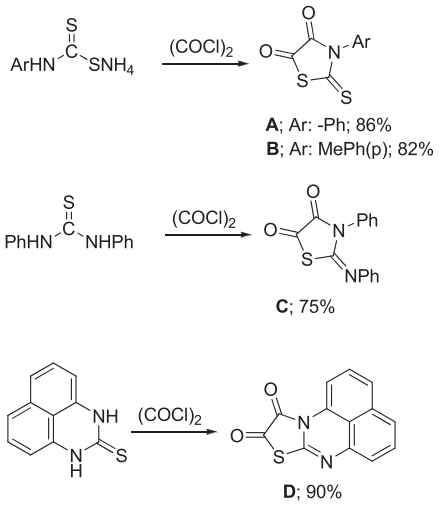
In this study, we propose a new useful method for synthesis of 5-acylidene and 5-imino rhodanine series by rection of 1,3-thiazolidine-4,5-diones (α-dioxothiazole derivatives) with Wittig reagents. The chemical behavior of the Wittig reagents towards α-dioxothiazole derivatives has not been investigated previously, however, the Wittig reactions of similar structures such as α-dioxoimidazole, α-dioxofurane were reported earlier.[14]

In addition to our synthesis study, we have investigated antibacterial and antioxidant properties of the newly synthesized rhodanine analogues.

2. Results and discussion

2.1. Synthesis

First, 3-aryl-2-thioxo-1,3-thiazolidine-4,5-diones (**A**, **B**) were prepared from corresponding ammonium dithiocarbamates with oxalyl chloride at reflux condition in benzene.[15] 2-Arylimino substituted 1,3-thiazolidinedione analogues (**C**, **D**) were synthesized with similar pathway as second-type of starting materials in MeCN (as shown Scheme 1).[16,13a]



Scheme 1. Preparations of 1,3-thiazolidine-4,5-dione structures as substrates (**A**–**D**).

Subsequently, heating a benzene solution of compounds **A**–**D** with various methylenephosphoranes leads to the regioselectively formation of 1,3-thiazolidine-5-ylidene derivatives at good yields as shown Table 1. Also, iminophosphoranes are reacted on the S–*C*=*O* group, but not N–*C*=*O* group of the substrates, similarly. The alkylidene substituted products were isolated in *Z*-form.

In the ^{13}C NMR spectra of **A**–**D**, S–*C*=O signals of α-dioxotihiazole derivatives were observed in the range of 178–190 ppm. In the ^{13}C NMR spectrum of the Wittig reaction products, these signals were disappeared and new signals, which belong to substituted group of the products were appeared. For example, 16 resonances were seen in the ^{13}C NMR spectra of **29**, and signals of a methyl group and two carbonyl group (acetyl and amide) were observed at 30.7, 196.7, 153.0 ppm, respectively. The other carbon signals are convenient for the proposed structure.

Validation studies for the proposed method were performed by using reported spectroscopic data of compounds **27**[17] and **20**.[13a,d] These compounds can be prepared from the reaction of dimethylacetylene dicarboxylate with corresponding thiourea derivatives in methanol. According to published ^{1}H NMR data of the compound **20**, which is formed in *Z*-geometry, and also supported with X-ray analyses,[13d] the olefinic proton signal is observed at δ 7.00 ppm. In this study, the same compound (**20**) showed a signal at δ 7.01 ppm in $CDCl_3$ due to the olefinic proton in *Z*-form. Thus, we have clearly proved the structures of the synthesized compounds in *Z*-geometry.

Before performing biological studies of the novel rhodanine derivatives, two chalcone analogues of 5-acylidene rhodanines were synthesized from **13** with aldehydes for structural diversity of 5-acylidene rhodanines. Therefore, structure–activity relationship of antibacterial and antioxidant properties of the new rhodanine derivatives would be better understood.

The condensation reactions occurred in presence of BF_3 as catalyst, in moderate yields, (Table 2). The chalcone derivatives (**33**, **34**) were purified by column chromatography, and their spectroscopic data were correspond with proposed structures.

2.2. In vitro antioxidant activity

The inhibitory effects of some of the synthesized compounds (**1**–**20**, **33**, **34**) on DPPH radical are presented as % inhibition in Table 3. Statistical differences among the DPPH scavenger activities of the compounds were important ($p<0.05$). DPPH radical scavenging activity of the synthesized compounds was detected to be good to moderate as compared to the standard BHA. % Inhibition value of the compound **3** (90.8%) was near to that of standard BHT (93.6%) at the same concentration. It appears that compounds **3**, **13**, **14**, **4**, **1**, **11** and **17** were found to be a significant scavenger of the DPPH radical (90.8%, 82.1%, 81.2%, 71.2%, 71.2%, 55.9% and 54.4%, respectively) when compared to BHT. The other compounds except for **20** were showed moderate inhibitory effect and inhibition rates in the range of 42.2–11.6%. Compound **20** was exhibited the weakest inhibitory effect with 6.1%.

The study reveals that the sulfur atom attached on C-2 atom of 1,3-thiazolidine skeleton increases the antioxidant potential of the rhodanine derivatives, compared to effect of nitrogen atom attached on the same point. 5-Carbonylmethylen substituted 1,3-thiazolidines have much more antioxidant properties from the 5-arylimino substituted ones, generally. Moreover, in the event that there are methyl, methylene and methine groups attached to carbonyl group of 1,3-thiazolidine analogues, the protons of these groups provide additional antioxidant activity by transferring the protons to oxidizing agent.

2.3. Antimicrobial activity

The antimicrobial activity of compounds **1**–**34** against fourteen microorganisms determined by agar diffusion method was investigated. The results revealed that most of the synthesized rhodanine compounds (**2**–**7**, **13**–**18**) showed significant antibacterial activities (Table 4). Among the tested rhodanine compounds, **4**, **5**, **14** and **15** had the strongest antibacterial activity.

As clearly seen in Table 4, among the Gram (−) bacteria tested, the most sensitive bacteria were *Aeromonas hydrophila*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* while the most resistant bacteria were *Escherichia coli, Salmonella typhimurium, Proteus mirabilis* and *Yersinia enterocolitica*. Amongst the tested five Gram (+) bacteria the most sensitive bacteria were *Bacillus cereus, Bacillus subtilis, Listeria monocytogenes* and *Staphylococcus aureus* while none of the tested compounds had inhibitory activity against *Mycobacterium smegmatis*. **2** exhibited inhibitory activity against only *S. aureus* (7.0 mm) while **7** showed inhibitory activity against *B. cereus* (9.0 mm). All other compounds did not show antibacterial activity against the bacteria tested. Only **5**, **15** and **18** had an inhibitory effect on *Candida albicans* with inhibition zones of 11.0, 12.5 and 7.5, respectively. Compound **18** did not exhibit any activity

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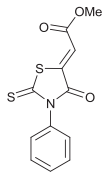
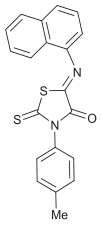
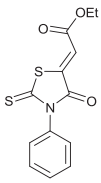
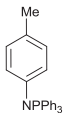
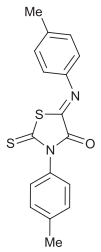
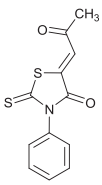
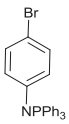
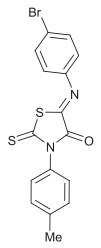
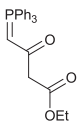
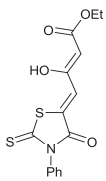
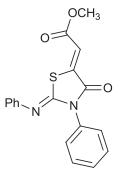
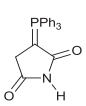
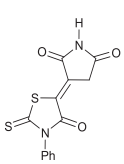
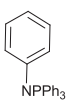
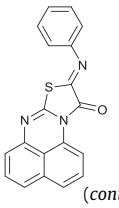
Table 1
5-Acylidene substituted thiazolidines (product no: **1**–**32**) prepared using Wittig/aza-Wittig reactions

