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Transformations of 2-alkylidene-4-oxothiazolidine vinyl bromides initiated by bromophilic attack of neutral and anionic nucleophiles

Marija Baranac-Stojanović [a,b,*], Jovana Tatar [b], Milovan Stojanović [b], Rade Marković [a,b,*]

[a] Faculty of Chemistry, University of Belgrade, Studentski trg 16, PO Box 158, 11000 Belgrade, Serbia
[b] Center for Chemistry ICTM, PO Box 473, 11000 Belgrade, Serbia

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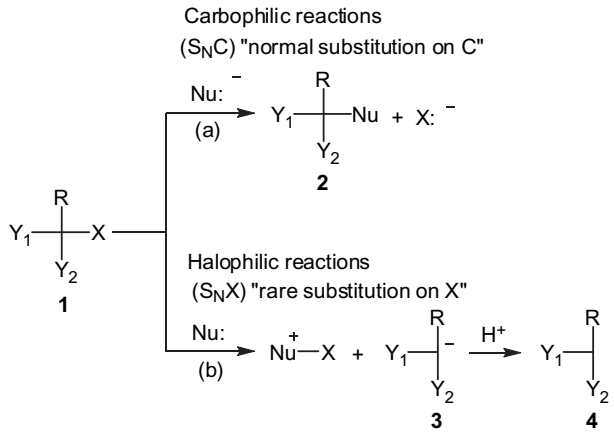
ABSTRACT

Vinyl bromides derived from 2-alkylidene-4-oxothiazolidines represent a class of vinyl halides, which readily undergo a bromophilic attack by a range of nucleophiles. With Ph_3P, AcS^-, CN^-, I^-, F^-, Ac_2CH^- and N_3^- the attack ends up with reductive debromination, whereas the bromine substitution takes place with KSCN. When acetate anion and organic bases, such as pyridine, Et_3N or morpholine, are employed as nucleophiles the initial bromophilic attack is followed by bromine migration to the C(5) position of the ring, allowing the C(5) functionalization of this heterocyclic system.

1. Introduction

Nucleophilic substitutions occurring by an attack at the carbon atom of an alkyl halide are among the most widely studied organic reactions (Scheme 1, route a).[1]



Scheme 1.

In contrast to the great amount of experimental and theoretical work within this central class of carbophilic reactions, the nucleophilic substitutions taking place at the halogen atom X (route b), with the expulsion of a carbanion **3** as a leaving group, are to date relatively undeveloped. Referred to in the literature as *halophilic reactions*,[2] they usually occur with substrates giving rise to a carbanionic leaving group stabilized by the presence of electron withdrawing groups (EWGs), for example, in the case of α-halosulfones,[3] α-halo-β-keto-sulfones,[4] α-haloketones,[5] α-halonitriles,[6] halogenated nitroalkanes,[7] diethyl bromo-[8a] and diethyl dibromomalonate,[8b] or selected *ortho*-substituted α,α-dibromoacetophenones.[9] Perhaloalkanes are rather inert towards nucleophilic displacement reactions, but they can undergo a halophilic attack by various nucleophiles, including phenoxides and alkoxides,[10] thiophenoxides,[10c,10d] *sec*-amines or their salts,[10d,11] phosphorous ylides,[10d,12] triphenylphosphine,[13] enamines and enolates.[10d] Halophilic reactions have also been observed in the case of 3-methyl-5-trichloro-methyl-1,2,4-oxadiazole,[14] 2-halomethyl-5-nitrofurans,[15] pentafluorohalo-benzenes,[16] substituted pentabromo-benzenes,[17] geminal[5] and vicinal dihalides.[5,18] Protonation of the carbanion **3** to yield **4**, i.e., the product of reductive dehalogenation, is often observed in these reactions.[2–4,14,15,17]

Synthetically viable, but rather scarce, halophilic reactions of vinyl halides (VyX) are limited to a couple of examples. In particular, reductive dehalogenation of 1,1-dibromo alkenes leads to the synthesis of vinyl bromides.[19] An efficient halophilic ring-opening E2 elimination of β-iodo-α,β-unsaturated γ-sultones **5** (Scheme 2) to allensulfonate **6** in DMSO or acetone, mediated by soft nucleophiles, such as iodide or thioacetate, has been de-scribed by Braverman et al.[20]

* Corresponding authors. Tel.: +381 11 3336741; fax: +381 11 636061; e-mail addresses: mbaranac@chem.bg.ac.rs (M. Baranac-Stojanović), markovic@chem.bg.ac.rs (R. Marković).

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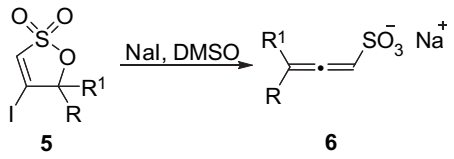
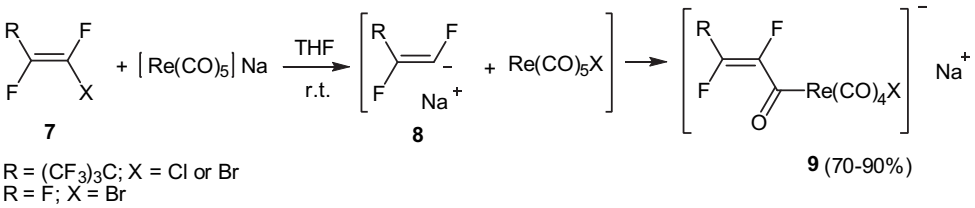


Scheme 2.

Another example of this chemistry involves a synthesis of halo (acyl)rhenate complexes **9** (Scheme 3) by a two-step sequence, initiated by halophilic attack of $[Re(CO)_5]^-Na^+$ on the halogen of polyfluorinated alkenyl halides **7**.[21] The nucleophilic addition of the resulting alkenyl carbanion intermediate **8** to CO gives rise to salts **9**.

2. Results and discussion

On the basis of the established susceptibility of 4-oxothiazolidines (*Z*)-**11** towards electrophilic attack on the enamine[24a] (Scheme 5), a number of the starting vinyl bromides **10** were prepared in moderate to high yields (Table 1) upon bromination under various experimental conditions. However, the *N*-substituted analogues of 5-unsubstituted 4-oxothiazolidines **11** are, due to the steric hindrance, regiospecifically brominated with molecular bromine or NBS at the C(5) position, yielding bromides **13**.[25]



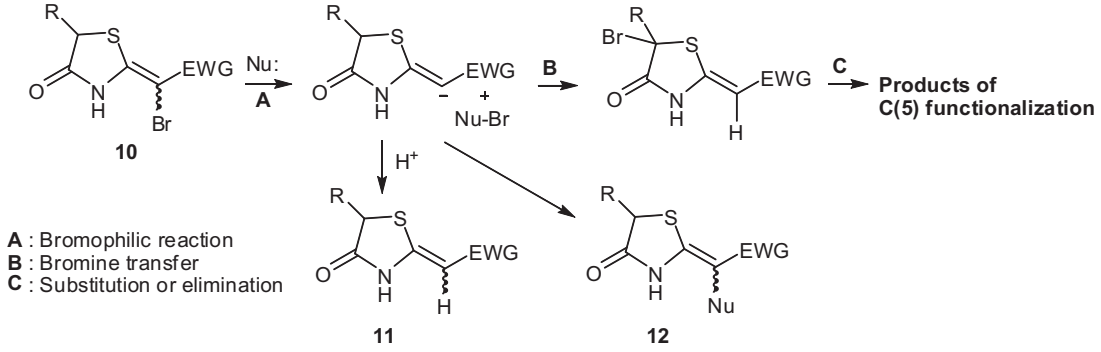
Scheme 3.

Extensive and systematic reactivity study on nucleophilic vinylic substitution (S_NV), has also been conducted by Rappoport et al.[22] on a range of selected substrates $Y_1Y_2C{=}CRX$, employing oxygen, sulfur or carbon nucleophiles.

Recently, we have shown that pyridine and a variety of pyridine derivatives possess chemical potential to rearrange 5-unsubstituted 4-oxothiazolidine vinyl bromides **10** (Scheme 4), via an initial bromophilic step, into a class of new pyridinium salts.[23] In this paper, we provide for the first time a full account on the overall strategy, outlined in Scheme 4, in which the bromophilic step **A** has been combined with bromine transfer (step **B**), followed by elimination/substitution (step **C**),

Likewise, upon changing the R substituent in *N*-methyl precursors **11** from H to Me, or CH_2CO_2Et, the corresponding products **15a** or **15b**, containing the two exocyclic double bonds, were readily formed in good yields, by dehydrobromination of an initially formed C(5) alkyl bromide **14**.

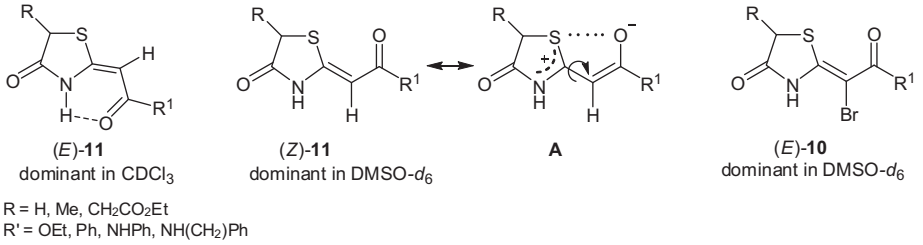
Regarding the configuration of the exocyclic C=C bond, all vinyl bromides **10a** and **10c–o** were isolated as a mixture of the *E*- and *Z*-isomers, and **10b** was formed as a single *Z*-isomer. These vinyl bromides and parent compounds **11** (R=H), are susceptible to *Z*/*E* isomerization[24] due to the lowering of the rotational barrier. This isomerization is a result of the electronic interactions between the donor and acceptor groups via the C=C bond, imparting a partial single

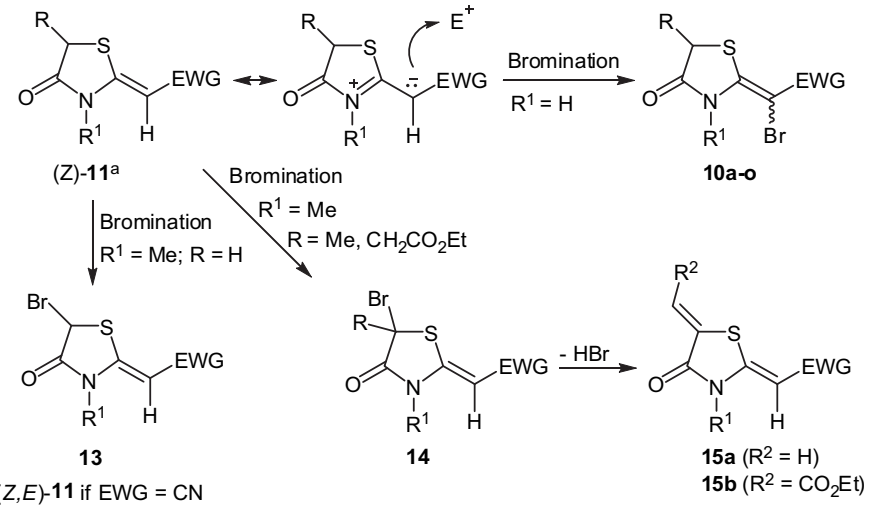


Scheme 4.

to allow the functionalization of 5-unsubstituted and substituted 4-oxothiazolidines. We also report reactions of selected substrate **10** with a series of neutral and anionic nucleophiles, leading to debromination product **11** and bromine substitution product **12**.

bond character, and is controlled by the appropriate choice of solvent. In accordance to the earlier generalization for a large number of thiazolidines **11** (R=H), the *E*-isomers (R=H) are the dominant species for the equilibrated *Z*/*E* mixtures in nonpolar $CDCl_3$ as the NH···O=C noncovalent interaction leads to favourable six-membered H-bonding.[24b,c]





Scheme 5.

Table 1
Synthesis of vinyl bromides *Z*/*E*-**10** from 2-alkylidene-4-oxothiazolidines **11**

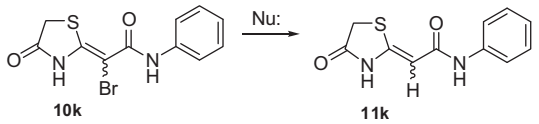
Substrate	R	EWG	Product (*Z*/*E* ratio)	Yield[a] (%)
R^1=H				
11a	CH_2CO_2Et	CONHPh	**10a** (39:61)	60[b]
11b	CH_2CO_2Et	$CONH(CH_2)_2Ph$	**10b** (100:0)	78[c]
11c	CH_2CO_2Et	CO_2Et	**10c** (54:46)	85[b]
11d	CH_2CO_2Et	COPh	**10d** (14:86)	53[b]
11e	CH_2CO_2Et	CN	**10e** (65:35)[b]	75[b]; 64[c]
11f	CH_3	CONHPh	**10f** (43:57)	64[d]
11g	CH_3	$CONH(CH_2)_2Ph$	**10g** (60:40)	99[d]
11h	CH_3	CO_2Et	**10h** (7:93)	68[d]
11i	CH_3	COPh	**10i** (20:80)	54[d]
11j	CH_3	CN	**10j** (54:46)	84[d]
11k	H	CONHPh	**10k** (85:15)	91[e]
11l	H	$CONH(CH_2)_2Ph$	**10l** (85:15)	79[e]
11m	H	CO_2Et	**10m** (86:14)	76[e]
11n	H	COPh	**10n** (18:82)	72[e]
11o	H	CN	**10o** (64:36)	65[e]
R^1=CH_3				
11p	H	CO_2Et	**13** (100:0)	98[f]
11q	CH_3	CO_2Et	**15a** (100:0)	71[f]
11r	CH_2CO_2Et	CO_2Et	**15b** (100:0)	63[f]

[a] Yield of isolated products.
[b] Br_2 (1 equiv), dry EtOH, rt.
[c] Br_2 (1 equiv), CCl_4, reflux.
[d] Br_2 (1 equiv), dry EtOH, −10 °C.
[e] Br_2 (1 equiv), $CHCl_3$, reflux.
[f] Br_2 (1 equiv), $CHCl_3$, rt.

