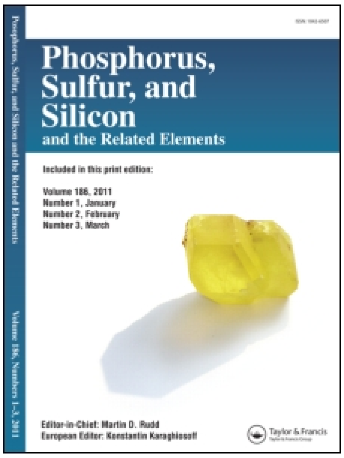

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SYNTHESIS OF SOME NEW THIAZOLIDIN-5-ONE DERIVATIVES OF PHARMACEUTICAL INTEREST

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SYNTHESIS OF SOME NEW THIAZOLIDIN-5-ONE DERIVATIVES OF PHARMACEUTICAL INTEREST

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Condensation of thiazolidin-5-one derivative ***1*** *with different aromatic aldehydes gave the corresponding arylidenes* ***2a–e****. Compound* ***2e*** *was reacted with urea and thiourea to give the corresponding thiazolo[5,4-d]pyrimidine derivatives* ***3a,b****, respectively. Treatment of compound* ***1*** *with phenyl isothiocyanate in basic DMF gave the nonisolable potassium salt of the adduct* ***4****, which underwent heterocyclization upon treatment with chloroacetyl chloride and phenacyl bromide to give the corresponding [2,4′] bisthiazolidinylidenes* ***5*** *and* ***8****. Moreover, the reactions of compound* ***1*** *with a variety of reagents, e.g., ninhydrin and isatin, were investigated. The structures of these compounds were established by analytical and spectral data.*

Keywords: Bisthiazolidinylidene-5,5′-dione; isothiocyanates; thiazolidin-5-ones

INTRODUCTION

Diverse biological activities such as bactericidal,[1,2] fungicidal,[3,4] insecticidal,[5,6] anticonvulsant,[7–9] tuberculostatic,[10,11] herbicidal,[12,13] antiviral,[14,15] and antiprotozoal[16] have been found with thiazolidinone derivatives. The diversity of biological and physiological activities of organic sulfur heterocycles may be attributed to the presence of the N—C—S fragment, which is characteristic of thiazoles, thiazolines, and thiazolidines.[17] This encouraged us to investigate the synthesis of some new thiazolidin-5-one derivatives of pharmaceutical interest.

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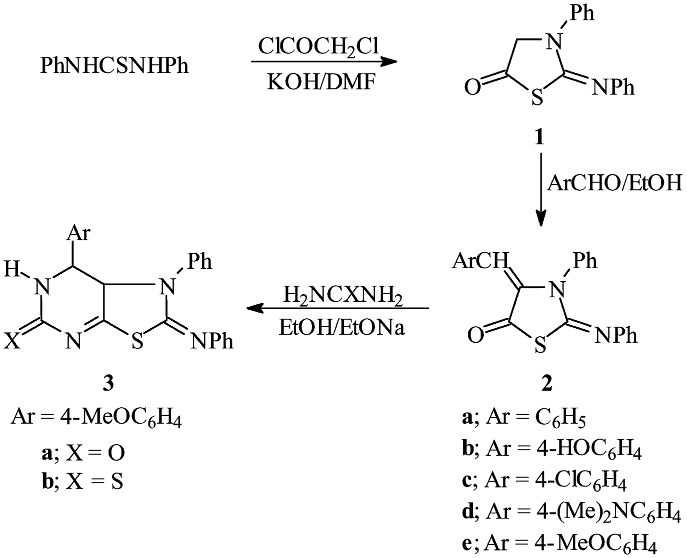
RESULTS AND DISCUSSION

3-Phenyl-2-phenyliminothiazolidin-5-one (**1**)[18] was prepared by the reaction of diphenylthiourea and chloroacetyl chloride in DMF containing a quantitative amount of KOH. IR, ^{1}H NMR, and ^{13}C NMR analyses confirmed the chemical structure of compound **1**. The ^{1}H NMR spectrum of 1 showed a singlet signal at δ 3.85 corresponding to the methylene protons and a multiplet signal at δ 6.85–7.50 due to the aromatic protons.

