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Rearrangement with Oxide Ion Transfer in Reactions of 4-Chloro-2-oxo-2,3-dihydrothiazole-5-carbaldehyde with Ureas. *cis*-(*Z*)–*trans*-(*E*) Isomerism of *N*-(2,4-Dioxothiazolidin-5-ylidenemethyl)ureas

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Abstract—4-Chloro-2-oxo-2,3-dihydrothiazole-5-carbaldehyde reacted with monosubstituted ureas to give *cis*-(*Z*)- and *trans*-(*E*)-*N*-(2,4-dioxothiazolidin-5-ylidenemethyl)ureas via rearrangement involving oxide ion transfer. *cis* (*Z*) Isomers were formed in methanol or dimethylformamide, while both individual *cis* (*Z*) and *trans* (*E*) isomers and their mixtures were isolated in the reaction performed in acetic acid.

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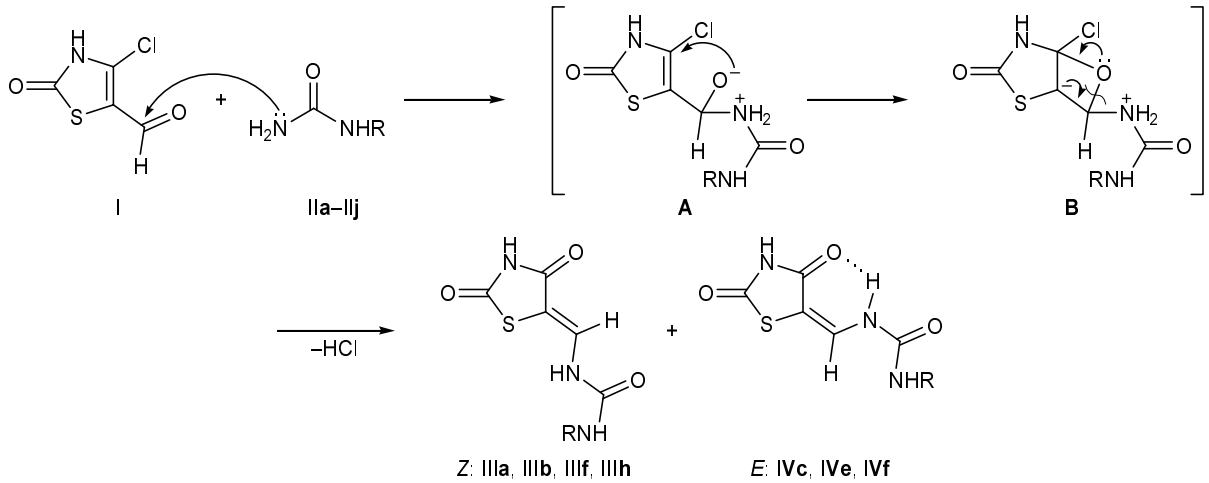
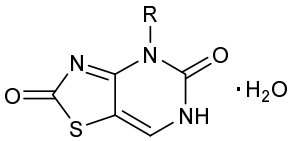
Reactions of β-halovinyl aldehydes with formamide [1] and guanidine or urea derivatives [2] lead to the corresponding pyrimidine derivatives; however, publications on the reactions with ureas are few in number. We examined reactions of 4-chloro-2-oxo-2,3-dihydrothiazole-5-carbaldehyde (**I**) with monosubstituted ureas **IIa**–**IIj**. The reactions were carried out in methanol, DMF, and acetic acid. As a result, we isolated 40–70% of isomeric *cis*-(*Z*)- and *trans*-(*E*)-*N*-(2,4-dioxothiazolidin-5-ylidenemethyl)ureas **IIIa**, **IIIb**, **IIIf**, **IIIh**, **IVc**, **IVe**, and **IVf** which were formed via rearrangement involving oxide ion transfer according to Scheme 1. Alternative structures of hydrated thiazolopyrimidinones like **V** and **VI** were ruled out on the basis of the ^{1}H NMR data.

