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RESEARCH ARTICLE

Synthesis of some new fused thiopyrano[2,3-*d*]thiazoles and their derivatives

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A series of some new fused thiopyrano[2,3-*d*]thiazole derivatives have been synthesized by a stereoselective hetero-Diels-Alder reaction of 5-(2,4-dihydroxy-benzylidene)-4-thioxo-thiazolidine derivatives **3a**,**b** with acrylonitrile, ethyl acrylate, *N*-phenylmale-imide, *ω*-nitrostyrene and *N*-phenyl-1, 3, 4-triazole-2,5-dione. 5-Amino-9-hydroxy-dihydro-benzopyrano[3′,4′:4,5]thiopyrano[2,3-*d*]thiazol-6-one derivatives **14a,b** have been synthesized by Michael addition of **3a**,**b** with malononitrile. Structures and conceivable mechanisms are discussed.

Keywords: 5-(2, 4-Dihydroxybenzylidene)-4-thioxo-thiazolidines; Thiopyrano[2,3-*d*]thia-zoles; Benzopyrano [3′,4′:4,5]thiopyrano[2,3-*d*]thiazole derivatives

1. Introduction

In recent decades we have been involved in a program aiming at the synthesis of heterocyclic compounds with anticipated biological activity [1, 2]. Thiazolidinone derivatives represent a well-known class of patented drugs and substances at different stages of research, which possess anti-inflammatory, diuretic, and other activities [3, 4]. Recently, attention has been paid to the antitumor activity of thiazolidinone derivatives as novel potential anticancer agents [3, 5–8]. The use of thiopyrano derivatives as antimalarial drugs [9, 10] has prompted us to continue our program for the construction of a condensed heterocyclic system having both thiazolidine and thiopyrano moieties starting from 2,4-thiazolidenedione (**1a**) and 2-thioxo-thiazolidin-4-one (**1b**) [11–15].

2. Results and discussion

Thionation of 4-thiazolidinones, in general, is performed in dry dioxane by phosphorus pentasulfide [16, 17]. Thionation of 2,4-thiazolidinedione (**1a**) by Lawesson's reagent in

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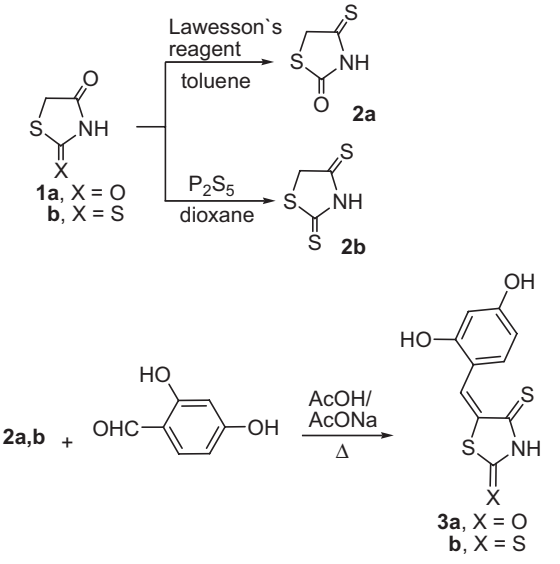
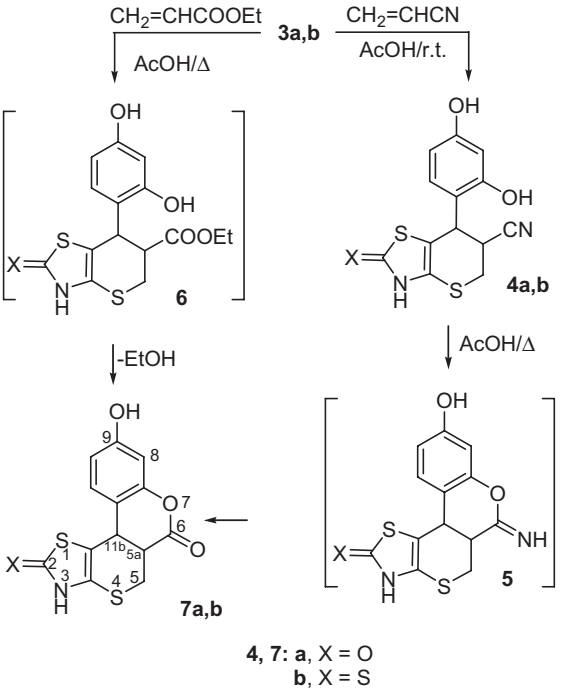


