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A NOVEL SYNTHESIS OF 1,4-Bis(THIOPYRANO[2,3-*d*] THIAZOLYL) BENZENE DERIVATIVES

Nadia Hanafy Metwally

Department of Chemistry, Faculty of Science, University of Cairo, Giza, Egypt
E-mail: nhmmohamed@yahoo.com

Abstract - The novel 5-(4-formylphenyl)methylene-thiazolidine-2,4-dithione **3** and 1,4-bis[(4-thioxo-thiazolidinyl)methylene]benzene derivatives **4a,b** were synthesized by condensation of each of 4-thioxo-thiazolidin-2-one (**1a**) and thiazolidine-2,4-dithione (**1b**) with terephthalaldehyde (**2**), in good yields depending on the molar ratio of **1** to **2**. The cycloaddition of the newly synthesized compounds to *N*-arylmaleimides, ethyl acrylate, *ω*-nitrostyrene and malononitrile was studied. The structures of the synthesized compounds were established by elemental analyses and spectral data.

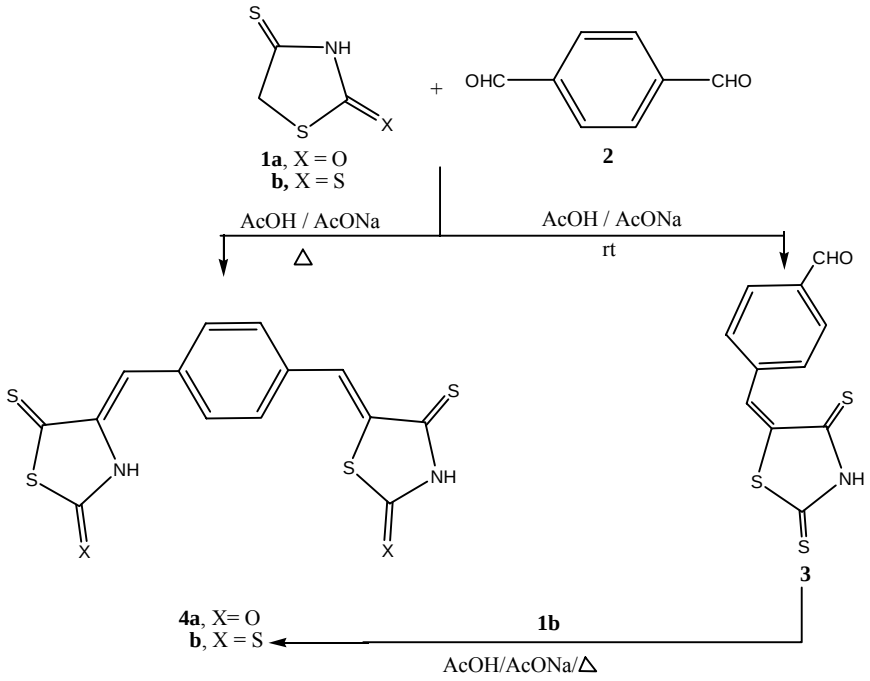
INTRODUCTION

4-Thiazolidinone derivatives are known to possess various biological activity such as hypnotic,[1] anesthetic,[2] antifungal,[3] anathelmintic[4] and antiviral agents[5] as well as CNS[6] stimulants. Moreover, the heterocyclic systems having both thiazolidine and thiopyrano moieties were found to be important in the field of medicinal chemistry.[7-9] Recently, it was reported that the bis-heterocyclic compounds exhibit much higher antibacterial activity than heterocyclic compounds[10,11] as well as various biological activities[12-16] including antibacterial, fungicidal and tuberculostatic, in addition, much higher antibacterial activity than heterocyclic compounds.[15,16] In view of this and in the course of our studies on the chemistry of 4-thiazolidinones,[17-24] I found the synthetic routs of the novel 5-arylmethylene-thiazolidine-2,4-dithione **3** and 1,4-bis(4-thioxo-thiazolidinylmethylene)benzene derivati-ves **4a,b** which can be used as active heterodiene components in hetero-Diels-Alder reactions. The latter reaction led to formation of the hitherto unknown compounds which containing two thiopyrano-thiazole units, starting from 4-thioxo-thiazolidinones and terephthalaldehyde.

