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Stereo- and regiocontrol of electrophile-initiated rearrangement of push–pull 5-substituted 4-oxothiazolidine derivatives

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Abstract—Regioselective α-bromination of (*Z*)-5-substituted-2-alkylidene-4-oxothiazolidine derivatives affords, under mild experimental conditions, vinyl bromides **3** in good yields. They undergo rearrangement providing a highly efficient route to the stereodefined 4-oxothiazolidine derivatives possessing two fully delocalized exocyclic double bonds at C(2) and C(5) positions. A mechanism of this novel rearrangement reaction via base-promoted proton transfer from one carbanionic site to another, followed by the bromination–dehydrobromination sequence, is proposed.

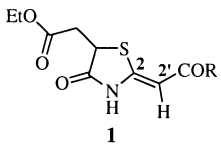
1. Introduction

Synthetic and naturally occurring 4-oxothiazolidines continue to attract attention both as biologically active compounds[1] and as precursors for synthetic purposes.[2] Furthermore, an investigation of the physical and chemical properties of the push–pull 4-oxothiazolidine derivatives[3] that may serve as an entry to conducting polymers is of special interest.[4] In this regard, development of new methods for the synthesis of push–pull alkenes which contain conjugated chains of various lengths, bearing electron donors and acceptors at the termini, is a very active field in current organic chemistry.[5] Following our recent report describing a method for the synthesis of new push–pull thiazolidinones **1** from diethyl ester of thiomalic acid and activated β-oxonitriles, via the regio- and stereoselective base-catalyzed two-step reaction sequence,[6] we have turned our attention to the reactivity of these compounds. Previous ^{13}C NMR spectroscopy studies using a wide range of known push–pull alkenes have been done by Kleinpeter et al.[7] who revealed that the charge polarization of the exocyclic double bond can be estimated on the basis of large chemical shift differences between olefinic carbon atoms. In particular, we also found a consistent set of high field shifts of the C(2′) atoms and low field shifts for the C(2) atoms which reflects the charge polarization of C=C in thiazolidine derivatives **1** (Table 1).

This fact implies the nucleophilic character of the C(2′) atom of **1**, which should generally correspond to an increase in the enaminic susceptibility of the push–pull alkenes **A** at C(α) position toward electrophiles (Scheme 1).[8]

Tokimitsu et al.[9] provided evidence that primary and secondary nitroenamines **A** (EWG=NO_2) undergo electronically controlled α-substitution with electrophilic reagents such as *N*-halosuccinimides, *o*-nitrobenzenesulfenyl chloride or benzoyl isothiocyanate, which can be accounted for by the contribution of a resonance structure **B**. There have been, however, only a few studies of halogenation of push–pull alkenes[3a,8a] and no investigations or other studies that revealed the position and stereochemistry of the

Table 1. ^{13}C NMR chemical shifts (ppm) of olefinic signals of (*Z*)-**1a–c** isomers in DMSO-d_6

		C-2′	C-2	$\Delta\delta_{C2,C2'}$
 **1**	*Z*-**1a** (R=$NHCH_2CH_2Ph$)	93.23	150.82	57.59
	Z-**1b** (R=NHPh)	93.34	153.54	60.20
	Z-**1c** (R=Ph)	94.94	161.56	66.62

Keywords: thiazolidines; halogenation; regiochemistry; rearrangement.
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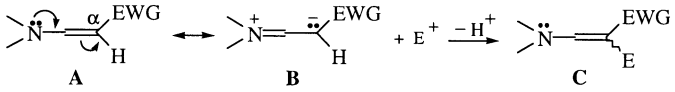


Scheme 1.

initial electrophilic attack. In a recent communication we have demonstrated that the regioselective bromination of **1a–c** at C(2′) provides a highly effective means for the incorporation of another double bond at C(5) via the novel rearrangement process.[10] Initial promising results prompted us to take a thorough look into the scope and limitations of viable synthesis of the push–pull 4-oxothiazolidine derivatives containing two fully conjugated C–C double bonds.

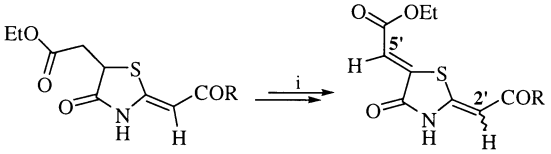
2. Results and discussion

2.1. Preparation and spectral properties of 4-oxothiazolidine derivatives 2a–c

In an initial experiment (*Z*)-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-*N*-(2-phenylethyl)ethanamide (**1a**), synthesized via our reported route,[6] was treated with an equimolar quantity of bromine in $CHCl_3$ at 0°C under controlled conditions, as observed by an almost instantaneous disappearance of bromine color upon dropwise addition (~20 min) and complete consumption of **1a** (TLC). Upon slow vacuum evaporation (ca. 5.5 h, rt), an initially pale-yellow reaction solution gradually became yellow in color, giving rise to nearly quantitative formation of only one product. The structure of the isolated yellow compound was deduced as **2a** (Table 2). Given the constitutional similarity between the starting 4-oxothiazolidine derivative **1a** and product **2a**, it was possible to determine unequivocally the configuration of exocyclic double bonds at C(2) and C(5) as being 2*Z*,5*Z* (vide infra).

As evidenced by the examples in Table 2, bromination of 4-oxothiazolidine derivatives **1a–d** (method **A**) of varying levels of olefin substitution afforded push–pull alkenes **2a–d** in excellent yields. The scope of this reaction involving derivatives **1a–c** is given further extension by employing NBS, or pyridinium hydrobromide perbromide ($C_5H_5NH^+Br_3^-$) as a brominating reagent (entries 2, 6 and 8). In addition to nearly quantitative yields of alkenes **2a–c** (method B), the high geometrical preference for the 2*E*,5*Z*-isomers over the 2*Z*,5*Z*- at ca. 10:1, should be emphasized regarding the sterochemical aspect of this reaction. To our knowledge, only one stereoselective synthesis of 4-oxothiazolidine compounds, possessing two exocyclic double bonds, has been recently reported, i.e. one based on the cyclization of malonthioamide derivatives with DMAD.[11] Purification of the crude products **2a–c** (method A) by column chromatography on silica-gel, led to mixtures containing, in varying proportions, the original 2*Z*,5*Z*-diastereomer (in the case of **2a** and **2b**) or 2*E*,5*Z*-diastereomer (in the case of **2c**) and the corresponding counterpart. This type of silica-gel induced *E–Z*-isomerization, being at the same time solvent-dependent, was monitored by 200 MHz ^{1}H NMR spectroscopy. The olefinic proton at C(2′) of isomers **2a–c** was easily distinguishable according to its

Table 2. Selected analytical and ^{1}H NMR data for the configurational isomers **2a–d** in bromine-mediated rearrangement **1⇒2**



Z-**1a** (R = $NHCH_2CH_2Ph$)
Z-**1b** (R = NHPh)
Z-**1c** (R = Ph)
Z-**1d** (R = CO_2Et)

