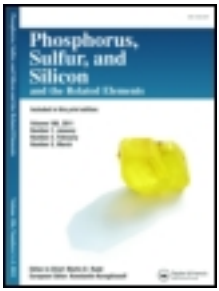

Phosphorus, Sulfur, and Silicon and the Related Elements

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A Convenient Synthesis of Some New 5-Substituted-4-Thioxo-Thiazolidinones and Fused Thiopyrano[2,3-d]thiazole Derivatives

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A Convenient Synthesis of Some New 5-Substituted-4-Thioxo-Thiazolidinones and Fused Thiopyrano[2,3-*d*]thiazole Derivatives

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The new Z-5-arylmethylene-4-thioxo-thiazolidine derivatives have been synthesized by condensation of ω-(4-formylphenoxy)acetophenone derivatives with 4-thioxo-thiazolidine derivatives, in good yields. The cycloaddition of the newly synthesized compounds to N-arylmaleimides, N-phenyl-1,2,4-triazole-3,5-dione, ethyl acrylate and ω-nitrostyrene has been studied. Under thermal reaction conditions [4 + 2] cycloaddition proceeds with complete site- and regioselectivity to yield the new fused thiopyrano[2,3-d]thiazole derivatives.

Keywords 4-Thioxo-thiazolidine derivatives; 5-[(4-benzoylmethoxy)phenylmethylene]-4-thioxo-thiazolidines; ω-(4-formylphenoxy)acetophenones; thiopyrano[2,3-d]-thiazole derivatives

INTRODUCTION

As a part of the general interest in heterocyclic synthesis, which has been explored for developing pharmaceutically important compounds, thiazolidinones have been studied extensively due to their ready accessibility, diverse chemical reactivity and broad spectrum of biological activity.[1–13] Recently, it was established, that the modified 5-substituted thiazolidinone derivatives exhibited diverse pharmacological activities.[14–17]In addition, heterocyclic systems having both thiazolidine and thiopyrano moieties have important applications in the field of medicinal chemistry.[18–20] Our objective is that 4-thioxo-thiazolidinones are synthetic precursors of thiopyrano[2,3-*d*]thiazole compounds, which could imitate some pharmacologically important molecular fragments of thiazolidinones. In continuation of our previous studies on 4-thioxo-thiazolidines,[21–28] I report here the synthesis

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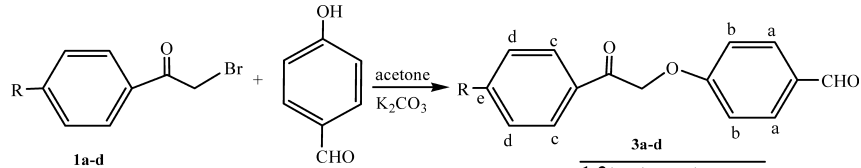
of some new thiopyrano[2,3-*d*]thiazole derivatives, starting from *ω*-(4-formylphenoxy)acetophenone derivatives and 4-thioxo-thiazolidinone derivatives.

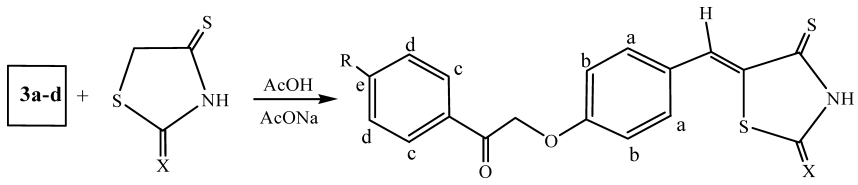
RESULTS AND DISCUSSION

The etherification of *ω*-bromoacetophenone derivatives **1a-d** with 4-hydroxybenzaldehyde (**2**) in refluxing acetone and in the presence of anhydrous K_2CO_3, afforded the corresponding *ω*-(4-formylphenoxy)acetophenone derivatives **3a-d** in almost quantitative yields (Scheme 1). The structure of the isolated products **3a-d** were deduced from elemental analyses and spectral data. For example, the IR spectrum of **3a** showed an absorption band near 2848, 2763 cm^{-1}, due to aldehydic CH group and 1681–1683 cm^{-1}, due to two C=O groups, in addition to other absorptions correlated to the assigned structures. Furthermore, the ^1H NMR spectrum of the same product revealed a singlet signal at $\delta = 5.76$ attributed to the active methylene protons and a singlet signal at $\delta = 9.87$ attributed to aldehydic proton. Also, the mass spectrum showed correct molecular ion peak at *m/z* 240 (M^+) beside some of the abundant fragments. Elemental analyses are in agreement with the structures **3a-d** (cf. Experimental).

The aldehydes **3a-d** were allowed to condense with 4-thioxo-thiazolidin-2-one (**4a**) and /or 2,4-dithioxo-thiazolidine (**4b**) in glacial acetic acid and in the presence of anhydrous sodium acetate to afford 5-arylmethylene-4-thioxo-thiazolidine derivatives **5a-h**, respectively, in good yields. The structures of products **5a-h** were established via their elemental analyses and spectral data. For example, the IR spectrum of **5a** showed absorption bands at 3055 and 1700–1702 cm^{-1} due to NH and two C=O groups, and in addition to other absorptions correlated to the assigned structure. Its ^1H NMR spectrum revealed a singlet signal at $\delta = 5.72$ due to methylene protons, a singlet signal at $\delta = 8.07$ due to olefinic proton and a D_2O-exchangeable signal at $\delta = 13.73$ attributed to NH proton, beside the other expected signals. The mass