Aldehyde **I** reacted with *N*-*p*-tolylurea to give compounds having the same composition and similar melting points but different ^{1}H NMR spectra. From ureas **IId**, **IIg**, **IIi**, and **IIj** in acetic acid we obtained mixtures of products. Comparison of the ^{1}H NMR

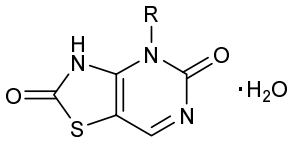
Scheme 1.



R = CH_2=$CHCH_2$ (**a**), $PhCH_2$ (**b**), Ph (**c**), *o*-MeC_6H_4 (**d**), *m*-MeC_6H_4 (**e**), *p*-MeC_6H_4 (**f**), *o*-$MeOC_6H_4$ (**g**), *p*-$MeOC_6H_4$ (**h**), *p*-BrC_6H_4 (**i**), *p*-ClC_6H_4 (**j**).



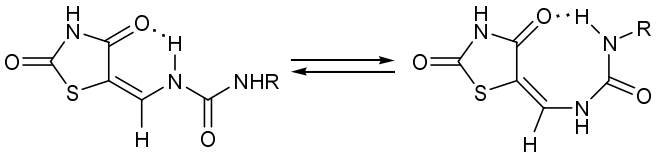
V



VI

spectra (DMSO-d_6) of compounds **IIIf** [δ, ppm: 11.83 s (1H, NH, ring), 9.65 d (1H, N^1H, urea, J = 12 Hz), 9.15 s (1H, N^3H, urea), 8.02 d (1H, =C**H**NH, J = 12 Hz), 7.35 d (2H, H_{arom}, J = 8 Hz), 7.07 d (2H, H_{arom}, J = 8 Hz), 2.28 s (3H, CH_3)] and **IVf** [δ, ppm: 11.93 s (1H, NH, ring), 10.26 d (1H, N^1H, urea, J = 12 Hz), 9.90 s (1H, N^3H, urea), 7.62 d (1H, =C**H**NH, J = 12 Hz), 7.33 d (2H, H_{arom}, J = 8 Hz), 7.03 d (2H, H_{arom}, J = 8 Hz), 2.29 s (3H, CH_3)] revealed an appreciable downfield shift of the N^1H and N^3H signals of compound **IVf** relative to the corresponding signals of urea **IIIf**. The observed shift is typical of structures with an intramolecular hydrogen bond [3]. In our case, it may result from participation of the N^1H and N^3H protons in dynamic equilibrium between quasipseudoaromatic structures [4] with six- and eight-membered H-bonded rings (structures **IVA** and **IVB**, respectively; Scheme 2). Thus the presence or absence of intramolecular hydrogen bond is indicative of *trans* (*E*) or *cis* (*Z*) structure of the isolated products.

Scheme 2.



IVA IVB

In view of the above stated, compound **IVf** is *trans* (*E*) isomer, while **IIIf** is *cis* (*Z*) isomer. Likewise, the *trans*-(*E*)-isomer structure was assigned to compounds **IVc** and **IVe** which were isolated in the reactions of chloroaldehyde **I** with ureas **IIc** and **IIe** in acetic acid, while the reactions of **I** with ureas **IIa** and **IIb** in methanol were assumed to give *cis* (*Z*) isomers. In addition, we were able to identify particular isomers in the isomer mixtures obtained by the reactions of compound **I** with ureas **IId**, **IIg**, **IIi**, and **IIj** in acetic acid.

The proposed reaction mechanism (Scheme 1) follows from the fact that in all cases the reaction gives only the corresponding ureas, regardless of the solvent; therefore, the process cannot be regarded as substitution with subsequent cleavage involving acetate ion.

