E—Z-Izomerization of 2-methylenethiazolidin-4-ones

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The equilibrium concentrations of *E*- and *Z*-isomers of thiazolidin-4-ones containing exocyclic double bonds in positions 2 and 5 of the cycle were determined in DMSO-d_6. The influence of the nature of the substituents on the equilibrium position was found. Electron-releasing substituents stabilize the *E,Z*-configuration and electron-withdrawing substituents stabilize the *Z,Z*-configuration. The association constants of *E*- and *Z*-2-ethoxycarbonylmethylenethiazolidin-4-ones with the sodium cation were determined by ^{1}H NMR spectroscopy.

Key words: sulfur-containing heterocycles, nitrogen-containing heterocycles, exocyclic double bond, complex formation, *E—Z*-izomerization.

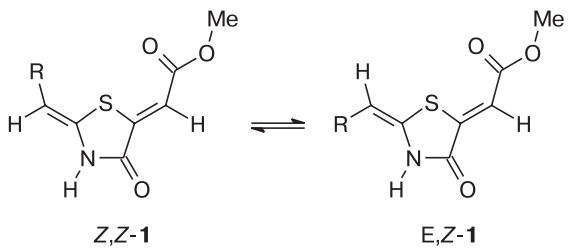
Thiazolidin-4-ones containing exocyclic trisubstituted double bonds attract attention due to their geometry. The presence of carbonyl groups in the neighbor position to the cyclic sulfur and nitrogen atoms assumes the use of these compounds as ligands for binding complexes of various metal ions. We have previously developed a convenient method for the synthesis of 5-methylenethiazolidin-4-ones by the reaction of malonothioamides with dimethyl acetylenedicarboxylate (DMAD).[1] The exocyclic double bond in position 5 of the cycle was shown to have the *Z*-configuration. The compounds containing the exocyclic double bond in position 2 of the thiazolidinone cycle can be considered as cyclic enamines[2] and exhibit *E—Z*-isomerism.[1,3]

The purpose of this work is to study isomerization about the exocyclic double bond of thiazolidines and their complex formation with the sodium cation.

Results and Discussion

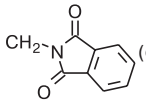
We have found that the mutual transformations of compounds *Z,Z*-**1a—s** and *E,Z*-**1a—s** occur in various solvents (Scheme 1). The condensation of thioamides of malonic acid with dimethyl acetylenedicarboxylate almost always affords mixtures of isomers **1**, whose composition depends on the nature of the solvent, namely, the fraction of the *E,Z*-isomer increases in chloroform, and that of the *Z,Z*-isomer increases in DMSO. Note that isomerization occurs only about the exocyclic bond in position 2 of the cycle. This fact is easily explained if the RCH=C—NH fragment in these compounds is considered as enaminic.

Scheme 1



Z,Z-**1** E,*Z*-**1**

R = CN (**a**), $CONMe_2$ (**b**), COOEt (**c**), $CON(CH_2CH_2)_2O$ (**d**), $CON(CH_2CH_2)_2CH_2$ (**e**), CONHMe (**f**),



(**g**), $CONHC_6H_{11}$-*cyclo* (**h**),

$CONHCH_2Ph$ (**i**), CONHPh (**j**), $CONHC_6H_4OMe$-4 (**k**), $CONHC_6H_4OMe$-3 (**l**), $CONHC_6H_5Me$-4 (**m**), $CONHC_6H_4Me$-3 (**n**), $CONHC_6H_4F$-4 (**o**), $CONHC_6H_4F$-2 (**p**), $CONHC_6H_3Cl_2$-2,6 (**q**), $CONHC_6H_2Cl_3$-2,4,6 (**r**), $CONHC_6H_4COOEt$-4 (**s**).

Individual isomers *Z,Z*-**1a—f,h,m,p—s** and *E,Z*-**1a—g,m,p—s** were isolated by fractional crystallization from chloroform (isomers *E,Z*-**1a**,**m**,**p**, unlike *Z,Z*-**1a**,**m**,**p**, are poorly soluble in chloroform). Other compounds were used as mixtures of two isomers. The equilibrium concentration of both isomers, which remains unchanged in time within a measurement error characteristic of NMR spectroscopy, is established during 2—3 days in DMSO solutions of compounds **1a—s** (Table 1). We failed to achieve the equilibrium concentration of the isomers in such solvents as acetone-d_6 and $CDCl_3$ even when solutions were stored for 10—15 days.