SCHEME 1



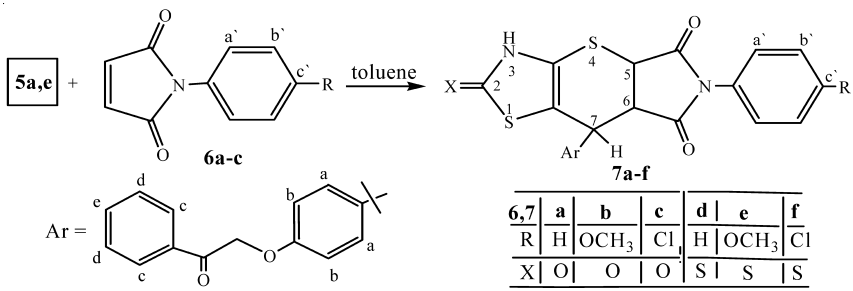
5	a	b	c	d	e	f	g	h
R	H	CH_3	Br	Cl	H	CH_3	Br	Cl
X	O	O	O	O	S	S	S	S

SCHEME 2

spectrum of **5a** showed correct molecular ion peak at m/z 355 (M^+). In addition, an evidence to support the structural assignment was gained from the ^{13}C NMR spectrum of the same compound, which showed two characteristic signals at δ 70.32 and 195.07 attributed to methylene and carbonyl carbon atoms. In addition, two characteristic signals at $\delta = 170.55$ and 193.89 corresponding to carbonyl and thiocarbonyl carbon atoms of thiazolidine ring, respectively, beside the other expected signals (cf. Experimental). From these data the *Z*-configuration was assigned to structures **5** on the basis that the olefinic proton of the *Z*-configured isomer is more deshielded by the thioxo group of the thiazole moiety compared with the *E*-isomer and appears at lower field ($\delta \sim 8.0$–8.50 ppm) relative to the *E*-isomer[29–31] ($\delta \sim 7.30$–7.80 ppm) (cf. Scheme 2 and Experimental).

Next, my study is extended to explore the utility of compounds **5a,e** in Diels-Alder reaction with different dienophiles. Thus, heating equimolar amounts of the deeply colored **5a,e** and *N*−arylmaleimides **6a-c** under reflux in toluene gave colorless 1:1 adducts. The IR spectrum of the isolated product **7b** taken as typical example of the prepared series, showed absorption bands at 1677 cm^{-1} and 1716 cm^{-1}, corresponding to CO groups. Furthermore, the ^1H NMR data of this adduct showed two doublets at $\delta = 3.88$ and 3.95 with J values 5.6 and 8.6 Hz attributed to H-6, in addition to two doublets at $\delta = 4.45$ and 5.24 with J values 5.6 and 8.6 Hz, respectively, corresponding to H-5 and H-7, beside the other expected signals. Based on the coupling constant, the cis-configurations[32] was assigned to the cycloadducts **7b**. Based on the elemental analyses and spectral data, structures **7a-f** were assigned to these adducts (cf. Scheme 3 and Experimental).

Similarly, the reaction of **5a,e** with N-phenyl-1, 2, 4-triazole-3,5-dione (**8**) in refluxing toluene afforded the 1:1 adducts **9a,b** (cf. Scheme 4). The structures of the isolated adducts **9a,b** were deduced from their elemental analyses and spectral data (cf. Experimental).



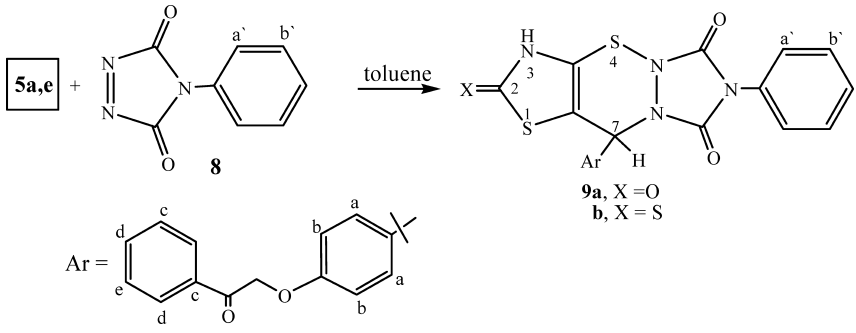
6,7	a	b	c	d	e	f
R	H	OCH_3	Cl	H	OCH_3	Cl
X	O	O	O	S	S	S

SCHEME 3

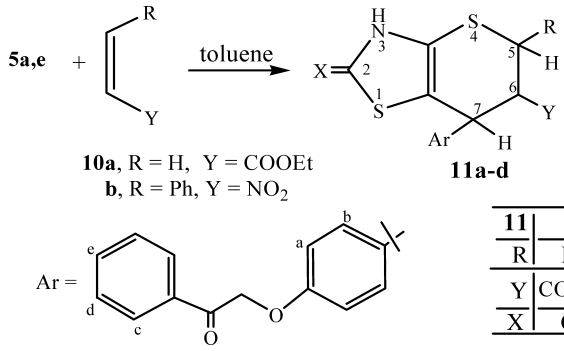
Also, the cycloaddition of **5a,e** with ethyl acrylate (**10a**) and *ω*-nitrostyrene (**10b**) in refluxing toluene gave the thiazolothiopyrano cycloadducts, **11a-d** (cf. Scheme 5). The structures of **11a-d** were assigned based on their elemental analyses and spectral data. The ^{1}H NMR spectra of compounds **11a,b** revealed in each case one doublet at $\delta \sim 4.45$ corresponding to H-7 and two doublets at ~ 3.28 and 3.37 corresponding to H-5ax and H-5eq in addition to multiplet at $\delta \sim 3.04$–3.15 corresponding to H-6. The formation of compounds **11a-d** can be explained in terms of [4 + 2] cycloaddition to thiocarbonyl system (cf. Experimental).

