Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. 76 (3) 317–328 (2011) UDC 547.78/.79+547.313:66.095.21:543.422.25
JSCS–4120 *Original scientific paper*

Thermal solid-state *Z*/*E* isomerization of 2-alkylidene-4--oxothiazolidines: effects of non-covalent interactions

ZDRAVKO DŽAMBASKI[1#], MILOVAN STOJANOVIĆ[1#], MARIJA BARANAC-STOJANOVIĆ[1,2#], DRAGICA M. MINIĆ[1,3#] and RADE MARKOVIĆ[1,2*#]

[1]*Centre for Chemistry, ICTM, P. O. Box 473, 11001 Belgrade,* [2]*Faculty of Chemistry, University of Belgrade, Studentski trg 16 P. O. Box 158, 11001 Belgrade and* [3]*Faculty of Physical Chemistry, University of Belgrade, Studentski trg 16, 11000 Belgrade, Serbia*

(Received 7 July 2010)

Abstract: Configurational isomerization of stereo-defined 5-substituted and unsubstituted 2-alkylidene-4-oxothiazolidines (**1**) in the solid state, giving the *Z*/*E* mixtures in various ratios, was investigated by ^{1}H-NMR spectroscopy, X-ray powder crystallography and differential scanning calorimetry (DSC). The *Z*/*E* composition can be rationalized in terms of non-covalent interactions, involving intermolecular and intramolecular hydrogen bonding and directional non-bonded 1,5-type S···O interactions. X-Ray powder crystallography, using selected crystalline (*Z*)-4-oxothiazolidine substrate, revealed transformation to the amorphous state during the irreversible *Z*→*E* process. A correlation between previous results on the *Z*/*E* isomerization in solution and now in the solid state was established.

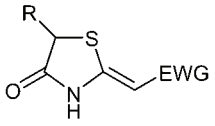
Keywords: 4-thiazolidinones; solid-state isomerisation; non-covalent interactions; dynamic ^{1}H-NMR spectroscopy.

INTRODUCTION

Over the last decade, the chemistry of an extensive series of 5-substituted and unsubstituted 4-oxothiazolidines (**1**, Fig. 1), bearing a trisubstituted exocyclic C–C double bond at position C-2 was investigated.[1]

They undergo a number of useful transformations into diverse heterocyclic systems, including 1,2-dithioles,[2a] 1,3-thiazines,[2b] pyridinium salts containing a 4-oxothiazolidinyl moiety,[2c] tetrahydrofuro[2,3-*d*]thiazolo derivatives[2d] and other thiazolidine-condensed 5-, 6- and 7-membered heterocycles.[2e,f] The thiazolidine derivatives **1** belong to a class of push-pull compounds,[3] usually represented by the general formula D-π-A, where D and A denote electron donor(s) and electron acceptor(s), respectively, bonded to a C–C double bond or a π-conjugating spacer.[4]

* Corresponding author. E-mail: markovic@chem.bg.ac.rs
# Serbian Chemical Society member.
doi: 10.2298/JSC100607038D

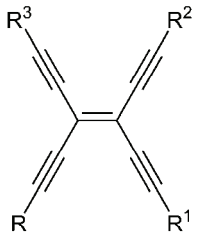


1

R = H, Me, CH_2CO_2Et
EWG = CO_2Et, COPh, CONHPh, $CONH(CH_2)Ph$, CN

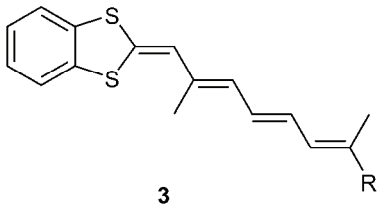
Fig. 1. 2-Alkylidene-4-oxothiazolidinones.

The strong D–A interactions *via* C=C bond(s) in various push-pull derivatives, for example in D–A-substituted tetraethynylethenes **2**,[4a] or benzodithiole polyenes **3**,[4b] (Fig. 2) are associated with their interesting electrochemical and non-linear optical properties.[5]



2

R, R^1 = *p*-$C_6H_4NO_2$; R^2, R^3 = *p*-$C_6H_4NMe_2$
R = *p*-$C_6H_4NMe_2$; R^1, R^2, R^3 = $SiMe_3$
R = *p*-$C_6H_4NMe_2$; R^1 = *p*-$C_6H_4NO_2$; R^2, R^3 = Si(*i*Pr)$_3$



3

R =

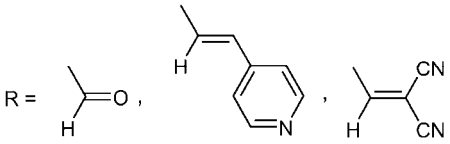


Fig. 2. D–A-Substituted tetraethynylethenes and benzodithiole polyenes.

