# Synthesis and Spectral Data of New 1,2-*Bis*-(2-hetaryl-4-oxothiazolidin-3-yl)ethanes and 1,4-*Bis*-(2-hetaryl-4-oxothiazolidin-3-yl)butanes



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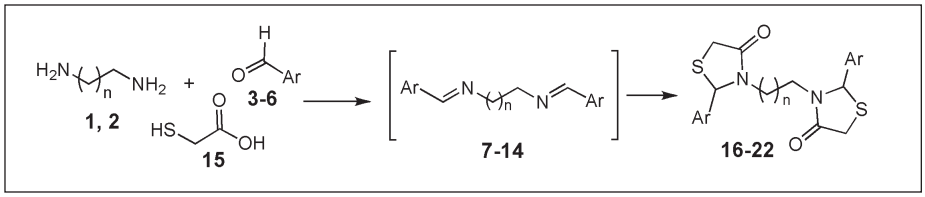


New α,ω-*bis*-(2-hetaryl-4-oxothiazolidin-3-yl)alkanes were prepared *via* a common two step procedure using *N,N-bis*-hetarylidenamines condensation with α-mercaptoacetic acid. The used *bis*-aldimines were obtained from reaction between ethylenediamine or putrescine and benzaldehyde or the isomeric pyridinecarboxyaldehydes. The *bis*-(2-phenyl-4-oxothiazolidin-3-yl)alkanes were prepared by one-pot three component reaction of diamine, aldehyde and α-mercaptoacetic acid under very mild conditions.

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## Introduction.

Thiazolidinones are important heterocyclic compounds, which exhibit a broad range of biological activities [1-4], including interesting profile as fungicidal [5,6], pesticide [7], antibacterial [8,9], anticonvulsant [10], antihistaminic [11], antioxidant [12], anti-inflammatory and antinociceptive [13,14] agents *etc*. As a consequence many different protocols have been developed that allow the synthesis of 4-thiazolidinone skeletons. The method more used employs a two step preparation: reaction of aromatic ketones (aldehydes) and amines and condensation of the prepared Schiff bases and α-mercaptoalkanoic acids [1-3]. However, a one-pot three-component reaction of amine, aldehyde and mercaptoacetic acid is recently emerged as an efficient synthesis of 4-thiazolidinones [15-18]. In both cases the reaction is believed to proceed first *via* an imine formation followed by attack of sulphur nucleophile on the imine carbon and finally intramolecular cyclization with loss of a molecule of water [19,20]. Little is known about α,ω-*bis*-(2-hetaryl-4-oxothiazolidin-3-yl)alkanes [1-4]. However, several studies have revealed their anti-inflammatory, antihistaminic and analgesic activities [21,22]. Moreover, recently, it was found that some *bis*-(2-aryl-4-oxothiazolidin-3-yl)ethanes act as good cyclooxygenase-2 inhibitory agents [23,24].

Based on these facts and in continuation of our research on bioactive heterocycles including thiazolidinone derivatives [25-27], we prepared two new series of 1,2-*bis*-(4-oxothiazolidin-3-yl)ethanes and 1,4-*bis*-(4-oxothiazolidin-3-yl)butanes with phenyl and pyridinyl fragments. Furthermore, having in mind the polyamine properties in living systems as well as the already mentioned thiazolidinone advantages, the incorporation of a diamine moiety between two thiazolidinone rings seems to be a good idea and so does the synthesis of these heterocycles, potentially promising molecules in the bioactive studies against fungi and bacteria. Herein, we describe its synthesis and some physical-chemical properties.

## Results and Discussion.

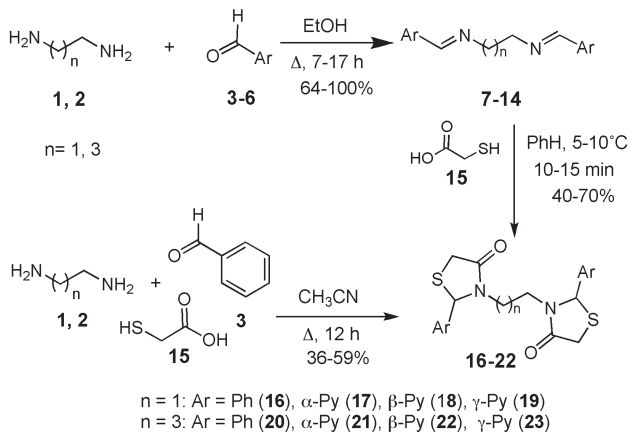
The *N,N-bis*-[phenylmethylen(pyridinylmethylene)]-ethane-1,2-diamines **7-10** and *N,N-bis*-[phenylmethylen (pyridinylmethylene)]butene-1,4-diamines **11-14** used in the preparation of these series were obtained by refluxing for 7 to 17 hours the solution in dry ethanol of the respective diamines (ethylenediamine **1** or putrescine **2**) and aromatic aldehydes (benzaldehyde **3**, pyridinecarboxyaldehydes **4-6**) with the ratio 1:2 of reactants. Almost all *bis*-imines were stable solid products which were easily characterized by the strong and sharp absorption band at 1639-1649 $cm^{-1}$ corresponding to the C=N bonds.