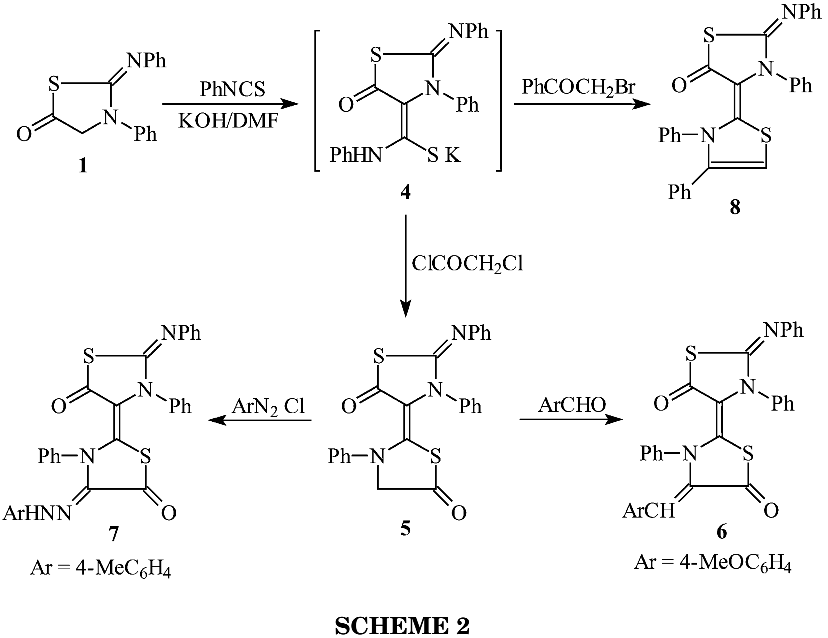
A series of 4-arylidene-3-phenyl-2-phenyliminothiazolidin-5-ones **2a–e** was synthesized by condensation of compound **1** with a variety of aromatic aldehydes in ethanol containing a catalytic amount of piperidine (Scheme 1). Assignment of the products **2a–e** was based on their elemental analyses, IR, ^{1}H NMR, ^{13}C NMR, and MS spectral data. The IR spectra of **2a–e** revealed absorption bands at 1713–1698 cm^{-1} (C=O) and 1641–1633 cm^{-1} (C=N). The ^{1}H NMR spectra of 2a–e showed the disappearance of the characteristic for singlet CH_2 of the thiazolidinone ring in **1** at δ 3.85.



SCHEME 1

Compound **2e** was refluxed with urea and thiourea in ethanol–sodium ethoxide to give the corresponding thiazolo[5,4-d]pyrimidine derivatives **3a**,**b**, respectively (Scheme 1). The structures of the products **3a**,**b** were established from their analytical and spectral data. The IR spectrum of compound **3a** showed absorption bands at 3322 cm^{-1} (NH), 1673 cm^{-1} (C=O), and 1640 cm^{-1} (C=N). The ^1H NMR spectrum of compound **3b** revealed signals for two paraffinic protons, methoxy, and aromatic protons at δ 2.60–2.70, 3.85, and 6.85–8.00, respectively, in addition to broad signal at δ 9.60 for NH proton.

The base promoted nucleophilic addition of 3-phenyl-2-phenylimino-thiazolidin-5-one (**1**) to an equimolar amount of phenyl isothiocyanate in DMF containing potassium hydroxide and afforded the corresponding, nonisolable intermediate potassium sulphide salt **4**. In situ heterocyclization of **4** was achieved by the reaction with chloroacetyl chloride to furnish the corresponding 3,3′-diphenyl-2′-phenylimino[2,4′]bisthiazolidinylidene-5,5′-dione (**5**) (Scheme 2). The structure of **5** was confirmed by analytical and spectral data. The IR spectrum revealed an intense bands at 1737, 1685 cm^{-1} (2 C=O), and 1625 cm^{-1} (C=N). The ^1H NMR spectrum of **5** showed a singlet signal at δ 3.80 due to the methylene protons and multiplet at δ 6.60–7.60 due to aromatic protons.



SCHEME 2

The condensation of **5** with *p*-anisaldehyde gave the corresponding product 4-(4′-methoxybenzylidene)-3,3″ -diphenyl-2″-phenylimino-[2,4″]bisthiazolidin- ylidene-5,5″-dione (**6**). The structure of the latter product was supported by analytical and spectral data. The ^{1}H NMR spectrum of **6** showed singlet signal at δ 3.90 for OCH_3 protons, a multiplet at δ 6.90–7.80 for aromatic protons, and a singlet signal at δ 8.00 for the olefinic proton.