It was previously shown that electronic interactions in the (*Z*)-4-oxothiazolidine derivatives **1** in solution, between the two electron-releasing substituents –NH and –S–, and an electron-withdrawing substituent (COPh, CO_2Et, CONHPh, *etc*.) through the π-conjugated bond, have a decisive influence on lowering the rotational barrier of the exocyclic C=C bond at position C-2.[6] As a result of the partial single bond character of the C=C bond, configurational isomerization of these highly dipolar compounds, controlled by an appropriate choice of solvent, occurs in solution. On the other hand, the literature contains only a few examples describing the *Z*/*E* isomerization of organic compounds in the solid state.[7]

It is the intent of this paper to report herein *i*) a ^{1}H-NMR investigation of the stereodynamic behaviour of the stereo-defined 2-alkylidene-4-oxothiazolidines **1** in the solid state, proving that a rare type of thermally induced configurational isomerization occurs to form *Z*/*E* mixtures in different ratios. This is combined with *ii*) X-ray powder analysis and DSC measurements in terms of an evaluation of the crystallinity change occurring during the heating process of a representta-

tive of the push-pull alkenes **1**, *i.e.*, (*Z*)-ethyl 4-oxo-2-[2-oxo-2-[(2-phenylethyl)amino]ethylidene]-5-thiazolidineacetate (**1d**) (Fig. 3).

(*Z*)-**1a** (R = CH_2CO_2Et; EWG = CO_2Et)
(*Z*)-**1b** (R = CH_2CO_2Et; EWG = CONHPh)
(*Z*)-**1c** (R = CH_3; EWG = CONHPh)
(*Z*)-**1d** (R = CH_2CO_2Et; EWG = $CONHCH_2CH_2Ph$)
(*Z*)-**1e** (R = CH_2CO_2Et; EWG = COPh)
(*Z*)-**1f** (R = H; EWG = COPh)

(2*E*,5*Z*)-**1g**

Fig. 3. Structures of 2-alkylidene-4-oxothiazolidines.

RESULTS AND DISCUSSION

Several structural features of compounds **1**, that is, their polyfunctional nature, the stereogenic centre at the C-5 position of the thiazolidine ring, the *Z*- or *E*-geometry of the exocyclic donor–acceptor substituted C=C bond, and, importantly, the *cis*-configured –S–C=C–C=O unit of the *Z*-isomers, make them interesting substrates for investigating their properties and reactivity. To probe the impact of inter- and intramolecular interactions on the solid state thermal *Z*/*E*-isomerization of the structurally related (*Z*)-5-substituted and unsubstituted 2-alkylidene-4-oxothiazolidines **1a**–**f** (Fig. 3), the behaviour of ethyl (*Z*)-ethyl 2-[2--(ethoxycarbonyl)ethylidene]-4-oxo-5-thiazolidineacetate (**1a**) was examined first.

The *Z*-configuration of the thiazolidines **1a**–**f**, obtained from the corresponding β-oxonitriles and α-mercaptoesters,[1a,b] was previously elucidated from ^{1}H--NMR spectroscopic data, including 1D nuclear Overhauser effect measurements in the case of the enaminoketone **1e**. X-ray structural analysis confirmed the configuration of the trisubstituted C=C bond in **1a**, having the lactam hydrogen involved in intermolecular hydrogen bonding to the C-4 carbonyl oxygen of an adjacent molecule. Upon slow heating of the solid crystalline compound **1a** (1–2 °C min^{-1}), from room temperature to 120 °C, which is slightly above its melting point, followed by fast cooling of the melt to 0 °C, the extent of the *Z*/*E* process was determined by ^{1}H-NMR spectroscopy, employing DMSO-d_6 or $CDCl_3$ as solvents. As Fig. 4 depicts, the spectrum of **1a** in DMSO-d_6 contained two sets of signals, including typical resonances of the olefinic protons at δ 5.44 ppm for the original *Z*-isomer and δ 5.21 ppm assigned to the newly formed *E*-isomer (the characteristic δ values of the olefinic protons are given in Experimental). The *Z*/*E* ratio, determined by integration of the corresponding chemical shifts, was 83/17.

Likewise, the composition of the *Z*/*E* mixtures of all thiazolidines **1a**–**g**, based on assignments of the characteristic signals for the vinylic protons in the corresponding ^{1}H-NMR spectra, recorded in DMSO-d_6 and/or $CDCl_3$, is compiled in Table I.

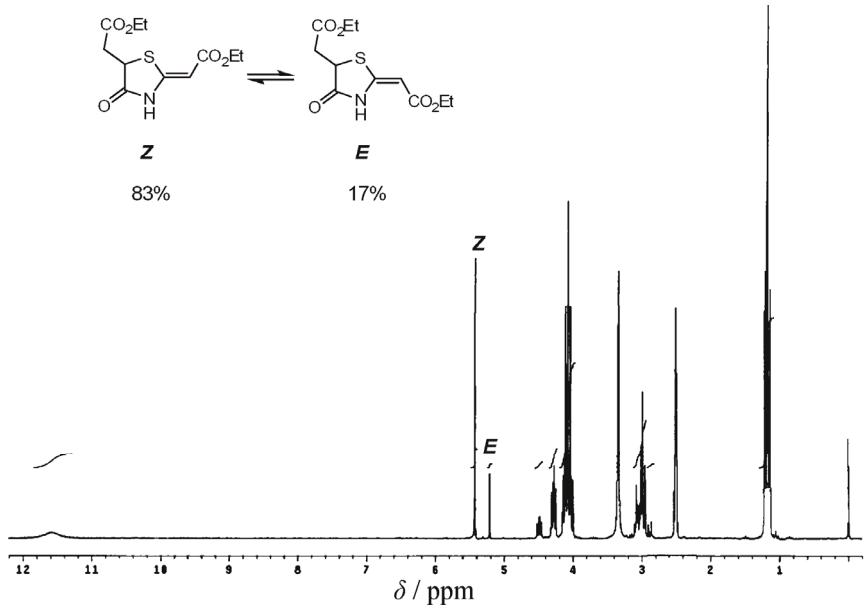
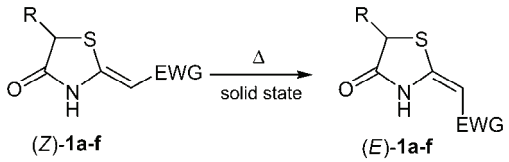