2a-c

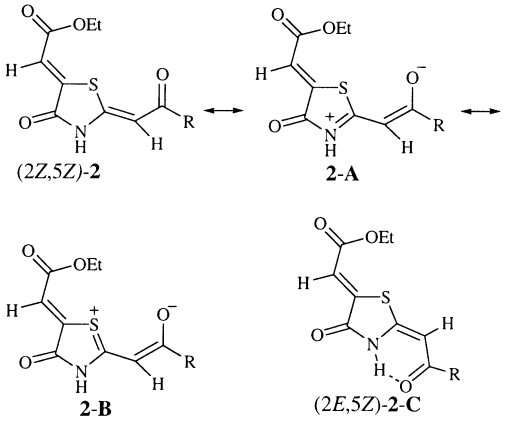
Entry	Compound	NH (ring)	C(2′)H	C(5′)H	Yield (%); Method A[a] or B[b]	
1	2*Z*,5*Z*-**2a** ($CDCl_3$)	9.53	5.73	6.74	94 (A)[c]	
2	2*E*,5*Z*-**2a** ($CDCl_3$)	11.63	5.13	6.86		quant. (B)[d]
3	2*Z*,5*Z*-**2b** (DMSO-d_6)	12.47	6.08	6.53	91 (A)[c]	
4	2*E*,5*Z*-**2b** (DMSO-d_6)	11.78	5.72	6.68		
5	2*Z*,5*Z*-**2b** ($CDCl_3$)	9.20	6.07	6.76		
6	2*E*,5*Z*-**2b** ($CDCl_3$)	11.60	5.50	6.86		quant. (B)[d]
7	2*Z*,5*Z*-**2c** ($CDCl_3$)[e]	9.70	6.91	6.95		
8	2*E*,5*Z*-**2c** ($CDCl_3$)	12.07	6.49	6.96	82 (A)[f]	quant. (B)[d]
9	2*Z*,5*Z*-**2d**[g] ($CDCl_3$)	9.81	5.78	6.81		
10	2*E*,5*Z*-**2d** ($CDCl_3$)	10.82	5.35	6.89	82 (A)[f]	

[a] (i) Br_2 (1 equiv.), $CHCl_3$, 0°C (10–30 min); then vacuum evaporation at rt or prolonged standing at rt.
[b] (i) $C_5H_5NH^+Br_3^-$ (1 equiv.), $CHCl_3$, rt (5–10 min); then prolonged standing during the HBr evolution at rt (2–3 days).
[c] Isolated after column chromatography purification.
[d] Determined by ^{1}H NMR.
[e] Isolated after isomerization in EtOH as a 89:11 mixture of 2*Z*,5*Z* and 2*E*,5*Z* isomers; chemical shifts for olefinic protons not certain; they may be reversed.
[f] Isolated after prolonged standing (72 h).
[g] Preliminary results.

spatial relationship. Hence, HC(2′) of the 2*Z*,5*Z*-**2a**–**c** isomers absorbed at lower field, namely, at δ 5.73, 6.07 and 6.91 ppm, respectively (Table 2, entries 1, 5 and 7) due to the deshielding effect of the *syn*-lactam nitrogen. The chemical shift of the corresponding proton in 2*E*,5*Z*-**2a**–**c** isomers, positioned *syn* to sulfur atom, appears upfield relative to the 2*Z*,5*Z*-counterparts, i.e. at δ 5.13, 5.50, and 6.49 ppm, respectively (Table 2, entries 2, 6 and 8).

Another diagnostic feature in ^{1}H NMR spectra of **2a**–**c**, recorded in $CDCl_3$, is the notable and consistent difference in the chemical shifts of the lactam protons in 2*E*,5*Z*-2 versus 2*Z*,5*Z*-2-isomers. For example, in the ^{1}H NMR spectra of the 2*E*,5*Z*-**2a** and **2c**-isomers recorded in $CDCl_3$ NH-proton, bound to the carbonyl group through intramolecular H-bonding, resonates at significantly lower field (δ 11.63 and 12.07, respectively) relative to the corresponding proton in the 2*Z*,5*Z*-**2a** (δ 9.53) and **2c**-isomer (δ 9.70).

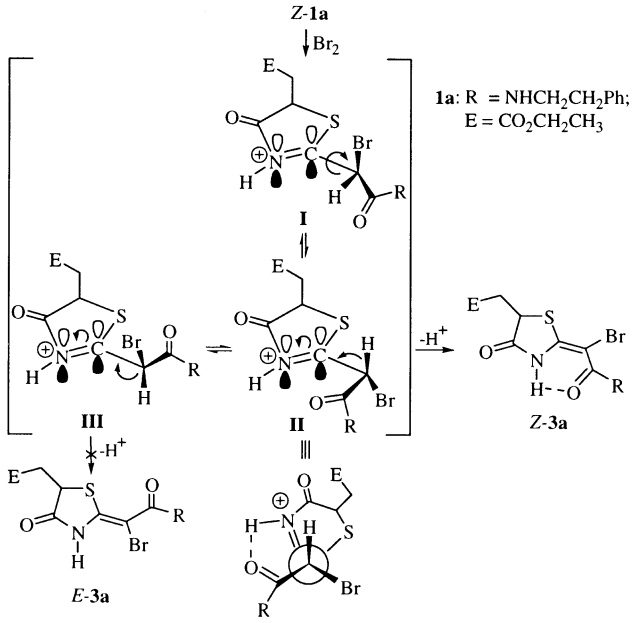
The equilibrated ratio of ca. 9/91 favoring 2*E*,5*Z*-**2a** isomer in nonpolar $CDCl_3$, confirms prevailing contribution of the neutral intramolecularly H-bonded structure (general structure 2-C) to the ground state. On the other hand, the push–pull structures 2*Z*,5*Z*-**2a**–**c**, with strong electron donor and acceptor groups, can be represented as a combination of the neutral structure **2** and charge-separated dipolar resonance forms **2-A** and **2-B**.[3c,10] Polar solvents enhance sulfur or nitrogen participation in the ground-state polarization making the **2-A** and **2-B** forms more dominant. In fact, they increase the stability of 2*Z*,5*Z*-configurated structures **2a**–**c** via strong electrostatic interactions (structure **2-B**) and intermolecular H-bonding.[5b]



In general terms, the fixed and unaffected *Z*-stereochemistry of the configurationally stable exocyclic double bond at C(5) in all compounds **2a**–**c** during the solvent-promoted isomerization of the exocyclic double bond at C(2) at ambient temperature is attributable to severe steric crowding between the lactam carbonyl and carboethoxy group in the respective *E*-configuration, as evidenced by similar examples.[12]

2.2. Mechanistic aspects

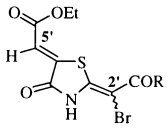
In an attempt to determine the structure of an initial intermediate in the general and surprisingly facile **1**⇒**2** single-pot transformation, the bromination reaction of *Z*-**1a** in $CDCl_3$ (~45 min) was monitored by ^{1}H NMR spectroscopy prior to evaporation of the reaction mixture. A single set of signals, virtually identical to those of the educt **1a** was observed. However, as the resonance of the vinylic proton at δ 5.44 ppm of **1a** completely faded out, obviously, the initial regioselective electrophilic attack occurred at the vinylic position, giving rise to vinyl bromide **3a**. In addition, an appearance of the NH lactam proton at much lower field (δ 11.46 ppm) relative to that of the precursor *Z*-**1a** (δ 9.53 ppm), was recognized as evidence for the *Z*-stereochemistry of the hydrogen-bonded vinyl bromide **3a**, thus indicating complete reversal of stereochemistry in *Z*-**3a** versus *Z*-**1a** (Scheme 2).



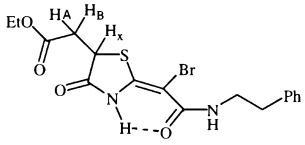
Scheme 2.