However, an increase of the ground-state polarization of thiazolidines **11** in polar solvents, such as DMSO, enhances the presence of the *Z*-isomers because of the favourable 1,5-type electrostatic S···O interactions depicted in structure **A**. Based on this well-established direction of the *Z*/*E* isomerization in polar DMSO, it is obvious that the corresponding *E*-isomer will be the major species in the case of vinyl bromides **10**. Therefore, the correlation of the ^1H and ^{13}C NMR spectroscopic data obtained for vinyl bromides **10** with these of the previously reported for an extensive series of **11**, in combination with the 1D nuclear Overhauser effect measurements and an X-ray structural analysis studies of the selected thiazolidine **11**,[24] allowed us to carry out proper structure elucidation of the *Z*- and *E*-isomers **10**. It suffices to point out that the reactions of vinyl bromides **10** with various nucleophiles, discussed below, are not influenced by the configuration of the exocyclic C=C bond.

A range of soft nucleophiles (Ph_3P, AcS^-, I^-, Ac_2CH^-), as well as the intermediate nucleophiles (CN^-, N_3^-) and one hard nucleophile (F^-) can debrominate the double bond of vinyl bromide **10k** to parent compound **11k**, probably via bromophilic attack, followed by protonation of the vinyl carbanion (Table 2). To the best of our knowledge, this is the first example of bromophilic attack exerted by a fluoride ion.

Table 2
Reductive debromination of vinyl bromide **10k** to **11k**

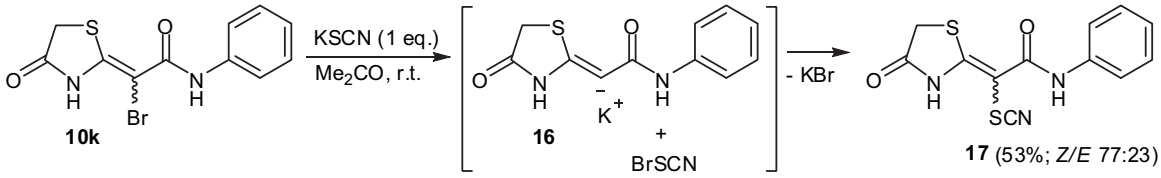


Nu: = Ph_3P, AcS^-, CN^-, I^-, F^-, Ac_2CH^-, N_3^-

Nucleophile	Solvent	*T*	Yield[a] (%) (*Z*/*E* ratio)
Ph_3P; 10 equiv	$CHCl_3$	Reflux	88 (49:51)
AcS^-; 2 equiv	Me_2CO/H_2O (7:1)	rt	72 (100:0)
CN^-; 10 equiv	MeCN	Reflux	51 (100:0)
I^-; 3 equiv	$MeCN/H_2O$	rt	71 (100:0)
F^-; 3 equiv	DMF	70 °C	25[b] (56:44)
Ac_2CH^-; 2 equiv	MeCN	rt	24[b] (53:47)
N_3^-; 2 equiv	Me_2CO/H_2O (7:1)	rt	34[b] (41:59)

[a] Yield of isolated product.
[b] The rest of the organic mixture decomposed.

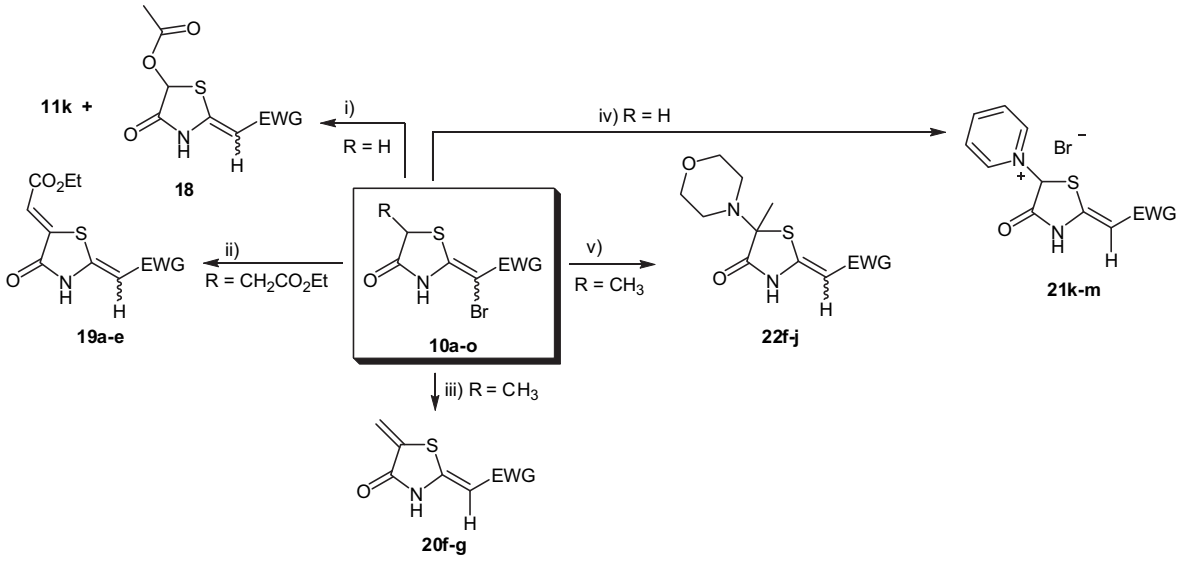
Amongst the tested nucleophiles, it is especially noteworthy that another reaction pathway was established with KSCN. The first step of the reaction of vinyl bromide **10k** with 1 equiv of KSCN was



Scheme 6.

again nucleophilic attack on bromine, furnishing the carbanion **16** (Scheme 6), which then rapidly reacted with BrSCN yielding the tetra-substituted alkene **17**. In support of this mechanism is the finding that a small amount of 4-oxothiazolidine **11k** (6%) was formed when the reaction was conducted in Me_2CO/H_2O 7:1 (v/v).

The mechanism for the formation of new pyridinium salts **21**, containing 4-oxothiazolidine fragment bonded through the C(5)-position to the pyridine nitrogen, was investigated in more details. The lack of inhibition in the presence of a strong electron acceptor, such as *p*-dinitrobenzene, both in catalytic and equimolar amounts, is indicative of an ionic mechanism. In order to distinguish between the intra- and intermolecular process, two separate crossover reactions have been carried out: (1) a mixture of equimolar amounts of vinyl bromide **10k** and 4-oxothiazolidine **11l**, and (2) vinyl bromide **10l** and



Scheme 7. Reagents and conditions: (i) AcOK (2 equiv), Me_2CO/H_2O, rt, 5 h; (ii) Method A: pyridine (10 equiv), $CHCl_3$, reflux, 6–59 h; Method B: Et_3N (5 equiv), $CHCl_3$, rt, 20 min–12 h; (iii) pyridine (20 equiv), $CHCl_3$, reflux, 21–64 h; (iv) pyridine, (10 equiv), $CHCl_3$, reflux, 4–7 days; (v) morpholine (10 equiv), $CHCl_3$, rt, 4–59 h.

Interestingly, on examination of a reductive dehalogenation ability of the hard acetate nucleophile in the reaction with vinyl bromide **10k**, the experimental results showed that the same anion was also capable of inducing rearrangement into the C(5) acetate **18** (Scheme 7, Table 3), though in low yield.

However, we have found that the organic bases, such as pyridine, Et_3N and morpholine,[26] can be used as the major and very efficient reagents for rearranging vinyl bromides **10a**–**o** to various C(5)-functionalized 4-oxothiazolidines **19**–**22** (Scheme 7). The yields of the rearranged products are good to high (Table 3).

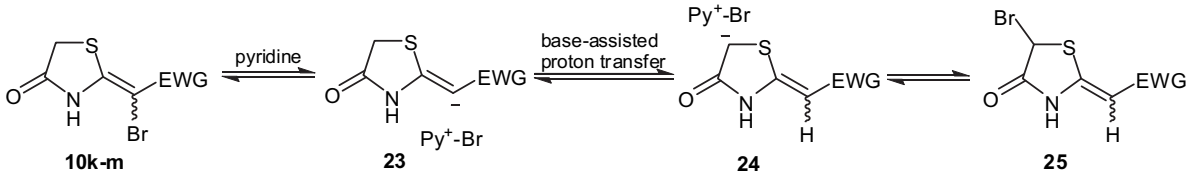
All these observations are in accordance with an ionic, intramolecular process, depicted in Scheme 8 with pyridine acting as a nucleophile and base. The first step, i.e., the bromophilic reaction, is followed by the bromine migration[27] to the C(5) position of the ring, which occurs through the base-assisted proton transfer from the C(5) to the vinylic position of the anion **23**. The resulting C(5)-carbanion **24** is brominated to the C(5) alkyl bromide **25**, which undergoes substitution with pyridine to form salts **21**. The mechanism for the formation of other C(5)-functionalized products, such as **19a**–**e**, **20f**–**g** and **22f**–**j**, is probably similar, with the difference being the last step. Consequently, the last step is either substitution (when morpholine is used as a nucleophile), or HBr elimination, occurring in the presence of pyridine and Et_3N.

In these rearrangements the *bromophilic reaction/bromine transfer/elimination(substitution)* cascade process implies a multiple role of nucleophile, bromine transfer agent and base, for the organic base.

Table 3
Rearrangement reactions of vinyl bromides **10**

Entry	Substrate	R	EWG	Product(s) (*Z*/*E* ratio)	Yield[a] (%)
1	**10k**	H	CONHPh	**11k**; **18** (91:9)	17[b]; 28[b]
2	**10a**	CH_2CO_2Et	CONHPh	**19a** (100:0)[c]	67[c]; 91[d]
3	**10b**	CH_2CO_2Et	$CONH(CH_2)_2Ph$	**19b** (82:18)[c]	51[c]; 92[d]
4	**10c**	CH_2CO_2Et	CO_2Et	**19c** (66:34)[c]	49[c]; 92[d]
5	**10d**	CH_2CO_2Et	COPh	**19d** (60:40)[c]	61[c]; 89[d]
6	**10e**	CH_2CO_2Et	CN	**19e** (14:86)[c]	76[c]; 93[d]
7	**10f**	CH_3	CONHPh	**20f** (100:0)	10
8	**10g**	CH_3	$CONH(CH_2)_2Ph$	**20g** (100:0)	35
9	**10k**	H	CONHPh	**21k** (100:0)	89
10	**10l**	H	$CONH(CH_2)_2Ph$	**21l** (100:0)	87
11	**10m**	H	CO_2Et	**21m** (100:0)	77
12	**10f**	CH_3	CONHPh	**22f** (13:87)	90
13	**10g**	CH_3	$CONH(CH_2)_2Ph$	**22g** (44:56)	62
14	**10h**	CH_3	CO_2Et	**22h** (60:40)	90
15	**10i**	CH_3	COPh	**22i** (100:0)	74
16	**10j**	CH_3	CN	**22j** (100:0)	83

[a] Yield of isolated products.
[b] Calculated from ^1H NMR spectrum, since a minor part of compound **18** was isolated in a mixture with **11k**.
[c] Method A (see Scheme 7 and Experimental section).
[d] Method B (see Scheme 7 and Experimental section).

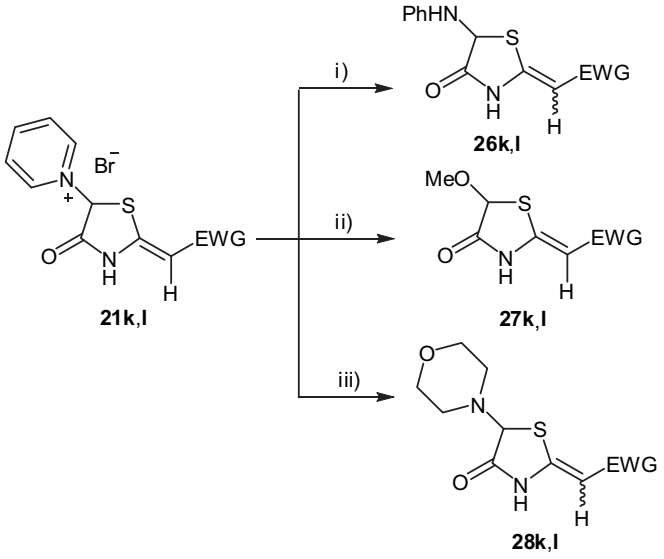


Scheme 8.

4-oxothiazolidine **11k** were treated with 10-fold molar excess of pyridine in refluxing $CHCl_3$. In reaction 1 the corresponding pyridinium salt **21k** and unchanged 4-oxothiazolidine **11l** were isolated, whereas in the case of reaction 2, the pyridinium salt **21l** and unchanged 4-oxothiazolidine **11k** were isolated from the reaction mixture. Furthermore, monitoring of the reaction of **10k** with excess of pyridine in $CDCl_3$ by ^1H NMR spectroscopy revealed that the parent 4-oxothiazolidine **11k** is not formed as an intermediate.

