Synthesis of New Thiazolidine and Imidazolidine Derivatives of Pharmacological Interest

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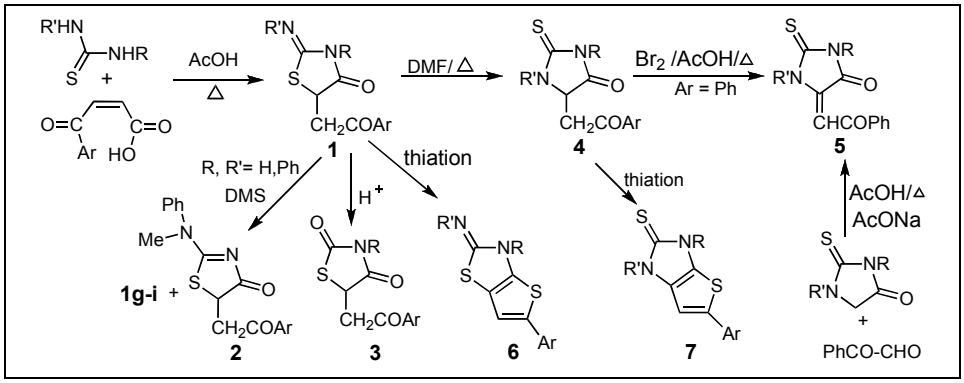

The hitherto unknown 5-(2-aryl-2-oxoethyl)-4-oxo-1,3-thiazolidines **1a-l** have been synthesized *via* cycloaddition process between thiourea and/or its derivatives with 3-aroylpropenoic acids. ^{1}H NMR spectra revealed the presence of **1a-c** as a tautmeric mixture. The presence of the thiazoline tautmers **(1a-c)'** was confirmed by methylating the tautmeric mixture, to the respective methylated derivatives 2-*N*-methylanilino-5-(2-aryl-2-oxoethyl)-4-oxo-1,3-thiazolines **2a-c** and **1g-i**. Acidic treatment of **1** provided the respective 2-oxo homologues **3a-i**. When **1a-d**, **k** were refluxed with DMF, molecular rearrangement was achieved, providing the 4-oxo-2-thioxoimidazolidine isomers **4a-d**, **k**. Bromination of **4a** and **4d** in hot acetic acid afforded the respective (*E,Z*)-5-benzoylmethylene derivatives **5a**, **d** which were prepared authentically. Thiation of **1a-c** and **4a-c** gave 5-aryl-2,3-dihydro-2-phenyliminothieno[2,3-*d*]thiazoles **6a-c** and 1-phenyl-5-aryl-2,3-dihydro-2-thioxothieno[2,3-*d*]imidazoles **7a-c**, respectively. The proposed structures have been confirmed by elemental analysis and spectroscopic data. The selected products showed different antimicrobial effect.

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INTRODUCTION

The reported biological activity for many thiazolidine derivatives [1] such as antifungal [2], antiviral [3], anticonvulsant [4] and antitubercular [5] as well as those reported for imidazolidines [6-9] stimulated the authors to prepare new derivatives of these classes.

Un-substituted thiourea has been reported to react with maleic anhydride, maleic acid, fumaric acid and methyl hydrogen fumarate, to afford 4-oxo-1,3-thiazolidines [10]. Similar to these methods, the thiazolidinone derivatives **1** were synthesized from thioureas and 3-aroylpropenoic acids [11]. The study provides also a mild and facile route to the 4-oxo-2-thioxoimidazolidines **4**, compared with previous methods for similar synthesis [12]. Moreover, the reported biological activity for different thiophenes [13] encouraged us to synthesize thiazole **6** and imidazole **7** derivatives containing this moiety, easily by thiation of **1** and **4**, respectively with Lawesson's reagent [14].

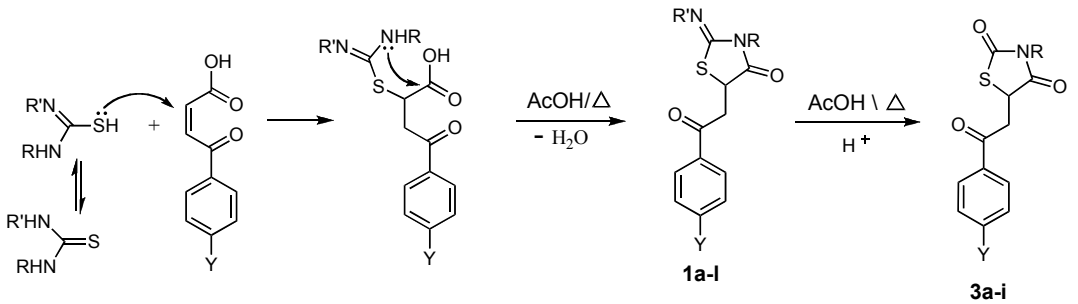
RESULTS AND DISCUSSION

When thiourea, phenyl-, 1-methyl-3-phenyl- and/or 1,3-diphenylthiourea was conducted to react with 3-aroyl-propenoic acids [11], cycloaddition process was achieved providing 5-(2-aryl-2-oxoethyl)-4-oxo-1,3-thiazolidines **1a-l** in a good yield (Scheme 1).

IR spectrum of **1a** exhibited absorption bands for aroyl CO group at 1684 cm^{-1}, ν_{CO} for cyclic amide at 1614 cm^{-1} besides two absorption bands for ν_{NH} at 3179, 3141 cm^{-1}. The mass spectrum of **1a** exhibited an intense molecular ion peak m/e 310 (80 %) and a base peak m/e 205 (100%) for the ionic radical [M- PhCO]$^+$, besides other pattern of intense peaks corresponding to the fragments, [PhCOCH$_2$]$^{+\cdot}$ m/e 119 (31 %), [PhCO]$^+$ m/e 105 (65 %) and [Ph]$^+$ m/e 77 (77 %). The ^{1}H NMR spectra of **1a-c** exhibited patterns of successive doublets in the aromatic H region at δ 7- 8 ppm, besides complicated multiplet for the thiazolidinone proton at ~ 4.6 ppm and deformed multiplet ~4.0- 4.2 ppm for the (CH$_2$) protons (-CO-*CH*$_2$). These complicated spectra were interpreted due to the existence of **1a-c** as a tautmeric mixture.