SCHEME 1

refluxing dry toluene leads to 4-thioxo-thiazolidin-2-one (isorhodanine) **2a** in high yield (98%) (scheme 1). The Knoevenagel condensation of **2a**,**b** with 2,4-dihydroxybenzaldehyde afforded the highly coloured 5-(2,4-dihydroxy-benzylidene)thiazolidine derivatives **3a**,**b** (cf. exp.). The presence of the hydroxyl groups in the phenyl moiety gives an advantage to these compounds in that it renders them easily soluble in ethanol and basic aqueous media at room temperature (scheme 1).

The reactivity of the sulfur atom at position-4 in 5-arylidene-4-thioxo-thiazolidin-ones allows it to be used as a highly active heterodiene component in hetero-Diels-Alder reactions [18–21].

Thus, the highly coloured **3a**,**b** react with acrylonitrile in acetic acid at room temperature to afford 1:1 adducts. The IR spectra of the isolated products showed in each case an absorption band at $\nu = 2228$–$2230\,cm^{-1}$, corresponding to CN group. Furthermore, the ^1H NMR data of these adducts showed a multiplet at $\delta = 3.25$–3.65 ppm attributed to C-5 proton, a multiplet at $\delta = 3.73$–4.20 ppm corresponding to C-6 proton, a doublet at $\delta = 4.70$–4.77 ppm attributed to C-7 proton, beside the other expected signals (cf. exp.). Also, the mass spectra reveal in each case a molecular ion peak which is consistent with the assigned structure. Based on the spectral data, structures **4a**,**b** were assigned to these adducts (scheme 2). Refluxing **4a**,**b** in acetic acid afforded directly fused 9-hydroxy- [1]benzo[3′,4′:4,5]thiopyrano[2,3-*d*]thiazole derivatives **7a**,**b**, respectively. The IR spectrum of the isolated product **7a** showed absorption band at $\nu = 1737\,cm^{-1}$ corresponding to carbonyl group of pyrane ring, in addition to the other carbonyl group of thiazolidine ring which appears at $\nu = 1684\,cm^{-1}$. The ^1H NMR data of this adduct showed a doublet at $\delta = 3.59$ ppm, J = 1.2 Hz attributed to C-5 proton, a multiplet at $\delta = 3.90$ ppm, J = 6.2 Hz corresponding to C-5a proton and a doublet at $\delta = 4.23$ ppm, J = 5.8 Hz attributed to C-11b proton. The ^{13}C NMR spectrum of **7a** showed two characteristic signals at 170.25 ppm and 174.74 ppm corresponding to carbonyl carbons of thiazolidine ring and pyrane ring, respectively, beside the other expected signals (cf. exp.). Mass spectrum and analytical data are in agreement with structure **7a**. The formation of the adducts **7a**,**b** is assumed to proceed through [4 + 2] cycloaddition to afford **4a**,**b**, followed by the addition



SCHEME 2

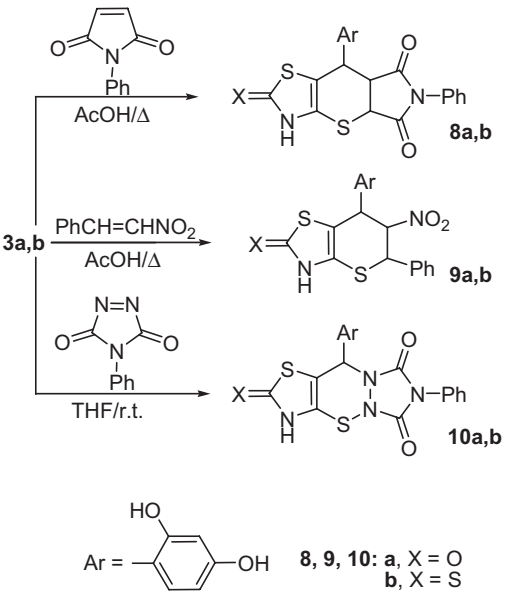
of hydroxyl group to the cyano group to afford the imino non-isolable intermediate **5** which converted in turn to **7a**,**b** by hydrolysis (scheme 2).

The same products **7a**,**b** are also formed *via* reaction of **3a**,**b** with ethyl acrylate in refluxing acetic acid which affords an evidence to our suggested mechanism (scheme 2).