The importance of the ethoxycarbonyl group for stabilization of the system with two exocyclic C=C bonds is clearly seen on the basis of the yields of the products **19a**–**e**, which depending on the applied method, range from 49 to 76% or 89 to 93% (Table 3; entries 1–6) and only 10–35% for **20f** and **g** (entries 7 and 8). In the case of **19a**–**e** the stable, fully conjugated system is formed. In addition, moderate yields of the products **19a**–**e**, obtained by the use of pyridine as the bromine transfer agent, were later improved by the use of a stronger base, Et_3N. The synthesis of **19a**–**e** was optimized by the treatment of 4-oxothiazolidines **11a**–**e** with pyridinium hydrobromide perbromide (PHBP),[28] allowing quantitative yields (94–100%) to be obtained. As can be seen from Scheme 7 and Table 3, the formation of the less stable derivatives **20f** and **g** was restricted to the bromides **10f** and **g**, having an amide substituent at the double bond. Under the same reaction conditions (20-fold molar excess of pyridine, $CHCl_3$, reflux) only unchanged vinyl bromide **10h** was isolated from the reaction mixture, whereas bromides **10i** and **10j** yielded 4-oxothiazolidines **11i** and **11j** in 23% and 14% yields, respectively. Vinyl bromides **10n** and **10o** were not suitable precursors for the synthesis of pyridinium salts under similar reaction conditions, since **10n** yielded only the product of reductive dehalogenation **11n** (18%), while **10o** gave inseparable complex mixture.

It is worth noting that pyridine in pyridinium salts **21k** and **l** can efficiently be replaced by neutral nitrogen and oxygen nucleophiles to give new 5-amino- and 5-alkoxy-4-oxothiazolidines **26**–**28** (Scheme 9, Table 4). In spite of the fact that pyridine is a relatively poor leaving group and susceptibility of the pyridinium ring to nucleophilic attack at the 2-, 4- and 6-positions, [29] and in some cases was followed by ring cleavage,[30] we have demonstrated that the pyridinium salts **21** are excellent substrates for substitution reactions with these neutral nucleophiles.



Scheme 9. Reagent and conditions: (i) aniline (excess), MeOH/H_2O, rt, 0.5–1.45 h; (ii) K_2CO_3, MeOH, reflux, 24 h; (iii) morpholine (excess), $CHCl_3$, rt, 6.5–25 h.

Table 4
Nucleophilic substitution reactions of pyridinium salts **21**

Substrate	EWG	Product (*Z*/*E* ratio)	Yield[a,b] (%)
21k	CONHPh	**26k** (76:24)	63
21l	$CONH(CH_2)_2Ph$	**26l** (20:80)	86
21k	CONHPh	**27k** (100:0)	69
21l	$CONH(CH_2)_2Ph$	**27l** (100:0)	66
21k	CONHPh	**28k** (9:91)	91
21l	$CONH(CH_2)_2Ph$	**28l** (18:82)	87

[a] Yield of isolated products.
[b] Based on vinyl bromides **10k** and **10l**.

3. Conclusion

This paper describes reactions of 2-alkylidene-4-oxothiazolidine vinyl bromides with a variety of ionic and neutral nucleophiles, leading to (i) reductive debromination, (ii) bromine substitution or (iii) efficient C(5) functionalization of the ring, all of them initiated by the nucleophilic attack on bromine. Combination of this rare bromophilic reaction with bromine transfer was used for the first time to achieve a number of synthetically useful transformations of 4-oxothiazolidines.

4. Experimental

4.1. General

Melting points below 215 °C were determined on a Büchi apparatus and those above 215 °C on a Mikroheitztich Boetius PMHK 05 apparatus and are uncorrected. The IR spectra were recorded on a Perkin–Elmer FTIR 1725X spectrophotometer and are reported as wave numbers (cm^{-1}). Samples for IR spectral measurements were prepared as KBr discs. The NMR spectra were recorded on a Varian Gemini 2000 spectrometer (^1H at 200 MHz, ^{13}C at 50.3 MHz) in DMSO-d_6 or $CDCl_3$ and on Bruker Avance III 500 (^1H at 500.26 MHz, ^{13}C at 125.79 MHz) in DMSO-d_6. Chemical shifts are reported in parts per million (ppm) on the δ scale from TMS as an internal standard. Elemental analyses were performed at the microanalysis laboratory at the Centre for Chemistry ICTM. HRMS was carried out on 6210 TOF LC/MS coupled with HPLC 1200 Series Agilent Technologies. Thin-layer chromatography (TLC) was carried out on Kieselgel Gnach 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). Aniline, carbontetrachloride, methanol, toluene, petrolether (40–70 °C) and ethyl acetate were distilled before use. Pyridine, triethylamine and morpholine were dried over NaOH or KOH and then distilled. Chloroform was extracted several times with water, dried over $CaCl_2$ or K_2CO_3 and distilled prior to use. Absolute ethanol was obtained by azeotropic distillation with benzene. 2-Alkylidene-4-oxothiazolidines were prepared from α-mercaptoesters and α-substituted nitriles, according to our procedure.[31] All vinyl bromides **10** should be stored in a freezer, at −15 °C.

4.2. General procedure for synthesis of 5-ethoxycarbonylmethyl-4-oxothiazolidine vinyl bromides 10a–e

4.2.1. Method A. To a suspension of 4-oxothiazolidine **11a**–**e** (1 mmol) in abs EtOH (20 mL) 2% bromine solution in the same solvent (ca. 1 equiv of bromine) was added dropwise at rt until complete consumption of the starting material (TLC). The bromine solution should be added at the rate, which is roughly the same as the rate of disappearance of bromine colour in the reaction mixture, though in some cases a pale yellow colour can appear before the addition is

completed. The reaction mixture was evaporated to a smaller volume and bromides were allowed to crystallize at rt or in a freezer. The products were isolated by filtration, as pure substances.

*4.2.1.1. 2-Bromo-2-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**10a**)*[24]. *Z*/*E* ratio: 39:61; yield: 60%; pale yellow solid, mp 122–123 °C; IR (KBr, cm^{-1}): ν_{max} 3371, 3227, 3180, 3090, 1719, 1634, 1595, 1558, 1528, 1499, 1443, 1378, 1312, 1234, 1195, 858, 834, 801, 755, 691; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 1.18 (t, J=7.2 Hz, 3H, CH_3), 2.99–3.03 (m, 2H, CH_AH_BCOO), 4.10 (q, J=7.2 Hz, 2H, CH_2O), 4.34 (dd, J_{Ax}=6.9 Hz, J_{Bx}=5.1 Hz, 1H, CH_xS), 7.09 (t, J=7.4 Hz, 1H, *p*-Ph), 7.28–7.35 (m, 2H, *m*-Ph), 7.60 (d, J=8.2 Hz, 2H, *o*-Ph), 9.29 (s, 1H, NH_{amide}), 11.22 (s, 1H, NH_{lactam}), (*Z* isomer) δ 1.19 (t, J=7.1 Hz, 3H, CH_3), 3.08–3.13 (m, 2H, CH_AH_BCOO), 4.11 (q, J=7.1 Hz, 2H, CH_2O), 4.53 (dd, J_{Ax}=7.5 Hz, J_{Bx}=4.8 Hz, 1H, CH_xS), 7.13 (t, J=7.4 Hz, 1H, *p*-Ph), 7.30–7.38 (m, 2H, *m*-Ph), 7.60 (d, J=8.2 Hz, 2H, *o*-Ph), 9.40 (s, 1H, NH_{amide}), 11.29 (br s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 14.2 (CH_3), 36.4 (CH_2COO), 43.5 (CHS), 60.9 (CH_2O), 79.4 (=CBr), 121.4 (*o*-Ph), 124.2 (*p*-Ph), 128.7 (*m*-Ph), 138.6 (C1-Ph), 151.1 (C=), 162.5 (CO_{amide}), 170.4 (CO_{ester}), 175.5 (CO_{lactam}), (*Z* isomer) δ 14.2 (CH_3), 36.1 (CH_2COO), 43.8 (CHS), 61.0 (CH_2O), 83.6 (=CBr), 122.2 (*o*-Ph), 124.8 (*p*-Ph), 128.7 (*m*-Ph), 138.1 (C1-Ph), 153.2 (C=), 162.2 (CO_{amide}), 170.4 (CO_{ester}), 174.8 (CO_{lactam}). Anal. Calcd for $C_{15}H_{15}BrN_2O_4S$: C, 45.12; H, 3.79; N, 7.02; S, 8.03; found: C, 45.34; H, 4.01; N, 6.77; S, 7.85.

*4.2.1.2. Ethyl 2-bromo-2-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)ethanoate (**10c**).* *Z*/*E* ratio: 54:46; yield 85%; pale yellow crystals, mp 86–88 °C; IR (KBr, cm^{-1}): ν_{max} 3196, 1719, 1671, 1583, 1449, 1374, 1316, 1273, 1235, 886, 858, 813, 756; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 1.20 (t, J=7.0 Hz, 3H, CH_3), 1.23 (t, J=7.0 Hz, 3H, CH_3), 3.08–3.12 (m, 2H, CH_AH_BCOO), 4.16 (q, J=7.0 Hz, 2H, CH_2O), 4.22 (q, J=7.0 Hz, 2H, CH_2O), 4.53 (dd, J_{Ax}=6.9 Hz, J_{Bx}=5.1 Hz, 1H, CH_xS), 10.84 (s, 1H, NH), (*E* isomer) δ 1.17 (t, J=7.2 Hz, 3H, CH_3), 1.22 (t, J=7.2 Hz, 3H, CH_3), 3.01–3.04 (m, 2H, CH_AH_BCOO), 4.09 (q, J=7.2 Hz, 2H, CH_2O), 4.12 (q, J=7.2 Hz, 2H, CH_2O), 4.41 (dd, J_{Ax}=6.6 Hz, J_{Bx}=5.4 Hz, 1H, CH_xS), 11.35 (s, 1H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 14.2 (CH_3), 14.4 (CH_3), 36.0 (CH_2COO), 44.1 (CHS), 61.0 (CH_2O), 61.9 (CH_2O), 81.8 (=CBr), 156.5 (C=), 162.6 (=CHCOO), 170.4 (CH_2COO), 175.4 (CO_{lactam}), (*E* isomer) δ 14.2 (CH_3), 14.4 (CH_3), 36.2 (CH_2COO), 43.9 (CHS), 60.9 (CH_2O), 61.5 (CH_2O), 77.3 (=CBr), 154.6 (C=), 163.9 (=CHCOO), 170.4 (CH_2COO), 175.7 (CO_{lactam}). Anal. Calcd for $C_{11}H_{14}BrNO_5S$: C, 37.51; H, 4.01; N, 3.98; S, 9.10; found: C, 37.34; H, 4.09; N, 4.28; S, 9.05.

*4.2.1.3. 2-Bromo-2-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**10d**)*[24]. *Z*/*E* ratio: 14:86; yield: 53%; pale yellow crystals, mp 87 °C; IR (KBr, cm^{-1}): ν_{max} 3471, 3407, 3061, 1728, 1626, 1542, 1446, 1377, 1316, 1230, 1201, 785, 745, 697; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 1.19 (t, J=7.0 Hz, 3H, CH_3), 3.08 (d, J=5.9 Hz, 2H, CH_2COO), 4.11 (q, J=7.0 Hz, 2H, CH_2O), 4.44 (t, J=5.9 Hz, 1H, CHS), 7.41–7.63 (m, 5H, Ph), 11.61 (s, 1H, NH), (*Z* isomer) δ 1.19 (t, J=7.0 Hz, 3H, CH_3), 3.14–3.18 (m, 2H, CH_AH_BCOO), CH_2O is masked by the signal of the *E* isomer, 4.58 (dd, J_{Ax}=6.8 Hz, J_{Bx}=5.2 Hz, 1H, CH_xS), 7.41–7.63 (m, 5H, Ph), 11.61 (s, 1H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 14.2 (CH_3), 35.8 (CH_2COO), 43.5 (CHS), 61.0 (CH_2O), 85.8 (=CBr), 127.9 (*o*-Ph), 128.2 (*m*-Ph), 131.0 (*p*-Ph), 139.4 (C1-Ph), 157.4 (C=), 170.4 (CO_{ester}), 176.0 (CO_{lactam}), 190.4 (CO_{ketone}), (*Z* isomer) δ 14.2 (CH_3), 35.8 (CH_2COO), 44.0 (CHS), 61.1 (CH_2O), 89.8 (=CBr), 127.9 (*o*-Ph), 128.3 (*m*-Ph), 131.6 (*p*-Ph), 138.9 (C1-Ph), 159.0 (C=), 170.4 (CO_{ester}), 176.2 (CO_{lactam}), 189.6 (CO_{ketone}). Anal. Calcd for $C_{15}H_{14}BrNO_4S$: C, 46.88; H, 3.65; N, 3.65; S, 8.34; found: C, 46.58; H, 3.63; N, 3.41; S, 8.27.