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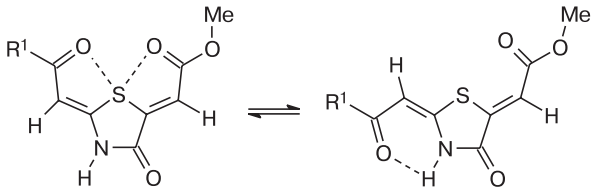
Table 1. Ratio of *E,Z*- to *Z,Z*-isomers of compound **1** in DMSO-d_6 solutions

Compound	Content of isomers (%)		Equilibrium constant *E,Z*/*Z,Z*
	E,Z	*Z,Z*	
1a	26	74	0.351
1b	>99	<1	
1c	81	19	4.26
1d	80	20	4.00
1e	75	25	3.00
1f	55	45	1.22
1g	61	39	1.56
1h	6	94	0.064
1I	49	51	0.960
1j	86	14	6.14
1k	92	8	3.34
1l	37	63	0.587
1m	88	12	7.33
1n	82	18	4.55
1o	42	58	0.538
1p	10	90	0.111
1q	0	100	0
1r	2	98	0.020
1s	1	99	0.010

Scheme 2



Z,Z-**1** *E,Z*-**1**

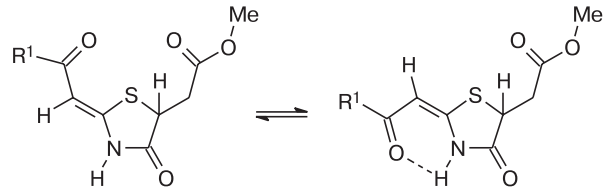
The data obtained show that the introduction of electron-withdrawing substituents into the aryl residue (R^1 = NHAr) stabilizes the *Z,Z*-isomers of compound **1**. For example, *Z,Z*-isomers predominate for compounds **1p**,**s** containing fluorine and the ethoxycarbonyl group in the *ortho*- and *para*-positions of the aryl substituent, respectively. This can be explained by the stabilizing S...O interaction[1,4] (Scheme 2). An increase in the stability of the *E,Z*-isomer of compound **1** can be explained by the stabilizing effect of the hydrogen bond, whose formation is favored by the electron-releasing substituents in the carbamoyl groups. The steric factor substantially affects the ratio of *Z,Z*- and *E,Z*-isomers. For example, for compounds containing the cyclohexyl, 2,6-dichlorophenyl, 2-fluorophenyl, and 2,4,6-trichlorophenyl substituents in the carboxamoyl fragment, the equilibrium is almost completely shifted toward *Z,Z*-isomer **1h**,**q**,**p**,**r**.

Unlike compounds **1**, in thiazolidines **2a**—**e** containing only one C=C bond the equilibrium is shifted toward the *E*-isomer. The content of the *Z*-isomer is at most

Table 2. Ratio of *E*- to *Z*-isomers of compound **2** in DMSO-d_6 solutions

Compound	Content of isomers (%)		Equilibrium constant *Z*/*E*
	E	*Z*	
2a	90	10	9.00
2b	85	15	5.67
2c	60	40	1.50
2d	93	7	13.3
2e	98	2	49

5—15% (Table 2), except for *ortho*-substituted anilide **2c**. Note that the reduction[5] of compounds **1** always produces only the *E*-isomer of **2**. This is related, most likely, to a higher thermodynamic stability of the *E*-isomer.