The reaction of **3a**,**b** with *N*-phenylmaleimide, *ω*-nitrostyrene and *N*-phenyl-1, 3, 4-triazole-2,5-dione afforded the 1:1 adducts **8**, **9** and **10**, respectively. The structures of compounds **8**, **9** and **10** were assigned on the basis of their analytical and spectral data (scheme 3 and cf. exp.).

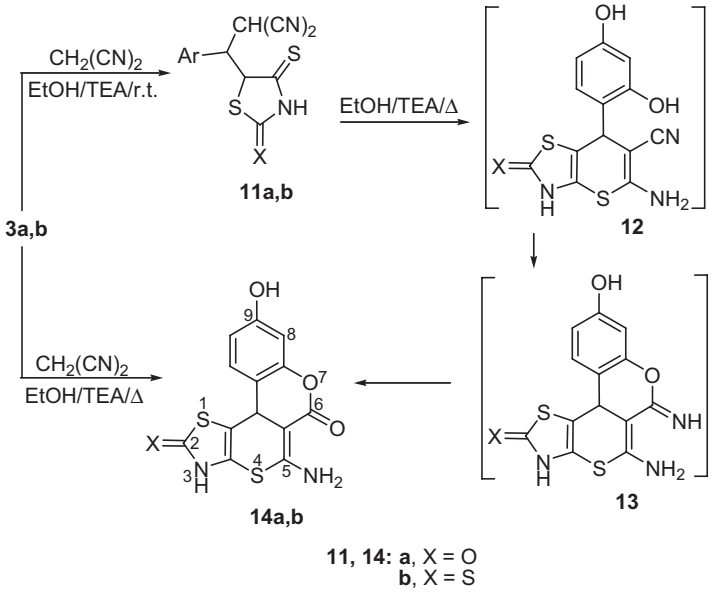
The behaviour of **3a**,**b** toward the action of malononitrile has also been investigated. Thus, treatment of **3a**,**b** with malononitrile, at room temperature in absolute ethanol and in the presence of few drops of triethylamine afforded products **11a,b**. Structures of **11a,b** were based on their analytical and spectral data. For example the IR spectrum of **11a** showed absorption band at $\nu = 2203\,\mathrm{cm}^{-1}$ corresponding to CN group. The ^{1}H NMR spectrum of **11a** showed a doublet at $\delta = 1.35$ ppm integrated for 1H (C<u>H</u>-CN) proton, a triplet at $\delta = 3.41$ ppm attributable to 1H (Ar-C<u>H</u>) and a doublet at $\delta = 4.16$ ppm integrated for 1H (C<u>H</u>-C=S) proton, beside the other expected signals (cf. exp.). Refluxing **11a,b** in ethanol in the presence of few drops of triethylamine, the fused 9-hydroxy-benzopyrano[3′,4′:4,5]-thiopyrano[2,3-*d*]thiazol-6-one derivatives **14a,b** were obtained apparently *via* the intermediates **12** and **13** (scheme 4). Structures of **14a,b** were deduced from their analytical and spectral data (cf. exp.).

Compounds **3a**,**b** react with methyl iodide, ethyl bromoacetate and/or phenacyl bromide in alcoholic potassium hydroxide to afford one and the same products for which structure **16a,b** were assigned. The IR spectrum of the isolated product **16a** showed absorption band at $\nu = 3410\,\mathrm{cm}^{-1}$ corresponding to phenolic OH group. The ^{1}H NMR data of this

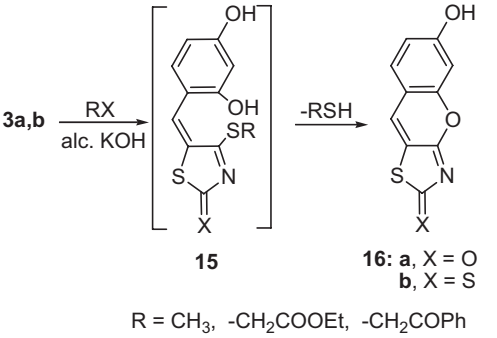


SCHEME 3

product showed a multiplet at $\delta = 7.11$ ppm integrated for 1H and aromatic protons and a singlet at $\delta = 13.64$ ppm attributed to phenolic proton. Structures **16a,b** were ascertained on the basis of their analytical and spectral data. The reaction seems to took place *via* S-alkylation followed by cyclization through elimination of alkane thiol (RSH) to afford **16a,b** (scheme 5).



