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Original scientific paper

Thionation of *N*-methyl- and *N*-unsubstituted thiazolidine enaminones*

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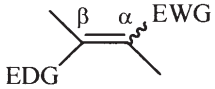
Abstract: The potential of directional non-bonded 1,5-type S···O interactions to initiate the incipient stage of an *in situ* rearrangement of *N*-unsubstituted thiazolidine enaminones to functionalized 1,2-dithioles has been demonstrated. The spectral characteristics, as well as X-ray structural analysis of a selected rearranged product, indicate that a dynamic interconversion occurs in solution between the 1,2-dithiole and the 3,3aλ^4,4-trithia-1-azapentalene bicylic form. The lack of the rearrangement in the case of a *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 groups(s) (EDG) on C(β) and strongly resonatively electron-withdrawing groups(s) (EWG) on C(α), is an on-going topic in organic chemistry.[1,2]



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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

* Dedicated to Professor Živorad Čeković on the occasion of his 70th birthday.

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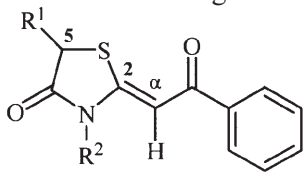
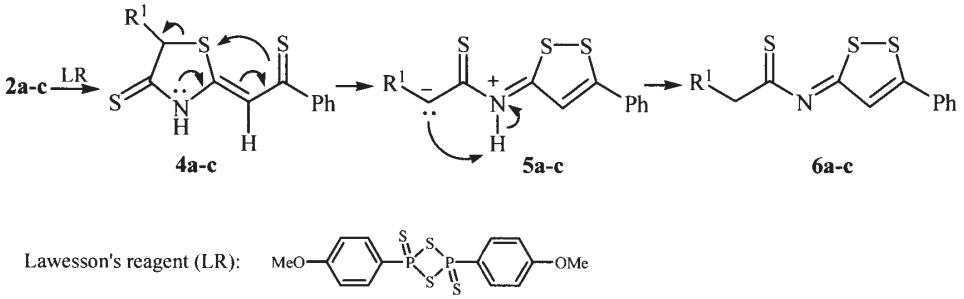
attention because they exhibit diverse biological effects.[5,6]



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

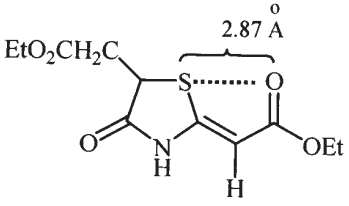


Scheme 1.

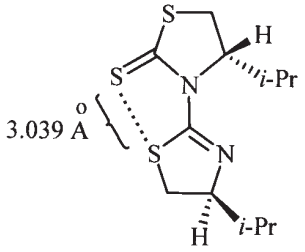
As a continuation of our studies on the chemistry of thiazolidines, experimental evidence regarding the postulated mechanistic pathway of the **2**→→**6** rearrangement, including the controlled formation of intermediate(s) *en route* to product **6**, is presented. The effect of structural change, *i.e.*,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

RESULTS AND DISCUSSION

Based on the complete understanding of the structures and physicochemical properties of parent thiazolidines **2**, the (*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 **2d** (R^1: CH_2CO_2Et and CO_2Et instead of COPh) was determined by X-ray crystallography.[10] The determined distance between the sulfur and oxygen atoms of 2.873(2) Å, which corresponds to 89 % of the sum of the van der Waals radii (3.22 Å),[11] implies strong non-bonded interactions. It is assumed that upon direct replacement of the carbonyl oxygen in **2d** with a sulfur atom, the non-bonded S···S distance in the intermediate **4d**, 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 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 a concerted thioxothiazolidine ring opening-closing process, followed by H-transfer (steps **4→5→6**). Amongst other recent examples, a similar close contact of the sulfur atoms has been recently recognized in the crystallographic structure of another thiazolidine derivative depicted by structure **7**.[13]