Fig. 4. ^{1}H-NMR spectrum of the *Z*/*E* mixture of thiazolidine derivative **1a**, recorded in DMSO-d_6 after thermal solid-state isomerization.

TABLE I. Configurational isomerization of compounds **1a**–**g** in the solid state

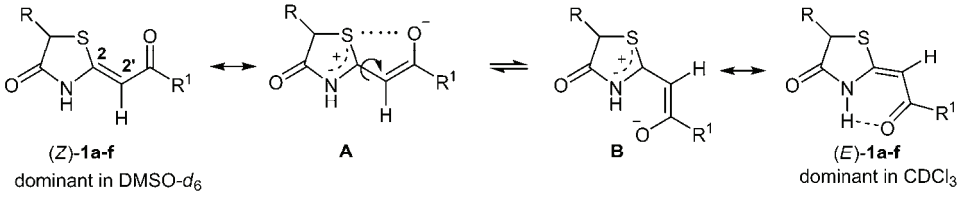


Entry	Substrate	R	EWG	Temperature range, °C[a]	Z/*E* ratio (DMSO-d_6)[b]	Z/*E* ratio ($CDCl_3$)[b]
	Z-**1a**	CH_2CO_2Et	CO_2Et	rt[c]–120	83/17	78/22
1				rt–120		49/51[e]
				rt–110[d]		90/10
2	*Z*-**1b**	CH_2CO_2Et	CONHPh	rt–195	41/59	–[e,f]
3	*Z*-**1c**	CH_3	CONHPh	rt–203	48/52	–
4	*Z*-**1d**	CH_2CO_2Et	$CONH(CH_2)_2Ph$	rt–166	58/42	–
5	*Z*-**1e**	CH_2CO_2Et	COPh	rt–90	100/0	57/43
6	*Z*-**1f**	H	COPh	rt–245	100/0	69/31
7	2*E*,5*Z*-**1g**	$=CHCO_2Et$	CO_2Et	rt–180	70/30 (2*E*,5*Z*/2*Z*,5*Z*)	–

[a]From room temperature to ≈5–10 °C above the melting point; [b]0 time (1–2 min after dissolution of a sample); [c]room temperature; [d]precursor heated below the melting point; [e]2nd heating; [f]insoluble in $CDCl_3$

It is interesting to note that in the case of substrates **1e** or **1f** of the thiazolidine series **1a**–**f** with one exocyclic C=C bond, the corresponding *Z*-isomers were the only species at the end of the heating process, as detected by ^{1}H-NMR

in DMSO-d_6 (Table I, entries 5 and 6). Apparently, the precursors *Z*-**1e** and *Z*-**1f** are either unable to undergo thermally induced solid state *Z*/*E* isomerization (*vide infra*) or, more likely, the *E*-isomer of the *Z*/*E* mixture formed during the isomerization, as found for 4-oxothiazolidines **1a**–**d** (Table I, entries 1–4), transforms in a rapid DMSO-induced $E \rightarrow Z$ interconversion back to original *Z*-form. Indeed, the observation of two ^{1}H-NMR vinylic signals at δ 6.83 and 6.32 ppm in non-polar $CDCl_3$ for substrate **1e**, ascribed to the *Z*- and *E*-isomer, respectively, in a 57/43 ratio (Table I, entry 5), verifies that the solid state isomerization does occur. This is consistent with the finding that the ^{1}H-NMR spectrum of the second enaminoketone **1f**, similarly to **1e**, displayed a pair of =CH signals in $CDCl_3$ at δ 6.78 ppm for *Z*-**1f** and at δ 6.33 ppm for *E*-**1f**, whereas the ^{1}H-NMR spectrum in DMSO-d_6 of the same sample **1f** after heating, showed only the vinylic proton of the *Z*-isomer at δ 6.82 ppm. This is in line with the fact that the ^{1}H-NMR spectra of the highly dipolar compounds **1a**–**f**, or, in principle, related push-pull compounds,[8] are solvent-dependent. The ^{13}C values of C-2 at rather low field for a vinylic carbon (151–163 ppm) of compounds **1a**–**f**, together with a high field position for vinylic C-2' atom (89–95 ppm) reflect their dipolar character[1,3] and hydrogen bonding ability. In some cases, depending on the relative rate of the configurational isomerization pertinent to dipolar compounds of the type **1**, the *Z*/*E* ratio can be appreciably affected in accordance to the general Scheme 1, even during the shortest NMR recording time possible.



