Tetrahedron xxx (2013) 1–12

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

2-Alkylidene-4-oxothiazolidine *S*-oxides: synthesis and stereochemistry

Zdravko Džambaski [a,b], Rade Marković [a,c,†], Erich Kleinpeter [b,*], Marija Baranac-Stojanović [a,c,*]

[a] *Center for Chemistry ICTM, University of Belgrade, P.O. Box 473, 11000 Belgrade, Serbia*
[b] *Chemisches Institut der Universität Potsdam, Karl-Liebknecht Str. 24-25, D-14476 Potsdam (Golm), Germany*
[c] *Faculty of Chemistry, University of Belgrade, Studentski trg 16, P.O. Box 158, 11000 Belgrade, Serbia*

ARTICLE INFO

Article history:
Received 23 March 2013
Received in revised form 9 May 2013
Accepted 20 May 2013
Available online xxx

Keywords:
2-Alkylidene-4-oxothiazolidine
Sulfoxide
Diastereoselectivity
Density functional calculations
CH···O hydrogen bonds

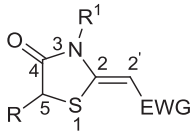
ABSTRACT

A series of 5-unsubstituted and 5-substituted 2-alkylidene-4-oxothiazolidine-*S*-oxides were synthesized by the sulfur-oxidation with *m*-CPBA. The stereochemistry of 5-substituted sulfoxides was determined by means of NMR spectroscopy and DFT theoretical calculations. It was found that the thermodynamically less stable *anti*-isomer was initially formed in the course of the oxidation, but it underwent epimerization to the mixture enriched in the more stable *syn*-isomer, during the work-up process. The higher stability of *syn*-isomers is ascribed to the stronger hyperconjugative $\sigma_{C-H} \rightarrow \sigma^*_{S-O}$ interaction versus the weaker $\sigma_{C-C} \rightarrow \sigma^*_{S-O}$ delocalization in their *anti*-counterparts and to the existence of intramolecular 1,5-CH···O hydrogen bonds.

1. Introduction

The 4-oxothiazolidine core is an important structural motif of biologically active compounds.[1] A wide range of pharmacological activities, such as antibacterial,[2] antiviral,[3] anti-inflammatory,[4] antifungal,[5] analgesic,[6] or anticancer[7] have been reported. A subclass constitutes 4-oxothiazolidine derivatives possessing an exocyclic double bond at the C-2 position of the ring, with some of them registered as nontoxic, active substances in treatment of neurological diseases (Ralitoline—an antiepileptic),[8] liver diseases (Piprozoline—a choleretic), or for treatment of hypertension (Etozolin—a diuretic) (Fig. 1).

The sulfoxide functional group is common in pharmaceutically important compounds and many sulfoxides are known to have high biological activity. Sulfur-oxidation of 4-oxothiazolidine ring may result in more potent compounds.[9] Having this in mind, we investigated the oxidation of a series of 2-alkylidene-4-oxothiazolidines **1** into sulfoxides and analyzed the origin of diastereoselectivity observed in the case of 5-substituted derivatives. In addition, sulfoxides are important synthetic intermediates and can be employed for further functionalization of thiazolidines **1**.



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R = H, Me, CH_2CO_2Et
R^1 = Me, Bn, $(CH_2)_3Br$, CH_2CO_2Et
EWG (electron-withdrawing group) = CONHPh, $CONH(CH_2)_2Ph$, CO_2Et, COPh

2. Results and discussion

The starting 4-oxothiazolidines **4** were prepared by the base-catalyzed reaction of α-mercapto esters **2** and α-substituted nitriles **3**, as already described[10] (Scheme 1). N-Alkylation was achieved with MeI, BnBr, $Br(CH_2)_3Br$ or $BrCH_2CO_2Et$ in moderate to high yields (53–97%), under mild reaction conditions (Table 1 and Scheme 1). After an initial screening of different agents, *meta*-chloroperbenzoic acid (*m*-CPBA) was chosen for the oxidation step (Table 2). When used in reagent/substrate 1.5–2/1 molar ratio, sulfone formation was minimized[11] and sulfoxides **5** were isolated in good yields (65–95%, Table 1). All the products **1**, **4** and **5** were obtained exclusively as *Z* isomers, concerning the configuration around the C=C double bond.[12] 5-Substituted substrates **1j**–**r** were oxidized with moderate to good diastereoselectivity, as evidenced

* Corresponding authors. Tel.: +381 11 3336740; fax: +381 11 2636061 (M.B.-S.); tel.: +49 331 977 5210/5211; fax: +49 331 977 5064/5057 (E.K.); e-mail addresses: ekleinp@uni-potsdam.de (E. Kleinpeter), mbaranac@chem.bg.ac.rs (M. Baranac-Stojanović).
† 1946–2012.

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http://dx.doi.org/10.1016/j.tet.2013.05.087

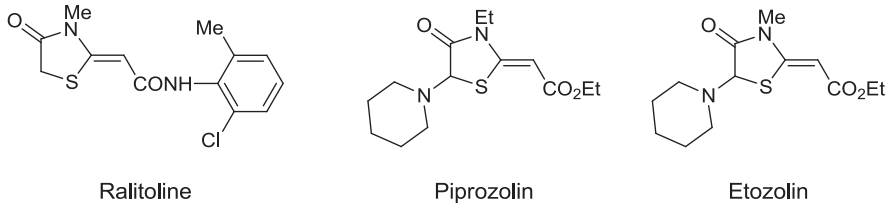
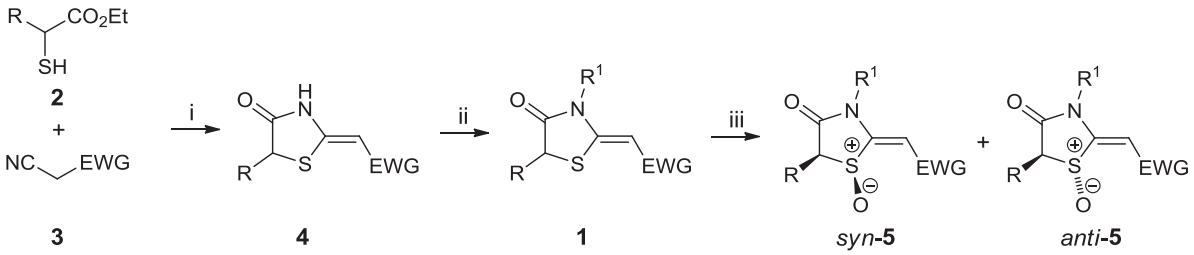


Fig. 1. Thiazolidine derivatives registered as drugs.



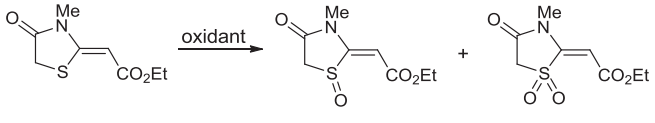
Scheme 1. Reagents and conditions: (i) K_2CO_3 cat., EtOH, reflux; (ii) MeI, BnBr, $Br(CH_2)_3Br$, or $BrCH_2CO_2Et$ (1.1–1.5 equiv), K_2CO_3 (1 equiv), DMF, rt; (iii) *m*-CPBA (1.5–2 equiv), CH_2Cl_2, 0 °C.

Table 1
Yields[a] of N-alkylated products **1**, sulfoxides **5**, experimental and calculated[b] *syn*/*anti* ratio for 5-substituted derivatives **5** and their relative free energy

R	R^1	EWG	**1** (%)	**5** (%)	Ratio *syn*/*anti* exp (calcd)	Relative free energy (kcal/mol) *syn*/*anti*
H	Me	CONHPh	**1a** (97)	**5a** (75)	—	—
H	Me	$CONH(CH_2)_2Ph$	**1b** (95)	**5b** (85)	—	—
H	Me	CO_2Et	**1c** (73)	**5c** (80)	—	—
H	Me	COPh	**1d** (95)	**5d** (74)	—	—
H	Bn	CONHPh	**1e** (64)	**5e** (72)	—	—
H	Bn	CO_2Et	**1f** (82)	**5f** (95)	—	—
H	Bn	COPh	**1g** (89)	**5g** (69)	—	—
H	$(CH_2)_3Br$	CO_2Et	**1h** (94)	**5h** (84)	—	—
H	CH_2CO_2Et	CO_2Et	**1i** (93)	**5i** (84)	—	—
Me	Me	CONHPh	**1j** (89)	**5j** (71)	85/15 (87/13)	0/1.15
Me	Me	$CONH(CH_2)_2Ph$	**1k** (87)	**5k** (65)	86/14 (81/19)	0/0.87
Me	Me	CO_2Et	**1l** (79)	**5l** (93)	86/14 (85/15)	0/1.01
Me	Me	COPh	**1m** (53)	**5m** (73)	85/15 (87/13)	0/1.13
Me	Bn	CONHPh	**1n** (66)	**5n** (76)	87/13 (93/7)	0/1.58
Me	Bn	CO_2Et	**1o** (92)	**5o** (85)	86/14 (91/9)	0/1.41
Me	$(CH_2)_3Br$	CO_2Et	**1p** (72)	**5p** (85)	87/13 (83/17)	0/0.93
CH_2CO_2Et	Bn	CONHPh	**1q** (77)	**5q** (79)	79/21[c] (94/6)	0/1.60
CH_2CO_2Et	Bn	COPh	**1r** (93)	**5r** (71)	77/23[c] (90/10)	0/1.27

[a] Yields of isolated products.
[b] At the B3LYP/6-31G* level, based on the relative free energy of diastereomers.
[c] Not completely equilibrated.

Table 2
Screening of oxidizing agents



Oxidant	Solvent	Temp (°)/Time (h)	Yield[a]	
			5c	**6c**
H_2O_2 (7.5 equiv)	$CHCl_3$/MeOH 2/1 v/v	0/1	0	0
H_2O_2 (7.5 equiv)	$CHCl_3$/MeOH 2/1 v/v	25/20	0	0
H_2O_2 (7.5 equiv)	$CHCl_3$/MeOH 2/1 v/v	Reflux/6	0	0
$NaIO_4$ (1.2 equiv)	MeOH/H_2O 3/1 v/v	25/72	21	0
Oxone (1.2 equiv)	MeOH/H_2O 1/1 v/v	0/1	27	19
m-CPBA (1.125 equiv)	CH_2Cl_2	0/1	80	1

[a] Yields of isolated products.

from the NMR spectroscopic data of isolated products where two sets of signals appeared, one prevailing. On the basis of ^{1}H NMR data, diastereomeric ratio was calculated to range from ~79/21 for **5q**,**r** to ~87/13 for **5j**–**p**. It was necessary to identify whether the *syn* or *anti* diastereomer was the major product.

Having a sulfoxide in hand, it is often a challenge to determine its configuration. Apart from an X-ray analysis requiring well-defined single crystals, general and reliable methods for configurational assignments are lacking. An assessment of stereochemistry directly from NMR spectroscopic data is not possible since coupling constants or NOE contacts with oxygen are inaccessible. Some relations between chemical shifts of neighbouring hydrogen and carbon atoms and the configuration of the sulfoxide group have been observed,[13] but are applicable only to specific cases. Although magnetic anisotropy of the sulfoxide group has been predicted to be acetylene-like,[14] it is weak due to the single bond character of the SO bond.[15] Unfortunately, in the synthesized compounds **5j**–**r** the ^{1}H NMR chemical shift difference of C5–H and C5–CH_3

between the two diastereomers is too small (0.1–0.3 ppm, Table 3) to be of use for structure determination. In addition, all attempts to obtain a single crystal suitable for an X-ray analysis resulted in a mixture of isomers. So, we turned our attention to computational methods, the use of which is now widespread among experimental chemists to solve various stereochemical problems.[16] Using quantum chemical calculations it is possible to accurately predict NMR chemical shifts,[17] which then allows one to distinguish between stereoisomers by comparing calculated and experimental values. documented γ-*gauche* effect. It has been suggested by Dračínský et al.[16a,b] to employ ^{13}C NMR chemical shift changes ($\Delta\delta$) induced by sulfur-oxidation as a means to differentiate between stereoisomeric sulfoxides in which the sulfoxide group is contained in various five- and six-membered rings. The corresponding experimental and theoretically calculated values for the synthesized sulfoxides **5j**–**r** are listed in Table 3 and they proved useful in the present case, as well. These differences obviously arise from the above mentioned steric and electric field effects and go in the following direction:

Table 3
Selected experimental[a] and calculated[b] ^{1}H NMR and ^{13}C NMR chemical shifts, and the ^{13}C NMR chemical shifts changes ($\Delta\delta$) induced by the oxidation

Compound		^{1}H NMR (ppm)		^{13}C NMR (ppm)				$\Delta\delta^c$ (ppm)			
		Exp $CDCl_3$/DMSO-d_6		C5		C5–CH_3		C5		C5–CH_3	
		C5–H	C5–CH_3	Exp	Calcd	Exp	Calcd	Exp	Calcd	Exp	Calcd
5j	*syn*	–/3.89	–/1.36	52.5	57.1	6.6	8.6	12.7	12.5	−12.3	−11.4
	anti	–/3.65	–/1.40	59.5	63.0	11.7	14.4	19.7	18.3	−7.2	−5.5
5k	*syn*	3.31/3.82	1.57/1.33	53.2	56.9	6.8	8.6	12.7	12.3	−12.2	−11.6
	anti	3.50/3.56	1.49/1.35	59.6	65.5	12.4	13.6	19.2	20.9	−6.6	−6.6
5l	*syn*	3.42/3.95	1.63/1.36	53.3	57.4	6.7	8.4	12.8	12.3	−12.3	−11.6
	anti	3.63/3.74	1.56/1.44	59.9	63.5	12.3	14.6	19.3	18.4	−6.7	−5.4
5m	*syn*	3.44/3.98	1.65/1.38	53.1	57.0	6.9	8.6	12.9	12.4	−11.6	−11.1
	anti	3.67/3.78	1.59/1.48	59.7	62.9	12.4	14.6	19.5	18.3	−6.2	−5.1
5n	*syn*	–/4.11	–/1.42	52.6	58.0	6.6	8.7	13.0	13.7	−12.5	−11.8
	anti	–/3.80	–/1.46	59.2	63.1	11.7	13.3	19.6	18.8	−7.4	−7.2
5o	*syn*	3.48/4.16	1.67/1.42	53.5	58.4	6.7	8.5	13.2	13.7	−12.6	−12.0
	anti	3.71/3.90	1.58/1.48	59.6	63.5	12.4	13.2	19.2	18.7	−7.0	−7.3
5p	*syn*	3.39/–	1.62/–	53.5	57.1	6.6	8.4	13.1	12.4	−12.4	−11.6
	anti	3.63/–	1.54/–	59.6	63.2	12.2	14.4	19.2	18.5	−6.8	−5.6
		C5–H	C5–CH_2	C5		C5–CH_2		C5		C5–CH_2	
5q	*syn*	–/4.47	–/2.94, 3.09	53.8	59.5	27.4	27.5	12.8	13.6	−9.4	−12.8
	anti	–/3.93	–/3.23, 3.54	61.6	66.6	31.8	33.5	20.6	20.7	−4.9	−6.8
5r	*syn*	4.01/4.48	3.23, 3.27/2.95; 3.10	54.6	59.4	27.3	27.6	13.3	13.3	−9.9	−12.5
	anti	3.75/3.97	3.41, 3.44/–	62.1	66.6	32.3	32.8	20.8	20.8	−5.0	−7.3

[a] Data are from DMSO-d_6 solution for **5j**, **5n** and **5q**, and from $CDCl_3$ solution for all others.
[b] At the B3LYP/6-31G* theory level, in the gas phase, relative to TMS.
[c] Difference between chemical shift values of sulfoxides **5** and thiazolidines **1**.