This type of stereochemical control in α-bromination of *Z*-**1a** should not be attributed to the anticipated, albeit, very slow *Z*/*E* isomerization, which favors the same **3a**-*Z* isomer in relatively nonpolar solvent, such as chloroform. Thus, irrespective of the solvent-induced isomerization, the observed stereochemical change at C(2′) in *Z*-**3a** versus *Z*-**1a** can be rationalized by considering conformations **I**–**III** of intermediary cation, similar to the one reported by Armstrong et al.[13] concerning the studies on selective bromination of some α,β-dehydroamino acid derivatives. The subsequent proton abstraction by the bromide ion from the reactive conformer **II**, having the C–H orbital parallel to the π-bond of iminium double bond, yields the vinyl bromide *Z*-**3a**, stabilized by intramolecular H-bond. Alternative deprotonation of the α-carbon via rotamer **III**, having equally favorable positioned orbitals, would yield the (*E*)-**3a** isomer which was not detected by ^{1}H NMR spectroscopy. ^{1}H NMR spectral analysis revealed also another series of signals assigned to the minor dibromide *Z*-**4a**. On standing **4a** undergoes dehydrobromination reaction to give vinyl bromide (2*Z*,5*Z*)-**5a** with two exocyclic double bonds.

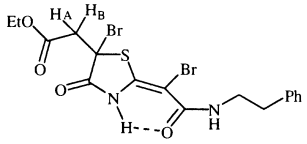
Table 3. Preparation of vinyl bromides **5a–c** via regioselective bromination of 4-oxothiazolidine derivatives **2a–c** at C(2′)

Product		Yield (%)	Mp (°C)	2*Z*,5*Z*/2*E*,5*Z*	λ_{max} ($CHCl_3$)
	**5a** (R=$NHCH_2CH_2Ph$)	94[a]	144–145	98/2[b]	257.0; 363.5
	5b (R=NHPh)	92[c]	187–188	95/5[b]	277.5; 374.0
	5c (R=Ph)	92[a]	148–151	95/5[b]	294.0; 386.0

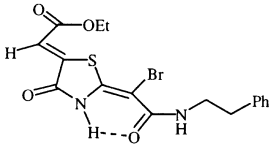
[a] Represent isolated, chromatographically purified materials.
[b] Determined for crude reaction mixture.
[c] Crude product.



3a



4a



5a

In practice, yellow colored vinyl bromides **5a–c** were synthesized, in generally high yields (Table 3), by clean and rapid regioselective bromination of **2a–c**.

An overwhelming preference for electrophilic attack at C(2′) site reflects the increased push–pull character, i.e. the greater polarization of the C–C double bond at C(2) versus that of the double bond at C(5). This can be quantitatively substantiated on the basis of ^{13}C chemical shift differences of the olefinic carbon atoms ($\Delta\delta_{C,C}$ values).[7] Thus, the significant decrease of $\Delta\delta_{C5,C5'}$ values, ranging from 22 to 33 ppm in **2a–c**, versus $\Delta\delta_{C2,C2'}$ ranges of 49–56 ppm in **2a–c** (see Section 3) and 58–67 ppm and in **1a–c** (Table 1), is parallel to an absolute reluctance of the exocyclic double bond at C(5) to undergo electrophilic substitution.

On a preparative scale, rapid regioselective α-bromination (~10–25 min) of **1a–c** at rt, in alcohol (**1b** and **1c** as precursors) or in boiling CCl_4 as a solvent (**1a** as the precursor), resulted in the isolation of the primary bromination compounds **3a–c** in good yields of 60–66%.[14]

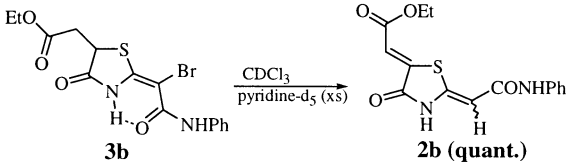
To establish further the fact that the initial intermediate, in general, in one-pot process **1⇒2** (Table 2) is indeed the vinyl bromide **3**, the anticipated rearrangement of stereoisomerically pure vinyl bromide *Z*-**3b** in $CDCl_3$ to **2b** was carried out in the presence of deuterated pyridine.

Compound **3b** completely disappeared after 83 h (Table 4) and ^1H NMR spectrum showed the presence of **2b** as a mixture (ca. 3:7) of (2*Z*,5*Z*)- and (2*E*,5*Z*)-isomers. Inferring vinyl bromide **3** as the intermediate in the direct **1⇒2** rearrangement process was also supported by the fact that in the separate experiment after bromination of **1a** ($CHCl_3$, 0°C) one half of the reaction mixture upon addition of ethanol afforded the expected bromide **3a** (2 days). The other portion however, containing obviously the same bromide, **3a**, rearranged to (2*Z*,5*Z*)-**2a** during vacuum evaporation (5 h, rt).

The most likely pathway for the vinyl bromide rearrangement to **2** in the presence of pyridine, starts with the base-assisted heterolytic cleavage of the C–Br bond (Scheme 3), thereby leading to the carbanion **6** and bis-(pyridine)bromonium cation, presumably in equilibrium with the mono(pyridine)bromonium species.

Subsequent very rapid hydrogen transfer, occurring via pyridine-induced C(5) proton capture and protonation at C(2′), leads to reversible formation of another carbanion–Br^+–pyridine complex **7**. It is conceivable, then, that an unprecedented migration of the pyridine-bound bromonium ion ($Py–Br^+$), from one carbanionic site of the ion pair complex **6** to the other of the complex **7** is actually the consequence of a conducted tour mechanism[15] in which pyridine transports a proton from the C(5) atom to C(2′). This type of ion pair reorganization reaction, followed by the irreversible collapse of **7** occurring by bromination within the ion pair complex **7**, affords the alkyl bromide **8**. This one, as a transient species, was not observed due to its

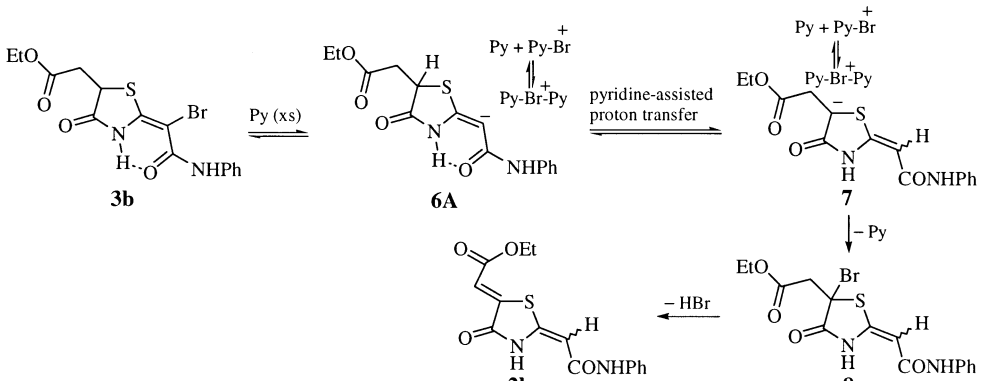
Table 4. Pyridine-initiated rearrangement of **3b** to **2b**

	Time (h)	Molar ratio **3b**/**2b**
	0	100/0
	9	92/8
	25	66/34
	31	44/56
	57	8/92
	73	~0/100[a]
	83.5	0/100

3b → **2b (quant.)**

2*Z*,5*Z*/2*E*,5*Z* = 32/68

[a] Hardly visible signals for **3b**.



Scheme 3.

facile pyridine-catalyzed dehydrobromination to **2b**. ^{1}H NMR study on the **3b**+$CDCl_3$+pyridine-d_5 system indicating slow, nevertheless complete, disappearance of **3b** and concomitant accumulation of **2b**, offers (conclusive) evidence that the heterolytic C–Br cleavage is likely to be the rate determining step in the overall process.