Z-**2a—e** *E*-**2a—e**

Based on the position of the carboxyl substituents in compounds **1** and **2**, we can assume that the latter can be used as ligands for various cations. We obtained the ^{1}H NMR spectra of compounds *Z,Z*-**1c** and *E,Z*-**1c** in acetone-d_6 in the presence of NaI in different concentrations. The *E,Z*-isomer of **2c** exhibits the shift of the signal from the methine proton at the double bond in position 2 of the cycle by 0.2—0.8 ppm, whereas the position of the signal from the methine proton at the exocyclic double bond in position 5 remains virtually unchanged (Fig. 1). The intensity of signals from the

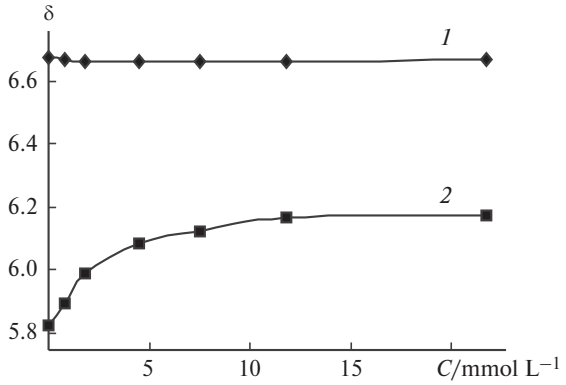


Fig. 1. Dependence of chemical shifts of methine protons in compound *E,Z*-**1c** on the concentration of NaI in acetone-d_6: *1*, for the proton at the exocyclic bond in position 5 of the cycle; and *2*, for the proton at the exocyclic bond in position 2 of the cycle.

NH protons also decreases strongly. For the *Z*,*Z*-isomer of **1c** the addition of NaI does not result in any substantial changes in the NMR spectra. We can conclude that the effects observed in the case of the *E*,*Z*-isomer of **1c**