SCHEME 4



SCHEME 5

The ^{1}H NMR spectra showed that only one stereoisomer was present for all products, indicating that the reaction is stereoselective.

3. Experimental

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 200 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 PX (Japan) with ionization potential 70 eV. Elemental analyses were carried out by the Microanalysis Center at Cairo University, Giza, Egypt. The starting compound **2b** was prepared according to literature procedure [16].

3.1 *Thionation of 1a: Preparation of 4-thioxo-thiazolidin-2-one (2a)*

To a solution of 1.22 g (0.01 mol) of **1a** in 25 mL of dry toluene was added 4.44 g (0.01 mol) of Lawesson's reagent. The reaction mixture was refluxed for 2 h and filtered off, the solid so formed was crystallized from acetone to afford 1.31 g (98%) of **2a** as a rose crystals, mp 158 °C Lit. (158 °C) [16, 17].

3.2 *5-(2,4-Dihydroxy-benzylidene)-4-thioxo-thiazolidin-2-one (3a)*

To a solution of 1.33 g (0.01 mol) of **2a** in 25 mL acetic acid was added 1.38 g (0.01 mol) of 2,4-dihydroxybenzaldehyde in presence of 0.82 g (0.01 mol) fused sodium acetate. The mixture was refluxed for 20 min., cooled to room temperature, then poured onto ice-cold water, the resulting precipitate was filtered off and recrystallized from acetic acid to afford a reddish-violet crystals, mp 265 °C, 1.55 g (61%); IR ν (cm^{-1}): 3386 (OH), 3134 (N-H), 1694 (CO); ^{1}H NMR δ 6.42 (d, 1H, J = 8.6 Hz, phenyl H), 6.46 (s, 1H, phenyl H) 7.29 (d, 1H, J = 9.2 Hz, phenyl H), 8.51 (s, 1H, CH), 10.47 (s, 1H, N−H), 10.70 (s, 1H, OH phenolic) and 13.52 (s, 1H, OH phenolic). Anal. for $C_{10}H_7NO_3S_2$ (253), Calc.: C 47.42; H 2.79; N 5.53; S 25.32; found: C 47.14; H 3.07; N 5.30; S 25.14.

3.3 *5-(2,4-Dihydroxy-benzylidene)-thiazolidin-2,4-dithione (3b)*

To a solution of 1.49 g (0.01 mol) of **2b** in 25 mL acetic acid was added 1.38 g (0.01 mol) of 2,4-dihydroxybenzaldehyde in presence of 0.82 g (0.01 mol) fused sodium acetate. The reaction mixture was stirred for 3 h at room temperature, then poured onto ice-cold water, the resulting precipitate was filtered off and recrystallized from acetic acid to afford a violet crystals **3b**, mp above 280 °C, 1.60 g (59%); IR ν (cm^{-1}): 3385 (OH), 3133 (N-H); ^{1}H NMR δ 6.40 (d, 1H, J = 8.8 Hz, phenyl H), 6.47 (s, 1H, phenyl H), 7.25 (d, 1H, J = 9.0 Hz, phenyl H), 8.55 (s, 1H, CH), 10.35 (s, 1H, N-H), 10.60 (s, 1H, OH phenolic) and 13.32 (s, 1H, OH phenolic). Anal. for $C_{10}H_7NO_2S_3$ (269); Calc.: C 44.59; H 2.62; N 5.20; S 35.71; found: C 44.37; H 2.45; N 5.45; S 35.50.

3.4 *Reaction of 3a,b with acrylonitrile (general procedure)*

A solution of equimolecular amounts (0.01 mol) of **3a**,**b** and acrylonitrile in acetic acid (50 ml) was stirred at room temperature for 2 hrs. The solid so formed was filtered off and recrystallized from the appropriate solvent.