2d



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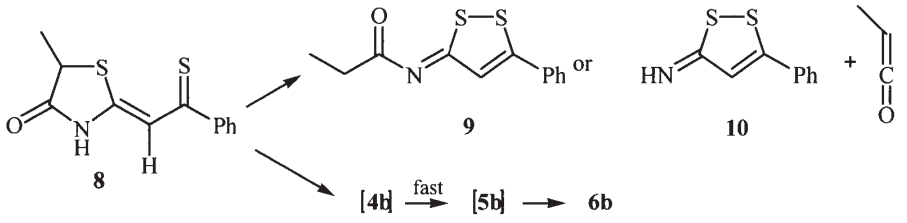
In general, starting from a colorless solution of equimolar quantities of **2** and LR in dry toluene, the corresponding orange crystalline 1,2-dithiole **6** was formed in high yield (90–98 %) upon heating the reaction mixture (3–4 h) in an oil bath at 90–95 °C. In order to test the mechanistic pathway (Scheme 1), **2b** was subjected to a controlled thionation which was carefully monitored by TLC. The green crystalline thione derivative **8** was isolated in a moderate yield (44 %) after ten minutes, along with a small

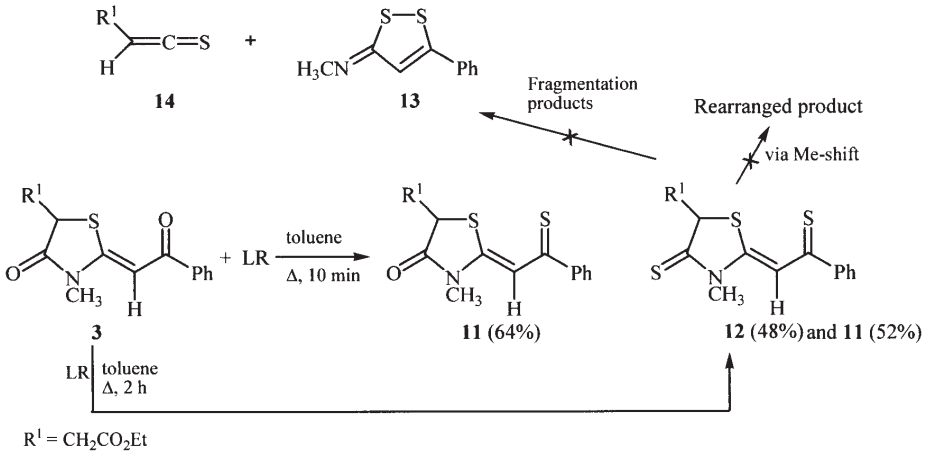


8 **9** **10**

Scheme 2.

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-3*H*-1,2-dithiol-3-ylidene)propionamide (**9**), or 1,2-dithiole **10**, respectively, might be yet other processes (Scheme 2).

However, these side products were not formed under the conditions employed. In addition, the dithione intermediate **4b**, arising from 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, which act in the same direction. The thionation of the lactam carbonyl is probably the rate-determining step (**8**→**4b**) of the whole process. An alternative formation of the final product **6b** by thionation of the 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 intermediate **8**, the strongly 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 the less electron-attracting thioxo group. It is worth mentioning that the green substrate **8** was converted in a preliminary solvent-free reaction, under relatively drastic conditions (30 min, ≈175 ºC) into an orange-red 1,2-dithiole-type product, the structure of which, not presently characterized, should be either **9** or **10**. In anticipation of obtaining the key intermediate **4**, the *N*-methyl thiazolidine precursor **3** was then prepared. It was reasoned that in this instance the required methyl shift, analogous to the hydrogen shift **5**→**6**, as the final step ultimately leading to the rearranged product, would be disfavored. This proved to be the case, as treatment of **3** with LR under similar conditions as for the generation of 1,2-dithioles **6a–c**, afforded the expected dithione intermediate **12** and the initial thionation product **11** (Scheme 3).



Scheme 3.