The presence of the thiazoline tautmers **(1a-c)'** has been confirmed by treating **1a-c** with ethanolic KOH solution, providing the respective potassium salts. Alkylating [15] the hypothetically formed salts with dimethyl sulphate, afforded the expected methyl derivatives Ph-N-CH$_3$; 2-*N*-

Scheme 1

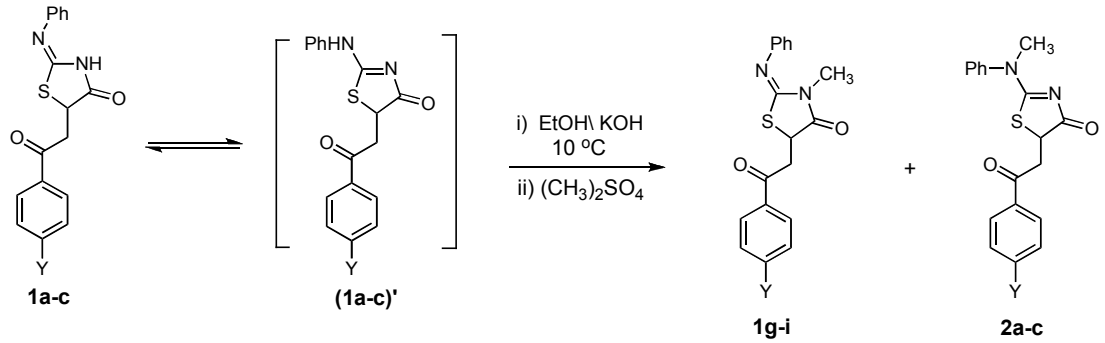


R,R',Y = **1a;**H, Ph, H, **e;**Ph, Ph, Br **i;**Me,Ph,Cl
b;H, Ph, Br **f;**Ph, Ph, Cl **j;**H, H, H
c;H, Ph, Cl **g;**Me, Ph, H **k;**H, H, Br
d;Ph,Ph, H, **h;**Me, Ph, Br **l;**H, H, Cl

R,Y = **3a;**H, H, **b;**H, Br, **c;**H, Cl,
d;Ph, H, **e;**Ph, Br, **f;**Ph,Cl
g;Me, H **h;**Me, Br, **i;**Me, Cl,

Synthesis of **1, 3**

Scheme 2



Y = **1, 2a;** H, **b;** Br, **c;** Cl

Synthesis of **1g-i, 2a-c**

methylanilino-5-(2-aryl-2-oxoethyl)-4-oxo-1,3-thiazolines **2a-c** and CO-N-CH_3; 2-phenylimino-3-methyl-5-(2-aryl-2-oxoethyl)-4-oxo-1,3-thiazolidines **1g-i** (Scheme 2).

The structure of the methylated products **1g-i** has been supported by elemental analysis and spectroscopic data. Methylation was further confirmed by m.p matching with the previous samples, the appearance of N-CH_3 signal in the ^{1}H NMR spectra δ ~ 3.3 s 3H, (CH_3), rather than the disappearance of the NH signal. Besides the IR spectra which were devoid of any NH absorption bands.

The structure of **2** has been proven via authentic samples were prepared from 1-phenyl-1-methylthiourea [16] and 3-aroylpropenoic acids. Moreover, the structure of **2** was also confirmed by the appearance of Ph-N-CH_3 singlet in their ^{1}H NMR at δ ~ 3.6, besides the mass spectra which displayed the expected molecular ion peaks.

When the 2-phenyl/imino **1a-l** was treated with HCl in boiled acetic acid solution, hydrolysis was achieved [15,17], providing the corresponding 2-oxy derivatives **3a-i** (Scheme 1). The structure for compound **3** was confirmed by correct elemental analysis, ^{1}H NMR and the IR spectra which recorded the appearance of thiolactone absorption bands ~1735-1760 cm^{-1}. Moreover, the structure was further supported by mass spectra, which showed the correct molecular ion peaks. The ^{1}H NMR spectrum of **3a** showed at δ 7.96 d, 2H; 7.64, 7.06 two deformed t, 1H, 2H (Ph), at δ 7.26, 1H (NH), at δ 4.68, dd, 1H (H-5), δ 4.69, 3.59 ppm 2dd, each1H (PhCO-CH_2) and the EI-MS exhibited [$M^{+\cdot}$] m/e 235 (21.9 %).

Upon reflux with dimethylformamide, the derivatives under investigation **1a-c**, **d** and **k** were found to undergo molecular rearrangement into the respective 1-phenyl-, 1,3-diphenyl-, and 5-(2-aryl-2-oxoethyl)-4-oxo-2-thioxo-imidazolidines **4a-c**, **d** and **k**, respectively (Scheme 3). The 2-imino **1k** was refluxed for longer hours to undergo this rearrangement, though in a poor yield of **4k**.

Under the acidic conditions, Edman reaction described a previous conversion for similar thiazolidinones [18].

Accordingly, rearrangement of **1** with boiled DMF, in the absence of any acidic conditions, could not be rationalized in terms of Edman's mechanism. Moreover, the acidic conditions were previously found to effect the conversion of **1** into **3** [15,17].

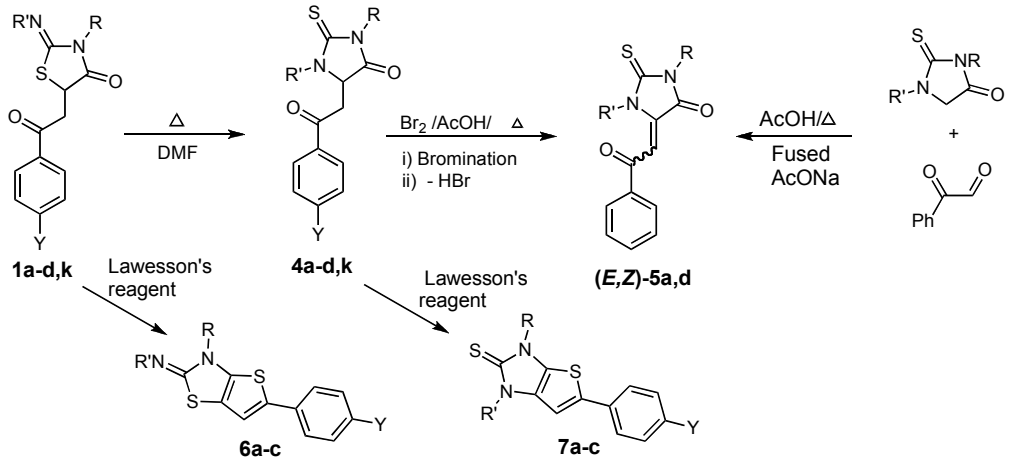
Conversion of **1** into the imidazolidines **4** has occurred most likely, via the suggested ionic intermediate [**E**], which was believed to be generated through the dipolar form **II**, by heterolytic cleavage along the 1, 5; S–C bond (Scheme 4). The charges of the ionic resonance forms **I**, **II** and the intermediate have stabilized by the polar DMF solvent [19,20], while further stabilization was provided by the phenyl group present at position-2. Therefore, the 2-phenylimino **1a-d** were sufficiently supported to undergo this rearrangement, in a good yield of **4a-d**. Whilst, the 2-imino **1k**, which is devoid of this stabilizing phenyl group, was unable to endure the transformation, providing poor yield of **4k**.

In spite of the disappointing yield of **4k**, nevertheless it was the result that supported the proposed mechanism.