Scheme 1. Configurational isomerization of compounds **1a**–**g** in solvents of different polarity.

In accordance to earlier generalization, the *E*-isomers **1a**–**f** are the preferred species for equilibrated *Z*/*E* mixtures in non-polar $CDCl_3$, as the NH···O=C non-covalent interaction leads to favourable six-membered H-bonding.[6a,b] Upon increasing the ground-state polarization of thiazolidines **1a**–**f** in polar DMSO, the neutral, intramolecularly H-bonded structure of *E*-**1a**–**f** is no longer the dominant one. The strong 1,5-type electrostatic S···O interaction due to the maximum charge stabilization in DMSO, as depicted in Scheme 1, enhances the contribution of the resonance form **A**.[9] Thus, the intramolecular H-bonding in the original *E*-isomer is suppressed at the expense of its *Z*-counterpart. The formation of competitive intermolecular H-bonding between the solvent and corresponding *Z*-**1**,

acting in the same direction, favouring the *Z*-form, further attenuates the fast process of C=C bond isomerization. This is obviously a draw-back of using DMSO-d_6 for ^{1}H-NMR determination of the *Z*/*E* composition for **1e** and **1f** after heating, due to the rapid *E*→*Z* isomerization. Fortunately, in contrast to the counter-effect of DMSO on reliable determination of the *Z*/*E* ratio, the kinetic data obtained for the configurational isomerization at room temperature of (*Z*)-ethyl 4-oxo-2-(2-oxo-2-phenylethylidene)-5-thiazolidineacetate (**1e**), and a series of related compounds, in $CDCl_3$ show that the configurational change at room temperature is rather slow. More precisely, starting from the pure (*Z*)-**1e** isomer, the $t_{1/2}$, *i.e.*, the time needed to obtain a 50:50 mixture of the isomers during the *Z*/*E* process in $CDCl_3$ at 25 °C, monitored at regular time intervals (1 h) by dynamic ^{1}H-NMR, was 5 h. The variable-temperature ^{1}H-NMR data for the isomerization of **1e** in $CDCl_3$ indicated that the rotational barrier $\Delta G^{\#}$, separating the (*Z*)-**1e** and (*E*)-**1e** isomers, is 98.5 kJ mol^{-1} (at 298 K).[6a,b] The use of $CDCl_3$ can actually circumvent the problem of rapid *E*→*Z* isomerization, or specifically that of the enaminoketones (*E*)-**1e** or (*E*)-**1f** (EWG = COPh) in DMSO. Thus, an accurate estimate of the relative amounts of each isomer and, consequently, an evaluation of the extent of the thermally induced configurational isomerization of **1a**–**f** in the solid state is possible.

An interesting point concerning the different percentages of the *Z*-isomers in the *Z*/*E* mixtures **1a**–**f**, as determined by ^{1}H-NMR in DMSO-d_6, revealed clearly the influence of the EWGs on an extent of the dictated *E*→*Z* isomerization in polar solvents, as illustrated in Scheme 1. Namely, an increase of the Z-isomers in the order **1e**, **1f** > **1a** > **1b** (Table I, entries 5, 6, 1 and 2, respectively) parallels the order COPh > CO_2Et > CONHR in terms of the stronger electron withdrawing effect of the keto group present in **1e** and **1f**, *vs*. the ester group in **1a**, with the amido group in **1b** being somewhat weaker. Consequently, the better electron withdrawing ability of the keto group to decrease the double bond character at C-2 enhances the contribution of the resonance forms **A** and **B**, enabling faster *E*→*Z* isomerization. This is indicated by the fact that the ^{1}H-NMR spectrum of **1e** (EWG = COPh) after the thermal process showed the presence of only the *Z*-isomer, whereas a *Z*/*E* ratio of 57/43 was determined for the same compound in $CDCl_3$. In contrast, the corresponding *Z*/*E* ratio was 78/22 for **1a** (EWG = CO_2Et) in $CDCl_3$ and only slightly higher (83/17) in DMSO-d_6, which convincingly suggest a slower *E*/*Z* interconversion on the NMR scale. On a second heating of the melt **1a** under identical conditions (Experimental), the *Z*/*E* composition, as determined by ^{1}H-NMR in $CDCl_3$, as for the other substrates **1b**–**f**, amounted to 49/51 (Table I, entry 1). Obviously, the greater percentage of the *E*-isomer in the second melt *vs*. that of the first melt proves the progressive extent of the *Z*→*E* process. When the thermal process, employing **1a** was performed from rt to 110 °C, which is below its melting point, the *Z*/*E* ratio was 90/10.

For stereodefined ethyl (2*E*,5*Z*)-ethyl 2-[2-[2-(ethoxycarbonyl)ethylidene)-4--oxo-5-thiazolidinylilidene]acetate (**1g**), possessing two exocyclic C=C bonds at positions C-2 and C-5, a 2*E*,5*Z*/2*Z*,5*Z* ratio of 70/30 was observed in DMSO-d_6 after thermal isomerization (Table I, entry 7). The *Z*-configuration at the C-5 position stayed intact due to the unfavourable steric interactions in the respective *E*-configuration.[10] By analysis of variable-temperature ^{1}H-NMR data for the solvent-initiated isomerization of 2*E*,5*Z*-**1g** into 2*Z*,5*Z*-**1g** in DMSO-d_6 from room temperature (Fig. 5) to 55 °C, the reliability of the extent of this isomerization occurring in the solid state was assessed.