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 in deuterated dimethylsulfoxide at 300 MHz on a Varian Gemini NMR spectrometer using tetramethylsilane as



SCHEME 4



11	a	b	c	d
R	H	H	Ph	Ph
Y	COOEt	COOEt	NO_2	NO_2
X	O	S	O	S

SCHEME 5

internal reference, and results are expressed as δ values. Mass spectra were taken on a Shimadzu GCMS-QP 1000 Ex mass spectrometer at 70 eV. Elemental analyses were carried out at the Microanalysis Center of Cairo University, Giza, Egypt. The starting compounds **4a** and **4b** were prepared according to the reported literature.[33,34]

ω-(4-Formylphenoxy)acetophenone Derivatives 3a-d—General Procedure

ω-Bromoacetophenone derivatives **1a-d** (10 mmol) was added to a mixture of 4-hydroxybenzaldehyde (**2**) (1.22 g, 10 mmol) and anhydrous K_2CO_3 (2.90 g, 30 mmol) in dry acetone (30 ml). The mixture was refluxed on a water bath for 6 h, left to cool, poured into cold water, filtered off, and recrystallized from ethanol to afford pale brown crystals.

ω-(4-Formylphenoxy)acetophenone (3a)

Yield (98%); m.p. 117°C; IR (cm^{-1}) ν 2848, 2763 (aldehydic CH) and 1681–1683 (C=O); ^{1}H NMR (DMSO) δ 5.76 (s, 2H, CH_2), 7.16 (d, $2H_b$, $J = 9.0$, Hz, ArH's), 7.57 (t, $2H_d$, $J = 7.2$ Hz, ArH's), 7.70 (t, $1H_e$, $J = 7.4$ Hz, ArH's), 7.88 (d, H_a, $J = 8.7$ Hz, ArH's), 8.04 (d, $2H_c$, $J = 7.2$ Hz, ArH's), 9.87 (s, 1H, CHO); MS (*m/z*): 240 (M^+, 5.7%), 121 (4.9%), 105 (100%), 91 (16.4%), 77 (36.7%), 61 (4.6%), and 50 (18.6%). Anal. for $C_{15}H_{12}O_3$ (240.25) calcd.: C, 74.99; H, 5.03. Found: C, 74.87; H, 5.16.

ω-(4-Formylphenoxy)-4-methylacetophenone (3b)

Yield (92%); m.p. 105°C; IR (cm^{-1}) ν 2859, 2789 (aldehydic CH) and 1698–1700 (C=O); ^{1}H NMR (DMSO) δ 2.37 (s, 3H, CH_3), 5.70 (s, 2H, CH_2), 7.15 (d, $2H_b$, $J = 9.0$ Hz, ArH's), 7.39 (d, $2H_d$, $J = 6.1$ Hz, ArH's), 7.85 (d, $2H_a$, $J = 8.7$ Hz, ArH's), 7.92 (d, $2H_c$, $J = 8.4$ Hz, ArH's), 9.87

(s, 1H, CHO). MS (*m/z*): 254 (M^+, 6.3%), 119 (100%), 91 (36.4%), 77 (17.4%), and 61 (2.1%). Anal. for $C_{16}H_{14}O_3$ (254.28) calcd.: C, 75.57; H, 5.55. Found: C, 75.71; H, 5.38.

ω-(4-Formylphenoxy)-4-bromoacetophenone (3c)

Yield (97%); m.p. 122°C; IR (cm^{-1}) ν 2832, 2762 (aldehydic CH) and 1706–1710 (C=O); ^{1}H NMR (DMSO) δ 5.76 (s, 2H, CH_2), 7.18 (d, $2H_b$, $J = 9.0$ Hz, ArH's), 7.71 (d, $2H_d$, $J = 8.6$ Hz, ArH's), 7.88 (d, $2H_a$, $J =$ 8.8 Hz, ArH's), 8.01 (d, $2H_c$, $J = 8.2$ Hz, ArH's), 9.01 (s, 1H, CHO). MS (*m/z*): 320 (M^{+1}, 12.9%), 183 (100%), 169 (8.1%), 155 (23.7%), 105 (14.6%), 90 (19.9%), 77 (23.2%), 63 (13.2%), and 50 (37.7%). Anal. for $C_{15}H_{11}BrO_3$ (319.15) calcd.: C, 56.45; H, 3.47; Br, 25.04 . Found: C, 56.28; H, 3.32, Br, 25.20.

ω-(4-Formylphenoxy)-4-chloroacetophenone (3d)

Yield (94%); m.p. 128°C; IR (cm^{-1}) ν 2865, 2782 (aldehydic CH) and 1708–1710 (C=O); ^{1}H NMR (DMSO) δ 5.77 (s, 2H, CH_2), 7.19 (d, $2H_b$, $J = 9.0$ Hz, ArH's), 7.68 (d, $2H_d$, $J = 8.6$ Hz, ArH's), 7.84 (d, $2H_a$, $J =$ 8.6 Hz, ArH's), 8.04 (d, $2H_c$, $J = 8.2$ Hz, ArH's), and 8.98 (s, 1H, CHO). Anal. for $C_{15}H_{11}ClO_3$ (274.04) calcd.: C, 65.58; H, 4.04; Cl, 12.91. Found: C, 65.43; H, 4.17; Cl, 12.78.