A-D **1-32**

No	Subs	Reagent	Product	Time (min) Yield (%) Mp (°C)	No	Subs	Reagent	Product	Time (min) Yield (%)[a] Mp (°C)
1	A			10 82 (EtOH) 168–169	**17**	B			10 61 (MeOH) 175–176
2	A			10 78 (MeOH) 127–128	**18**	B			10 61 (2-PrOH) 195–196
3	A			10 65 (EtOH) 191–192	**19**	B			10 69 (MeOH) 158–159
4	A			10 76 (MeCN) 185–186	**20**	C			30 90 (n-Hex.) 126–127[b]
5	A			180 63 (MeCN) 261–262	**21**	D			15 76 (EtOAc) 201–202

(*continued on next page*)

Table 1 (*continued*)

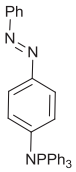
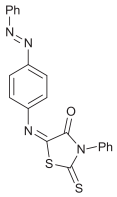
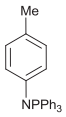
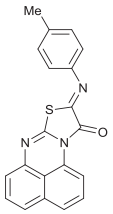
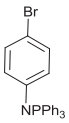
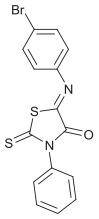
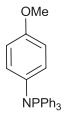
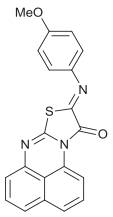
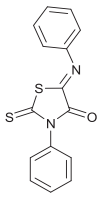
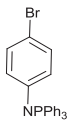
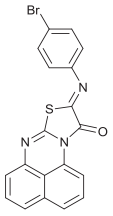
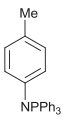
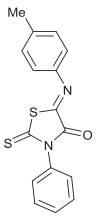
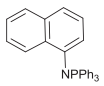
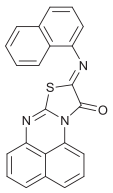
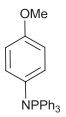
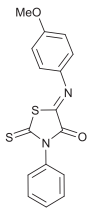
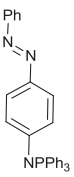
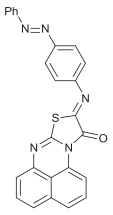
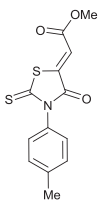
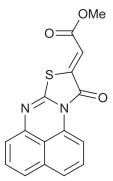
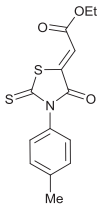
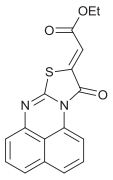
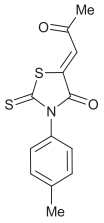
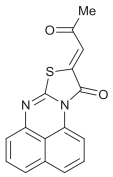
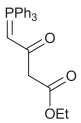
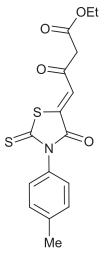
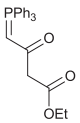
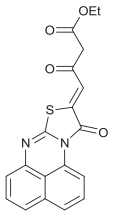
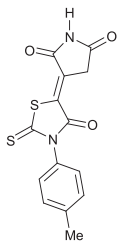
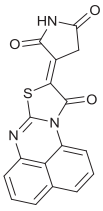
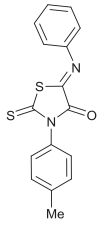
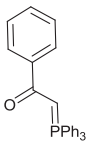
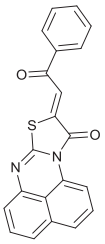
No	Subs	Reagent	Product	Time (min) Yield (%) Mp (°C)	No	Subs	Reagent	Product	Time (min) Yield (%)[a] Mp (°C)
6	A			10 68 (EtOH) 187–188	**22**	D			10 77 (MeCN) 172–173
7	A			10 86 (MeCN) 138–139	**23**	D			10 77 (EtOAc) 229–230
8	A			10 73 (2-PrOH) 146–147	**24**	D			10 81 (EtOAc) 232–233
9	A			20 82 (n-Hex.) 128–129	**25**	D			30 83 (MeCN) 198–199
10	A			10 88 (2-PrOH) 170–171	**26**	D			15 73 (DMF) 225–226
11	B			10 82 (MeOH) 150–151	**27**	D			10 87 (MeCN) 215–216[c]
12	B			10 88 (2-PrOH) 121–122	**28**	D			10 81 (MeCN) 179–180

Table 1 (*continued*)

No	Subs	Reagent	Product	Time (min) Yield (%) Mp (°C)	No	Subs	Reagent	Product	Time (min) Yield (%)[a] Mp (°C)
13	B			10 61 (MeOH) 206–207	**29**	D			10 89 (MeCN) 203–204
14	B			10 76 (2-PrOH) 187–188	**30**	D			20 83 (Xylene) 193–194
15	B			60 75 (Toluene) 242–243	**31**	D			60 54 (DMF) 307–308
16	B			10 79 (MeOH) 125–126	**32**	D			15 88 (MeCN) 239–240

[a] Isolated yield.
[b] Lit.[13d] Mp: 128–130 °C.
[c] Lit.[13a] Mp: 215–218 °C.

against bacterial strains and *Aspergillus parasiticus* while it had inhibitory effect on *C. albicans* (7.5 mm). Antifungal activities of Natamycin as positive control against *C. albicans* (24.0 mm) was higher than that of rhodanine compounds tested.

The MICs (minimum inhibitory concentrations) of the compounds against these microorganisms are summarized in Table 5 (a smaller MIC value corresponds to higher activity). As shown in Table 5, **15** exhibited the highest antibacterial activity against *A. hydrophila*, *K. pneumonia, P. aeruginosa* and *B. cereus* with an MIC as low as 0.63 mg/mL **14** exhibited excellent activity against *Morganella morganii* and *P. aeruginosa* with MIC of 0.63 mg mL^{-1}. Compound **5** exhibited the most potent antibacterial activity with MIC of 0.63 mg mL^{-1} against *B. subtilis* and MIC of 0.16 mg/mL against *L. monocytogenes*. The best antibacterial activity was observed for **4** against *L. monocytogenes* (MIC=0.08 mg/mL). Among the synthesized compounds, **2**, **3**, **4**, **5**, **13** and **14** exhibited moderate activity with MIC of 2.5–5.0 mg mL^{-1} against *S. aureus*. **15** and **18** exhibited moderate antifungal activity against *C. albicans* with MIC of 2.5–5.0 mg mL^{-1} (except for **5**, MIC=0.31 mg/mL).

A rough order of antimicrobial activity of substituted rhodanine analogues is outlined in Fig. 1. The highest antimicrobial activities of the new rhodanine series were observed in case of the compounds **5** and **15**, which have the alkyliden-amide group at the C-5 position of the 1,3-thiazolidine ring.

3. Conclusions

We have described stereo- and regioselective method for simple synthesis of 5-acylidene and 5-imino substituted rhodanine framework. The generalized procedure gave 32 samples in total, and is a new route to these potentially bioactive materials. Our investigation reveals that 5-acylidene rhodanines having an amide group attached to alkylidene moiety can be candidates for broad-spectrum antibiotics.