Table 3. ^{1}H NMR spectra of compounds *Z,Z*-**1f—s** and *E,Z*-**1f—s**

Compound	δ (*J*/Hz)
Z,Z-**1f**	10.23 (t, 1 H, NH); 6.52 (s, 1 H, CH=C(5)); 5.87 (s, 1 H, CH=C(2)); 3.77 (s, 3 H, OMe); 2.51 (d+s, 3 H, NMe)
Z,Z-**1g**	12.16 (br.s, 1 H, NH); 7.80—7.90 (m, 4 H, ArH); 6.52 (s, 1 H, CH=C(5)); 5.46 (t, 1 H, CH=C(5), *J* = 7.6); 4.28 (d, 2 H, CH_2, *J* = 7.6); 3.73 (s, 3 H, OMe)
Z,Z-**1h**	12.18 (s, 1 H, NH); 7.99 (d, 1 H, NH, *J* = 7.6); 6.48 (s, 1 H, CH=C(5)); 5.87 (s, 1 H, CH=C(2)); 3.76 (s, 3 H, OMe); 3.40—3.50 (m, 1 H, NCH); 1.00—2.00 (m, 10 H, C_5H_{10})
Z,Z-**1i**	12.16 (br.s, 1 H, NH); 8.62 (t, 1 H, NH, *J* = 6.2); 7.20—7.36 (m, 5 H, Ph); 6.50 (s, 1 H, CH=C(5)); 5.94 (s, 1 H, CH=C(2)); 4.36 (d, 2 H, CH_2, *J* = 6.2); 3.77 (s, 3 H, OMe)
Z,Z-**1j**	12.29 (s, 1 H, NH); 10.05 (s, 1 H, NH); 7.60 (d, 2 H, ArH, *J* = 7.4); 7.25 (dd, 2 H, ArH, *J* = 7.4, *J* = 8.0); 7.00 (t, 1 H, ArH, *J* = 8.0); 6.54 (s, 1 H, CH=C(5)); 6.06 (s, 1 H, CH=C(2)); 3.80 (s, 3 H, OMe)
Z,Z-**1k**	12.36 (br.s, 1 H, NH); 10.05 (s, 1 H, NH); 7.53 (d, 2 H, ArH, *J* = 9.2); 6.97 (d, 2 H, ArH, *J* = 9.2); 6.54 (s, 1 H, CH=C(5)); 6.05 (s, 1 H, CH=C(2)); 3.78 (s, 3 H, OMe); 3.73 (s, 3 H, OMe)
Z,Z-**1l**	12.4 (br.s, 1 H, NH); 10.15 (s, 1 H, NH); 7.10—7.36 (m, 3 H, ArH); 6.30—6.33 (m, 1 H, ArH); 6.56 (s, 1 H, CH=C(5)); 6.07 (s, 1 H, CH=C(2)); 3.75 (s, 3 H, OMe); 3.74 (s, 3 H, OMe)
Z,Z-**1m**	11.6 (br.s, 1 H, NH); 10.09 (s, 1 H, NH); 7.48 (d, 2 H, ArH, *J* = 8.2); 7.10 (d, 2 H, ArH, *J* = 8.2); 6.54 (s, 1 H, CH=C(5)); 6.06 (s, 1 H, CH=C(2)); 3.78 (s, 3 H, OMe); 2.25 (s, 3 H, Me)
Z,Z-**1n**	12.40 (s, 1 H, NH); 10.10 (s, 1 H, NH); 7.51 (s, 1 H, ArH); 7.38 (d, 1 H, ArH, *J* = 7.9); 7.18 (dd, 1 H, ArH, *J* = 7.9, *J* = 7.5); 6.86 (d, 1 H, ArH, *J* = 7.5); 6.55 (s, 1 H, CH=C(5)); 6.08 (s, 1 H, CH=C(2)); 3.79 (s, 1 H, OMe); 2.28 (s, 3 H, Me)
Z,Z-**1o**	12.8 (s, 1 H, NH); 10.1 (s, 1 H, NH); 7.62—7.69 (m, 2 H, ArH); 7.08—7.19 (m, 2 H, ArH); 6.56 (s, 1 H, CH=C(5)); 6.06 (s, 1 H, CH=C(2)); 3.79 (s, 3 H, OMe)
Z,Z-**1p**	12.44 (s, 1 H, NH); 10.00 (s, 1 H, NH); 7.95—8.10 (m, 1 H, ArH); 7.10—7.30 (m, 3 H, ArH); 6.56 (s, 1 H, CH=C(5)); 6.30 (s, 1 H, CH=C(2)); 3.78 (s, 3 H, OMe)
Z,Z-**1r**	12.70 (s, 1 H, NH); 9.70 (s, 1 H, NH); 8.52 (s, 1 H, ArH); 7.62 (s, 1 H, ArH); 6.55 (s, 1 H, CH=C(5)); 6.32 (s, 1 H, CH=C(2)); 3.81 (s, 3 H, OMe)
Z,Z-**1s**	12.48 (s, 1 H, NH); 10.50 (s, 1 H, NH); 7.90 (d, 9.2, 2 H, ArH); 7.75 (d, 9.2, 2 H, ArH); 6.58 (s, 1 H, CH=C(5)); 6.10 (s, 1 H, CH=C(2)); 4.28 (q, 2 H, OMe, *J* = 7.1); 3.79 (s, 3 H, OMe); 1.31 (t, 3 H, Me, *J* = 7.1)