The structures of **4** were proved by elemental analysis and mass spectra, which exhibited the same [$M^{+\cdot}$] peak values as their parent isomers **1**. The ^{1}H NMR and IR spectra supported the structural nature between **1** and **4**.

Moreover, treatment of **4a**, **d** with bromine in hot acetic acid solution [21], was carried out affording the expected (*E,Z*) 5-benzoylmethylene analogues **5a**, **d**. Then, it was verified that compound **4** acquires the imidazolidinone conformation when **5a**, **d** were authentically prepared, by condensing 1-phenyl and 1,3-diphenyl-4-oxo-2-thioxo-imidazolidine [22,23], respectively with phenylglyoxal (Scheme 3).

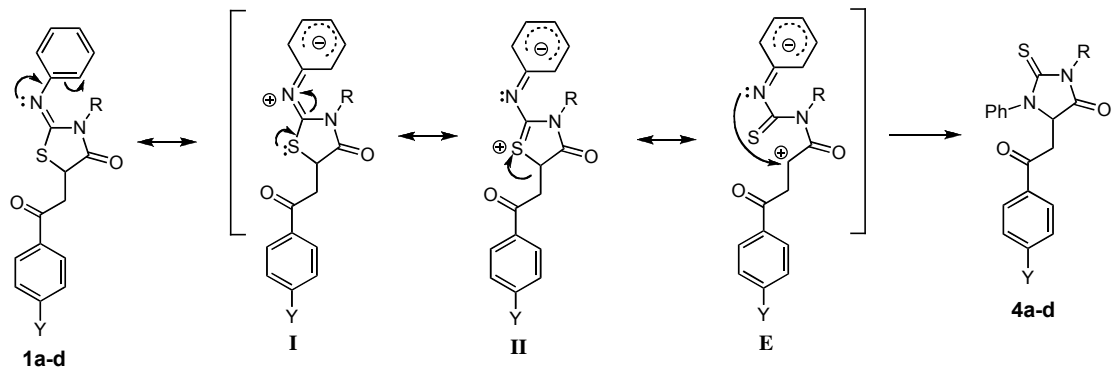
Scheme 3



	R	R'	Y
1-7a;	H,	Ph	H,
b;	H	Ph	Br,
c;	H	Ph	Cl,
d;	Ph	Ph	H,
k;	H	H	Br

Synthesis of **4- 7**

Scheme 4



Isomerisation of **1** into **4**

Table 1

Antimicrobial activity of tested products

Inhibition zone diameter (mm/ mg Sample)

Micro organism	Sample No. (20 mg/ mL)															
	T*	**A****	**1e**	**1g**	**1h**	**1j**	**1l**	**3c**	**3d**	**3i**	**3j**	**4a**	**4b**	**4k**	**6b**	**7c**
Bacillus subtilis	**30**	-	13	14	14	15	14	17	14	13	15	14	14	13	14	13
Staphylococcus aureus	**34**	-	12	11	13	12	11	15	13	12	14	13	11	12	12	0.0
Escherichia coli	**32**	-	12	14	14	14	13	16	13	13	14	13	14	13	13	12
Pseudomonas aeruginosa	**35**	-	12	14	14	14	13	16	13	12	15	13	13	13	13	11
Aspergillus flavus	-	**17**	0.0	0.0	0.0	0.0	0.0	11	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Aspergillus niger	-	**16**	11	0.0	0.0	0.0	0.0	14	13	12	0.0	0.0	0.0	0.0	0.0	11
Candida albicans	-	**18**	11	11	12	0.0	12	14	12	12	13	12	12	12	12	11
Candida Parapsilosis	-	**20**	12	12	12	12	11	15	13	12	13	12	11	13	12	12

* Tetracycline; standared antibacterial agent. ** Amphotricine-B; standared antifungal agent

On the other hand, the structure of compound **5** was also supported by elemental analysis and spectroscopic data. The ^{1}H NMR spectrum of **5a** displayed at δ 6.2 (s, 42%, olefinic H) for isomer (*E*) and 6.84 (s, 58%, olefinic H) for isomer (*Z*), 7.0- 7.63 m, 6H (aromatic H), 7.9, 7.07 each d, 2H (aromatic H), 9.45 s, 1H (NH). The configuration assignment of these isomers is based on the accepted assumption that the olefinic proton in isomer (*Z*) is more deshielded by the 4-oxo group, compared with the (*E*) counterpart [24].

According to our previous studies [25], thiation of **1a-c** and **4a-c** with Lawesson's reagent [14] was carried out (Scheme 3), affording 5-aryl-2,3-dihydro-2-phenylimino-thieno[2,3-*d*]thiazole derivatives **6a-c** and 1-phenyl-5-aryl-2,3-dihydro-2-thioxothieno[2,3-*d*]imidazoles **7a-c**, respectively. The IR spectra of either **6** or **7** were devoid of any CO absorption bands. The mass spectra of **6a-c** as well as **7a-c** displayed the same molecular ion peak values, showing the isomeric relationship between these compounds. The spectra showed also pattern of other fragments supporting the construction of these molecules.

Antimicrobial activity (Table 1) was measured in Micro Analytical Center, Cairo University, Giza, Egypt. The method was performed by saturating a sterilized filter paper disc with the selected sample with concentration of 20 mg/mL. Then, it was placed on a plate containing solid bacterial medium (nutrient agar both) or fungal medium (Dox's medium) to be seeded with the spore suspension of the tested organism. After inoculation, the diameter of the clear zone of inhibition surrounding the sample was taken as a measure of the inhabitation power against the particular tested organism [26-29]. The selected samples were screened against 2 bacterial Gram-positive; *Bacillus subtilis* and *Staphylococcus aureus*; and 2 bacterial Gram-negative; *Pseudomonas aeruginosa* and *Escherichia coli*. Antifungal activity was tested against *Aspergillus flavus*, *Aspergillus niger, Candida albicans* and *Candida Parapsilosis*. The recorded results were compared with Tetracycline and Amphotricine-B, respectively as standared antibacterial and antifungal agents. All the tested samples showed activity against the four bacterial strains, in 25-55% and activity against *Candida albicans* and *Candida Parapsilosis*, in (60-75%). Whilst, the activity against *Aspergillus niger* was only shown by the samples having the 2,4-dioxy- structure (class **3**), besides **1e** and **7c** of other classes, in (68-87%). In general, compound **3c** was the most effective sample and it was the only one that displayed activity against *Aspergillus flavus* in 64%.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on Perkin Elmer 1600 FT.IR spectrophotometer. ^{1}H-NMR spectra were measured on Varian Gemini 200 MHz instrument; chemical shifts (δ) are reported in ppm downfield from (*TMS*). Mass spectra were recorded on a Shimadzu GC-MS-QP 1000X spectrometer operating at 70 eV. Chromatography was carried out with Silica gel S 0.63 - 0.1 mm Riedel-de-Haen on a column with l = 17 cm, ϕ = 1.7 cm. dimensions. Thin layer chromatography was performed on Merck Kieselgel 60 F_{254} aluminum packed plates. Light petroleum is referred to the fraction b.p: (60-80 °C).