*4.2.1.4. 2-Bromo-2-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)ethanonitrile (**10e**).* *Z*/*E* ratio: 65:35; yield: 75%; pale yellow solid, mp 124–125 °C; IR (KBr, cm^{-1}): ν_{max} 3185, 3116, 2212, 1737, 1713, 1605, 1448, 1313, 1289, 1251, 1214, 1192, 849, 752; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 1.18 (t, J=7.1 Hz, 3H, CH_3), 3.08–3.13 (m, 2H, CH_AH_BCOO), 4.10 (q, J=7.1 Hz, 2H, CH_2O), 4.57 (t, J=6.2 Hz, 1H, CH_xS), (*E* isomer) δ 1.18 (t, J=7.1 Hz, 3H, CH_3), 3.08–3.13 (m, 2H, CH_AH_BCOO), 4.10 (q, J=7.1 Hz, 2H, CH_2O), 4.72 (t, J=5.9 Hz, 1H, CH_xS); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 14.1 (CH_3), 35.9 (CH_2COO), 45.6 (CHS), 56.4 (=CBr), 61.0 (CH_2O), 115.2 (CN), 159.5 (C=), 170.4 (CO_{ester}), 176.0 (CO_{lactam}), (*E* isomer) δ 14.1 (CH_3), 36.1 (CH_2COO), 45.9 (CHS), 51.3 (=CBr), 61.0 (CH_2O), 116.7 (CN), 156.3 (C=), 170.3 (CO_{ester}), 175.5 (CO_{lactam}). Anal. Calcd for $C_9H_9BrN_2O_3S$: C, 35.42; H, 2.97; N, 9.18; S, 10.51; found: C, 35.19; H, 3.08; N, 9.10; S, 10.73.

4.2.2. Method B. To a suspension of 4-oxothiazolidine **11b** (or **11e**) (1 mmol) in CCl_4 (48 mL) 2% bromine solution in the same solvent (ca. 1 equiv of bromine) was added dropwise under reflux until complete disappearance of the starting material (TLC). The bromine solution should be added at the rate, which is roughly the same as the rate of disappearance of bromine colour in the reaction mixture, though in some cases a pale yellow or pale orange colour can appear before the addition is completed. The reaction mixture was evaporated to a smaller volume and bromides were allowed to crystallize at rt. The products were isolated by filtration, as pure substances.

*4.2.2.1. (Z)-2-Bromo-2-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-N-(2-phenylethyl)ethanamide (**10b**)*[24]. Yield: 78%; pale yellow crystals, mp 116–118 °C; IR (KBr, cm^{-1}): ν_{max} 3369, 3176, 3025, 1722, 1609, 1585, 1523, 1451, 1374, 1347, 1308, 1229, 1192, 858, 749, 705; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): δ 1.18 (t, J=7.1 Hz, 3H, CH_3), 2.78 (t, J=7.5 Hz, 2H, CH_2Ph), 3.06–3.11 (m, 2H, CH_AH_BCOO), 3.33–3.43 (m, 2H, NCH_2), 4.10 (q, J=7.1 Hz, 2H, CH_2O), 4.49 (dd, J_{Ax}=7.5 Hz, J_{Bx}=4.9 Hz, 1H, CH_xS), 7.16–7.34 (m, 5H, Ph), 7.89 (t, J=5.6 Hz, 1H, NH_{amide}), 11.42 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): δ 14.1 (CH_3), 35.2 (CH_2Ph), 36.2 (CH_2COO), 41.4 (NCH_2), 43.7 (CHS), 61.0 (CH_2O), 84.2 (=CBr), 126.4 (*p*-Ph), 128.6 (*o*-Ph), 128.9 (*m*-Ph), 139.4 (C1-Ph), 151.7 (C=), 163.4 (CO_{amide}), 170.4 (CO_{ester}), 174.4 (CO_{lactam}). Anal. Calcd for $C_{17}H_{19}BrN_2O_4S$: C, 47.78; H, 4.48; N, 6.56; S, 7.50; found: C, 48.14; H, 4.56; N, 6.33; S, 7.60.

*4.2.2.2. 2-Bromo-2-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)ethanonitrile (**10e**).* Yield: 64%.

4.3. General procedure for synthesis of 5-methyl-4-oxothiazolidine vinyl bromides 10f–j

A suspension of 4-oxothiazolidine **11f–j** (1 mmol) in abs EtOH (49 mL) was cooled in an ice-NaCl bath and 2% bromine solution in the same solvent (ca. 1 equiv of bromine) was added dropwise until complete disappearance of the starting material (TLC). The bromine solution should be added at the rate, which is nearly the same as the rate of disappearance of bromine colour in the reaction mixture. In some cases the appearance of pale yellow colour of the formed solution indicates completion of the reaction. The reaction mixture was evaporated to a smaller volume, a few drops of water were added and bromides were allowed to crystallize in a freezer. The products were isolated by filtration, as pure substances. Vinyl bromide **10g** was isolated by extraction with CH_2Cl_2 and could not be crystallized or chromatographically purified.

*4.3.1. 2-Bromo-2-(5-methyl-4-oxothiazolidine-2-ylidene)-N-phenylethanamide (**10f**).* *Z*/*E* ratio: 43:57; yield: 64%; white solid with no sharp mp; IR (KBr, cm^{-1}): ν_{max} 3434, 3393, 3251, 1721, 1627, 1586,

1528, 1441, 1372, 1313, 1238, 1209, 1170, 898, 822, 756, 694; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 1.46 (d, J=7.2 Hz, 3H, CH_3), 4.12 (q, J=7.2 Hz, 1H, CHS), 7.05–7.13 (m, 1H, *p*-Ph), 7.27–7.35 (m, 2H, *m*-Ph), 7.58–7.62 (m, 2H, *o*-Ph), 9.28 (s, 1H, NH_{amide}), 11.12 (s, 1H, NH_{lactam}), (*Z* isomer) δ 1.54 (d, J=7.2 Hz, 3H, CH_3), 4.30 (q, J=7.2 Hz, 1H, CHS), 7.09–7.16 (m, 1H, *p*-Ph), 7.30–7.37 (m, 2H, *m*-Ph), 7.58–7.62 (m, 2H, *o*-Ph), 9.39 (s, 1H, NH_{amide}), 11.22 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 18.5 (CH_3), 42.3 (CHS), 79.4 (=CBr), 121.4 (*o*-Ph), 124.2 (*p*-Ph), 128.7 (*m*-Ph), 138.6 (C1-Ph), 150.2 (C=), 162.4 (CO_{amide}), 177.2 (CO_{lactam}), (*Z* isomer) δ 18.5 (CH_3), 42.8 (CHS), 83.7 (=CBr), 122.1 (*o*-Ph), 124.7 (*p*-Ph), 128.7 (*m*-Ph), 138.1 (C1-Ph), 152.6 (C=), 162.1 (CO_{amide}), 176.5 (CO_{lactam}). Anal. Calcd for $C_{12}H_{11}BrN_2O_2S$: C, 44.05; H, 3.39; N, 8.56; S, 9.80; found: C, 44.35; H, 3.44; N, 8.46; S, 9.95.

*4.3.2. 2-Bromo-2-(5-methyl-4-oxothiazolidine-2-ylidene)-N-(2-phenylethyl)ethanamide (**10g**). Z/E* ratio: 60:40; yield: 99% (crude product); colourless oil; IR (KBr, cm^{-1}): ν_{max} 3445, 3410, 3260, 3028, 1725, 1622, 1582, 1523, 1452, 1372, 1308, 1263, 1218, 749, 703; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 1.52 (d, J=7.2 Hz, 3H, CH_3), 2.74–2.81 (m, 2H, CH_2Ph), 3.29–3.43 (m, 2H, CH_2N), 4.26 (q, J=7.2 Hz, 1H, CHS), 7.16–7.34 (m, 5H, Ph), 7.88 (t, J=5.7 Hz, 1H, NH_{amide}), 11.37 (s, 1H, NH_{lactam}), (*E* isomer) δ 1.43 (d, J=7.2 Hz, 3H, CH_3), 2.72–2.78 (m, 2H, CH_2Ph), 3.29–3.43 (m, 2H, CH_2N), 4.05 (q, J=7.2 Hz, 1H, CHS), 7.16–7.34 (m, 5H, Ph), 7.75 (t, J=5.6 Hz, 1H, NH_{amide}), 10.94 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 18.5 (CH_3), 35.2 (CH_2Ph), 41.4 (NCH_2), 42.7 (CHS), 84.3 (=CBr), 126.4 (*p*-Ph), 128.6 (*o*-Ph), 128.9 (*m*-Ph), 139.5 (C1-Ph), 151.2 (C=), 163.4 (CO_{amide}), 176.1 (CO_{lactam}), (*E* isomer) δ 18.6 (CH_3), 35.4 (CH_2Ph), 41.4 (NCH_2), 42.1 (CHS), 80.2 (=CBr), 126.4 (*p*-Ph), 128.6 (*o*-Ph), 129.0 (*m*-Ph), 139.6 (C1-Ph), 148.0 (C=), 163.4 (CO_{amide}), 177.2 (CO_{lactam}); HRMS: calcd for $C_{14}H_{16}BrN_2O_2S$ $(M+H)^+$: 355.0110; found: 355.0119.

*4.3.3. Ethyl 2-bromo-2-(5-methyl-4-oxothiazolidin-2-ylidene)ethanoate (**10h**). Z/E* ratio: 7:93; yield 68%; white solid, mp 75–77 °C; IR (KBr, cm^{-1}): ν_{max} 3175, 1720, 1669, 1567, 1458, 1367, 1306, 1269, 1193, 1172, 881, 822, 788, 753; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 1.23 (t, J=7.2 Hz, 3H, CH_3CH_2), 1.47 (d, J=7.2 Hz, 3H, CH_3CH), 4.16 (q, J=7.2 Hz, 3H, CH_2O and CHS), 11.27 (s, 1H, NH), (*Z* isomer) δ 1.24 (t, J=7.1 Hz, 3H, CH_3CH_2), 1.53 (d, J=7.2 Hz, 3H, CH_3CH), 4.21 (q, J=7.1 Hz, 2H, CH_2O), 4.31 (q, J=7.2 Hz, 1H, CHS), 10.77 (s, 1H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 14.4 (CH_3CH_2), 18.4 (CH_3CH), 42.7 (CHS), 61.5 (CH_2O), 77.3 (=CBr), 153.8 (C=), 163.8 (CO_{ester}), 177.3 (CO_{lactam}), (*Z* isomer) δ 14.4 (CH_3CH_2), 18.4 (CH_3CH), 43.1 (CHS), 61.8 (CH_2O), 81.8 (=CBr), 156.0 (C=), 162.6 (CO_{ester}), 177.1 (CO_{lactam}). Anal. Calcd for $C_8H_{10}BrNO_3S$: C, 34.30; H, 3.60; N, 5.00; S, 11.45; found: C, 34.56; H, 3.62; N, 5.05; S, 11.65.

*4.3.4. 2-Bromo-2-(5-methyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**10i**). Z/E* ratio: 20:80; yield: 54%; pale yellow solid with no sharp mp; IR (KBr, cm^{-1}): ν_{max} 3208, 3068, 1717, 1609, 1576, 1545, 1507, 1449, 1375, 1318, 1275, 1221, 1177, 842, 794, 764, 733, 701; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 1.50 (d, J=7.2 Hz, 3H, CH_3), 4.21 (q, J=7.2 Hz, 1H, CHS), 7.41–7.63 (m, 5H, Ph), 11.52 (s, 1H, NH), (*Z* isomer) δ 1.57 (d, J=7.2 Hz, 3H, CH_3), 4.35 (q, J=7.2 Hz, 1H, CHS), 7.41–7.63 (m, 5H, Ph), 11.52 (s, 1H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 18.0 (CH_3), 42.4 (CHS), 85.9 (=CBr), 128.0 (*o*-Ph), 128.1 (*m*-Ph), 131.0 (*p*-Ph), 139.4 (C1-Ph), 156.5 (C=), 177.6 (CO_{lactam}), 190.4 (CO_{ketone}), (*Z* isomer, visible signals) δ 18.2 (CH_3), 43.0 (CHS), 128.1 (*o*-Ph), 128.2 (*m*-Ph), 131.6 (*p*-Ph), 177.8 (CO_{lactam}). Anal. Calcd for $C_{12}H_{10}NO_2S$: C, 46.17; H, 3.23; N, 4.49; S, 10.27; found: C, 46.32; H, 3.22; N, 4.53; S, 10.26.

*4.3.5. 2-Bromo-2-(5-methyl-4-oxothiazolidin-2-ylidene)ethanonitrile (**10j**). Z/E* ratio: 54:46; yield: 84%; white crystals, mp 124 °C; IR (KBr, cm^{-1}): ν_{max} 3149, 2203, 1721, 1596, 1446, 1377, 1320, 1247, 1115, 888, 797, 734; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 1.51 (d, J=7.2 Hz, 3H, CH_3), 4.34 (q, J=7.2 Hz, 1H, CHS), 12.30 (s, NH), (*E* isomer) δ 1.53 (d, J=7.2 Hz, 3H, CH_3), 4.49 (q, J=7.2 Hz, 1H, CHS), 12.30 (s, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 18.4 (CH_3), 44.7 (CHS), 56.5 (=CBr), 115.3 (CN), 158.9 (C=), 177.7 (CO), (*E* isomer) δ 18.6 (CH_3), 45.1 (CHS), 51.4 (=CBr), 116.7 (CN), 155.7 (C=), 177.2 (CO). Anal. Calcd for $C_6H_5BrN_2OS$: C, 30.92; H, 2.16; N, 12.02; S, 13.76; found: C, 31.27; H, 2.18; N, 12.08; S, 13.94.