The preferential formation of intermediate **12** was not necessarily the only outcome, since a potential fragmentation process may give rise to the 1,2-dithiole **13** and the thioketene **14**. In fact, Vialle *et al.*,[14] reported a fragmentation of this type for *N*-phenyl-5,5-disubstituted 4-thiazolidinones under 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 necessary methyl migration being unfavorable, whereas the analogous hydrogen shift in the case of precursors **2a–c** is favorable (see Scheme 1, step **5→6**). Upon reducing the reaction time (10 min), the reaction of **3** with LR proceeded in a stepwise manner to give exclusively the initial thionation derivative **11** in 64 % yield. In light of these results, the reactivity of the carbonyl groups of thiazolidines **2** and **3** toward LR reflects the established trend of the rates of thionation, as follows: ketone > lactam >>> ester.[15,16] Actually, the ester functionality at C(5) stayed intact even after a 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 that of the carbonyl group (Table I).[17–20]

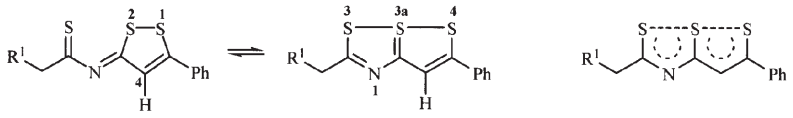
TABLE I. Selected ^{13}C and ^{1}H chemical shifts (ppm) for the parent thiazolidines **2b** and **3** and the thionation derivatives **8**, **11** and **12**

Entry	Compound	C(2α)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 a 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).

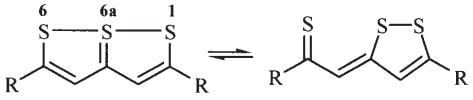
The ^{13}C-NMR data are also consistent with the increased anisotropic effect of a thiocarbonyl moiety. The signals at δ 174.5 and 187.8 ppm for the compound (*Z*)-**3** (entry 3) are ascribed to the lactam carbonyl and the C=O ketone, respectively. As discussed above, the chemical shifts of the thiocarbonyl groups of the 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 the derivatives **6a**, **6b** and **6c** absorbs at a very low field, *i.e.*, at 8.37, 8.42 and 8.37 ppm, respectively, which is indicative of the aromatic nature of these compounds. Interconversions of the **6↔6A** type have been the 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 structure **6A** implies a σ bond connecting the internal hypervalent sulfur atom with the terminal S(3) and S(4) atoms. As discussed in a comprehensive review by N. Lozac'H,[12] the related 1,6,6aλ^4-trithiapentalenes **15**, as typical 10 π-electron with C_{2v} symmetry, are best represented as being in 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**. The single-crystal X-ray analysis of **6c** shown in Fig. 1, confirmed the trithiaazapentalene structure (formulae **6A** or **6B**; $R^1 = CH_2CO_2Et$).

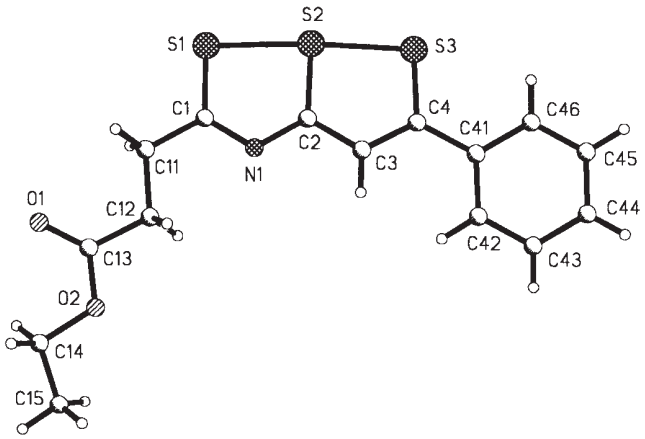


Fig. 1. Solid-state structure for compound **6c** as established by X-ray diffraction with the atom numbering-scheme for non-hydrogen atoms.