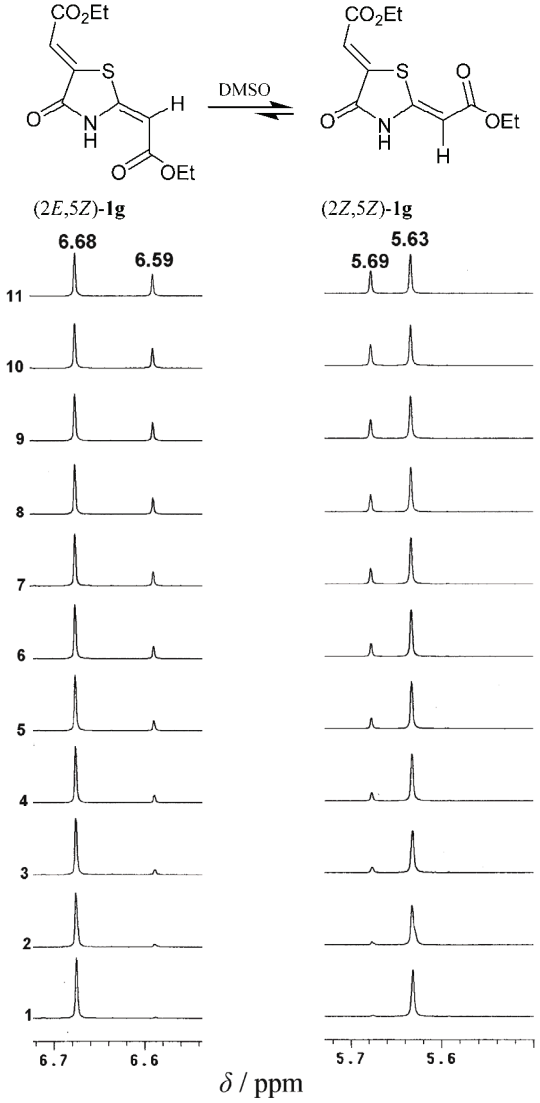


Fig. 5. Spectral evidence for the presence of the 2*E*,5*Z*-**1g** isomer (olefinic signals at δ 5.63 and 6.68 ppm, and 2*Z*,5*Z*-**1g** isomer (olefinic signals at δ 5.69 and 6.59 ppm) in DMSO-d_6 at rt; 30 min ^{1}H-NMR recording interval; partial ^{1}H-NMR spectrum **1** at initial recording time indicates the presence of the starting 2*E*,5*Z*-**1g** isomer, based on the observation of the olefinic signals at δ 5.63 and 6.68 ppm; partial ^{1}H-NMR spectrum **11**, recorded after 5 h, indicates the presence of both isomers, 2*E*,5*Z*-**1g** and 2*Z*,5*Z*-**1g**, in the 72/28 ratio; partial ^{1}H-NMR spectrum **21** (not given), recorded after 10 h, indicates that the signals of 2*E*,5*Z*-**1g** at δ 5.63 and 6.68 ppm, and these of 2*Z*,5*Z*-**1g** at δ 5.69 and 6.59 ppm, have almost the same intensities.

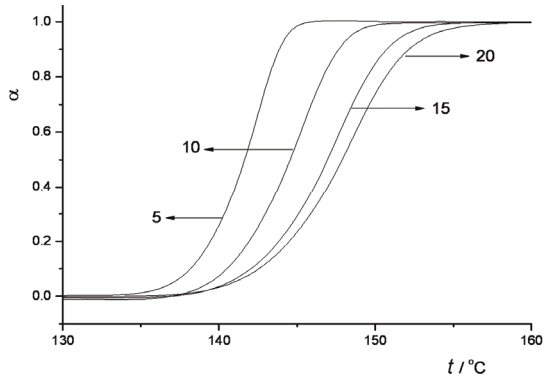
Thus, Fig. 5, displaying the partial ^{1}H-NMR spectra of 2*E*,5*Z*-**1g** and 2*Z*,5*Z*--**1g** isomers recorded during a 5-h period at 30-min intervals at room temperature, indicates only the characteristic signals of the olefinic protons. As seen from Fig. 5, the 2*E*,5*Z*/2*Z*,5*Z* ratio reached a value of 72/28 after 5 h (spectrum 11). By monitoring the kinetics of the configurational isomerization during an extended period (20 h), a relatively long isomerization half-life ($t_{1/2}$) of around 10 h was observed. An equilibrated 2*E*,5*Z*/2*Z*,5*Z* ratio of 10/90 was established after 20 h. These data clearly suggest that the 2*E*,5*Z*→2*Z*,5*Z* process in DMSO-d_6 is rather slow at room temperature. Accordingly, it was concluded that the overall estimate of the thermally induced isomerization of isomer 2*E*,5*Z*-**1g** (Table I, entry 7), based on the determination of the 2*E*,5*Z*/2*Z*,5*Z* ratio in this polar solvent, is quite accurate. The same conclusion applies to the 4-oxothiazolidine **1a**, differing from 2*E*,5*Z*-**1g** only at the C-5 atom that is not sp^2 but sp^3 hybridized.