Synthesis of 2-(Phenyl)/imino-3-(un)/substituted-5-(2-aryl-2-oxoethyl)-4-oxo-1,3-thiazolidines 1a-l (1g-i Method I); An acetic acid (50 mL) solution containing (5.0 mmol) of each of phenyl- (0.67 g), 1,3-diphenyl- (1.14 g), 1-methyl-3-phenyl- (0.88 g) and/or thiourea (0.38 g), was added to (5.0 mmol) of the required 3-benzoyl- (0.88 g), 3-(4-bromobenzoyl)- (1.27 g) or 3-(4-chlorobenzoyl)-2-propenoic acid (1.0 g). The whole mixture was refluxed either for an hour or till a sudden precipitation of the crude **1j-l**. The solution of **1a-i** was concentrated (20 mL) and left to cool. The solid precipitated was filtered off, dried and recrystallized from the proper solvent to afford **1a-l**.

2-Phenylimino-5-(2-phenyl-2-oxoethyl)-4-oxo-1,3-thiazolidine (1a). 2.8 g (85.3%); mp 215-217° (acetic acid). ir: ν 3179, 3141 (N-H, hetero, exo), 3035, 3006 (=CH), 2904 (C-H), 1684, 1660 (C=O, aroyl and hetero ring), 1617 (C=N), 760, 690 cm^{-1}.

^{1}H nmr: δ 11.32 (brs, 1H, NH), 7.08- 8.11 (four deformed m, 10H_{arom}), 4.65-4.63 (complicated m, 1H_A), 4.18- 4.01 (deformed m, 2H, H_M, H_X) ; ms: m/z 310 (79.0), 205 (100), 119 (31), 105 (54.8),77 (77.1). *Anal.* Calcd for $C_{17}H_{14}N_2O_2S$ (310): C, 65.8; H, 4.51; N, 9.03. Found: C, 65.82; H, 4.48; N, 9.1.

2-Phenylimino-5-[2-(4-bromophenyl)-2-oxoethyl]-4-oxo-1,3-thiazolidine (1b). 3.5 g (87.5%); mp 241-243° (acetic acid). ir: ν 3266, 3207, 3412 (N-H), 3080, 3000 (=CH), 2924, 2860 (C-H), 1668 br (C=O, aroyl and hetero ring), 1638 (C=N), 818, 750, 690 cm^{-1}. ^{1}H nmr: δ 11.99, 11.25 (brs, 2H, CO*NH*, Ph*NH*), 7.0-7.93 (four deformed m. 9H_{arom}), 4.56– 4.53 (complicated m. 1H_A), 4.08- 3.97, 3.75- 3.53 (two deformed m. 2H, H_M, H_X); ms: m/z 388 (20.4), 205 (100), 183 (28.1), 77(33.1). Anal. Calcd for $C_{17}H_{13}BrN_2O_2S$ (388): C, 52.72; H, 3.35; N, 7.21. Found: C, 52.70; H, 3.33; N, 7.11.

2-Phenylimino-5-[2-(4-chlorophenyl)-2-oxoethyl]-4-oxo-1,3-thiazolidine (**1c**). 3.2 g (80.4%); mp 233-235° (acetic acid). ir: ν 3262, 3205,3142 (N-H), 3030-3000 (=CH), 2913-2858 (C-H), 1676 br (C=O, aroyl and hetero ring), 1629 (C=N), 820, 750, 700 cm^{-1}. ^{1}H nmr: δ 11.90, 11.15 (brs, 2H, CO*NH*, Ph*NH*), 6.98-8.01 (five deformed m, 9H_{arom}), 4.53- 4.50 (complicated m, 1H_A), 4.05-3.94, 3.71-3.62 (two deformed m. 2H, H_M, H_X); ms: m/z 344 (54.7), 205 (100) 139 (39.3), 118 (16.6), 77(22.6). *Anal*. Calcd for $C_{17}H_{13}ClN_2O_2S$ (344.5): C, 59.21; H, 3.77; N, 8.13. Found: C, 59.19; H, 3.78; N, 8.14.

2-Phenylimino-3-phenyl-5-(2-phenyl-2-oxoethyl)-4-oxo-1,3-thiazolidine (**1d**). 1.62 g (84.0%); mp 138-140° (light petroleum /chloroform). ir: ν 3054, 3031 (=CH), 2919 (C-H), 1723, 1672 (C=O, aroyl and hetero ring), 1634 (C=N), 768, 691 cm^{-1}. ^{1}H nmr: δ 7.96 (d, 2H, H_{arom}, J = 7.8 Hz), 7.45-7.62 (m, 8H, H_{arom}), 7.29 (apt., 2H, H_{arom}, J = 7.6 Hz), 7.68 (apt., 1H, H_{arom}, J = 7.6 Hz), 6.92 (d, 2H, H_{arom}, J = 7.8 Hz), 4.64 (dd, 1H_A, J_{AX} = 10.6, J_{AM} = 2.8 Hz), 4.14 (dd, 1H_M, J_{MX} = 18.4, J_{AM} = 2.8 Hz), 3.62 (dd, 1H_X, J_{MX} = 18.4, J_{AX} = 10.6 Hz); ms: m/z. 386 (56.7), 105 (40), 281 (100), 77 (75.7). *Anal.* Calcd for $C_{23}H_{18}N_2O_2S$ (386): C, 71.5; H, 4.66; N, 7.25. Found: C, 71.48; H, 4.62; N, 7.31.

2-Phenylimino-3-phenyl-5-[2-(4-bromophenyl)-2-oxoethyl]-4-oxo-1,3-thiazolidine (**1e**). 2.07 g (89.6%); mp 169-171° (light petroleum/chloroform). ir: ν 3059 (=CH), 2917 (C-H), 1718, 1685 (C=O, aroyl and hetero ring), 1631 (C=N), 817, 766, 693 cm^{-1}. ^{1}H nmr: δ 7.81, 7.63 each (d, 2H, H_{arom}, J = 8.8 Hz), 7.54 (d, 2H, H_{arom}, J = 7.8 Hz), 7.43-7.48 (m, 3H, H_{arom}), 7.29 (apt., 2H, H_{arom}, J = 7.8 Hz), 7.1 (apt., 1H, H_{arom}, J = 7.4 Hz), 6.92 (dd, 2H, H_{arom}, J = 8.2, 1.4 Hz), 4.62 (dd, 1H, H_A, J_{AX} = 10.2, J_{AM} = 2.8 Hz), 4.09 (dd, 1H, H_M, J_{MX} = 18.7, J_{AM} = 2.8 Hz), 3.58 (dd, 1H, H_X, J_{MX} = 18.7, J_{AX} = 10.2 Hz;); ms: m/z. 464 (25.3), 282 (100), 183 (15.9), 77 (33.1). *Anal*. Calcd for $C_{23}H_{17}BrN_2O_2S$ (464): C, 59.48; H, 3.66; N, 6.03. Found: C, 59.42; H, 3.68; N, 6.02.