In conclusion, the experimental data show that regioselective α-bromination of the 5-substituted-2-alkylidene-4-oxothiazolidine derivatives **1a–c** affords vinyl bromides **3a–c** in good yields. The driving force for the novel rearrangement process **1**⇒**2** leading, via intermediate vinylbromide **3**, to the stereodefined push–pull thiazolidine derivatives **2** stems obviously from an extensive π-delocalization, as exemplified by the unusually large bathochromic shift induced upon incorporation of the new C–C double bond into the precursors **1** (Table 5).

The stabilization of this kind of products **2a–c**, in conjunction with the relative ease of C–Br cleavage in intermediates **3a–c**, should therefore account for the observed high yields in this rearrangement reaction of a general character. Though the intermolecular transfer of Br^+ or I^+ from bis(*sym*-collidine)bromonium triflate and bis-(pyridine)-iodinium nitrate to acceptor alkenes are well documented,[16] this is the first example of an in situ bromonium transfer between relatively distant reactive sites within the same molecule. Possible dependence of the transformation process **1**⇒**2** on the presence or absence of various substituents at C(5) in the 4-oxothiazolidine derivatives is under current investigation.

Table 5. UV data $\lambda_{max}(\varepsilon)$ of the starting precursors **1a–c** and products **2a–c**. (Mixture of 2*Z*,5*Z*- and 2*E*,5*Z*- isomers)

2a (DMSO)[a]	357 (19,400)
Z-**1a** (DMSO)	282 (25,300)
2b (DMSO)	276 (19,200); 374.5 (25,600)
Z-**1b** (DMSO)	306 (30,900)
2c ($CHCl_3$)	286 (11,400); 368 (29,400)
Z-**1c** (DMSO)	335 (19,100)

Comparison of the UV spectral data of **2a–c** with these of the corresponding precursors **1a–c** (respective λ_{max} values for **1a–c** are 282, 306 and 335 nm) indicate, for example, a 75 nm red shift observed upon synthesis of **2a** (λ_{max} 357 nm) and 68.5 nm red shift in the case of **2b** (λ_{max} 357 nm).
[a] Another absorption maximum at 260 nm masked by solvent absorption.

3. Experimental

Melting points were determined on a Micro-Heiztisch Boetius PHMK apparatus and Buchi apparatus and are uncorrected. The IR spectra were recorded on a Perkin–Elmer FT-IR spectrophotometer 1725X and are reported as wave numbers (cm^{-1}). Samples for IR spectral measurements were prepared as KBr disks. The NMR spectra were obtained using a Varian Gemini 2000 instrument (^{1}H at 200 MHz, ^{13}C at 50.3 MHz). Chemical shifts are reported in parts per million (ppm) on the δ scale from TMS as an internal standard in the solvents specified. Low-resolution mass spectra were recorded using a Finnigan MAT 8230 BE spectrometer. Isobutane was used as the ionizing gas for the chemical ionization (CI) mass spectra. The UV spectra were measured on a Beckman DU-50 spectrophotometer. Analytical thin-layer chromatography (TLC) was carried out on Kieselgel G nach Stahl, and the spots were visualized by iodine. Column chromatography was carried out on SiO_2 (silica gel 60 Å, 12–26, ICN Biomedicals). Elemental analyses were performed at the microanalysis laboratory at the Department of Chemistry, University of Belgrade.

3.1. Rearrangement reactions of 4-oxothiazolidine derivatives (*Z*)-1a–c

3.1.1. (2*E*,5*Z*)- and (2*Z*,5*Z*)-(5-Ethoxycarbonylmethylidene-4-oxothiazolidin-2-ylidene)-*N*-(2-phenylethyl)-ethanamide (2a). The thiazolidine derivative (*Z*)-**1a** (300 mg, 0.86 mmol) was suspended in 42 mL of $CHCl_3$ and cooled in an ice bath. Equimolar quantity of bromine as a 2% solution in $CHCl_3$ was added slowly, with stirring over the period of 10 min until the yellowish color persisted due to the slight excess of bromine (TLC indicated the complete disappearance of the starting material). The resulting mixture was stirred for additional 20 min, warmed to room temperature and the solvent evaporated under reduced pressure at room temperature. Analysis of the yellow residue (402.0 mg), left by removal of the solvent and prolonged evacuation (5.5 h), by ^{1}H NMR spectroscopy indicated the presence of (2*Z*,5*Z*)-**2a** isomer as the major compound. The crude residue was purified by column chromatography (silica gel) with toluene/ethyl acetate as eluent (solvent gradient 100/0–0/100, v/v), followed by ethanol, to give 279.0 mg (94%) of **2a** as a mixture of (2*E*,5*Z*)- and (2*Z*,5*Z*)-isomers as a yellow solid. Recrystallization from

ethanol gave an analytically pure sample. Anal. Calcd for $C_{17}H_{18}N_2O_4S$: C, 58.94; H, 5.24; N, 8.09; S, 9.26. Found: C, 59.15; H, 5.28; N, 8.38; S, 9.51. Samples of each isomer were obtained from the chromatography:

*Isomer (2E,5Z)-**2a***: ((mixture of (2*E*,5*Z*)-**2a** and (2*Z*,5*Z*)-**2a** in the 93/7 ratio)). Mp 169–171°C (the configurational change of structure at 151–153°C due to the thermal isomerization); IR (KBr) ν_{max} 3372, 3212, 3094, 3044, 2987, 2868, 1732, 1651, 1602, 1541, 1370, 1332, 1219, 1196, 868, 715, 697 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.26 (3H, t, J=7.2 Hz, CH_3), 2.76 (2H, t, J=7.3 Hz, CH_2Ph), 3.34–3.43 (2H, m, J=7.3, 5.5 Hz, $NHCH_2CH_2$), 4.24 (2H, q, J=7.2 Hz, CH_2O), 5.55 (1H, s, =CH(2′)), 6.65 (1H, s, =CH(5′)), 7.20–7.34 (5H, m, Ph), 8.31 (1H, t, J=5.5 Hz, NH_{exo}), 11.89 ppm (1H, s, NH ring); ^{13}C NMR (DMSO-d_6): δ 14.3 (CH_3), 35.2 (CH_2Ph), C of CH_2N not visible, 61.6 (CH_2O), 96.5 (=C(2′)), 113.7 (=C(5′)), 126.4 (*p*-Ph), 128.6 (*o*-Ph), 128.9 (*m*-Ph), 139.5 (C(1)– Ph), 145.0 (=C(2)) and (=C(5)), 165.4 (C(4)), 165.7 (CO_{ester}), 165.9 (CO_{exo}).

*Isomer (2Z,5Z)-**2a***: Mp 169–171°C (configurationally pure); IR (KBr) ν_{max} 3323, 3125, 3069, 3022, 2981, 2969, 2830, 1710, 1691, 1660, 1625, 1561, 1462, 1370, 1071, 848, 794, 761, 699 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.26 (3H, t, J=7.1 Hz, CH_3), 2.74 (2H, t, J=7.3 Hz, CH_2Ph), 3.30–3.40 (2H, m, J=7.3, 5.5 Hz, $NHCH_2CH_2$), 4.23 (2H, q, J=7.1 Hz, CH_2O), 5.85 (1H, s, =CH(2′)), 6.48 (1H, s, =CH(5′)) 7.16–7.35 (5H, m, Ph), 8.26 (1H, t, J=5.5 Hz, NH_{exo}), 12.21 ppm (1H, s, NH ring); ^{13}C NMR (DMSO-d_6): δ 14.3 (CH_3), 35.4 (CH_2Ph), C of CH_2N not visible, 61.2 (CH_2O), 97.2 (=CH(2′)), 113.0 (=C(5′)), 126.4 (*p*-Ph), 128.6 (*o*-Ph), 129.9 (*m*-Ph), 139.6 (C(1)– Ph), 145.8 (=C(2)) and (=C(5)), 165.4 (C(4)), 165.7 (CO_{ester}), 165.9 (CO_{exo}); MS (CI) 347 (M+1); MS (EI) *m/z* (rel. intensity) 346 (M^+, 6), 301 (8), 300 (15), 255 (6), 242 (9), 226 (100), 198 (11), 180 (5), 104 (10).

