THIONATION OF *N*-METHYL- AND *N*-UNSUBSTITUTED THIAZOLIDINE ENAMINONES*

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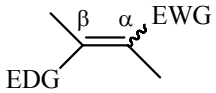
Abstract: The potential of the directional non-bonded 1,5-type S···O interactions to initiate an incipient stage of an *in situ* rearrangement of *N*-unsubstituted thiazolidine enaminones to the functionalized 1,2-dithioles has been demonstrated. Spectral characteristics, as well as an X-ray structural analysis of the selected rearranged product, indicate that a dynamic interconversion occurs in a solution between the 1,2-dithiole and 3,3aλ^4,4-trithia-1-azapentalene bicylic form. The lack of the rearrangement in the case of the *N*-methyl substituted enaminone precursor is attributed to an unfavorable methyl migration in the last reaction step.

Keywords: thiazolidine, enaminone, Lawesson's reagent, 1,2-dithiole, 3,3aλ^4,4-trithia-1-azapentalene

INTRODUCTION

Investigation of the physicochemical properties and chemical reactivity of push-pull alkenes **1**, carrying electron-donating group(s) (EDG) on C(β) and strongly resonatively electron-withdrawing group(s) (EWG) on C(α), is an on-going topic in organic chemistry.[1-2]

*Dedicated to Professor @ivorad ^ekovi} on the occasion of his 70th birthday.



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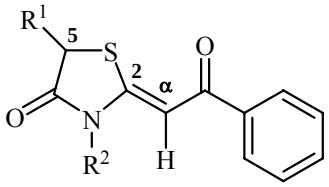
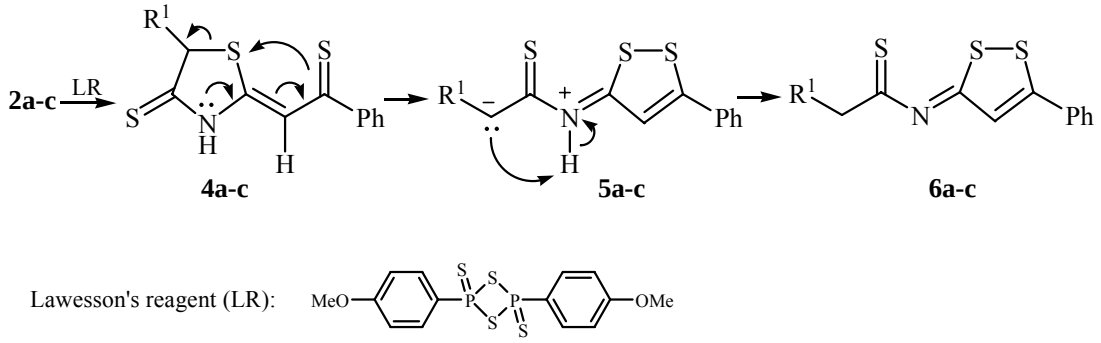
4-Oxothiazolidines **2-3**, containing an exocyclic C=C bond at the position C(2), belong to push-pull enaminones which are widely used in organic synthesis.[3-4] In addition, numerous thiazolidine derivatives have attracted considerable attention because they exhibit diverse biological effects. [5-6]



2a: R^1 = H; R^2=H
2b: R^1 = CH_3; R^2=H
2c: R^1 = CH_2CO_2Et; R^2=H
3: R^1 = CH_2CO_2Et; R^2=CH_3

During the course of our studies on polarized thiazolidines, we have shown that an enaminone moiety, HN–C_β=C_α–C=O, can be protected under the alkaline conditions, thus permitting the regioselective reduction of a series of thiazolidine esters, such as **2c**, to alcohols.[7] Similar concept, based on a prior protection of **2c** *via N*-alkylation, was successfully exploited, at present in a single case, for a reductive heteroannulation of *N*-methyl derivative **3** to fused bicyclic 2-alkylidenethiazolidine. On the other hand, we have experimentally demonstrated a higher electrophilic reactivity of the enaminone electron-rich centre C_α toward various brominating reagents, as compared to the electrophilic position C(5).[8] Furthermore, recently reported rearrangement of 4-oxothiazolidines **2a-c** to 1,2-dithioles **6a-c** (Scheme 1) induced by Lawesson's reagent [LR: (2,4-bis(4-methoxyphenyl)-1,2,3,4-dithiadiphosphetane 2,4-disulfide], is dictated by the intermolecular 1,5-interactions of nonbonded S and O in the *cis*–S–C=C–C=O enaminone fragment of the corresponding precursor **2**.[9]



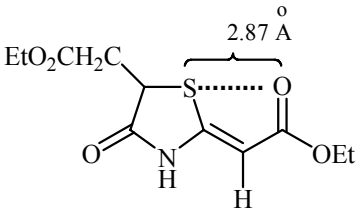
Scheme 1

As a continuation of our studies on the thiazolidine chemistry we present experimental evidence regarding the postulated mechanistic pathway of the **2→→6** rearrangement, including the controlled formation of intermediate(s) *en route* to product **6**. The effect of the structural change, that is, the introduction of the methyl group at the *N*-position of the thiazolidine ring in the selected parent substrate, on the reaction course of the ring transformation, and the overall reactivity of different carbonyl groups in the substrates **2-3** toward LR, has also been investigated.