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 the 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 structure **6A** and in analogous trithiapentalenes in the solid state[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 a Büchi 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 the numbers of attached hydrogens. The 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 60 Å, 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 the 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 ºC (the initially heterogeneous system at room temperature became homogenous upon heating at around 75 ºC). 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 an additional hour when TLC indicated the substrate **2a-c** had been completely consumed. 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 the isolated products were made on the basis of spectroscopic data (IR, ^1H 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}; ^1H-NMR ($CDCl_3$): δ 2.86 (3H, *s*, CH_3), 7.42–7.53 (3H, *m*, *m*- and *p*-Ph), 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 (petroleum ether/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}; ^{1}H-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), 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}; ^{1}H-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), 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 (15,990) and 446.1 nm (12,720). Anal: Calcd. for $C_{15}H_{15}NO_2S_3$: 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*)-2-(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*)-2-(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*)-2-(5-Ethoxycarbonylmethyl-*N*-methyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (***3***)*

To a vigorously stirred mixture of (*Z*)-2-(5-ethoxycarbonylmethyl-4-oxothiazolidin-2-ylidene)-1-phenylethanone (**2c**) (100 mg, 0.33 mmol) 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 starting material had disappeared. After column chromatography (toluene/EtOAc, 100/0 → 80/20, v/v), the pure *N*-methylthiazolidine derivative **3** was isolated; yield 90 mg (86 %); mp 114–115 ºC. 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*H*$_3$CH$_2$), 2.94–3.18 (2H, *m*, CH_AH_B; chemical shifts and coupling constants can not be precisely determined as the signals are of a 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, $CH_AH_BCH_X$), 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 (*C*H_3CH$_2$), 30.5 (NCH_3), 36.3 (CH_AH_B), 41.1 (CH_X), 60.8 (CH_3CH_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, 70 eV): *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, 10.4; Found: C, 59.88; H, 5.32; N, 4.39; S, 10.13.

*(Z)-2-(5-Ethoxycarbonylmethyl-*N*-methyl-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 %); 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}; ^{1}H-NMR ($CDCl_3$): δ 1.27 (3H, *t*, *J* = 7.2 Hz, CH_3CH_2), 2.97 (1H, *dd*, J_{AX} = 8.3 Hz, J_{AB} = 17.7 Hz, $OCCH_AH_B$), 3.19 (1H, *dd*, J_{BX} = 4.1 Hz, J_{AB} = 17.7 Hz, $OCCH_AH_B$), 3.40 (3H, *s*, $N–CH_3$), 4.12 (1H, *dd*, J_{AX} = 8.3 Hz, J_{BX} = 4.1 Hz, $CH_AH_BCH_X$), 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)-2-(5-Ethoxycarbonylmethyl-*N*-methyl-4-thioxothiazolidin-2-ylidene)-1-phenylethanethione (***12***)*

From **3** (50 mg, 0.156 mmol) in toluene (3 mL) and LR (63 mg, 0.156 mmol) (2 h, reflux) after column chromatography (toluene/EtOAc 3:1 to 1:1), the thioxothiazolidine derivative **12** was isolated in addition to **11** (52 %); yield 25 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}; ^{1}H-NMR ($CDCl_3$): δ 1.28 (3H, *t*, *J* = 7.1 Hz, CH_3CH_2), 2.98 (1H, *dd*, J_{AX} = 9.5 Hz, J_{AB} = 17.7 Hz, $OCCH_AH_B$), 3.51 (1H, *dd*, J_{BX} = 3.8 Hz, J_{AB} = 17.6 Hz, $OCCH_AH_B$), 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, $CH_AH_BCH_X$), 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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ИЗВОД

ТИОНОВАЊЕ *N*-МЕТИЛ- И *N*-НЕСУПСТИТУИСАНИХ ТИАЗОЛИДИНОНСКИХ ЕНАМИНОНА

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Показан је потенцијал усмерених невезивних S···O интеракција 1,5-типа да иницирају почетну фазу *in situ* премештања *N*-несупституисаних тиазолидинонских енаминона у функционализоване 1,2-дитиоле. Спектралне карактеристике, као и кристалографска структурна анализа изабраног премештеног производа, указују на брзу интерконверзију између 1,2-дитиола и 3,3aλ^4,4-тритија-1-азапенталенског бицикличног облика. Одсуство премештања у случају *N*-метил-супституисаног енаминомског прекурсора приписано је нефаворизованом премештању метил-групе у завршној фази реакције.