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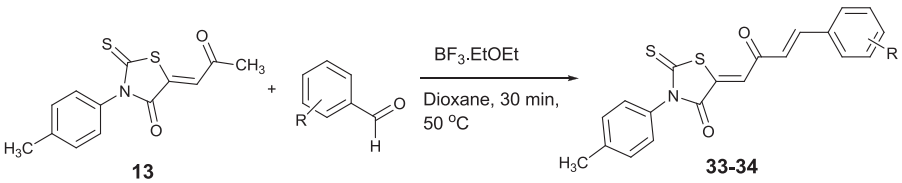
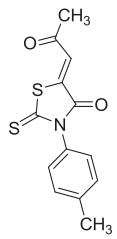
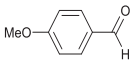
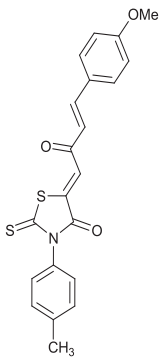
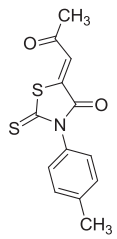
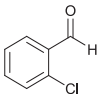
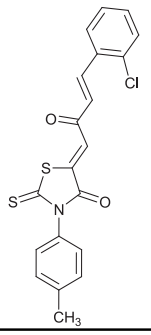
Table 2
Synthesis and experimental data of chalcone derivatives of 5-acylidene rhodanines



13 33-34

No	Subst.	Reagent	Product	t (min)	Yield (%)	Mp (°C)
33				30	66	172–173
34				30	48	191–192

4. Experimental

Melting points were measured on an Electro thermal 9100 apparatus and uncorrected. Elemental analyses for C, H and N were carried out using a LECO-932 CHNS–O Elemental Analyzer. ^{1}H and ^{13}C NMR spectra were measured with Bruker Advance 400 spectrometer using $CDCl_3$ or DMSO–d_6 solvents. The IR spectra were obtained with ATR method using a Shimadzu 8400 and Perkin Elmer Spectrum Two Model FTIR spectrometer. The progress of reactions was monitored by thin layer chromatography (TLC) on silica gel GF254 using $CHCl_3$ as mobile phase.

The antioxidant activity of the synthesized compounds was evaluated by 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging method.[18] All the synthesized rhodanine compounds were dissolved to prepare a stock solution of 1 mg/mL using dimethyl sulfoxide (DMSO). Fifty microliter solutions of compounds were added to 1 mL of a 0.1 mM solution of DPPH in methanol. After 2 h, absorbance values were measured at 517 nm. Butylated hydroxyl anisole (BHA) was used as the standard. The percentage inhibition activity was calculated by means of a Formula: % Antioxidant activity (% İnhibition)=100×(1- OD of test compound/OD of control compound).

The agar well diffusion method[19] was used for the determination of antibacterial activity of synthesized rhodanine compounds against fifteen microorganism including five Gram (+), eight Gram (−) bacterial strains, one yeast and one fungal strain. *A. hydrophila* ATCC7965, *B. cereus* RSKK 863, *B. subtilis* ATCC 6633, *E. coli* ATCC 25922, *K. pneumoniae* ATCC 27736, *L. monocytogenes* 1/2B, *M. smegmatis RUT*, *M. morganii*, *P. mirabilis* BC 3624, *P. aeruginosa* ATCC 27853, *S. typhimurium* NRRLE 4463, *S. aureus* ATCC 25923, *Y. enterocolitica* ATCC 1501 were used to determine antibacterial activity. As for antifungal activity, standard strain of *C. albicans* ATCC 10231 and *A. parasiticus* DSM 577 were used. Tetracycline (10 mg/mL, Sigma T3258-T6) and Natamycin (30 mg mL^{-1}, Delvocid DMS) were used as positive control. All the synthesized rhodanine compounds were dissolved to prepare a stock solution of 10 mg mL^{-1} using DMSO. The bacterial culture strains and fungal spore suspensions were adjusted to give a final concentration of 10^6–10^7 cfu mL^{-1}. About 25 mL of media (Mueller Hinton Agar, Malt Extract Agar and Patoto Dextrose Agar for bacteria, yeast and mold, respectively) were poured into Petri plates (9 cm in diameter) and inoculated with respective test organism. Wells (6 mm) were made with cork borer on the solid agar and loaded with 50 μL of the test compounds. *Y. enterocolitica*, *C. albicans* and *A. parasiticus* were

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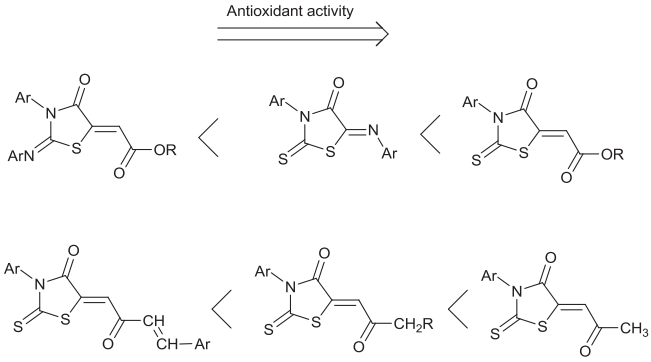
Table 3
In vitro antioxidant activity of some of the compounds (No: **1**–**20**, **33**, **34**)



No	% Inhibition*	No	% Inhibition*
1	71.2±0.8[d]	**2**	21.1±0.4[k]
3	90.8±0.3[b]	**4**	71.2±0.4[d]
5	12.1±0.4[n]	**6**	33.3±0.9[i]
7	20.8±0.2[k]	**8**	16.8±1.8[l]
9	13.8±2.2[m]	**10**	11.6±0.3[n]
11	55.9±0.6[e]	**12**	42.2±0.5[g]
13	82.1±0.6[c]	**14**	81.2±0.3[c]
15	13.9±0.7[m]	**16**	21.3±0.4[k]
17	54.4±0.2[e]	**18**	26.3±0.2[j]
19	41.5±1.3[g]	**20**	6.1±0.1[o]
33	14.8±0.4[m]	**34**	37.3±0.8[h]
BHT	93.6±0.1[a]		

(*) In each column, means of three independent experiments (± SD) with different superscript letters are significantly different ($p<0.05$).

Table 4
In vitro antimicrobial activity of newly synthesized compounds (**2**–**7**, **13**–**15**, **18**)

Microorganisms	Rhodanine compounds (10 mg/mL)										Tetracycline (10 mg/mL)
Gram (−)	**2**	**3**	**4**	**5**	**6**	**7**	**13**	**14**	**15**	**18**	
A. hydrophila	—	—	13.0±1.4	11.0±0.0	9.5±0.7	—	—	10.5±0.7	12.0±1.4		25.0±0.0
E. coli	—	—	—	—	—	—	—	—	—		26.0±0.0
K. pneumoniae	—	10.0±0.0[a]	13.0±1.4	10.5±0.7	—	—	8.0±0.0	11.0±0.0	11.5±0.7		25.0±0.0
M. morganii	—	—	—	9.5±0.7	—	—	—	10.0±0.0	11.5±0.7		18.0±0.0
P. mirabilis	—	—	—	—	—	—	—	—	—		21.0±0.0
P. aeruginosa	—	7.5±0.7	13.5±0.7	10.0±0.0	9.0±1.4	—	—	11.0±0.0	12.5±0.7		23.0±0.0
S. typhimurium	—	—	—	—	—	—	—	—	—		18.0±0.0
Y. enterocolitica	—	—	—	—	—	—	—	—	—		29.0±0.0
Gram (+)											
B. cereus	—	—	9.5±0.7	12.0±1.4	7.0±0.0	9.0±0.0	—	9.0±0.0	9.5±0.7		33.0±0.0
B. subtilis	—	—	10.0±0.0	10.5±0.7	—	—	—	8.0±0.0	12.5±0.7		30.0±0.0
L. monocytogenes	—	7.0±0.0	12.0±0.0	10.0±0.0	—	—	7.0±0.0	9.0±0.0	12.5±0.7		27.0±0.0
M. smegmatis	—	—	—	—	—	—	—	—	—		17.0±0.0
S. aureus	7.0±0.0	9.0±0.0	11.5±0.7	11.0±0.0	—	—	9.0±0.0	7.75±0.4	—		22.0±0.0
Yeast											Natamisin (30 mg mL−1)
C. albicans				11.0±0.0					12.5±0.7	7.5±0.7	24.0±0.0

—: No inhibition.
[a] Inhibition zones include diameter of hole (6 mm). Sample amount 50 μL.

incubated at 27 °C while other microorganisms were incubated at 35 °C for 28–48 h. The average diameter of the inhibition zone surrounding the wells was measured as mm.