Condensation of 3a-d with 4-Thioxo-thiazolidin-2-one (4a) and/or 2,4-Dithioxo-thiazolidine (4b)—*General Procedure*

To a solution of **4a** or **4b** (10 mmol) in glacial acetic acid (25 ml) and anhydrous sodium acetate (1.64 g, 20 mmol) was added the appropriate aldehyde **3a-d** (10 mmol). The reaction mixture was refluxed for 30 min. on a water bath, cooled and then poured into cold water. The solid so formed was filtered off and recrystallized from EtOH/dioxane to give orange or reddish crystals of **5a-d**.

Z-5-[4-(Benzoylmethoxy)phenylmethylene]-4-thioxo-thiazolidin-2-one(5a)

Yield (75%); m.p. 198°C; IR (cm^{-1}) υ 3055 (NH) and 1700–1702 (C=O); ^{1}H NMR (DMSO) δ 5.72 (s, 2H, CH_2), 7.14 (d, $2H_b$, $J = 9.3$ Hz, ArH's), 7.56 (d, $2H_a$, $J = 7.5$ Hz, Ar's), 7.60 (t, $2H_d$, $J = 8.7$ Hz, ArH's), 7.69 (t, $1H_e$, $J = 7.5$ Hz, ArH's), 8.02 (d, $2H_c$, $J = 7.2$ Hz, Ar's), 8.07 (s, 1H, CH), 13.73 (brs, NH, exchangeable with D_2O). ^{13}C NMR (DMSO-d_6,) δ 70.32 (CH_2), 115.18, 126.31, 127.15, 127.87, 128.84, 132.71, 133.90, 134.18, 136.15, 160.27, 170.55 (C=O), 193.89 (C = S) and 195.07 (C=O). MS m/z (%): 355 (M^+, 19.3%), 235 (7.5%), 193 (4.4%), 181 (3.1%), 165

(2.7%), 149 (3.5%), 106 (8.3%), 105 (100%), 89 (7.5%), and 77 (47.5%). Anal. for $C_{18}H_{13}NO_3S_2$ (355.43) calcd.: C, 60.83; H, 3.69; N, 3.94; S, 18.04. Found: C, 60.68; H, 3.57; N, 3.78; S, 17.89.

Z-5-[4-(4-Methylbenzoylmethoxy)phenylmethylene]-4-thioxo-thiazolidin-2-one(5b)

Yield (72%), m.p. 170°C; IR (cm^{-1}) υ 3120 (NH) and 1690 (C=O); ^1H NMR (DMSO) δ 3.36 (s, 3H, CH_3), 5.72 (s, 2H, CH_2), 7.12 (d, $2H_b$, $J =$ 8.8 Hz, ArH's), 7.53–7.62 (m, $4H_{a,d}$, ArH's), 7.98 (d, $2H_c$, $J = 7.6$ Hz, ArH's), 8.0 (s, 1H, CH), and 13.71 (brs, NH, exchangeable with D_2O). Anal. for $C_{19}H_{15}NO_3S_2$ (369.46) calcd.: C, 61.77; H, 4.09; N, 3.79; S, 17.36. Found: C, 61.63; H, 4.21; N, 3.62; S, 17.50.

Z-5-[4-(4-Bromobenzoylmethoxy)phenylmethylene]-4-thioxo-thiazolidin-2-one(5c)

Yield (80%); m.p. 227°C; IR (cm^{-1}) υ 3175 (NH) 1686 and 1690 (C=O); ^1H NMR (DMSO) δ 5.74 (s, 2H, CH_2), 7.12 (d, $2H_b$, $J = 8.8$ Hz, ArH's), 7.66 (d, $2H_a$, $J = 8.4$ Hz, ArH's), 7.77 (d, $2H_d$, $J = 8.2$ Hz, ArH's), 7.82 (d., $2H_c$, $J = 8.4$ Hz, ArH's), 8.02 (s, 1H, CH), and 13.70 (brs, NH, exchangeable with D_2O). Anal. for $C_{18}H_{12}BrNO_3S_2$ (434.33) calcd.: C, 49.78; H, 2.78; Br, 18.40; N, 3.22; S, 14.77. Found: C, 49.91; H, 2.90; Br, 18.24; N, 3.37; S, 14.63.

Z-5-[4-(4-Chlorobenzoylmethoxy)phenylmethylene]-4-oxo-thiazolidin-2-one(5d)

Yield (82%), m.p. 218°C; IR (cm^{-1}) υ 3183 (NH), 1687 and 1690 (C=O); ^1H NMR (DMSO) δ 5.73 (s, 2H, CH_2), 7.14 (d, $2H_b$, $J =$ 9.0 Hz, ArH's), 7.60 (d, $2H_a$, $J = 8.2$ Hz, Ar's), 7.74 (d, $2H_d$, $J = 8.4$ Hz, ArH's), 8.88 (d, $2H_c$, $J = 8.2$ Hz, Ar's), 8.04 (s, 1H, CH), and 13.73 (brs, NH, exchangeable with D_2O). Anal. for $C_{18}H_{12}ClNO_3S_2$ (389.88) calcd.: C, 55.45; H, 3.10; Cl, 9.09; N, 3.59; S, 16.45. Found: C, 55.57; H, 3.23; Cl, 9.23; N, 3.42; S, 16.58.