For this purpose the structures **5j**–**r** were optimized in the gas phase at the B3LYP/6-31G* level.[18] NMR chemical shifts were calculated at the same level using the GIAO method[19] and were plotted against the experimental values (Fig. 2).[20] An excellent correlation gave evidence for reliable calculated structures and allowed the stereochemistry determination: the major isomer proved to be *syn*. The most diagnostic chemical shift values are those for carbon atoms at the α- (C5) and β-positions (C5–CH_3), which differ by ~6 ppm between the two isomers (Table 3). A diamagnetic shift observed for *syn*-isomers arises from steric and electric field effects, in the case of the C5–CH_3 being the well

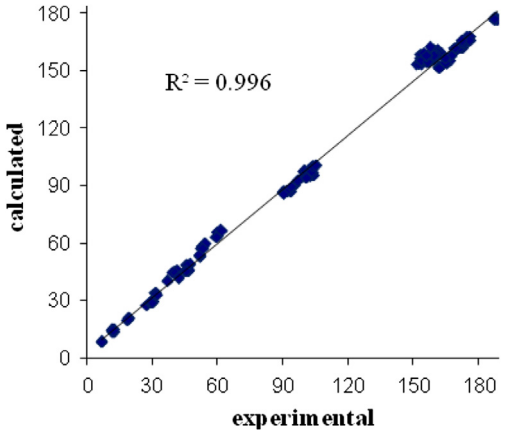


Fig. 2. Computed ^{13}C NMR chemical shifts against the experimental ones.

paramagnetic shift for the α-carbon is higher for *anti*-isomers, whereas diamagnetic shift for the β-carbon (CH_3/CH_2 group) is larger for *syn*-isomers. Interestingly, the C5–CH_3 and C5–H signals in the proton NMR spectra exchange their relative position upon shifting from the non-polar solvent to the polar one. Thus, the C5–CH_3 (C5–H) protons of *syn*-isomers resonate at lower (higher) field with respect to *anti*-isomers in chloroform solution, but at higher (lower) field in DMSO solution (Table 3, Fig. S1 in the Supplementary data).

Almost no change in the ^{13}C NMR chemical shifts of the C2 atoms experimentally observed after the sulfur-oxidation (Table 4) results from the two opposing effects: paramagnetic shift due to the –I effect of the sulfoxide group and diamagnetic shift coming from the decrease in the push–pull effect of the C=C double bond. This latter effect is the reason for the observed paramagnetic movement of the C2′ carbon resonances. The overall result is the decrease in the ^{13}C NMR chemical shift difference between the two carbons of the double bond, $\Delta\delta_{C=C}$, in the oxidized products (Table 4). Namely, all thiazolidine derivatives **1a**–**r** and **5a**–**r** belong to the class of the so-called push–pull alkenes, possessing one or two electron-donating substituents at one end of the double bond and one or two electron-accepting groups at the other. Electronic interactions between the donor and acceptor groups via the C=C double bond reduces its π-bond order and strongly influences its dynamic behaviour and chemical reactivity.

Among several parameters, such as the restricted rotation about the partial C=C double bond,[21] bond length[22] and the occupation quotient π^*/π,[21d,23] this push–pull effect can also be quantified by the ^{13}C NMR chemical shift difference between the two carbons of the double bond, which increase with increasing push–pull

Table 4
Experimental[a] ^{13}C NMR chemical shifts for the two carbons of the C=C double bond and their difference ($\Delta\delta_{C=C}$)

	^{13}C NMR (ppm)					^{13}C NMR (ppm)		
	C2	C2′	$\Delta\delta_{C=C}$			C2	C2′	$\Delta\delta_{C=C}$
1a	155.3	93.7	61.6	**5a**		156.5	102.4	54.1
1b	152.9	93.6	59.3	**5b**		155.2	102.8	52.4
1c	158.6	90.7	67.9	**5c**		158.4	100.2	58.2
1d	161.8	95.7	66.1	**5d**		159.2	102.7	56.5
1e	154.5	94.4	60.1	**5e**		155.7	102.8	52.9
1f	158.6	90.3	68.3	**5f**		159.4	98.93	60.5
1g	160.6	97.0	63.6	**5g**		157.7	104.3	53.4
1h	157.6	90.6	67.0	**5h**		157.5	100.5	57.0
1i	157.3	90.7	66.6	**5i**		157.2	100.7	56.5
1j	153.5	93.5	60.0	**5j**	*syn*	154.7	103.2	51.5
					anti	154.7	103.8	50.8
1k	153.6	92.3	61.4	**5k**	*syn*	153.5	103.8	49.6
					anti	153.5	104.1	49.4
1l	157.3	90.2	67.1	**5l**	*syn*	157.1	100.6	56.5
					anti	157.1	100.9	56.2
1m	160.4	95.3	65.1	**5m**	*syn*	157.8	103.1	54.7
					anti	158.0	103.3	54.7
1n	152.5	94.1	58.4	**5n**	*syn*	153.8	103.8	50.0
					anti	153.8	104.6	49.2
1o	156.2	91.4	64.8	**5o**	*syn*	155.9	101.7	54.2
					anti	156.0	102.1	53.9
1p	156.3	90.1	66.2	**5p**	*syn*	156.1	100.8	55.3
					anti	156.1	101.1	55.0
1q	153.2	94.3	58.9	**5q**	*syn*	154.2	103.9	50.3
					anti	154.8	102.8	52.0
1r	159.3	97.0	62.3	**5r**	*syn*	156.4	105.4	51.0
					anti	157.6	103.3	54.3

[a] Data are from DMSO-d_6 solution for **1a**/**5a**, **1b**/**5b**, **1e**/**5e**, **1f**/**5f**, **1j**/**5j**, **1n**/**5n** and **1q**/**5q**, and from $CDCl_3$ solution for all others.

character.[21b,23a,24] The experimental chemical shifts for the C2 and C2′ atoms and their differences, $\Delta\delta_{C=C}$, for compounds **1a**–**r** and **5a**–**r** are given in Table 4. The observed decrease in the push–pull activity results from the substitution of a good electron donor, the sulfide, by a poor donor, the sulfoxide. The stabilization energies of the sulfur lone pair conjugative interaction with the π*-antibonding orbital of the C=C double bond drastically decrease upon oxidation. For example, this energy, obtained from the second order perturbation theory analysis of Fock matrix in the NBO basis,[25] for **1c** amounts 24.4 kcal/mol, but only 0.7 kcal/mol for **5c**. Though significantly reduced, the sulfur lone pair $n\rightarrow\pi^*_{C=C}$ donation in sulfoxides still exists and it has already been shown that the sulfoxide group can act as an electron donor.[26] However, its net effect on the double bond of compounds **5** is electron attraction: the π-electron density is attracted into the σ* S–O orbital, as evidenced from the corresponding stabilization energy of 2.6 kcal/mol for **5c**. The reduction in the sulfur lone pair donation to the C=C double bond is mainly caused by the presence of the electronegative oxygen at the sulfur atom, but also by stereoelectronic factors: while one of the sulfur's lone pairs in compounds **1** is p-like and is in plane with the π* orbital of the double bond, which allows a significant $n_S\rightarrow\pi^*_{C=C}$ delocalization, this is not the case for sulfoxides with the sp^3 hybridization of the sulfur (Fig. 3). The difference in the $\Delta\delta_{C=C}$ values between the *syn*- and *anti*-isomers is, however, too small and not regular to be of use for stereochemistry determination.

The free energies, predicted at the same theory level employed for the structure optimizations, favour *syn*-isomers by 0.9–1.6 kcal/mol (Table 1). Experimentally observed and computed *syn*/*anti* ratios are in good agreement and they point to a thermodynamic control of the oxidation reactions. This was corroborated when the oxidation of **1l** was monitored by NMR spectroscopy in $CDCl_3$, at 0 °C: *anti*-**5l** was initially formed as the major product, as a result of steric approach control (attack of the oxidizing agent from the less hindered side) (Fig. S2 in the Supplementary data). The initial *syn*/*anti* ratio of 28/72 did not change during the reaction time. However, due to the facile isomerization of sulfoxides having an α-hydrogen,[13b,27] the *anti*-**5l** underwent epimerization to the equilibrium mixture (*syn*/*anti* 86/14, Table 1) during the work-up process. In order to learn why *syn*-isomers are more stable than their *anti*-counterparts donor–acceptor interactions and their stabilization energies have been examined. The main difference in the hyperconjugative interactions between the two isomers comes from the $\sigma_{C5-H}\rightarrow\sigma^*_{S-O}$ existing in the *syn*-isomers (E2 values: 1.42–1.6 kcal/mol; dihedral H–C5–S–O angles: from −161.2 to −167.7°), but replaced by the weaker $\sigma_{C5-C5'}\rightarrow\sigma^*_{S-O}$ interaction in the *anti*-isomers (E2 values: 0.63–0.79 kcal/mol; dihedral H_3C–C5–S–O angles: from −109.5 to −158.2°) (Fig. 4 and Table 5).

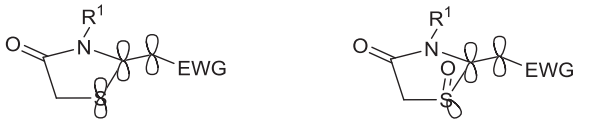


Fig. 3. Orbitals in the parent compounds **1** and sulfoxides **5**.

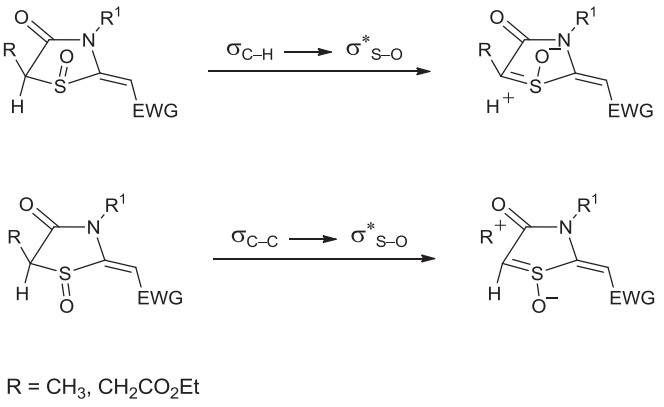


Fig. 4. Hyperconjugative interactions in *syn*- and *anti*-sulfoxides **5**.

Please cite this article in press as: Džambaski, Z.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.05.087

Table 5
Calculated dihedral angles and energies (E2)[a] of $\sigma_{C-H}\rightarrow\sigma^*_{S-O}$ and $\sigma_{C-C}\rightarrow\sigma^*_{S-O}$ interactions for *syn*- and *anti*-**5**, respectively

Compound	*syn*-isomer		*anti*-isomer	
	$\tau_{H-C5-S-O}$ (°)	$\sigma_{C-H}\rightarrow\sigma^*_{S-O}$ (kcal/mol)	$\tau_{C-C5-S-O}$ (°)	$\sigma_{C-C}\rightarrow\sigma^*_{S-O}$ (kcal/mol)
5j	−161.6	1.56	−145.1	0.67
5k	−161.2	1.55	−109.5	—
5l	−161.3	1.56	−141.4	0.63
5m	−161.4	1.55	−143.6	0.65
5n	−167.7	1.55	−158.2	0.79
5o	−167.4	1.60	−157.5	0.79
5p	−162.2	1.57	−144.1	0.67
5q	−163.4	1.44	−119.4	—
5r	−162.7	1.42	−113.3	—

[a] Obtained from the second order perturbation theory analysis of Fock matrix in the NBO basis.

In addition, the *syn*-isomers are also preferred by the electrostatic effects, the so-called CH···O hydrogen bonds[28] occurring between the positively charged methyl/methylene hydrogens and the negatively charged sulfoxide oxygen atom (Fig. 5; optimized structures of *syn*-**5l** and *syn*-**5q** are shown). The calculated partial charge of the hydrogen atom of *syn*-**5l** (0.20e; $1e=1.602\times10^{-19}$ C) that interacts with the oxygen (−0.60e) is larger than the charges of the other hydrogen atoms (0.16 and 0.18e) and the H···O distance of 2.56 Å is shorter than the expected van der Waals separation of 2.72 Å. In the case of *syn*-**5q** the H···O distance is even shorter and amounts 2.47 Å. Here, another methylene hydrogen is involved in hydrogen bonding with the carbonyl oxygen atom and the calculated partial charges of the two H atoms are very similar (0.224 and 0.215e, Fig. 5). Now, the above mentioned puzzling reversal of position of the C5−CH_3 signals in the ^{1}H NMR spectra of *syn*- and *anti*-isomers in the two solvents of different polarity (Table 3) can be rationalized. Intramolecularly hydrogen bonded CH_3 in *syn*-isomers resonates at lower field in the chloroform solution with respect to the CH_3 in *anti*-isomers. In DMSO solution the intermolecular hydrogen bonds formed between the CH_3 and the solvent molecules become stronger with the *anti*-isomers, resulting in paramagnetic shift of their signals. The downfield movement of proton chemical shift of hydrogen bonded CH protons has already been observed.[28d,29] In the same manner, the ^{1}H NMR chemical shift position reversal observed for the C5−H signals can be accounted for by the formation of a hydrogen bond between the C5−H and sulfoxide oxygen in the *anti*-isomers. This hydrogen bond is weaker than that of the CH_3 group (the CH···O distance for *anti*-**5l** amounts 2.64 Å). Substituents attached at the N3 and C2′ positions do not affect the relative stability of isomers and diastereoselectivity of the reaction.

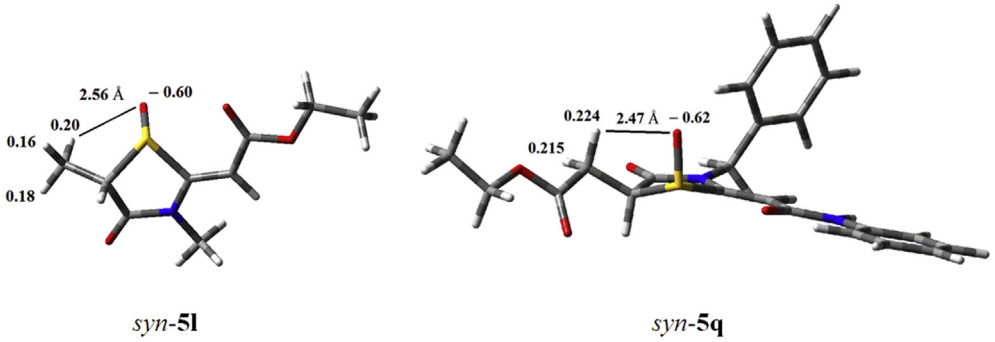


Fig. 5. Optimized structures (B3LYP/6-31G*) of *syn*-**5l** and *syn*-**5q**.