The condensation of the Schiff bases **7-14** with the α-mercaptoacetic acid **15** with the ratio 1:2 by stirring in dry benzene with temperatures between 5 and 10 ºC did not take more than 20 min and allowed us to get the α,ω-*bis*-(2-hetaryl-4-oxothiazolidin-3-yl)alkanes **16-23** as solid products in good yields (Scheme 1).

Finally, the 1,2-*bis*-(2-phenyl-4-oxothiazolidin-3-yl)ethane **16** and the 1,4-*bis*-(2-phenyl-4-oxothiazolidin-3-yl)butane **20** were also obtained *via* the one-pot three-com-

ponent condensation by the reaction of diamines (ethylenediamine, putrescine), benzaldehyde and the mercaptoacetic acid with ratios 1:2.5:2.5 respectively, in refluxing dry acetonitrile for 12 hours to get solid products, which can be filtered and recrystallized in ethanol from the reaction mixture (Scheme 1).

Scheme 1




n = 1: Ar = Ph (**16**), α-Py (**17**), β-Py (**18**), γ-Py (**19**)
n = 3: Ar = Ph (**20**), α-Py (**21**), β-Py (**22**), γ-Py (**23**)

The IR spectra of the compounds **16-23** show the typical C(=O)-N stretching band appearing in the region of 1643-1680 $cm^{-1}$. The strong and sharp band of the azomethine bonds was missing, which was a faithful evidence of the cyclocondensation.

The structure of all the *bis*-thiazolidinones was also confirmed by $^1$H-NMR, $^{13}$C-NMR, DEPT and bi-dimensional techniques as $^1$H,$^1$H-COSY, HMQC and HMBC. These analyses indicated the magnetic non-equivalence in the ethanic fragment protons as in the proton of the chiral C-2 at δ 5.74-5.89 ppm. A doublet is displayed due to its interaction with the proton $H_A$ at C-5.

According to the gc-ms analysis made to the compound **17**, there are two chromatographic peaks with almost equal retention times (40.30 min, 41.81 min), which are sign of corresponding racemate (*2R,2'R/2S,2'S)* and *meso*-form (*2R,2'S-meso*), as has been already proved [21-23]. But not only the *bis*-thiazolidinone **17** showed diastereoisomeric presence, the gc analysis of **16-19** exhibits broad chromatographic peaks, typical for overlapped peaks with very similar retention times. We were unable to separate these mixtures of isomers by conventional column chromatography.

The NMR spectra showed a set of signals for the corresponding protons of thiazolidinone rings and a resonance system AA'BB' for the ethanic fragment protons of non-first-order spectra. The $^1$H-NMR spectra of the compounds **16-19** displayed a doublet of doublets at δ 3.84-3.94 ppm due to the methylene proton $H_A$ at C-5 because of its interaction with the geminal proton $H_B$ and the proton at the chiral C-2; doublet of doublets at δ 3.59-3.71 ppm due to the methylene proton $H_B$ at C-5 because of its interaction with the geminal proton $H_A$ and a diastereotopic proton $H_A$ (6´-$H_A$) at the C-1´ of the ethylene fragment. This last proton displayed a doublet of doublets or a multiplet at δ 2.55-2.79 ppm because of its interaction with the geminal proton $H_B$ (6´-$H_B$) and the proton $H_B$ at the C-5. The 6´-$H_B$ proton at the C-1´ aliphatic chain suffered the anisotropic effect from the near amide group or aryl substituents and it went to down field at δ 3.37-4.01 ppm appearing overlapped with $H_B$ as a multiplet. These geminal protons of each methylene group reside in magnetic non-equivalent environments. The $^1$H-NMR spectra of the compounds **20-23** basically displayed similar shifts plus a multiplet at δ 1.14-1.30 ppm due to the methylene protons (7-$H_A$, 7-$H_B$) of the butane fragment.

We found also *anisochronous* chemical shifts along the whole molecules not only by the ethanic fragment protons but also the heterocyclic ring protons that proves the existence of a mixture of isomers.

The cross-peak in the COSY two dimensional spectrum was very useful in assigning signals. As an example, the compound **18** displays signals at 2.73 ppm, which present contours correlated at 3.55 ppm revealing a AA'BB' system. The contours corresponding at 3.66 ppm are correlated with the signals displayed at 3.92 ppm, these are heterocyclic 5-$CH_2$ signals, an AB system, and the last one (3.92 ppm) is also correlated with the signal at 5.82 ppm, the chiral proton. In turn there are contours that correlate this chiral proton with signals of two aromatic protons, a doublet of doublets at 7.43 and a multiplet at 8.57-8.58 ppm. The remaining aromatic proton contours of the pyridin-3-yl fragments behave as expected.

The HMQC two dimensional spectrum of **20** presents contours correlating the carbon signals at 24 ppm and the proton signals of the multiplet at 1.41-1.43 ppm and the carbon signal at 42.9 ppm with the multiplets at 2.49-2.51 and 3.51-3.70 ppm, exposing the presence of the alkanic fragment. The contours correlating the signal at 37.9 ppm and the multiplets at 3.51-3.70 and 3.81-3.89 ppm belong to the diastereotopic 5-$CH_2$ of the thiazolidinone ring and two smaller contours correlate the signals at 64 and 5.82 ppm, the chiral 2-CH. The aromatic carbons signals between 126.9 and 128.9 ppm are correlated with the aromatic proton multiplet signal at 7.32-7.41. The $^{13}$C-nmr shows the carbonyl carbon signals at 171.2 ppm.