Z-5-[4-(Benzoylmethoxy)phenylmethylene]-2,4-dithioxo-thiazolidine(5e)

Yield (83%); m.p. 202°C; IR (cm^{-1}) υ 3100 (NH) and 1690 (C=O); ^1H NMR (DMSO) δ 5.73 (s, 2H, CH_2), 7.12 (d, $2H_b$, $J = 8.8$ Hz, ArH's), 7.53 (d, $2H_a$, $J = 7.4$, Ar's), 7.59 (t, $2H_d$, $J = 7.4$ Hz, ArH's), 7.70 (t, $1H_e$, $J =$ 7.6 Hz, ArH's), 8.0 (d, $2H_c$, $J = 7.2$ Hz, Ar's), 8.08 (s, 1H, CH), 13.70 (brs, NH, exchangeable with D_2O). Anal. for $C_{18}H_{13}NO_2S_3$ (371.50) calcd.: C, 58.20; H, 3.53; N, 3.77; S, 25.89. Found: C, 58.33; H, 3.70; N, 3.64; S, 25.77.

Z-5-[4-(4-Methylbenzoylmethoxy)phenylmethylene]-2,4-dithioxo-thiazolidine(5f)

Yield (78%); m.p. 215°C; IR (cm^{-1}) υ 3126 (NH) and 1690 (C=O); ^1H NMR (DMSO) δ 3.37 (s, 3H, CH_3), 5.72 (s, 2H, CH_2), 7.12 (d, $2H_b$, J = 9.0 Hz, ArH's), 7.55–7.66 (m, $4H_{a,d}$, ArH's), 7.97 (d, $2H_c$, J = 7.8 Hz, ArH's), 8.02 (s, 1H, CH), 13.68 (brs, NH, exchangeable with D_2O). MS m/z (%): 385 (21.3%), 252 (10.9%), 193 (5.2%), 177 (5.2%), 191 (2.1%), 177 (5.8%), 165 (4.3%), 150 (6.3%), 105 (28.6%), 119 (100%), 91 (36.3%), and 77 (17.1%). Anal. for $C_{19}H_{15}NO_2S_3$ (385.52) calcd.: C, 59.19; H, 3.92; N, 3.63; S, 24.95. Found: C, 59.33; H, 3.75; N, 3.49; S, 24.78.

Z-5-[4-(4-Bromobenzoylmethoxy)phenylmethylene]-2,4-dithioxo-thiazolidine(5g)

Yield (83%); m.p. 242°C; IR (cm^{-1}) υ 3177 (NH) and 1690 (C=O); ^1H NMR (DMSO) δ 5.72 (s, 2H, CH_2), 7.12 (d, $2H_b$, J = 8.8 Hz, ArH's), 7.60 (d, $2H_a$, J = 7.6 Hz, ArH's), 7.74 (d, $2H_d$, J = 8.4 Hz, ArH's), 7.88 (d., $2H_c$, J = 8.4 Hz, ArH's), 8.07 (s, 1H, CH), and 13.64 (brs, NH, exchangeable with D_2O). Anal. for $C_{18}H_{12}BrNO_2S_3$ (450.39) calcd.: C, 48.0; H, 2.69; Br, 17.74; N, 3.11; S, 21.36. Found: C, 48.18; H, 2.54; Br, 17.90; N, 3.28; S, 21.49.

Z-5-[4-(4-Chlorobenzoylmethoxy)phenylmethylene]-2,4-dithioxo-thiazolidine(5h)

Yield (87%); m.p. 230°C; IR (cm^{-1}) υ 3187 (NH) and 1690 (C=O); ^1H NMR (DMSO)δ 5.75 (s, 2H, CH_2), 7.15 (d, $2H_b$, J = 8.6 Hz), 7.58 (d, $2H_a$, J = 7.8 Hz), 7.70 (d, $2H_d$, J = 7.8 Hz), 8.02 (d, $2H_c$, J = 8.2 Hz), 8.04 (s, 1H, CH), and 13.65 (brs, NH, exchangeable with D_2O). Anal. for $C_{18}H_{12}ClNO_2S_3$ (405.94) calcd.: C, 53.26; H, 2.98; Cl, 8.73; N, 3.45; S, 23.70. Found: C, 53.39; H, 2.86; Cl, 8.88; N, 3.29; S, 23.58.

Reactions of 5a,e with N-arylmaleimides, N-phenyl-1,2,4-triazole-3,5-dione, Ethyl Acrylate and ω-Nitrostyrene—General Procedure

A solution of equimolecular amounts (10 mmol) of **5a,e,** and the appropriate dienophile in toluene (30 ml) was refluxed for 1 h. The solid so formed was filtered off and crystallized from the appropriate solvent.