3.1.2. (2*E*,5*Z*)- and (2*Z*,5*Z*)-(5-Ethoxycarbonylmethylidene-4-oxothiazolidin-2-ylidene)-*N*-phenylethanamide (2b). Rearrangement reaction of (*Z*)-**1b** (205.0 mg, 0.64 mmol in 44 mL of chloroform) with small equimolar excess of bromine was carried out under similar conditions as described for **1a**. Evaporation to dryness, followed by prolonged evacuation at room temperature (5 h) gave 254 mg of a yellowish-orange mixture which contained (2*Z*,5*Z*)-isomer **2b** as the major compound. The crude residue was chromatographed on silica gel, using the toluene/ethyl acetate mixture (solvent gradient 100/0–0/100, v/v), to give 186 mg (91%) of **2b** (a mixture of (2*E*,5*Z*)- and (2*Z*,5*Z*)-isomers) as a yellow solid. Analytically pure sample was obtained by crystallization of this solid from toluene–ethyl acetate mixture 9:1 (v/v). Anal. Calcd for $C_{15}H_{14}N_2O_4S$: C, 56.59; H, 4.43; N, 8.80; S, 10.07. Found: C, 56.30; H, 4.62; N, 8.62; S, 9.62. Samples of each isomer were obtained from the chromatography:

*Isomer (2E,5Z)-**2b*** (mixture of (2*E*,5*Z*)-**2b** and (2*Z*,5*Z*)-**2b** in the 97/3 ratio). Mp 217–221°C (the configurational change of structure at 197–200°C due to the thermal isomerization); IR (KBr) ν_{max} 3462, 3329, 3044, 3028, 2974, 1687, 1653, 1599, 1372, 1314, 1196, 1095, 852, 805, 756, 692 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.27 (3H, t, J=7.1 Hz, CH_3), 4.25 (q, 2H, J=7.1 Hz, CH_2O), 5.72 (1H, s, =CH(2′)), 6.68 (1H, s, =CH(5′)), 7.04–7.11 (1H, m, *p*-Ph), 7.30–7.33 (2H, m, *m*-Ph), 7.61–7.65 (2H, m, *o*-Ph), 10.22 (1H, s, NH_{exo}), 11.78 ppm (1H, s, NH ring); ^{13}C NMR (DMSO-d_6): δ 14.3 (CH_3), 61.6 (CH_2O), 96.7 (=C(2′)), 114.0 (=C(5′)), 119.5 (*o*-Ph), 123.7 (*p*-Ph), 129.0 (*m*-Ph), 139.0 (C(1)– Ph), 145.3 (=C(5)), 148.0 (=C(2)), 164.6 (C4), 165.4 (CO_{ester}), 165.9 (CO_{exo}).

*Isomer (2Z,5Z)-**2b*** (2*Z*,5*Z*/2*E*,5*Z* ratio: 96/4). Mp 218–222°C; IR (KBr) ν_{max} 3323, 3197, 2987, 1708, 1674, 1654, 1600, 1548, 1373, 1321, 1202, 1149, 833, 751, 690 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.27 (3H, t, J=7.0 Hz, CH_3), 4.25 (2H, q, J=7.0 Hz, CH_2O), 6.08 (1H, s, =CH(2′)), 6.53 (1H, s, =CH(5′)), 7.01–7.08 (1H, m, *p*-Ph), 7.27–7.35 (2H, m, *m*-Ph), 7.57–7.65 (2H, m, *o*-Ph), 10.23 (1H, s, NH_{exo}), 12.47 ppm (1H, s, NH ring); ^{13}C NMR (DMSO-d_6): δ 14.3 (CH_3), 61.3 (CH_2O), 97.3 (=C(2′)), 113.6 (=C(5′)), 119.1 (*o*-Ph), 123.4 (*p*-Ph), 129.0 (*m*-Ph), 139.5 (C(1)– Ph), 145.2 (=C(5), 148.0 (=C(2)), 164.6 (C4), 165.4 (CO_{ester}), 165.9 (CO_{exo}); MS (CI) 319 (M+1); MS (EI) *m/z* (rel. intensity) 318 (M^+, 8), 226 (14), 198 (9), 180 (4), 103 (4), 93 (100), 85 (11), 67 (15).

3.1.3. (2*E*,5*Z*)- and (2*Z*,5*Z*)-(5-Ethoxycarbonylmethylidene-4-oxothiazolidine-2-ylidene)-1-phenylethanone (2c). A suspension of **2c** (300 mg, 0.98 mmol) and NBS (196 mg, 1.1 mmol) in 8 mL of $CHCl_3$ was stirred at room temperature for 20 min, until TLC analysis (toluene/EtOAc, 4/1) indicated complete consumption of the starting material. The residual solid was filtered and rinsed with additional chloroform. The slightly colored filtrate was washed with saturated aqueous sodium bicarbonate and then with water. Drying and evaporation of the solvent under reduced pressure for an extended period of time (5 h) afforded a yellow residue which was chromatographed on a silica gel column eluting with toluene/ethyl acetate (95/5, v/v) to give the *title compound* **2c** (244.0 mg, 82%; ratio 2*E*,5*Z*/2*Z*,5*Z*=78/22).

Almost pure sample of the major (2*E*,5*Z*)-isomer **2c** as yellow crystals, was obtained by isomerization in chloroform: mp 166–167°C (the configurational change of structure at 153–158°C due to thermal isomerization); IR (KBr) ν_{max} 3197, 2997, 1692, 1641, 1607, 1595, 1579, 1559, 1449, 1364, 1317, 1199, 1024, 998, 872, 857, 816, 777, 761, 685 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.36 (3H, t, J=7.2 Hz, CH_3), 4.33 (2H, q, J=7.2 Hz, CH_2O), 6.49 (1H, s, =CH(2′)), 6.96 (1H, s, =CH(5′)), 7.42–7.61 (3H, m, *m*- and *p*-Ph), 7.94–7.97 (2H, m, *o*-Ph), 12.07 ppm (1H, s, NH ring); ^{13}C NMR ($CDCl_3$): δ 14.2 (CH_3), 61.9 (CH_2O), 97.1 (=CH(2′)), 117.3 (=CH(5′)), 128.0 (*o*-Ph), 128.8 (*m*-Ph), 133.1 (*p*-Ph), 137.6 (C(1)– Ph), 139.5 (=C(5), 153.5 (=C(2)), 165.9 (C4), 166.2 (CO_{ester}), 189.0 CO_{exo}); MS (CI) *m/z* 304 (M+1); MS (EI) *m/z* (rel. intensity) 303 (M^+, 100), 257 (18), 226 (17), 131 (12), 105 (19), 85 (16), 77 (17), 68 (5). Anal. Calcd for $C_{15}H_{13}NO_4S$: C, 59.39; H, 4.32; N, 4.62; S, 10.57. Found: C, 59.19; H, 4.24; N, 4.90; S, 10.30.