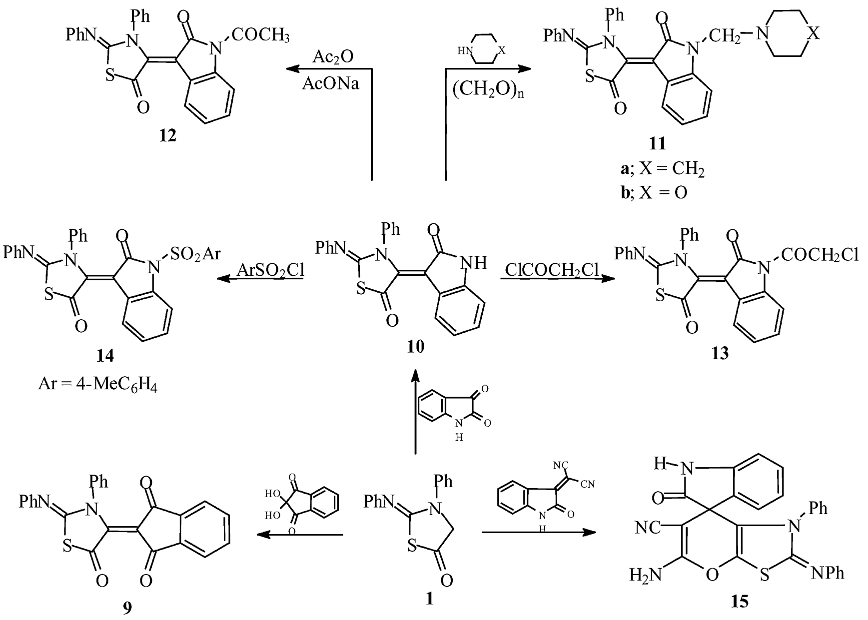
The active methylene of the [2,4′]bisthiazolidinylidene-5,5′-dione **5** was coupled with 4-methylbenzenediazonium chloride in ethanol buffered with sodium acetate at 0–5°C to yield the corresponding monohydrazone product 3,3″-diphenyl-2″-phenylimino-4-(4′-tolylhydrazono)[2,4″]bisthiazolidinylidene-5,5″-dione (**7**). The structure of the product **7** was assigned on the basis of the elemental analysis and spectral data. The IR spectrum exhibited bands at 3250 cm^{-1} (NH), 1718, 1695 cm^{-1} (2 C=O), and 1634 cm^{-1} (C=N). The ^{1}H NMR spectrum revealed a singlet signal at δ 2.30 corresponding to CH_3 protons and a multiplet in the region of δ 6.80–7.90 for the aromatic protons, in addition to a broad signal at δ 8.60 for the NH proton.

Subsequent treatment of **4** with equimolar amount of phenacyl bromide furnished 3,4,3′-triphenyl-2′-phenylimino-2′,3′-dihydro-3H-[2,4′]-bisthiazolyliden-5′-one (**8**) (Scheme 2). The structure of the latter product was established via inspection of its spectral data. The ^{1}H NMR spectrum revealed a multiplet signal in the region δ 6.70–7.60 corresponding to the aromatic protons together with the olefinic proton.

On the other hand, compound **1** was reacted with ninhydrin in ethanol containing a catalytic amount of triethylamine to yield 2-(5′-oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene)indan-1,3-dione (**9**) (Scheme 3). The structure of the latter product was established on the basis of its analytical and spectral data. The IR spectrum showed bands at 1711 cm^{-1} (C=O), 1688 (2 C=O), and 1635 cm^{-1} (C=N).

Furthermore, compound **1** was condensed with isatin in glacial acetic acid to yield 3-(5′-oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene)-1,3-dihydro-indol-2-one (**10**). The latter product was established from the correct elemental analysis and spectral data. The IR spectrum showed bands at 3181 cm^{-1} (NH), 1711, 1688 cm^{-1} (2 C=O), and 1634 cm^{-1} (C=N). The ^{1}H NMR spectrum of **10** revealed the presence of a multiplet signal corresponding to the aromatic protons at δ 6.90–7.75.

Treatment of compound **10** with paraformaldehyde and piperidine or morpholine in absolute ethanol afforded the corresponding Mannich products **11a**,**b** (Scheme 3). Assignment of the products was based on their analytical and spectral data. The ^{1}H NMR spectrum for compound **11a** showed a multiplet signal in the region δ 1.35–1.55 for three methylene groups, at δ 2.55 for two methylene groups, a singlet signal at δ 4.50 for one methylene group, and a multiplet signal for the aromatic protons at δ 6.90–7.60.



SCHEME 3

1-Acetyl-3-(5′-oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene) - 1,3-dihydroindol-2-one (**12**) was synthesized by treatment of the thiazolidin-4-ylidene derivative **10** with acetic anhydride and sodium acetate at 80°C. The spectral data of the amide **12** were consistent with its structure. The ^{1}H NMR spectrum displayed a singlet at δ 2.30 for CH$_3$ protons and a multiplet at δ 6.90–7.70 for the aromatic protons.