7-[4-(Benzoylmethoxy)phenyl]-N-phenyl-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-oxo-5,6-dicarboximide (7a)

White crystals (EtOH/dioxane); yield (57%); m.p. 218°C; IR (cm^{-1}) υ 3186 (NH), 1711 (CO) and 1677 (CO); ^1H NMR (DMSO) δ 3.85–3.91

(dd, 1H, $J = 5.6$ Hz, 8.6 Hz, H-6), 4.42 (d, 1H, $J = 5.6$ Hz, H-5), 5.22 (d, 1H, $J = 8.6$ Hz, H-7), 5.60 (s, 2H, CH_2), 6.50 (d, $2H_b$, $J = 8.8$ Hz, ArH's), 6.88 (m, $3H_{a,c'}$, ArH's), 7.18 (t, $2H_{b'}$, $J = 8.4$ Hz, ArH's), 7.32 (m, $2H_{a'}$, ArH's), 7.35 (t, $2H_d$, $J = 7.6$ Hz, Ar's), 7.57 (t, $1H_e$, $J = 7.0$ Hz, Ar's), 8.01 (d, $2H_c$, $J = 7.2$ Hz, ArH's), and 11.80 (s, 1H, NH). Anal. for $C_{28}H_{20}N_2O_5S_2$ (528.60) calcd.: C, 63.62; H, 3.81; N, 5.30; S, 12.13. Found: C, 63.45; H, 3.65; N, 5.48; S, 12.28.

7-[4-(Benzoylmethoxy)phenyl]-N-(4-methoxyphenyl)-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-oxo-5,6-dicarboximide (7b)

Pale brown crystals (EtOH/dioxane); yield (63%); m.p. 225°C; IR (cm^{-1}) υ 3165 (NH), 1716 (CO) and 1677 (CO); ^{1}H NMR (DMSO) δ 3.75 (s, 3H, OCH_3), 3.88–3.95 (dd, 1H, $J = 5.6$, 8.6 Hz, H-6), 4.45 (d, 1H, $J = 5.6$ Hz, H-5), 5.24 (d, 1H, $J = 8.6$ Hz, H-7), 5.62 (s, 2H, CH_2), 6.53 (d, $2H_b$, $J = 9.0$ Hz, ArH's), 6.91–7.0 (m, $2H_a$, $2H_{b'}$, ArH's), 7.22 (d, $2H_{a'}$, $J = 8.6$ Hz, ArH's), 7.55 (t, $2H_d$, $J = 7.8$ Hz, ArH's), 7.65 (t, $1H_e$, $J = 7.4$ Hz, ArH's), 8.03 (d, $2H_c$, $J = 6.8$ Hz, ArH's), and 11.82 (s, 1H, NH). Anal. for $C_{29}H_{22}N_2O_6S_2$ (558.62) calcd.: C, 62.35; H, 3.97; N, 5.01; S, 11.48. Found: C, 62.20; H, 3.80; N, 5.18; S, 11.65.

7-[4-(Benzoylmethoxy)phenyl]-N-(4-chlorophenyl)-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-oxo-5,6-dicarboximide (7c)

Pale brown crystals (EtOH/dioxane); yield (65%); m.p. 235°C; IR (cm^{-1}) υ 3176 (NH), 1710 (CO) and 1680 (CO); ^{1}H NMR (DMSO) δ 3.98–4.11 (dd, 1H, $J = 6.0$, 8.8 Hz, H-6), 4.71 (d, 1H, $J = 6.0$ Hz, H-5), 5.10 (d, 1H, $J = 8.8$ Hz, H-7), 5.70 (s, 2H, CH_2), 6.62 (d, $2H_b$, $J = 8.8$, ArH's), 6.93–7.10 (m, $2H_a$, $2H_{b'}$, ArH's), 7.25 (d, $2H_{a'}$, $J = 8.6$ Hz, ArH's), 7.58 (t, $2H_d$, $J = 7.6$ Hz, ArH's), 7.67 (t, $1H_e$, $J = 7.2$ Hz, ArH's), 8.04 (d, $2H_c$, $J = 6.8$ Hz, ArH's), and 11.78 (s, 1H, NH). Anal. for $C_{28}H_{19}ClN_2O_5S_2$ (563.04) calcd: C, 59.73; H, 3.40; Cl, 6.30; N, 4.98; S, 11.39. Found: C, 59.56; H, 3.24; Cl, 6.20; N, 4.80; S, 11.57.

7-[4-(Benzoylmethoxy)pheny]-N-phenyl-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-thioxo-5,6-dicarboximide (7d)

White crystals (EtOH); yield (57%); m.p. 228°C; IR (cm^{-1}) υ 3173 (NH) and 1717 (CO); ^{1}H NMR (DMSO) δ 3.90–3.98 (dd, 1H, $J = 6.2$, 9.0 Hz, H-6), 4.63 (d, 1H, $J = 6.2$ Hz, H-5), 5.30 (d, 1H, $J = 9.0$ Hz, H-7), 5.59 (s, 2H, CH_2), 6.62 (d, $2H_b$, $J = 8.0$ Hz, ArH's), 6.91 (d, $3H_{a,c'}$, ArH's), 7.21 (t, $1H_{b'}$, $J = 8.6$ Hz, ArH's) 7.42 (t, $2H_{a'}$, $J = 7.0$ Hz, ArH's), 7.57 (t, $2H_d$, $J = 7.2$ Hz, Ar's), 7.69 (t, $1H_e$, $J = 7.6$ Hz, Ar's), 8.05 (d,

$2H_c$, $J = 7.0$ Hz, ArH's), and13.77 (s, 1H, NH). Anal. for $C_{28}H_{20}N_2O_4S_3$ (544.66) calcd.: C, 61.74; H, 3.70; N, 5.14; S, 17.66. Found: C, 61.86; H, 3.58; N, 5.26; S, 17.73.