RESULTS AND DISCUSSION

The condensation of equimolar amounts of thiazolidine-2,4-dithione (**1b**) and terephthalaldehyde (**2**) in glacial acetic acid and in the presence of sodium acetate at room temperature yielded a brown solid of mp 226 ^{o}C, in good yield. The structure of the isolated product was established based on elemental

analyses and spectral data. The IR spectrum of this product showed a characteristic absorption band at 3028 cm^{-1} assignable to NH. In addition, the characteristic absorption bands at 2855, 2738 and 1686 cm^{-1} due to the aldehydic group appeared in the IR spectrum. Its ^1H NMR spectrum revealed a singlet signal at δ 8.11 due to olefinic proton, a singlet signal at δ 10.03 exhibited by the aldehydic CH proton and a D_2O-exchangeable singlet signal at δ 13.73 attributed to NH proton, beside the other expected signals due to the aromatic protons. In addition, the mass spectrum of the product gave the molecular ion peak at *m/z* 265 which is exactly consistent with the molecular weight of structure **3**. Based on the elemental analysis and spectral data, structure **3** was assigned to the product **3** (see EXPERIMENTAL and Scheme 1).

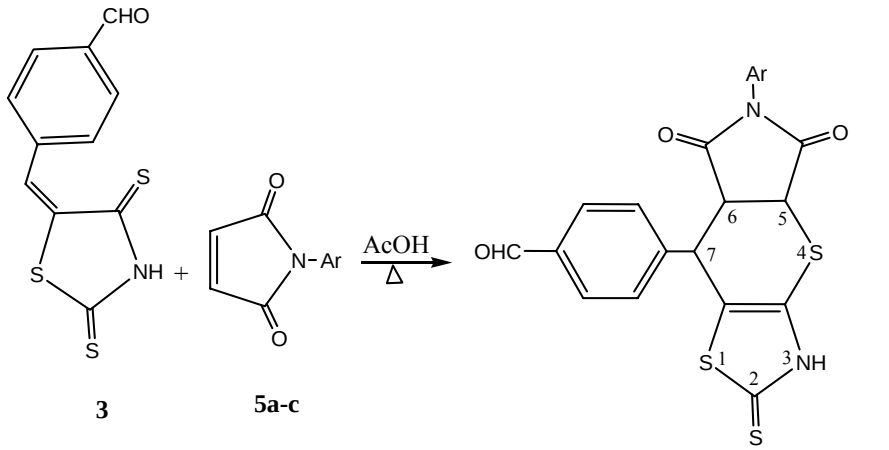


Scheme 1

On the other hand, condensation of terephthalaldehyde with two equivalents of each of 4-thioxo-thiazolidin-2-one (**1a**) and thiazolidine-2,4-dithione (**1b**) in refluxing glacial acetic acid and in the presence of sodium acetate afforded the highly coloured products, bis-arylidenes **4a,b**, respectively, in good yields. The structures of the bis-products **4a,b** were confirmed based on elemental analyses and spectral data. For example, the IR spectrum of **4a** showed characteristic absorption bands at 3071 and 1724 cm^{-1} assignable to NH and C=O groups. Its ^1H NMR spectrum revealed a singlet signal at δ 8.07 due to olefinic proton and a D_2O-exchangeable singlet signal at δ 13.75 attributed to NH proton, beside the other expected signals. In addition, the mass spectrum of **4a** gave the expected molecular ion peak at *m/z* 364. Configurational assignments of compounds **3** and **4** were based exclusively on ^1H NMR

spectroscopy by comparing the observed chemical shifts value;[25] and according to literature data for analogous 4-thiazolidinone.[26-29] The olefinic protons of the *Z*-isomers are relatively deshielded by the thioxo groups of the thiazole moiety compared with the *E*-isomers (see EXPERIMENTAL and Scheme 1). The compound **4b** can be also obtained by refluxing equimolar amounts of **3** with **1b** in glacial acetic acid and in the presence of fused sodium acetate.

In the course of study of cycloaddition reactions of α,β-unsaturated thiocarbonyl heterocycles with electron-poor dienophiles, new 1:1 adducts, thiopyrano[2,3-*d*]thiazoles **6a-c** *via* the reaction of **3** with *N*-arylmaleimides **5a-c** in refluxing acetic acid were obtained. The IR spectrum of the isolated product **6b** showed absorption bands at 3023, 2745, 2859, 1719 and 1702 cm^{-1}, corresponding to NH, aldehydic CH and CO groups, respectively. Furthermore, the ^1H NMR spectrum of this adduct showed signals reasonably assignable to the structures proposed (see EXPERIMENTAL and Scheme 2). Based on the elemental analyses and spectral data, structures **6a-c** were proposed to these adducts.