The three-dimensional molecular geometry adopted for these *bis*-thiazolidinones depicted in Figure 1 was deduced from computational geometry programs of the type HYPERCHEM 7.0 with a molecular mechanic optimization MM+. From them, the most probable conformation acquired for the compounds **18** and **20** can be noted, named as “exo”- conformation, in which the phenyl groups are spaced at the maximal distance in a different plane.

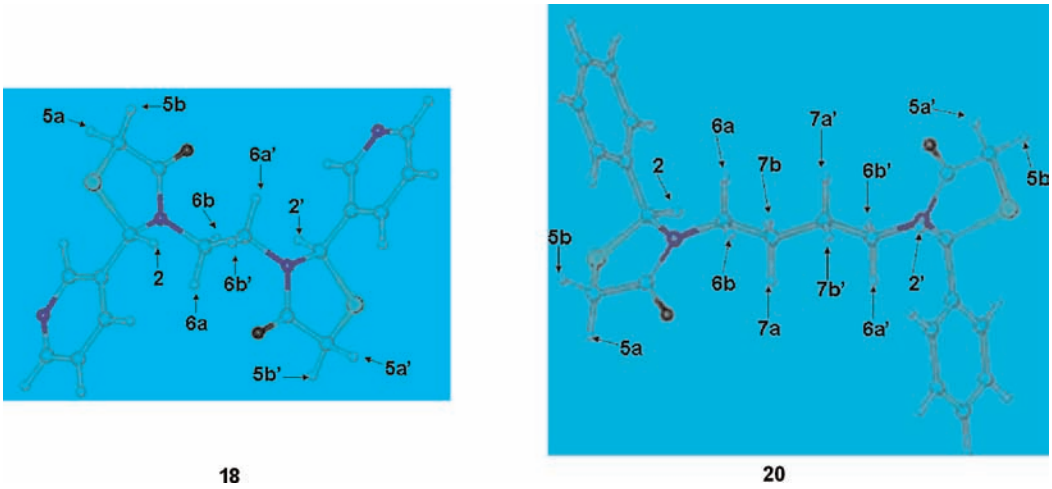



Figure 1. Structure of compounds **18** and **20**.

The antifungal and antibacterial properties of all obtained α,ω-*bis*-(2-hetaryl-4-oxothiazolidin-3-yl)alkanes were not evaluated in full measure due to the poor solubility of these compounds. However, preliminary assays showed that compound **23** was active against the fungi *Penicillium notatum* with a diameter of inhibition zone of 30 mm per 50 µg, and compound **20** against the bacteria *Bacillus brevis* with a diameter of inhibition zone of 10 mm per 100 µg [28].

## EXPERIMENTAL

General Method. The same experimental techniques were used as was previously reported [27].

General Procedure for Reaction of Diamine and Pyridinecarboxyaldehydes (or Benzaldehyde).

To diamine (1 mmol) in dry ethanol (25-30 ml) was added the hetaryl aldehyde (2 mmol). The reaction mixture was stirred and refluxed for 7 to 17 hours. The crystalline solid products were collected by filtration and washed with heptanes. The liquid products were concentrated by distilling the ethanol off.

*N,N-Bis*-(phenylmethylen)ethane-1,2-diamine (**7**).

This compound was obtained in 100% yield as a yellow solid, mp 37-39 ºC; ir (potassium bromide): ν =CH 2847, ν C=N 1643 $cm^{-1}$; gc-ms: $t_R$= 25.05 min, ms: m/z 236 (molecular ion).

*Anal*. Calcd. for $C_{16}H_{16}N_2$: C, 81.32%; H, 6.82%; N, 11.85%. Found: C, 81.39%; H, 6.77%; N, 11.84%.

*N,N-Bis*-(pyridin-2-ylmethylene)ethane-1,2-diamine (**8**).

This compound was obtained in 86% yield as a dark red liquid; ir (potassium bromide): ν =CH 2916, ν C=N 1649 $cm^{-1}$; gc-ms: $t_R$= 25.72 min, ms: m/z 238 (molecular ion).

*Anal*. Calcd. for $C_{14}H_{14}N_4$: C, 70.57%; H, 5.92%; N, 23.51%. Found: C, 70.47%; H, 6.02%; N, 23.51%.

*N,N'-Bis*-(pyridin-3-ylmethylene)ethane-1,2-diamine (**9**).

This compound was obtained in 100% yield as a yellow solid, mp 84-85 ºC; ir (potassium bromide): ν =CH 2848, ν C=N 1647 $cm^{-1}$.

*Anal*. Calcd. for $C_{14}H_{14}N_4$: C, 70.57%; H, 5.92%; N, 23.51%. Found: C, 70.65%; H, 6.07%; N, 23.28%

*N,N-Bis*-(pyridin-4-ylmethylene)ethane-1,2-diamine (**10**).

This compound was obtained in 71% yield as a white solid, mp 134-135 ºC; ir (potassium bromide): ν =CH 2844, ν C=N 1649 $cm^{-1}$; gc-ms: $t_R$= 27.42 min, ms: m/z 238 (molecular ion).