2-Phenylimino-3-phenyl-5-[2-(4-chlorophenyl)-2-oxoethyl]-4-oxo-1,3-thiazolidine (**1f**). 1.85 g (88.4%); mp 168-169° (light petroleum/chloroform). ir: ν 3059 (=CH), 2954, 2919 (C-H), 1719, 1686 (C=O, aroyl and hetero ring), 1634 (C=N), 818, 766, 693 cm^{-1}. ^{1}H nmr: δ 7.88 (d, 2H, H_{arom}, J = 8.6 Hz), 7.56 (d, 2H, H_{arom}, J = 8.6 Hz), 7.41- 7.52 (m, 5H, H_{arom}), 7.27 (apt., 2H, H_{arom}, J = 7.8 Hz), 7.09 (apt., 1H, H_{arom}, J = 7.6 Hz), 6.91 (d, 2H, H_{arom}, J = 7.6 Hz), 4.62 (dd, 1H_A, J_{AX} = 10.0, J_{AM} = 2.8 Hz), 4.09 (dd, 1H_M, J_{MX} = 18.4, J_{AM} = 2.8 Hz), 3.58 (dd, 1H_X, J_{MX} = 18.4, J_{AX} = 10.0 Hz); ms: m/z. 420 (45.4),281 (100) 139 (29.8), 77 (25.1). *Anal*. Calcd for $C_{23}H_{17}ClN_2O_2S$ (420.5): C, 65.63; H, 4.04; N, 6.66. Found: C, 65.66; H, 4.11; N, 6.71.

2-Phenylimino-3-methyl-5-(2-phenyl-2-oxoethyl)-4-oxo-1,3-thiazolidine (**1g**). 1.43 g (87.7%); mp 67-70° (light petroleum/chloroform). ir: ν 3058,3027 (=CH), 2924 (C-H), 1716, 1674 (C=O, aroyl and hetero ring), 1639 (C=N), 761, 688 cm^{-1}. ^{1}H nmr: δ 7.92 (d, 2H, H_{arom}, J = 8.0 Hz), 7.39-7.60 (m, 3H, H_{arom}), 7.33 (apt., 2H, H_{arom}, J = 7.4 Hz), 7.116 (apt., 1H, H_{arom}, J = 7.4 Hz), 6.96 (d, 2H, H_{arom}, J = 7.4 Hz), 4.49 (dd, 1H_A, J_{AX} = 11.0, J_{AM} = 3.0 Hz), 4.11 (dd, 1H_M, J_{MX} = 18.7, J_{AM} = 3.0 Hz), 3.44 (dd, 1H_X, J_{MX} = 18.7, J_{AM} = 11.0 Hz), 3.37 (s, 3H, CH_3) ; ms: m/z. 324 (100), 105 (2.48), 219 (40.6), 77 (6.83). *Anal.* Calcd for $C_{18}H_{16}N_2O_2S$ (324): C, 66.66; H, 4.93; N, 8.64. Found: C, 66.63; H, 4.91; N, 8.71.

2-Phenylimino-3-methyl-5-[2-(4-bromophenyl)-2-oxoethyl]-4-oxo-1,3-thiazoildine (**1h**). 1.77 g (88.0%); mp 141-143° (light petroleum/chloroform). ir: ν 3070, 3025 (=CH), 2923 (C-H), 1715, 1674 (C=O, aroyl and hetero ring), 1639 (C=N), 826 cm^{-1}. ^{1}H nmr: δ 7.79, 7.61 each (d, 2H, H_{arom}, J = 8.0 Hz), 7.32 (apt., 2H, H_{arom}, J = 8.2 Hz), 7.14 (apt., 1H, H_{arom}, J = 8.2 Hz), 6.957 (d, 2H, H_{arom}, J = 8.2 Hz), 4.47 (dd, 1H_A, J_{AX} = 11.0, J_{AM} = 2.6 Hz), 4.05 (dd, 1H_M, J_{MX} = 18.6, J_{AM} = 2.6 Hz), 3.39 (dd, 1H_X, J_{MX} = 18.6, J_{AX} = 11.0 Hz), 3.362 (s, 3H, CH_3) ; ms: m/z. 402 (28.9) 219 (100)183 (3.27). *Anal.* Calcd for $C_{18}H_{15}BrN_2O_2S$ (402): C, 53.73; H, 3.73; N, 6.96. Found: C, 53.69; H, 3.72; N, 6.98.

2-Phenylimino-3-methyl-5-[2-(4-chlorophenyl)-2-oxoethyl]-4-oxo-1,3-thiazolidine (**1i**). 1.6 g (89.1% Method I) , 0.26 g (26.1% Method II); mp 128-130° (light petroleum/ chloroform). ir: ν 3065, 3024 (=CH), 2924 (C-H), 1716, 1674 (C=O, aroyl and hetero ring), 1642 (C=N), 831, 765, 694 cm^{-1}. ^{1}H nmr: δ 7.86 (d, 2H, H_{arom}, J = 8.8 Hz), 7.45 (d, 2H, H_{arom}, J = 8.6 Hz), 7.11 (apt., 2H, H_{arom}, J = 7.2 Hz), 6.95 (d, 2H, H_{arom}, J = 7..2 Hz), 6.84 (apt., 1H, H_{arom}, J = 7.2 Hz), 4.47 (dd, 1H_A, J_{AX} = 10.8, J_{AM} = 2.8 Hz), 4.05 (dd, 1H_M, J_{MX} = 18.6, J_{AM} = 2.8 Hz), 3.39 (dd, 1H_X, J_{MX} = 18.6, J_{AX} = 10.8 Hz), 3.36 (s, 3H, CH_3) ; ms: m/z. 358 (46.00), 219 (100),111 (18.2), 139 (20.10). *Anal.* Calcd for $C_{18}H_{15}ClN_2O_2S$ (358.5): C, 60.25; H, 4.81; N, 7.81. Found: C, 60.23; H, 4.79; N, 7.8.

2-Imino-5-(2-phenyl-2-oxoethyl)-4-oxo-1,3-thiazolidine (**1j**). 1.03 g (87.4%); m.p. > 300°C (DMF/ EtOH). ir: ν 3194 br (N-H), 3060-2940 br (=CH, C-H), 1677 br (C=O, aroyl and hetero ring), 761, 684 cm^{-1}. ^{1}H nmr: δ 9.10 (brs., 1H, NH_{hetero}), 8.91 (s, 1H, NH_{imino}), 8.08 (d, 2H, H_{aroyl}, J = 7.6 Hz), 7.77 (apt., 1H, H_{arom}, J = 7.2 Hz), 7.64 (apt., 2H, H_{arom}, J = 7.2 Hz), 4.52 (dd, 1H_A, J_{AX} = 10.6, J_{AM} = 2.8 Hz), 4.06 (dd, 1H_M, J_{MX} = 18.6, J_{AM} = 2.8 Hz), 3.56 (dd, 1H_X, J_{MX} = 18.6, J_{AX} = 10.6 Hz) ; ms: m/z. 234 (18.9), 129 (100),105 (74.8), 77 (80.8). *Anal.* Calcd for $C_{11}H_{10}N_2O_2S$ (234): C, 56.41; H, 4.27; N, 11.96. Found: C, 56.38; H, 4.21; N, 11.93.