The solid-state *Z*→*E* process of (*Z*)-ethyl 4-oxo-2-[2-oxo-2-[(2-phenylethyl)-amino]ethylidene]-5-thiazolidineacetate (**1d**) was also studied by powder X-ray diffraction and DSC in the temperature interval from rt to m.p.[11] The crystalline structure of *Z*-**1d** was stable up to approximately 136 °C when a breakdown of the ordered crystal structure and melting occurred (t_p = 145 °C at a heating rate β = 5 °C min^{-1}). The diffractogram of the melted structure, characterized by ^{1}H-NMR as the expected *E*-isomer, indicated the formation of an amorphous compound. The observation of a sharp peak of very low intensity was evidence for the presence of a small quantity of the crystalline *E*-isomer in a matrix of amorphous material. An analysis of the X-ray diffraction data obtained for a melt stored under inert conditions for four months showed an increase in the intensity of this peak. This fact suggested a slow and progressive conversion of the amorphous *E*-isomer into the crystalline form.

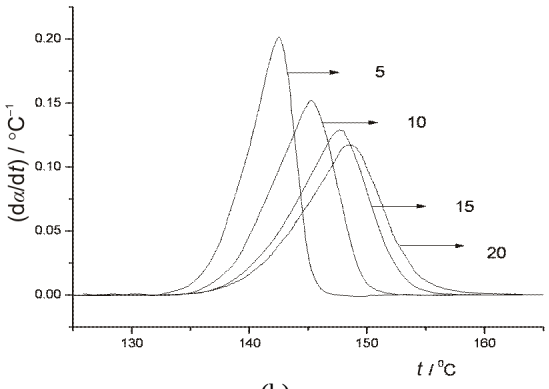
DSC measurements of the *E*-isomer **1d** demonstrated that, in comparison to the *Z*-isomer, the *E*-isomer melts at a significantly lower temperature (t_p = 130.9 °C for β = 5 °C min^{-1}). The volume fraction, α, *i.e.*, the fractional conversion of the *Z*→*E* process from the starting *Z*-isomer, was determined from the DSC curves as a function of the temperature (Fig. 6a). A consistent shifting of the DSC curves towards higher temperatures with increasing heating rate indicates that the well-defined endothermic peak on each DSC curve involves, in addition to the melting of the compound and the *Z*→*E* process, other thermally activated steps, such as cleavage of the crystal lattice, disruption of the stabilizing non-bonded 1,5-type S···O interaction and inter-molecular hydrogen bonds, as integral parts of the phase transformation.

As depicted in Figs. 6a and 6b, all curves, depending on the heating rate, exhibit a slow initial period ranging from 7–27 min, which corresponded to the dominant transformation step, followed by the faster steps of the transformation.

The well-shaped sigmoid pattern of the fractional conversion curves (Fig. 6a) indicates that the overall transformation occurs in the bulk of material.



(a)



(b)

Fig. 6 a) Fractional conversion, α, as a function of temperature for the $Z \rightarrow E$ process of (*Z*)-**1d** and b) differential rate curves at different heating rates: 5, 10, 15 and 20 °C/min.

For a preliminary determination of the kinetic model of the phase transformation, the Dollimore method was applied.[12] The procedure was applied to the conversion and differential rate curves for the thiazolidine derivative **1d** (Figs. 6a and 6b), the asymmetry of which was observed between the initial temperature (t_i) and final temperature (t_f) for the differential rate curves. The other parameters, such as the conversion at the rate of maximum crystallization, α_{max}, peak temperature, t_p, at $(d\alpha/dt)_{max}$, and asymmetry (shape factor), which is the ratio between the low and high temperature at the half-width of the differential rate curve peak, are presented in Table II.

Fig. 6b depicts that the position of the broad endotherms, which are pertinent to the phase transformation, involving the $Z \rightarrow E$ isomerization, are shifted towards higher temperatures with increasing heating rate (Table II, column 4). Simultaneously, the symmetry of curves decreased (column 3). These features suggest that the investigated process should not be characterized by a definite critical

temperature independent of the heating rate. The determined values of α_{max} for all heating rates were 0.58 and the values of the half-width of peaks were in the range of 5.4–8.0 °C. Thus, the sharpness of the initial and final part of differential curve, together with other parameters presented in Table II, indicate that the investigated process corresponds to the Avrami–Erofe'ev Equation, $f(\alpha) = n(1-\alpha)(-\ln(1-\alpha))^{1/n}$, where n = 2, 3 or 4, describes the random nucleation and growth of the nuclei. In the case of continuous heating, the generalization of the Avrami–Erofe'ev Equation, by applying the Kissinger equation,[13] gives the relations:

$$\beta\left(\frac{E_a}{k_p R T_p^2}\right) = 1 \text{ and } \left(\frac{d\alpha}{dt}\right)_p = 0.37 n k_p$$

where n is the Avrami exponent, T_p is the peak temperature and k_p is the rate constant at the peak temperature.