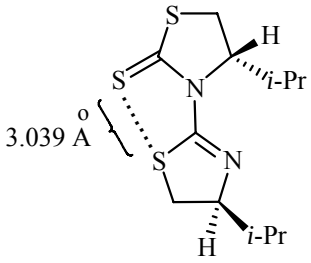
RESULTS AND DISCUSSION

Based on the complete understanding of the structures and physicochemical properties of parent thiazolidines **2,** (*Z*)-thioxothiazolidine-4-thione species **4** (Scheme 1) is proposed as the key intermediate responsible for the formation of the sole product **6** from the (*Z*)-**2** substrate and LR. In particular, the exact molecular structure of the prototype compound **2e** (R^1: CH_2CO_2Et and CO_2Et instead of COPh) was determined by an X-ray crystallography.[10] The distance between the sulfur and oxygen atoms being 2.873(2) Å, which corresponds to 89% of the sum of the van der Waals radii (3.22 Å),[11] implies the strong non-bonded interactions. We assume that upon direct replacement of the carbonyl oxygen in **2e** by sulfur atom the non-bonded S···S distance in the intermediate **4e,** as well as in **4a-c**, has to be very similar to the original value of 2.873(2) Å determined for the S···O distance. The distance is approximately 0.75 Å shorter than the corresponding van der Waals distance between the two sulfur atoms.[12] The significant shortening of the non-bonded distance promotes close 1,5-contact. Subsequently,

through-bond S-S interaction initiates an intramolecular rearrangement by concerted thioxothiazolidine ring opening-closing process, followed by the H-transfer (steps **4**→ **5**→ **6**). Amongst the recent examples, similar close contact between the sulfur atoms has been recently recognized in the crystallographic structure of another thiazolidine derivative depicted by structure **7**.[13]



2e



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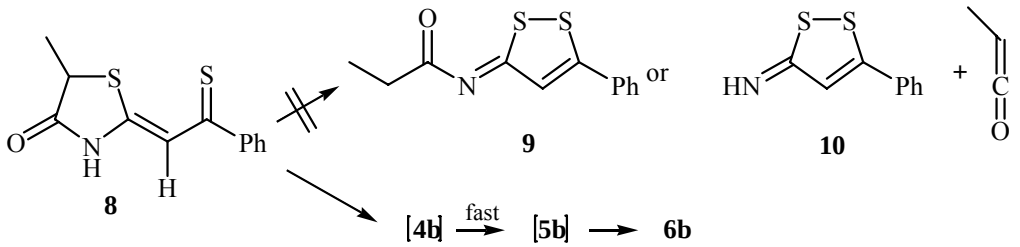
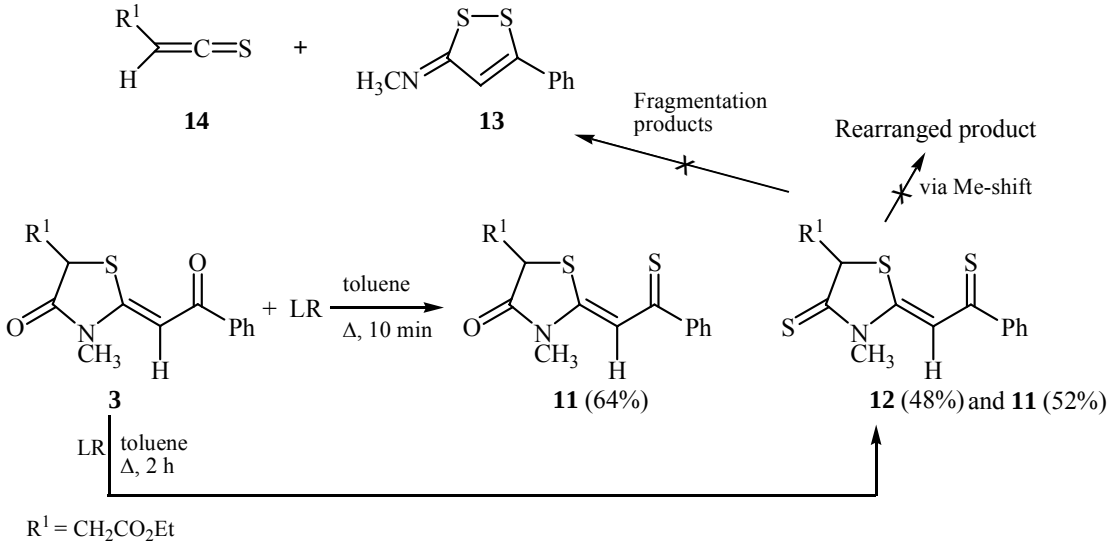
In general, starting from a colorless solution of equimolar quantities of **2** and LR in dry toluene, the corresponding orange crystalline 1,2-dithiole **6** was formed in a high yield (90-98%) upon heating the reaction mixture (3-4 h) in an oil bath at 90-95 °C. In order to test the mechanistic pathway (Scheme 1), **2b** was subjected to a controlled thionation carefully monitored by TLC. The green crystalline thione derivative **8** was isolated in a moderate yield (44%) after ten minutes, along with the low amount of 1,2-dithiole **6b** (10%). In terms of the rearrangement observed for **2a-c** (Scheme 1), similar ring transformation and/or fragmentation of the initial thionation intermediate **8** to *N*-(5-phenyl-3H-1,2-dithiol-3-ylidene)propionamide **9**, or 1,2-dithiole **10**, respectively, might be yet another processes (Scheme 2).