Compound **10** was reacted with chloroacetyl chloride in DMF containing catalytic amount of triethylamine to give the corresponding chloroacetyl derivative **13**. The structure of **13** was confirmed by the IR, ^{1}H NMR, and MS spectral data. The IR spectrum revealed an intense broad band at 1700 cm^{-1} corresponding to the carbonyl groups and 1638 cm^{-1} (C=N).

Moreover, compound **10** was treated with *p*-toluenesulphonyl chloride in pyridine to give the corresponding sulphonyl derivative **14**. The spectral data of **14** were consistent with its structure. The IR spectrum showed a broad band in the region 1699 cm^{-1} (2 C=O) and a strong band at 1634 cm^{-1} (C=N).

The medicinal applications of spiro-2-oxoindolines as muscle relaxants and anti-inflammatory agents is well known.[19,20] Several spiro-2-oxoindoline derivatives have been reported to exhibit analgesic activity[21] and were also platelet-aggregation inhibitors.[22] Based on the above facts, we investigated the Michael addition reaction of the thiazolidin-5-one derivative **1** with 3-dicyanomethylidene-2-oxoindoline to obtain the spiro-2-oxoindoline derivative **15**. The structure of the spiro-2-oxoindoline **15** was secured by its elemental analysis and spectral data (see the Experimental section below).

EXPERIMENTAL

All melting points were uncorrected. Elemental analyses were carried out in the microanalytical unit, Faculty of Science, University of Cairo, Egypt. IR spectra were recorded on a Mattson 5000 Fourier transform infrared (FTIR) spectrometer. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker WP 300 in $CDCl_3$, DMSO-d_6, or CF_3COOD as solvent using TMS as an internal standard. Mass spectra were recorded on a Finnigan MAT 212 instrument.

3-Phenyl-2-phenyliminothiazolidin-5-one (1)

A mixture of diphenylthiourea (2.29 g, 0.01 mol) and chloroacetyl chloride (2.27 g, 0.02 mol) was stirred in DMF (25 ml) containing (0.56 g, 0.01 mol) KOH for 10 h. The reaction mixture was poured onto crushed ice. The precipitate that formed was filtered off, dried, and recrystallized (ethanol) to give compound **1** as buff crystals, m.p. 170–171°C, lit.[18] m.p. 172–173°C. Yield, 84%. IR (KBr) (ν, cm^{-1}): 1724 (C=O), 1637 (C=N). ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 2H, CH2), 6.85–7.50 (m, 10H, Ar-H). ^{13}C NMR ($CDCl_3$) ppm 32.75, 120.76 (2C), 124.53, 127.86 (2C), 128.88, 129.04 (2C), 129.24 (2C), 134.56, 147.89, 154.89, 171.29. MS (m/z, %): 268 (M$^+$, 100), 194 (38), 149 (65), 104 (40), 77 (25). $C_{15}H_{12}N_2OS$ (268.33) requires C, 67.14; H, 4.51; N, 10.44. Found: C, 67.05; H, 4.42; N, 10.34.

4-Arylidene-3-phenyl-2-phenyliminothiazolidin-5-ones (2a–e)

A mixture of compound **1** (2.68 g, 0.01 mol) and appropriate aldehyde (0.01 mol) in ethanol (20 ml) containing a catalytic amount of piperidine was refluxed for 4 h. The mixture was cooled, and the solid products formed were filtered, dried, and recrystallized (ethanol) to afford compounds **2a–e**.

4-Benzylidene-3-phenyl-2-phenyliminothiazolidin-5-one (2a)

Yellow crystals. m.p. 200–202°C. Yield, 73%. IR (KBr) (ν, cm^{-1}): 1713 (C=O), 1641 (C=N). ^{1}H NMR (DMSO-d$_6$) δ 7.10–7.80 (m, 15H, Ar-H), 8.05 (s, 1H, olefinic CH). $C_{22}H_{16}N_2OS$ (356.44) requires C, 74.13; H, 4.52; N, 7.86. Found: C, 74.26; H, 4.40; N, 7.74.

4-(4′-Hydroxybenzylidene)-3-phenyl-2-phenyliminothiazolidin-5-one (2b)

Yellow crystals. m.p. $>$300°C. Yield, 84%. IR (KBr) (ν, cm^{-1}): 1698 (C=O), 1639 (C=N). ^{1}H NMR (CDCl$_3$/CF$_3$COOD) δ 6.95–7.70 (m, 14H, Ar-H), 8.15 (s, 1H, olefinic CH). ^{13}C NMR (CDCl$_3$/CF$_3$COOD) ppm 110.80, 117.17 (2C), 124.13, 125.12 (2C), 127.75 (2C), 129.76, 130.79 (2C), 131.15 (2C), 131.26, 132.40, 133.53, 133.76 (2C), 142.77, 160.38, 164.58, 170.91. MS (m/z, %): 372 (M$^+$, 35), 194 (13), 150 (100), 121(9), 77(15). $C_{22}H_{16}N_2O_2S$ (372.44) requires C, 70.95; H, 4.33; N, 7.52. Found: C, 70.78; H, 4.45; N, 7.63.