*Anal*. Calcd. for $C_{14}H_{14}N_4$: C, 70.57%; H, 5.92%; N, 23.51%. Found: C, 70.69%; H, 6.12%; N, 23.29%

*N,N-Bis*-(phenylmethylene)butane-1,4-diamine (**11**).

This compound was obtained in 100% yield as a yellow liquid; ir (potassium bromide): ν =CH 2925, ν C=N 1645 $cm^{-1}$; gc-ms: $t_R$= 29.28 min, ms: m/z 264 (molecular ion).

*Anal*. Calcd. for $C_{18}H_{20}N_2$: C, 81.78%; H,7.63%; N, 10.60%. Found: C, 81.85%; H,7.54%; N, 10.61%.

*N,N-Bis*-(pyridin-2-ylmethylene)butane-1,4-diamine (**12**).

This compound was obtained in 64% yield as an orange solid, mp 41-42 ºC; ir (potassium bromide): ν =CH 2912, ν C=N 1639 $cm^{-1}$.

*Anal*. Calcd. for $C_{16}H_{18}N_4$: C, 72.15%; H, 6.81%; N, 21.04%. Found: C, 72.02%; H, 6.91%; N, 21.03%.

*N,N-Bis*-(pyridin-3-ylmethylene)butane-1,4-diamine (**13**).

This compound was obtained in 100% yield as a yellow viscous liquid; ir (potassium bromide): ν =CH 2933, ν C=N 1647 $cm^{-1}$.

*Anal*. Calcd. for $C_{16}H_{18}N_4$: C, 72.15%; H, 6.81%; N, 21.04%. Found: C, 72.23%; H, 6.65%; N, 21.22%.

*N,N-Bis*-(pyridin-4-ylmethylene)butane-1,4-diamine (**14**).

This compound was obtained in 97% yield as a white solid, mp 73-74 ºC; ir (potassium bromide): ν =CH 2941, ν C=N 1643 $cm^{-1}$.

*Anal*. Calcd. for $C_{16}H_{18}N_4$: C, 72.15%; H, 6.81%; N, 21.04%. Found: C, 72.01%; H, 6.98%; N, 21.01%.

General Procedure for Reaction of *Bis*-aldimines (**7-14**) with α-Mercaptoacetic Acid.

A mixture of the appropriate *bis*-aldimine (**7-14**) (4.20 mmoles) and the α-mercaptoacetic acid (8.40 mmoles) was

stirred in dry benzene in ice cold bath for 15-20 min. The benzene was distilled off and the solid *bis*-thiazolidinones (**16-23**) were obtained from ethanol recrystallization.

1,2-*Bis*-(2-phenyl-4-oxo-1,3-thiazolidin-3-yl)ethane (**16**).

This compound was obtained in 68% yield as a white solid, mp 155-157 ºC; ir (potassium bromide): ν -$CH_2$- 2924, ν C(=O)-N 1666 $cm^{-1}$; $^1H$ nmr (DMSO-$d_6$): δ 2.72-2.79 (m, 2H, $CH_2CH_2$), 3.62-3.64 (m, 2H, $CH_2CH_2$), 3.71 (d, *J*= 16.0 Hz, 2H, 5-$CH_2$; $H_A$), 3.84 (ddd, *J*= 2.0, 11.0, 16.0 Hz, 2H, 5-$CH_2$; $H_B$), 5.89 (d, *J*= 2.0 Hz, 2H, 2-CH), 7.30-7.42 (m, 10H, $H_{Ph}$); $^{13}C$ nmr (100 MHz): δ 171.4 (2C=O), 140 (2C, Ph), 128.9 (4C, Ph), 127.2 (4C, Ph), 127 (2C, Ph), 62.4 (2C, 2-CH), 43.3 (2C, $CH_2CH_2$), 32 ppm (2C, 5-$CH_2$); COSY correlations [$\delta_H/\delta_H$ (H/H)]: 2.72-2.79/3.62-3.64 ($2H_A$, $CH_2CH_2/2H_B$, $CH_2CH_2$), 3.62-3.64/3.84 ($2H_B$, $CH_2CH_2/2H_B$, 5-$CH_2$), 3.71/3.84 ($2H_A$, 5-$CH_2/2H_B$, 5-$CH_2$), 3.84/5.89 ($2H_B$, 5-$CH_2$/2H, 2-CH); HMQC correlations [$\delta_C/\delta_H$ (C/H)]: 32.0/3.71 (2C/$2H_A$, 5-$CH_2$), 32.0/3.84 (2C/$2H_B$, 5-$CH_2$), 43.3/2.72-2.79 (2C/$2H_A$, $CH_2CH_2$), 43.3/3.62-3.64 (2C/$2H_B$, $CH_2CH_2$), 62.4/5.89 (2C/2H, 2-CH), 127/7.30-7.42 (2C/2H, Ph), 127.2/7.30-7.42 (4C/4H, Ph), 128.9/7.30-7.42 (4C/4H, Ph); gc-ms: $t_R$= 43.66 min, ms: m/z 384 (molecular ion).

*Anal*. Calcd. for $C_{20}H_{20}N_2O_2S_2$: C, 62.47%; H, 5.24%; N,7.29%. Found: C, 62.29%; H, 5.37%; N,7.01%.