Spectral characterization of (2*Z*,5*Z*)-(5-ethoxycarbonylmethylidene-4-oxothiazolidine-2-ylidene)-1-phenylethanone

(**2c**) was carried out using the product obtained after isomerization in ethanol (ratio 2*Z*,5*Z*/2*E*,5*Z*=89/11): mp 166–167°C; IR (KBr) ν_{max} 3193, 3079, 1727, 1616, 1550, 1467, 1421, 1402, 1220, 1046, 862,762, 707, 651 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.37 (3H, t, J=7.1 Hz, CH_3), 4.34 (2H, q, J=7.1 Hz, CH_2O), 6.91 (or 6.95) (1H, s, =C(2′)), 6.95 (or 6.91) (1H, s, =CH(5′)), 7.42–7.61 (3H, m, *m*- and *p*-Ph), 7.94–7.97 (2H, d, *o*-Ph) 9.70 ppm (1H, s, NH ring); ^{13}C NMR ($CDCl_3$): δ 14.2 (CH_3), 61.7 (CH_2O), 98.0 (=C(2′), 118.7 (=C(5′), 127.8 (*o*-Ph), 128.8 (*m*-Ph), 132.9 (*p*-Ph), 137.6 (C(1) or *ipso* Ph), 139.5 (=C (5)), 152.5 (=C(2)), 165.7 (C4), 166.2 (CO_{ester}), 189.0 (CO_{exo}).

3.2. Preparation of vinylbromides 3a–c

3.2.1. (*Z*)-(5-Ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-*N*-(2-phenylethyl)-2-bromoethanamide (3a). The suspension of (*Z*)-**1a** (150 mg, 0.43 mmol) in 21 mL of CCl_4 was brought to reflux and equimolar amount of Br_2 as a 2% solution in CCl_4 was added, with stirring, over the period of 25 min whereas the starting compound completely dissolved. The resulting nearly colorless solution was stirred for additional 15 min and then concentrated under reduced pressure to about 2 mL. Pale yellowish crystals were precipitated, filtered, washed with CCl_4 and dried to give (*Z*)-**3a** (121 mg, 66%), mp 113–114°C; IR (KBr): ν 3374, 3169, 3145, 3023, 2986, 2948, 1719, 1608, 1584, 1524, 1376, 1347, 1312, 1302, 1229, 1191, 853, 749, 703, 689 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.28 (3H, t, J=7.2 Hz, CH_3), 2.84 (1H, dd, J_{AB}=17.7 Hz, J_{AX}=10.2 Hz, CH_AH$_B$CH$_X$S) 2.85 (2H, t, J=7.0 Hz, CH_2Ph), 3.27 (1H, dd, J_{AB}=17.7 Hz, J_{BX}=3.4 Hz, CH$_A$$H_BCH_X$S) 3.50–3.60 (2H, m, J=7.0, 5.4 Hz, NHCH_2CH_2), 4.21 (2H, q, J=7.2 Hz, CH_2O), 4.26 (1H, dd, J_{AX}=10.2 Hz, J_{BX}=3.4 Hz, CH$_X$S), 6.27 (1H, t, J=5.4 Hz, NH_{exo}), 7.19–7.39 (5H, m, Ph), 11.46 ppm (s, 1H, NH_{ring}); ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 35.6 (CH_2Ph), 37.7 (CH_2COO) 41.4 (CH_2N), 44.0 (CHS), 61.6 (CH_2O), 85.3 (=CBr), 126.7 (*p*-Ph), 128.8 (*o*- and *m*-Ph), 138.4 (C(1)– Ph), 151.4 (=C(2)), 163.1 (CO_{exo}), 170.2 (C(4)), 173.9 (CO_{ester}); MS (CI) *m*/*z* 427/429 (M+1); MS (EI) *m*/*z* (rel. intensity) 426 (70)/428 (79) (M^+), 381 (15)/383 (15), 347 (27), 335 (10)/337 (11), 306 (100)/308 (92), 260 (22)/262 (25), 259 (17), 243 (12), 232 (25)/234 (28), 228 (28), 226 (18), 206 (13)/208 (12), 120 (14), 105 (38), 104 (17), 103 (14), 91 (30), 87 (17), 77 (12), 67 (12); UV ($CHCl_3$): λ_{max} (ε) 292.0 nm (26,100). Purification by chromatography using a gradient of pure toluene to pure EtOAc as eluent, followed by concentration of the collected fractions and precipitation by CCl_4 gave analytically pure sample **3a**. 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.

3.2.2. (*E*)-(5-Ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-*N*-(2-phenylethyl)-2-bromoethanamide (3a). This compound was obtained by isomerization of (*Z*)-**3a** isomer in DMSO-d_6 (10 days) giving rise to the equilibrated 40:60 mixture of the (*Z*)-**3a** and (*E*)-**3a** isomers. ^1H NMR (DMSO-d_6) for **3a**-*E*: δ 1.18 (3H, t, J=7.2 Hz, CH_3), 2.74 (2H, t, J=6.8 Hz, CH_2Ph), 2.93 (1H, dd, J_{AX}=7.3 Hz, CH_AH$_B$CH$_X$S; due to the small chemical shift difference of H_A and H_B protons the signal does not show typical ABX pattern; thus J_{AB} can't be determined), 3.12 (1H, dd, J_{BX}=4.9 Hz, CH$_A$$H_BCH_X$S), NCH_2 signal not visible, 4.09 (2H, q, J=7.2 Hz, CH_2O), 4.27 (1H, dd, J_{AX}=7.3 Hz, J_{BX}=4.9 Hz, CH$_X$S), 7.16–7.34 (5H, m, Ph), 7.77 (1H, t, J=5.7 Hz, NH_{exo}), 11.02 (1H, s, NH_{ring}).

3.2.3. (*E*)-(5-Ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-*N*-(phenyl)-2-bromoethanamide (3b). The equimolar amount of Br_2 as a 2% solution in dry alcohol was added dropwise at room temperature to the suspension of (*Z*)-**1b** (110 mg, 0.34 mmol) in 7 mL of dry ethanol, with stirring, over the period of 7–8 min whereupon the starting compound dissolved. The resulting pale yellowish solution, which became cloudy at the end of the Br_2 addition, was stirred for additional 20 min. Upon standing for several hours pale yellowish crystals were precipitated, filtered, washed with alcohol and dried to give (*E*)-**3b** 83 mg (60%), mp 118–120°C; IR (KBr): ν 3437, 3371, 3205, 3028, 2953, 2935, 1735, 1719, 1636, 1599, 1557, 1529, 1380, 1313, 1235, 1196, 812, 755, 689 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.27 (3H, t, J=7.0 Hz, CH_3), 2.96 (1H, dd, J_{AB}=17.5 Hz, J_{AX}=8.5 Hz, CH_AH$_B$CH$_X$S), 3.13 (1H, dd, J_{AB}=17.5 Hz, J_{BX}=4.0 Hz, CH$_A$$H_BCH_X$S), 4.19 (2H, q, J=7.0 Hz, CH_2O), 4.31 (1H, dd, J_{AX}=8.5 Hz, J_{BX}=4.0 Hz, CH$_X$S), 7.10–7.18 (1H, m, *p*-Ph), 7.26–7.38 (2H, m, *m*-Ph), 7.52–7.57 (2H, m, *o*-Ph), 8.01 (1H, s, NH_{exo}), 8.11 (1H, s, NH_{ring}); ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 37.3 (CH_2COO), 44.3 (CHS), 61.6 (CH_2O), 87.2 (=CBr), 120.1 (*o*-Ph), 124.9 (*p*-Ph), 129.1 (*m*-Ph), 137.3 (C(1)– Ph), 154.2 (C=), 161.2 (CO_{exo}), 169.7 (CO_{ring}), 173.6 (CO_{ester}). MS (CI) *m*/*z* 399/401 (M+1); MS (EI) *m*/*z* (rel. intensity) 398 (4)/400 (5) (M^+), 397 (12)/399 (13), 353 (7)/355 (4), 319 (100), 306 (9)/308 (8), 273 (30), 260 (13)/262 (13), 245 (12), 232 (14)/234 (16), 231 (19), 206 (4)/208 (4),159 (5), 146 (3)/148 (3), 131 (7), 93 (85), 87 (6), 77 (9), 66 (3), 65 (2); UV ($CHCl_3$): λ_{max} (ε) 308.0 nm (28.400). Analytically pure sample **3b** was isolated under the conditions described above for vinyl bromide **3a** using ethanol for precipitation. 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.