2-Imino-5-[2-(4-bromophenyl)-2-oxoethyl]-4-oxo-1,3-thiazolidine (**1k**). 1.44 g (92.3%); mp > 300° (DMF/ EtOH). ir: ν 3230 br (N-H), 3023 br (=CH), 2930 br (C-H), 1671 br (C=O, aroyl and hetero ring), 821 cm^{-1}. ^{1}H nmr: δ 9.09 (brs., 1H, NH_{hetero}), 8.78 (brs, 1H, NH_{imino}), 7.93 (d, 2H, H_{arom}, J = 8.6 Hz), 7.76 (d, 2H, H_{arom}, J = 8.4 Hz), 4.42 (dd, 1H_A, J_{AX} = 10.6, J_{AM} = 2.6 Hz), 3.95 (dd, 1H_M, J_{MX} = 18.4, J_{AM} = 2.6 Hz), 3.49 (dd, 1H_X, J_{MX} = 18.4, J_{AX} = 10.6 Hz); ms: m/z. 312 (8.30), 129 (100),183 (21.60). *Anal*. Calcd for $C_{11}H_9BrN_2O_2S$ (312): C, 42.3; H, 2.88; N, 8.97. Found: C, 42.23; H, 2.81; N, 8.98.

2-Imino-5-[2-(4-chlorophenyl)-2-oxoethyl]-4-oxo-1,3-thiazolidine (**1l**). 1.23 g (92.7%); mp > 300° (DMF/ EtOH). ir: ν 3217 br (N-H), 3060-2940 br (=CH, C-H), 1672 br (C=O, aroyl and hetero ring), 826 cm^{-1}. ^{1}H nmr: δ 9.95 (s, 1H, $NH_{hetero.}$), 9.10

(brs., 1H, NH_{imino}), 8.08 (d, 2H, H_{arom}, J = 8.4 Hz), 7.69 (d, 2H, H_{arom}, J = 8.4 Hz), 4.510 (dd, $1H_A$, J_{AX} = 10.6, J_{AM} = 3.0 Hz), 4.04 (dd, $1H_M$, J_{MX} = 18.8, J_{AM} = 3.0 Hz), 3.57 (dd, $1H_X$, J_{MX} = 18.8, J_{AX} = 10.6 Hz) ; ms: m/z. 268 (12.10), 219 (100),139 (38.50). *Anal.* Calcd for $C_{11}H_9ClN_2O_2S$ (268.5): C, 49.16; H, 3.35; N, 10.43. Found: C, 49.22; H, 3.31; N, 10.46.

Synthesis of 2-*N*-methylanilino-5-(2-aryl-2-oxoethyl)-4-oxo-1,3-thiazolines 2a-c (Method Ⅰ): A solution of acetic acid (50 mL) containing 1-methyl-1-phenylthiourea (0.83 gm, 5.0 mmol) was refluxed for 1h with (5.0 mmol) of 3-benzoyl- (0.88 gm), 3-(4-bromobenzoyl)- (1.27 gm) or 3-(4-chlorobenzoyl)-2-propenoic acid (1.0 gm). The solution was concentrated (20 mL) and worked out as above to give **2a-c**.

Synthesis of 1g-i and 2a-c (Method Ⅱ): To a cold solution of ethanol (15 mL) containing KOH (0.17 g, 3 mmol), **1a, b** and/or **c** (3 mmol) was added. The mixture was stirred (20 min) in an ice bath, then treated with $(CH_3)_2SO_4$ (0.5 mL). The stirring was continued (20 min). The reaction mixture was poured into cold water (25 mL), extracted with two portions of chloroform (50 mL). The organic layers were combined together, dried ($CaCl_2$ anhydrous) and concentrated (1 mL). The residue was chromatographed on a column silica gel with light petroleum/ ethylacetate mixture first by (80/ 20 v/v) to afford **1g-i** then with (50/50 v/v) to give **2a-c**.

Compounds **1g-i** were matched (mp, admixing mp) with the respective sample previously obtained by (Method Ⅰ).

2-*N*-Methylanilino-5-(2-phenyl-2-oxoethyl)-4-oxo-1,3-thiazoline (**2a**) 1.1 gm (67.5% Method I); 0.50 gm (51.3 % Method II); mp 180-182° (Light petroleum/ chloroform). ir: ν 3070 br (=CH), 2918 br (C-H), 1695 (C=O, aroyl and hetero ring), 750 cm^{-1}. ^1H nmr: δ 7.92 (dd, 2H, H_{arom}, J = 3.5, 1.6 Hz), 7.29-7.62 (m, 8H, H_{arom}), 4.49 (dd, $1H_A$, J_{AX} = 11.8, J_{AM} = 2.8 Hz), 4.19 (dd, $1H_M$, J_{MX} = 18.6, J_{AM} = 2.8 Hz), 3.66 (s, 3H, CH_3), 3.31 (dd, $1H_X$, J_{MX} = 18.6, J_{AX}= 11.8 Hz) ; ms: m/z. 324 (3), 219 (18), 133 (50.75), 155 (35.5) 77 (100). *Anal.* Calcd for $C_{18}H_{16}N_2O_2S$ (324): C, 66.66; H, 4.93; N, 8.64. Found: C, 66.64; H, 4.91; N, 8.66.

2-*N*-Methylanilino-5-[2-(4-bromophenyl)-2-oxoethyl]-4-oxo-1,3-thiazoline (**2b**). 1.4 g (69.6% Method I), 0.63 g (52.6% Method II); mp 140-142° (Light petroleum/ chloroform). ir: ν 3060 (=CH), 2918 (C-H), 1705, 1676 (C=O, aryl and hetero ring), 1620 (C=N), 816 cm^{-1}. ^1H nmr: δ 7.78 (d, 2H, H_{arom}, J = 8.6 Hz), 7.59 (d, 2H, H_{arom}, J = 8.6 Hz), 7.44- 7.48 (m, 3H, H_{arom}), 7.30 (dd, 2H, H_{arom}, J = 5.0, 2.0 Hz), 4.47 (dd, $1H_A$, J_{AX} = 11.6, J_{AM} = 3.0 Hz), 4.13 (dd, $1H_M$, J_{MX} = 18.8, J_{AM} = 3.0 Hz), 3.659 (s, 3H, CH_3), 3.26 (dd, $1H_X$, J_{MX} = 18.8, J_{AX} = 11.6 Hz); ms: m/z. 402 (31), 219 (100).183 (31.95) 77 (67.16). *Anal.* Calcd for $C_{18}H_{15}BrN_2O_2S$ (402): C, 53.73; H, 3.73; N, 6.96. Found: C, 53.72; H, 3.63; N, 6.99.