EXPERIMENTAL

The ^1H NMR spectra were recorded on a Varian Gemini 200 spectrometer from solutions in DMSO-d_6. Initial 4-chloro-2-oxo-2,3-dihydrothiazole-5-carbaldehyde was synthesized by the procedure developed previously [5]. Substituted ureas were synthesized by the cyanate method [6].

***N*-[(*Z*)-2,4-Dioxothiazolidin-5-ylidenemethyl]-ureas IIIa and IIIb (*general procedure*).** A mixture of 1.64 g (10 mmol) of 4-chloro-2-oxo-2,3-dihydrothiazole-5-carbaldehyde (**I**), 0.82 g (10 mmol) of sodium acetate, and 10 mmol of *N*-allyl- or *N*-benzylurea in 8 ml of methanol was heated for 4 h under reflux. The mixture was then kept for 1 h at room temperature, and the precipitate was filtered off and washed with cold water and 5 ml of methanol.

***N*-Allyl-*N′*-[(*Z*)-2,4-dioxothiazolidin-5-ylidenemethyl]urea (IIIa).** Yield 1.25 g (45%), fine colorless crystals, mp 208–210°C. ^1H NMR spectrum, δ, ppm: 12.03 s (1H, NH, ring), 9.55 d (1H, N^1H, urea, J = 12 Hz), 7.91 d (1H, =C**H**NH, J = 12 Hz), 6.73 t (1H, N^3H, urea), 5.84 m (1H, =CH, allyl), 5.11 t (2H, $=CH_2$, allyl), 3.76 t (2H, CH_2, allyl). Found, %: C 42.35; H 4.02; N 18.53; S 14.00. $C_8H_9N_3O_3S$. Calculated, %: C 42.38; H 3.99; N 18.49; S 14.11.

***N*-Benzyl-*N′*-[(*Z*)-2,4-dioxothiazolidin-5-ylidenemethyl]urea (IIIb).** Yield 1.11 g (40%), yellowish crystals, mp 237–239°C. ^1H NMR spectrum, δ, ppm: 12.04 s (1H, NH, ring), 9.60 d (1H, N^1H, urea, J = 12 Hz), 7.95 d (1H, =C**H**NH, J = 12 Hz), 7.27 m (5H, H_{arom}, J = 8 Hz), 7.04 t (1H, N^3H, urea), 4.33 t (2H, PhCH_2). Found, %: C 52.02; H 4.03; N 15.18; S 11.51. $C_{12}H_{11}N_3O_3S$. Calculated, %: C 51.98; H 4.00; N 15.15; S 11.56.

***N*-[(*Z*)-2,4-Dioxothiazolidin-5-ylidenemethyl]-*N′*-(4-tolyl)urea (IIIf).** A mixture of 1.63 g (10 mmol) of compound **I**, 1.50 g (10 mmol) of *N*-*p*-tolylurea, and 8 ml of DMF was heated for 3 h at 70°C. After 24 h, the precipitate was filtered off and washed with 1 ml of DMF and 5 ml of ice water. Yield 1.75 g (63%), colorless crystals, mp 246–248°C. ^1H NMR spectrum, δ, ppm: 11.83 s (1H, NH, ring), 9.65 d (1H, N^1H, urea, J = 12 Hz), 9.15 s (1H, N^3H, urea), 8.02 d (1H, =C**H**NH, J = 12 Hz), 7.35 d (2H, H_{arom}, J = 8 Hz), 7.08 d (2H, H_{arom}, J = 8 Hz). Found, %: C 52.10; H 4.05; N 15.23; S 11.67. $C_{12}H_{11}N_3O_3S$. Calculated, %: C 51.98; H 4.00; N 15.15; S 11.56.