The in vitro minimum inhibitory concentrations (MICs) of the synthesized rhodanine compounds were determined using microdilution assay in 96–well plates according to the methods recommended by Sarker et al.[20] The compounds were dissolved in DMSO to obtain a concentration of 10 mg mL^{-1}. Then this solution was added to the first two wells on a micro-titer plate and twofold dilutions were done in (Mueller Hinton Broth, Malt Extract Broth and Patoto Dextrose Broth for bacteria, yeast and mold, respectively from well two. The final range was from 0.078 to 5.000 mg/mL. Each well was inoculated with the microbial suspensions (10^6–10^7 cfu mL^{-1}) and incubated at 35 °C for 28 h.

Same procedure was conducted for Tetracycline and Natamycin. MIC_s values of test compounds were determined by colorimetric assay using Resazurin Sodium Salt (RSS). A change in color from blue to pink pointed out the growth of bacteria, and the MIC was defined as the lowest concentration of the compound that prevented this change in color. The lowest concentration at, which there was no visible growth was taken as the minimal inhibitory concentration (MIC) and expressed in mg ml^{-1}.

Statistical analysis: Data from the experiments were subjected to analysis of variance (ANOVA) using SPSS (2001) for Windows.[21] Percentage data were transformed using arcsine $\sqrt{x}$ before ANOVA. Means were separated at the 5% significance level by the least significant difference (LSD) test.

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Table 5
MIC values (mg mL^{-1}) for the rhodanine compounds (**2**–**7**, **13**–**15**, **18**)

Microorganisms	Tetracycline	Rhodanine derivatives									
Gram (−)	μg mL^{-1}	**2**	**3**	**4**	**5**	**6**	**7**	**13**	**14**	**15**	**18**
A. hydrophila	<7.8	—	—	2.5	2.5	2.5	—	—	1.25	0.63	
E. coli	<7.8	—	—	—	—	—	—	—	—	—	
K. pneumoniae	<7.8	—	1.25	10.0	1.25	—	—	2.5	2.5	0.63	
M. morganii	31.3	—	—	—	2.5	—	—	—	0.63	1.25	
P. mirabilis	31.3	—	—	—	—	—	—	—	—	—	
P. aeruginosa	15.6	—	1.25	0.31	0.63	2.5	—	—	0.63	0.63	
S. typhimurium	62.5	—	—	—	—	—	—	—	—	—	
Y. enterocolitica	15.6	—	—	—	—	—	—	—	—	—	
Gram (+)											
B. cereus	62.5	—	—	2.5	1.25	5.0	2.5	—	2.5	0.63	
B. subtilis	7.8	—	—	10.0	0.63	—	—	—	2.5	1.25	
L. monocytogenes	62.5	—	10.0	0.08	0.16	—	—	2.5	2.5	1.25	
M. smegmatis	125	—	—	—	—	—	—	—	—	—	
S. aureus	15.6	5.0	2.5	2.5	2.5	—	—	2.5	2.5	—	
Yeast	Natamycin										
C. albicans	0.0625				0.31					2.5	5.0

—: No inhibition.

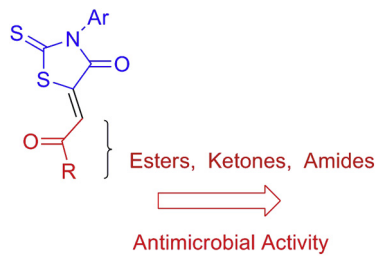

Fig. 1. Order of antimicrobial activity of substituted rhodanine analogues.

4.1. General procedure for the preparation of substrates A–D

A solution of dry ammonium aryldithiocarbamates or thioureas (1 mmol) and oxalyl chloride (1.1 mmol) in 30 mL dry benzene (for **C** and **D** in 30 mL CH_3CN) were stirred for 10 min, and then refluxed for 30 min. After removal of the solvents, the residues were treated with 15 mL n-hexane to give pure **A**–**D**.

*4.1.1. 3-Phenyl-2-(phenylimino)-1,3-thiazolidine-4,5-dione (**C**).* Yellow crystals, mp 168–169 °C; recrystallized from cyclohexane, yield 0.212 g 75%; IR (ATR): υ_{max}=3061 (Ar–H), 1770, 1748, 1728 (C=O), 1644 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66–6.92 (m, 10H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 179.9 (S–C=O), 157.1 (N–C=O), 146.3 (C=N), 145.2, 133.3, 129.7, 129.5, 129.4, 127.4, 126.1, 120.6 (C=C); Anal. Calcd for $C_{15}H_{10}N_2O_2S$ (282.3 g/mol): C, 63.81; H, 3.57; N, 9.92; S, 11.36. Found: C, 63.99; H, 3.65; N, 10.10; S, 11.48%.

*4.1.2. [1,3]Thiazolo[3,2-a]perimidine-9,10-dione (**D**).* Red crystals, mp 208–209 °C, Lit[13a] mp 207–209, recrystallized from CH_3CN, yield 0.228 g 90%; IR (ATR): υ_{max}=1751, 1705 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.63–7.17 (m, 6H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.0 (S–C=O), 153.8 (N–C=O), 145.2 (C=N), 136.9, 133.6, 130.0, 128.3, 127.6, 126.5, 126.3, 126.6, 118.6, 111.9 (C=C); Anal. Calcd for $C_{13}H_6N_2O_2S$ (254.3 g/mol): C, 61.41; H, 2.38; N, 11.02; S, 12.61. Found: C, 61.52; H, 2.38; N, 10.91; S, 12.88%.

*4.1.3. General procedure for the preparation of compounds **1**–**32**.* The solution of compounds **A**–**D** (1 mmol) and corresponding Wittig reagents (1 mmol) in 30 mL dry toluene (in 30 mL xylene for **5**, **15**, **31**) were refluxed for optimized time. After removal of the solvent, the residues were washed with hot 10 mL cyclohexane and recrystallized from corresponding solvent (see Table 1) to give pure compounds **1**–**32**.

5. Methyl (2*Z*)-(5-oxo-3-phenyl-2-thioxo-1,3-thiazolidin-4-ylidene)acetate (1)

Yellow crystals; mp 168–169 °C; yield 0.229 g 82%; IR (ATR): υ_{max}=1723 (COOMe), 1699 (NC=O), 1610 (C=C), 1346 (C=S) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.48–7.25 (m, 5H, Ar–H), 6.92 (s, 1H, C=CH), 3.91 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 195.7 (C=S), 166.2 (COOMe), 165.7 (N–C=O), 142.4, 130.0, 129.7, 128.2 (Ar–C), 134.1, 117.0 (C=CH), 53.0 (OMe); Anal. Calcd for $C_{12}H_9NO_3S_2$ (279.3 g/mol): C, 51.60; H, 3.25; N, 5.01; S, 22.96. Found: C, 51.71; H, 3.23; N, 4.91; S, 22.83%.

6. Ethyl (2*Z*)-(5-oxo-3-phenyl-2-thioxo-1,3-thiazolidin-4-ylidene)acetate (2)

Yellow crystals; mp 127–128 °C; yield 0.228 g 78%; IR (ATR): υ_{max}=1717 (COOEt), 1682 (NC=O), 1610 (C=C), 1350 (C=S) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.48–7.25 (m, 5H, Ar–H), 6.91 (s, 1H, C=CH), 4.36 (q, J=7.12 Hz, 2H, OCH_2), 1.40 (t, J=7.12 Hz, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 195.9 (C=C), 166.3 (COOEt), 165.2 (N–C=O), 142.1, 130.0, 129.6, 128.2 (Ar–C), 134.1, 117.6 (C=CH), 62.3 (OCH_2), 14.2 (Me); Anal. Calcd for $C_{13}H_{11}NO_3S_2$ (293.4 g/mol): C, 53.22; H, 3.78; N, 4.77; S, 21.86. Found: C, 53.41; H, 3.71; N, 4.61; S, 21.99%.