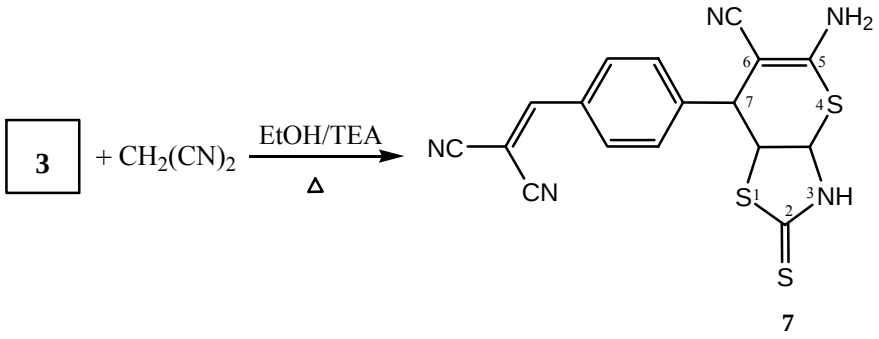


3 **5a-c**

6a, Ar = C_6H_5
b, Ar = 4-$MeOC_6H_4$
c, Ar = 4-ClC_6H_4

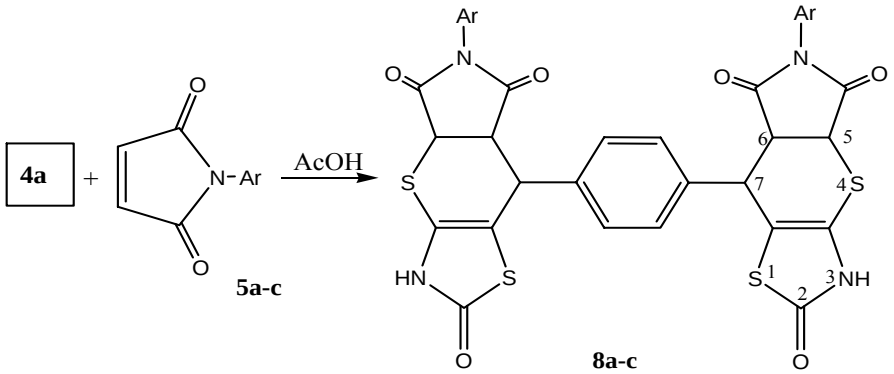
Scheme 2

Reaction of **3** with two equivalents of malononitrile in refluxing absolute ethanol in the presence of triethylamine, afforded coloured product **7** (Scheme 3). Structure of **7** was deduced from its elemental analysis and spectral data. Thus the IR spectrum of this isolated product showed absorption bands at 3310, 3128 and 3101 cm^{-1} corresponding to NH_2 and NH groups, and characteristic absorption bands at 2214 and 2184 cm^{-1} corresponding to CN groups and the absence of CHO band. Its ^1H NMR data showed signals assignable reasonably to the proposed structure (see EXPERIMENTAL). From these results, the structure **7** was assigned to this adduct. (see EXPERIMENTAL and Scheme 3).



Scheme 3

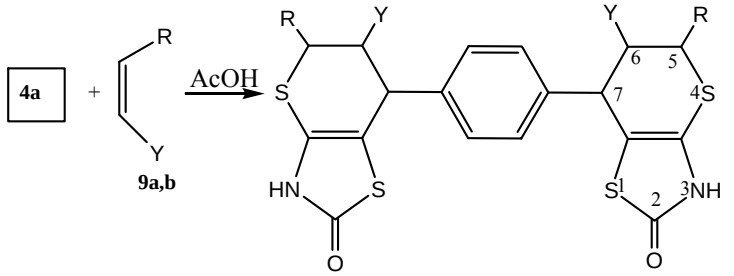
It is interesting to explore the utility of the novel 1,4-bis[(2-oxo-4-thioxo-thiazolidinyl)methylene]benzene (**4a**) as heterodienes in Diels-Alder reaction with various dienophiles. Thus, refluxing compound **4a** with two equivalents of *N*-arylmaleimides **5a-c** in glacial acetic acid gave colorless adducts. The ^{1}H NMR spectrum of the adduct **8b** showed double doublets at δ 3.39-3.45 (J = 6.0 and 9.0 Hz) attributed to H-6, in addition to two doublets at δ 4.64 and 5.24 (J = 5.7 and 9.3 Hz), respectively, corresponding to H-5 and H-7, beside the other expected signals due to the aromatic protons (see EXPERIMENTAL). IR spectrum of product **8b** also showed the absorptions consistent with the proposed structure (see EXPERIMENTAL). Based on the elemental analyses and spectral data, structures **8a-c** were assigned to these adducts (see EXPERIMENTAL and Scheme 4).