4.4. General procedure for synthesis of 4-oxothiazolidine vinyl bromides 10k–o

To a suspension of 4-oxothiazolidine **11k–o** (1 mmol) in $CHCl_3$ (37 mL) 2% bromine solution in the same solvent (ca. 1 equiv of bromine) was added dropwise under reflux until complete disappearance of the starting material (TLC). The bromine solution should be added at the rate, which is roughly the same as the rate of disappearance of bromine colour in the reaction mixture, though in some cases a pale yellow or pale orange colour can appear before the addition is completed. The reaction mixture was evaporated to dryness, bromides were precipitated with EtOH (in some cases a few drops of water were also added) and filtered.

*4.4.1. 2-Bromo-2-(4-oxothiazolidine-2-ylidene)-N-phenylethanamide (**10k**). Z/E* ratio: 85:15; yield: 91%; white solid, mp 139–140 °C (decomp.); IR (KBr, cm^{-1}): ν_{max} 3400, 3215, 3184, 1728, 1642, 1597, 1574, 1532, 1492, 1441, 1317, 1239, 1212, 1171, 834, 758, 733, 690; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 3.99 (s, 2H, CH_2), 7.09–7.17 (m, 1H, *p*-Ph), 7.30–7.38 (m, 2H, *m*-Ph), 7.58–7.63 (m, 2H, *o*-Ph), 9.36 (s, 1H, NH_{amide}), 11.24 (s, 1H, NH_{lactam}), (*E* isomer) δ 3.86 (s, 2H, CH_2), 7.06–7.13 (m, 1H, *p*-Ph), 7.28–7.36 (m, 2H, *m*-Ph), 7.58–7.63 (m, 2H, *o*-Ph), 9.26 (s, 1H, NH_{amide}), 11.14 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 33.4 (CH_2), 83.6 (=CBr), 122.1 (*o*-Ph), 124.7 (*p*-Ph), 128.7 (*m*-Ph), 138.1 (C1-Ph), 154.4 (C=), 162.1 (CO_{amide}), 173.8 (CO_{lactam}), (*E* isomer) δ 34.0 (CH_2), 79.2 (=CBr), 121.4 (*o*-Ph), 124.2 (*p*-Ph), 128.7 (*m*-Ph), 138.6 (C1-Ph), 152.3 (C=), 162.6 (CO_{amide}), 174.4 (CO_{lactam}). Anal. Calcd for $C_{11}H_9BrN_2O_2S$: C, 42.19; H, 2.90; N, 8.94; S, 10.24; found: C, 42.36; H, 3.16; N, 9.00; S, 10.01.

*4.4.2. 2-Bromo-2-(4-oxothiazolidine-2-ylidene)-N-(2-phenylethyl) ethanamide (**10l**)*[26]*. Z/E* ratio: 85:15; yield: 79%; white crystals, mp 140–142 °C; IR (KBr, cm^{-1}): ν_{max} 3360, 3139, 3022, 1723, 1615, 1585, 1517, 1452, 1431, 1350, 1312, 1257, 1219, 1190, 887, 786, 750, 699; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 2.78 (t, J=7.3 Hz, 2H, CH_2Ph), 3.33–3.43 (m, 2H, NCH_2), 3.95 (s, 2H, CH_2S), 7.19–7.34 (m, 5H, Ph), 7.84 (t, J=5.6 Hz, 1H, NH_{amide}), 11.37 (s, 1H, NH_{lactam}), (*E* isomer, visible signals, others are masked by the signals of the *Z* isomer) δ 3.79 (s, 2H, CH_2S), 7.17 (t, J=5.2 Hz, 1H, NH_{amide}), 10.93 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 33.2 (CH_2S), 35.1 (CH_2Ph), 41.4 (NCH_2), 84.2 (=CBr), 126.3 (*p*-Ph), 128.6 (*o*-Ph), 128.8 (*m*-Ph), 139.4 (C1-Ph), 152.8 (C=), 163.3 (CO_{amide}), 173.3 (CO_{lactam}), (*E* isomer) δ 33.8 (CH_2S), 35.4 (CH_2Ph), 41.4 (NCH_2), 80.0 (=CBr), 126.3 (*p*-Ph), 128.6 (*o*-Ph), 128.8 (*m*-Ph), 139.4 (C1-Ph), 149.9 (C=), 163.3 (CO_{amide}), 174.3 (CO_{lactam}). Anal. Calcd for $C_{13}H_{13}BrN_2O_2S$: C, 45.76; H, 3.84; N, 8.21; S, 9.40; found: C, 45.94; H, 3.90; N, 8.16; S, 9.56.

*4.4.3. Ethyl 2-bromo-2-(4-oxothiazolidin-2-ylidene)ethanoate (**10m**). Z/E* ratio: 86:14; yield 76%; white solid, mp 103–105 °C; IR (KBr, cm^{-1}): ν_{max} 3251, 1735, 1708, 1665, 1590, 1444, 1371, 1307, 1271, 1230, 1183, 868, 824, 757, 715; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 1.24 (t, J=7.1 Hz, 3H, CH_3), 4.01 (s, 2H, CH_2S), 4.21 (q, J=7.1 Hz, 2H, CH_2O), 10.76 (s, 1H, NH), (*E* isomer) δ 1.24 (t, J=7.1 Hz, 3H, CH_3), 3.93 (s, 2H, CH_2S), 4.16 (q, J=7.1 Hz, 2H, CH_2O), 11.27 (s, 1H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer)

δ 14.4 (CH_3), 33.9 (CH_2S), 61.8 (CH_2O), 81.6 (=CBr), 157.7 (C=), 162.6 (CO_{ester}), 174.2 (CO_{lactam}), (*E* isomer) δ 14.4 (CH_3), 34.2 (CH_2S), 61.4 (CH_2O), =CBr uncertain, 155.8 (C=), 164.0 (CO_{ester}), 174.5 (CO_{lactam}). Anal. Calcd for $C_7H_8BrNO_3S$: C, 31.59; H, 3.03; N, 5.26; S, 12.05; found: C, 31.58; H, 3.10; N, 5.23; S, 12.01.

*4.4.4. 2-Bromo-2-(4-oxothiazolidin-2-ylidene)-1-phenylethanone (**10n**).* *Z*/*E* ratio: 18:82; yield: 72%; light pink-coloured crystals, mp 118–120 °C; IR (KBr, cm^{-1}): ν_{max} 3220, 3063, 1724, 1620, 1603, 1576, 1532, 1445, 1319, 1277, 1221, 1181, 880, 790, 723, 698; ^1H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 3.96 (s, 2H, CH_2), 7.41–7.65 (m, 5H, Ph), 11.53 (s, 1H, NH), (*Z* isomer) δ 4.06 (s, 2H, CH_2), 7.41–7.65 (m, 5H, Ph), 11.53 (s, 1H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): δ (*E* isomer) 34.00 (CH_2), 85.62 (=CBr), 127.92 (*o*-Ph), 128.12 (*m*-Ph), 130.96 (*p*- Ph), 139.44 (C1- Ph), 158.65 (C=), 174.75 (CO_{lactam}), 190.30 (CO_{ketone}), (*Z* isomer, visible signals) 33.75 (CH_2), 75.44 (=CBr), 128.03 (*o*- Ph), 128.21 (*m*-Ph), 131.54 (*p*- Ph), 175.05 (CO_{lactam}), CO_{ketone}. Anal. Calcd for $C_{11}H_8BrNO_2S$: C, 44.31; H, 2.70; N, 4.70; S, 10.75; found: C, 44.64; H, 2.79; N, 4.76; S, 10.89.

*4.4.5. 2-Bromo-2-(4-oxothiazolidin-2-ylidene)ethanonitrile (**10o**).* *Z*/*E* ratio: 64:36; yield: 65%; brownish solid, mp 163 °C (decomp.); IR (KBr, cm^{-1}): ν_{max} 3452, 3136, 2202, 1713, 1595, 1417, 1318, 1248, 787; ^1H NMR (200 MHz, DMSO-d_6, 25 °C): δ 4.03 (s, 2H, CH_2), 4.16 (s, 2H, CH_2, *E* isomer), 12.38 (br s, 2H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 35.3 (CH_2), 56.4 (=CBr), 115.3 (CN), 160.6 (C=), 174.4 (CO), (*E* isomer) δ 35.3 (CH_2), 51.1 (=CBr), 116.8 (CN), 157.4 (C=), 174.9 (CO). Anal. Calcd for $C_5H_3BrN_2OS$: C, 27.41; H, 1.38; N, 12.79; S, 14.64; found: C, 27.35; H, 1.51; N, 12.51; S, 14.72.

4.5. Synthesis of (*Z*)-ethyl 2-(*N*-methyl-5-bromo-4-oxothiazolidin-2-ylidene)ethanoate (13)

To a solution of 4-oxothiazolidine **11p** (180.7 mg, 0.9 mmol) in $CHCl_3$ (4 mL) 2% bromine solution in the same solvent (ca. 1 equiv of bromine) was added dropwise at rt until the complete disappearance of the starting material (TLC). The reaction mixture was diluted with $CHCl_3$ (6 mL), washed with 5% $Na_2S_2O_3$, water, dried with anhydrous Na_2SO_4 and evaporated to give **13** (245.5, 98%), as a pale yellow solid, mp 72–73 °C. IR (KBr, cm^{-1}): ν_{max} 1719, 1679, 1576, 1430, 1278, 1188, 1120, 804; ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ 1.31 (t, *J*=7.2 Hz, 3H, CH_3), 3.25 (s, 3H, NCH_3), 4.23 (q, *J*=7.2 Hz, 2H, CH_2O), 5.62 (s, 1H, =CH), 5.72 (s, 1H, CHS); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ 14.3 (CH_3), 30.7 (NCH_3), 41.8 (CHS), 60.6 (CH_2O), 93.2 (=CH), 153.9 (C=), 167.1 (CO_{ester}), 169.9 (CO_{lactam}). Anal. Calcd for $C_8H_{12}BrNO_4S$ (**13**×H_2O): C, 32.23; H, 4.06; N, 4.70; S, 10.75; found: C, 31.89; H, 3.86; N, 4.53; S, 10.79.

4.6. Synthesis of (*Z*)-ethyl 2-(*N*-methyl-5-methylidene-4-oxothiazolidin-2-ylidene)ethanoate (15a)

To a solution of 4-oxothiazolidine **11q** (22.0 mg; 0.1 mmol) in $CHCl_3$ (2 mL) 2% bromine solution in the same solvent (ca. 1 equiv of bromine) was added dropwise at rt until complete disappearance of the starting material (TLC). The reaction mixture was diluted with $CHCl_3$ (10 mL), washed with water and dried with anhydrous Na_2SO_4 for 3 days. During this period the initially formed C(5) bromide **14** was completely dehydrobrominated to **15a**. The extract was evaporated and chromatographed (eluent: gradient petrolether/ethyl acetate 100:0 to 70:30) to give **15a** (15.5 mg, 71%), as a white solid, mp 133–134 °C; IR (KBr, cm^{-1}): ν_{max} 1717, 1681, 1569, 1422, 1271, 1178, 1036, 790; ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ 1.31 (t, *J*=7.2 Hz, 3H, CH_3), 3.28 (s, 3H, NCH_3), 4.23 (q, *J*=7.2 Hz, 2H, CH_2O), 5.55 (s, 1H, =CH), 5.75 (s, 1H, =CH_2), 6.42 (s, 1H, =CH_2); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ 14.3 (CH_3), 30.1 (NCH_3), 60.3 (CH_2O), 90.8 (=CH), 116.5 (=CH_2), 132.6 (C(5)=), 152.9 (C(2)=), 165.0 (CO_{lactam}), 167.2 (CO_{ester}); HRMS: calcd for $C_{18}H_{23}N_2O_6S_2$ $(2M+H)^+$: 427.09920; found: 427.10366.

4.7. Synthesis of (2*Z*,5*Z*)-ethyl-2-(*N*-methyl-5-ethoxycarbonylmethylidene-4-oxothiazolidin-2-ylidene) ethanoate (15b)

To a solution of 4-oxothiazolidine **11r** (104.4 mg, 0.37 mmol) in $CHCl_3$ (5 mL) 2% bromine solution in the same solvent (ca. 1 equiv of bromine) was added dropwise at rt until the complete disappearance of the starting material (TLC). The reaction mixture was washed with 5% $Na_2S_2O_3$, water, stirred with 5% $NaHCO_3$ for 1 h, washed with water, dried with anhydrous Na_2SO_4, evaporated and chromatographed (eluent: gradient petrolether/ethyl acetate 100:0 to 80:20) to give **15b** (66.1 mg, 63%), as a pale yellow solid, mp 130–131 °C. IR (KBr, cm^{-1}): ν_{max} 1719, 1691, 1592, 1315, 1178, 1030, 819; ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ 1.32 (t, *J*=7.2 Hz, 3H, CH_3), 1.36 (t, *J*=7.2 Hz, 3H, CH_3), 3.32 (s, 3H, NCH_3), 4.25 (q, *J*=7.2 Hz, 2H, CH_2O), 4.31 (q, *J*=7.2 Hz, 2H, CH_2O), 5.65 (s, 1H, =C(2)H), 6.83 (s, 1H, =C(5)H); ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ 14.1 (CH_3), 14.2 (CH_3), 29.7 (NCH_3), 60.4 (CH_2O), 61.4 (CH_2O), 93.7 (=C(2)H), 116.7 (=C(5)H), 141.6 (C(5)=), 152.9 (C(2)=), 164.7 (CO), 165.6 (CO), 166.3 (CO). Anal. Calcd for $C_{12}H_{15}NO_5S$: C, 50.52; H, 5.30; N, 4.91; S, 11.24; found: C, 50.12; H, 5.23; N, 4.77; S, 10.87.