4-(4′-Chlorobenzylidene)-3-phenyl-2-phenyliminothiazolidin-5-one (2c)

Yellow crystals. m.p. 179–180°C. Yield, 78%. IR (KBr) (ν, cm^{-1}): 1708 (C=O), 1634 (C=N). ^{1}H NMR (CDCl$_3$) δ 7.00–7.60 (m, 14H, Ar-H), 8.10 (s, 1H, olefinic CH). $C_{22}H_{15}ClN_2OS$ (390.89) requires C, 67.60; H, 3.87; N, 7.17. Found: C, 67.73; H, 3.91; N, 7.08.

4-(4′-Dimethylaminobenzylidene)-3-phenyl-2-phenyliminothiazolidin-5-one (2d)

Yellow crystals. m.p. $>$ 300°C. Yield, 91%. IR (KBr) (ν, cm^{-1}): 1711 (C=O), 1633 (C=N). ^{1}H NMR (DMSO-d$_6$) δ 3.10 (s, 6H, N(CH$_3$)$_2$), 6.90–7.60 (m, 14H, Ar-H), 8.00 (s, 1H, olefinic CH). MS (m/z, %): 399 (M$^+$, 13), 177 (100), 77 (13). $C_{24}H_{21}N_3OS$ (399.51) requires C, 72.15; H, 5.30; N, 10.52. Found: C, 72.34; H, 5.42; N, 10.61.

4-(4′-Methoxybenzylidene)-3-phenyl-2-phenyliminothiazolidin-5-one (2e)

Yellow crystals. m.p. 210–212°C; Yield, 84%. IR (KBr) (ν, cm^{-1}): 1712 (C=O), 1641 (C=O). ^{1}H NMR (CDCl$_3$) δ 3.80 (s, 3H, OCH$_3$), 6.80–7.55 (m, 14H, Ar-H), 7.80 (s, 1H, olefinic CH). ^{13}C NMR (CDCl$_3$) ppm 55.32, 114.49 (2C), 118.19, 121.05 (2C), 124.70, 126.23, 128.00 (2C), 128.79, 129.20 (4C), 131.30, 131.88 (2C), 134.71, 148.27, 151.22, 160.83, 166.58. $C_{23}H_{18}N_2O_2S$ (386.47) requires C, 71.48; H, 4.69; N, 7.25. Found: C, 71.60; H, 4.80; N, 7.37.

2H-Thiazolo[5,4-d]pyrimidines (3a,b)

A mixture of compound **2e** (3.86 g, 0.01 mol) and urea or thiourea (0.01 mol) in EtONa/EtOH (prepared by dissolving 0.23 g of Na in 30 ml absolute EtOH) was refluxed for 3 h. The reaction mixture was cooled, poured onto crushed ice, left to cool, and neutralized with dilute HCl. The solid that was formed was filtered off, dried, and recrystallized (ethanol) to give **3a**,**b**, respectively.

*7-(4′-Methoxyphenyl)-1-phenyl-2-phenylimino-1,6,7,7a-tetrahydro-2H-thiazolo[5,4-*d*]pyrimidin-5-one (3a)*

Yellow crystals. m.p. 165–166°C; Yield, 48%. IR (KBr) (ν, cm^{-1}): 3322 (NH), 1673 (C=O), 1640 (C=N). ^{1}H NMR (DMSO-d$_6$) δ 2.55–2.70 (m, 2H, CH-CH), 3.80 (s, 3H, OCH$_3$), 6.80–8.00 (m, 14H, Ar-H), 8.50 (br. s, 1H, NH). $C_{24}H_{20}N_4O_2S$ (428.51) requires C, 67.27; H, 4.70; N, 13.07. Found: C, 67.41; H, 4.84; N, 13.20.

*7-(4′-Methoxyphenyl)-1-phenyl-2-phenylimino-1,6,7,7a-tetrahydro-2H-thiazolo[5,4-*d*]pyrimidine-5-thione (3b)*

Green crystals, m.p. 185–187°C; Yield, 54%. IR (KBr) (ν, cm^{-1}): 3313 (NH), 1638 (C=N). ^{1}H NMR (DMSO-d$_6$) δ 2.60–2.70 (m, 2H, CH—CH), 3.85 (s, 3H, OCH$_3$), 6.85–8.00 (m, 14H, Ar-H), 9.60 (br. s, 1H, NH). MS (m/z, %): 444 (M$^+$, 4), 429 (2), 369 (32), 310 (25), 299 (15), 234 (62), 164 (100), 140 (74). $C_{24}H_{20}N_4OS_2$ (444.57) requires C, 64.84; H, 4.53; N, 12.60. Found: C, 64.63; H, 4.66; N, 12.73.