7-[4-(Benzoylmethoxy)phenyl]-N-(4-methoxyphenyl)-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-thioxo-5,6-dicarboximide (7e)

White crystals (acetic acid); yield (61%); m.p. 195°C; IR (cm^{-1}) υ 3165 (NH), 1710 (CO) and 1680 (CO); ^{1}H NMR (DMSO) ^{1}H NMR (DMSO) δ 3.75 (s, 3H, OCH_3), 3.91–3.96 (dd, 1H, $J = 6.0$, 8.8 Hz, H-6), 4.65 (d, 1H, $J = 6.0$ Hz, H-5), 5.33 (d, 1H, $J = 8.8$ Hz, H-7), 5.60 (s, 2H, CH_2), 6.63 (d, $2H_b$, $J = 6.0$ Hz, ArH's), 6.91–7.22 (m, $2H_a$, $2H_{b'}$, ArH's), 7.28 (d, $2H_{a'}$, $J = 8.6$ Hz, ArH's), 7.57 (t, $2H_d$, $J = 7.0$ Hz, ArH's), 7.68 (t, $1H_e$, J = 7.2 Hz, ArH's), 8.05 (d, $2H_c$, $J = 6.8$Hz, ArH's), and 13.75 (s, 1H, NH). Anal. for $C_{29}H_{22}N_2O_5S_3$ (574.69) calcd.: C, 60.61; H, 3.86; N, 4.87; S, 16.74. Found: C, 60.51; H, 3.97; N, 4.71; S, 16.86.

7-[4-(Benzoylmethoxy)phenyl]-N-(4-chlorophenyl)-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-thioxo-5,6-dicarboximide (7f)

White crystals (acetic acid), yield (63%); m.p. 242°C; IR (cm^{-1}) υ 3187 (NH) and 1718 (CO); ^{1}H NMR (DMSO) δ 3.97–4.06 (dd, 1H, $J = 6.0$, 9.0 Hz, H-6), 4.71 (d, 1H, $J = 6.0$ Hz, H-5), 5.43 (d, 1H, $J = 9.0$ Hz, H-7), 5.65 (s, 2H, CH_2), 6.68 (d, $2H_b$, $J = 6.0$ Hz, ArH's), 6.93 (d, $2H_a$, $J = 8.8$, ArH's), 7.30 (d, $2H_{b'}$, $J = 8.8$ Hz, ArH's), 7.60 (t, $2H_d$, $J = 7.4$ Hz, ArH's), 7.71 (t, $1H_e$, J = 7.2 Hz, ArH's), 8.06 (d, $2H_c$, $J = 7.2$ Hz, ArH's), and 13.76 (s, 1H, NH). Anal. for $C_{28}H_{19}ClN_2O_4S_3$ (579.11) calcd.: C, 58.07; H, 3.31; Cl, 6.12; N, 4.84; S, 16.61. Found: C, 58.16; H, 3.44; Cl, 6.0; N, 4.95; S, 16.48.

10-[4-(Benzoylmethoxy)phenyl]-7-phenyl-thiazolo[5,4-e]thiadiazino[2′,3′-a]triazole-2,6,8-trione (9a)

White crystals (DMF); yield (45%); m.p. 297°C; IR (cm^{-1}) υ 3170 (NH) and 1711 (CO); ^{1}H NMR ($DMSO_6$)δ 5.30 (s, 1H, H-7), 5.73 (s, 2H, CH_2), 6.47 (d, $2H_b$, $J = 8.6$ Hz, ArH's), 6.85 (m, $3H_{a,c'}$, ArH's), 7.18 (t, $2H_{b'}$, $J = 8.6$ Hz, ArH's), 7.44 (d, $2H_{a'}$, $J = 7.4$ Hz, ArH's), 7.55 (t, $2H_d$, $J =$ 7.6 Hz, Ar's), 7.68 (t, $1H_e$, $J = 7.2$ Hz, Ar's), 8.0 (d, $2H_c$, $J = 7.4$ Hz, ArH's), and 11.76 (s, 1H, NH). Anal. for $C_{26}H_{18}N_4O_5S_2$ (530.57) . calcd.: C, 58.86; H, 3.42; N, 10.56; S, 12.09. Found: C 58.98; H, 3.53; N, 10.41; S, 12.28.

10-[4-(Benzoylmethoxy)pheny]-7-phenyl-2-thioxo-thiazolo[5,4-e]thiadiazino[2′,3′-a]triazole-6,8-dione (9b)

Pale brown crystals (DMF); yield (47%); m.p. 325°C; IR (cm^{-1}) υ 3174 (NH) and 1712 (CO); ^{1}H NMR (DMSO) δ 5.40 (s, 1H, H-7), 5.66 (s, 2H, CH_2), 6.45 (d, 2H_b, $J = 6.8$ Hz, ArH's), 6.90 (m, 3$H_{a,c'}$, ArH's), 7.23 (t, 2$H_{b'}$, $J = 8.6$ Hz, ArH's), 7.46 (d, 2$H_{a'}$, $J = 7.6$ Hz, ArH's), 7.58 (t, 3H_d, $J = 7.6$Hz, Ar's), 7.70 (t, 1H_e, $J = 7.4$ Hz, Ar's), 8.02 (d, 2H_c, $J = 7.4$ Hz, ArH's), and 13.73 (s, 1H, NH). Anal. for $C_{26}H_{18}N_4O_4S_3$ (546.64) calcd.: C, 57.13; H, 3.32; N, 10.25; S, 17.60. Found: C 57.25; H, 3.43; N, 10.41; S, 17.45.