4.8. Reductive debrominations of vinyl bromide 10k

4.8.1. Reaction with Ph_3P. A mixture of vinyl bromide **10k** (25 mg, 0.08 mmol) and Ph_3P (209.6 mg, 0.8 mmol) in $CHCl_3$ (1.6 mL) was heated under reflux for 2 h. The mixture was evaporated and chromatographed (eluent: gradient toluene/ethyl acetate 90:10 to 50:50) to give **11k** (16.5 mg, 88%) as a white solid, mp 287–289 °C; *Z*/*E* ratio: 49:51; IR (KBr, cm^{-1}): ν_{max} 3291, 3250, 3200, 3138, 3084, 1707, 1666, 1618, 1583, 1550, 1319, 1246, 1155, 836, 814, 780, 752, 694; ^1H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 3.70 (s, 2H, CH_2), 5.80 (s, 1H, =CH), 6.98 (t, *J*=7.6 Hz, 1H, *p*-Ph), 7.26 (t, *J*=7.6 Hz, 2H, *m*-Ph), 7.59 (d, *J*=7.6 Hz, 2H, *o*-Ph), 9.82 (s, 1H, NH_{amide}), 11.37 (s, 1H, NH_{lactam}), (*E* isomer) δ 3.91 (s, 2H, CH_2), 5.35 (s, 1H, =CH), 7.03 (t, *J*=7.6 Hz, 1H, *p*-Ph), 7.29 (t, *J*=7.6 Hz, 2H, *m*-Ph), 7.59 (d, *J*=7.6 Hz, 2H, *o*-Ph), 9.91 (s, 1H, NH_{amide}), 11.26 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 32.3 (CH_2), 92.8 (=CH), 118.8 (*o*-Ph), 122.6 (*p*-Ph), 128.9 (*m*-Ph), 140.1 (C1-Ph), 154.7 (C=), 165.6 (CO_{amide}), 174.5 (CO_{lactam}). Anal. Calcd for $C_{11}H_{10}N_2O_2S$: C, 56.39; H, 4.30; N, 11.96; S, 13.69; found: C, 56.17; H, 4.38; N, 11.92; S, 13.65.

4.8.2. Reaction with AcSK. A mixture of vinyl bromide **10k** (51.7 mg, 0.16 mmol) and AcSK (37.7 mg, 0.32 mmol) in Me_2CO/H_2O 7:1 (v/v) (3.9 mL) was stirred at rt for 24 h. The product **11k** was precipitated by the addition of water and isolated by filtration (24.9 mg, 72%); *Z*/*E* ratio: 100:0.

4.8.3. Reaction with KCN. A mixture of vinyl bromide **10k** (12.7 mg, 0.04 mmol) and KCN (26.4 mg, 0.04 mmol) in MeCN (0.7 mL) was heated under reflux for 2 h. The reaction mixture was cooled, evaporated and the residue was partitioned between ethyl acetate and water. The organic layer was dried with anhydrous Na_2SO_4 and evaporated to give **11k** (4.8 mg, 51%); *Z*/*E* ratio: 100:0.

4.8.4. Reaction with KI. A mixture of vinyl bromide **10k** (14.3 mg, 0.046 mmol) and KI (22.7 mg, 0.137 mmol) in $MeCN/H_2O$ 5:1 (v/v) (1.1 mL) was stirred at rt for 24 h. The product **11k** was precipitated by the addition of water and isolated by filtration (7.6 mg, 71%); *Z*/*E* ratio: 100:0.

4.8.5. Reaction with NaF. A mixture of vinyl bromide **10k** (28.3 mg, 0.09 mmol) and NaF (11.4 mg, 0.27 mmol) in DMF (1.4 mL) was heated at 70 °C for 46 h. The reaction mixture was cooled, water

was added and the product extracted with ethyl acetate. The organic layer was dried with anhydrous Na_2SO_4, evaporated and chromatographed (eluent: gradient toluene/ethyl acetate 90:10 to 50:50) to give **11k** (5.2 mg, 25%); *Z*/*E* ratio: 56:44.

4.8.6. Reaction with NaN_3. A mixture of vinyl bromide **10k** (20.0 mg, 0.064 mmol) and NaN_3 (8.3 mg, 0.13 mmol) in Me_2CO/H_2O 7:1 (v/v) (1.5 mL) was stirred at rt for 24 h. The reaction mixture was evaporated and the residue was partitioned between ethyl acetate and water. The organic layer was dried with anhydrous Na_2SO_4, evaporated and chromatographed (eluent: gradient toluene/ethyl acetate 90:10 to 50:50) to give **11k** (5.0 mg, 34%); *Z*/*E* ratio: 41:59.

4.8.7. Reaction with acetylacetone. A mixture of acetylacetone (22.1 mg, 0.22 mmol) and K_2CO_3 (30.5 mg, 0.22 mmol) in MeCN (2.4 mL) was stirred at rt for 15 min and vinyl bromide **10k** (34.6 mg, 0.11 mmol) was added at once. The mixture was stirred at rt for additional 30 h, evaporated and the residue was partitioned between ethyl acetate and water. The organic layer was dried with anhydrous Na_2SO_4, evaporated and chromatographed (eluent: gradient toluene/ethyl acetate 90:10 to 50:50) to give **11k** (6.1 mg, 24%); *Z*/*E* ratio: 53:47.

4.9. Reaction of vinyl bromide 10k with KSCN

A mixture of vinyl bromide **10k** (30.6 mg, 0.098 mmol) and KSCN (9.5 mg, 0.098 mmol) in acetone (2.1 mL) was stirred at rt for 50 h. The mixture was evaporated and partitioned between ethyl acetate and water. The organic layer was dried with anhydrous Na_2SO_4, evaporated and chromatographed (eluent: gradient toluene/ethyl acetate 100:0 to 70:30) to give **17** (15.0 mg, 53%), as a white solid, mp 197 °C; *Z*/*E* ratio: 77:23; IR (KBr, cm^{-1}): ν_{max} 3367, 3348, 3139, 2154, 1732, 1627, 1596, 1528, 1492, 1440, 1324, 1207, 1168, 840, 763, 694; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 3.93 (s, 2H, CH_2), 7.13 (t, *J*=7.4 Hz, 1H, *p*-Ph), 7.35 (t, *J*=7.4 Hz 2H, *m*-Ph), 7.63 (d, *J*=7.4 Hz, 2H, *o*-Ph), 9.70 (s, 1H, NH_{amide}), 11.78 (br s, 1H, NH_{lactam}), (*Z* isomer) δ 4.10 (s, 2H, CH_2), 7.13 (t, *J*=7.4 Hz, 1H, *p*-Ph), 7.35 (t, *J*=7.4 Hz 2H, *m*-Ph), 7.63 (d, *J*=7.4 Hz, 2H, *o*-Ph), 9.85 (s, 1H, NH_{amide}), 12.09 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): *E*+*Z* isomer δ 34.4 (CH_2), 80.3 and 82.1 (=CSCN), 112.0 (SCN), 121.4 and 121.8 (*o*-Ph), 124.1 and 124.4 (*p*-Ph), 128.7 (*m*-Ph), 138.4 and 138.8 (C1-Ph), 163.2 and 164.0 (C=), 167.9 (CO_{amide}), 175.0 (CO_{lactam}). Anal. Calcd for $C_{12}H_9N_3O_2S_2$: C, 49.47; H, 3.11; N, 14.42; S, 22.01; found: C, 49.38; H, 3.26; N, 14.08; S, 21.63.

4.10. Reaction of vinyl bromide 10k with AcOK

A mixture of vinyl bromide **10k** (24.9 mg, 0.08 mmol) and AcOK (15.6 mg, 0.16 mmol) in acetone/H_2O 7:1 v/v (1.4 mL) was stirred at rt for 5 h. The mixture was evaporated and the residue was partitioned between ethyl acetate and water. The organic layer was dried with anhydrous Na_2SO_4, evaporated and chromatographed (eluent: gradient toluene/acetone 100:0 to 80:20) to give **18** (6.5 mg, 28%; 4.4 mg was isolated pure, *Z*/*E* 91:9, and 2.1 mg in a mixture with **11k**), as a white solid, mp 103–105 °C and **11k** (3.2 mg, 17%; isolated in a mixture with **18**); IR (KBr, cm^{-1}): ν_{max} 3353, 3271, 3208, 3145, 1715, 1671, 1623, 1598, 1547, 1499, 1443, 1317, 1210, 761, 693; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 2.15 (s, 3H, CH_3), 5.45 (s, 1H, =CH), 6.36 (s, 1H, CHS), 7.00 (t, *J*=7.2 Hz, 1H, *p*-Ph), 7.27 (t, *J*=7.2 Hz, 2H, *m*-Ph), 7.56 (d, *J*=7.2 Hz, 2H, *o*-Ph), 10.08 (s, 1H, NH_{amide}), 11.98 (s, 1H, NH_{lactam}), (*Z* isomer) δ 2.13 (s, 3H, CH_3), 5.88 (s, 1H, =CH), 6.16 (s, 1H, CHS), 7.00 (t, *J*=7.2 Hz, 1H, *p*-Ph), 7.27 (t, *J*=7.2 Hz 2H, *m*-Ph), 7.56 (d, *J*=7.2 Hz, 2H, *o*-Ph), 10.02 (s, 1H, NH_{amide}), 11.98 (s, 1H, NH_{lactam}); ^{13}C NMR (125 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 20.4 (CH_3), 73.3 (CHS), 95.1 (=CH), 119.0 (*o*-Ph), 123.1 (*p*-Ph), 128.9 (*m*-Ph), 139.5 (C1-Ph), 149.8 (C=), 165.0 (CO_{amide}), 170.1 (CO_{ester}), 174.4 (CO_{lactam}); HRMS: calcd for $C_{13}H_{13}N_2O_4S$ (M+H) 293.05905, found 293.05909.

4.11. General procedure for synthesis of 5-ethoxycarbonylmethylidene-4-oxothiazolidines 19a–e[24,28]

4.11.1. Method A. To a suspension, or a solution of 4-oxothiazolidine **11a–e** (0.37 mmol) in $CHCl_3$ (8 mL) 2% bromine solution in the same solvent (ca. 1 equiv of bromine) was added dropwise at 0 °C (an ice bath) until complete disappearance of the starting material (TLC). The bromine solution should be added at the rate, which is nearly the same as the rate of disappearance of bromine colour in the reaction mixture, though a yellow or orange colour can appear before the addition is completed. The reaction mixture was warmed to rt, pyridine (3.7 mmol) was added and the mixture refluxed until the complete disappearance of the vinyl bromide (TLC). Only in the case of compound **11d** the mixture should be stirred at rt for 24 h without pyridine added. In all cases the reaction mixture was evaporated to dryness and the crude product purified by column chromatography.

4.11.2. Method B. To a suspension, or a solution of vinyl bromide **10a–e** (0.21 mmol) in $CHCl_3$ (2 mL) 2% solution of Et_3N in the same solvent (5 equiv of Et_3N) was added dropwise at rt and the mixture stirred at rt for additional period until complete disappearance of the starting material (TLC). The reaction mixture was evaporated to dryness and the crude product purified by column chromatography.

4.12. General procedure for synthesis of 5-methylidene-4-oxothiazolidines 20f–g

To a suspension of vinyl bromide **10f–g** (0.2 mmol) in $CHCl_3$ (4.4 mL) a 20-fold molar excess of pyridine was added and the mixture refluxed until the disappearance of the vinyl bromide (TLC). The reaction mixture was then cooled to rt and filtered (if there was a precipitate). The filtrate was evaporated to 1.5–2.5 mL and chromatographed.

*4.12.1. (Z)-(5-Methylidene-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**20f**).* Reflux time: 21 h; purification: gradient toluene/ethyl acetate 30:20 to 10:90; yield: 10%; pale yellow solid with no sharp mp; IR (KBr, cm^{-1}): ν_{max} 3303, 3209, 3065, 1709, 1663, 1596, 1549, 1500, 1314, 1244, 1157, 789, 752, 695; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): δ 5.84 (s, 1H, =C(2)H), 5.93 (s, 1H, =C(5)H), 6.10 (s, 1H, =C(5)H), 7.01 (t, *J*=7.2 Hz, 1H, *p*-Ph), 7.28 (t, *J*=7.8 Hz, 2H, *m*-Ph), 7.60 (d, *J*=7.8 Hz, 2H, *o*-Ph), 10.05 (s, 1H, NH_{amide}), 12.06 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): δ 94.1 (=CH), 114.9 (=CH_2), 119.0 (*o*-Ph), 123.1 (*p*-Ph), 129.0 (*m*-Ph), 134.8 (C(5)=), 139.7 (C1-Ph), 147.6 (C(2)=), 165.0 and 165.9 (CO_{amide} and CO_{lactam}); HRMS: calcd for $C_{12}H_{11}N_2O_2S$ $(M+H)^+$: 247.0536; found: 247.0543.