1,2-*Bis*-[2-(pyridin-2-yl)-4-oxo-1,3-thiazolidin-3-yl]ethane (**17**).

This compound was obtained in 40% yield as a brown solid, mp 167-169 ºC; ir (potassium bromide): ν -$CH_2$- 2941, ν C(=O)-N 1680 $cm^{-1}$; $^1H$ nmr (deuteriumcloroform): δ 2.71 (dd, *J*= 8.0, 18.0 Hz, 2H, $CH_2CH_2$), 3.65 (d, *J*= 16.0 Hz, 2H, 5-$CH_2$; $H_A$), 3.84 (dd, *J*= 2.0, 16.0 Hz, 2H, 5-$CH_2$; $H_B$), 3.93-4.00 (m, 2H, $CH_2CH_2$), 5.87 (d, *J*= 2.0 Hz, 2H, 2-CH), 7.22 (ddd, *J*= 2.0, 5.0, 8.0 Hz, 2H, $H_{Py}$), 7.28 (dd, *J*= 2.0, 16.0 Hz, 2H, $H_{Py}$), 7.71 (ddd, *J*= 2.0, 8.0, 16.0 Hz, 2H, $H_{Py}$), 8.5 (dd, *J*= 2.0, 5.0 Hz, 2H, $H_{Py}$); $^{13}C$ nmr (100 MHz): δ 172.5 (2C=O), 158.6 (2C, Py), 150.1 (2C, Py), 137.3 (2C, Py), 123.6 (2C, Py), 121.1 (2C, Py), 63.7 (2C, 2-CH), 39.9 (2C, $CH_2CH_2$), 32.4 ppm (2C, 5-$CH_2$); COSY correlations [$\delta_H/\delta_H$ (H/H)]: 2.71/3.93-4.0 ($2H_A$, $CH_2CH_2/2H_B$, $CH_2CH_2$), 2.71/7.28 ($2H_A$, $CH_2CH_2$/2H, Py), 3.65/3.84 ($2H_A$, 5-$CH_2/2H_B$, 5-$CH_2$), 3.84/5.87 ($2H_B$, 5-$CH_2$/2H, 2-CH), 7.22/7.28 (2H, Py/2H, Py), 7.22/7.71 (2H, Py/2H, Py), 7.22/8.5 (2H, Py/2H, Py), 7.28/7.71 (2H, Py/2H, Py), 7.71/8.5 (2H, Py/2H, Py); HMQC correlations [$\delta_C/\delta_H$ (C/H)]: 32.4/3.65 (2C/$2H_A$, 5-$CH_2$), 32.4/3.84 (2C/$2H_B$, 5-$CH_2$), 39.9/2.71 (2C/$2H_A$, $CH_2CH_2$), 39.9/3.93-4.0 (2C/$2H_B$, $CH_2CH_2$), 63.7/5.87 (2C/2H, 2-CH), 121.1/7.28 (2C/2H, Py), 123.6/7.22 (2C/2H, Py), 137.3/7.71 (2C/2H, Py), 150.1/8.5 (2C/2H, Py); gc-ms: $t_{R1}$= 40.30 min, $t_{R2}$= 41.81 min, ms: m/z 386 (molecular ion).

*Anal*. Calcd. for $C_{18}H_{18}N_4O_2S_2$: C, 55.94%; H, 4.69%; N, 14.50%. Found: C, 56.05%; H, 4.57%; N, 14.66%.

1,2-*Bis*-[2-(pyridin-3-yl)-4-oxo-1,3-thiazolidin-3-yl]ethane (**18**).

This compound was obtained in 40% yield as a white solid, mp 198-200 ºC; ir (potassium bromide): ν -$CH_2$- 2930, ν C(=O)-N 1670 $cm^{-1}$; $^1H$ nmr (DMSO-$d_6$): δ 2.73 (dd, *J*= 5.8, 14.0 Hz, 2H, $CH_2CH_2$), 3.55 (dd, *J*= 5.8, 14.2 Hz, 2H, $CH_2CH_2$), 3.66 (d, *J*= 15.6 Hz, 2H, 5-$CH_2$, $H_A$), 3.92 (dd, *J*= 1.4, 15.4 Hz, 2H, 5-$CH_2$, $H_B$), 5.82 (d, *J*= 1.4 Hz, 2H, 2-CH), 7.43 (dd, *J*= 5.2, 7.9 Hz, 2H, $H_{Py}$), 7.78-7.81 (m, 2H, $H_{Py}$), 8.57-8.58 (m, 4H, $H_{Py}$); $^{13}C$ nmr (100 MHz): δ 171 (2C=O), 150 (2C, Py), 148.4 (2C, Py), 135.6 (2C, Py), 134.7 (2C, Py), 123.9 (2C, Py), 60 (2C, 2-CH), 39.5 (2C, $CH_2CH_2$), 31.6 ppm (2C, 5-$CH_2$); COSY correlations [$\delta_H/\delta_H$ (H/H)]: 2.73/3.55 ($2H_A$, $CH_2CH_2/2H_B$, $CH_2CH_2$), 3.66/3.92 ($2H_A$, 5-$CH_2/2H_B$, 5-$CH_2$), 3.92/5.82 ($2H_B$, 5-$CH_2$/2H, 2-CH), 5.82/7.43 (2H, 2-CH/2H, Py), 5.82/8.57-8.58 (2H, 2-CH/4H, Py), 7.43/7.78-7.81 (2H, Py/2H, Py), 7.43/8.57-8.58 (2H, Py/4H, Py), 7.78-7.81/8.57-8.58 (2H, Py/4H, Py); HMQC correlations [$\delta_C/\delta_H$ (C/H)]: 31.6/3.66 (2C/$2H_A$, 5-$CH_2$), 31.6/3.92 (2C/$2H_B$, 5-$CH_2$), 39.5/2.73 (2C/$2H_A$, $CH_2CH_2$), 39.5/3.55 (2C/$2H_B$, $CH_2CH_2$), 60.0/5.82 (2C/2H, 2-CH), 123.9/7.43 (2C/2H, Py), 134.7/7.9 (2C/2H, Py), 148.4/8.57-8.58 (2C/2H, Py), 150/8.57-8.58 (2C/2H, Py).