***N*-[(*Z*)-2,4-Dioxothiazolidin-5-ylidenemethyl]-*N′*-(4-methoxyphenyl)urea (IIIh).** A mixture of 1.63 g

(10 mmol) of aldehyde **I**, 1.83 g (11 mmol) of *N*-*p*-methoxyphenylurea, and 10 ml of acetic acid was heated for 30 min under reflux. The mixture was left to stand for 30 min at room temperature, and the precipitate was filtered off and washed with 3 ml of acetic acid and 10 ml of ice water. Yield 1.90 g (65%), slightly colored crystals, mp 246–248°C. ^{1}H NMR spectrum, δ, ppm: 11.89 s (1H, NH, ring), 9.24 d (1H, N^{1}H, urea, *J* = 12 Hz), 8.64 s (1H, N^{3}H, urea), 7.98 d (1H, =C**H**NH, *J* = 12 Hz), 7.34 d (2H, H_{arom}, *J* = 8 Hz), 6.82 d (2H, H_{arom}, *J* = 8 Hz), 3.75 s (3H, CH_3). Found, %: C 49.26; H 3.85; N 14.29; S 10.80. $C_{12}H_{11}N_3O_4S$. Calculated, %: C 49.14; H 3.78; N 14.33; S 10.93.

Compounds **IVc**, **IVe**, and **IVf** were synthesized in a similar way.

***N*-[(*E*)-2,4-Dioxothiazolidin-5-ylidenemethyl]-*N′*-phenylurea (IVc).** Yield 1.32 g (50%), colorless crystals, mp 250–252°C. ^{1}H NMR spectrum, δ, ppm: 11.97 s (1H, NH, ring), 10.30 d (1H, N^{1}H, urea, *J* = 12 Hz), 10.04 s (1H, N^{3}H, urea), 7.70 d (1H, =C**H**NH, *J* = 12 Hz), 7.50 d (2H, H_{arom}, *J* = 8 Hz), 7.29 t (2H, H_{arom}, *J* = 8 Hz), 7.01 t (1H, H_{arom}, *J* = 8 Hz). Found, %: C 50.29; H 3.51; N 16.03; S 12.30. $C_{11}H_9N_3O_3S$. Calculated, %: C 50.18; H 3.45; N 15.96; S 12.18.

***N*-[(*E*)-2,4-Dioxothiazolidin-5-ylidenemethyl]-*N′*-(*m*-tolyl)urea (IVe).** Yield 1.88 g (68%), light brown crystals, mp 235–237°C. ^{1}H NMR spectrum, δ, ppm: 11.98 s (1H, NH, ring), 10.29 d (1H, N^{1}H, urea, *J* = 12 Hz), 9.96 s (1H, N^{3}H, urea), 7.65 d (1H, =C**H**NH, *J* = 12 Hz), 7.19 m (3H, H_{arom}, *J* 8 Hz), 6.80 d (1H, H_{arom}, *J* = 8 Hz), 2.33 s (3H, CH_3). Found, %: C 52.06; H 4.08; N 15.25; S 11.67. $C_{12}H_{11}N_3O_3S$. Calculated, %: C 51.98; H 4.00; N 15.15; S 11.56.

***N*-[(*E*)-2,4-Dioxothiazolidin-5-ylidenemethyl]-*N′*-(*p*-tolyl)urea (IVf).** Yield 1.94 g (70%), slightly colored crystals, mp 248–250°C. ^{1}H NMR spectrum, δ, ppm: 11.94 s (1H, NH, ring), 10.26 d (1H, N^{1}H, urea, *J* = 12 Hz), 9.90 s (1H, N^{3}H, urea), 7.62 d (1H, =C**H**NH, *J* = 12 Hz), 7.33 d (2H, H_{arom}, *J* = 8 Hz), 7.03 d (1H, H_{arom}, *J* = 8 Hz), 2.29 s (3H, CH_3). Found, %: C 51.83; H 4.05; N 15.23; S 11.69. $C_{12}H_{11}N_3O_3S$. Calculated, %: C 51.98; H 4.00; N 15.15; S 11.56.

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