*4.12.2. (Z)-(5-Methylidene-4-oxothiazolidin-2-ylidene)-N-(2-phenylethyl)ethanamide (**20g**).* Reflux time: 64 h; purification: gradient petrolether/ethyl acetate 100:0 to 60:40; yield: 35%; pale yellow solid with no sharp mp; IR (KBr, cm^{-1}): ν_{max} 3288, 3090, 3060, 1697, 1652, 1586, 1498, 1455, 1308, 1188, 867, 828, 788, 746, 699; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): δ 2.72 (t, *J*=7.4 Hz, 2H, CH_2Ph), NCH_2 is masked by water, 5.70 (s, 1H, =C(2)H), 5.76 (s, 1H, =C(5)H), 6.04 (s, 1H, =C(5)H), 7.16–7.34 (m, 5H, Ph), 8.08 (t, *J*=5.4 Hz, 1H, NH_{amide}), 11.80 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): δ 35.5 (CH_2Ph), 40.3 (NCH_2), 94.0 (=CH), 113.9 (=CH_2), 126.3 (*p*-Ph), 128.6 (*o*-Ph), 128.9 (*m*-Ph), 135.2 (C(5)=), 139.8

(C1-Ph), 145.2 (C(2)=), 165.8 and 166.2 (CO_{amide} and CO_{lactam}); HRMS: calcd for $C_{14}H_{15}N_2O_2S$ $(M+H)^+$: 275.0849; found: 275.0856.

4.13. General procedure for synthesis of pyridinium salts 21k–m[23b]

To a suspension, or a solution of vinyl bromide **10k–m** (0.5 mmol) in $CHCl_3$ a 10-fold molar excess of pyridine was added and the mixture refluxed, or heated at 50 °C, until the disappearance of the starting bromide (TLC). The reaction mixture was evaporated to dryness to afford the crude product.

4.14. General procedure for synthesis of 5-methyl-5-morpholino-4-oxothiazolidines 22f–j

A mixture of vinyl bromide **10f–j** (0.2 mmol) and morpholine (0.18 mL; 2.0 mmol) in $CHCl_3$ (8.7 mL) was stirred at rt for 1.5–50 h in dry atmosphere. The reaction mixture was then evaporated to dryness and purified by column chromatography.

*4.14.1. (5-Methyl-5-morpholino-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**22f**).* Reaction time: 50 h; purification: gradient toluene/ethyl acetate 60:40 to 0:100; yield: 90%; white solid, mp 165–167 °C (decomp.); *Z*/*E* ratio: 13:87; IR (KBr, cm^{-1}): 3456, 3329, 3250, 3056, 1720, 1643, 1596, 1539, 1498, 1446, 1382, 1314, 1245, 1181, 1118, 849, 782, 736, 694; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 1.78 (s, 3H, CH_3), 2.20–2.28 (m, 2H, NCH_A), 2.66–2.72 (m, 2H, NCH_B), 3.61–3.65 (m, 4H, CH_2O), 5.45 (s, 1H, =CH), 7.04 (t, *J*=7.3 Hz, 1H, *p*-Ph), 7.31 (t, *J*=7.8 Hz, 2H, *m*-Ph), 7.59 (d, *J*=7.8 Hz, 2H, *o*-Ph), 9.95 (s, 1H, NH_{amide}), 11.51 (s, 1H, NH_{lactam}), (*Z* isomer) δ 1.68 (s, 3H, CH_3), 2.20–2.28 (m, 2H, NCH_A), 2.66–2.72 (m, 2H, NCH_B), 3.61–3.65 (m, 4H, CH_2O), 5.82 (s, 1H, =CH), 6.99 (t, *J*=7.4 Hz, 1H, *p*-Ph), 7.27 (t, *J*=7.8 Hz, 2H, *m*-Ph), 7.61 (d, *J*=7.8 Hz, 2H, *o*-Ph), 9.88 (s, 1H, NH_{amide}), 11.66 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 26.2 (CH_3), 47.5 (CH_2N), 65.7 (CH_2O), 83.1 (*C*(CH_3)S), 92.6 (=CH), 119.5 (*o*-Ph), 123.5 (*p*-Ph), 129.0 (*m*-Ph), 139.2 (C1-Ph), 148.8 (C=), 165.4 (CO_{amide}), 173.2 (CO_{lactam}), (*Z* isomer) δ 26.0 (CH_3), 47.2 (CH_2N), 65.9 (CH_2O), 79.1 (*C*(CH_3)S), 94.3 (=CH), 118.9 (*o*-Ph), 122.8 (*p*-Ph), 128.9 (*m*-Ph), 140.0 (C1-Ph), 149.5 (C=), 165.2 (CO_{amide}), 174.8 (CO_{lactam}). Anal. Calcd for $C_{16}H_{19}N_3O_3S$: C, 57.64; H, 5.74; N, 12.60; S, 9.62; found: C, 57.88; H, 5.62; N, 12.27; S, 9.64.

*4.14.2. (5-Methyl-5-morpholino-4-oxothiazolidin-2-ylidene)-N-(2-phenylethyl)ethanamide (**22g**).* Reaction time: 48 h; purification: gradient toluene/ethyl acetate 60:40 to 0:100; yield: 62%; yellowish oil; *Z*/*E* ratio: 44:56; IR (KBr, cm^{-1}): 3310, 3230, 3084, 3028, 1720, 1637, 1592, 1546, 1452, 1371, 1277, 1177, 1119, 869, 747, 701; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 1.75 (s, 3H, CH_3), 2.16–2.27 (m, 2H, NCH_A), 2.63–2.76 (m, 4H, NCH_B and CH_2Ph), NCH_2 is masked by water, 3.59–3.64 (m, 4H, CH_2O), 5.22 (s, 1H, =CH), 7.20–7.36 (m, 5H, Ph), 8.03 (t, *J*=5.6 Hz, 1H, NH_{amide}), 11.70 (br s, 1H, NH_{lactam}), (*Z* isomer) δ 1.63 (s, 3H, CH_3), 2.17–2.26 (m, 2H, NCH_A), 2.63–2.74 (m, 4H, NCH_B and CH_2Ph), NCH_2 is masked by water, 3.56–3.63 (m, 4H, CH_2O), 5.56 (s, 1H, =CH), 7.20–7.33 (m, 5H, Ph), 7.89 (t, *J*=5.6 Hz, 1H, NH_{amide}), 11.38 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 26.2 (CH_3), 35.4 (CH_2Ph), 40.8 ($NHCH_2$) 47.5 (CH_2N), 65.7 (CH_2O), 83.1 (*C*(CH_3)S), 92.3 (=CH), 126.4 (*p*-Ph), 128.6 (*o*-Ph), 128.9 (*m*-Ph), 139.6 (C1-Ph), 146.6 (C=), 166.9 (CO_{amide}), 172.9 (CO_{lactam}), (*Z* isomer) δ 26.1 (CH_3), 35.6 (CH_2Ph), 40.4 ($NHCH_2$), 47.1 (CH_2N), 65.9 (CH_2O), 78.7 (*C*(CH_3)S), 94.2 (=CH), 126.3 (*p*-Ph), 128.6 (*o*-Ph), 128.9 (*m*-Ph), 139.9 (C1-Ph), 146.9 (C=), 166.3 (CO_{amide}), 174.6 (CO_{lactam}); HRMS: calcd for $C_{18}H_{23}N_3O_3S$ (M^+): 361,1460, found: 361,1466.

*4.14.3. Ethyl (5-methyl-5-morpholino-4-oxothiazolidin-2-ylidene) ethanoate (**22h**).* Reaction time: 6 h; purification: gradient toluene/ethyl acetate 80:20 to 50:50; yield: 90%; white solid, mp 123–125 °C; *Z*/*E* ratio: 60:40; IR (KBr, cm^{-1}): 3445, 1730, 1674, 1598, 1450, 1371, 1274, 1223, 1184, 1143, 1119, 868, 740; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 1.18 (t, *J*=7.1 Hz, 3H, CH_3CH_2), 1.69 (s, 3H, CH_3CS), 2.15–2.25 (m, 2H, NCH_A), 2.61–2.72 (m, 2H, NCH_B), 3.60–3.64 (m, 4H, CH_2O), 4.06 (q, *J*=7.1 Hz, 2H, CH_3CH_2O), 5.47 (s, 1H, =CH), 11.70 (br s, 1H, NH), (*E* isomer) δ 1.20 (t, *J*=7.0 Hz, 3H, CH_3CH_2), 1.76 (s, 3H, CH_3CS), 2.15–2.25 (m, 2H, NCH_A), 2.61–2.72 (m, 2H, NCH_B), 3.60–3.64 (m, 4H, CH_2O), 4.10 (q, *J*=7.0 Hz, 2H, CH_3CH_2O), 5.28 (s, 1H, =CH), 10.84 (br s, 1H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 14.6 (CH_3CH_2), 25.9 (CH_3CS), 47.3 (CH_2N), 59.3 (CH_3CH_2O), 65.8 (CH_2O), 80.8 (*C*(CH_3)S), 90.3 (=CH), 154.1 (C=), 166.8 (CO_{ester}), 174.8 (CO_{lactam}), (*E* isomer) δ 14.6 (CH_3CH_2), 26.0 (CH_3CS), 47.5 (CH_2N), 59.8 (CH_3CH_2O), 65.6 (CH_2O), 83.1 (*C*(CH_3)S), 89.0 (=CH), 152.9 (C=), 166.8 (CO_{ester}), 173.8 (CO_{lactam}). Anal. Calcd for $C_{12}H_{18}N_2O_4S$: C, 50.33; H, 6.34; N, 9.78; S, 11.20; found: C, 50.32; H, 6.26; N, 9.49; S, 11.33.

*4.14.4. (Z)-(5-Methyl-5-morpholino-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**22i**).* Reaction time: 6 h; purification: gradient toluene/ethyl acetate 70:30 to 60:40; yield: 74%; white solid, mp 160–162 °C (decomp.); IR (KBr, cm^{-1}): 3169, 3088, 1706, 1637, 1601, 1578, 1531, 1469, 1373, 1316, 1281, 1193, 1176, 1116, 857, 792, 762, 695; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): δ 1.72 (s, 3H, CH_3), 2.21–2.31 (m, 2H, NCH_A), 2.66–2.76 (m, 2H, NCH_B), 3.60–3.62 (m, 4H, CH_2O), 6.80 (s, 1H, =CH), 7.48–7.60 (m, 3H, *m*- and *p*-Ph), 7.80–7.85 (m, 2H, *o*-Ph), 11.98 (br s, 1H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): δ 25.6 (CH_3), 47.3 (CH_2N), 65.9 (CH_2O), 79.7 (*C*(CH_3)S), 95.9 (=CH), 127.2 (*o*-Ph), 129.0 (*m*-Ph), 132.4 (*p*-Ph), 138.6 (C1-Ph), 157.0 (C=), 175.4 (CO_{lactam}), 187.6 (CO_{ketone}). Anal. Calcd for $C_{16}H_{18}N_2O_3S$: C, 60.36; H, 5.70; N, 8.80; S, 10.07; found: C, 60.51; H, 5.77; N, 8.67; S, 10.27.

*4.14.5. (Z)-(5-Methyl-5-morpholino-4-oxothiazolidin-2-ylidene) ethanonitrile (**22j**).* Reaction time: 1.5 h; purification: gradient toluene/ethyl acetate 100:0 to 20:80; yield: 83%; light brown oil; IR (KBr, cm^{-1}): 3446, 3200, 2204, 1727, 1599, 1449, 1240, 1116, 796; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): δ 1.77 (s, 3H, CH_3), 2.14–2.24 (m, 2H, NCH_A), 2.62–2.72 (m, 2H, NCH_B), 3.60–3.64 (m, 4H, CH_2O), 5.00 (s, 1H, =CH), 10.54 (br s, 1H, NH); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): δ 29.2 (CH_3), 49.4 (CH_2N), 66.2 (CH_2O), *C*(CH_3)S uncertain, 65.9 (=CH), 119.2 (CN), 155.5 (C=), 169.8 (CO_{lactam}); HRMS; calcd for $C_{10}H_{14}N_3O_2S$ $(M+H)^+$: 240.0801; found: 240.0791.

4.15. General procedure for synthesis of 5-anilino-4-oxothiazolidines 26k–l

A mixture of the crude pyridinium salt **21k–l** and aniline in a MeOH/H_2O was stirred at rt. The reaction mixture was filtered, brown precipitate was washed with water, dried and purified by column chromatography.

*4.15.1. (5-Anilino-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**26k**).* Pyridinium salt **21k** (22 mg), aniline (0.005 mL, 0.056 mmol), MeOH (1 mL)/H_2O (0.5 mL); stirred for 1 h and 45 min; crude **26k**-*Z* (78%), mp 180–184 °C; purification: gradient petrolether/ethyl acetate 60:40 to 0:100; yield 63%; pale orange solid, mp 180–184 °C; *Z*/*E* ratio: 76:24; IR (KBr, cm^{-1}): ν_{max} 3464, 3412, 3298, 3056, 1704, 1658, 1600, 1578, 1539, 1496, 1440, 1318, 1244, 1154, 796, 754, 693; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 5.84 (s, 1H, =CH), 5.91 (d, *J*=10.0 Hz, 1H, CHS), 6.65–6.75 (m, 3H, *o*- and *p*-aniline), 6.79 (d, *J*=10.0 Hz, 1H, NH_{amine}), 6.97 (t, *J*=7.4 Hz, 1H, *p*-Ph), 7.13–7.29 (m, 4H, *m*-aniline and *m*-Ph), 7.57 (d, *J*=7.4 Hz, 2H, *o*-Ph), 9.87 (s, 1H, NH_{amide}), 11.71 (s, 1H, NH_{lactam}), (*E* isomer, visible signals, others are masked by the signals of the *Z* isomer) δ 5.41 (s, 1H, =CH), 6.30 (d, 1H, CHS, *J*=10.6 Hz), 9.94 (s, 1H, NH_{amide}), 11.52 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*Z* isomer) δ 60.0 (CHS), 94.0

(=CH), 113.6 (*o*-aniline),118.3 (*p*-aniline), 118.8 (*o*-Ph), 122.7 (*p*-Ph), 128.9 (*m*-Ph), 129.4 (*m*-aniline), 140.0 (C1-Ph), 146.2 (C1-aniline), 151.3 (C=), 165.2 (CO_{amide}), 172.8 (CO_{lactam}), (*E* isomer) δ 61.8 (CHS), 92.7 (=CH), 113.8 (*o*-aniline), 119.2 (*p*-aniline), 119.5 (*o*-Ph), 123.5 (*p*-Ph), 129.1 (*m*-Ph), 129.5 (*m*-aniline), 139.2 (C1-Ph), 145.6 (C1-aniline), 150.3 (C=), 165.2 (CO_{amide}), 171.2 (CO_{lactam}). Anal. Calcd for $C_{17}H_{15}N_3O_2S$: C, 62.75; H, 4.65; N, 12.91; S, 9.85; found: C, 62.58; H, 4.76; N, 12.79; S, 9.91.