2-*N*-Methylanilino-5-[2-(4-chlorophenyl)-2-oxoethyl]-4-oxo-1,3-thiazoline (**2c**). 1.4 g (61.3% Method I), 0.61 g (57.0% Method II); mp 151-153° (Light petroleum/ chloroform); ir: ν 3063 (=CH), 2924 (C-H), 1687 br (C=O, aryl and hetero ring), 813 cm^{-1}. ^1H nmr: δ 7.86 (d, 2H, J = 8.6 Hz), 7.413-7.484 (m, 5H, H_{arom}), 3.32 (dd, 2H, H_{arom}, J = 5.40, 2.4 Hz), 4.48 (dd, $1H_A$, J_{AX} = 11.6, J_{AM} = 2.8 Hz), 4.15 (dd, $1H_M$, J_{MX} = 18.8, J_{MX} = 2.8 Hz), 3.66 (s, 3H, Me), 3.27 (dd, $1H_X$, J_{MX} = 18.8, J_{AX} = 11.6 Hz); ms: m/z. 358 (5.17), 219 (91.87), 139 (82), 111 (100). *Anal.* Calcd for $C_{18}H_{15}ClN_2O_2S$ (358.5): C, 60.25; H, 4.2; N, 7.81. Found: C, 60.26; H, 4.21; N, 7.83.

Synthesis of 3-un/substituted-5-(2-aryl-2-oxoethyl)-2,4-dioxo-1,3-thiazolidines 3a-i. A solution of glacial acetic acid (25 mL) containing **1a-k** or **l** 0.5 g (1.0- 2.5 mmol) was refluxed with conc. HCl (2 mL) for 10 hours (5 hours for **1j-l**). The solution was concentrated and poured into ice-cold water (30 mL). The solid separated was collected by filtration, washed, dried and crystallized from the proper solvent to give:

5-(2-Phenyl-2-oxoethyl)-2,4-dioxo-1,3-thiazolidine (**3a**). (from **1a** or **1j**) 0.46 g (90%); mp 153-155° (toluene); ir: ν 3167 (N-H), 3053 (=CH), 2789, 2959 (C-H), 1753 (C=O), 1677 br (C=O, aroyl and hetero ring), 772, 685 cm^{-1}. ^1H nmr: δ 7.96 (d, 2H, H_{arom}, J = 7.8 Hz), 7.64 (ap.t., 1H, H_{arom}, J = 7.6 Hz), 7.506 (apt., 2H, H_{arom}, J = 7.6 Hz), 7.26 (s, 1H, NH), 4.68 (dd, 1H, H_A, J_{AX} = 10.4, J_{AM} = 3.0 Hz), 4.69 (dd, 1H, H_M, J_{MX} = 18.6, J_{AM} = 3.0 Hz), 3.594 (dd, 1H, H_X, J_{MX} = 18.6, J_{AX} = 10.4 Hz); ms: m/z. 235 (21.9), 130 (8.20), 105 (100), 77 (59.2). .*Anal.* Calcd for $C_{11}H_9NO_3S$ (235): C, 56.17; H, 3.84; N, 5.95. Found: C, 56.13; H, 3.79; N, 5.96.

5-[2-(4-Bromophenyl)-2-oxoethyl]-2,4-dioxo-1,3-thiazolidine (**3b**) (from **1b** or **1k**). 0.47 g (95.5%); mp 184-185° (toluene); ir: ν 3173 (N-H), 3066 (=CH), 2950, 2799 (C-H), 1760 (C=O), 1689 br (C=O, aroyl and hetero ring), 816 cm^{-1}. ^1H nmr: δ 7.82, 7.65 each (d, 2H, H_{arom}, J = 8.6 Hz), 7.36 (s, 1H, NH). 4.67 (dd, 1H, H_A, J_{AX} = 10.4, J_{AM} = 3.0 Hz), 4.04 (dd, 1H, H_M, J_{MX} = 18.6, J_{AM} = 3.0 Hz), 3.54 (dd, 1H, H_X, J_{MX} = 18.6, J_{AX} = 10.4 Hz); ms: m/z. 313 (29.40)130 (45), 183 (100)155 (17.50). *Anal.* Calcd for $C_{11}H_8BrNO_3S$ (313): C, 42.17; H, 2.55; N, 4.47. Found: C, 42.14; H, 2.55; N, 4.46.

5-[2-(4-Chlorophenyl)-2-oxoethyl]-2,4-dioxo-1,3-thiazolidine (**3c**) (from **1c** or **1l**). 0.46 g (92%); mp 161-163° (toluene); ir: ν 3168 (N-H), 3067 (=CH), 2950, 2799 (C-H), 1756 (C=O), 1690 br (C=O, aroyl and hetero ring), 822 cm^{-1}. ^1H nmr: δ 8.6 (br, NH), 7.9, 7.48 each (d, 2H, H_{arom}, J = 8.4 Hz), 4.66 (dd, 1H, H_A, J_{AX} = 10.2, J_{AM} = 3.0 Hz), 4.04 (dd, 1H, H_M, J_{MX} = 18.8, J_{AM} = 3.0 Hz), 3.55 (dd, 1H, H_X, J_{MX} = 18.4, J_{AX} = 10.2 Hz); ms: m/z. 269 (27),130 (21), 139 (100), 111 (41). *Anal.* Calcd for $C_{11}H_8ClNO_3S$ (269.5): C, 48.97; H, 2.97; N, 5.19. Found: C, 48.93; H, 2.96; N, 5.18

3-Phenyl-5-(2-phenyl-2-oxoethyl)-2,4-dioxo-1,3-thiazolidine (**3d**) (from **1d**). 9.1 g (91%); mp 117- 118° (EtOH); ir: ν 3067 (=CH), 2917 (C-H), 1735 (C=O), 1674 br (C=O, aroyl and hetero ring), 754, 688 cm^{-1}. ^1H nmr: δ 7.98 (d, 2H, H, J = 7.8 Hz), 7.64 (apt., 1H, H_{arom}, J = 7.2 Hz), 7.45-7.57 (m, 5H, H_{arom}), 7.336 (dd, $2H_{arom}$, J = 6.7, 2.0 Hz), 4.742 (dd, 1H, H_A, J_{AX} = 9.9, J_{AM} = 3.0 Hz), 4.15 (dd, 1H, H_M, J_{MX} = 18.7, J_{AM} = 3.0 Hz), 3.70 (dd, 1H, H_X, J_{MX} = 18.7, J_{AX} = 9.8 Hz); ms: m/z. 311 (34), 206 (59), 105 (100), 77 (67). *Anal.* Calcd for $C_{17}H_{13}NO_3S$ (311): C, 65.59; H, 4.18; N, 4.50. Found: C, 65.61; H, 4.20; N, 4.53.