E,Z-**1f**	9.65 (t, 1 H, NH); 6.85 (s, 1 H, CH=C(5)); 5.46 (s, 1 H, CH=C(2)); 3.78 (s, 3 H, OMe); 2.53 (d+s, 3 H, NMe)
E,Z-**1g**	11.88 (br.s, 1 H, NH); 7.80—7.90 (m, 4 H, ArH); 6.53 (s, 1 H, CH=C(5)); 5.00 (t, 1 H, CH=C(5), *J* = 7.3); 4.50 (d, 2 H, CH_2, *J* = 7.3); 3.72 (s, 3 H, OMe)
E,Z-**1h**	12.10 (s, 1 H, NH); 8.02 (d, 7.5, 1 H, NH); 6.72 (s, 1 H, CH=C(5)); 5.45 (s, 1 H, CH=C(2)); 3.77 (s, 3 H, OMe); 3.40—3.50 (m, 1 H, NCH); 1.00—2.00 (m, 10 H, C_5H_{10})
E,Z-**1i**	12.6 (br.s, 1 H, NH); 8.65 (t, 1 H, NH, *J* = 6.2); 7.20—7.36 (m, 5 H, Ph); 6.77 (s, 1 H, CH=C(5)); 5.73 (s, 1 H, CH=C(2)); 4.37 (d, 2 H, CH_2, *J* = 6.2); 3.76 (s, 3 H, OMe)
E,Z-**1j**	11.79 (s, 1 H, NH); 9.51 (s, 1 H, NH); 7.58 (d, 2 H, ArH, *J* = 7.6); 7.28 (dd, 2 H, ArH, *J* = 7.6, *J* = 7.9); 7.09 (t, 1 H, ArH, *J* = 7.9); 6.84 (s, 1 H, CH=C(5)); 5.86 (s, 1 H, CH=C(2)); 3.77 (s, 3 H, OMe)
E,Z-**1k**	12.33 (br.s, 1 H, NH); 9.85 (s, 1 H, NH); 7.52 (d, 2 H, ArH, *J* = 9.2); 6.87 (d, 2 H, ArH, *J* = 9.2); 6.69 (s, 1 H, CH=C(5)); 5.85 (s, 1 H, CH=C(2)); 3.77 (s, 3 H, OMe); 3.72 (s, 3 H, OMe)
E,Z-**1l**	11.9 (br.s, 1 H, NH); 10.15 (s, 1 H, NH); 7.10—7.36 (m, 3 H, ArH); 6.70 (s, 1 H, CH=C(5)); 6.30—6.35 (m, 1 H, ArH); 5.70 (s, 1 H, CH=C(2)); 3.79 (s, 3 H, OMe); 3.78 (s, 3 H, OMe)
E,Z-**1m**	12.38 (br.s, 1 H, NH); 10.08 (s, 1 H, NH); 7.50 (d, 8.2, 2 H, ArH); 7.11 (d, 8.2, 2 H, ArH); 6.70 (s, 1 H, CH=C(5)); 5.70 (s, 1 H, CH=C(2)); 3.78 (s, 3 H, OMe); 2.25 (s, 3 H, Me)
E,Z-**1n**	12.00 (s, 1 H, NH); 10.05 (s, 1 H, NH); 7.51 (s, 1 H, ArH); 7.37 (d, 1 H, ArH, *J* = 7.9); 7.17 (dd, 1 H, ArH, *J* = 7.9, *J* = 7.5); 6.85 (d, 1 H, ArH, *J* = 7.5); 6.85 (s, 1 H, CH=C(5)); 5.68 (s, 1 H, CH=C(2)); 3.77 (s, 3 H, OMe); 2.29 (s, 3 H, Me)
E,Z-**1o**	12.68 (s, 1 H, NH); 10.21 (s, 1 H, NH); 7.62—7.69 (m, 2 H, ArH); 7.08—7.19 (m, 2 H, ArH); 6.71 (s, 1 H, CH=C(5)); 5.70 (s, 1 H, CH=C(2)); 3.78 (s, 3 H, OMe)
E,Z-**1p**	12.48 (s, 1 H, NH); 10.00 (s, 1 H, NH); 7.95—8.10 (m, 1 H, ArH); 7.10—7.30 (m, 3 H, ArH); 6.76 (s, 1 H, CH=C(5)); 5.80 (s, 1 H, CH=C(2)); 3.79 (s, 3 H, OMe)
E,Z-**1r**	12.57 (s, 1 H, NH); 9.74 (s, 1 H, NH); 8.52 (s, 1 H, ArH); 7.62 (s, 1 H, ArH); 6.78 (s, 1 H, CH=C(5)); 5.82 (s, 1 H, CH=C(2)); 3.81 (s, 3 H, OMe)
E,Z-**1s**	12.00 (s, 1 H, NH); 10.46 (s, 1 H, NH); 7.91 (d, 2 H, ArH, *J* = 9.2); 7.74 (d, 2 H, ArH, *J* = 9.2); 6.85 (s, 1 H, CH=C(5)); 5.95 (s, 1 H, CH=C(2)); 4.27 (q, 2 H, OCH_2, *J* = 7.1); 3.77 (s, 3 H, OMe); 1.25 (t, 3 H, Me, *J* = 7.1)