3.5 *7-(2,4-Dihydroxy-phenyl)-2-oxo-3,5,6,7-tetrahydro-2H-thiopyrano[2,3-d]thiazole-6-carbonitrile (4a)*

Whitish brown crystals (acetic acid), mp 245 °C, (1.93 g, 63%); IR ν (cm^{-1}): 3422 (OH), 3160 (N-H), 2230 (CN), 1705 (CO); ^{1}H NMR δ 3.53 (m, 2H, C-5 proton), 3.98 (m, 1H, C-6 proton), 4.77 (d, 1H, J = 5.8 Hz, C-7 proton), 6.40 (s, 1H, phenyl H), 6.63 (d, 1H, J = 8.6 Hz, phenyl H), 7.11 (d, 1H, J = 8.2 Hz, phenyl H), 10.40 (s, 1H, N-H), 11.0 (s, 1H, OH phenolic) and 13.55 (s, 1H, OH phenolic). Anal. for $C_{13}H_{10}N_2O_3S_2$ (306); Calc.: C 50.97; H 3.29; N 9.14; S 20.93; found: C 51.22; H 3.53; N 9.41; S 21.15.

3.6 *7-(2,4-Dihydroxy-phenyl)-2-thioxo-3,5,6,7-tetrahydro-2H-thiopyrano[2,3-d]thiazole-6-carbonitrile (4b)*

Pale violet crystals (acetic acid), mp 210 °C, (1.35 g, 42%); IR ν (cm^{-1}): 3418 (OH), 3140 (N-H), 2228 (CN); ^{1}H NMR δ 3.43 (m, 2H, C-5 proton), 3.87 (m, 1H, C-6 proton), 4.70 (d, 1H, J = 6.0 Hz, C-7 proton), 6.35 (s, 1H, phenyl H), 6.67 (d, 1H, J = 8.6 Hz, phenyl H), 7.23 (d, 1H, J = 8.2 Hz, phenyl H), 10.11 (s, 1H, N-H), 10.90 (s, 1H, OH phenolic) and 13.50 (s, 1H, OH phenolic). Anal. for $C_{13}H_{10}N_2O_2S_3$ (322); Calc.: C 48.43; H 3.13; N 8.69; S 29.83; found: C 48.70; H 3.34; N 8.96; S 30.08.

3.7 *Reaction of 3a,b with acrylonitrile and/or ethyl acrylate (general procedure)*

A solution of equimolecular amounts (0.01 mol) of **3a**,**b** and acrylonitrile and/or ethyl acrylate in acetic acid (50 mL), was refluxed for 30 min, cooled to room temperature and the solid, so formed, was filtered off and recrystallized.

3.8 *9-Hydroxy-2,3,5,5a,6,11b-hexahydro[1]benzo[3′,4′:4,5]thiopyrano[2,3-d]thiazol-2,6-dione (7a)*

Yellowish brown crystals (acetic acid), mp 275 °C (1.55 g, 50%); IR ν (cm^{-1}): 3464 (OH), 3177 (N-H), 1737 (CO), 1684 (CO); ^{1}H NMR δ 3.59 (d, 2H, J = 1.2 Hz, C-5 proton), 3.90

(m, 1H, C-6 proton), 4.23 (d, 1H, J = 5.8 Hz, C-7 proton), 6.51 (s, 1H, phenyl H), 6.62 (d, 1H, J = 8.6 Hz, phenyl H), 7.15 (d, 1H, J = 8.2 Hz, phenyl H), 9.90 (s, 1H, N-H) and 11.40 (s, 1H, OH phenolic). ^{13}C NMR δ 25.83, 33.25, 66.36, 103.85, 111.91, 114.15, 119.56, 128.93, 150.80, 158.30, 166.50, 170.25, 174.74. Anal. for $C_{13}H_9NO_4S_2$ (307); Calc.: C 50.80; H 2.95; N 4.56; S 20.87; found: C 51.04; H 2.73; N 4.80; S 20.59.

3.9 *9-Hydroxy-2-thioxo-2,3,5,5a,6,11b-hexahydro[1]benzo[3,4:4,5]thiopyrano[2,3-d]thiazol-6-one (7b)*

Whitish brown crystals (acetic acid), mp above 300 °C (1.63 g, 50%); IR ν (cm^{-1}): 3460 (OH), 3175 (N-H), 1725 (CO); ^{1}H NMR δ 3.40 (d, 2H, J = 1.2 Hz, C-5 proton), 3.85 (m, 1H, C-6 proton), 4.11 (d, 1H, J = 6.0 Hz, C-7 proton), 6.48 (s, 1H, phenyl H), 6.60 (d, 1H, J = 8.6 Hz, phenyl H), 7.17 (d, 1H, J = 8.2 Hz, phenyl H), 9.75 (s, 1H, N-H) and 11.25 (s, 1H, OH phenolic). Anal. for $C_{13}H_9NO_3S_3$ (323); Calc.: C 48.28; H 2.80; N 4.33; S 29.74; found: C 48.53; H 2.57; N 4.58; S 29.96.