3.2.4. (*Z*)-(5-Ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-*N*-(phenyl)-2-bromoethanamide (3b). This compound was isolated as a pure (*Z*)-isomer by column chromatography on silica gel of the (*Z*)-**3b** and (*E*)-**3b** mixture, using relatively nonpolar toluene/EtOAc solvent gradient (100/0–50/50, v/v): mp 96–100°C; IR (KBr): ν 3399, 3127, 3031, 3013, 2993, 2976, 2935, 2906, 1725, 1713, 1625, 1597, 1541, 1530, 1377, 1320, 1233, 1217, 764, 750, 691 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.29 (3H, t, J=7.3 Hz, CH_3), 2.88 (1H, dd, J_{AB}=17.8 Hz, J_{AX}=10.2 Hz, CH_AH$_B$CH$_X$S), 3.28 (1H, dd, J_{AB}=17.8 Hz, J_{BX}=3.5 Hz, CH$_A$$H_BCH_X$S), 4.22 (2H, q, J=7.3 Hz, CH_2O), 4.30 (1H, dd, J_{AX}=10.2 Hz, J_{BX}=3.5 Hz, CH$_X$S), 7.05–7.13 (1H, m, *p*-Ph), 7.27–7.35 (2H, m, *m*-Ph), 7.58–7.63 (2H, m, *o*-Ph), 7.96 (1H, s, NH_{exo}), 11.42 (1H, s, NH_{ring}); ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 37.6 (CH_2COO), 44.1 (CHS), 61.7 (CH_2O), 84.7 (=CBr), 120.5 (*o*-Ph), 125.1 (*p*-Ph), 129.1 (*m*-Ph), 137.0 (C(1)– Ph), 153.1 (C=), 161.4 (CO_{exo}), 170.2 (CO_{ring}), 174.0 (CO_{ester}).

3.2.5. (*Z*)-(5-Ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-2-bromo-1-phenylethanone (3c). An equimolar

amount of Br_2 as a 2% solution in dry alcohol was added dropwise at room temperature to a suspension of (*Z*)-**1c** (100 mg, 0.33 mmol) in 3 mL of dry ethanol, with stirring, over the period of 10 min whereupon the starting compound started to dissolve. The resulting slightly yellowish solution was then concentrated to about 2 mL. Pale yellowish crystals were precipitated, filtered, washed with ethanol and dried to give crude (*Z*)-**3c** (80 mg, 64%), mp 83–85°C; IR (KBr): ν 3431, 3203, 3042, 2992, 1724, 1625, 1541, 1377, 1317, 1270, 1230, 1201, 787, 744, 696 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.30 (3H, t, J=7.2 Hz, CH_3), 2.94 (1H, dd, J_{AB}=17.7 Hz, J_{AX}=9.9 Hz, $CH_AH_BCH_XS$), 3.30 (1H, dd, J_{AB}=17.7 Hz, J_{BX}=3.5 Hz, $CH_AH_BCH_XS$), 4.24 (2H, q, J=7.2 Hz, CH_2O), 4.30 (1H, dd, J_{AX}=9.9 Hz, J_{BX}=3.5 Hz, CH_XS), 7.38–7.51 (3H, m, *m*- and *p*-Ph), 7.63–7.68 (2H, m, *o*-Ph), 11.63 (1H, s, NH); ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 37.2 (CH_2COO), 43.9 (CHS), 61.8 (CH_2O), 91.0 (=CBr), 127.8 (*o*-Ph), 128.2 (*m*-Ph), 131.4 (*p*-Ph), 138.7 (C(1)– Ph), 160.7 (C=), 170.0 (CO_{ring}), 175.2 (CO_{ester}), 190.8 (CO_{exo}); MS (EI) *m*/*z* (rel. intensity) 383 (40)/385 (32) (M^+), 338 (3)/340 (2), 304 (7), 258 (5), 230 (8), 159 (3), 131 (8), 128 (10), 105 (88), 87 (16), 77 (100), 73 (7), 55 (28); UV ($CHCl_3$): λ_{max} (ε) 255.0 nm (5300), 341.0 nm (11,900). Analytical sample was obtained by column chromatography purification of the crude (*Z*)-**3c** on silica gel, eluting with toluene/ethyl acetate (100/0–50/50, v/v), followed by concentration of the fractions containing the desired compound **3c**. 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.

3.3. Preparation of vinylbromides with two exocyclic double bonds 5a–c

3.3.1. (2*Z*,5*Z*)-(5-Ethoxycarbonylmethylidene-4-oxothiazolidin-2-ylidene)-*N*-(2-phenylethyl)-2-bromoethanamide (5a). To a solution of 65 mg (0.19 mmol) of **2a** (as a mixture of 2*Z*,5*Z*- and 2*E*,5*Z*-isomers) in chloroform (9.0 mL), an equimolar amount of Br_2 as a 2% solution in $CHCl_3$ was added dropwise, at room temperature, with stirring, over the period of 5 min. The reaction mixture was monitored by TLC for loss of the starting material at which time additional drop of Br_2 caused sudden change of yellow color to yellow–orange. After additional stirring for 10 min, reaction mixture was evaporated to dryness at 30°C, affording 86 mg of crude intensively yellow (2*Z*,5*Z*)-**5a** and 2*E*,5*Z*-**5a** isomers in a 98:2 ratio (^1H NMR, $CDCl_3$).The mixture was purified by column chromatography on silica gel using gradient of toluene/EtOAc from 100/0 to 0/100, v/v) to give 75 mg (94%) of **5a**. Spectral data for the major dark yellow product (2*Z*,5*Z*)-**5a**, mp 144–145°C (after additional crystallization from ethanol) are as follows: IR (KBr): ν 3387, 3138, 3050, 3024, 2944, 1713, 1687, 1618, 1587, 1518, 1371, 1317, 1207, 1190, 856, 757, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.35 (3H, t, J=7.1 Hz, CH_3), 2.87 (2H, t, J=6.9 Hz, CH_2Ph), 3.54–3.64 (2H, m, J=6.9, 5.8 Hz, $NHCH_2CH_2$), 4.32 (2H, q, J=7.1 Hz, CH_2O), 6.41 (1H, t, J=5.8 Hz, NH_{exo}), 6.91 (1H, s, =CH), 7.20–7.40 (5H, m, Ph), 11.68 (1H, s, NH_{ring}); ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 35.4 (CH_2Ph), 41.5 (NCH_2), 61.8 (CH_2O), 89.0 (=CBr), 116.9 (=CH), 126.8 (*p*-Ph), 128.7 (*o*-Ph), 128.8 (*m*-Ph), 138.2 (C(1)– Ph), 141.4 (=C(5)), 148,1 (=C(2)), 162.8 (CO_{exo}), 165.3 (CO_{ring}), 16.3 (CO_{ester}); MS (CI) *m*/*z* 425/427 $(M+1)^+$; MS (EI) *m*/*z* (rel. intensity) 424(15)/426 (14) (M^+), 345 (37), 304 (71)/306 (100), 299 (6), 276 (18)/278 (20), 258 (9)/260 (6), 226 (26), 180 (6), 158 (8), 148 (12), 120 (7), 105 (42), 104 (13), 103 (27), 91 (60), 85 (76), 77 (21), 67 (13), 57 (21); UV ($CHCl_3$): λ_{max} (ε) 257.0 nm (11.000), 363.5 nm (18.400). Anal. Calcd for $C_{17}H_{17}BrN_2O_4S$: C, 48.01; H, 4.03; N, 6.59; S, 7.54. Found: C, 48.29; H, 3.93; N, 6.49; S, 7.48.