are caused by the coordination of the sodium cation to the ester group at the exocyclic bond in position 2 of the cycle and to the nitrogen atom of the cycle. No coordination involves the ester group at the double exocyclic bond in position 5 of the cycle, as well as the ester group in position 2 of the cycle for the *Z*,*Z*-isomer, and to the sulfur atom. We calculated the association constant (105±12 L mol^{-1}) from the chemical shift of the methine proton in the ^{1}H NMR spectrum at different concentrations of NaI using the method proposed previously.[6] The *E*-isomer of **2** exhibits the downfield shift of the signals from the methine proton depending on the concentration of NaI, while no shift of the signal from the methine proton is observed for the *Z*-isomer of **1a**. The association constant of the *E*-isomer of **1a** is 112±8 L mol^{-1}.

Thus, it was shown that isomerization in solutions of 2,5-dimethylenethiazolidin-4-ones in DMSO-d_6, $CDCl_3$, and acetone-d_6 occurs only about the double exocyclic bond in position 2 of the heterocycle. The influence of substituents on the position of equilibrium was found, and electron-donating substituents were shown to stabilize the *E*,*Z*-isomer. It was revealed that the *E*,*Z*-isomer of **1c** and the *E*-isomer of **2a** form complexes with NaI in acetone, whereas Z,*Z*-**1c** and *Z*-**2a** cannot form complexes.

Experimental

NMR spectra were recorded on Bruker 250 (250 MHz for ^{1}H) and Bruker DRX-500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) instruments using HMDS as internal standard. IR spectra were recorded on an IR-75 spectrometer in KBr pellets. The reaction course and purity of compounds were monitored by TLC on the Silufol UV-254 plates in chloroform or ethyl acetate—hexane (1 : 1) and chloroform—ethanol (9 : 1) systems. Corrections for melting points were not introduced. Solvents were purified and dried using standard procedures.

Table 4. Physicochemical data for compounds *E,Z*-**1f**—**s** and *E*-**2c**—**e**

Compound	Yield (%)	M.p./°C	Found / Calculated (%)		Molecular formula	IR ν(C=O)/cm^{-1}
			N	S		
1f	45	285—287	10.23	8.12	$C_9H_{10}N_2O_4S$	1705, 1685
			10.42	7.95		
1g	28	205—206	8.56	6.02	$C_{16}H_{12}N_2O_5S$	1710, 1690
			8.31	6.34		
1h	44	213—215	9.12	7.00	$C_{14}H_{18}N_2O_4S$	1705, 1685
			8.91	6.80		
1i	55	140—141	8.75	6.53	$C_{15}H_{14}N_2O_4S$	1705, 1695
			8.76	6.69		
1j	47	195—196	9.12	7.02	$C_{14}H_{12}N_2O_4S$	1710, 1680
			9.03	6.89		
1k	62	240—242	8.65	6.50	$C_{15}H_{14}N_2O_5S$	1710, 1685
			8.48	6.47		
1l	42	249—252	8.53	6.48	$C_{15}H_{14}N_2O_5S$	1705, 1685
			8.48	6.47		
1m	55	245—248	9.02	6.88	$C_{15}H_{14}N_2O_4S$	1710, 1690
			8.76	6.69		
1n	60	222—225	8.77	6.45	$C_{15}H_{14}N_2O_4S$	1710, 1680
			8.76	6.69		
1o	56	200—204	8.99	6.53	$C_{14}H_{11}FN_2O_4S$	1705, 1685
			8.69	6.63		
1p	57	239—242	8.78	6.78	$C_{14}H_{11}FN_2O_4S$	1705, 1690
			8.69	6.63		
1r	62	268—269	7.58	5.55	$C_{14}H_9Cl_3N_2O_4S$	1710, 1695
			7.39	5.64		
1s	58	254—255	7.45	5.77	$C_{17}H_{16}N_2O_6S$	1710, 1700, 1680
			7.40	5.65		
2c	47	170	8.55	6.27	$C_{15}H_{16}N_2O_5S$	1700, 1680
			8.45	6.44		
2d	49	185	8.95	6.67	$C_{12}H_{16}N_2O_5S$	1700, 1690
			9.11	6.95		
2e	52	178	9.45	6.77	$C_{13}H_{18}N_2O_4S$	1700, 1680
			9.14	6.98		

Table 5. ^{1}H NMR spectra (DMSO-d_6) for compounds *Z*-**2c**—**e** and *E*-**2c**—**e**