Scheme 4

Similarly, refluxing **4a** with ethyl acrylate (**9a**) and/or *ω*-nitrostyrene (**9b**) in molar ratio 1:2 in glacial acetic acid gave the symmetric *N*-aryl-1,4-bis(thiazolothiopyranyl)benzenes **10a,b** (Scheme 5). The structures of **10a,b** were also assigned on the basis of their elemental analyses and spectral data (see

EXPERIMENTAL). The ^{1}H NMR spectrum of compounds **10a** revealed a doublet at δ 4.45 corresponding to H-7 and double doublets at δ 3.28-3.37 corresponding to H-5*ax* and H-5*eq* in addition to multiplet at δ 3.04-3.15 corresponding to H-6. The formation pathway of compound **10a** from **4a** and **9a,b** is similar to these of compounds **9a,b** (Scheme 5 and see EXPERIMENTAL).

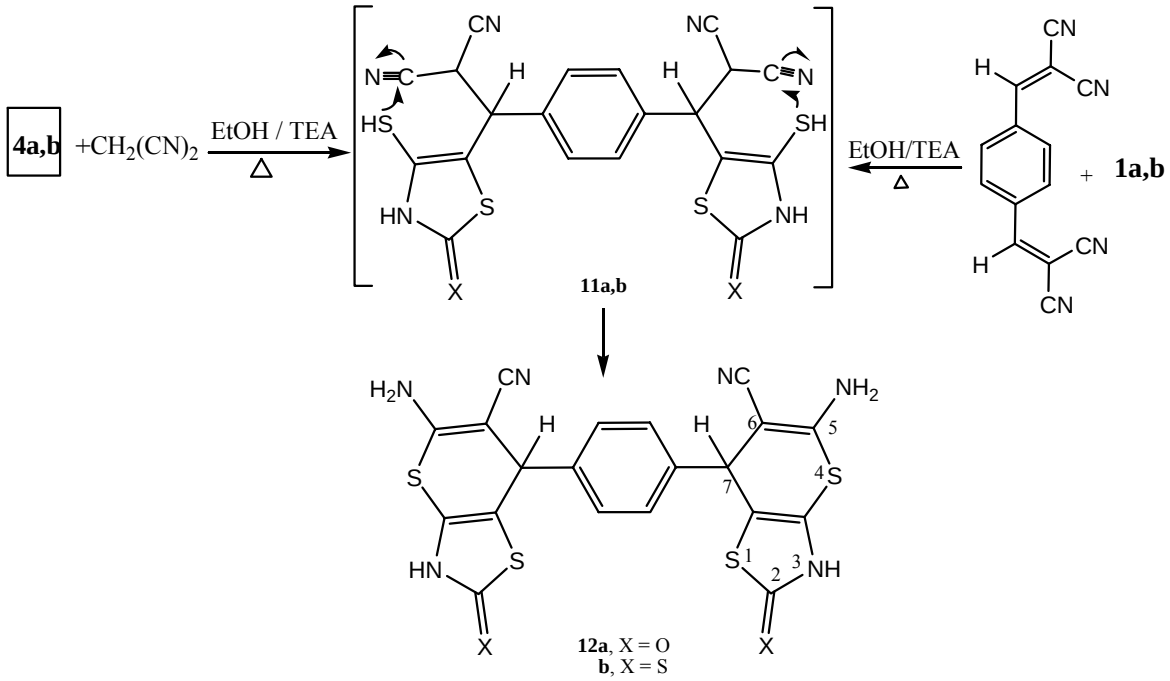


10a, R = H, Y = CO_2Et
b, R = C_6H_5, Y = NO_2

Scheme 5

All the new adducts **6a-c**, **8a-c** and **10a,b** showed only one isomer in the ^{1}H NMR spectra (see EXPERIMENTAL) and this seems logic, since the endo-adduct is obtained as a kinetically controlled product at room temperature, but under thermal conditions it is transformed into the exo-adduct which is thermally stable controlled product.