TABLE II. Parameters describing the asymmetry of the differential curves

β / °C min^{-1}	$(d\alpha/dt)_{max}$ °C^{-1}	Asymmetry	Half-width °C	Shape of initial part	Shape of final part	α_{max}
5	0.20	0.78	5.4	Sharp	Sharp	0.58
10	0.15	0.75	5.5	Sharp	Sharp	0.58
15	0.13	0.67	6.5	Sharp	Sharp	0.58
20	0.12	0.64	8.0	Sharp	Sharp	0.58

The average value of n = 1.83 obtained by applying these relations is very close to the value n = 2, suggesting the validity of the Avrami–Erofe'ev equation, $f(\alpha) = n(1-\alpha)(-\ln(1-\alpha))^{1/n}$ (n = 2), for a description of the whole phase transformation occurring in the bulk of the material. Based on previously reported kinetic parameters,[8] the overall structural transformation, including the $Z \rightarrow E$ isomerization of (*Z*)-ethyl 4-oxo-2-(2-oxo-2-[(2-phenylethyl)amino]ethylidene]-5-thiazolidineacetate (**1d**), can be described by the kinetic triplet, *i.e.*, E_a = 317.7 kJ mol^{-1}, ln A = 93.4 min^{-1} and $f(\alpha) = 2(1-\alpha)(-\ln(1-\alpha))^{1/2}$.

In summary, it has been shown that an irreversible configurational isomerization of a series of stereo-defined 2-alkylidene-4-oxothiazolidines occurs in the solid state.

EXPERIMENTAL

General Procedures

The configurational isomerization of the stereo-defined 5-substituted and unsubstituted 2-alkylidene-4-oxothiazolidines **1a–g** was investigated by the slow heating (1–2 °C min^{-1}) of the corresponding solid crystalline compounds from room temperature to a temperature which is 5––10 °C above the melting point, followed by fast cooling to 0 °C. The extent of the isomerization process was determined by ^{1}H-NMR spectroscopy, employing DMSO-d_6 or $CDCl_3$ as solvents. The structural assignments of all configurational isomers of 4-oxothiazolidines **1a–g** were

made based on reported spectroscopic data (IR, ^{1}H- and ^{13}C-NMR, MS and UV) and elemental analysis.[1a,6b] The ^{1}H-NMR data for the characteristic olefinic hydrogens of the configurational isomers **1a**–**g**, employed for monitoring the extent of the solid state isomerization, are listed in Table III.

TABLE III. Diagnostic ^{1}H-NMR chemical shifts (the ^{1}H-NMR spectra were recorded on a Varian Gemini 2000 instrument (^{1}H at 200 MHz); the chemical shifts are given in ppm downfield from TMS as the internal standard) of the olefinic hydrogens in the configurational isomers **1a–g**

Substrate	R	EWG	DMSO-d_6	$CDCl_3$
Z-**1a**	CH_2CO_2Et	CO_2Et	5.44	5.59
E-**1a**	CH_2CO_2Et	CO_2Et	5.21	5.12
Z-**1b**	CH_2CO_2Et	CONHPh	5.79	–
E-**1b**	CH_2CO_2Et	CONHPh	5.36	–
Z-**1c**	CH_3	CONHPh	5.80	–
E-**1c**	CH_3	CONHPh	5.36	–
Z-**1d**	CH_2CO_2Et	$CONH(CH_2)_2Ph$	5.55	5.44
E-**1d**	CH_2CO_2Et	$CONH(CH_2)_2Ph$	5.15	4.88
Z-**1e**	CH_2CO_2Et	COPh	6.78	6.83
E-**1e**	CH_2CO_2Et	COPh	–[a]	6.32
Z-**1f**	H	COPh	6.82	6.78
E-**1f**	H	COPh	–[a]	6.33
2*Z*,5*Z*-**1g**	$=CHCO_2Et$	CO_2Et	5.68	5.83
2*E*,5*Z*-**1g**	$=CHCO_2Et$	CO_2Et	5.64	5.35

[a]Due to the instantaneous *E*→*Z* isomerisation, there were no signals for the olefinic *E*-**1e** and *E*-**1f** isomers in DMSO-d_6

The overall thermally induced process of the structural transformation of (*Z*)-ethyl 4--oxo-2-(2-oxo-2-[(2-phenylethyl)amino]ethylidene]-5-thiazolidineacetate (**1d**) was also investigated non-isothermally by differential scanning calorimetry (DSC) using a DuPont Thermal analyzer (model 1090). Samples weighing several milligrams (3–7 mg) were heated in the DSC cell from room temperature to 170 °C, at heating rates in the range 5–20 °C min^{-1}, in a stream of nitrogen at normal pressure. The temperature peaks (t_p) were determined from the DSC curves using the program Interactive DSC V1.1. Then X-ray powder diffraction patterns of the *Z*- and *E*-isomer **1d** were investigated.

Acknowledgements. This research was partially supported by the Ministry of Science and Technological Development of the Republic of Serbia, Grant No. 142007 (to R. M.).