Compound	δ (*J*/Hz)
Z-**2c**	11.20 (s, 1 H, NH); 8.77 (s, 1 H, NH); 8.00—8.08 (m, 1 H, ArH); 6.83—7.00 (m, 3 H, ArH); 5.65 (s, 1 H, CH=); 4.27 (dd, 1 H, CH, *J* = 4.8, *J* = 7.9); 3.84 (s, 3 H, OMe); 3.67 (s, 3 H, OMe); 3.11 (dd, 1 H, CH, *J* = 4.8, *J* = 17.8); 2.84 (dd, 1 H, CH, *J* = 7.9, *J* = 17.8)
Z-**2d**	11.58 (s, 1 H, NH); 5.62 (s, 1 H, CH=); 4.124 (dd, 1 H, CH, *J* = 4.6, *J* = 7.6); 3.65 (s, 3 H, OMe); 3.40—3.60 (m, 8 H, 4 CH_2); 3.12 (dd, 1 H, CH, *J* = 4.6, *J* = 17.2); 2.86 (dd, 1 H, CH, *J* = 7.6, *J* = 17.2)
Z-**2e**	11.00 (s, 1 H, NH); 5.68 (s, 1 H, CH=); 4.09 (dd, 1 H, CH, *J* = 4.6, *J* = 7.7); 3.66 (s, 3 H, OMe); 3.40—3.60 (m, 4 H, 2 NCH_2); 3.00 (dd, 1 H, CH, *J* = 4.6, *J* = 17.5); 2.72 (dd, 1 H, CH, *J* = 7.7, *J* = 17.5); 1.40—1.70 (m, 6 H, 3 CH_2)
E-**2c**	11.42 (s, 1 H, NH); 8.87 (s, 1 H, NH); 8.00—8.08 (m, 1 H, ArH); 6.83—7.00 (m, 3 H, ArH); 5.97 (s, 1 H, CH=); 4.04 (dd, 1 H, CH, *J* = 4.7, *J* = 7.9); 3.84 (s, 3 H, OMe); 3.67 (c, 3 H, OMe); 3.08 (dd, 1 H, CH, *J* = 4.7, *J* = 17.8); 2.85 (dd, 1 H, CH, *J* = 7.9, *J* = 17.8)
E-**2d**	11.29 (s, 1 H, NH); 5.84 (s, 1 H, CH=); 4.04 (dd, 1 H, CH, *J* = 4.6, *J* = 7.6); 3.66 (s, 3 H, OMe); 3.40—3.60 (m, 8 H, 4 CH_2); 3.08 (dd, 1 H, CH, *J* = 4.6, *J* = 17.2); 2.85 (dd, 1 H, CH, *J* = 7.6, *J* = 17.2)
E-**2e**	11.18 (s, 1 H, NH); 5.88 (s, 1 H, CH=); 4.01 (dd, 1 H, CH, *J* = 4.8, *J* = 7.7); 3.66 (s, 3 H, OMe); 3.40—3.60 (m, 4 H, 2 NCH_2); 2.98 (dd, 1 H, CH, *J* = 4.8, *J* = 17.5); 2.75 (dd, 1 H, CH, *J* = 7.7, *J* =17.5); 1.40—1.70 (m, 6 H, 3 CH_2)

The thioacetamides RCH_2—C(S)NH_2 (**3a—c**) were synthesized by a previously described procedure.[7] Compounds **1a—s** were synthesized from dimethyl acetylenedicarboxylate and corresponding substituted thioacetamides **3a—s** according to a described procedure.[1] Compounds **2a**,**b** were synthesized by the reduction of corresponding thiazolidinones **1** with Zn(AcOH) as described in Ref. 5. Compounds **2c—d** were prepared similarly. The physicochemical characteristics of the compounds are presented in Tables 3—6.

Preparation of thioacetamides 3d—s (general procedure). A suspension of the corresponding acetonitrile RCH_2CN (0.1 mol) and triethylamine (1.4 mL, 0.01 mol) in ethanol (100 mL) saturated with H_2S (5.1 g, 0.15 mol) was placed in an autoclave and heated for 1.5 h at 70 °C. The reaction mixture was cooled, and the precipitate of thioamide RCH_2CSNH_2 (**3d—s**) was filtered off. The product was recrystallized from ethanol.

Preparation of 2,5-dimethylenethiazolidin-4-ones (1a—s) (general procedure). Dimethyl acetylenedicarboxylate (0.4 mL, 3.17 mmol) was added to a suspension of the corresponding thioacetamide **3** (3 mmol) in 30 mL of ethanol (40 mL of chloroform or 2 mL of DMSO) at ~20 °C. The reaction mixture was stirred for 2 h and cooled. The precipitate was filtered off, and the product was recrystallized from ethanol.