The reaction of **4a,b** toward malononitrile was also investigated. Thus, the reaction of **4** and two equivalents of malononitrile in refluxing absolute ethanol in the presence of triethylamine, afforded highly coloured products **12ab** (Scheme 6). Structures of **12a,b** were proposed from their analytical and spectral data. Absorption bands of the IR spectrum of **12b** of at 3428, 3320 and 3085 cm^{-1} corresponding to NH_2 and NH groups and a strong absorption band at 2188 cm^{-1} due to CN group were observed. In the ^{1}H NMR spectrum of this adduct, a singlet signal at δ 4.43 attributed to H-7 and two D_2O-exchangeable signals at δ 9.93 and 8.63 attributed to NH_2 and NH protons appeared. Further more, the adducts **12a,b** were synthesised separately by another reaction between 1,4-bis(2,2`-dicyanovinyl)benzene and two equivalents of each of **1a** and **1b**. The formation of the adducts **12** is assumed to proceed *via* initial Michael addition to yield acyclic adducts **11**, followed by the cyclization *via* the attack of the mercapto group on the cyano group.



Scheme 6

EXPERIMENTAL

All melting points were determined on an electrothermal (9100) apparatus and are uncorrected. The IR spectra were recorded as KBr pellets on a Perkin Elmer 1430 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer (TMS as internal standard, DMSO-d_6 as solvent, δ values in ppm). Mass spectra were taken on a Shimadzu GCMS-QP-1000 EX (Japan) with ionization potential 70 eV. Elemental analyses were carried out by the Microanalysis Center at Cairo University, Giza, Egypt.

5-(4-Formylphenyl)methylenethiazolidine-2,4-dithione (3).

To a solution of **1b** (10 mmol) in glacial acetic acid (25 mL) and sodium acetate (1.64 g, 20 mmol) was added terephthalaldehyde (**2**) (10 mmol). The reaction mixture was stirred at rt for 15 min. The solid which separated from the reaction mixture, was collected and recrystallized from acetic acid.

Brown crystals; yield (85%); mp 226 °C; IR (KBr) υ 3028 (NH) and 2855, 2738, 1686 (aldehydic CHO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.80 (m, 4H, ArH's), 8.11 (s, 1H, CH), 10.03 (s, 1H, aldehydic CH), 13.73 (brs, NH, exchangeable). MS, m/z 265 (M^+, 100%), 236 (46.7%), 177 (65.1%), 161 (37.5%), 133 (21.7%), 89 (38.2%), 64 (50.7%). Anal. Calcd for $C_{11}H_7NOS_3$ (265.37): C, 49.79; H, 2.66; N, 5.28; S, 36.25%. Found: C, 49.67; H, 2.53; N, 5.44; S, 36.37%.

Condensation of terephthaldehyde with 4-thioxothiazolidin-2-one (1a) and thiazolidine-2,4-dithione (1b).

General procedure.

To a solution of each of **1a** and **1b** (20 mmol) in glacial acetic acid (25 mL) and sodium acetate (3.82 g, 40 mmol) was added terephthalaldehyde (**2**) (10 mmol). The reaction mixture was refluxed for 1 h on water bath, cooled and then poured into cold water. The solid, which separated, was collected and recrystallized from DMF/EtOH.

(Z)-1,4-Bis(2-oxo-4-thioxothiazolidinylmethylene)benzene (4a).

Red crystals; yield (75%); mp >300 °C; IR (KBr) υ 3071 (NH) and 1724 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.80 (s, 4H, ArH's), 8.07 (s, 2H, 2CH), 13.75 (br, 2NH, exchangeable). ^{13}C NMR: δ = 117.21, 121.10, 127.30, 134.18, 169.32 (C=O) and 198.80 (C=S); MS, m/z 364 (M^+, 100%), 276 (27.5%), 233 (75%), 190 (29.9%), 145 (20%), 95 (43.4%). Anal. Calcd for $C_{14}H_8N_2O_2S_4$ (364.49): C, 46.13; H, 2.21; N, 7.69; S, 35.19%. Found: C, 46.25; H, 2.34; N, 7.83; S, 35.32%.