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REFERENCES

1. S. Rajappa, *Tetrahedron* **55** (1999) 7065
2. J. Sandström, *J. Top. Stereochem.* **14** (1983) 83
3. S. P. Singh, S. S. Parmar, K. Raman, V. I. Stenberg, *Chem. Rev.* **81** (1981) 175
4. J. V. Metzger, in *Comprehensive Heterocyclic Chemistry*, A. R. Katritzky and C. W. Rees, Eds., Pergamon, Oxford, 1984; Vol. 6, Chapter 19, pp. 235–331
5. D. J. Faulkner, *Nat. Prod. Rep.* **15** (1998) 113
6. N. Sokolenko, G. Abbenante, M. J. Scanlon, A. Jones, R. Gahan, G. R. Hanson, D. P. Fairlie, *J. Am. Chem. Soc.* **121** (1999) 2603
7. R. Marković, M. Baranac, M. Stojanović, *Synlett* (2004) 1034
8. R. Marković, Z. Džambaski, M. Baranac, *Tetrahedron* **57** (2001) 5833
9. R. Marković, M. Baranac, S. Jovetić, *Tetrahedron Lett.* **44** (2003) 7087
10. R. Marković, M. Baranac, Z. Džambaski, M. Stojanović, P. J. Steel, *Tetrahedron* **59** (2003) 7803
11. J. G. Ángyán, R. A. Poirier, Á. Kucsman, I. G. Csizmadia, *J. Am. Chem. Soc.* **109** (1987) 2237 and references cited therein
12. N. Lozac'H, in *Comprehensive Heterocyclic Chemistry*, K. T. Potts, Ed., Pergamon, Oxford, 1984, Vol. 6, pp. 1049–1070
13. Y. Nagao, H. Nishijima, H. Iimori, H. Ushirogochi, S. Sano, M. Shiro, *J. Organometallic Chem.* **611** (2000) 172
14. P. G. Hervieu, P. Rioult, J. Vialle, *Bull. Soc. Chim. Fr.* (1971) 4380
15. For a review regarding Lawesson's reagent, see: (a) M. P. Cava, I. M. Levinson, *Tetrahedron* **41** (1985) 5061; (b) R. A. Cherkasov, G. A. Kutyrev, A. N. Pudovik, *Tetrahedron* **41** (1985) 2567
16. M. Ori, T. Nishio, *Heterocycles* **54** (2001) 201
17. D. M. McKinnon, in *Comprehensive Heterocyclic Chemistry*; K. T. Potts, Ed., Pergamon, Oxford, 1984, Vol. 6, pp. 783–811
18. H. Mastalerz, M. S. Gibson, *J. Chem. Soc., Perkin Trans. 1* (1981) 2952
19. J. G. Dingwall, S. McKenzie, D. H. Reid, *J. Chem. Soc. (C)* (1968) 2543
20. B. S. Pedersen, S.-O. Lawesson, *Tetrahedron* **35** (1985) 2433
21. W. Zhang, Y. Henry, *Synlett* (2001) 1129
22. K. T. Potts, S. A. Nye, K. A. Smith, *J. Org. Chem.* **57** (1992) 3895
23. S. Wang, J. P. Fackler, *Chem. Commun.* (1988) 22
24. M. Yokoyama, T. Shiraishi, H. Hatanaka, K. Ogata, *Chem. Commun.* (1985) 1704
25. R. Čmelik, M. Čajan, J. Marek, P. Pazdera, *Collect. Czech. Chem. Commun.* **68** (2003) 1243
26. A. Hordvik, E. Sletten, J. Sletten, *Acta Chem. Scand.* **23** (1969) 1377
27. C. Th. Pedersen, C. Lohse, *J. Chem. Soc., Perkin Trans. 1* (1977) 994
28. G. Ammick, J. Vialle, *Bull. Soc. Chim. Fr.* (1971) 4002.