Scheme 2

However, these side products were not formed under the conditions employed. In addition, the intermediacy of the dithione **4b**, arising from the subsequent thionation of the intermediate **8**, was not detected, as the facile ring opening, occurring with the

concomitant ring-closing step to give **5b**, immediately follows. The close proximity of the sulfur atoms, combined with the push-pull effect of the enaminone unit are the two main factors acting in the same direction. The thionation of the lactam carbonyl is probably the rate-determining step (**8→4b**) of the whole process. Alternative formation of the final product **6b** by the thionation of 1,2-dithiole **9**, generated *via* the **8→9** sequence, should not be completely ruled out. However, regardless of the strongly directing interaction between the two sulfur atoms in the intermediate **8**, the strong electron-attracting ring carbonyl will make this ring opening-closing process less feasible. The related process in the case of the dithione **4b** is enhanced as the oxygen/sulfur exchange at C(4) leads to less electron-attracting thioxo group. It is worth mentioning that the green substrate **8** in a preliminary solvent-free reaction was converted under relatively drastic conditions (30 min, ~175 ^{o}C) into an orange-red 1,2-dithiole-type product, whose structure, not presently characterized, should be either **9** or **10**. In an anticipation of obtaining the key intermediate **4**, we then prepared *N*-methyl thiazolidine precursor **3**. We reasoned that in this instance the required methyl shift, analogous to the hydride shift **5→6**, as a final step ultimately leading to a rearranged product, will be disfavored. This proved to be the case, as treatment of **3** with LR under the similar conditions as for the generation of 1,2-dithioles **6a-c**, afforded the expected dithione intermediate **12** and an initial thionation product **11** (Scheme 3).



Scheme 3

The preferential formation of the intermediate **12** was not necessarily the only outcome, since potential fragmentation process may give rise to 1,2-dithiole **13** and thioketene **14**. In fact, Vialle et. al.,[14] reported the fragmentation of this type for *N*-phenyl-5,5-disubstituted 4-thiazolidinones under the harsh experimental conditions. However, compounds **13** and **14** were not observed under the experimental reaction conditions employed. As observed in the reaction scheme, a rearranged product was not obtained from **12**, most likely due to the unfavorable methyl migration as a necessary step, analogous to the hydrogen shift in the case of precursors **2a-c** (see Scheme 1, step **4→5**). Upon the reduced reaction time (10 min) the reaction of **3** with LR proceeded in the stepwise manner to give exclusively an initial thionation derivative **11** in 64% yield. In the light of these results the reactivity of the carbonyl groups of thiazolidines **2** and **3** toward LR reflects a established trend of the thionation rates as follows: ketone > lactam >> > ester.[15,16] Actually, the ester functionality at C(5) stayed intact even after the prolonged reaction time (5-7 h).

The structures of all thionation and rearranged products were elucidated on the basis of their spectroscopic and analytical data (see Experimental). Comparison of the selected ^{1}H and ^{13}C NMR chemical shifts for the pairs of parent thiazolidine and corresponding thionation product **2b/8, 3/11** and **3/12** revealed a complete regularity based on the enhanced anisotropic effect of the thiocarbonyl group relative to the carbonyl anisotropic effect (Table 1).[17-20]

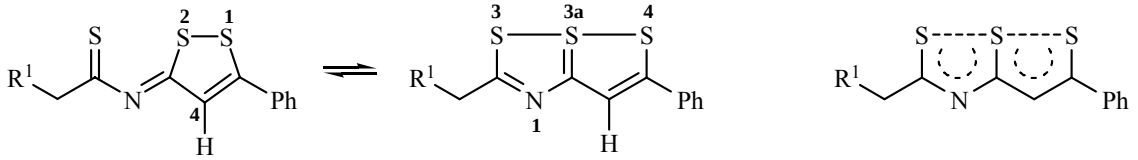
Table 1. Selected ^{13}C and ^{1}H chemical shifts (ppm) for the parent thiazolidines **2b** and **3** and thionation derivatives **8**, **11** and **12**

Entry	Compound	C(2')H	NCH_3	$C{=}O_{exo}$	$C{=}S_{exo}$	$C{=}O_{lactam}$	$C{=}S_{lactam}$
1	(*Z*)-**2b** (DMSO-d_6)	6.78		187.4			
2	(*Z*)-**8** (DMSO-d_6)	7.58			213.6		
3	(*Z*)-**3** ($CDCl_3$)	6.95	3.28	187.8		174.5	
4	(*Z*)-**11** ($CDCl_3$)	7.43	3.40		217.5		
5	(*Z*)-**12** ($CDCl_3$)	7.61	3.83		217.6		205.0

The signals for the olefinic protons of thiazolidines (entries 1 and 3) are at higher field than those of the corresponding sulfur analogues (entries 2, 4 and 5). The same feature is illustrated for the pair **3/12**, where the downfield shift of *ca.* 0.5 ppm is observed for the methyl protons in **12** (δ 3.83 ppm) relative to **3** (δ 3.28 ppm).

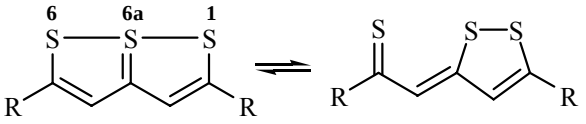
The ^{13}C NMR data are also consistent with the increased anisotropic effect of a thiocarbonyl moiety. The signals at δ 174.5 and 187.8 ppm for the compound (*Z*)-**3** (entry 3) are ascribed to lactam carbonyl and C=O ketone, respectively. As discussed above, the chemical shifts of thiocarbonyl groups of dithione **12** (entry 5) resulting from the oxygen-sulfur exchange, are in the 205-218 ppm range i.e., at a lower field than those of the parent thiazolidine **3**.