(Z)-1,4-Bis(2,4-dithioxothiazolidinylmethylene)benzene (4b).

Brown crystals; yield (82%), mp >300 °C; IR (KBr) υ 3028 (NH) cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.85 (s, 4H, ArH's), 8.11 (s, 2H, CH), 13.73 (brs, 2NH, exchangeable). Anal. Calcd for $C_{14}H_8N_2S_6$ (396.62): C, 42.40; H, 2.03; N, 7.07; S, 48.51%. Found: C, 42.55; H, 2.16; N, 7.23; S, 48.37%.

Reaction of 3 with N-arylmaleimides

A mixture of **3** (10 mmol) and *N*-arylmaleimides **5a-c** (10 mmol) in glacial acetic acid (30 mL) was refluxed for 30 min. The separated solid, was collected and recrystallized from the appropriate solvent.

7-(4-Formylphenyl)-N-phenyl-5,6-dihydrothiopyrano[2,3-d]thiazolidine-2-thioxo-5,6-dicarboximide-(6a).

White crystals (EtOH/dioxane); yield (60%); mp 268 °C; IR (KBr) υ 3017 (NH), 2743, 2855 (aldehydic CH), 1720 (CO), 1695 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.40-3.46 (dd, H, J = 6.8 Hz, 8.8 Hz, H-6), 4.80 (d, 1H, J = 7.0 Hz, H-5), 5.24 (d, 1H, J = 9.0 Hz, H-7), 6.60-7.34 (m, 5H, ArH's), 7.57 (d, 2H, J = 8.4 Hz, ArH's), 7.88 (d, 2H, J = 8.4 Hz, ArH's), 10.0 (s, 1H, aldehydic CH), 13.78 (s, 1H, NH). Anal. Calcd for $C_{21}H_{14}N_2O_3S_3$ (438.54): C, 57.52; H, 3.22; N, 6.38; S, 21.94%. Found: C, 57.65; H, 3.36; N, 6.55; S, 22.08%.

7-(4-Formylphenyl)-N-(4-methoxyphenyl)-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-thioxo-5,6-dicarboximide (6b).

White crystals (EtOH/dioxane); yield (63%); mp 255 ^{o}C; IR (KBr) υ 3023 (NH), 2745, 2859 (aldehydic CH), 1719 (CO), 1702 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.72 (s, 3H, OMe), 3.42-3.48 (dd, 1H, J = 6.9, 9.1 Hz, H-6), 4.81 (d, 1H, J = 7.2 Hz, H-5), 5.26 (d, 1H, J = 9.0 Hz, H-7), 6.51 (d, 1H, J = 8.7 Hz, ArH's), 6.88 (d, 1H, J = 9.3 Hz, ArH's), 7.56 (d, 1H, J = 7.8 Hz, ArH's), 7.87 (d, 1H, J = 8.1 Hz, ArH's), 9.99 (s, 1H, aldehydic CH), 13.80 (s, 1H, NH). Anal. Calcd for $C_{22}H_{16}N_2O_4S_3$ (468.57): C, 56.39; H, 3.44; N, 5.97; S, 20.53%. Found: C, 56.52; H, 3.58; N, 6.14; S, 20.67%.

7-(4-Formylphenyl)-N-(4-chlorophenyl)-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-thioxo-5,6-dicarboximide (6c).

White crystals (AcOH); yield (65%); mp 285 ^{o}C; IR (KBr) υ 3025 (NH), 2744, 2861 (aldehydic CH), 1723 (CO), 1700 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.42-3.51 (dd, 1H, J = 6.9, 9.1 Hz, H-6), 4.82 (d, 1H, J = 7.2 Hz, H-5), 5.28 (d, 1H, J = 9.2 Hz, H-7), 6.54 (d, 1H, J = 8.8 Hz, ArH's), 6.90 (d, 1H, J = 9.2 Hz, ArH's), 7.60 (d, 1H, J = 7.6 Hz, ArH's), 7.89 (d, 1H, J = 8.1 Hz, ArH's), 10.01 (s, 1H, aldehydic CH), 13.80 (s, 1H, NH). Anal. Calcd for $C_{21}H_{13}ClN_2O_3S_3$ (472.99): C, 53.33; H, 2.77; Cl, 7.50; N, 5.92; S, 20.33%. Found: C, 53.46; H, 2.91; Cl, 7.64; N, 6.10; S 20.49%.