3. Conclusion

A series of 5-unsubstituted and 5-substituted 2-alkylidene-4-oxothiazolidine-*S*-oxides **5** were synthesized by the sulfur-oxidation of the parent sulfides **1** with *m*-CPBA. The products were obtained in good yields, 65–95%, and with moderate to good diastereoselectivity in the case of 5-substituted derivatives (de 54–74%). The stereochemistry of 5-substituted products was elucidated by means of NMR spectroscopy and theoretical calculations. While the stereochemistry of the oxidation step is controlled by the reagent (*m*-CPBA) approach from the less hindered side, the final stereochemical outcome is governed by the relative stability of the isomers and is the result of the facile epimerization at the α-carbon. The greater stability of *syn*-isomers arises from intramolecular 1,5-CH···O hydrogen bonding stabilization and stronger $\sigma_{C-H}\rightarrow\sigma^*_{S-O}$ hyperconjugative interaction versus the weaker $\sigma_{C-C}\rightarrow\sigma^*_{S-O}$ overlap in the *anti*-isomers.

4. Computational details

All calculations were done using Gaussian 03 program package.[30] Geometries were optimized at the B3LYP/6-31G* level of theory,[18] followed by frequency calculations to verify the nature of stationary points and to obtain thermochemical parameters. Magnetic shieldings were computed at the same level using the GIAO method.[19] NMR chemical shifts were calculated relative to TMS. Solvent effects on chemical shift values were modelled as IEF-PCM.[31]

5. Experimental

5.1. General

Melting points were determined on a Stuart SMP10 apparatus. The IR spectra were recorded on a Perkin–Elmer FT-IR 1725X spectrophotometer and are reported as wave numbers (cm^{-1}). The NMR spectra were recorded on a Varian Gemini 2000 spectrometer (^{1}H at 200 MHz, ^{13}C at 50.3 MHz) and on a Bruker Ultrashield Advance III (^{1}H at 500.26 MHz, ^{13}C at 125.79 MHz) in DMSO-d_6 or $CDCl_3$. Chemical shifts are given in parts per million downfield from TMS as an internal standard. ^{13}C NMR resonance assignments were aided by the use of the DEPT technique to determine the number of attached hydrogens. Elemental analyses were performed at the microanalysis laboratory at the Centre for Chemistry ICTM. HRMS was carried out on 6210 Time-of-Flight LC/MS (G1969A, Agilent Technologies) coupled with 1200 Series HPLC system (Agilent Technologies). Thin-layer chromatography (TLC) was carried out on Kieselgel G nach Stahl and spots were visualized by iodine or by 50% H_2SO_4. Column chromatography was carried out on SiO_2 (silica

gel 60 Å, 12–26, ICN Biomedicals). All solvents were distilled before use. DMF was distilled over CaH_2.

5.2. General procedure for the preparation of *N*-methyl derivatives 1a–d and 1j–m

Methyl iodide (1.1–1.5 mmol) was added to a stirred mixture of 4-oxothiazolidine **4** (1 mmol) and K_2CO_3 (1 mmol) in DMF (2–5 mL) and stirring was continued at rt until the disappearance of the starting material (TLC). The products were precipitated by pouring a threefold quantity of water onto the reaction mixture, filtrated and air-dried. In the case of **1k** and **1m** the precipitate was not suitable for filtration and the aqueous phase was extracted with ethyl acetate (**1k**) or CH_2Cl_2 (**1m**) and the organic layer was washed with water (3×8 mL), brine solution (1×8 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (gradient toluene/ethyl acetate).

*5.2.1. (Z)-(3-Methyl-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**1a**).* Compound **1a** was obtained from **4** (1.76 g; 7.50 mmol; R=H, EWG=CONHPh), K_2CO_3 (1.04 g; 7.50 mmol), CH_3I (1.60 g; 11.25 mmol; 1.5 equiv) in DMF (20 mL) according to the general procedure (reaction time 2 h) as a white solid (1.80 g; 97%); mp 205–208 °C; R_f=0.32 (toluene/ethyl acetate 3/2); IR (ATR): ν=3544, 3457, 3296, 2964, 1712, 1649, 1594, 1560, 1540, 1489, 1441, 1344, 1307, 1195, 1118, 795, 754, 690 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 3.09 (s, 3H, CH_3), 3.78 (s, 2H, CH_2S), 5.79 (s, 1H, =CH), 6.70 (t, J=7.3 Hz, 1H, *p*-Ph), 7.28 (m, 2H, *m*-Ph), 7.59 (d, J=7.8 Hz, 2H, *o*-Ph), 9.90 (s, 1H, NH_{amide}), 11.53 (broad s, 1H, NH_{lactam}); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 29.9 (CH_3), 31.4 (CH_2S), 93.7 (=CH), 118.8 (*o*-Ph), 122.9 (*p*-Ph), 129.0 (*m*-Ph), 140.0 (C1–Ph), 155.3 (C=), 165.3 (CO_{amide}), 172.5 (CO_{lactam}); HRMS: calcd for $C_{12}H_{13}N_2O_2S$ $[M+H]^+$ 249.0692, found 249.0696; Anal. Calcd for $C_{12}H_{12}N_2O_2S$: C, 58.05; H, 4.87; N, 11.28; S, 12.91; found: C, 58.01; H, 4.92; N, 10.98; S, 12.63.

*5.2.2. (Z)-(3-Methyl-4-oxothiazolidin-2-ylidene)-N-(2-phenylethyl) ethanamide (**1b**).* Compound **1b** was obtained from **4** (1.31 g; 5.00 mmol; R=H, EWG=CONH$(CH_2)_2$Ph), K_2CO_3 (0.69 g; 5.00 mmol), CH_3I (0.85 g; 6.00 mmol; 1.2 equiv) in DMF (15 mL) according to the general procedure (reaction time 1.5 h) as a white solid (1.31 g; 95%); mp 177–179 °C; R_f=0.52 (toluene/acetone 7/3); IR (ATR): ν=3260, 3066, 2968, 2934, 1712, 1629, 1569, 1550, 1451, 1338, 1286, 1216, 1121, 863, 803, 752, 701 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 2.72 (t, J=7.3 Hz, 2H, CH_2Ph), 3.02 (s, 3H, CH_3), 3.28–3.38 (m, 2H, NCH_2), 3.72 (s, 2H, CH_2S), 5.59 (s, 1H, =CH), 7.16–7.34 (m, 5H, Ph), 7.84 (t, J=5.6 Hz, 1H, NH_{amide}); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 29.7 (CH_3), 31.3 (CH_2S), 35.6 (CH_2Ph), 40.3 (NCH_2), 93.6 (=CH), 126.3 (*p*-Ph), 128.6 (*o*-Ph), 128.8 (*m*-Ph), 139.8 (C1–Ph), 152.9 (C=), 166.5 (CO_{amide}), 172.4 (CO_{lactam}); ^1H NMR ($CDCl_3$, 200 MHz): δ 2.86 (t, J=6.8 Hz, 2H, CH_2Ph), 3.11 (s, 3H, CH_3), 3.55–3.66 (m, 2H, NCH_2), 3.66 (s, 2H, CH_2S), 5.31 (s, 1H, =CH), 5.42 (broad t, 1H, NH_{amide}), 7.19–7.34 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 29.8 (CH_3), 31.8 (CH_2S), 35.8 (CH_2Ph), 40.5 (NCH_2), 92.7 (=CH), 126.5 (*p*-Ph), 128.6 (*o*-Ph), 128.8 (*m*-Ph), 139.0 (C1–Ph), 155.2 (C=), 166.8 (CO_{amide}), 172.4 (CO_{lactam}); HRMS: calcd for $C_{14}H_{17}N_2O_2S$ $[M+H]^+$ 277.1005, found 277.1005; Anal. Calcd for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14; S, 11.60; found: C, 61.15; H, 6.06; N, 10.13; S, 11.33.

*5.2.3. (Z)-Ethyl (3-methyl-4-oxothiazolidin-2-ylidene)ethanoate (**1c**).* Compound **1c** was obtained from **4** (1.17 g; 6.25 mmol; R=H, EWG=CO_2Et), K_2CO_3 (0.86 g; 6.25 mmol), CH_3I (0.98 g; 6.88 mmol; 1.1 equiv) in DMF (15 mL) according to the general procedure (reaction time 1.5 h) as a white solid (0.94 g; 73%); mp 99–100 °C; R_f=0.57 (toluene/ethyl acetate 7/3); IR (KBr): ν=2982, 2942, 1708, 1676, 1562, 1427, 1366, 1340, 1275, 1180, 1118, 805 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 1.20 (t, J=7.2 Hz, 3H, CH_3CH_2), 3.08 (s, 3H, NCH_3), 3.85 (s, 2H, CH_2S), 4.10 (q, J=7.2 Hz, 2H, CH_2O), 5.57 (s, 1H, =CH); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 14.5 (CH_3CH_2), 29.9 (NCH_3), 31.6 (CH_2S), 59.4 (CH_2O), 89.6 (=CH), 159.7 (C=), 167.2 (CO_{ester}), 172.7 (CO_{lactam}); ^1H NMR ($CDCl_3$, 200 MHz): δ 1.30 (t, J=7.2 Hz, 3H, CH_3CH_2), 3.17 (s, 3H, NCH_3), 3.72 (s, 2H, CH_2S), 4.22 (q, J=7.2 Hz, 2H, CH_2O), 5.49 (s, 1H, =CH); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 14.3 (CH_3CH_2), 29.9 (NCH_3), 31.8 (CH_2S), 60.0 (CH_2O), 90.7 (=CH), 158.6 (C=), 167.6 (CO_{ester}), 172.3 (CO_{lactam}); HRMS: calcd for $C_8H_{12}NO_3S$ $[M+H]^+$ 202.0532, found 202.0525; Anal. Calcd for $C_8H_{11}NO_3S$: C, 47.75; H, 5.51; N, 6.96; S, 15.93; found: C, 47.71; H, 5.40; N, 7.04; S, 16.12.

*5.2.4. (Z)-(3-Methyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**1d**).* Compound **1d** was obtained from **4** (1.64 g; 7.50 mmol; R=H, EWG=COPh), K_2CO_3 (1.04 g; 7.50 mmol), CH_3I (1.17 g; 8.25 mmol; 1.1 equiv) in DMF (15 mL) according to the general procedure (reaction time 1.5 h) as a pale yellow solid (1.67 g; 95%); mp 173–174 °C; R_f=0.39 (toluene/ethyl acetate 4/1); IR (ATR): ν=3062, 3032, 2974, 2921, 1724, 1614, 1573, 1513, 1419, 1345, 1266, 1206, 1111, 1053, 909, 888, 745, 697 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 3.25 (s, 3H, CH_3), 3.85 (s, 2H, CH_2S), 6.92 (s, 1H, =CH), 7.47–7.63 (m, 3H, *m*- and *p*-Ph), 8.01–8.06 (m, 2H, *o*-Ph); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 30.3 (CH_3), 31.5 (CH_2S), 95.5 (=CH), 127.7 (*o*-Ph), 128.8 (*m*-Ph), 132.4 (*p*-Ph), 138.4 (C1–Ph), 162.68 (C=), 172.2 (CO_{lactam}), 187.5 (CO_{ketone}); ^1H NMR ($CDCl_3$, 200 MHz): δ 3.30 (s, 3H, CH_3), 3.70 (s, 2H, CH_2S), 6.68 (s, 1H, =CH), 7.42–7.58 (m, 3H, *m*- and *p*-Ph), 7.92–7.97 (m, 2H, *o*-Ph); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 30.2 (CH_3), 31.7 (CH_2S), 95.7 (=CH), 127.5 (*o*-Ph), 128.5 (*m*-Ph), 132.2 (*p*-Ph), 138.3 (C1–Ph), 161.8 (C=), 172.7 (CO_{lactam}), 188.6 (CO_{ketone}); HRMS: calcd for $C_{12}H_{12}NO_2S$ $[M+H]^+$ 234.0583, found 234.0572; Anal. Calcd for $C_{12}H_{11}NO_2S$: C, 61.78; H, 4.75; N, 6.00; S, 13.74; found: C, 61.44; H, 4.75; N, 5.94; S, 14.01.

*5.2.5. (Z)-(3,5-Dimethyl-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**1j**).* Compound **1j** was obtained from **4** (248 mg; 1.00 mmol; R=Me, EWG=CONHPh), K_2CO_3 (138 mg; 1.00 mmol), CH_3I (213 mg; 1.50 mmol; 1.5 equiv) in DMF (5 mL) according to the general procedure (reaction time 2.5 h) as a white solid (0.234 g; 89%); mp 168–170 °C; R_f=0.30 (toluene/ethyl acetate 7/3); IR (ATR): ν=3341, 1697, 1658, 1567, 1492, 1440, 1337, 1302, 1175, 1130, 1054, 761, 692 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 1.46 (d, J=7.3 Hz, 3H, CH_3CH), 3.11 (s, 3H, NCH_3), 4.02 (q, J=7.3 Hz, 1H, CHS), 5.80 (s, 1H, =CH), 7.00 (t, J=7.3 Hz, 1H, *p*-Ph), 7.28 (m, 2H, *m*-Ph), 7.59 (d, J=7.2 Hz, 2H, *o*-Ph), 9.88 (s, 1H, NH_{amide}); ^{13}C NMR (DMSO-d_6, 50,3 MHz): δ 18.9 (CH_3CH), 29.6 (NCH_3), 39.8 (CHS), 93.5 (=CH), 118.7 (*o*-Ph), 122.8 (*p*-Ph), 128.9 (*m*-Ph), 139.9 (C1–Ph), 153.5 (C=), 165.1 (CO_{amide}), 175.2 (CO_{lactam}); HRMS: calcd for $C_{13}H_{15}N_2O_2S$ $[M+H]^+$ 263.0849, found 263.0855.