7. (4*Z*)-4-(2-Oxopropylidene)-3-phenyl-2-thioxo-1,3-thiazolidin-5-one (3)

Yellow crystals; mp 192–193 °C; yield 0.171 g 65%; IR (ATR): υ_{max}=1709 (MeC=O), 1668 (NC=O), 1346 (C=S) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.80–7.24 (m, 5H, Ar–H), 7.05 (s, 1H, C=CH), 2.51 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.0 (MeC=O), 196.6 (C=S), 167.1 (N–C=O), 140.3, 130.0, 129.6, 128.2 (Ar–C), 134.1, 120.6 (C=CH), 31.0 (Me); Anal. Calcd for $C_{12}H_9NO_2S_2$ (263.3 g/mol): C, 54.73; H, 3.44; N, 5.32; S, 24.35. Found: C, 54.60; H, 3.47; N, 5.39; S, 24.42%.

8. Ethyl (4*Z*)-3-oxo-4-(5-oxo-3-phenyl-2-thioxo-1,3-thiazolidin-4-ylidene)butanoate (4)

Orange crystals; mp 185–186 °C; yield 0.255 g 76%; IR (ATR): υ_{max}=1710 (EtC=O), 1642 (NC=O), 1620 (C=C), 1341 (C=S) cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 12.27 (s, 1H, enol–OH), 7.59–7.24 (m, 5H, Ar–H), 7.00 (s, 1H, ring=CH), 5.52 (s, 1H, C=CHCOOEt), 4.29 (q, J=7.12 Hz, 2H, OCH_2), 1.35 (t, J=7.12 Hz, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 195.3 (C=S), 172.1 (O=*C*–CH_2), 167.0 (COOEt), 165.2 (NC=O), 134.5, 132.5, 129.2, 128.3, 123.8, 99.2 (C=C), 61.2 (OCH_2), 14.2 (Me); Anal. Calcd for $C_{15}H_{13}NO_4S_2$ (335.4 g/mol): C, 53.72; H, 3.91; N, 4.18; S, 19.12. Found: C, 53.90; H, 3.98; N, 4.26; S, 19.02%.

9. 3-(5-Oxo-3-phenyl-2-thioxo-1,3-thiazolidin-4-ylidene)pyrrolidine-2,5-dione (5)

Orange crystals; mp 261–262 °C; yield 0.191 g 63%; IR (ATR): υ_{max}=3162 (NH), 1776, 1758, 1721, 1694, 1683, 1644 (C=O), 1620 (C=C), 1345 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, DMSO–d_6): δ (ppm) 12.10 (s, 1H, NH), 7.58–7.36 (m, 5H, Ar–H), 3.66 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 175.8 (C=S), 171.1 (CH_2*C*=O), 170.9 (NHC=O), 166.6 (Ar–N–C=O), 135.1, 130.1, 129.8, 129.5, 129.1, 127.1 (C=C), 36.5 (CH_2); Anal. Calcd for $C_{13}H_8N_2O_3S_2$ (304.3 g/mol): C, 51.30; H, 2.65; N, 9.20; S, 21.07. Found: C, 51.45; H, 2.72; N, 9.33; S, 21.16%.

10. 3-Phenyl-4-({4-[phenyldiazenyl]phenyl}imino)-2-thioxo-1,3-thiazolidin-5-one (6)

Yellow crystals; mp 188–189 °C; yield 0.273 g 68%; IR (ATR): υ_{max}=1738 (C=O), 1615 (C=N), 1343 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, DMSO–d_6): δ (ppm) 8.08–7.44 (m, 14H, Ar–H); ^{13}C NMR (100 MHz, DMSO–d_6): δ (ppm) 193.7 (C=S), 160.9 (C=O), 154.0, 152.4, 151.4, 151.0, 135.1, 132.3, 130.2, 130.0, 129.9, 129.0, 124.9, 123.1, 121.8 (C=C and C=N); Anal. Calcd for $C_{21}H_{14}N_4OS_2$ (402.5 g/mol): C, 62.67; H, 3.51; N, 13.92; S, 15.93. Found: C, 62.83; H, 3.62; N, 13.98; S, 15.63%.

11. 4-[(4-Bromophenyl)imino]-3-phenyl-2-thioxo-1,3-thiazolidin-5-one (7)

Yellow crystals; mp 138–139 °C; yield 0.324 g 86%; IR (ATR): υ_{max}=1726 (C=O), 1658 (C=N), 1344 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.69–7.14 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.9 (C=S), 161.4 (C=O), 151.3 (C=N), 147.2, 133.8, 132.9, 130.2, 129.8, 128.2, 122.6, 122.1 (C=C, arom.); Anal. Calcd for $C_{15}H_9BrN_2OS_2$ (377.3 g/mol): C, 47.75; H, 2.40; N, 7.43; S, 17.00. Found: C, 47.87; H, 2.38; N, 7.63; S, 17.16%.

12. 3-Phenyl-4-(phenylimino)-2-thioxo-1,3-thiazolidin-5-one (8)

Yellow crystals; mp 146–147 °C; yield 0.244 g 73%; IR (ATR): υ_{max}=1737 (C=O), 1666 (C=N), 1342 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.87–7.01 (m, 10H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.8 (C=S), 161.5 (N–C=O), 157.5 (C=N), 150.7, 148.5, 130.10, 129.8, 129.30, 120.90, (C=C ve C=N). Anal. Calcd for $C_{15}H_{10}N_2OS_2$ (298.4 g/mol): C, 60.38; H, 3.38; N, 9.39; S, 21.49. Found: C, 60.52; H, 3.30; N, 9.46; S, 21.61%.

13. 4-[(4-Methylphenyl)imino]-3-phenyl-2-thioxo-1,3-thiazolidin-5-one (9)

Yellow crystals; mp 128–129 °C; yield 0.256 g 82%; IR (ATR): υ_{max}=1738 (C=O), 1615 (C=N), 1342 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61–7.21 (m, 9H, Ar–H), 2.43 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 192.1 (C=S), 161.7 (NC=O), 148.9 (C=N), 145.6, 139.1, 134.0, 130.3, 130.0, 129.8, 129.7, 128.2, 121.6 (C=C ve C=N), 21.3 (CH_3). Anal. Calcd for $C_{16}H_{12}N_2OS_2$ (312.4 g/mol): C, 61.51; H, 3.87; N, 8.97; S, 20.53. Found: C, 61.65; H, 3.76; N, 8.83; S, 20.60%.

14. 4-[(4-Methoxyphenyl)imino]-3-phenyl-2-thioxo-1,3-thiazolidin-5-one (10)

Yellow crystals; mp 170–171 °C; yield 0.288 g 88%; IR (ATR): υ_{max}=1730 (C=O), 1613 (C=N), 1343 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.59–7.03 (m, 9H, Ar–H), 3.89 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 192.1 (C=S), 162.0 (N–C=O), 146.0 (C=N), 160.3, 140.5, 134.1, 130.0, 129.7, 124.6, 114.9 (C=C ve C=N), 55.6 (CH_3). Anal. Calcd for $C_{16}H_{12}N_2O_2S_2$ (328.4 g/mol): C, 58.52; H, 3.68; N, 8.53; S, 19.53. Found: C, 58.60; H, 3.61; N, 8.58; S, 19.42%.

15. Methyl (2*Z*)-[3-(4-methylphenyl)-5-oxo-2-thioxo-1,3-thiazolidin-4-ylidene]acetate (11)

Yellow crystals; mp 150–151 °C; yield 0.240 g 82%; IR (ATR): υ_{max}=1729 (COOMe), 1698 (NC=O), 1609 (C=C), 1348 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.37–7.13 (m, 4H, Ar–H), 6.91 (s, 1H, C=CH), 3.91 (s, 3H, OMe), 2.45 (s, 3H, PhMe); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 195.9 (C=S), 166.3 (COOMe), 165.7 (N–C=O), 142.5, 131.4, 130.4, 127.9 (Ar–C), 140.22, 117.0 (C=CH), 53.0 (OMe), 21.4 (Ar-CH_3). Anal. Calcd for $C_{13}H_{11}NO_3S_2$ (293.4 g/mol): C, 53.22; H, 3.78; N, 4.77; S, 21.86. Found: C, 53.28; H, 3.91; N, 4.86; S, 21.71%.