*Anal*. Calcd. for $C_{18}H_{18}N_4O_2S_2$: C, 55.94%; H, 4.69%; N, 14.50%. Found: C, 56.07%; H, 4.58%; N, 14.76%.

1,2-*Bis*-[2-(pyridin-4-yl)-4-oxo-1,3-thiazolidin-3-yl]ethane (**19**).

This compound was obtained in 33% yield as a white solid, mp 224-225 ºC; ir (potassium bromide): ν -$CH_2$- 2933, ν C(=O)-N 1670 $cm^{-1}$; $^1H$ nmr (DMSO-$d_6$): δ 2.71 (dd, *J*= 5.8, 14.0 Hz, 2H, $CH_2CH_2$), 3.59-3.63 (m, 4H, 5-$CH_2$; $H_A$, $CH_2CH_2$), 3.85 (dd, *J*= 1.8, 16.0 Hz, 2H, 5-$CH_2$; $H_B$), 5.74 (d, *J*= 1.8 Hz, 2H, 2-CH), 7.31 (dd, *J*= 1.2, 4.5 Hz, 4H, $H_{Py}$), 8.55 (dd, *J*= 1.2, 4.5 Hz, 4H, $H_{Py}$); $^{13}C$ nmr (100 MHz): δ 171.2 (2C=O), 150.2 (4C, Py), 149 (2C, Py), 121.4 (4C, Py), 60.8 (2C, 2-CH), 40.1 (2C, $CH_2CH_2$), 31.3 ppm (2C, 5-$CH_2$); COSY correlations [$\delta_H/\delta_H$ (H/H)]: 2.71/3.59-3.63 ($2H_A$, $CH_2CH_2/2H_B$, $CH_2CH_2$), 2.71/7.31 ($2H_A$, $CH_2CH_2$/4H, Py), 3.59-3.63/3.85 ($2H_A$, 5-$CH_2/2H_B$, 5-$CH_2$), 3.85/5.74 ($2H_B$, 5-$CH_2$/2H, 2-CH), 5.74/7.31 (2H, 2-CH/4H, Py), 7.31/8.55 (4H, Py/4H, Py); HMQC correlations [$\delta_C/\delta_H$ (C/H)]: 31.3/3.59-3.63 (2C/$2H_A$, 5-$CH_2$), 31.3/3.85 (2C/$2H_B$, 5-$CH_2$), 40.1/2.71 (2C/$2H_A$, $CH_2CH_2$), 40.1/3.59-3.63 (2C/$2H_B$, $CH_2CH_2$), 60.8/5.74 (2C/2H, 2-CH), 121.4/7.31 (4C/4H, Py), 150.2/8.55 (4C/4H, Py); ms: m/z 386 (molecular ion).

*Anal*. Calcd. for $C_{18}H_{18}N_4O_2S_2$: C, 55.94%; H, 4.69%; N, 14.50%. Found: C, 55.78%; H, 4.55%; N, 14.63%.

1,4-*Bis*-(2-phenyl-4-oxo-1,3-thiazolidin-3-yl)butane (**20**).