3,3′-Diphenyl-2′-phenylimino[2,4′]bithiazolidinylidene-5,5′-dione (5)

A mixture of compound **1** (2.68 g, 0.01 mol), KOH (0.56 g, 0.01 mol), and phenyl isothiocyanate (1.35 g, 0.01 mol) was stirred in DMF (20 ml) at 0–5°C for 10 h. Simultaneously chloroacetyl chloride (1.13 g, 0.01 mol) was added dropwise, and stirring was continued for 4 h. The reaction mixture was poured onto crushed ice. The precipitate that was formed was filtered off, dried, and recrystallized (ethanol) to afford compound **5** as brown crystals, m.p. 198–200°C. Yield, 64%. IR (KBr) (ν, cm^{-1}): 1737 (C=O), 1685 (C=O), 1625 (C=N). ^{1}H NMR (CDCl$_3$) δ 3.80 (s, 2H, CH$_2$), 6.60–7.60 (m, 15H, Ar-H). ^{13}C NMR (CDCl$_3$) ppm 31.90, 93.79, 121.14 (2C), 124.27, 128.00 (2C), 128.65 (2C), 129.10 (2C), 129.36 (2C), 129.79 (2C), 130.56, 131.63, 133.17, 134.36, 145.58, 147.71, 151.76, 166.76, 172.66. MS (m/z, %): 443 (M$^+$, 95), 384 (18), 249 (20), 221 (100), 179 (57), 135 (13), 103 (19), 77 (23). $C_{24}H_{17}N_3O_2S_2$ (443.54) requires C, 64.99; H, 3.86; N, 9.47. Found: C, 64.83; H, 3.95; N, 9.59.

4-(4′-Methoxybenzylidene)-3,3″-diphenyl-2″-phenylimino[2,4″]bithiazolidinylidene-5,5″-dione (6)

A mixture of compound **5** (4.43 g, 0.01 mol) and *p*-methoxybenzaldehyde (1.22 g, 0.01 mol) in ethanol (30 ml) containing a catalytic amount of piperidine was refluxed for 4 h. The reaction mixture was left to cool. The solid formed was filtered off, dried, and recrystallized (ethanol) to give compound **6** as orange crystals, m.p. 96–97°C; Yield: 78%. IR (KBr) (ν, cm^{-1}): 1702 (C=O), 1679 (C=O), 1610 (C=N). ^1H NMR ($CDCl_3/CF_3COOD$) δ 3.90 (s, 3H, OCH_3), 6.90–7.80 (m, 19H, Ar-H), 8.00 (s, 1H, olefinic CH). MS (m/z, %): 561 (M^+, 8), 368 (12), 339 (20), 281 (12), 207 (27), 149 (40), 57 (100). $C_{32}H_{23}N_3O_3S_2$ (561.67) requires C, 68.43; H, 4.13; N, 7.48. Found: C, 68.62; H, 4.32; N, 7.57.

3,3″-Diphenyl-2″-phenylimino-4-(4′-tolylhydrazono) [2,4″]-bithiazolidinylidene-5,5″-dione (7)

A solution of compound 5 (4.43 g, 0.01 mol) in ethanol (25 ml) and sodium acetate (4 g) was stirred in ice-bath at 0–5°C. A diazotized solution of *p*-toluidine (0.01 mol) was added to the stirred solution over a period 30 min, and stirring was continued for 2 h with cooling. The reaction mixture was left in an ice bath and the solid formed was filtered off, dried, and recrystallized (ethanol) to afford compound **7** as dark red crystals, m.p. 120–121°C. Yield, 70%. IR (KBr) (ν. cm^{-1}): 3250(NH), 1718 (C=O), 1695 (C=O), 1634 (C=N). ^1H NMR ($CDCl_3$) δ 2.30 (s, 3H, CH_3), 6.80–7.90 (m, 19H, Ar-H), 8.60(NH). $C_{31}H_{23}N_5O_2S_2$ (561.68) requires C, 66.29; H, 4.13; N, 12.47. Found: C, 66.10; H, 4.00; N, 12.56.