16. Ethyl (2*Z*)-[3-(4-methylphenyl)-5-oxo-2-thioxo-1,3-thiazolidin-4-ylidene]acetate (12)

Yellow crystals; mp 121–122 °C; yield 0.270 g 88%; IR (ATR): υ_{max}=1720 (COOEt), 1685 (NC=O), 1613 (C=C), 1356 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.71–7.13 (m, 4H, Ar–H), 6.91 (s, 1H, C=CH), 4.36 (q, J=7.12 Hz, 2H, OCH_2), 1.38 (t, J=7.12 Hz, 3H, Me), 2.44 (s, 3H, Ph-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 196.0 (C=C), 166.3 (COOEt), 165.2 (N–C=O), 142.1, 140.2, 130.3, 127.9 (Ar–C), 131.4, 117.6 (C=CH), 62.2 (OCH_2), 21.4 (CH_2–CH_3), 14.2 (Ar-CH_3). Anal. Calcd for $C_{14}H_{13}NO_3S_2$ (307.4 g/mol): C, 54.70; H, 4.26; N, 4.56; S, 20.86. Found: C, 54.78; H, 4.38; N, 4.48; S, 20.94%.

17. (4*Z*)-3-(4-Methylphenyl)-4-(2-oxopropylidene)-2-thioxo-1,3-thiazolidin-5-one (13)

Yellow crystals; mp 206–207 °C; yield 0.169 g 61%; IR (ATR): υ_{max}=1711 (MeC=O), 1667 (NC=O), 1350 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.37–7.12 (m, 4H, Ar–H), 7.23 (s, 1H, C=CH), 2.50 (s, 3H, $ArCH_3$), 2.45 (s, 3H, $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.1 (MeC=O), 196.6 (C=S), 167.2 (N–C=O), 140.3, 131.4, 130.3, 127.9 (Ar–C), 140.2, 120.5 (C=CH), 31.0 ($COCH_3$), 21.4 ($ArCH_3$). Anal. Calcd for $C_{13}H_{11}NO_2S_2$ (277.4 g/mol): C, 56.29; H, 4.00; N, 5.05; S, 23.12. Found: C, 56.38; H, 4.12; N, 4.91; S, 23.28%.

18. Ethyl (4*Z*)-4-[3-(4-methylphenyl)-5-oxo-2-thioxo-1,3-thiazolidin-4-ylidene]-3-oxobutanoate (14)

Orange crystals; mp 187–188 °C; yield 0.265 g 76%; IR (ATR): υ_{max}=1712 (EtC=O), 1651 (NC=O), 1619 (C=C), 1356 (C=S) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 12.27 (s, 1H, enol–OH), 7.37–7.12 (m, 4H, Ar–H), 7.00 (s, 1H, C=CH), 5.51 (s, 1H, C=CHCOOEt), 4.29 (q, J=7.12 Hz, 2H, OCH_2), 3.75 (s, 2H, CH_2, keto form), 2.44 (s, 3H, $PhCH_3$), 1.35 (t, J=7.12 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 195.5 (C=S), 172.1 (O=*C*–CH_2), 167.1 (COOEt), 165.2 (N–C=O), 140.1, 132.5, 131.8, 130.3, 127.9, 123.7, 99.1 (C=C), 61.2 (OCH_2), 21.4 ($PhCH_3$),14.2 (CH_3). Anal. Calcd for

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$C_{15}H_{13}NO_4S_2$ (335.4 g/mol): C, 53.72; H, 3.91; N, 4.18; S, 19.12. Found: C, 53.76; H, 3.96; N, 4.22; S, 19.14%.

19. 3-[3-(4-Methylphenyl)-5-oxo-2-thioxo-1,3-thiazolidin-4-ylidene]pyrrolidine-2,5-dione (15)

Green crystals; mp 242–243 °C; yield 0.238 g 75%; IR (ATR): υ_{max}=3153 (NH), 1759, 1705, 1686 (C=O), 1343 (C=S) cm^{-1}; ^1H NMR (400 MHz, DMSO–d_6): δ (ppm) 12.10 (s, 1H, NH), 7.92–7.17 (m, 4H, Ar–H), 3.43 (s, 2H, CH_2), 2.50 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO–d_6): δ (ppm) 176.0 (C=S), 171.1 (CH_2C=O), 170.9 (NHC=O), 166.6 (ArN–C=O), 139.8, 134.5, 130.8, 128.8, 126.2, 120.3 (C=C), 36.6 (CH_2), 21.3 ($ArCH_3$). Anal. Calcd for $C_{14}H_{10}N_2O_3S_2$ (318.4 g/mol): C, 52.82; H, 3.17; N, 8.80; S, 20.14. Found: C, 52.87; H, 3.18; N, 8.78; S, 20.17%.

20. 3-(4-Methylphenyl)-4-(phenylimino)-2-thioxo-1,3-thiazolidin-5-one (16)

Yellow crystals; mp 125–126 °C; yield 0.302 g 79%; IR (ATR): υ_{max}=1740 (C=O), 1667 (C=N), 1346 (C=S) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.70–7.19 (m, 9H, Ar–H), 2.46 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 192.0 (C=S), 161.6 (NC=O), 150.8 (C=N), 148.5, 140.4, 130.4, 129.7, 129.3, 128.3, 127.8, 120.9, (C=C and C=N), 21.4 ($ArCH_3$). Anal. Calcd for $C_{16}H_{12}N_2OS_2$ (312.4 g/mol): C, 61.51; H, 3.87; N, 8.97; S, 20.53. Found: C, 61.68; H, 3.85; N, 8.92; S, 20.47%.

21. 3-(4-Methylphenyl)-4-(1-naphthylimino)-2-thioxo-1,3-thiazolidin-5-one (17)

Red crystals; mp 175–176 °C; yield 0.220 g 61%; IR (ATR): υ_{max}=1733 (C=O), 1697 (C=N), 1347 (C=S) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.23–7.16 (m, 11H, Ar–H), 2.48 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 192.2 (C=S), 161.3 (NC=O), 151.5 (C=N), 145.6, 140.4, 134.2, 131.3, 130.5, 128.7, 127.9, 127.8, 127.7, 127.3, 126.8, 125.4, 123.3, 113.0 (C=C and C=N), 21.4 ($ArCH_3$). Anal. Calcd for $C_{20}H_{14}N_2OS_2$ (362.5 g/mol): C, 66.27; H, 3.89; N, 7.73; S, 17.69. Found: C, 66.41; H, 3.86; N, 7.80; S, 17.81%.

22. 3-(4-Methylphenyl)-4-[(4-methylphenyl)imino]-2-thioxo-1,3-thiazolidin-5-one (18)

Yellow crystals; mp 195–196 °C; yield 0.199 g 61%; IR (ATR): υ_{max}=1737 (C=O), 1659 (C=N), 1343 (C=S) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.58–7.19 (m, 8H, Ar–H), 2.46 (s, 3H, $ArCH_3$), 2.43 (s, 3H, $ArCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 192.3 (C=S), 161.8 (NC=O), 145.6, 140.3, 139.0, 131.3, 130.4, 130.3, 127.9, 121.6, 119.8 (C=C and C=N), 21.4, 21.3 (2×$ArCH_3$). Anal. Calcd for $C_{17}H_{14}N_2OS_2$ (326.4 g/mol): C, 62.55; H, 4.32; N, 8.58; S, 19.65. Found: C, C, 62.21; H, 4.53; N, 8.38; S, 19.54%.