3.10 *Reactions of 3a,b with N-phenylmaleimide and ω-nitrostyrene (general procedure)*

A solution of equimolecular amounts (0.01 mole) of **3a**,**b** and *N*-phenylmaleimide or *ω*-nitrostyrene in acetic acid (50 ml) was refluxed for 10 min. The solid, so formed, was filtered off and crystallized from the appropriate solvent.

3.11 *7-(2,4-Dihydroxyphenyl)-N-phenyl-5,6-dihydrothiopyrano[2,3-d]thiazolidine-2-oxo-5,6-dicarboximide (8a)*

Whitish brown crystals (acetic acid), mp 208 °C (2 g, 47%); IR ν (cm^{-1}): 3360 (OH), 3173 (N-H), 1711 (CO), 1660 (CO); ^{1}H NMR δ 4.20 (dd, 1H, 6.2, 9.1 Hz, C-6 proton), 4.95 (d, 1H, J = 6.2 Hz, C-5 proton), 5.30 (d, 1H, J = 8.0 Hz, C-7 proton), 6.79 (m, 8H, phenyl H), 10.40 (s, 1H, N-H), 11.0 (s, 1H, OH phenolic) and 13.56 (s, 1H, OH phenolic). Anal. for $C_{20}H_{14}N_2O_5S_2$ (426); Calc.: C 56.32; H 3.31; N 6.56; S 15.03; found: C 56.11; H 3.53; N 6.34; S 15.28.

3.12 *7-(2,4-Dihydroxyphenyl)-N-phenyl-5,6-dihydrothiopyrano[2,3-d]thiazolidine-2-thioxo-5,6-dicarboximide (8b)*

Whitish brown (acetic acid), mp 195 °C (2.35 g, 53%); IR ν (cm^{-1}): 3358 (OH), 3165 (N-H), 1710 (CO); ^{1}H NMR δ 4.12 (dd, 1H, J = 6.0, 9.0 Hz, C-6 proton), 4.71 (d, 1H, J = 6.0 Hz, C-5 proton), 5.10 (d, 1H, J = 7.6 Hz, C-7 proton), 6.76 (m, 8H, phenyl H), 10.30 (s, 1H, N-H), 10.86 (s, 1H, OH phenolic) and 13.50 (s, 1H, OH phenolic). Anal. for $C_{20}H_{14}N_2O_4S_3$ (442); Calc.: C 54.28; H 3.18; N 6.33; S 21.73; found: C 54.56; H 3.41; N 6.57; S 21.53.

3.13 *7-(2,4-Dihydroxy-phenyl)-6-nitro-5-phenyl-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-one (9a)*

Yellowish brown crystals (dil. acetic acid), mp 158 °C (1.97 g, 49%); IR ν (cm^{-1}): 3470 (OH), 3175 (N-H), 1689 (CO); ^{1}H NMR δ 3.57 (d, 1H, J = 8.0 Hz, C-7 proton), 4.07 (m, 1H, C-5 proton), 4.80 (m, 1H, C-6 proton), 6.66 (m, 8H, phenyl H), 10.40 (s, 1H, N-H), 11 (s, 1H, OH phenolic) and 13.56 (s, 1H, OH phenolic). Anal. for $C_{18}H_{14}N_2O_5S_2$ (402); Calc.: C 53.72; H 3.51; N 6.96; S 15.94; found: C 53.52; H 3.28; N 6.58; S 16.17.

3.14 *7-(2,4-Dihydroxy-phenyl)-6-nitro-5-phenyl-5,6-dihydrothiopyrano[2,3-d]thiazolidine-2-thione (9b)*

Whitish brown crystals (dil. acetic acid), mp 165 °C (1.52 g, 36%); IR ν (cm^{-1}): 3460 (OH), 3165 (N-H); ^{1}H NMR δ 3.35 (d, 1H, J = 8.0 Hz, C-7 proton), 4.0 (m, 1H, C-5 proton), 4.74 (m, 1H, C-6 proton), 6.65 (m, 8H, phenyl H), 10.33 (s, 1H, N-H), 10.97 (s, 1H, OH phenolic) and 13.50 (s, 1H, OH phenolic). Anal. for. $C_{18}H_{14}N_2O_4S_3$ (418). Calc.: C 51.66; H 3.37; N 6.69; S 22.99; found: C 51.88; H 3.58; N 6.48; S 23.24.