The MS, UV, ^{1}H and ^{13}C NMR spectroscopic data for the rearranged products are in good agreement with the 1,2-dithiole structure **6** and the fused bicyclic aromatic 3,3aλ^4,4-trithia-1-azapentalene system **6A** in a continuous equilibrium.[12] In the ^{1}H NMR spectra (in $CDCl_3$) the proton at C(4) of derivatives **6a**, **6b** and **6c** absorbs at very low field, *i.e.*, at 8.37, 8.42 and 8.37 and ppm, respectively, which is indicative of the aromatic nature of these compounds. The interconversion of the **6↔6A** type has been a subject of numerous investigations.[21-25]



6 **6A** **6B**

Formula **6B**, depicting a partial bonding between the sulfur atoms, is another acceptable bonding pattern for this trisulfur bicyclic ring system, whereas the structure **6A** implies the σ bond connecting an internal hypervalent sulfur atom with the terminal S(6) and S(1) atoms. As discussed in a comprehensive review by N. Lozac'H,[12] related 1,6,6aλ^4-trithiapentalenes **15**, as typical 10 π-electron with C_{2v} symmetry, are best represented as being in a rapid interconversion with the 1,2-dithiol-3-ylidene thiones **15A**.



15 **15A**

Finally, as indicated in Scheme 1 the scope of this rearrangement reaction is demonstrated by employing the thiazolidine-type enaminones **2a-c**. A single-crystal X-ray analysis of **6c**, shown in Figure 1, confirmed the trithiaazapentalene structure (formulae **6A** or **6B**; $R^1 = CH_2CO_2Et$).

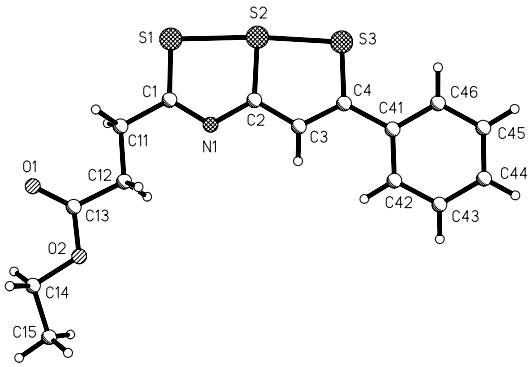


Figure 1. Solid-state structure for compound **6c** as established by X-ray diffraction with atom numbering-scheme for non-hydrogen atoms.

In addition to the nearly linear S(1)-S(2)-S(3) array (175º), the two S-S bonds, being 2.36 and 2.29 Å, respectively, are not of exactly same length as the structures of the two fused rings differ. The computed sulfur-sulfur single bond length in a *cis* planar disulphide group is 2.08 Å and accordingly, the order of this bond is 1. Based on a correlation between the bond order and bond length, the assumed bond order in the solid state structure **6A** and in analogous trithiapentalenes[26,27] is lower than 1 supporting the partial covalent bonding of the trisulfur-sequence.

EXPERIMENTAL

Melting points were determined on a Micro-Heiztisch Boetius PHMK apparatus or Bηchi apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer FT-IR 1725X spectrophotometer 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 (^1H at 200 MHz, ^{13}C at 50.3 MHz). ^{13}C NMR resonance assignments were aided by the use of the DEPT technique to determine numbers of attached hydrogens. 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 at 70 eV (EI). 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 60Å, 12-26, ICN Biomedicals). Elemental analyses were performed at the microanalysis laboratory at the Department of Chemistry, University of Belgrade.

General procedure for the preparation of rearranged derivatives 6a-c

A colorless solution of (*Z*)-2-alkylidene-4-oxothiazolidine **2a-c** (0.164 mmol) and LR (0.164 mmol) in dry toluene (3 mL) was heated in an oil bath at 90-95 °C (initially heterogeneous solution at room temperature becomes homogenous upon heating at around 75 °C). After a few minutes, the color of the reaction mixture turned dark reddish brown. **CAUTION:** *All reactions involving Lawesson's reagent, due to the unpleasant odor, should be carried out in a well-ventilated hood.* The mixture was stirred at this temperature for additional hour when TLC indicated the complete consumption of substrate **2a-c**. After cooling to room temperature, the solvent was evaporated *in vacuo*. The residue was chromatographed (toluene/ethyl acetate, 10:0→8:2, v/v) affording the dark orange crystalline 1,2-dithiole **6a-c** in high yields (90-98 %). The structural assignments of all isolated products were made on the basis of spectroscopic data (IR, ^{1}H and ^{13}C NMR, MS, UV) and elemental analysis. Compound **6a** was previously described.[28] Note: It should be emphasized that the assignments are based on 1,2-dithiole structures **6** which are in continuous equilibrium with the 3,3aλ^4,4-trithia-1-azapentalene forms **6A**.