This compound was obtained in 44% yield as a white solid, mp 168-170 ºC; ir (potassium bromide): ν -$CH_2$- 2931, ν C(=O)-N 1666 $cm^{-1}$; $^1H$ nmr (DMSO-$d_6$): δ 1.41-1.43 (m, 4H, $CH_2(CH_2)_2CH_2$), 2.49-2.51 (m, 2H, $CH_2(CH_2)_3$), 3.51-3.70 (m, 4H, $CH_2(CH_2)_3$, 5-$CH_2$; $H_A$), 3.81-3.89 (m, 2H, 5-$CH_2$; $H_B$), 5.82 (d, *J*= 1.0 Hz, 2H, 2-CH), 7.32-7.41 (m, 10H, $H_{Ph}$); $^{13}C$ nmr (100 MHz): δ 171.2 (2C=O), 140.3 (2C, Ph), 128.9 (4C, Ph), 128.9 (4C, Ph), 126.9 (2C, Ph), 64.0 (2C, 2-CH), 42.9 (2C, $CH_2(CH_2)_3$), 37.9 (2C, 5-$CH_2$), 24.0 ppm (2C, $CH_2(CH_2)_2CH_2$); COSY correlations [$\delta_H/\delta_H$ (H/H)]: 1.41-1.43/2.49-2.51 (4H, $CH_2(CH_2)_2CH_2/2H_A$, $CH_2(CH_2)_3$), 1.41-1.43/3.51-3.70 (4H, $CH_2(CH_2)_2CH_2/2H_B$, $CH_2(CH_2)_3$), 2.49-2.51/3.51-3.70 ($2H_A$, $CH_2(CH_2)_3/2H_B$, $CH_2(CH_2)_3$), 3.51-3.70/3.81-3.89 ($2H_A$, 5-$CH_2/2H_B$, 5-$CH_2$), 3.81-3.89/5.82 ($2H_B$, 5-$CH_2$/2H, 2-CH); HMQC correlations [$\delta_C/\delta_H$ (C/H)]: 24.0/1.41-1.43 (2C/4H, $CH_2(CH_2)_2CH_2$), 37.9/3.51-3.70 (2C/$2H_A$, 5-$CH_2$), 37.9/3.81-3.89 (2C/$2H_B$, 5-$CH_2$), 42.9/2.49-2.51 (2C/$2H_A$, $CH_2(CH_2)_3$), 42.9/3.51-3.70 (2C/$2H_B$, $CH_2(CH_2)_3$), 64.0/5.82 (2C/2H, 2-CH), 126.9/7.32-7.41 (2C/2H, Ph), 128.9/7.32-7.41 (4C/4H, Ph), 128.9/7.32-7.41 (4C/4H, Ph).

*Anal*. Calcd. for $C_{22}H_{24}N_2O_2S_2$: C, 64.05%; H, 5.86%; N, 6.79%. Found: C, 64.17%; H, 5.77%; N, 6.84%.

1,4-Bis-[2-(pyridin-2-yl)-4-oxo-1,3-thiazolidin-3-yl]butane (**21**).

This compound was obtained in 50% yield as a yellow solid, mp 162-163 ºC; ir (potassium bromide): ν -$CH_2$- 2927, ν C(=O)-N 1643 $cm^{-1}$; $^1H$ nmr (DMSO-$d_6$): δ 1.23-1.30 (m, 4H,

$CH_2(CH_2)_2CH_2$), 2.49-2.59 (m, 2H, $CH_2(CH_2)_3$), 3.43-3.51 (m, 2H, $CH_2(CH_2)_3$), 3.55-3.62 (m, 2H, 5-$CH_2$; $H_A$), 3.82 (d, *J*= 15.0 Hz, 2H, 5-$CH_2$; $H_B$), 5.79 (d, *J*= 1.2 Hz, 2H, 2-CH), 7.32-7.36 (m, 2H, $H_{Py}$), 7.38 (d, *J*= 8.0 Hz, 2H, $H_{Py}$), 7.37 (m, 2H, $H_{Py}$), 8.54 (dd, *J*= 1.5, 4.5 Hz, 2H $H_{Py}$); $^{13}$C nmr (100 MHz): δ 171.2 (2C=O), 159.3 (2C, Py), 149.7 (2C, Py), 137.4 (2C, Py), 123.5 (2C, Py), 121.0 (2C, Py), 62.6 (2C, 2-CH), 42.2 (2C, $CH_2(CH_2)_3$), 31.6 (2C, 5-$CH_2$), 23.8 ppm (2C, $CH_2(CH_2)_2CH_2$); COSY correlations [$\delta_H/\delta_H$ (H/H)]: 1.23-1.30/2.49-2.59 (4H, $CH_2(CH_2)_2CH_2/2H_A$, $CH_2(CH_2)_3$), 1.23-1.30/3.43-3.51 (4H, $CH_2(CH_2)_2CH_2/2H_B$, $CH_2(CH_2)_3$), 2.49-2.59/3.43-3.61 ($2H_A$, $CH_2(CH_2)_3/2H_B$, $CH_2(CH_2)_3$), 3.55-3.62/3.82 ($2H_A$, 5-$CH_2/2H_B$, 5-$CH_2$), 3.82/5.79 ($2H_B$, 5-$CH_2$/2H, 2-CH), 7.32-7.36/7.38 (2H, Py/2H, Py), 7.32-7.36/7.37 (2H, Py/2H, Py), 7.32-7.36/8.54 (2H, Py/2H, Py), 7.38/7.37 (2H, Py/2H, Py); HMQC correlations [$\delta_C/\delta_H$ (C/H)]: 23.8/1.23-1.30 (2C/4H, $CH_2(CH_2)_2CH_2$), 31.6/3.55-3.62 (2C/$2H_A$, 5-$CH_2$), 31.6/3.82 (2C/$2H_B$, 5-$CH_2$), 42.2/2.49-2.59 (2C/$2H_A$, $CH_2(CH_2)_3$), 42.2/3.43-3.51 (2C/$2H_B$, $CH_2(CH_2)_3$), 62.6/5.79 (2C/2H, 2-CH), 121/7.38 (2C/2H, Py), 123.5/7.32-7.36 (2C/2H, Py), 137.4/7.37 (2C/2H, Py), 149.7/8.54 (2C/2H, Py).

*Anal*. Calcd. for $C_{20}H_{22}N_4O_2S_2$: C, 57.95%; H, 5.35%; N, 13.52%. Found: C, 58.13%; H, 5.21%; N, 13.77%.