*5.2.6. (Z)-(3,5-Dimethyl-4-oxothiazolidin-2-ylidene)-N-(2-phenylethyl) ethanamide (**1k**).* Compound **1k** was obtained from **4** (275 mg; 1.00 mmol; R=Me, EWG=CONH$(CH_2)_2$Ph), K_2CO_3 (138 mg; 1.00 mmol), CH_3I (170 mg; 1.20 mmol; 1.2 equiv) in DMF (4 mL) according to the general procedure (reaction time 1.5 h). Column chromatography (eluent: gradient toluene/ethyl acetate 100/0 to 60/40) gave pure **1k** as a colourless oil (234 mg; 87%). Crystallization from ethanol/water mixture 2/1 (v/v) gave a white solid, mp 87–89 °C; R_f=0.33 (toluene/ethyl acetate 3/2); IR (ATR): ν=3313, 3058, 2979, 2933, 1712, 1644, 1575, 1285, 1202, 1132, 1054, 794, 736, 702 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 1.42 (d, J=7.2 Hz, 3H, CH_3CH), 2.72 (t, J=7.3 Hz, 2H, CH_2Ph), 3.03 (s, 3H, NCH_3), 3.28–3.38 (m, 2H, NCH_2), 3.94 (q, J=7.2 Hz, 1H, CHS), 5.59 (s, 1H, =CH), 7.17–7.33 (m, 5H, Ph), 7.82 (t, J=5.6 Hz, 1H, NH); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 19.1 (CH_3CH), 29.8 (NCH_3), 35.6 (CH_2Ph), 39.6 (NCH_2), 40.2 (CHS), 93.4 (=CH), 126.3 (*p*-Ph), 128.6 (*o*-Ph), 128.8 (*m*-Ph), 139.8 (C1–Ph), 151.2 (C=), 166.4 (CO_{amide}), 175.2 (CO_{lactam}); ^1H NMR ($CDCl_3$, 200 MHz): δ 1.58 (d,

J=7.1 Hz, 3H, CH_3CH), 2.85 (t, J=7.0 Hz, 2H, CH_2Ph), 3.10 (s, 3H, NCH_3), 3.53–3.63 (m, 2H, NCH_2), 3.83 (q, J=7.1 Hz, 1H, CHS), 5.32 (s, 1H, =CH), 5.58 (broad t, 1H, NH), 7.18–7.36 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$, 50,3 MHz): δ 19.0 (*C*H_3CH), 29.9 (NCH_3), 35.8 (CH_2Ph), 40.2 (NCH_2), 40.5 (CHS), 92.3 (=CH), 126.4 (*p*-Ph), 128.6 (*o*-Ph), 128.7 (*m*-Ph), 138.9 (C1–Ph), 153.6 (C=), 166.8 (CO_{amide}), 175.5 (CO_{lactam}); HRMS: calcd for $C_{15}H_{19}N_2O_2S$ $[M+H]^+$ 291.1162, found 291.1167.

*5.2.7. (Z)-Ethyl (3,5-dimethyl-4-oxothiazolidin-2-ylidene)ethanoate (**1l**).* Compound **1l** was obtained from **4** (R=Me, EWG=CO_2Et) as already described.[32]

*5.2.8. (Z)-(3,5-Dimethyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**1m**).* Compound **1m** was obtained from **4** (350 mg; 1.50 mmol; R=H, EWG=COPh), K_2CO_3 (207 mg; 1.50 mmol), CH_3I (245 mg; 1.725 mmol; 1.15 equiv) in DMF (6 mL) according to the general procedure (reaction time 1.5 h). Column chromatography (eluent: gradient toluene/ethyl acetate 100/0 to 80/20) gave pure **1m** as a white solid (196 mg; 53%); mp 130–132 °C; R_f=0.52 (toluene/ethyl acetate 4/1); IR (ATR): ν=3394, 3061, 2980, 2938, 1711, 1624, 1516, 1347, 1224, 1052, 756, 704 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz): δ 1.49 (d, J=7.2 Hz, 3H, C*H*$_3$CH), 3.27 (s, 3H, NCH_3), 4.08 (q, J=7.2 Hz, 1H, CHS), 6.93 (s, 1H, =CH), 7.47–7.63 (m, 3H, *m*- and *p*-Ph), 8.01–8.06 (m, 2H, *o*-Ph); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 18.4 (*C*H_3CH), 30.5 (NCH_3), 39.8 (CHS), 95.4 (=CH), 127.7 (*o*-Ph), 128.8 (*m*-Ph), 132.4 (*p*-Ph), 138.4 (C1–Ph), 160.9 (C=), 176.1 (CO_{lactam}), 187.6 (CO_{ketone}); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.63 (d, J=7.3 Hz, 3H, C*H*$_3$CH), 3.31 (s, 3H, NCH_3), 3.88 (q, J=7.3 Hz, 1H, CHS), 6.67 (s, 1H, =CH), 7.42–7.57 (m, 3H, *m*- and *p*-Ph), 7.92–7.98 (m, 2H, *o*-Ph); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 18.6 (*C*H_3CH), 30.3 (NCH_3), 40.2 (CHS), 95.3 (=CH), 127.5 (*o*-Ph), 128.5 (*m*-Ph), 132.2 (*p*-Ph), 138.4 (C1–Ph), 160.4 (C=), 176.0 (CO_{lactam}), 188.6 (CO_{ketone}); HRMS: calcd for $C_{13}H_{14}NO_2S$ $[M+H]^+$ 248.0740, found 248.0746.

5.3. General procedure for the preparation of *N*-benzyl derivatives 1e–g, 1n,o and 1q,r

Benzyl bromide (1.2 mmol) was added to a stirred mixture of 4-oxothiazolidine **4** (1 mmol) and K_2CO_3 (1–1.05 mmol) in DMF (2–10 mL) and stirring was continued at rt until the disappearance of the starting material (TLC). The reaction mixture was neutralized with satd NH_4Cl solution. The aqueous phase was extracted with ethyl acetate (3×2–5 mL) and the organic layer was washed with water (3×2–5 mL), brine solution (1×2–5 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (gradient toluene/ethyl acetate).

*5.3.1. (Z)-(3-Benzyl-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**1e**).* Compound was **1e** obtained from **4** (234.3 mg; 1.00 mmol; R=H, EWG=CONHPh), K_2CO_3 (138.2 mg; 1.00 mmol), benzyl bromide (205.3 mg, 1.20 mmol) in DMF (5 mL) according to the general procedure (reaction time 2.5 h). Column chromatography (eluent: gradient toluene/ethyl acetate 100/0 to 70/30) gave pure **1e** as a white solid (208.9 mg; 64%); mp 216–218 °C; R_f=0.64 (toluene/ethyl acetate 3/2); IR: ν=3283, 3244, 3142, 1712, 1595, 1547, 1489, 1440, 1317, 1243, 1156, 861, 792, 752, 691 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz): δ 3.92 (s, 2H, CH_2S), 4.85 (s, 2H, CH_2Ph), 5.78 (s, 1H, =CH), 6.95–7.56 (m, 10H, 2× Ph), 9.82 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 31.4 (CH_2S), 46.3 (CH_2Ph), 94.4 (=CH), 119.0, 123.0, 127.0, 127.9, 129.1, 135.2, 139.8, 154.5 (C=), 165.3 (CO_{amide}), 173.2 (CO_{lactam}); HRMS: calcd for $C_{18}H_{17}N_2O_2S$ $[M+H]^+$ 325.1005, found 325.1008; Anal. Calcd for $C_{18}H_{16}N_2O_2S$: C, 66.64; H, 4.97; N, 8.64; S, 9.88; found: C, 66.25; H, 5.07; N, 8.61; S, 9.72.

*5.3.2. (Z)-Ethyl (3-benzyl-4-oxothiazolidin-2-ylidene)ethanoate (**1f**).* Compound **1f** was obtained from **4** (187.2 mg; 1.00 mmol; R=H, EWG=CO_2Et), K_2CO_3 (138.2 mg; 1.00 mmol), benzyl bromide (205.3 mg, 1.20 mmol) in DMF (5 mL) according to the general procedure (reaction time 2.5 h). Column chromatography (eluent: gradient toluene/ethyl acetate 100/0 to 85/15) gave pure **1f** as a white solid (227.4 mg; 82%); mp 89–91 °C; R_f=0.52 (toluene/ethyl acetate 4/1); IR (KBr): ν=2981, 2930, 1718, 1681, 1560, 1289, 1159, 1039, 967, 788, 691 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz): δ 1.15 (t, J=7.1 Hz, 3H, CH_3), 4.01 (s, 2H, CH_2S), 4.03 (q, J=7.1 Hz, 2H, CH_2O), 4.90 (s, 2H, CH_2Ph), 5.47 (s, 1H, =CH), 7.23–7.41 (m, 5H, Ph); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 14.4 (CH_3), 31.4 (CH_2S), 45.8 (*C*H_2Ph), 59.5 (CH_2O), 90.3 (=CH), 126.9 (*o*-Ph), 127.8 (*p*-Ph), 128.9 (*m*-Ph), 135.2 (C1–Ph), 158.6 (C=), 167.0 (CO_{ester}), 173.1 (CO_{lactam}); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.25 (t, J=7.3 Hz, 3H, CH_3), 3.81 (s, 2H, CH_2S), 4.15 (q, J=7.3 Hz, 2H, CH_2O), 4.88 (s, 2H, CH_2Ph), 5.47 (s, 1H, =CH), 7.20–7.36 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 14.3 (CH_3), 31.6 (CH_2S), 46.8 (*C*H_2Ph), 60.0 (CH_2O), 91.8 (=CH), 126.8 (*o*-Ph), 128.0 (*p*-Ph), 128.9 (*m*-Ph), 134.0 (C1–Ph), 157.5 (C=), 167.6 (CO_{ester}), 172.6 (CO_{lactam}); HRMS: calcd for $C_{14}H_{16}NO_3S$ $[M+H]^+$ 278.0845, found 278.0854; Anal. Calcd for $C_{14}H_{15}NO_3S$: C, 60.63; H, 5.45; N, 5.05; S, 11.56; found: C, 60.36; H, 5.42; N, 5.04; S, 11.65.

*5.3.3. (Z)-(3-Benzyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**1g**).* Compound **1g** was obtained from **4** (328.9 mg; 1.50 mmol; R=H, EWG=COPh), K_2CO_3 (207.4 mg; 1.50 mmol), benzyl bromide (307.8 g, 1.80 mmol) in DMF (7 mL) according to the general procedure (reaction time 1 h). Column chromatography (eluent: gradient toluene/ethyl acetate 100/0 to 90/10) gave pure **1g** as a white solid (412.3 mg; 89%); mp 169–170 °C; R_f=0.51 (toluene/ethyl acetate 4/1); IR: ν=3059, 3031, 2968, 2930, 1708, 1633, 1575, 1515, 1348, 1216, 1176, 915, 883, 764, 695 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz): δ 4.02 (s, 2H, CH_2S), 5.11 (s, 2H, CH_2Ph), 6.90 (s, 1H, =CH), 7.24–7.91 (m, 10H, 2× Ph); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 31.4 (CH_2S), 46.0 (*C*H_2Ph), 96.1 (=CH), 127.3, 127.5, 127.8, 128.9, 128.9, 132.4, 135.6, 138.8, 161.7 (C=), 173.7 (CO_{lactam}), 187.4 (CO_{ketone}); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 3.81 (s, 2H, CH_2S), 5.01 (s, 2H, CH_2Ph), 6.67 (s, 1H, =CH), 7.26–7.79 (m, 10H, 2× Ph); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 31.6 (CH_2S), 47.2 (CH_2Ph), 97.0 (=CH), 126.9, 127.4, 128.2, 128.5, 129.1, 132.2, 134.2, 138.3, 160.6 (C=), 173.1 (CO_{lactam}), 188.6 (CO_{ketone}); HRMS: calcd for $C_{18}H_{16}NO_2S$ $[M+H]^+$ 310.0896, found 310.0890; Anal. Calcd for $C_{18}H_{15}NO_2S$: C, 69.88; H, 4.89; N, 4.53; S, 10.36; found: C, 70.15; H, 4.94; N, 4.40; S, 10.28.

*5.3.4. (Z)-(3-Benzyl-5-methyl-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**1n**).* Compound **1n** was obtained from **4** (124.2 mg; 0.50 mmol; R=Me, EWG=CONHPh), K_2CO_3 (69.1 mg; 0.50 mmol), benzyl bromide (102.6 mg, 0.60 mmol) in DMF (5 mL) according to general procedure (reaction time 2 h). Column chromatography (eluent: gradient toluene/ethyl acetate 100/0 to 80/20) gave pure **1n** as a white solid (111.6 mg; 66%); mp 166–167 °C; R_f=0.47 (toluene/ethyl acetate 4/1); IR (ATR): ν=3291, 3056, 3030, 2976, 2932, 1717, 1644, 1560, 1493, 1440, 1317, 1159, 975, 731, 691 cm^{-1}; ^{1}H NMR (DMSO-d_6, 200 MHz): δ 1.52 (d, J=7.2 Hz, 3H, C*H*$_3$CH), 4.17 (q, J=7.2 Hz, 1H, CHS), 4.86 (s, 2H, CH_2Ph), 5.77 (s, 1H, =CH), 6.98 (t, J=7.3 Hz, 1H, *p*-Ph), 7.22–7.43 (m, 7H, Ph), 7.53 (d, J=7.8 Hz, 2H, *o*-Ph), 9.84 (s, 1H, NH_{amide}); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 19.1 (CH_3), 39.5 (CHS), 46.2 (*C*H_2Ph), 94.1 (=CH), 118.8, 122.9, 126.7, 127.7, 128.9, 135.1 (C1–Ph), 139.6 (C1–Ph), 152.6 (C=), 164.9 (CO_{amide}), 175.8 (CO_{lactam}); HRMS: calcd for $C_{19}H_{19}N_2O_2S$ $[M+H]^+$ 339.1162, found 339.1157.

*5.3.5. (Z)-Ethyl (3-benzyl-5-methyl-4-oxothiazolidin-2-ylidene)ethanoate (**1o**).* Compound **1o** was obtained from **4** (150.9 mg; 0.75 mmol; R=Me, EWG=CO_2Et), K_2CO_3 (103.6 mg; 0.75 mmol), benzyl bromide (153.9 mg, 0.90 mmol) in DMF (6 mL) according to the general procedure (reaction time 2.5 h). Column chromatography (eluent: gradient toluene/ethyl acetate 100/0 to 90/10) gave

Please cite this article in press as: Džambaski, Z.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.05.087

pure **1o** as a white solid (200.8 mg; 92%); mp 96–97 °C; R_f=0.48 (toluene/ethyl acetate 9/1); IR (KBr): ν=3028, 2976, 2936, 1714, 1686, 1568, 1372, 1342, 1290, 1156, 1041, 969, 784, 693 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 1.14 (t, J=7.0 Hz, 3H, CH_3CH$_2$), 1.54 (d, J=7.1 Hz, 3H, CH_3CH), 4.03 (q, J=7.0 Hz, 1H, CH$_2$O), 4.27 (q, J=7.1 Hz, 2H, CHS), 4.91 (s, 2H, CH$_2$Ph), 5.86 (s, 1H, =CH), 7.21–7.41 (m, 5H, Ph); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 14.4 (CH_3CH$_2$), 19.0 (CH_3CH), 40.1 (CHS), 45.9 (CH_2Ph), 59.5 (CH$_2$O), 90.3 (=CH), 126.8 (*o*-Ph), 127.8 (*p*-Ph), 129.0 (*m*-Ph), 135.2 (C1–Ph), 156.8 (C=), 166.9 (CO$_{ester}$), 176.1 (CO$_{lactam}$); ^1H NMR (CDCl$_3$, 200 MHz): δ 1.24 (t, J=7.2 Hz, 3H, CH_3CH$_2$), 1.68 (d, J=7.2 Hz, 3H, CH_3CH), 4.00 (q, J=7.2 Hz, 1H, CHS), 4.15 (q, J=7.2 Hz, 2H, CH$_2$O), 4.85 (d, J=15.8 Hz, 1H, CH_AH$_B$Ph), 4.90 (d, J=15.8 Hz, 1H, CH$_A$$H_B$Ph), 5.44 (s, 1H, =CH), 7.17–7.40 (m, 5H, Ph); ^{13}C NMR (CDCl$_3$, 50.3 MHz): δ 14.3 (CH_3CH$_2$), 19.3 (CH_3CH), 40.4 (CHS), 46.8 (CH_2Ph), 60.0 (CH$_2$O), 91.4 (=CH), 126.7 (*o*-Ph), 127.9 (*p*-Ph), 128.9 (*m*-Ph), 134.2 (C1–Ph), 156.2 (C=), 167.6 (CO$_{ester}$), 175.9 (CO$_{lactam}$); HRMS: calcd for $C_{15}H_{18}NO_3S$ $[M+H]^+$ 292.1002, found 292.1001; Anal. Calcd for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N, 4.81; S, 11.01; found: C, 61.50; H, 5.64; N, 4.90; S, 10.83.