И З В О Д

ТЕРМАЛНА *Z*/*E* ИЗОМЕРИЗАЦИЈА 2-АЛКИЛИДЕН-4-ОКСОТИАЗОЛИДИНА У ЧВРСТОМ СТАЊУ: УТИЦАЈ НЕКОВАЛЕНТНИХ ИНТЕРАКЦИЈА

ЗДРАВКО ЏАМБАСКИ[1], МИЛОВАН СТОЈАНОВИЋ[1], МАРИЈА БАРАНАЦ-СТОЈАНОВИЋ[1,2], ДРАГИЦА М. МИНИЋ[1,3] и РАДЕ МАРКОВИЋ[1,2]

[1]Центар за хемију, ИХТМ, п. пр. 473, 11001 Београд, [2]Хемијски факултет, Универзитет у Београду, Студентски трг 16, п. пр. 158, 11001 Београд и [3]Факултет за физичку хемију, Универзитет у Београду, Студентски трг 12, 11000 Београд

Конфигурациона изомеризација стереодефинисаних 5-супституисаних и несупституисаних 2-алкилиден-4-оксотиазолидина **1** у чврстом стању, при чему се ствара *Z*/*E* смеса у различитим односима, проучавана је помоћу ^{1}H-NMR спектроскопије, рендгенске кристало-

графије праха и диференцијалне скенирајуће калориметрије (ДСК). Однос *Z*/*E* изомера може се објаснити у контексту нековалентних интеракција, које обухватају интермолекулско и интрамолекулско водонично везивање и усмерене невезивне S···O интеракције 1,5-типа. Рендгенска кристалографија праха одабраног кристалног (*Z*)-4-оксотиазолидинског супстрата, потврдила је трансформацију у аморфно стање у току иреверзибилног *Z*→*E* процеса. Постављена је корелација између претходних резултата који се односе на *Z*/*E* изомеризацију у раствору, и сада, у чврстом стању.

(Примљено 7. јула 2010)

REFERENCES

1. a) R. Marković, M. Baranac, Z. Džambaski, M. Stojanović, P. J. Steel, *Tetrahedron* **59** (2003) 7803; b) R. Marković, M. M. Pergal, M. Baranac, D. Stanisavljev, M. Stojanović, *Arkivoc* (2006) 1; c) G. Satzinger, *Liebigs Ann. Chem.* (1978) 473
2. a) R. Marković, M. Baranac, S. Jovetić, *Tetrahedron Lett.* **44** (2003) 7087; b) A. Rašović, P. J. Steel, E. Kleinpeter, R. Marković, *Tetrahedron* **63** (2007) 1937; c) M. Baranac-Stojanović, J. Tatar, E. Kleinpeter, R. Marković, *Synthesis* (2008) 2117; d) R. Marković, M. Baranac, P. J. Steel, E. Kleinpeter, M. Stojanović, *Heterocycles* **65** (2005) 2635; e) R. Marković, M. Stojanović, *Synlett* (2009) 1997; f) A. V. Tverdokhlebov, A. P. Andrushko, A. A. Tolmachev, *Synthesis* (2006) 1433
3. a) E. Kleinpeter, S. Klod, W.-D. Rudorf, *J. Org. Chem.* **69** (2004) 4317; b) E. Kleinpeter, *J. Serb. Chem. Soc.* **71** (2006) 1; c) J. Sandström, *Top. Stereochem.* **14** (1983) 83
4. a) M. Kivala, F. Diederich, *Acc. Chem. Res.* **42** (2009) 235; b) J.-M. Lehn, *Angew. Chem. Int. Ed. Engl.* **29** (1990) 1304 (and references therein)
5. a) J. L. Brédas, G. B. Street, *Acc. Chem. Res.* **48** (1985) 309; b) A. O. Patil, A. J. Heeger, F. Wudl, *Chem. Rev.* **88** (1988) 183
6. a) R. Marković, A. Shirazi, Z. Džambaski, M. Baranac, D. Minić, *J. Phys. Chem.* **17** (2004) 118; b) R. Marković, M. Baranac, N. Juranić, S. Macura, I. Cekić, D. Minić, *J. Mol. Struct.* **800** (2006) 85
7. G. Kaupp, *Top. Stereochem.* **25** (2006) 303 (and references therein)
8. a) E. Kleinpeter, B. A. Stamboliyska, *J. Org. Chem.* **73** (2008) 8250; b) A. Basheer, Z. Rappoport, *Org. Biomol. Chem.* **6** (2008) 1071
9. a) J. G. Ángyán, R. A. Poirier, Á. Kucsman, I. G. Csizmadia, *J. Am. Chem. Soc.* **109** (1987) 2237; b) S. Wu, A. Greer, *J. Org. Chem.* **65** (2000) 4883
10. S. F. Tan, K. P. Ang, G. F. How, *J. Chem. Soc. Perkin Trans. 2* (1988) 2045
11. D. M. Minić, Z. Nedić, R. Marković, *J. Therm. Anal. Cal.* **95** (2009) 167
12. Y. F. Lee, D. Dollimore, *Thermochim. Acta* **323** (1998) 75
13. D. S. dos Santos, R.S. de Biasi, *J. Alloy Compd.* **335** (2002) 266.