7-[4-(Benzoylmethoxy)phenyl]-2-oxo-3,5,6,7-tetrahydro-2H-thiopyrano[2,3-d]thiazole-6-carboxylate (11a)

Pale brown crystals (acetic acid); yield (55%); m.p. 167°C; IR (cm^{-1}) υ 3177 (NH), 1735 (CO) and 1684 (CO); ^{1}H NMR (DMSO) δ 1.13 (t, 3H, $J = 7.2$ Hz, CH_3), 3.04–3.15 (m, 1H, H-6), 3.28–3.37 (dd, 1H, $J = 4.6$, 8.2 Hz, H-5), 3.99 (q, 2H, CH_2), 4.45 (d, 1H, $J = 5.1$ Hz, H-7), 5.53 (s, 2H, CH_2), 6.88 (d, 2H_b, $J = 8.7$ Hz, ArH's), 7.0 (d, 2H_a, $J = 9.0$ Hz, ArH's), 7.56 (t, 2H_d, $J = 7.8$ Hz, ArH's), 7.67 (t, 1H_e, $J = 7.5$ Hz, ArH's), 8.0 (d, 2H_c, $J = 7.0$ Hz, ArH's), and 11.37 (s, 1H, NH). Anal. for $C_{23}H_{21}NO_5S_2$ (455.55) calcd.: C, 60.64; H, 4.65; N, 3.07; S, 18.04. Found: C, 60.50; H, 4.77; N, 3.22; S, 18.19.

7-[4-(Benzoylmethoxy)phenyl]-2-thioxo-3,5,6,7-tetrahydro-2H-thiopyrano-[2,3-d]thiazole-6-carboxylate (11b)

Pale brown crystals (acetic acid); yield (58%); m.p. 188°C; IR (cm^{-1}) υ 3165 (NH) 1733 (CO) and 1686 (CO); ^{1}H NMR (DMSO) δ 1.14 (t, 3H, $J = 7.2$ Hz, CH_3), 3.08–3.17 (m, 1H, H-6), 3.30–3.41 (dd, 1H, $J = 4.1$, 8.4 Hz, H-5), 4.09 (q, 2H, CH_2), 4.46 (d, 1H, $J = 5.2$ Hz, H-7), 5.57 (s, 2H, CH_2), 6.91 (d, 2H_b, $J = 8.8$ Hz, ArH's), 7.11 (d, 2H_a, $J = 9.0$ Hz, ArH's), 7.55 (t, 2H_d, $J = 7.8$ Hz, ArH's), 7.68 (t, 1H_e, $J = 7.6$ Hz, ArH's), 8.03 (d, 2H_c, $J = 7.2$ Hz, ArH's), and 13.67 (s, 1H, NH). Anal. for $C_{23}H_{21}NO_4S_3$ (471.61) calcd.: C, 58.57; H, 4.49; N, 2.97; S, 20.40. Found: C, 58.40; H, 4.62; N, 2.80; S, 20.52.

7-[4-(Benzoylmethoxy)phenyl]-6-nitro-5-phenyl-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-one (11c)

Pale yellow crystals (acetic acid); yield (60%); m.p. 188°C; IR (cm^{-1}) υ 3178 (NH), 1680 (CO); ^{1}H NMR (DMSO) δ 3.76 (d, 1H, $J = 15.3$ Hz, H-5), 3.85 (d, 1H, $J = 14.4$ Hz, H-7) 4.71–4.93 (dd, 1H, $J = 5.7$, 11.4 Hz, H-6), 5.58 (s, 2H, CH_2), 6.92 (d, 2H_b, $J = 8.7$ Hz, ArH's), 7.03 (d, 2H_a, $J = 8.6$ Hz, ArH's), 7.31 (m, 5H, ArH's), 7.68 (t, 2H_d, $J = 7.2$ Hz, Ar's), 8.02 (d,

$2H_c$, $J = 8.4$ Hz, ArH's), and 11.63 (s, 1H, NH). Anal. for $C_{26}H_{20}N_2O_5S_2$ (504.58) calcd.: C, 61.89; H, 4.0; N, 5.55; S, 12.71. Found: C, 61.76; H, 4.12; N, 5.72; S, 12.53.

7-[4-(Benzoylmethoxy)phenyl]-6-nitro-5-phenyl-5,6-dihydrothiopyrano[2,3-d]thiazolidin-2-thione (11d)

Pale violet crystals (acetic acid); yield (63%); m.p. 165°C; IR (cm^{-1}) υ 3175 (NH) and 1702 (CO); ^{1}H NMR (DMSO) δ 3.78 (d, 1H, $J = 15.4$ Hz, H-5), 3.86 (d, 1H, $J = 14.6$ Hz, H-7) 4.70–4.94 (dd, 1H, $J = 5.6$, 11.2 Hz, H-6), 5.56 (s, 2H, CH_2), 6.93 (d, $2H_b$, $J = 8.8$ Hz, ArH's), 7.0 (d, $2H_a$, $J = 8.6$ Hz, ArH's), 7.33 (m, 5H, ArH's), 7.70 (t, $2H_d$, $J = 7.2$ Hz, Ar's), 8.0 (d, $2H_c$, $J = 8.8$ Hz, ArH's), and 13.73 (s, 1H, NH). Anal. for $C_{26}H_{20}N_2O_4S_3$ (520.64) calcd.: C, 59.98; H, 3.87; N, 5.38; S, 18.48. Found: C, 59.84; H, 4.0; N, 5.55; S, 18.34.

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