*5.3.6. (Z)-(3-Benzyl-5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**1q**).* Compound **1q** was obtained from **4** (160.2 mg; 0.50 mmol; R=CH$_2$CO$_2$Et, EWG=CONHPh), K_2CO_3 (69.1 mg; 0.50 mmol), benzyl bromide (102.6 mg, 0.60 mmol) in DMF (5 mL) according to the general procedure (reaction time 2.5 h). Column chromatography (eluent: gradient toluene/ethyl acetate 100/0 to 75/25) gave pure **1q** as a white solid (157.3 mg; 77%); R_f=0.36 (toluene/ethyl acetate 4/1); mp 209–211 °C; IR (ATR): ν=3307, 3137, 2985, 2927, 1715, 1648, 1598, 1569, 1497, 1444, 1326, 1164, 1030, 765, 697 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 1.18 (t, J=7.2 Hz, 3H, CH$_3$), 3.02 (dd, J_{AB}=17.4 Hz, J_{AX}=7.2 Hz, 1H, CH_AH$_B$CO$_2$Et), 3.14 (dd, J_{AB}=17.4 Hz, J_{BX}=4.6 Hz, 1H, CH$_A$$H_BCO_2$Et), 4.11 (q, J=7.2 Hz, 2H, CH$_2$O), 4.42 (dd, J_{AX}=7.2 Hz, J_{BX}=4.6 Hz, 1H, CH$_X$S), 4.87 (s, 2H, CH$_2$Ph), 5.75 (s, 1H, =CH), 6.98 (t, J=7.3 Hz, 1H, *p*-Ph), 7.22–7.43 (m, 7H, Ph), 7.53 (d, J=7.8 Hz, 2H, *o*-Ph), 9.82 (s, 1H, NH$_{amide}$); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 14.2 (CH$_3$), 36.8 (CH$_2$CO$_2$Et), 40.9 (CHS), 46.5 (CH$_2$Ph), 60.8 (CH$_2$O), 94.3 (=CH), 118.8, 122.9, 126.9, 127.7, 128.9, 135.1, 139.7, 153.2 (C=), 165.0 (CO$_{amide}$), 170.3 (CO$_{ester}$), 174.2 (CO$_{lactam}$); HRMS: calcd for $C_{22}H_{22}N_2NaO_4S$ $[M+Na]^+$ 433.1192, found 433.1177.

*5.3.7. (Z)-(3-Benzyl-5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**1r**).* Compound **1r** was obtained from **4** (305.4 mg; 1.00 mmol; R=CH$_2$CO$_2$Et, EWG=COPh), K_2CO_3 (138.2 mg; 1.00 mmol), benzyl bromide (205.3 mg, 1.20 mmol) in DMF (7 mL) according to the general procedure (reaction time 1 h). Column chromatography (eluent: gradient toluene/ethyl acetate 100/0 to 80/20) gave pure **1r** as a white solid (367.1 mg; 93%); mp 105–106 °C; R_f=0.57 (toluene/ethyl acetate 4/1); IR: ν=3422, 3063, 2990, 1715, 1609, 1573, 1501, 1486, 1371, 1214, 1172, 915, 763, 694 cm^{-1}; ^1H NMR (CDCl$_3$, 200 MHz): δ 1.26 (t, J=7.3 Hz, 3H, CH$_3$), 3.02 (dd, J_{AB}=14.4 Hz, J_{AX}=8.4 Hz, 1H, CH_AH$_B$CO$_2$Et), 3.21 (dd, J_{AB}=14.4 Hz, J_{BX}=4.0 Hz, 1H, CH$_A$$H_BCO_2$Et), 4.19 (q, J=7.3 Hz, 2H, CH$_2$O), 4.26 (dd, J_{AX}=8.4 Hz, J_{BX}=4.0 Hz, 1H, CH$_X$S), 5.03 (s, 2H, CH$_2$Ph), 6.66 (s, 1H, =CH), 7.26–7.78 (m, 10H, 2× Ph); ^{13}C NMR (CDCl$_3$, 50.3 MHz): δ 14.1 (CH$_3$), 37.2 (CH$_2$CO$_2$Et), 41.3 (CHS), 47.4 (CH$_2$Ph), 61.4 (CH$_2$O), 97.0 (=CH), 126.9, 127.4, 128.1, 128.5, 129.0, 132.2, 134.2, 138.3, 159.3 (C=), 169.7 (CO$_{ester}$), 174.7 (CO$_{lactam}$), 186.6 (CO$_{ketone}$); HRMS: calcd for $C_{22}H_{22}NO_4S$ $[M+H]^+$ 396.1264, found 396.1272; Anal. Calcd for $C_{22}H_{21}NO_4S$: C, 66.82; H, 5.35; N, 3.54; S, 8.11; found: C, 66.90; H, 5.46; N, 5.37; S, 8.30.

5.4. Synthesis of *N*-bromoalkyl derivatives 1h and 1p

Compounds **1h** and **1p** were obtained as already described.[33]

5.5. (*Z*)-Ethyl (3-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)ethanoate (1i)

Compound **1i** was obtained from **4** (187.2 mg; 1.00 mmol; R=H, EWG=CO$_2$Et), K_2CO_3 (145.1 mg; 1.05 mmol), ethyl 2-bromoacetate (200.4 mg, 1.20 mmol, 0.14 mL) in DMF (2 mL) at rt (reaction time 1 h). The reaction mixture was then diluted with $CHCl_3$ (3 mL) and water (3 mL) was added. The organic layer was separated and the water layer extracted with $CHCl_3$ (3×2 mL). The chloroform extracts were combined, washed with water (3×3 mL), brine (1×3 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure. Thus obtained product was stirred with *n*-hexane for 2 h and filtered to give pure **1i** as a white solid (111.6 mg; 93%); mp 103–104 °C; R_f=0.65 (toluene/ethyl acetate 7/3); IR (ATR): ν=2985, 1746, 1687, 1571, 1301, 1219, 1167, 1047, 1026, 976, 794 cm^{-1}; ^1H NMR (CDCl$_3$, 200 MHz): δ 1.19 (t, J=7.2 Hz, 6H, 2× CH$_3$), 3.79 (s, 2H, CH$_2$S), 4.20 (q, J=7.2 Hz, 2H, CH$_2$O), 4.24 (q, J=7.2 Hz, 2H, CH$_2$O), 4.40 (s, 2H, NCH$_2$), 5.33 (s, 1H, =CH); ^{13}C NMR (CDCl$_3$, 50.3 MHz): δ 14.0 (CH$_3$), 14.3 (CH$_3$), 31.4 (CH$_2$S), 44.2 (NCH$_2$), 60.1 (CH$_2$O), 62.1 (CH$_2$O), 90.7 (=CH), 157.3 (C=), 166.0 (CO$_{ester}$), 167.3 (CO$_{ester}$), 172.1 (CO$_{lactam}$); HRMS: calcd for $C_{11}H_{16}NO_5S$ $[M+H]^+$ 274.0744, found 274.0735.

5.6. General procedure for the oxidation of thiazolidine derivatives 1

A solution of *m*-CPBA (1.5–2.0 mmol) in CH_2Cl_2 was added dropwise within 5 min to a solution of thiazolidine **1** (1.0 mmol) in CH_2Cl_2 at 0 °C. The mixture was stirred at 0 °C for additional 30–60 min until the disappearance of the starting material (TLC). After the addition of 10% aq $Na_2S_2O_3$ (5–15 mL), the solution was extracted with CH_2Cl_2 (3×2–5 mL). The combined organic layers were washed with 10% K_2CO_3 (2×2–5 mL), water (2×2–5 mL) and finally with brine (1×2–5 mL). The organic layer was dried over Na_2SO_4 and solvent was removed under reduced pressure. Thus obtained crude product was purified by column chromatography.

*5.6.1. (Z)-(3-Methyl-1,4-dioxothiazolidin-2-ylidene)-N-phenylethanamide (**5a**).* Compound **5a** was obtained from **1a** (300 mg; 1.20 mmol; 18 mL CH_2Cl_2) and *m*-CPBA (428 mg; 2.48 mmol; 24 mL CH_2Cl_2) according to the general procedure (reaction time 30 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 30/70) gave pure **5a** as a white solid (248 mg; 75%);mp 228–231 °C (decomposes); R_f=0.39 (toluene/acetone 1/1); IR (KBr): ν=3303, 3263, 3198, 3097, 3054, 2931, 1711, 1677, 1625, 1552, 1493, 1439, 1339, 1108, 1041, 845, 771, 696 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 3.11 (s, 3H, CH$_3$), 3.50 (d, J=17.4 Hz, 1H, CH_aH$_b$S), 4.10 (d, J=17.4 Hz, 1H, CH$_a$$H_b$S), 6.04 (s, 1H, =CH), 7.08 (t, J=7.3 Hz, 1H, *p*-Ph), 7.35 (m, 2H, *m*-Ph), 7.66 (d, J=7.4 Hz, 2H, *o*-Ph), 10.35 (s, 1H, NH$_{amide}$); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 29.3 (CH$_3$), 52.1 (CH$_2$S), 102.6 (=CH), 119.3 (*o*-Ph), 123.8 (*p*-Ph), 129.2 (*m*-Ph), 139.2 (C1–Ph), 156.8 (C=), 162.3 (CO$_{amide}$), 170.1 (CO$_{lactam}$); HRMS: calcd for $C_{12}H_{13}N_2O_3S$ $[M+H]^+$ 265.0641, found 265.0637.

*5.6.2. (Z)-(3-Methyl-1,4-dioxothiazolidin-2-ylidene)-N-(2-phenylethyl) ethanamide (**5b**).* Compound **5b** was obtained from **1b** (156 mg; 0.60 mmol; 15 mL CH_2Cl_2) and *m*-CPBA (214 mg; 0.90 mmol; 20 mL CH_2Cl_2) according to the general procedure (reaction time 30 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 30/70) gave pure **5b** as a white solid (149 mg; 85%);mp 139–141 °C (decomposes); R_f=0.27 (toluene/acetone 1/1); IR (KBr): ν=3519, 3421, 3239, 3072, 2934, 1724, 1652, 1605, 1286, 1124, 1040, 850, 705 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 2.77 (t, J=7.3 Hz, 2H, CH$_2$Ph), 3.03 (s, 3H, CH$_3$), 3.36–3.46 (m, 3H, NCH$_2$ and CH_AH$_B$S), 4.03 (d, J=17.4 Hz, 1H, CH$_A$$H_B$S), 5.86 (s, 1H, =CH), 7.17–7.35 (m, 5H, Ph), 8.33 (t,

J=5.3 Hz, 1H, NH_{amide}); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 29.2 (CH_3), 35.3 (CH_2Ph), NCH_2 is covered by DMSO, 52.1 (CH_2S), 102.8 (=CH), 126.4 (*p*-Ph), 128.7 (*o*-Ph), 128.9 (*m*-Ph), 139.6 (C1–Ph), 155.2 (C=), 163.6 (CO_{amide}), 170.0 (CO_{lactam}); HRMS: calcd for $C_{14}H_{17}N_2O_3S$ $[M+H]^+$ 293.0954, found 293.0960.

*5.6.3. (Z)-Ethyl (3-methyl-1,4-dioxothiazolidin-2-ylidene)ethanoate (**5c**).* Compound **5c** was obtained from **1c** (151 mg; 0.75 mmol; 6 mL CH_2Cl_2) and *m*-CPBA (267 mg; 1.125 mmol; 10 mL CH_2Cl_2) according to the general procedure (reaction time 60 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 70/30) gave pure **5c** as a pale yellow solid (128 mg; 80%);mp 128–129 °C; R_f=0.36 (toluene/acetone 7/3); IR (KBr): ν=3046, 2924, 1711, 1619, 1276, 1185, 1116, 1040, 847 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 1.25 (t, J=7.1 Hz, 3H, CH_3CH_2), 3.09 (s, 3H, NCH_3) 3.54 (d, J=17.4 Hz, 1H, CH_AH_BS), 4.12 (d, J=17.4 Hz, 1H, CH_AH_BS), 4.20 (q, J=7.2 Hz, 2H, CH_2O), 5.87 (s, 1H, =CH); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 14.4 (CH_3CH_2), 29.4 (NCH_3), 52.2 (CH_2S), 60.6 (CH_2O), 98.3 (=CH), 160.6 (C=), 164.9 (CO_{ester}), 170.3 (CO_{lactam}); ^1H NMR ($CDCl_3$, 200 MHz): δ 1.34 (t, J=7.2 Hz, 3H, CH_3CH_2), 3.19 (s, 3H, NCH_3) 3.60 (d, J=17.7 Hz, 1H, CH_AH_BS), 3.86 (d, J=17.7 Hz, 1H, CH_AH_BS), 4.31 (q, J=7.2 Hz, 2H, CH_2O), 5.72 (s, 1H, =CH); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 14.0 (CH_3CH_2), 29.4 (NCH_3), 51.5 (CH_2S), 61.3 (CH_2O), 100.2 (=CH), 158.4 (C=), 164.6 (CO_{ester}), 168.6 (CO_{lactam}); HRMS: calcd for $C_8H_{12}NO_4S$ $[M+H]^+$ 218.0418, found 218.0486; Anal. Calcd for $C_8H_{11}NO_4S$: C, 44.23; H, 5.10; N, 6.45; S, 14.76; found: C, 44.33; H, 5.19; N, 6.43; S, 14.48.