Preparation of 5-methylenethiazolidin-4-ones (2a—e) (general procedure). Zinc dust (1 g) was added to a suspension of compound **1** (0.5 g) in glacial acetic acid (4 mL). The mixture was stirred for 24 h at 30—35 °C, 100 mL of water were added,

Table 6. Physicochemical data for thioacetamides *Z,Z*-**3d—s**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%) N	Found / Calculated (%) S	Molecular formula	MS, *m/z* (I_{rel} (%))
3d	85	120	15.28 14.88	16.65 17.03	$C_7H_{12}N_2O_2S$	188 (52)
3e	73	140	15.23 15.04	16.89 17.21	$C_8H_{14}N_2OS$	186 (17)
3f	92	105	21.00 21.19	24.62 24.26	$C_4H_8N_2OS$	132 (35)
3g	68	158	11.68 11.96	14.03 13.69	$C_{11}H_{10}N_2O_2S$	234 (8)
3h	71	98—100	14.19 13.99	15.42 16.01	$C_9H_{16}N_2OS$	200 (53)
3i	93	110	13.05 13.45	14.98 15.39	$C_{10}H_{12}N_2OS$	208 (65)
3j	96	106	14.02 14.42	16.08 16.51	$C_9H_{10}N_2OS$	194 (56)
3k	87	128	12.12 12.49	13.95 14.30	$C_{10}H_{12}N_2O_2S$	224 (18)
3l	89	142	12.59 12.49	14.12 14.30	$C_{10}H_{12}N_2O_2S$	224 (26)
3m	76	106—108	12.89 13.45	14.92 15.39	$C_{10}H_{12}N_2OS$	208 (12)
3n	86	114	13.69 13.45	15.65 15.39	$C_{10}H_{12}N_2OS$	208 (53)
3o	53	125 (decomp.)	—	14.92 15.11	$C_9H_9FN_2OS$	212 (56)
3p	48	112 (decomp.)	—	14.74 15.11	$C_9H_9FN_2OS$	212 (32)
3q	75	89	10.69 10.65	12.25 12.18	$C_9H_8Cl_2N_2OS$	264 (32), 262 (55)
3r	68	86	9.63 9.41	10.54 10.77	$C_9H_7Cl_3N_2OS$	298 (22), 296 (23)
3s	55	108	10.86 10.52	11.86 12.04	$C_{12}H_{14}N_2O_3S$	266 (8)

and the resulting mixture was stirred for 30 min. The precipitate was filtered off and recrystallized from ethanol.

Methyl *E,Z*-(2-[2-(1,3-dioxo-1,3-dihydroisoindol-2-yl)ethylidene]-4-oxothiazol-5-ylidene)acetate (*E,Z*-1g). ^{13}C NMR (DMSO-d_6), δ: 167.3 (CON); 166.3 (COOMe); 164.2 (C(3)); 144.1 (C(2)); 134.5, 123.1, 131.6 (Ar); 135.1 (C(5)); 110.7 (CH=C(5)); 99.6 (CH=C(2)); 52.1 (OCH_3), 34.7 (CH_2).

Methyl *Z,Z*-{2-[2-(1,3-dioxo-1,3-dihydroisoindol-2-yl)ethylidene]-4-oxothiazolidin-5-ylidene}acetate (*Z,Z*-1g). ^{13}C NMR (DMSO-d_6), δ: 167.2 (CON); 166.4 (COOMe); 165.3 (C(3)); 144.1 (C(2)); 134.4, 123.0, 131.7 (Ar); 132.4 (C(5)); 110.5 (CH=C(5)); 100.3 (CH=C(2)); 52.1 (OCH_3); 34.3 (CH_2).

Determination of association constant. To determine association constants, we used ^{1}H NMR spectroscopy in a solution of acetone-d_6 at 298 K at constant concentrations of compounds **1c** and **2a** (3 mmol L^{-1}) and varied concentrations of NaI (0.8, 1.8, 4.5, 7.5, 11.8, and 21.7 mmol L^{-1}). The chemical shift of the signal from the methine proton of the exocyclic double bond in position 2 was used for measurements. The association constant was calculated from the nonlinear regression as described in Ref. 6.

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