5-Amino-7-[4-(2,2-dicyanovinyl)phenyl]-3,7-dihydro-2-thioxothiopyrano[2,3-d]thiazole-6-carbonitr-ile (7).

A mixture of compound **3** (10 mmol) and malononitrile (20 mmol) in ethanol (100 mL), containing several drops of triethylamine, was refluxed for 2 h. The solid product was collected by filtration and recrystallized from EtOH/DMF to afford violet crystals.

Yield (62%); mp >300 ^{o}C; IR (KBr) υ 3310, 3128, 3101 (NH_2 and NH) and 2214, 2184 (CN) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 4.41 (s, 1H, H-7), 7.81 (s, 1H, CH), 7.88 (d, 2H, J = 8.4 Hz, ArH's), 8.02 (d, 2H, J = 8.4 Hz, ArH's), 8.10 (br., 1H, NH), 11.0 (s, 2H, NH_2). Anal. Calcd for $C_{17}H_9N_5S_3$ (379.48): C, 53.80; H, 2.39; N, 18.40; S, 25.35%. Found: C, 53.92; H, 2.52; N, 18.52; S, 25.22%.

Reaction of 4a with N-arylmaleimides, ethyl acrylate and ω-nitrostyrene.

General Procedure.

A mixture of **4a** (10 mmol) and the appropriate dienophile (20 mmol) in glacial acetic acid (30 mL) was refluxed for 2 h. The solid product was collected and recrystallized from appropriate solvent.

1,4-Bis(N-phenyl-3,5,6,7-tetrahydrothiopyrano[2,3-d]thiazolidin-2-oxo-5,6-dicarboximidyl)benzene (8a).

Pale brown crystals (AcOH); yield (45%); mp 277 °C; IR (KBr) υ 3095 (NH), 1716 (CO) and 1675 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.38-3.44 (dd, 2H, *J* = 5.7 Hz, 8.9 Hz, 2H-6), 4.63 (d, 2H, *J* = 5.8 Hz, 2H-5), 5.24 (d, 2H, *J* = 9.0 Hz, 2H-7), 6.62 (m, 10H, 2ArH), 7.33 (s, 4H, ArH's), 11.82 (s, 2H, 2NH). Anal. Calcd for $C_{34}H_{22}N_4O_6S_4$ (710.82): C, 57.45; H, 3.12; N, 7.88; S, 18.04%. Found: C, 57.57; H, 3.26; N, 7.72; S, 18.18%.

1,4-Bis(N-(4-methoxyphenyl)-3,5,6,7-tetrahydrothiopyrano[2,3-d]thiazolidin-2-oxo-5,6-dicarboximidyl)benzene (8b).

Pale brown crystals (EtOH/dioxane); yield (48%); mp 295 °C; IR (KBr) υ 3100 (NH), 1717 (CO) and 1677 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.73 (s, 6H, 2OMe), 3.39-3.45 (dd, 2H, *J* = 6.0, 9.0 Hz, 2H-6), 4.64 (d, 2H, *J* = 5.7 Hz, 2H-5), 5.24 (d, 2H, *J* = 9.3 Hz, 2H-7), 7.26 (s, 4H, ArH's), 7.56 (d, 2H, *J* = 8.1 Hz, 2ArH's), 7.87 (d, 2H, *J* = 8.1 Hz, 2ArH's), 11.84 (s, 2H, 2NH). Anal. Calcd for $C_{36}H_{26}N_4O_8S_4$ (770.87): C, 56.09; H, 3.40; N, 7.27; S, 16.64%. Found: C, 56.22; H, 3.52; N, 7.44; S, 16.50%.

1,4-Bis(N-(4-chlorophenyl)-3,5,6,7-tetrahydrothiopyrano[2,3-d]thiazolidin-2-oxo-5,6-dicarboximidyl)benzene (8c).

Brownish yellow crystals (EtOH/DMF); yield (52%); mp >300 °C; IR (KBr) υ 3098 (NH), 1717 (CO) and 1678 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.37-3.46 (dd, 2H, *J* = 6.0, 8.8 Hz, 2H-6), 4.65 (d, 2H, *J* = 6.0 Hz, 2H-5), 5.23 (d, 2H, *J* = 9.0 Hz, 2H-7), 7.30 (s, 4H, ArH's), 7.60 (d, 2H, *J* = 8.4 Hz, 2ArH's), 7.90 (d, 2H, *J* = 8.4 Hz, 2ArH's), 11.80 (s, 2H, 2NH). Anal. Calcd for $C_{34}H_{20}Cl_2N_4O_6S_4$ (779.71): C, 52.37; H, 2.59; Cl, 9.09; N, 7.19; S, 16.45%. Found: C, 52.24; H, 2.72; Cl, 9.22; N, 7.36; S 16.33%.