***N*-(5-Phenyl)-[1,2]dithiol-3-ylidene)-thioacetamide (6a)**

From **2a** (50 mg, 0.228 mmol) in toluene (4 mL) and LR (87 mg, 0.228 mmol) after column chromatography (toluene/EtOAc 10:0 to 8:2) the 1,2-dithiole **6a** was isolated; yield 57 mg (99 %); mp 98 ºC. IR (KBr): ν_{max} 3004, 2908, 1638, 1514, 1485, 1447, 1404, 1226, 1205, 989, 846, 757, 690, 642 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.86 (3H, s, CH_3), 7,42-7.53 (3H, m, *m*- and *p*-Ph), δ 7.75-7.84 (2H, m, *o*- Ph), 8.37 (1H, s, =CH); ^{13}C NMR ($CDCl_3$): δ 29.1 (CH_3), 125.8 (=CH), 127.4 (*o*- Ph), 129.0 (*m*-Ph), 131.0 (*p*-Ph),

136.2 (C_{ipso}- Ph), 178.5 (C=*C*-S), 187.3 (N=C-S), 198.6 (C=S); MS (EI): *m/z* (rel.intensity): 251 (M^+, 35), 236 (15), 210 (5), 193 (7), 174 (3), 145 (13), 121 (18), 102 (20), 89 (3), 77 (13), 59 (100), 39 (3); UV (DMSO): λ_{max} (ε) 333 nm (15,250) and 446 nm (11,300). Anal. calcd for $C_{11}H_9NS_3$: C, 52.56; H, 3.61; N, 5.57; S, 38.26; Found: C, 52.68; H, 3.71; N, 5.63; S, 37.88.

***N*-(5-Phenyl)-[1,2]dithiol-3-ylidene)-thiopropanamide (6b)**

From **2b** (40 mg, 0.17 mmol) in toluene (4 mL) and LR (70 mg, 0.17 mmol) after column chromatography (petrolether/EtOAc 10:0 to 10:0.4) the 1,2-dithiole **6b** was isolated; yield 39 mg (85 %); mp 54-56 ºC. IR (KBr): ν_{max} 3142, 3013, 2965, 2927, 2891 1518, 1481, 1448, 1396, 1290, 1227, 1195, 1065, 1000, 944, 841, 761, 693 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.44 (3H, t, *J*=7.4 Hz, CH_3), 3.12 (2H, q, *J*=7.4 Hz, CH_2), 7,47-7.50 (3H, m, *m*- and *p*-Ph), δ 7.83-7.88 (2H, m, *o*- Ph), 8.42 (1H, s, =CH); ^{13}C NMR ($CDCl_3$): δ 13.8 (CH_3), 35.8 (CH_2), 126.0 (=CH), 127.5 (*o*- Ph), 129.1 (*m*-Ph), 131.0 (*p*-Ph), 136.7 (C_{ipso}- Ph), 178.7 (C=*C*-S), 187.8 (N=C-S), 204.9 (C=S); UV (DMSO): λ_{max} (ε) 332 nm (15,250) and 446 nm (11,300). Anal. calcd for $C_{12}H_{11}NS_3$: C, 54.32; H, 4.15; N, 5.28. Found: C, 54.14; H, 4.18; N, 5.26.

Ethyl 3-(5-phenyl-[1,2]dithiol-3-ylidenethiocarbamoyl)propanoate (6c)

From **2c** (50 mg, 0.16 mmol) in toluene (4 mL) and LR (66 mg, 0.16 mmol) after column chromatography (toluene/EtOAc 3:1 to 1:1) the 1,2-dithiole **6c** was isolated; yield 51 mg (92 %); mp 65 ºC. IR (KBr): ν_{max} 3067, 3006, 2978, 2925, 2855, 1730, 1512, 1483, 1450, 1426, 1401, 1375, 1305, 1177, 1157, 1107, 1049, 1015, 945, 867, 830, 760, 687 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.26 (3H, t, *J*=7.2 Hz, CH_3), 2.92 (2H, t, *J*=7.3 Hz, CH_2-CO), 3.40 (2H, t, *J*=7.3 Hz, CH_2-CS), 4.17 (2H, q, *J*=7.0 Hz, CH_2-O), 7,41-7.53 (3H, m, *m*- and *p*-Ph), δ 7.78-7.87 (2H, m, *o*- Ph), 8.37 (1H, s, =CH); ^{13}C NMR ($CDCl_3$): δ 14.7 (CH_3), 32.9 (*C*H_2-CO), 37.5 (*C*H_2-CS), 60.6 (CH_2-O), 126.4 (=CH), 127.4 (*o*- Ph), 129.1 (*m*-Ph), 131.1 (*p*-Ph), 136.0 (C_{ipso}- Ph), 172.2 (CO_{ester}), 177.5 (C=*C*-S), 187.4 (N=C-S), 201.9 (C=S); MS (EI): *m/z* (rel.intensity): 337 (M^+, 38), 304 (65), 277 (7), 264 (8), 236 (100), 211 (15), 194 (10), 178 (20), 145 (38), 117 (73), 102 (33), 71 (45), 55 (65); UV (DMSO): λ_{max} (ε) 332.6 nm (15,990) and 446.1 nm (12,720).

Anal. calcd for $C_{15}H_{15}N\,O_2S_3$: C, 53.39; H, 4.48; N, 4.15; S, 28.50; Found: C, 53.15; H, 4.45; N, 4.24; S, 27.97.

(*Z*)-5-methyl-4-oxothiazolidin-2-ylidene)-1-phenylethanethione (8)