3.15 *Reaction of 3a,b with N-phenyl-1,3,4-triazole-2,5-dione (general procedure)*

A solution of equimolecular amounts (0.01 mole) of **3a**,**b** and *N*-phenyl-1, 3, 4-triazol-2,5-dione in tetrahydrofuran (THF) (25 ml) was stirred at room temperature. The solid, so formed, was filtered off and crystallized from dimethylformamide (DMF).

3.16 *10-(2,4-Dihydroxyphenyl)-7-phenyl-thiazolo[5,4-e]thiadiazino[2′,3′-a]triazole-2,6,8-trione (10a)*

White crystals, mp above 300 °C (1.58 g, 37%); IR ν (cm^{-1}): 3430 (OH), 3165 (N-H), 1719 (CO), 1686 (CO); ^{1}H NMR δ 5.66 (s, 1H, C-7 proton), 6.95 (m, 8H, phenyl H), 10.30 (s, 1H, N-H), 10.85 (s, 1H, OH phenolic) and 13.55 (s, 1H, OH phenolic). Anal. for $C_{18}H_{12}N_4O_5S_2$ (428), Calc.: C 50.46; H 2.82; N 13.08; S 14.97; found: C 50.70; H 3. 0; N 13.30; S 14.75.

3.17 *10-(2,4-Dihydroxyphenyl)-7-phenyl-2-thioxo-thiazolo[5,4-e]thiadiazino[2′,3′-a]-triazole-6,8-dione (10b)*

Whitish brown crystals, mp above 300 °C (1.75 g, 39%); IR ν (cm^{-1}): 3430 (OH) 3200 (N-H), 1719 (CO); ^{1}H NMR δ 5.63 (s, 1H, C-7 proton), 6.90 (m, 8H, phenyl H), 10.11 (s, 1H, N-H), 10.65 (s, 1H, OH phenolic) and 13.45 (s, 1H, OH phenolic). Anal. for $C_{18}H_{12}N_4O_4S_3$ (444). Calc.: C 48.64; H 2.72; N 12.60; S 21.64; found: C 48.87; H 2.94; N 12.85; S 21.86.

3.18 *Reaction of 3a,b with malononitrile to afford 5-[2,4-dihydroxy-phenyl(dicyano-methyl)methyl]-4-thioxo-thiazolidine derivatives (11a,b) (general procedure)*

A solution of equimolecular amounts (0.01 mol) of **3a**,**b** and malononitrile in ethanol (100 mL), containing few drops of triethylamine, was mechanically stirred at room temperature, until the color of the reaction mixture faded away and a complete precipitation of solid took place. The solid product so formed was filtered off and recrystallized.

3.19 *5-[2,4-Dihydroxy-phenyl(dicyanomethyl)methyl]-4-thioxo-thiazolidin-2-one (11a)*

Reddish-brown solid (DMF), mp above 300 °C, (1.53 g, 48%); IR ν (cm^{-1}): 3299 (OH), 3230 (N-H), 2203 (CN), 1687 (CO); ^{1}H NMR δ 1.40 (t, J = 13.5 Hz, 1H, Ar-C<u>H</u>), 3.61 (d, 1H, J = 6.8 Hz, C<u>H</u>-CN), 4.26 (d, J = 5.9 Hz, 1H, C<u>H</u>-CS), 6.51 (s, 1H, phenyl H), 6.76 (d, 1H, J = 8.6 Hz, phenyl H), 7.27 (d, 1H, J = 8.0 Hz, phenyl H), 8.78 (s, 1H, N-H), 11.36 (s, 1H, OH) and 13.73 (s, 1H, OH). Anal. for $C_{13}H_9N_3O_3S_2$ (319). Calc.; C 48.89; H 2.84; N 13.16; S 20.02; found: C 48.66; H 2.61; N 13.40; S 20.30.