3,4,3′-Triphenyl-2′-phenylimino-2′,3′-dihydro-3H-[2,4′]bisthiazolyliden-5′-one (8)

To a cold suspension of finally divided KOH (0.56 g, 0.01 mol) in DMF (20 ml) was added the thiazolidin-5-one derivative **1** (2.68 g, 0.01 mol), followed by phenyl isothiocyanate (1.35 g, 0.01 mol). The mixture was stirred at room temperature overnight, then treated with phenacyl bromide (1.99 g, 0.01 mol) and left to stand at room temperature for 24 h. The mixture was poured into cold water. The solid product that separated was filtered off, washed with water, dried, and recrystallized (ethanol) to give compound **8** as white crystals, m.p. 150–152°C. Yield, 48%. IR (KBr) (ν, cm^{-1}): 1659 (C=O), 1619 (C=N). ^1H NMR ($CDCl_3$) δ 6.70–7.60 (m, 21H, 20 Ar-H and olefinic CH). $C_{30}H_{21}N_3OS_2$ (503.64) requires C, 71.54; H, 4.20; N, 8.34. Found: C, 71.39; H, 4.34; N, 8.45.

2-(5′-Oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene) indan-1,3-dione (9)

A mixture of compound **1** (2.68 g, 0.01 mol) and ninhydrin (1.78 g, 0.01 mol) in ethanol (30 ml) containing a catalytic amount of triethylamine was refluxed for 4 h, and then was left to cool overnight. The solid formed was filtered off, dried, and recrystallized (ethanol) to give compound **9** as brown crystals, m.p. 105–107°C. Yield, 44%. IR (KBr) (ν, cm^{-1}): 1711 (C=O), 1688 (2 C=O), 1635 (C=N). ^{1}H NMR (DMSO-d$_6$) δ 7.10–7.85 (m, 14H, 14 Ar-H). $C_{24}H_{14}N_2O_3S$ (410.44) requires C, 70.23; H, 3.44; N, 6.83. Found: C, 70.07; H, 3.28; N, 6.74.

3-(5′-Oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene)-1,3-dihydro-indol-2-one (10)

A mixture of compound **1** (2.68 g, 0.01 mol) and isatin (1.47 g, 0.01 mol) in glacial acetic acid (30 ml) was refluxed for 3 h, left to cool at room temperature, and then poured into cold water. The solid formed was filtered off, dried, and recrystallized from AcOH:EtOH (2:1) to afford **10** as orange crystals, m.p. 229–230°C. Yield, 85%. IR (KBr) (ν, cm^{-1}): 3181 (NH), 1711 (C=O), 1688 (C=O), 1634 (C=N). ^{1}H NMR (CDCl$_3$/CF$_3$COOD) δ 6.90–7.75 (m, 14H, Ar-H). MS (m/z, %): 397 (M$^+$, 20), 268 (19), 194 (100), 175 (56), 149 (23), 120 (28), 104 (32), 91 (32), 77 (81). $C_{23}H_{15}N_3O_2S$ (397.45) requires C, 69.50; H, 3.80; N, 10.57. Found: C, 69.65; H, 3.94; N, 10.70.

3-(5′-Oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene)-1,3-dihydro-indol-2-ones (11a,b)

A mixture of compound **10** (3.97 g, 0.01 mol), paraformaldehyde (0.31 g, 0.01 mol), and piperidine or morpholine (0.01 mol) in absolute ethanol (30 ml) was refluxed in a water bath for 5 h. The reaction mixture was evaporated to its half volume and kept at room temperature overnight. The solid obtained was filtered off, dried, and recrystallized (ethanol) to give **11a**,**b**.

3-(5′-Oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene)-1-piperidin-1-yl-methyl-1,3-dihydroindol-2-one (11a)

Red crystals. m.p. 143–145 °C. Yield, 55%. IR (KBr) (ν, cm^{-1}): 1692 (broad, 2 C=O), 1638 (C=N).^{1}H NMR (CDCl$_3$/CF$_3$COOD) δ 1.35–1.55 (m, 6H, 3CH$_2$), 2.55 (m, 4H, 2CH$_2$), 4.50 (s, 2H, CH$_2$), 6.90–7.60 (m, 14H, Ar-H). $C_{29}H_{26}N_4O_2S$ (494.61) requires C, 70.42; H, 5.30; N, 11.33. Found: C, 70.30; H, 5.42; N, 11.40.

1-Morpholin-4-ylmethyl-3-(5′-oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene)-1,3-dihydroindol-2-one (11b)

Red crystals. m.p. 154–155°C. Yield, 63%. IR (KBr) (ν, cm^{-1}): 1702 (broad, 2 C=O), 1638 (C=N). ^{1}H NMR (DMSO-d$_6$) δ 2.60 (m, 4H, 2CH$_2$), 3.50 (m, 4H, 2CH$_2$), 4.45 (s, 2H, CH$_2$), 7.00–7.70 (m, 14H, Ar-H). MS (m/z, %): 496 (M$^+$, 5), 397 (43), 310 (5), 194 (84), 174 (37), 149 (17), 120 (11), 104 (20), 100 (100), 77 (35). $C_{28}H_{24}N_4O_3S$ (496.58) requires C, 67.72; H, 4.87; N, 11.28. Found: C, 67.85; H, 4.90; N, 11.35.