*5.6.4. (Z)-(3-Methyl-1,4-dioxothiazolidin-2-ylidene)-1-phenylethanone (**5d**).* Compound **5d** was obtained from **1d** (175 mg; 0.75 mmol; 12 mL CH_2Cl_2) and *m*-CPBA (269 mg; 1.13 mmol; 20 mL CH_2Cl_2) according to the general procedure (reaction time 40 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 70/30) gave pure **5d** as a pale yellow solid (187 mg; 74%);mp 177–178 °C (decomposes); R_f=0.32 (toluene/acetone 4/1); IR (ATR): ν=3064, 3004, 2941, 1729, 1645, 1565, 1279, 1220, 1119, 1042, 907, 776, 697 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 3.35 (s, 3H, CH_3), 3.56 (d, J=17.4 Hz, 1H, CH_aH_bS), 4.17 (d, J=17.4 Hz, 1H, CH_aH_bS), 7.09 (s, 1H, =CH), 7.54–7.73 (m, 3H, *m*- and *p*-Ph), 8.13–8.17 (m, 2H, *o*-Ph); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 29.8 (CH_3), 51.9 (CH_2S), 101.9 (=CH), 128.6 and 129.1 (*o*- and *m*-Ph), 133.6 (*p*-Ph), 137.6 (C1–Ph), 161.1 (C=), 170.6 (CO_{lactam}), 187.7 (CO_{ketone}); ^1H NMR ($CDCl_3$, 200 MHz): δ 3.31 (s, 3H, CH_3), 3.66 (d, J=17.7 Hz, 1H, CH_aH_bS), 3.87 (d, J=17.6 Hz, 1H, CH_aH_bS), 6.81 (s, 1H, =CH), 7.48–7.68 (m, 3H, *m*- and *p*-Ph), 8.00–8.06 (m, 2H, *o*-Ph); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 29.8 (CH_3), 51.4 (CH_2S), 102.7 (=CH), 128.4 and 128.6 (*o*- and *m*-Ph), 133.6 (*p*-Ph), 137.3 (C1–Ph), 159.2 (C=), 169.0 (CO_{lactam}), 187.6 (CO_{ketone}) HRMS: calcd for $C_{12}H_{12}NO_3S$ $[M+H]^+$ 250.0532, found 250.0542; Anal. Calcd for $C_{12}H_{11}NO_3S$: C, 57.82; H, 4.45; N, 5.62; S, 12.86; found: C, 57.58; H, 4.53; N, 5.54; S, 12.41.

*5.6.5. (Z)-(3-Benzyl-1,4-dioxothiazolidin-2-ylidene)-N-phenylethanamide (**5e**).* Compound **5e** was obtained from **1e** (97.3 mg; 0.30 mmol; 4 mL CH_2Cl_2) and *m*-CPBA (107.1 mg; 0.45 mmol; 5 mL CH_2Cl_2) according to the general procedure (reaction time 60 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 70/30) gave pure **5e** as a white solid (73.1 mg; 72%);mp 142–144 °C (decomposes); R_f=0.33 (toluene/acetone 7/3); IR (ATR): ν=3036, 1722, 1671, 1613, 1548, 1311, 1495, 1446, 1164, 1018, 758, 696 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 3.61 (d, J=17.2 Hz, 1H, CH_aH_bS), 4.26 (d, J=17.2 Hz, 1H, CH_aH_bS), 4.83 (d, J=16.0 Hz, 1H, CH_aH_bPh), 4.91 (d, J=16.0 Hz, 1H, CH_aH_bPh), 6.00 (s, 1H, =CH), 7.07 (t, J=5.5 Hz, 1H, *p*-Ph), 7.30–7.40 (m, 7H, 2× Ph), 7.61 (d, J=8.0 Hz, 2H, *o*-Ph), 10.25 (s, 1H, NH_{amide}); ^{13}C NMR (DMSO-d_6, 125.8 MHz): δ 45.4 (CH_2Ph), 51.7 (CH_2S), 102.8 (=CH), 119.2, 123.6, 126.6, 127.6, 128.7, 128.8, 134.2, 138.8, 155.7 (C=), 161.9 (CO_{amide}), 170.4 (CO_{lactam}); HRMS: calcd for $C_{18}H_{16}N_2NaO_3S$ $[M+Na]^+$ 363.0774, found 363.0775.

*5.6.6. (Z)-Ethyl (3-benzyl-1,4-dioxothiazolidin-2-ylidene)ethanoate (**5f**).* Compound **5f** was obtained from **1f** (69.3 mg; 0.25 mmol; 3 mL CH_2Cl_2) and *m*-CPBA (76.0 mg; 0.35 mmol; 4 mL CH_2Cl_2) according to the general procedure (reaction time 30 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 80/20) gave pure **5f** as a white solid (69.6 mg; 95%);mp 128–129 °C; R_f=0.30 (toluene/acetone 4/1); IR (ATR): ν=2985, 2933, 1706, 1616, 1292, 1156, 1048, 834, 733, 698 cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 1.20 (t, J=7.1 Hz, 3H, CH_3), 3.68 (d, J=17.4 Hz, 1H, CH_AH_BS), 4.14 (q, J=7.1 Hz, 2H, CH_2O), 4.29 (d, J=17.4 Hz, 1H, CH_AH_BS), 4.93 (m, 2H, CH_2Ph), 5.78 (s, 1H, =CH), 7.25–7.40 (m, 5H, Ph); ^{13}C NMR (DMSO-d_6, 50.3 MHz): δ 14.2 (CH_3), 45.0 (CH_2Ph), 52.1 (CH_2S), 60.6 (CH_2O), 98.9 (=CH), 127.0 (*o*-Ph), 127.9 (*p*-Ph), 128.9 (*m*-Ph), 134.5 (C1–Ph), 159.4 (C=), 164.7 (CO_{ester}), 170.9 (CO_{lactam}); ^1H NMR ($CDCl_3$, 200 MHz): δ 1.28 (t, J=7.3 Hz, 3H, CH_3), 3.65 (d, J=17.5 Hz, 1H, CH_AH_BS), 3.89 (d, J=17.5 Hz, 1H, CH_AH_BS), 4.23 (q, J=7.3 Hz, 2H, CH_2O), 4.87 (m, 2H, CH_2Ph), 5.66 (s, 1H, =CH), 7.19–7.36 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 14.0 (CH_3), 46.4 (CH_2Ph), 51.4 (CH_2S), 61.3 (CH_2O), 101.2 (=CH), 126.8 (*o*-Ph), 128.2 (*p*-Ph), 129.1 (*m*-Ph), 132.8 (C1–Ph), 157.3 (C=), 164.5 (CO_{ester}), 169.2 (CO_{lactam}); HRMS: calcd for $C_{14}H_{16}NO_4S$ $[M+H]^+$ 294.0795, found 294.0786.

*5.6.7. (Z)-(3-Benzyl-1,4-dioxothiazolidin-2-ylidene)-1-phenylethanone (**5g**).* Compound **5g** was obtained from **1g** (77.3 mg; 0.25 mmol; 3 mL CH_2Cl_2) and *m*-CPBA (76.3 mg; 0.375 mmol; 4 mL CH_2Cl_2) according to the general procedure (reaction time 40 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 90/10) gave pure **5g** as a yellow solid (55.8 mg; 69%);mp 173–175 °C (decomposes); R_f=0.30 (toluene/acetone 4/1); IR (KBr): ν=3062, 3006, 2932, 1723, 1649, 1563, 1322, 1176, 1038, 1018, 892, 780, 740, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 3.71 (d, J=17.5 Hz, 1H, CH_aH_bS), 3.93 (d, J=17.5 Hz, 1H, CH_aH_bS), 4.94 (d, J=15.7 Hz, 1H, CH_aH_bPh), 5.06 (d, J=15.7 Hz, 1H, CH_aH_bPh), 6.75 (s, 1H, =CH), 7.28–7.77 (m, 10H, 2× Ph); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 46.9 (CH_2Ph), 51.4 (CH_2S), 104.3 (=CH), 127.0, 128.2, 128.5, 128.8, 129.3, 133.1, 133.5, 137.2, 157.7 (C=), 169.5 (CO_{lactam}), 187.6 (CO_{ketone}); HRMS: calcd for $C_{18}H_{16}NO_3S$ $[M+H]^+$ 326.0845, found 326.0845; Anal. Calcd for $C_{18}H_{15}NO_3S$: C, 66.44; H, 4.65; N, 4.30; S, 9.85; found: C, 66.12; H, 4.80; N, 4.28; S, 9.48.

*5.6.8. (Z)-Ethyl (3-(3-bromopropyl)-1,4-dioxothiazolidin-2-ylidene) ethanoate (**5h**).* Compound **5h** was obtained from **1h** (77.0 mg; 0.25 mmol; 3 mL CH_2Cl_2) and *m*-CPBA (89.2 mg; 0.375 mmol; 4 mL CH_2Cl_2) according to the general procedure (reaction time 60 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 75/25) gave pure **5h** as a colourless oil (67.7 mg; 84%); R_f=0.47 (toluene/acetone 7/3); IR (ATR): ν=2985, 1708, 1614, 1306, 1237, 1181, 1144, 1048, 836, 735 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 1.35 (t, J=7.2 Hz, 3H, CH_3), 2.17–2.24 (m, 2H, CH_2), 3.40–3.48 (m, 3H, CH_2Br), 3.61 (d, J=18.0 Hz, 1H, CH_AH_BS), 3.80 (d, J=18.0 Hz, 1H, CH_AH_BS), 3.77–3.83 (m, 1H, NCH_aH_b), 3.87–3.93 (m, 1H, NCH_aH_b), 4.32 (q, J=7.2 Hz, 2H, CH_2O), 5.84 (s, 1H, =CH); ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 14.1 (CH_3), 28.8 ($CH_2CH_2CH_2$), 29.5 (CH_2Br), 41.8 (NCH_2), 51.5 (CH_2S), 61.5 (CH_2O), 100.5 (=CH), 157.5 (C=), 164.6 (CO_{ester}), 168.9 (CO_{lactam}); HRMS: calcd for $C_{10}H_{15}BrNO_4S$ $[M+H]^+$ 323.9900, found 323.9901.

*5.6.9. (Z)-Ethyl-(3-ethoxycarbonylmethyl-1,4-dioxothiazolidin-2-ylidene)ethanoate (**5i**).* Compound **5i** was obtained from **1i** (82.0 mg; 0.30 mmol; 5 mL CH_2Cl_2) and *m*-CPBA (107.0 mg; 0.45 mmol; 6 mL CH_2Cl_2) according to the general procedure (reaction time 40 min). Column chromatography (eluent: gradient

toluene/acetone 100/0 to 80/20) gave pure **5i** as a white solid (73.0 mg; 84%);mp 87–89 °C; R_f=0.32 (toluene/acetone 4/1); IR (ATR): ν=3065, 2985, 2938, 1739, 1708, 1620, 1359, 1293, 1213, 1162, 1052, 971, 841 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 1.30 (t, J=7.2 Hz, 3H, CH_3), 1.34 (t, J=7.2 Hz, 3H, CH_3), 3.65 (d, J=17.8 Hz, 1H, CH_AH_BS), 3.91 (d, J=17.8 Hz, 1H, CH_AH_BS), 4.25 (q, J=7.2 Hz, 2H, CH_2O), 4.31 (q, J=7.2 Hz, 2H, CH_2O), 4.12 (d, J=17.2 Hz, 1H, NCH_aH_b), 4.72 (d, J=17.2 Hz, 1H, NCH_aH_b), 5.58 (s, 1H, =CH); ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 13.9 (CH_3), 14.0 (CH_3), 44.0 (NCH_2), 51.4 (CH_2S), 61.5 (CH_2O), 62.4 (CH_2O), 100.7 (=CH), 157.2 (C=), 164.3 (CO_{ester}), 165.5 (CO_{ester}), 168.6 (CO_{lactam}); HRMS: calcd for $C_{11}H_{16}NO_6S$ $[M+H]^+$ 290.0693, found 290.0696; Anal. Calcd for $C_{11}H_{15}NO_6S$: C, 45.67; H, 5.23; N, 4.84; S, 11.08; found: C, 45.84; H, 5.11; N, 4.82; S, 10.77.

*5.6.10. (Z)-(3,5-Dimethyl-1,4-dioxothiazolidin-2-ylidene)-N-phenylethanamide (**5j**).* Compound **5j** was obtained from **1j** (98.4 g; 0.375 mmol; 8 mL CH_2Cl_2) and *m*-CPBA (178.6 mg; 0.75 mmol; 6 mL CH_2Cl_2) according to the general procedure (reaction time 60 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 60/40) gave pure **5j** as a pale yellow solid (74.3 mg; 71%; *syn*/*anti* 85/15);mp 204–207 °C (decomposes); R_f=0.42 and 0.47 (toluene/acetone 3/2); IR (ATR): ν=3330, 2914, 1722, 1673, 1606, 1538, 1311, 1039, 820, 758, 697 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): *syn*-**5j** δ 1.36 (d, J=7.5 Hz, 3H, CH_3CH), 3.12 (s, 3H, NCH_3), 3.89 (q, J=7.5 Hz, 1H, CHS), 6.11 (s, 1H, =CH), 7.09 (t, J=7.2 Hz, 1H, *p*-Ph), 7.35 (m, 2H, *m*-Ph), 7.66 (d, J=8.0 Hz, 2H, *o*-Ph), 10.34 (s, 1H, NH); *anti*-**5j** δ 1.40 (d, J=8.0 Hz, 3H, CH_3CH), 3.12 (s, 3H, NCH_3), 3.65 (q, J=8.0 Hz, 1H, CHS), 6.13 (s, 1H, =CH), 7.09 (t, J=7.2 Hz, 1H, *p*-Ph), 7.35 (m, 2H, *m*-Ph), 7.66 (d, J=8.0 Hz, 2H, *o*-Ph), 10.34 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 125.8 MHz): *syn*-**5j** δ 6.6 (CH_3CH), 29.4 (NCH_3), 52.5 (CHS), 103.2 (=CH), 119.1 (*o*-Ph), 123.6 (*p*-Ph), 128.9 (*m*-Ph), 138.9 (C1–Ph), 154.7 (C=), 162.0 (CO_{amide}), 172.5 (CO_{lactam}); *anti*-**5j** δ 11.7 (CH_3CH), 29.4 (NCH_3), 59.5 (CHS), 103.8 (=CH), 119.1 (*o*-Ph), 123.6 (*p*-Ph), 128.9 (*m*-Ph), 138.9 (C1–Ph), 154.7 (C=), 162.0 (CO_{amide}), 172.5 (CO_{lactam}); HRMS: calcd for $C_{13}H_{14}N_2NaO_3S$ $[M+Na]^+$ 301.0617, found 301.0624.