3.20 *5-[2,4-Dihydroxy-phenyl(dicyanomethyl)methyl]thiazolidine-2,4-dithione (11b)*

Reddish-violet solid (dil. acetic acid), mp 240 °C, (2 g, 60%); IR ν (cm^{-1}): 3366 (OH), 3217 (N-H), 2203 (CN); ^{1}H NMR δ 1.35 (t, J = 13.0 1H, Ar-C<u>H</u>), 3.41 (d, 1H, J = 6.6 Hz, C<u>H</u>-CN), 4.18 (d, J = 5.6 Hz, 1H, C<u>H</u>-CS), 6.37 (s, 1H, phenyl H), 6.70 (d, 1H, J = 8.6 Hz, phenyl H), 7.16 (d, 1H, J = 8.2 Hz, phenyl H), 8.68 (s, 1H, N-H), 11.30 (s, 1H, OH) and 13.70 (s, 1H, OH). Anal. for $C_{13}H_9N_3O_2S_3$ (335). Calc. C 46.55; H 2.70; N 12.53; S 28.68; found: C 46.30; H 2.49; N 12.31; S 28.48.

3.21 *Reaction of 3a,b with malononitrile to give 5-amino-9-hydroxy-3H,11bH-dihydro [1]benzopyrano[3′,4′:4,5]thiopyrano[2,3-d]thiazol-6-one derivatives 14a,b (general procedure)*

A solution of equimolecular amounts (0.01 mol) of **3a**,**b** and malononitrile in ethanol (100 mL), containing few drops of triethylamine, was refluxed for 1 h, then left at room temperature. The solid product so obtained was filtered off and crystallized from acetic acid.

14a, Reddish-brown solid, mp above 300 °C (1.65 g, 51%); IR ν (cm^{-1}): 3365 (OH), 3300, 3286 (NH_2), 3185 (N-H), 1710 (CO), 1680 (CO); ^{1}H NMR δ 4.40 (s, 1H, C 11b proton), 6.58 (s, 1H, phenyl H), 6.66 (d, 1H, J = 8.8 Hz, phenyl H), 7.25 (d, 1H, J = 8.4 Hz, phenyl H), 10 (s, 1H, N-H), 11.12 (br., 2H, NH_2, exch.) and 11.73 (s, 1H, OH phenolic). Anal. for $C_{13}H_8N_2O_4S_2$ (319). Calc.: C 48.89; H 2.52; N 8.74; S 20.02, found: C 48.65; H 2.75; N 8.50; S 20.25.

14b, Violet solid, mp above 300 °C (1.88 g, 56%); IR ν (cm^{-1}): 3389 (OH), 3318, 3287 (NH_2), 3188 (N-H), 1700 (CO); ^{1}H NMR δ 4.35 (s, 1H, C 11b proton), 6.51 (s, 1H, phenyl H), 6.68 (d, 1H, J = 8.8 Hz, phenyl H), 7.19 (d, 1H, J = 8.2 Hz, phenyl H), 9.85 (s, 1H, N-H), 10.90 (br., 2H, NH_2, exch.) and 11.55 (s, 1H, OH phenolic). Anal. for $C_{13}H_8N_2O_3S_3$ (336). Calc.: C 46.41; H 2.40; N 8.33; S 28.59, found: C 46.65; H 2.65; N 8.53; S 28.30.

3.22 *6-Hydroxy[1]benzopyrano[2,3-d]thiazole derivatives 16a,b (general procedure)*

To a solution of **3a**,**b** (0.01 mole) in ethanolic potassium hydroxide (20 mL, 10%) was added either methyl iodide, ethyl bromoacetate or phenacyl bromide (0.01 mol). The reaction mixture was refluxed for 30 min., cooled to room temperature, then poured onto ice-cold water; the resulting precipitate was filtered off and recrystallized from dil. acetic acid.

16a, reddish violet solid, mp 125 °C (1.6 g, 73%); IR ν (cm^{-1}): 3410 (OH), 1683 (CO); ^{1}H NMR δ 7.11 (m, 4H, phenyl H and CH) and 13.64 (s, 1H, OH phenolic). Anal. for $C_{10}H_5NO_3S$ (219). Calc.: C 54.79; H 2.30; N 6.39; S 14.63; found: C 54.58; H 2.52; N 6.18; S 14.40.

16b, reddish violet solid, mp 135 °C (1.53 g, 65%); IR ν (cm^{-1}): 3390 (OH); ^{1}H NMR δ 7.06 (m, 4H, phenyl H and CH) and 11.55 (s, 1H, OH). Anal. for $C_{10}H_5NO_2S_2$ (235). Calc.: C 51.05; H 2.14; N 5.95; S 27.26; found: C 51.25; H 2.38; N 5.76; S 27.04.

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