23. 4-[(4-Bromophenyl)imino]-3-(4-methylphenyl)-2-thioxo-1,3-thiazolidin-5-one (19)

Orange crystals; mp 158–159 °C; yield 0.269 g 69%; IR (ATR): υ_{max}=1739 (C=O), 1659 (C=N), 1334 (C=S) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.64–7.12 (m, 8H, Ar–H), 2.46 (s, 3H, $ArCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.0 (C=S), 161.5 (C=O), 151.4 (C=N), 147.2, 140.5, 133.0, 131.1, 130.5, 127.8, 122.6, 122.1, (C=C, arom.), 21.4 ($ArCH_3$). Anal. Calcd. For $C_{16}H_{11}BrN_2OS_2$ (391.3 g/mol): C, 49.11; H, 2.83; N, 7.16; S, 16.39. Found: C, 49.23; H, 2.80; N, 7.37; S, 16.51%.

24. Methyl (2*Z*)-[5-oxo-3-phenyl-2-(phenylimino)-1,3-thiazolidin-4-ylidene]acetate (20)

Yellow crystals; mp 126–127 °C; yield 0.304 g 90%; IR (ATR): υ_{max}=1728, 1698, 1651 (C=O, C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.58–6.94 (m, 10H, Ar–H), 7.01 (s, 1H, CH), 3.84 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.4 (C=O, ester), 164.6 (NC=O), 151.7, 147.4, 141.5, 134.0, 129.4, 129.3, 129.2, 127.9, 125.3, 120.9, 116.5 (C=C and C=N), 52.6 (OCH_3); Anal. Calcd. For $C_{18}H_{14}N_2O_3S$ (338.4 g/mol): C, 63.89; H, 4.17; N, 8.28; S, 9.48. Found: C, 63.72; H, 4.13; N, 8.36; S, 9.57%.

25. 9-(Phenylimino)[1,3]thiazolo[3,2-*a*]perimidin-10(9*H*)-one (21)

Orange solid; mp 201–202 °C; yield 0.250 g 76%; IR (ATR): υ_{max}=1717 (C=O), 1626 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.78–7.22 (m, 11H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.4 (N=C–S), 148.8 (C=O), 148.6 (C=N–Ar), 148.1, 137.8, 133.9, 131.1, 129.8, 128.2, 127.8, 127.6, 125.5, 125.4, 121.0, 120.4, 118.7, 111.7 (C=C, arom.); Anal. Calcd. For $C_{19}H_{11}N_3OS$ (329 g/mol): C, 69.28; H, 3.37; N, 12.76; S, 9.74 Found: C, 69.43; H, 3.31; N, 12.95; S, 9.92%.

26. 9-[(4-Methylphenyl)imino][1,3]thiazolo[3,2-*a*]perimidin-10(9*H*)-one (22)

Orange solid; mp 172–173 °C; yield 0.264 g 77%; IR (ATR): υ_{max}=1714 (C=O), 1626 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.75–7.21 (m, 10H, Ar–H), 2.43 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.5 (N=C–S), 148.9 (C=O), 146.5 (C=N–Ar), 146.0, 138.3, 137.9, 133.9, 131.1, 130.3, 128.2, 127.6, 125.4, 125.3, 120.9, 120.8, 118.7, 111.6, (C=C, arom.), 21.3 (Me); Anal. Calcd. For $C_{20}H_{13}N_3OS$ (343 g/mol): C, 69.95; H, 3.82; N, 12.24; S, 9.34 Found: C, 69.82; H, 3.89; N, 12.36; S, 9.25%.

27. 9-[(4-Methoxyphenyl)imino][1,3]thiazolo[3,2-*a*]perimidin-10(9*H*)-one (23)

Orange solid; mp 229–230 °C; yield 0.276 g 77%; IR (ATR): υ_{max}=1728 (C=O), 1626 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.76–6.99 (m, 10H, Ar–H), 3.89 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.8 (N=C–S), 149.1 (C=O), 143.8 (C=N–Ar), 159.7, 140.8, 138.0, 133.9, 131.2, 128.2, 127.6, 125.3, 125.2, 123.7, 120.7, 118.8, 114.9, 111.6 (C=C, arom.), 55.6 (OMe); Anal. Calcd. For $C_{20}H_{13}N_3O_2S$ (359 g/mol): C, 66.84; H, 3.65; N, 11.69; S, 8.92 Found: C, 66.71; H, 3.67; N, 11.48; S, 9.12%.

28. 9-[(4-Bromophenyl)imino][1,3]thiazolo[3,2-*a*]perimidin-10(9*H*)-one (24)

Orange solid; mp 232–233 °C; yield 0.330 g 81%; IR (ATR): υ_{max}=1716 (C=O), 1619 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.77–7.14 (m, 10H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.1 (N=C–S), 148.0 (C=O), 147.7 (C=N–Ar), 137.8, 133.8, 133.0, 131.1, 128.3, 127.6, 125.7, 125.6, 122.1, 121.3, 121.2, 118.6, 111.8, (C=C, arom.); Anal. Calcd. For $C_{19}H_{10}BrN_3OS$ (408 g/mol): C, 55.89; H, 2.47; N, 10.29; S, 7.85 Found: C, 55.68; H, 2.47; N, 10.18; S, 7.62%.

29. 9-(1-Naphthylimino)[1,3]thiazolo[3,2-*a*]perimidin-10(9*H*)-one (25)

Orange solid; mp 198–199 °C; yield 0.315 g 83%; FT–IR (ATR): υ_{max}=1717 (C=O), 1626 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.80–7.22 (m, 13H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.4 (N=C–S), 148.8 (C=O), 148.5 (C=N–Ar), 137.8,

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133.8, 131.1, 129.8, 128.2, 127.8, 127.6, 125.5, 125.4, 121.0, 120.4, 111.7 (C=C, arom.); Anal. Calcd. For $C_{23}H_{13}N_3OS$ (408 g/mol): C, 72.80; H, 3.45; N, 11.07; S, 8.45 Found: C, 72.99; H, 3.42; N, 11.01; S, 8.49%.

30. 9-(4-Phenyldiazenylphenylimino)[1,3]thiazolo[3,2-*a*]perimidin-10(9*H*)-one (26)

Red solid; mp 225–226 °C; yield 0.317 g 73%; IR (ATR): υ_{max}=1732 (C=O), 1625 (C=N) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.59–7.24 (m, 15H, Ar–H); ^{13}C NMR (100 MHz, Pyridine–d_5): δ (ppm) 159.8 (N=C–S), 151.7 (C=O), 150.6 (C=N–Ar), 154.3, 153.4, 152.7, 152.1, 140.0, 137.3, 136.3, 135.6, 133.2, 133.1, 131.0, 130.0, 129.1, 126.8, 126.7, 126.4, 124,7, 124.2, 122.6, 122.3, 120.4, 112.7 (C=C, arom.); Anal. Calcd. For $C_{25}H_{15}N_5OS$ (433 g/mol): C, 69.27; H, 3.49; N, 16.16; S, 7.40 Found: C, 69.12; H, 3.43; N, 16.32; S, 7.43%.

31. Methyl (2*Z*)-(10-oxo[1,3]thiazolo[3,2-*a*]perimidin-9(10*H*)-ylidene)acetate (27)

Red solid; mp 215–216 °C; yield 0.270 g 87%; IR (ATR): υ_{max}=1709 (COOMe), 1688 (NC=O), 1628 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.59–7.23 (m, 6H, Ar–H), 7.05 (s, 1H, C=CH), 3.91 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.6 (MeC=O), 140.3 (NC=O), 161.5, 138.2, 133.8, 131.5, 128.3, 127.3, 125.3, 125.0, 120.6, 118.2, 116.5, 111.3, 100.0 (C=C and C=N), 52.7 (OMe); Anal. Calcd. For $C_{16}H_{10}N_2O_3S$ (310 g/mol): C, 61.93; H, 3.25; N, 9.03; S, 10.33 Found: C, 62.16; H, 3.29; N, 9.22; S, 10.06%.