From **2b** (54 mg, 0.23 mmol) in toluene (5 mL) and LR (94 mg, 0.23 mmol), at 90-95 ºC, 10 min, after column chromatography (toluene/EtOAc 10:0 to 10:0.3) the (*Z*)-5-methyl-4-oxothiazolidin-2-ylidene)-1-phenylethanethione (**8**)

was isolated; yield 25 mg (44 %); mp 184-186 ºC. IR (KBr): ν_{max} 3405, 3094, 3022, 2935, 2896, 1691, 1535, 1476, 1447, 1367, 1308, 1219, 1073, 1000, 840, 768, 743, 692 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.52 (3H, d, *J*=7.4 Hz, CH_3), 4.10 (1H, q, *J*=7.4 Hz, SCH), 7,43-7.48 (3H, m, *m*- and *p*-Ph), 7.58 (1H, s, =CH), 7.70-7.74 (2H, m, *o*- Ph), 12.30 (1H, s, NH); ^{13}C NMR (DMSO-d_6): δ 17.3 (CH_3), 41.6 (SCH), 111.6 (=CH), 126.6 (*o*- Ph), 128.6 (*m*-Ph), 130.9 (*p*-Ph), 146.8 (C_{ipso}- Ph), 166.0 (C=*C*H), 178.0 (CO), 213.6 (C=S); UV ($CHCl_3$): λ_{max} (ε) 330 nm (17,300) and 416.0 nm (23,300). Anal. calcd for $C_{12}H_{11}NOS_2$: C, 57.81; H, 4.41; N, 5.62; S, 25.72; Found: C, 57.32; H, 4.60; N, 5.60; S, 25.15 .

(*Z*)-(5-Ethoxycarbonylmethyl-*N*-methyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (3)

To a vigorously stirred mixture of (*Z*)-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**2c**) (100 mg , 0.33 mmole) in dry acetone (1.5 mL) and K_2CO_3 (45 mg, 0.33 mmol) a solution of MeI (0.022 mL, 51 mg, 0.36 mmol) (10% molar excess) was added in one portion. The reaction mixture was refluxed for 2 h until the disappearance of the starting material. After column chromatography (toluene/EtOAc, 100/0 → 80/20, v/v) pure *N*-methylthiazolidine derivative **3** was isolated; yield 90 mg (86%)**;** mp 114-115 °C. IR (KBr): ν_{max} 3245, 3069, 2986, 2926, 1731, 1706, 1627, 1598, 1575, 1515, 1465, 1419, 1350, 1224, 1196, 1128, 1051 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.17 (3H, t, *J*=7.0 Hz, $C\underline{H}_3CH_2$), 2.94-3.18 (2H, m, CH_AH_B; chemical shifts and coupling constants can't be precisely determined as the signals are of the higher order); 3.28 (3H, s, NCH_3), 4.09 (2H, q, *J*= 7.0 Hz, CH_2O), 4.22 (1H, dd, J_1=7.0 Hz, J_2=4.6 Hz, $CH_AH_BC\underline{H}_X$), 6.95 (1H, s, =CH), 7.48-7.64 (3H, m, *p*-Ph and *m*-Ph), 8.04 (1H, dd, J_1=8.0 Hz, J_2=1.6 Hz, *o*-Ph); ^{13}C NMR (DMSO-d_6): δ 14.2 ($\underline{C}H_3CH_2$), 30.5 (NCH_3),

36.3 (CH_AH_B), 41.1 (CH_X), 60.8 ($CH_3\underline{C}H_2$), 95.5 (=CH), 127.8 (*m*-Ph), 128.8 (*o*-Ph), 132.4 (*p*-Ph), 138.3 (C_1-Ph), 161.2 (=CH), 170.3 (CO_{ester}) 174.5 (CO_{lactam}), 187.8 (CO_{exo}); MS (EI, 70eV): *m/z* (rel. intensity): 319 (M^+, 100), 302(3), 274(13), 245(100), 228(45), 168(63), 131(10), 105(67), 82(64), 77(56), 55(31); UV (DMSO): λ_{max} (ε) 336.0 nm (25,600); Anal. Calcd for $C_{13}H_{13}NO_3S$: C, 60.17; H, 5.36; N, 4.39; S, 10.04; Found: C, 59.88; H, 5.32; N, 4.39; S, 10.13.

(*Z*)-*N*-Methyl-5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-1-phenylethanethione (11)

From **3** (50 mg, 0.156 mmol) in toluene (3 mL) and LR (63 mg, 0.156 mmol) (10 min, reflux) after column chromatography (toluene/EtOAc 3:1 to 1:1) the yellowish thiazolidine derivative **11** was isolated; yield 33.5 mg (64 %); mp ºC. IR (KBr): ν_{max} 3080, 2978, 2927, 1723, 1587, 1521, 1452, 1422, 1379, 1336, 1302, 1258, 1224, 1191, 1107, 1070, 1027, 1001, 945, 872, 840, 809, 763, 688, 616 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.27 (3H, t, *J*=7.2 Hz, $C\underline{H}_3CH_2$), 2.97 (1H, dd, J_{AX} =8.3 Hz, J_{AB} =17.7 Hz, $OCC\underline{H}_AH_B$), 3.19 (1H, dd, J_{BX} =4.1 Hz, J_{AB} =17.7 Hz, $OCCH_A\underline{H}_B$), 3.40 (3H, s, N-CH_3), 4.12 (1H, dd, J_{AX} =8.3 Hz, J_{BX} =4.1 Hz, $CH_AH_BC\underline{H}_X$), 4.19 (2H, q, *J*=7.1 Hz, CH_2-O), 7.34-7.49 (3H, m, *m*- and *p*-Ph), 7.43 (1H, s, =CH), 7.75-7.80 (2H, m, *o*- Ph); ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 30.9 (N-CH_3), 36.5 (CH_AH_B), 41.6 (CH_X), 61.5 (CH_2-O), 112.0 (=CH), 126.7 (*o*- Ph), 128.3 (*m*-Ph), 130.8 (*p*-Ph), 147.8 (C_{ipso}- Ph), 162.8 (NC=), 169.8 (CO_{ester}), 174.8 (CO_{lactam}), 217.5 (C=S); MS (CI): *m/z* 336 (M + 1); Anal. calcd for $C_{16}H_{17}NO_3S_2$: C,57.29; H, 5.11; N, 4.18; S, 19.11; Found: C, 56.92; H, 5.01; N, 4.20; S, 19.08.