1-Acetyl-3-(5′-oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene)-1,3-dihydroindol-2-one (12)

A mixture of compound **10** (3.97 g, 0.01 mol) and sodium acetate (0.5 g) in acetic anhydride (10 ml) was heated in a water bath (at 80°C) for 6 h, left to cool, and poured into ice-cold water. The solid formed was filtered off, dried, and recrystallized (ethanol) to afford compound **12** as red crystals, m.p. 263–264°C. Yield, 76%. IR (KBr) (ν, cm^{-1}): 1712 (broad, 3 C=O), 1643 (C=N). ^{1}H NMR (DMSO-d$_6$) δ 2.30 (s, 3H, CH$_3$), 6.90–7.70 (m, 14H, Ar-H). $C_{25}H_{17}N_3O_3S$ (439.49) requires C, 68.32; H, 3.90; N, 9.56. Found: C, 68.49; H, 3.77; N, 9.45.

1-(2-Chloroacetyl)-3-(5′-oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene)-1,3-dihydroindol-2-one (13)

A mixture of compound **10** (3.97 g, 0.01 mol) and chloroacetyl chloride (1.13 g, 0.01 mol) in DMF containing a catalytic amount of triethylamine was stirred at room temperature for 2 h and was then poured into ice-cold water. The solid formed was filtered off, dried, and recrystallized from EtOH:DMF (3:1) to yield the chloroacetyl derivative **13** as orange crystals, m.p. 270–271°C. Yield, 68%. IR (KBr) (ν, cm^{-1}): 1700 (broad, 3 C=O), 1638 (C=N). ^{1}H NMR (DMSO-d$_6$) δ 4.15 (s, 2H, CH$_2$), 7.10–7.90 (m, 14H, Ar-H). $C_{25}H_{16}ClN_3O_3S$ (473.93) requires C, 63.36; H, 3.40; N, 8.87. Found: C, 63.53; H, 3.22; N, 9.00.

3-(5′-Oxo-3′-phenyl-2′-phenyliminothiazolidin-4′-ylidene)-1-(toluene-4-sulphonyl)-1,3-dihydroindol-2-one (14)

A mixture of compound **10** (3.97 g, 0.01mol) and *p*-toluenesulphonyl chloride (1.90 g, 0.01 mol) in pyridine (20 ml) was stirred at room temperature for 4 h. The reaction mixture was poured into ice-cold water and neutralized with acetic acid. The formed solid product was filtered off, dried, and recrystallized from ethanol to yield compound **14** as red crystals, m.p. 280–282°C. Yield, 77%. IR (KBr) (ν, cm^{-1}): 1699 (broad, 2 C=O), 1634 (C=N). ^1H NMR (DMSO-d_6) δ 2.40 (s, 3H, CH_3), 7.05–7.80 (m, 18H, Ar-H). MS (m/z, %): 551 (M^+, 5), 397 (41), 194 (100), 175 (50), 146 (13), 120 (10), 77 (20). $C_{30}H_{21}N_3O_4S_2$ (551.64) requires C, 65.32; H, 3.84; N, 7.62. Found: C, 65.20; H, 3.95; N, 7.51.

Spiro-pyrano[3,2-*d*]thiazole-2-oxoindoline Derivative (15)

A mixture of **1** (2.68 g, 0.01 mol) in ethanol (30 ml), 3-dicyanomethylidene-2-oxoindoline (1.96 g, 0.01 mol), and a few drops of piperidine was refluxed for 4 h and then left to cool overnight. The resulting solid product was filtered off, dried, and recrystallized (ethanol) to yield **15** as yellow crystals, m.p. 258–259°C. Yield, 54%. IR (KBr) (ν, cm^{-1}): 3394, 3311 (NH_2 and NH), 2197 (CN), 1705 (C=O). ^1H NMR ($CDCl_3/CF_3COOD$) δ 7.10–7.90 (m, 14H, Ar-H). MS (m/z, %): 463 (M^+, 4), 354 (4), 306 (100), 278 (82), 234 (25), 180 (10), 119 (22), 77 (65). $C_{26}H_{17}N_5O_2S$ (463.51) requires C, 67.37; H, 3.70; N, 15.11. Found: C, 67.50; H, 3.78; N, 15.22.

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