32. Ethyl (2*Z*)-(10-oxo[1,3]thiazolo[3,2-*a*]perimidin-9(10*H*)-ylidene)acetate (28)

Red solid; mp 179–180 °C; yield 0.262 g 81%; IR (ATR): υ_{max}=1710 (COOEt), 1680 (NC=O), 1625 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.62–7.24 (m, 6H, Ar–H), 7.06 (s, 1H, C=CH), 4.37 (q, J=7.1 Hz, 2H, OCH_2), 1.40 (t, J=7.1 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.1 (MeC=O), 139.9 (N–C=O), 161.6, 139.9, 138.3, 133.9, 131.5, 128.3, 127.3, 125.2, 125.0, 120.6, 118.2, 117.1, 111.3 (C=C and C=N), 61.9 (OCH_2), 14.2 (CH_3); Anal. Calcd. For $C_{17}H_{12}N_2O_3S$ (324 g/mol): C, 62.95; H, 3.73; N, 8.64; S, 9.89 Found: C, 62.82; H, 3.80; N, 8.78; S, 10.11%.

33. (9*Z*)-9-(2-Oxopropylidene)[1,3]thiazolo[3,2-*a*]perimidin-10(9*H*)-one (29)

Red–brown needles; mp 203–204 °C; yield 0.262 g 89%; IR (ATR): υ_{max}=1710 (C=O), 1626 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.52–7.16 (m, 6H, Ar–H), 7.37 (s, 1H, C=CH), 2.49 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 196.7 (MeC=O), 153.0 (NC=O), 162.1, 138.4, 138.2, 133.7, 131.3, 128.2, 127.3, 125.2, 125.0, 120.8, 120.8, 118.1, 111.3 (C=C and C=N), 30.7 (Me); Anal. Calcd. For $C_{16}H_{10}N_2O_2S$ (294 g/mol): C, 65.29; H, 3.42; N, 9.52; S, 10.89 Found: C, 65.46; H, 3.42; N, 9.41; S, 10.97%.

34. Ethyl (4*Z*)-3-oxo-4-(10-oxo[1,3]thiazolo[3,2-*a*]perimidin-9(10*H*)-ylidene)butanoate (30)

Red solid; mp 193–194 °C; yield 0.304 g 83%; IR (ATR): υ_{max}=1714 (C=O), 1626 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 12.37 (s, 1H, OH), 8.77–7.20 (m, 6H, Ar–H), 7.09 (d, J=1.8 Hz, 1H, C=CHC=O), 5.45 (s, 1H, enol's C=CH), 4.28 (q, J=7.1 Hz, 2H, CH_2), 1.35 (t, J=7.2 Hz, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.3 (EtOC=O), 165.9 (C–OH), 152.2 (NC=O), 162.7, 138.4, 138.5, 134.0, 131.8, 129.6, 128.3, 127.3, 125.0, 124.5, 123.1, 120.0, 118.4, 110.9, 97.4 (C=C and C=N), 61.0 (OCH_2), 14.2 (CH_3); Anal. Calcd. For $C_{19}H_{14}N_2O_4S$ (366 g/mol): C, 62.28; H, 3.85; N, 7.65; S, 8.75 Found: C, 62.32; H, 3.71; N, 7.44; S, 8.58%.

35. 3-(10-Oxo[1,3]thiazolo[3,2-*a*]perimidin-9(10*H*)-ylidene) pyrrolidine-2,5-dione (31)

Red solid; mp 307–308 °C; yield 0.181 g 54%; IR (ATR): υ_{max}=3176 (NH), 1764, 1694, (C=O), 1625 (C=N) cm^{-1}; ^1H NMR (400 MHz, DMSO–d_6): δ (ppm) 11.98 (s, 1H, NH), 8.51–7.18 (m, 6H, Ar–H), 3.78 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 175.9, 170.9, 153.0 (NHC=O), 162.7, 138.9, 134.1, 132.2, 128.9, 128.5, 128.0, 125.1, 119.8, 118.4, 110.3 (C=C and C=N), 39.1 (CH_2); Anal. Calcd. For $C_{17}H_9N_3O_3S$ (335 g/mol): C, 60.89; H, 2.71; N, 12.53; S, 9.56 Found: C, 60.96; H, 2.66; N, 12.39; S, 9.59%.

36. (9*Z*)-9-(2-Oxo-2-phenylethylidene)[1,3]thiazolo[3,2-*a*] perimidin-10(9*H*)-one (32)

Brown solid; mp 239–240 °C; yield 0.313 g 88%; IR (ATR): υ_{max}=1700, 1638 (C=O), 1624 (C=N) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.71–7.32 (m, 11H, Ar–H), 7.24 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 188.6 (PhC=O), 162.4 (NC=O), 153.3, 140.9, 138.4, 136.7, 134.0, 133.9, 131.6, 129.1, 128.6, 128.4, 127.4, 125.3, 125.2, 120.9, 118.3, 117.7, 111.5 (C=C and C=N); Anal. Calcd. For $C_{21}H_{12}N_2O_2S$ (356 g/mol): C, 70.77; H, 3.39; N, 7.86; S, 9.00 Found: C, 71.00; H, 3.35; N, 7.93; S, 9.11%.

37. General procedure for the preparation of chalcone derivatives 33 and 34

To solution of compound **13** (0.263 g, 1 mmol) and corresponding aldehyde (1.1 mmol) in 3 mL dioxane was added (0.185 g, 1.3 mmol) $BF_3{\cdot}(C_2H_5)_2O$, then the solution was stirred at 50 °C for 30 min. After addition of 5 mL water, the residue was subjected to column chromatography on silica gel 60 Hf_{254}; elution with $CHCl_3$ afforded the product.

38. (5*Z*)-5-[(3*E*)-4-(4-Methoxyphenyl)-2-oxobut-3-en-1-ylidene]-3-(4-methylphenyl)-2-thioxo-1,3-thiazolidin-4-one (33)

Red crystals; mp 172–173 °C; yield 0.253 g 66%; IR (ATR): υ_{max}=1728, 1694, 1646 (C=O, C=N), 1345 (C=S) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.81 (d, J=15.89 Hz, 1H,=CH), 7.62–6.96 (m, 8H, Ar–H), 7.58 (s, 1H,=CH), 6.94 (d, J=15.89 Hz, 1H,=CH), 3.89 (s, 3H, OCH_3), 2.45 (s, 3H, Ph–CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 189.9 (C=O, keton), 187.1 (C=S), 167.4 (NC=O), 162.6, 146.1, 140.5, 140.1, 131.6, 130.8, 130.3, 128.0, 126.8, 124.0, 120.6, 114.7 (C=C), 55.5 ($ArOCH_3$), 21.4 ($ArCH_3$); Anal. Calcd. For $C_{21}H_{17}NO_3S_2$ (395.5 g/mol): C, 63.77; H, 4.33; N, 3.54; S, 16.22. Found: C, 63.98; H, 4.33; N, 3.48; S, 16.02%.

39. (5*Z*)-5-[(3*E*)-4-(2-Chlorophenyl)-2-oxobut-3-en-1-ylidene]-3-(4-methylphenyl)-2-thioxo-1,3-thiazolidin-4-one (34)

Orange crystals; mp 191–192 °C; yield 0.186 g 48%; IR (ATR): υ_{max}=1724, 1696, 1637 (C=O, C=N), 1345 (C=S) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.25 (d, J=16.1 Hz, 1H,=CH), 7.75–6.93 (m, 8H, Ar–H), 7.62 (s, 1H,=CH), 6.94 (d, J=15.5 Hz, 1H,=CH), 2.46 (s, 3H, Ph-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.5 (C=O, keton), 187.3 (C=S), 167.2 (NC=O), 141.7, 141.5, 140.2, 136.0, 132.3, 132.1, 131.5, 130.5, 130.3, 128.3, 127.9, 127.8, 127.3, 119.7 (C=C), 21.4

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($ArCH_3$); Anal. Calcd. For $C_{20}H_{14}ClNO_2S_2$ (400 g/mol): C, 60.07; H, 3.53; N, 3.50; S, 16.04. Found: C, 60.12; H, 3.51; N, 3.53; S, 16.13%.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.04.069.

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