*5.6.11. (Z)-(3,5-Dimethyl-1,4-dioxothiazolidin-2-ylidene)-N-(2-phenylethyl)ethanamide (**5k**).* Compound **5k** was obtained from **1k** (147.5 mg; 0.51 mmol; 8 mL CH_2Cl_2) and *m*-CPBA (241.8 mg; 1.01 mmol; 7 mL CH_2Cl_2) according to the general procedure (reaction time 60 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 60/40) gave pure **5k** as a colourless oil (100.8 mg; 65%; *syn*/*anti* 86/14); R_f=0.28 (toluene/acetone 3/2); IR (ATR): ν=3299, 3066, 2937, 1721, 1660, 1610, 1288, 1046, 848, 735, 700 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): *syn*-**5k** δ 1.33 (d, J=7.5 Hz, 3H, CH_3), 2.79 (t, J=7.3 Hz, 2H, CH_2Ph), 3.04 (s, 1H, NCH_3), 3.40–3.46 (m, 2H, NCH_2), 3.82 (q, J=7.5 Hz, 1H, CHS), 5.93 (s, 1H, =CH), 7.20–7.32 (m, 5H, Ph), 8.33 (t, J=5.7 Hz, 1H, NH); *anti*-**5k** δ 1.35 (d, J=7.5 Hz, 3H, CH_3), 2.79 (t, J=7.3 Hz, 2H, CH_2Ph), 3.04 (s, 1H, NCH_3), 3.40–3.46 (m, 2H, NCH_2), 3.56 (q, J=7.5 Hz, 1H, CHS), 5.96 (s, 1H, =CH), 7.20–7.32 (m, 5H, Ph), 8.33 (t, J=5.7 Hz, 1H, NH); ^{13}C NMR (DMSO-d_6, 125.8 MHz): *syn*-**5k** δ 6.5 (CH_3CH), 29.3 (NCH_3), 35.0 (CH_2Ph), 40.3 (NCH_2), 52.5 (CHS), 103.4 (=CH), 126.2 (*p*-Ph), 128.4 and 128.6 (*o*- and *m*-Ph), 139.3 (C1–Ph), 153.2 (C=), 163.3 (CO_{amide}), 172.4 (CO_{lactam}); *anti*-**5k** δ 11.7 (CH_3CH), 29.3 (NCH_3), 40.0 (CH_2Ph), 40.3 (NCH_2), 59.3 (CHS), 104.1 (=CH), 126.5 (*p*-Ph), 128.6 and 128.7 (*o*- and *m*-Ph), 138.6 (C1–Ph), 153.2 (C=), 163.6 (CO_{amide}), 172.4 (CO_{lactam}); ^1H NMR ($CDCl_3$, 500 MHz): *syn*-**5k** δ 1.57 (d, J=7.5 Hz, 3H, CH_3), 2.85 (t, J=7.2 Hz, 2H, CH_2Ph), 3.11 (s, 1H, NCH_3), 3.31 (q, J=7.5 Hz, 1H, CHS), 3.50–3.68 (m, 2H, NCH_2), 5.76 (s, 1H, =CH), 6.54 (t, J=5.7 Hz, 1H, NH), 7.18–7.30 (m, 5H, Ph); *anti*-**5k** δ 1.49 (d, J=7.5 Hz, 3H, CH_3), 2.85 (t, J=7.2 Hz, 2H, CH_2Ph), 3.11 (s, 1H, NCH_3), 3.50 (q, J=7.5 Hz, 1H, CHS), 3.50–3.68 (m, 2H, NCH_2), 5.78 (s, 1H, =CH), 6.54 (t, J=5.7 Hz, 1H, NH), 7.18–7.30 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$, 125.8 MHz): *syn*-**5k** δ 6.8 (CH_3CH), 29.7 (NCH_3), 35.4 (CH_2Ph), 40.9 (NCH_2), 53.2 (CHS), 103.8 (=CH), 126.5 (*p*-Ph), 128.6 and 128.7 (*o*- and *m*-Ph), 138.6 (C1–Ph), 153.5 (C=), 163.6 (CO_{amide}), 171.7 (CO_{lactam}); *anti*-**5k** δ 12.4 (CH_3CH), 29.6 (NCH_3), 35.4 (CH_2Ph), 40.9 (NCH_2), 59.6 (CHS), 104.1 (=CH), 126.5 (*p*-Ph), 128.6 and 128.7 (*o*- and *m*-Ph), 138.6 (C1–Ph), 153.5 (C=), 163.6 (CO_{amide}), 171.7 (CO_{lactam}); HRMS: calcd for $C_{15}H_{18}N_2NaO_3S$ $[M+Na]^+$ 329.0930, found 329.09304.

*5.6.12. (Z)-Ethyl (3,5-dimethyl-1,4-dioxothiazolidin-2-ylidene)ethanoate (**5l**).* Compound **5l** was obtained from **1l** (150.7 mg; 0.70 mmol; 12 mL CH_2Cl_2) and *m*-CPBA (333.3 mg; 1.40 mmol; 10 mL CH_2Cl_2) according to the general procedure (reaction time 40 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 80/20) gave pure **5l** as a white solid (150.6 mg; 93%; *syn*/*anti* 86/14);mp 97–99 °C; R_f=0.37 (toluene/acetone 4/1); IR (KBr): ν=2983, 2937, 1705, 1614, 1262, 1183, 1131, 1056, 839, 732, 688 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): *syn*-**5l** δ 1.26 (t, J=7.0 Hz, 3H, CH_3CH_2), 1.36 (d, J=7.5 Hz, 3H, CH_3CH), 3.10 (s, 3H, NCH_3), 3.95 (q, J=7.5 Hz, 1H, CHS), 4.22 (q, J=7.0 Hz, 2H, CH_2O), 5.93 (s, 1H, =CH); *anti*-**5l** δ 1.26 (t, J=7.0 Hz, 3H, CH_3CH_2), 1.44 (d, J=7.5 Hz, 3H, CH_3CH), 3.10 (s, 3H, NCH_3), 3.74 (q, J=7.5 Hz, 1H, CHS), 4.20 (q, J=7.0 Hz, 2H, CH_2O), 5.94 (s, 1H, =CH); ^{13}C NMR (DMSO-d_6, 125.8 MHz): *syn*-**5l** δ 6.6 (CH_3CH), 14.1 (CH_3CH_2), 29.5 (NCH_3), 52.5 (CHS), 60.4 (CH_2O), 98.9 (=CH), 158.4 (C=), 164.6 (CO_{ester}), 172.9 (CO_{lactam}); *anti*-**5l** δ 11.5 (CH_3CH), 14.1 (CH_3CH_2), 29.5 (NCH_3), 59.9 (CHS), 60.4 (CH_2O), 99.3 (=CH), 158.6 (C=), 164.5 (CO_{ester}), 172.1 (CO_{lactam}); ^1H NMR ($CDCl_3$, 500 MHz): *syn*-**5l** δ 1.35 (t, J=7.1 Hz, 3H, CH_3CH_2), 1.63 (d, J=7.4 Hz, 3H, CH_3CH), 3.18 (s, 3H, NCH_3), 3.42 (q, J=7.4 Hz, 1H, CHS), 4.32 (q, J=7.1 Hz, 2H, CH_2O), 5.73 (s, 1H, =CH); *anti*-**5l** δ 1.35 (t, J=7.1 Hz, 3H, CH_3CH_2), 1.56 (d, J=7.9 Hz, 3H, CH_3CH), 3.18 (s, 3H, NCH_3), 3.63 (q, J=7.9 Hz, 1H, CHS), 4.32 (q, J=7.1 Hz, 2H, CH_2O), 5.76 (s, 1H, =CH); ^{13}C NMR ($CDCl_3$, 125.8 MHz): *syn*-**5l** δ 6.7 (CH_3CH), 14.1 (CH_3CH_2), 29.7 (NCH_3), 53.3 (CHS), 61.3 (CH_2O), 100.6 (=CH), 157.1 (C=), 164.6 (CO_{ester}), 172.0 (CO_{lactam}); *anti*-**5l** δ 12.3 (CH_3CH), 14.1 (CH_3CH_2), 29.8 (NCH_3), 59.9 (CHS), 61.3 (CH_2O), 100.9 (=CH), 157.1 (C=), 164.6 (CO_{ester}), 172.0 (CO_{lactam}); HRMS: calcd for $C_9H_{14}NO_4S$ $[M+H]^+$ 232.0638, found 232.0635.

*5.6.13. (Z)-(3,5-Dimethyl-1,4-dioxothiazolidin-2-ylidene)-1-phenyle thanone (**5m**).* Compound **5m** was obtained from **1m** (74.2 mg; 0.30 mmol; 4 mL CH_2Cl_2) and *m*-CPBA (142.8 mg; 0.60 mmol; 7 mL CH_2Cl_2) according to the general procedure (reaction time 45 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 75/25) gave pure **5m** as a white solid (57.8 mg; 73%; *syn*/*anti* 85/15); mp 132–134 °C (decomposes); R_f=0.30 and 0.40 (toluene/acetone 4/1); IR (ATR): ν=3065, 2915, 1729, 1644, 1558, 1348, 1224, 1038, 780, 702 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): *syn*-**5m** δ 1.38 (d, J=7.5 Hz, 3H, CH_3), 3.27 (s, 1H, NCH_3), 3.98 (q, J=7.5 Hz, 1H, CHS), 7.15 (s, 1H, =CH), 7.59 (m, 2H, *m*-Ph), 7.69 (t, J=7.5 Hz, 1H, *p*-Ph), 8.16 (d, J=8.2 Hz, 2H, *o*-Ph); *anti*-**5m** δ 1.48 (d, J=7.7 Hz, 3H, CH_3), 3.25 (s, 1H, NCH_3), 3.78 (q, J=7.7 Hz, 1H, CHS), 7.14 (s, 1H, =CH), 7.59 (m, 2H, *m*-Ph), 7.69 (t, J=7.5 Hz, 1H, *p*-Ph), 8.16 (d, J=8.2 Hz, 2H, *o*-Ph); ^{13}C NMR (DMSO-d_6, 125.8 MHz): *syn*-**5m** δ 6.8 (CH_3CH), 29.9 (NCH_3), 52.1 (CHS), 102.6 (=CH), 128.3 (*o*-Ph), 128.8 (*m*-Ph), 133.4 (*p*-Ph), 137.3 (C1–Ph), 158.8 (C=), 173.3 (CO_{lactam}), 187.5 (CO_{ketone}); *anti*-**5m** δ 11.5 (CH_3CH), 29.9 (NCH_3), 59.7 (CHS), 102.9 (=CH), 128.3 (*o*-Ph), 128.8 (*m*-Ph), 133.4 (*p*-Ph), 137.4 (C1–Ph), 159.4 (C=), 172.2 (CO_{lactam}), 187.5 (CO_{ketone}); ^1H NMR ($CDCl_3$, 500 MHz): *syn*-**5m** δ 1.65 (d, J=7.5 Hz, 3H, CH_3), 3.28 (s, 1H, NCH_3), 3.44 (q, J=7.5 Hz, 1H, CHS), 6.80 (s, 1H, =CH), 7.51 (m, 2H, *m*-Ph), 7.61 (t, J=7.2 Hz, 1H, *p*-Ph), 8.01 (d, J=8.5 Hz, 2H, *o*-Ph); *anti*-**5m** δ 1.59 (d, J=7.5 Hz, 3H, CH_3), 3.30 (s, 1H, NCH_3), 3.67 (q, J=7.5 Hz, 1H, CHS), 6.84 (s, 1H, =CH), 7.51 (m, 2H, *m*-Ph), 7.61 (t, J=7.2 Hz, 1H, *p*-Ph), 8.01 (d, J=8.5 Hz, 2H, *o*-Ph); ^{13}C NMR ($CDCl_3$, 125.8 MHz): *syn*-**5m** δ 7.0

(CH_3CH), 30.0 (NCH_3), 53.1 (CHS), 103.1 (=CH), 128.3 and 128.8 (*o*- and *m*-Ph), 133.5 (*p*-Ph), 137.5 (C1−Ph), 157.8 (C=), 172.5 (CO_{lactam}), 187.6 (CO_{ketone}); *anti*-**5m** δ 12.4 (CH_3CH), 30.0 (NCH_3), 59.7 (CHS), 103.3 (=CH), 128.3 and 128.8 (*o*- and *m*-Ph), 133.5 (*p*-Ph), 137.5 (C1−Ph), 158.0 (C=), 172.3 (CO_{lactam}), 187.6 (CO_{ketone}); HRMS: calcd for $C_{13}H_{13}NNaO_3S$ $[M+Na]^+$ 286.0508, found 286.0514.

*5.6.14. (Z)-(3-Benzyl-5-methyl-1,4-dioxothiazolidin-2-ylidene)-N-phenylethanamide (**5n**).* Compound **5n** was obtained from **1n** (67.7 mg; 0.20 mmol; 6 mL CH_2Cl_2) and *m*-CPBA (95.2 mg; 0.40 mmol; 5 mL CH_2Cl_2) according to the general procedure (reaction time 30 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 75/25) gave pure **5n** as a colourless oil (53.9 mg; 76%; *syn*/*anti* 87/13); R_f=0.36 and 0.42 (toluene/acetone 7/3); IR (ATR): ν=3300, 3198, 3173, 3060, 2931, 1726, 1671, 1613, 1549, 1467, 1445, 1322, 1163, 1040, 1010, 735, 697 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): *syn*-**5n** δ 1.42 (d, J=7.5 Hz, 3H, CH_3), 4.11 (q, J=7.5 Hz, 1H, CHS), 4.84 (d, J=16.5 Hz, 1H, CH_AH_BPh), 4.90 (d, J=16.5 Hz, 1H, CH_AH_BPh), 6.07 (s, 1H, =CH), 7.06−7.62 (m, 10H, 2× Ph), 10.28 (s, 1H, NH); *anti*-**5n** δ 1.46 (d, J=8.0 Hz, 3H, CH_3), 3.80 (q, J=8.0 Hz, 1H, CHS), 4.76 (d, J=16.3 Hz, 1H, CH_AH_BPh), 4.96 (d, J=16.3 Hz, 1H, CH_AH_BPh), 6.12 (s, 1H, =CH), 7.06−7.62 (m, 10H, 2× Ph), 10.28 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 125.8 MHz): *syn*-**5n** δ 6.6 (CH_3), 45.7 (CH_2Ph), 52.6 (CHS), 103.8 (=CH), 119.3, 123.7, 126.6, 127.6, 128.8, 128.9, 134.2, 138.8, 153.8 (C=), 161.9 (CO_{amide}), 173.1 (CO_{lactam}); *anti*-**5n** δ 11.7 (CH_3), 45.7 (CH_2Ph), 59.2 (CHS), 104.6 (=CH), 119.2, 125.3, 126.7, 128.2, 134.2, 137.4, 153.8 (C=), 161.9 (CO_{amide}), 173.1 (CO_{lactam}); HRMS: calcd for $C_{19}H_{19}N_2O_2S$ $[M+H]^+$ 355.1116, found 355.1120.