(*Z*)-*N*-Methyl-5-ethoxycarbonylmethyl-4-thioxothiazolidin-2-ylidene)-1-phenylethanethione (12)

From **3** (50 mg, 0.156 mmol) in toluene (mL) and LR (63 mg, 0.156 mmol) (2 hours, reflux) after column chromatography (toluene/EtOAc 3:1 to 1:1) the thioxothiazolidine derivative **12** was isolated in addition to **11** (52%); yield mg (48 %); mp 84-86 ºC. IR (KBr): ν_{max} 3026, 2967, 2928, 1730, 1597, 1485, 1377, 1253, 1100, 1025, 925, 855, 813, 759, 693, 587 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.28 (3H, t, *J*=7.1 Hz, $C\underline{H}_3CH_2$), 2.98 (1H, dd, J_{AX} =9.5 Hz, J_{AB} =17.7 Hz, $OCC\underline{H}_AH_B$), 3.51 (1H, dd, J_{BX} =3.8 Hz, J_{AB} =17.6

Hz, $OCCH_A\underline{H}_B$), 3.83 (3H, s, N-CH_3), 4.18 (2H, q, *J*=7.1 Hz, CH_2-O), 4.49 (1H, dd, J_{AX} =9.5 Hz, J_{BX} =3.8 Hz, $CH_AH_BC\underline{H}_X$), 7.35-7.48 (3H, m, *m*- and *p*-Ph), 7.61 (1H, s, =CH), 7.75-7.80 (2H, m, *o*- Ph); ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 36.4 (N-CH_3), 41.4 (CH_AH_B), 54.1 (CH_X), 61.4 (CH_2-O), 113.8 (=CH), 126.7 (*o*- Ph), 128.3 (*m*-Ph), 130.8 (*p*-Ph), 147.8 (C_{ipso}- Ph), 164.9 (NC=), 170.1 (CO_{ester}), 205.0 ($CS_{thiolactam}$), 217.6 (C=S); CIMS: *m/z* 352 (M + 1).

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I Z V O D

TIONOVANJE *N*-METIL- I *N*-NESUPSTITUISANIH TIAZOLIDINONSKIH ENAMINONA

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Pokazan je potencijal usmerenih nevezivnih S···O interakcija 1,5-tipa da iniciraju po~etnu fazu *in situ* preme{tanja *N*-nesupstituisanih tiazolidinonskih enaminona u funkcionalizovane 1,2-ditiole. Spektralne karakteristike, kao i kristalografska strukturna analiza izabranog preme{tenog proizvoda, ukazuju na brzu interkonverziju izme|u 1,2-ditiola i 3,3aλ^4,4-tritia-1-azapentalenskog bicikli~nog oblika. Odsustvo preme{tanja u slu~aju *N*-metil-supstituisanog enaminonskog prekursora pripisano je nefavorizovanom preme{tanju metil-grupe u zavr{noj fazi reakcije.

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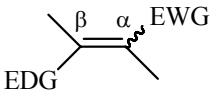
Strana 2



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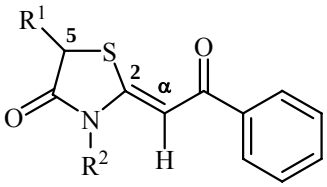
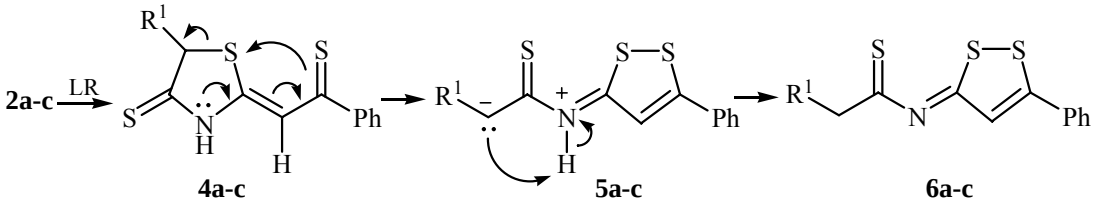
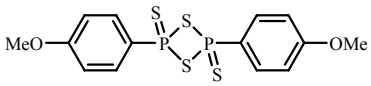
Strana 2



2a: R^1 = H; R^2=H
2b: R^1 = CH_3; R^2=H
2c: R^1 = CH_2CO_2Et; R^2=H
3: R^1 = CH_2CO_2Et; R^2=CH_3

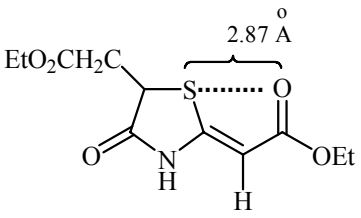


Lawesson's reagent (LR):