3.3.2. (2*E*,5*Z*)-(5-Ethoxycarbonylmethylidene-4-oxothiazolidin-2-ylidene)-*N*-(2-phenylethyl)-2-bromoethanamide (5a). On standing in $CDCl_3$ (11 days) crude reaction mixture containing the (2*Z*,5*Z*)-isomer (98%) and (2*E*,5*Z*)-isomer (2%) transformed into the 88/12 mixture of the (2*Z*,5*Z*)- and (2*E*,5*Z*)-isomers, as determined by the presence of new singlets in proton NMR spectrum at δ 6.78 (1H, s, =CH) and 8.33 (1H, s, NH_{ring}) assigned to the minor (2*E*,5*Z*)-**5a** isomer.

3.3.3. (2*Z*,5*Z*)-(5-Ethoxycarbonylmethylidene-4-oxothiazolidin-2-ylidene)-*N*-(phenyl)-2-bromoethanamide (5b). The procedure was similar to that used above for **5a** except for the purification of the final product. Thus, the crude product (126 mg, 92%; mp 183–185°C), isolated and characterized as the 95:5 mixture of (2*Z*,5*Z*)-**5b** and (2*E*,5*Z*)-**5b**, was obtained by bromination of 110 mg (0.35 mmol) of **2a** (employed as the mixture of both isomers). Crystallization from ethanol afforded the 86:14 mixture of (2*Z*,5*Z*)-**5b** and (2*E*,5*Z*)-**5b**, mp 187–188°C; melting point of **5b** varies due to the different isomer ratio. Spectral data for the major intensively colored yellow product (2*Z*,5*Z*)-**5b** are as follows: IR (KBr): ν 3160, 3041, 3016, 2959, 1735, 1703, 1688, 1668, 1631, 1597, 1530, 1368, 1318, 1199, 857, 836, 756, 688 cm^{-1}; ^1H NMR (2*Z*,5*Z* izomer, $CDCl_3$): δ 1.36 (3H, t, J=7.2 Hz, CH_3), 4.34 (2H, q, J=7.2 Hz, CH_2O), 6.94 (1H, s, =CH), 7.16–7.24 (1H, m, *p*-Ph), 7.34–7.43 (2H, m, *m*-Ph), 7.51–7.60 (2H, m, *o*-Ph), 8.08 (1H, s, NH_{exo}), 11.64 (1H, s, NH_{ring}); ^{13}C NMR ($CDCl_3$): δ 14.2 (CH_3), 62.0 (CH_2O), 88.4 (=CBr), 117.4 (=CH), 120.5 (*o*-Ph), 125.5 (*p*-Ph), 129.2 (*m*-Ph), 136.7 (C(1)– Ph), 141.1 (=C(5)), 149.6 (=C(2)), 161.0 (CO_{exo}), 165.4 (CO_{ring}), 166.2 (CO_{ester}); MS (EI) *m*/*z* (rel. intensity) 396 (2)/398 (3) (M^+), 353 (1), 318 (47), 305 (8)/307 (8), 277 (7)/279 (7), 272 (21), 259 (2)/261 (2), 226 (1), 198 (2), 180 (2), 159 (6), 158 (4), 131 (13), 120 (2), 103 (11), 93 (100), 85 (36), 77 (8), 68 (3), 67 (2), 66 (7), 65 (12), 57 (6); UV ($CHCl_3$): λ_{max} (ε) 277.5 nm (11,500), 374.0 nm (24.200); Anal. Calcd for $C_{15}H_{13}BrN_2O_4S$: C, 45.35; H, 3.30; N, 7.05; S, 8.07; Found: C, 45.65; H, 3.52; N, 7.16; S, 8.29.

3.3.4. (2*E*,5*Z*)-(5-Ethoxycarbonylmethylidene-4-oxothiazolidin-2-ylidene)-*N*-(phenyl)-2-bromoethanamide (5b). ^1H NMR data ($CDCl_3$) for the minor isomer are as follows: δ 1.35 (3H, t, J=7.1 Hz, CH_3), 4.32 (2H, q, J=7.1 Hz, CH_2O), 6.82 (1H, s, =CH), 7.16–7.24 (1H, m, *p*-Ph), 7.34–7.43 (2H, m, *m*-Ph), 7.51–7.60 (2H, m, *o*-Ph), NH_{exo} not visible, 8.38 (1H, s, NH_{ring}).

3.3.5. (2*Z*,5*Z*)-(5-Ethoxycarbonylmethylidene-4-oxothiazolidin-2-ylidene)-2-bromo-1-phenylethanone (5c). According to the procedure similar to that used above, the bromination of 50 mg (0.17 mmol) of **2c** in chloroform (5.0 mL) afforded, after purification of the crude mixture

by column chromatography on silica gel using toluene/EtOAc as eluent (100/0–0/100, v/v), (2*Z*,5*Z*)-**5c** isomer as a 70:30 mixture (with (2*E*,5*Z*)-**5c**), mp 148–151°C, in 92% overall yield (58 mg). Spectral data for the major yellow product (2*Z*,5*Z*)-**5c** are as follows: ^{1}H NMR ($CDCl_3$): δ 1.37 (3H, t, J=7.2 Hz, CH_3), 4.35 (2H, q, J=7.2 Hz, CH_2O), 7.01 (1H, s, =CH), 7.40–7.58 (3H, m, *m*- and *p*-Ph), 7.68–7.75 (2H, m, *o*-Ph), 11.58 (1H, s, NH); ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 62.1 (CH_2O), 93.7 (=CBr), 118.6 (=CH), 127.9 (*o*-Ph), 128.4 (*m*-Ph), 131.9 (*p*-Ph), 138.2 (C(1)– Ph), 140.3 (=C(5)), 153.9 (=C(2)), 166.0 (CO_{ring}), 166.4 (CO_{ester}), 191.5 (CO_{exo}); MS (EI) *m*/*z* (rel. intensity) 381 (52)/383 (43) (M^+), 380 (42)/382 (66), 352 (19)/354 (12), 335 (19)/337 (17), 307 (10)/309 (13), 302 (6), 276 (2)/278 (2), 256 (1), 159 (2), 158 (2), 131 (21), 105 (100), 103 (22), 85 (63), 77 (30), 57 (10); UV ($CHCl_3$): λ_{max} (ε) 294.0 nm (6000), 386.0 nm (18,400); Anal. Calcd $C_{15}H_{12}BrNO_4S$: C, 47.13; H, 3.16; N, 3.66; S, 8.39. Found: C, 47.30; H, 3.34; N, 3.97; S, 8.13.

3.3.6. (2*E*,5*Z*)-(5-Ethoxycarbonylmethylidene-4-oxothiazolidin-2-ylidene)-2-bromo-1-phenylethanone (5c). ^{1}H NMR ($CDCl_3$) data for the minor isomer (2*E*,5*Z*)-**5c** are as follows: δ 1.36 (3H, t, J=7.1 Hz, CH_3), 4.33 (2H, q, J=7.1 Hz, CH_2O), 6.89 (1H, s, =CH), 7.40–7.58 (3H, m, *m*- and *p*-Ph), 7.68–7.75 (2H, m, *o*-Ph), 8.65 (1H, s, NH).

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