1,4-Bis[6-ethoxycarbonyl-2-oxo-3,5,6,7-tetrahydro-2H-thiopyrano[2,3-d]thiazolyl]benzene (10a).

Pale brown crystals (acetic acid); yield (44%); mp 265 °C; IR (KBr) υ 3132 (NH), 1732 (CO) and 1686 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.13 (t, 6H, *J* = 7.2 Hz, 2Me), 3.04-3.15 (m, 2H, 2H-6), 3.28-3.37 (dd, 2H, *J* = 4.6, 8.2 Hz, 2H-5), 3.99 (q, 4H, $2CH_2$), 4.45 (d, 2H, *J* = 5.1 Hz, 2H-7), 7.35 (s, 4H, ArH's), 11.37 (s, 2H, 2NH). MS, *m/z* 564 (M^+, 11%), 346 (25.3%), 320 (6.8%), 233 (16%), 190 (4.3%), 177 (4.1%), 152 (5%), 129 (6.7%), 95 (8.0%), 55 (100%). Anal. Calcd for $C_{24}H_{24}N_2O_6S_4$ (564.72): C, 51.04; H, 4.28; N, 4.96; S, 22.71%. Found: C, 51.16; H, 4.44; N, 4.80; S, 22.88%.

1,4-Bis(6-nitro-5-phenyl-2-oxo-3,5,6,7-tetrahydrothiopyrano[2,3-d]thiazolyl)benzene (10b).

Pale yellow crystals (acetic acid); yield (49%); mp 288 °C; IR (KBr) υ 3138 (NH), 1685 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.76 (d, 2H, *J* = 15.3 Hz, 2H-5), 3.85 (d, 2H, *J* = 14.4 Hz, 2H-7) 4.71-4.93 (dd, 1H, *J* = 5.7, 11.4 Hz, 2H-6), 6.70 (s, 10H, 2ArH's), 7.42 (s, 4H, ArH's), 11.85 (s, 2H, 2NH). Anal. Calcd for $C_{30}H_{22}N_4O_6S_4$ (662.78): C, 54.37; H, 3.35; N, 8.45; S, 19.35%. Found: C, 54.50; H, 3.48; N, 8.30; S, 19.47%.

1,4-Bis [thiopyrano[2,3-d]thiazolyl]benzene derivatives 12a,b

A mixture of **4a,b** (10 mmol) and malononitrile (20 mmol) in EtOH (100 mL), containing a few drops of triethylamine, was refluxed for 2 h then left at rt overnight. The solid product so obtained was filtered off and recrystallized from EtOH/DMF.

1,4-Bis (5-amino-6-cyano-2-oxo-thiopyrano[2,3-d]thiazolyl)benzene (12a).

Orange crystals; yield (60%); mp >300 °C; IR (KBr) υ 3425, 3318, 3081 (NH_2 and NH), 2190 (CN) and1680 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 4.40 (s, 2H, 2H-7), 7.31 (s, 4H, ArH's), 8.60 (br., 4H, $2NH_2$), 9.90 (s, 2H, 2NH). Anal. Calcd for $C_{20}H_{12}N_6O_2S_4$ (496.61): C, 48.37; H, 2.44; N, 16.92; S, 25.83%. Found: C, 48.50; H, 2.56; N, 16.75; S, 25.96%.

1,4-Bis(5-amino-6-cyano-2- thioxothiopyrano[2,3-d]thiazolyl)benzene (12b).

Violet crystals; yield (62%); mp >300 °C; IR (KBr) υ 3428, 3320, 3085 (NH_2 and NH) and 2188 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 4.43 (s, 2H, 2H-7), 7.26 (s, 4H, ArH's), 8.63 (s, 2H, 2NH), 9.93 (s, 4H, 2NH). Anal. Calcd for $C_{20}H_{12}N_6S_6$ (528.74): C, 45.43; H, 2.29; N, 15.89; S, 36.39%. Found: C, 45.58; H, 2.46; N, 15.72; S, 36.53%.

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