1,4-*Bis*-[2-(pyridin-3-yl)-4-oxo-1,3-thiazolidin-3-yl]butane (**22**).

This compound was obtained in 40% yield as a yellow solid, mp 143-145 ºC; ir (potassium bromide): ν -$CH_2$- 2928, ν C(=O)-N 1643 cm$^{-1}$; $^1$H nmr (DMSO-$d_6$): δ 1.14-1.30 (m, 4H, $CH_2(CH_2)_2CH_2$), 2.55-2.60 (m, 2H, $CH_2(CH_2)_3$), 3.37-3.43 (m, 2H, $CH_2(CH_2)_3$), 3.65 (d, *J*= 15.5 Hz, 2H, 5-$CH_2$; $H_A$), 3.94 (dd, *J*= 1.0, 15.5 Hz, 2H, 5-$CH_2$; $H_B$), 5.83 (d, *J*= 1.0 Hz, 2H, 2-CH), 7.41-7.45 (m, 2H, $H_{Py}$), 7.78-7.81 (m, 2H, $H_{Py}$), 8.55-8.58 (m, 4H, $H_{Py}$); $^{13}$C nmr (100 MHz): δ 170.5 (2C=O), 149.9 (2C, Py), 148.2 (2C, Py), 136.3 (2C, Py), 134.6 (2C, Py), 124 (2C,Py), 59.6 (2C, 2-CH), 41.9 (2C, $CH_2(CH_2)_3$), 31.7 (2C, 5-$CH_2$), 23.6 ppm (2C, $CH_2(CH_2)_2CH_2$); COSY correlations [$\delta_H/\delta_H$ (H/H)]: 1.14-1.30/2.55-2.60 (4H, $CH_2(CH_2)_2CH_2/2H_A$, $CH_2(CH_2)_3$), 1.14-1.30/3.37-3.43 (4H, $CH_2(CH_2)_2CH_2/2H_B$, $CH_2(CH_2)_3$), 2.55-2.60/3.37-3.43 ($2H_A$, $CH_2(CH_2)_3/2H_B$, $CH_2(CH_2)_3$), 3.65/3.94 ($2H_A$, 5-$CH_2/2H_B$, 5-$CH_2$), 3.94/5.83 ($2H_B$, 5-$CH_2$/2H, 2-CH), 5.83/7.41-7.45 (2H, 2-CH/2H, Py), 7.41-7.45/7.78-7.81 (2H, Py/2H, Py), 7.41-7.45/8.55-8.58 (2H, Py/4H, Py), 7.78-7.81/8.55-8.58 (2H, Py/4H, Py); HMQC correlations [$\delta_C/\delta_H$ (C/H)]: 23.6/1.14-1.30 (2C/4H, $CH_2(CH_2)_2$-$CH_2$), 31.7/3.65 (2C/$2H_A$, 5-$CH_2$), 31.7/3.94 (2C/$2H_B$, 5-$CH_2$), 41.9/2.55-2.60 (2C/$2H_A$, $CH_2(CH_2)_3$), 41.9/3.37-3.43 (2C/$2H_B$, $CH_2(CH_2)_3$), 59.6/5.83 (2C/2H, 2-CH), 124/7.41-7.45 (2C/2H, Py), 134.6/7.78-7.81 (2C/2H, Py), 148.2/8.55-8.58 (2C/4H, Py), 149.9/8.55-8.58 (2C/4H, Py).

*Anal*. Calcd. for $C_{20}H_{22}N_4O_2S_2$: C, 57.95%; H, 5.35%; N, 13.52%. Found: C, 58.14%; H, 5.23%; N, 13.44%.

1,4-*Bis*-[2-(pyridin-4-yl)-4-oxo-1,3-thiazolidin-3-yl]butane (**23**).

This compound was obtained in 40% yield as a white solid, mp 164-166 ºC; ir (potassium bromide): ν -$CH_2$- 2949, ν C(=O)-N 1720 cm$^{-1}$.

*Anal*. Calcd. for $C_{20}H_{22}N_4O_2S_2$: C, 57.95%; H, 5.35%; N, 13.52%; O, 7.72%; S, 15.47%. Found: C, 58.09%; H, 5.47%; N, 13.33%.

General Procedure for One-Pot Three-Component Reaction of Diamine with Benzaldehyde and α-Mercaptoacetic Acid.

The appropriate diamine (1.0 mmol) and aldehyde (2.5 mmol) were stirred and refluxed in acetonitrile for 1 hour, followed by addition of mercaptoacetic acid (2.5 mmol). The reaction mixture was stirred and refluxed for 12 more hours. The precipitate product was filtered and the filtrate was concentrated. The residue was taken up with ethanol, where the remainder of product crystallized. After the filtered precipitate was washed with ethanol and dried to give the *bis*-thiazolidinones **16** and **20** in 59 and 36% yields, respectively.

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[28] For example, comp. **20** had diameter of growth inhibition zone of 10 mm at 100 μg/disk for *B. brevis*. Chlorophenicol inhibition was 25 mm. The biological results about antiparasitic activities of these α,β-*bis*-(2-hetaryl-4-oxothiazolidin-3-yl)alkanes will be published elsewhere.