*5.6.15. (Z)-Ethyl (3-benzyl-5-methyl-1,4-dioxothiazolidin-2-ylidene) ethanoate (**5o**).* Compound **5o** was obtained from **1o** (58.3 mg; 0.20 mmol; 3 mL CH_2Cl_2) and *m*-CPBA (81.2 mg; 0.40 mmol; 4 mL CH_2Cl_2) according to the general procedure (reaction time 30 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 85/15) gave pure **5o** as a colourless oil (52.3 mg; 85%; *syn*/*anti* 86/14); R_f=0.30 (toluene/acetone 9/1); IR (ATR): ν=3063, 2983, 2937, 1727, 1707, 1616, 1293, 1154, 1056, 836, 734, 698 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): *syn*-**5o** δ 1.21 (t, J=7.3 Hz, 3H, CH_3CH_2), 1.42 (d, J=7.0 Hz. 3H, CH_3CH), 4.12−4.19 (m, 3H, CHS and CH_2O), 4.92 (d, J=16.0 Hz, 1H, CH_AH_BPh), 4.94 (d, J=16.0 Hz, 1H, CH_AH_BPh), 5.85 (s, 1H, =CH), 7.25 (d, J=7.0 Hz, 2H, *o*-Ph), 7.29 (t, J=7.3 Hz, 1H, *p*-Ph), 7.35 (m, 2H, *m*-Ph); *anti*-**5o** δ 1.20 (t, J=7.3 Hz, 3H, CH_3CH_2), 1.48 (d, J=7.5 Hz, 3H, CH_3CH), 3.90 (q, J=7.5 Hz, 1H, CHS), CH_2O is covered by *syn*-**5o**, 4.82 (d, J=16.0 Hz, 1H, CH_AH_BPh), 4.99 (d, J=16.0 Hz, 1H, CH_AH_BPh), 5.88 (s, 1H, =CH), 7.24−7.37 (m, 5H, Ph); ^{13}C NMR (DMSO-d_6, 125.8 MHz): *syn*-**5o** δ 6.6 (CH_3CH), 14.0 (CH_3CH_2), 45.1 (CH_2Ph), 52.7 (CHS), 60.5 (CH_2O), 99.6 (=CH), 126.7 (*o*-Ph), 127.6 (*p*-Ph), 128.7 (*m*-Ph), 134.3 (C1−Ph), 157.2 (C=), 164.5 (CO_{ester}), 173.4 (CO_{lactam}); *anti*-**5o** δ 11.5 (CH_3CH), 14.0 (CH_3CH_2), 45.2 (CH_2Ph), 59.6 (CHS), 60.5 (CH_2O), 100.3 (=CH), 126.8 (*o*-Ph), 127.7 (*p*-Ph), 128.7 (*m*-Ph), 134.3 (C1−Ph), 157.3 (C=), 164.3 (CO_{ester}), 173.0 (CO_{lactam}); ^1H NMR ($CDCl_3$, 500 MHz): *syn*-**5o** δ 1.29 (t, J=7.3 Hz, 3H, CH_3CH_2), 1.67 (d, J=7.5 Hz, 3H, CH_3CH), 3.48 (q, J=7.5 Hz, 1H, CHS), 4.24 (q, J=7.3 Hz, 2H, CH_2O), 4.79 (d, J=15.5 Hz, 1H, CH_AH_BPh), 4.94 (d, J=15.5 Hz, 1H, CH_AH_BPh), 5.67 (s, 1H, =CH), 7.18−7.39 (m, 5H, Ph); *anti*-**5o** δ 1.29 (t, J=7.3 Hz, 3H, CH_3CH_2), 1.58 (d, J=7.5 Hz, 3H, CH_3CH), 3.71 (q, J=7.5 Hz, 1H, CHS), 4.24 (q, J=7.3 Hz, 2H, OCH_2), 4.81 (d, J=15.5 Hz, 1H, CH_AH_BPh), 4.91 (d, J=15.5 Hz, 1H, CH_AH_BPh), 5.70 (s, 1H, =CH), 7.18−7.39 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$, 125.8 MHz): *syn*-**5o** δ 6.7 (CH_3CH), 14.0 (CH_3CH_2), 46.8 (CH_2Ph), 53.5 (CHS), 61.3 (CH_2O), 101.7 (=CH), 126.7 (*o*-Ph), 128.2 (*p*-Ph), 129.1 (*m*-Ph), 133.1 (C1−Ph), 155.9 (C=), 164.5 (CO_{ester}), 172.4 (CO_{lactam}); *anti*-**5o** δ 12.4 (CH_3CH), 14.0 (CH_3CH_2), 46.6 (CH_2Ph), 59.6 (CHS), 61.3 (CH_2O), 102.1 (=CH), assignation for Ph is not certain, 133.0 (C1−Ph), 156.0 (C=), 164.5 (CO_{ester}), 172.8 (CO_{lactam}); HRMS: calcd for $C_{15}H_{18}NO_4S$ $[M+H]^+$ 308.0951, found 308.0963.

*5.6.16. (Z)-Ethyl (3-(3-bromopropyl)-5-methyl-1,4-dioxothiazolidin-2-ylidene)ethanoate (**5p**).* Compound **5p** was obtained from **1p** (64.4 mg; 0.20 mmol; 4 mL CH_2Cl_2) and *m*-CPBA (95.1 mg; 0.40 mmol; 4 mL CH_2Cl_2) according to the general procedure (reaction time 35 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 85/15) gave pure **5p** as a colourless oil (57.5 mg; 85%; *syn*/*anti* 87/13); R_f=0.39 (toluene/acetone 4/1); IR (ATR): ν=2983, 2939, 1709, 1615, 1306, 1236, 1182, 1145, 1059, 838 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): *syn*-**5p** δ 1.35 (t, J=7.0 Hz, 3H, CH_3CH_2), 1.62 (d, J=7.0 Hz, 3H, CH_3CH), 2.16−2.21 (m, 2H, $CH_2CH_2CH_2$), 3.39 (q, J=7.0 Hz, 1H, CHS), 3.37−3.44 (m, 2H, CH_2Br), 3.76−3.82 (m, 1H, NCH_aH_b), 3.85−3.91 (m, 1H, NCH_aH_b), 4.32 (q, J=7.0 Hz, 2H, CH_2O), 5.85 (s, 1H, =CH); *anti*-**5p** δ 1.35 (t, J=7.0 Hz, 3H, CH_3CH_2), 1.54 (d, J=8.0 Hz, 3H, CH_3CH), 2.16−2.21 (m, 2H, $CH_2CH_2CH_2$), 3.37−3.44 (m, 2H, CH_2Br), 3.63 (q, J=8.0 Hz, 1H, CHS), 3.76−3.82 (m, 1H, NCH_aH_b), 3.85−3.91 (m, 1H, NCH_aH_b), 4.32 (q, J=7.0 Hz, 2H, CH_2O), 5.88 (s, 1H, =CH); ^{13}C NMR ($CDCl_3$, 125.8 MHz): *syn*-**5p** δ 6.6 (CH_3CH), 14.2 (CH_3CH_2), 28.9 ($CH_2CH_2CH_2$), 29.5 (CH_2Br), 41.9 (NCH_2), 53.5 (CHS), 61.4 (CH_2O), 100.8 (=CH), 156.1 (C=), 164.6 (CO_{ester}), 172.3 (CO_{lactam}); *anti*-**5p** δ 12.2 (CH_3CH), 14.2 (CH_3CH_2), 28.9 ($CH_2CH_2CH_2$), 29.5 (CH_2Br), 41.9 (NCH_2), 59.6 (CHS), 61.4 (CH_2O), 101.1 (=CH), 156.1 (C=), 164.6 (CO_{ester}), 172.3 (CO_{lactam}); HRMS: calcd for $C_{11}H_{17}BrNO_4S$ $[M+Na]^+$ 338.0056, found 338.0041.

*5.6.17. (Z)-(3-Benzyl-5-ethoxycarbonylmethyl-1,4-dioxothiazolidin-2-ylidene)-N-phenylethanamide (**5q**).* Compound **5q** was obtained from **1q** (102.6 mg; 0.25 mmol; 5 mL CH_2Cl_2) and *m*-CPBA (119.0 mg; 0.50 mmol; 8 mL CH_2Cl_2) according to the general procedure (reaction time 45 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 70/30) gave pure **5q** as a colourless oil (88.4 mg; 83%; *syn*/*anti* 79/21); R_f=0.42 and 0.61 (toluene/acetone 7/3); IR (KBr): ν=3259, 3196, 3061, 2981, 2930, 1723, 1673, 1602, 1549, 1323, 1165, 1018, 839, 756, 695 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): *syn*-**5q** δ 1.23 (t, J=7.0 Hz, 3H, CH_3), 2.94 (dd, J_{AB}=17.8 Hz, J_{AX}=10.5 Hz, 1H, $CH_AH_BCO_2Et$), 3.09 (dd, J_{AB}=17.8 Hz, J_{BX}=4.0 Hz, 1H, $CH_AH_BCO_2Et$), 4.16 (q, J=7.0 Hz, 2H, CH_2O), 4.47 (dd, J_{AX}=10.5 Hz, J_{BX}=4.0 Hz, 1H, CH_XS), 4.86 (d, J=16.2 Hz, 1H, CH_AH_BPh), 4.90 (d, J=16.2 Hz, 1H, CH_AH_BPh), 6.08 (s, 1H, =CH), 7.06−7.64 (m, 10H, 2× Ph), 10.29 (s, 1H, NH); *anti*-**5q** δ 1.15 (t, J=7.2 Hz, 3H, CH_3), 3.23 (dd, J_{AB}=18.4 Hz, J_{AX}=5.5 Hz, 1H, $CH_AH_BCO_2Et$), 3.54 (dd, J_{AB}=18.4 Hz, J_{BX}=4.2 Hz, 1H, $CH_AH_BCO_2Et$), 3.93 (m, J_{AX}=5.5 Hz, J_{BX}=4.2 Hz, 1H, CH_XS), 4.03−4.11 (q, J=7.2 Hz, 2H, CH_2O), CH_AH_BPh are covered by *syn*-**5q**, 6.08 (s, 1H, =CH), 7.06−7.64 (m, 10H, 2× Ph), 10.26 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 125.8 MHz): *syn*-**5q** δ 14.0 (CH_3), 27.4 (CH_2CO_2Et), 45.7 (CH_2Ph), 53.8 (CHS), 60.8 (CH_2O), 103.9 (=CH), 119.2, 123.7, 126.6, 127.6, 128.7, 128.8, 134.0, 138.8, 154.2 (C=), 161.9 (CO_{amide}), 170.2 and 171.6 (CO_{lactam} and CO_{ester}); *anti*-**5q** δ 13.8 (CH_3), 31.8 (CH_2CO_2Et), 45.7 (CH_2Ph), 61.2 (CH_2O), 61.6 (CHS), 102.8 (=CH), 119.2, 123.6, 125.3, 126.8, 127.7, 128.2, 134.1, 138.8, 154.8 (C=), 161.8 (CO_{amide}), 170.7 and 171.3 (CO_{lactam} and CO_{ester}); HRMS: calcd for $C_{22}H_{23}N_2O_5S$ $[M+H]^+$ 427.1322, found 427.1313.

*5.6.18. (Z)-(3-Benzyl-5-ethoxycarbonylmethyl-1,4-dioxothiazolidin-2-ylidene)-1-phenylethanone (**5r**).* Compound **5r** was obtained from **1r** (79.1 mg; 0.20 mmol; 3 mL CH_2Cl_2) and *m*-CPBA (81.2 mg; 0.40 mmol; 4 mL CH_2Cl_2) according to the general procedure (reaction time 90 min). Column chromatography (eluent: gradient toluene/acetone 100/0 to 60/40) gave pure **5r** as a colourless oil (58.7 mg; 71%; *syn*/*anti* 77/23); R_f=0.30 (toluene/acetone 7/3); IR (KBr): ν=3063, 3032, 2980, 2930, 1720, 1650, 1575, 1320, 1292, 1175, 1042, 1019, 778, 740, 699 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): *syn*-**5r** δ 1.30 (t, J=7.0 Hz, 3H, CH_3), 3.23 (dd, J_{AB}=18.5 Hz, J_{AX}=9.5 Hz, 1H, $CH_AH_BCO_2Et$), 3.27

(dd, J_{AB}=18.5 Hz, J_{BX}=4.3 Hz, 1H, $CH_AH_BCO_2Et$), 4.01 (dd, J_{AX}=9.5 Hz, J_{BX}=4.3 Hz, 1H, CH_XS), 4.23 (q, J=7.0 Hz, 2H, CH_2O), 4.86 (d, J=15.5 Hz, 1H, CH_AH_BPh), 5.11 (d, J=15.5 Hz, 1H, CH_AH_BPh), 6.78 (s, 1H, =CH), 7.26–7.74 (m, 10H, 2× Ph); *anti*-**5r** δ 1.21 (t, J=7.0 Hz, 3H, CH_3), 3.41 (dd, J_{AB}=18.5 Hz, J_{AX}=4.3 Hz, 1H, $CH_AH_BCO_2Et$), 3.44 (dd, J_{AB}=18.5 Hz, J_{BX}=4.3 Hz, 1H, $CH_AH_BCO_2Et$), 3.75 (t, J_{AX}=J_{BX}=4.3 Hz, 1H, CH_XS), 4.07–4.14 (m, 2H, CH_2O), 4.90 (d, J=16.0 Hz, 1H, CH_AH_BPh), 5.16 (d, J=16.0 Hz, 1H, CH_AH_BPh), 6.75 (s, 1H, =CH), 7.26–7.74 (m, 10H, 2× Ph); ^{13}C NMR ($CDCl_3$, 125.8 MHz): *syn*-**5r** δ 14.1 (CH_3), 27.3 (CH_2CO_2Et), 47.1 (CH_2Ph), 54.6 (CHS), 61.6 (CH_2O), 105.4 (=CH), 126.9, 128.2, 128.7, 129.2, 133.2, 133.4, 137.2, 156.4 (C=), 170.3 and 171.5 (CO_{lactam} and CO_{ester}), 187.4 (CO_{ketone}); *anti*-**5r** δ 13.9 (CH_3), 32.3 (CH_2CO_2Et), 47.4 (CH_2Ph), 62.1 and 62.2 (CH_2O and CHS), 103.3 (=CH), 127.0, 128.4, 128.6, 129.1, 133.1, 133.2, 137.4, 157.6 (C=), 170.4 and 171.3 (CO_{lactam} and CO_{ester}), 187.4 (CO_{ketone}); ^{1}H NMR (DMSO-d_6, 500 MHz): *syn*-**5r** δ 1.22 (t, J=7.0 Hz, 3H, CH_3), 2.95 (dd, J_{AB}=17.8 Hz, J_{AX}=10.5 Hz, 1H, $CH_AH_BCO_2Et$), 3.10 (dd, J_{AB}=17.8 Hz, J_{BX}=4.0 Hz, 1H, $CH_AH_BCO_2Et$), 4.14 (q, J=7.0 Hz, 2H, CH_2O), 4.48 (dd, J_{AX}=10.5 Hz, J_{BX}=4.0 Hz, 1H, CH_XS), 5.10 (s, 2H, CH_2Ph), 7.10 (s, 1H, =CH), 7.27–7.97 (m, 10H, 2× Ph); ^{13}C NMR (DMSO-d_6, 125.8 MHz): *syn*-**5r** δ 14.1 (CH_3), 27.7 (CH_2CO_2Et), 44.6 (CH_2Ph), 53.7 (CHS), 61.0 (CH_2O), 103.6 (=CH), 127.2, 128.2, 128.8, 129.0, 133.7, 134.5, 137.3, 158.1 (C=), 170.3 and 172.4 (CO_{lactam} and CO_{ester}), 187.6 (CO_{ketone}); *anti*-**5r** δ 13.5 (CH_3), 31.8 (CH_2CO_2Et), 45.4 (CH_2Ph), 61.3 and 61.5 (CH_2O and CHS), 102.6 (=CH), assignation for Ph is not certain, 158.7 (C=), 170.9 and 171.7 (CO_{lactam} and CO_{ester}), 187.2 (CO_{ketone}); HRMS: calcd for $C_{22}H_{22}NO_5S$ $[M+H]^+$ 412.1213, found 412.1211.

Acknowledgements

This work was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia, Grant No. 172020 and Deutscher Akademischer Austauschdienst (DAAD)—project ID: 504 252 70.

Supplementary data

^{1}H NMR spectra for *syn*- and *anti*-**5l**, absolute energies and *x*, *y*, *z* coordinates of the optimized structures. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.05.087.

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