*4.15.2. (5-Anilino-4-oxothiazolidin-2-ylidene)-N-(2-phenylethyl) ethanamide (**26l**).* Pyridinium salt **21l** (30.3 mg), aniline (0.006 mL, 0.071 mmol), MeOH (1.3 mL)/H_2O (0.65 mL); stirred for 30 min; crude **26l**-*E* (89%), mp 189–191 °C; purification: gradient toluene/ethyl acetate 60:40 to 0:100; yield 86%; pale yellow solid, mp 189–191 °C; *Z*/*E* ratio: 20:80; IR (KBr, cm^{-1}): ν_{max} 3338, 3284, 3062, 1712, 1629, 1598, 1563, 1314, 1281, 1227, 1190, 1137, 812, 749, 698; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 2.74 (t, *J*=7.3 Hz, 2H, CH_2Ph), NCH_2 is masked by water, 5.19 (s, 1H, =CH), 6.24 (d, *J*=10.5 Hz, 1H, CHS), 6.68 (d, *J*=7.5 Hz, 2H, *o*-aniline), 6.75 (t, *J*=7.5 Hz, 1H, *p*-aniline), 7.03 (d, *J*=10.5 Hz, 1H, NH_{amine}), 7.15–7.34 (m, 7H, *m*-aniline and Ph), 8.01 (t, *J*=5.6 Hz, 1H, NH_{amide}), 11.72 (s, 1H, NH_{lactam}), (*Z* isomer) δ 2.69 (t, *J*=7.4 Hz, 2H, CH_2Ph), NCH_2 is masked by water, 5.60 (s, 1H, =CH), 5.82 (d, *J*=9.4 Hz, 1H, CHS), 6.63–6.76 (m, 4H, *o*-aniline, *p*-aniline and NH_{amine}), 7.12–7.32 (m, 7H, *m*-aniline and Ph), 7.88 (t, *J*=5.5 Hz, 1H, NH_{amide}), 11.44 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 35.3 (CH_2Ph), NCH_2 is masked by DMSO, 61.7 (CHS), 92.5 (=CH), 113.8 (*o*-aniline), 119.0 (*p*-aniline), 126.4 (*p*-Ph), 128.6 (*o*-Ph), 128.9 (*m*-Ph), 129.5 (*m*-aniline), 139.6 (C1-Ph), 145.7 (C1-aniline), 148.2 (C=), 166.9 (CO_{amide}), 170.9 (CO_{lactam}), (*Z* isomer) δ 35.6 (CH_2Ph), NCH_2 is masked by DMSO, 59.8 (CHS), 93.9 (=CH), 113.6 (*o*-aniline), 118.2 (*p*-aniline), 126.3 (*p*-Ph), 128.6 (*o*-Ph), 128.8 (*m*-Ph), 129.3 (*m*-aniline), 139.8 (C1-Ph), 146.2 (C1-aniline), 148.7 (C=), 166.4 (CO_{amide}), 172.6 (CO_{lactam}). Anal. Calcd for $C_{19}H_{19}N_3O_2S$: C, 64.57; H, 5.42; N, 11.89; S, 9.07; found: C, 64.50; H, 5.43; N, 11.83; S, 9.43.

4.16. General procedure for synthesis of 5-methoxy-4-oxothiazolidines 27k–l

A mixture of the crude pyridinium salt **21k–l** and anhydrous K_2CO_3 in MeOH was refluxed for 24 h in dry atmosphere. After cooling to rt the reaction mixture was evaporated to dryness and purified by column chromatography.

*4.16.1. (Z)-(5-Methoxy-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**27k**).* Pyridinium salt **21k** (50.2 mg), anhydrous K_2CO_3 (7.0 mg, 0.05 mmol), MeOH (3.7 mL); purification: gradient petrolether/ethyl acetate 20:80 to 0:100; yield 69%; yellowish solid, mp 155–158 °C; IR (KBr, cm^{-1}): ν_{max} 3319, 3146, 3098, 3021, 1720, 1656, 1599, 1549, 1497, 1441, 1315, 1242, 1194, 1156, 850, 802, 752, 689; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): CH_3 is masked by water, δ 5.66 (s, 1H, CHS), 5.86 (s, 1H, =CH), 7.00 (t, *J*=7.4 Hz, 1H, *p*-Ph), 7.27 (t, *J*=7.8 Hz, 2H, *m*-Ph), 7.59 (d, *J*=7.6 Hz, 2H, *o*-Ph), 9.96 (s, 1H, NH_{amide}), 11.79 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): δ 55.2 (CH_3), 82.0 (CHS), 95.2 (=CH), 118.9 (*o*-Ph), 123.0 (*p*-Ph), 128.9 (*m*-Ph), 139.7 (C1-Ph), 149.8 (C=), 165.0 (CO_{amide}), 171.4 (CO_{lactam}). Anal. Calcd for $C_{12}H_{12}N_2O_3S$: C, 54.53; H, 4.58; N, 10.60; S, 12.13; found: C, 54.27; H, 4.57; N, 10.52; S, 12.24.

*4.16.2. (Z)-(5-Methoxy-4-oxothiazolidin-2-ylidene)-N-(2-phenylethyl)ethanamide (**27l**).* Pyridinium salt **21l** (40.4 mg), anhydrous K_2CO_3 (5.3 mg, 0.04 mmol), MeOH (2.8 mL); purification: gradient toluene/ethyl acetate 60:40 to 0:100; yield 66%; yellowish solid, mp 147–149 °C; IR (KBr, cm^{-1}): ν_{max} 3312, 3196, 3055, 1722, 1641, 1563, 1461, 1305, 1186, 1101, 817, 761, 699; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): δ 2.71 (t, *J*=7.3 Hz, 2H, CH_2Ph), 3.30 (s, 3H, CH_3), NCH_2 is masked by water, 5.60 and 5.64 (2×s, 1H, =CH and CHS), 7.19–7.34 (m, 5H, Ph), 8.00 (s, *J*=5.6 Hz, 1H, NH_{amide}), 11.54 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): δ 35.5 (CH_2Ph), 40.3 (NCH_2), 55.0 (CH_3), 81.9 (CHS), 95.1 (=CH), 126.3 (*p*-Ph), 128.6 (*o*-Ph), 128.9 (*m*-Ph), 139.8 (C1-Ph), 147.3 (C=), 166.1 (CO_{amide}), 171.3 (CO_{lactam}). Anal. Calcd for $C_{14}H_{16}N_2O_3S$: C, 57.52; H, 5.52; N, 9.58; S, 10.97; found: C, 57.20; H, 5.50; N, 9.51; S, 11.08.

4.17. General procedure for synthesis of 5-morpholino-4-oxothiazolidines 28k–l

A mixture of the crude pyridinium salt **21k–l** and morpholine in $CHCl_3$ was stirred at rt in dry atmosphere. After evaporation of the solvent under reduced pressure, the residue was purified by column chromatography.

*4.17.1. (5-Morpholino-4-oxothiazolidin-2-ylidene)-N-phenylethanamide (**28k**).* Pyridinium salt **21k** (90.4 mg), morpholine (0.08 mL, 0.91 mmol), $CHCl_3$ (9 mL); stirred for 25 h; purification: gradient toluene/ethyl acetate 80:20 to 0:100; yield 91%; pale orange solid, mp 160–162 °C (decomp.); *Z*/*E* ratio: 9:91; IR (KBr, cm^{-1}): ν_{max} 3345, 3172, 3033, 1718, 1655, 1599, 1545, 1490, 1441, 1310, 1254, 1182, 1131, 1108, 857, 776, 750, 700; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 2.24–2.38 (m, 2H, NCH_A), 2.59–2.70 (m, J_{ax-eq}=11.4 Hz, 2H, NCH_B), 3.60–3.65 (m, 4H, CH_2O), 5.44 (s, 1H, =CH), 5.78 (s, 1H, CHS), 7.04 (t, *J*=7.3 Hz, 1H, *p*-Ph), 7.31 (t, *J*=7.9 Hz, 2H, *m*-Ph), 7.58 (d, *J*=7.9 Hz, 2H, *o*-Ph), 9.94 (s, 1H, NH_{amide}), 11.49 (s, 1H, NH_{lactam}), (*Z* isomer) δ 2.26–2.36 (m, 2H, NCH_A), 2.65–2.72 (m, 2H, NCH_B), 3.59–3.63 (m, 4H, CH_2O), 5.38 (s, 1H, CHS), 5.82 (s, 1H, =CH), 6.99 (t, *J*=7.3 Hz, 1H, *p*-Ph), 7.27 (t, *J*=7.8 Hz, 2H, *m*-Ph), 7.60 (d, *J*=7.8 Hz, 2H, *o*-Ph), 9.89 (s, 1H, NH_{amide}), 11.71 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 48.7 (CH_2N), 65.6 (CH_2O), 75.2 (CHS), 92.9 (=CH), 119.5 (*o*-Ph), 123.5 (*p*-Ph), 129.0 (*m*-Ph), 139.2 (C1-Ph), 149.9 (C=), 165.3 (CO_{amide}), 170.3 (CO_{lactam}), (*Z* isomer) δ 48.5 (CH_2N), 65.9 (CH_2O), 72.8 (CHS), 94.6 (=CH), 118.9 (*o*-Ph), 122.8 (*p*-Ph), 128.9 (*m*-Ph), 140.0 (C1-Ph), 150.8 (C=), 165.2 (CO_{amide}), 171.9 (CO_{lactam}). Anal. Calcd for $C_{15}H_{17}N_3O_3S$: C, 56.41; H, 5.37; N, 13.16; S, 10.04; found: C, 56.41; H, 5.24; N, 12.97; S, 10.07.

*4.17.2. 5-Morpholino-4-oxothiazolidin-2-ylidene-N-(2-phenylethyl) ethanamide (**28l**)*[26]. Pyridinium salt **21l** (94.3 mg), morpholine (0.08 mL, 0.91 mmol), $CHCl_3$ (8.7 mL); stirred for 6.5 h; purification: gradient toluene/ethyl acetate 40:60 to 0:100; yield 87%; pale yellow solid, mp 114–115 °C; *Z*/*E* ratio: 18:82; IR (KBr, cm^{-1}): ν_{max} 3437, 3267, 3212, 3077, 1718, 1635, 1565, 1454, 1280, 1249, 1113, 858, 831, 768, 703; ^{1}H NMR (200 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 2.21–2.31 (m, 2H, NCH_A), 2.57–2.76 (m, 4H, NCH_B and CH_2Ph), NCH_2 is masked by water, 3.61 (t, *J*=4.4 Hz, 4H, CH_2O), 5.23 (s, 1H, =CH), 5.72 (s, 1H, CHS), 7.16–7.34 (m, 5H, Ph), 8.02 (t, *J*=5.6 Hz, 1H, NH_{amide}), 11.70 (s, 1H, NH_{lactam}), (*Z* isomer) 2.24–2.30 (m, 2H, NCH_A), 2.62–2.74 (m, 4H, NCH_B and CH_2Ph), 3.24–3.34 (m, 2H, NCH_2), 3.57–3.60 (m, 4H, CH_2O), 5.30 (s, 1H, CHS), 5.58 (s, 1H, =CH), 7.16–7.34 (m, 5H, Ph), 7.90 (t, *J*=5.5 Hz, 1H, NH_{amide}), 11.42 (s, 1H, NH_{lactam}); ^{13}C NMR (50.3 MHz, DMSO-d_6, 25 °C): (*E* isomer) δ 35.3 (CH_2Ph), 40.3 ($NHCH_2$), 48.6 (CH_2N), 65.8 (CH_2O), 75.1 (CHS), 92.7 (=CH), 126.4 (*p*-Ph), 128.6 (*o*-Ph), 128.8 (*m*-Ph), 139.6 (C1-Ph), 147.7 (C=), 166.8 (CO_{amide}), 170.0 (CO_{lactam}), (*Z* isomer) δ 35.6 (CH_2Ph), 40.4 ($NHCH_2$), 48.4 (CH_2N), 65.9 (CH_2O), 72.6 (CHS), 94.5 (=CH), 126.3 (*p*-Ph), 128.6 (*o*-Ph), 128.8 (*m*-Ph), 139.8 (C1-Ph), 148.1 (C=), 166.3 (CO_{amide}), 171.7 (CO_{lactam}). Anal. Calcd for $C_{17}H_{23}N_3O_4S$ (**9g**×H_2O): C, 55.87; H, 6.34; N, 11.50; S, 8.77; found: C, 55.90; H, 6.34; N, 11.42; S, 9.05.

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