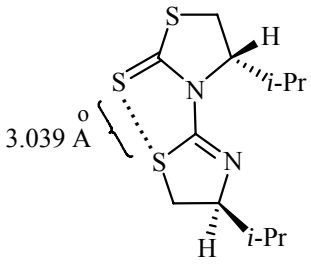


Scheme 1

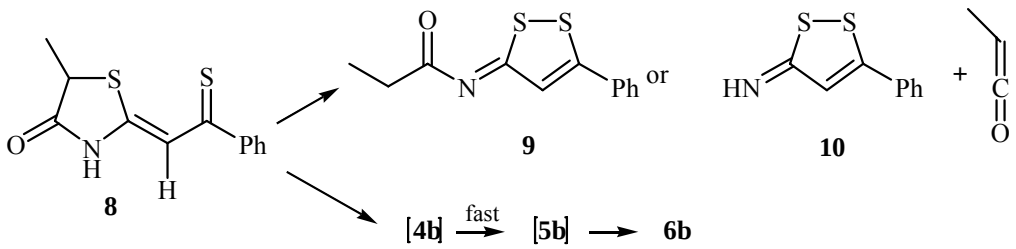
Strana 4



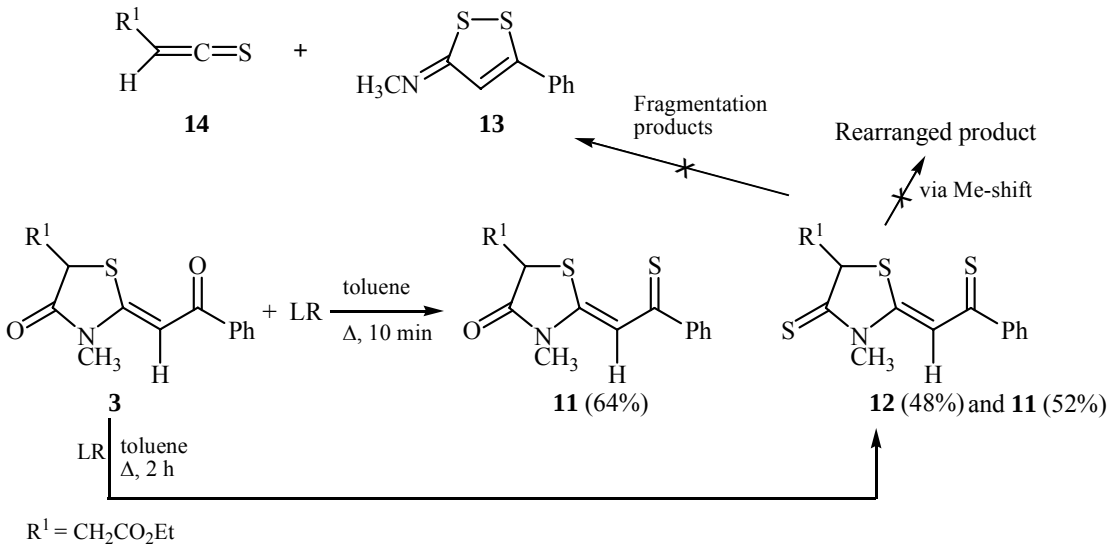
2e



7



Scheme 2

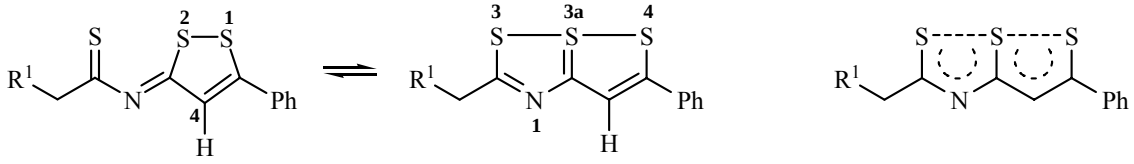

R1
C=S
H
+
S—S
H3CN
Ph
14
13
Fragmentation products
Rearranged product
via Me-shift
R1
S
O
O
N
CH3
H
Ph
+ LR
toluene
Δ, 10 min
S
S
3
11 (64%)
12 (48%) and 11 (52%)
LR
toluene
Δ, 2 h
R1 = CH2CO2Et

Scheme 3

Table 1. Selected ^{13}C and ^{1}H chemical shifts (ppm) for the parent thiazolidines **2b** and **3** and thionation derivatives **8**, **11** and **12**

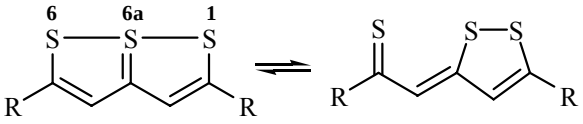
Entry	Compound	C(2')H	NCH_3	$C{=}O_{exo}$	$C{=}S_{exo}$	$C{=}O_{lactam}$	$C{=}S_{lactam}$
1	(*Z*)-**2b** (DMSO-d_6)	6.78		187.4			
2	(*Z*)-**8** (DMSO-d_6)	7.58			213.6		
3	(*Z*)-**3** ($CDCl_3$)	6.95	3.28	187.8		174.5	
4	(*Z*)-**11** ($CDCl_3$)	7.43	3.40		217.5		
5	(*Z*)-**12** ($CDCl_3$)	7.61	3.83		217.6		205.0

Strana 7



6 **6A** **6B**

Strana 7



15 **15A**

Strana 8

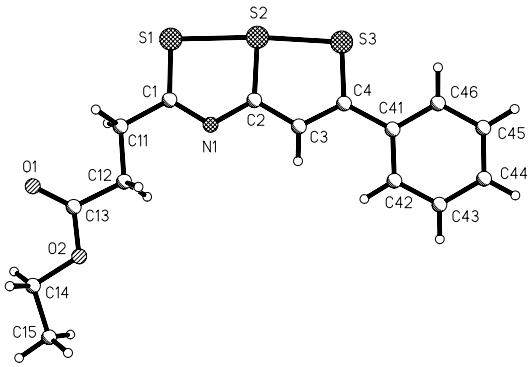


Figure 1. Solid-state structure for compound **6c** as established by X-ray diffraction with atom numbering-scheme for non-hydrogen atoms.