3-Phenyl-5-[2-(4-bromophenyl)-2-oxoethyl]-2,4-dioxo-1,3-thiazolidine (**3e**) (from **1e**). 1.0 g (93.0%); mp 182-184° (EtOH); ir: ν 3064 (=CH), 2943, 2909 (C-H), 1751 (C=O), 1678 br (C=O, aroyl and hetero ring), 816, 750, 689 cm^{-1}. ^1H nmr: δ 7.85, 7.66 each (d, 2H, H_{arom}, J = 8.6 Hz), 7.45-7.57 (m, 3H, H_{arom}), 7.33 (d, 2H, H_{arom}, J = 8.6 Hz), 4.73 (dd, 1H, $1H_A$, J_{AX} = 9.8, J_{AM} = 3.0 Hz), 4.10 (dd, 1H, H_M, J_{MX} = 18.6, J_{AM} = 3.0 Hz), 3.67 (dd, 1H, H_X, J_{MX} = 18.6, J_{AX} = 9.8 Hz); ms: m/z. 389 (24), 206 (100), 183 (52), 155 (21). *Anal.* Calcd for $C_{17}H_{12}BrNO_3S$ (389): C, 52.44; H, 3.08; N, 3.59. Found: C, 52.50; H, 3.11; N, 3.62.

3-Phenyl-5-[4-(chlorophenyl)-2-oxoethyl]-2,4-dioxo-1,3-thiazolidine (**3f**) (from **1f**). Yield: 1.8 g (92.0%); mp 180-182° (EtOH); ir: ν 3098, 3065 (=CH), 2943, 2911 (C-H), 1749 (C=O), 1680 br (C=O, aroyl and hetero ring), 825, 751, 691 cm^{-1}. ^1H nmr: δ 7.8, 7.64 each (d, 2H, H_{arom}, J = 8.8 Hz), 7.30-

7.44 (m, 5H, H_{arom}), 4.58 (dd, 1H, H_A, J_{AX} = 10.6, J_{AM} = 3.0 Hz), 4.05 (dd, 1H, H_M, J_{MX} = 18.6, J_{AM} = 3.0 Hz), 3.42 (dd, 1H, H_X, J_{MX} = 18.6, J_{AX} = 10.6 Hz) ; ms: m/z. 345 (35), 206 (97) 139 (100) 111 (46.80). *Anal.* Calcd for $C_{17}H_{12}ClNO_3S$ (345.5): C, 59.04; H, 3.47; N, 4.05. Found: C, 59.10; H, 3.46; N, 4.12.

3-Methyl-5-(2-phenyl-2-oxoethyl)-2,4-dioxo-1,3-thiazolidine (**3g**) (from **1g**). 0.41 g (82.0%); mp 85-87° (EtOH); ir: ν 3065 (=CH), 2961, 2920 (C-H), 1740 (C=O), 1678 br (C=O, aroyl and hetero ring), 686, 745 cm^{-1}. ^1H nmr: δ 7.95 (d, 2H, H_{arom}, J = 7.2 Hz), 4.63 (apt., 1H, H_{arom}, J = 7.2 Hz), 7.46 (apt., 2H, H_{arom}, J = 7.2 Hz), 4.59 (dd, $1H_A$, J_{AX} = 10.6, J_{AM} = 2.8 Hz), 4.12 (dd, $1H_M$, J_{MX} = 18.6, J_{AM} = 2.8 Hz), 3.51 (dd, $1H_X$, J_{MX} = 18.6, J_{AX} = 10.6 Hz), 3.16 (s, 3H, CH_3) ; ms: m/z. 249 (100), 144 (77.23),105 (65.00), 77 (84.68). 235 (21.9)130 (8.20),105 (100),77 (59.2). *Anal.* Calcd for $C_{12}H_{11}NO_3S$ (249): C, 57.83; H, 4.41; N, 5.62. Found: C, 57.81; H, 4.43; N, 5.61.

3-Methyl-5-[2-(4-bromophenyl)-2-oxoethyl]-2,4-dioxo-1,3-thiazolidine (**3h**) (from **1h**). 0.46 g (92.0%); mp 148-150° (EtOH); ir: ν 3072, 3040 (=CH), 2983, 2906 (C-H), 1752 (C=O), 1675 br (C=O, aroyl and hetero ring), 818 cm^{-1}. ^1H nmr: δ 7.87 (d, 2H, H_{arom}, J = 8.0 Hz), 7.46 (d, 2H, H_{arom}, J = 8.2 Hz), 4.57 (dd, $1H_A$, J_{AX} = 10.6, J_{AM} = 3.0 Hz), 3.97 (dd, $1H_M$, J_{MX} = 18.4, J_{AM} = 3.0 Hz), 3.46 (dd, $1H_X$, J_{MX} = 18.4, J_{AX}= 10.6 Hz), 3.14 (s, 3H, CH_3); ms: m/z. 327 (24.7), 206(100), 155 (21.2), 183 (52.50). *Anal.* Calcd for $C_{12}H_{10}BrNO_3S$ (328): C, 43.93; H, 3.08; N, 4.27. Found: C, 43.96; H, 3.05; N, 4.31.

3-Methyl-5-[2-(4-chlorophenyl)-2-oxoethyl]-2,4-dioxo-1,3-thiazolidine (**3i**) (from **1i**). 0.43 g (86.0%); mp 128-130° (EtOH). ir: ν 3072, 3033 (=CH), 2946, 2906 (C-H), 1748 (C=O), 1678 br (C=O, aroyl and hetero ring), 821 cm^{-1}. ^1H nmr: δ 7.80 (d, 2H, H_{arom}, J = 8.6 Hz), 7.64 (d, 2H, H_{arom}, J = 8.6 Hz), 4.57 (dd, $1H_A$, J_{AX} = 10.6, J_{AM} = 2.8 Hz), 4.06 (dd, $1H_M$, J_{MX} = 18.4, J_{AM} = 2.8 Hz), 3.46 (dd, $1H_X$, J_{MX} = 18.4, J_{AX} = 10.6 Hz), 3.16 (s, 3H, CH_3); ms: m/z. 283 (31), 144 (87), 139 (100), 111(49.20). *Anal.* Calcd for $C_{12}H_{10}ClNO_3S$ (283.5): C, 50.79; H, 3.53; N, 4.94. Found: C, 50.77; H, 3.56; N, 4.93.

Rearrangement of 1a-c, d and k into 1-phenyl-, 1,3-diphenyl-, and 5-(2-aryl-2-oxoethyl)-4-oxo-2-thioxoimidazolidines 4a-c, d and k. A solution of DMF (50 mL) containing **1a, b, c, d** or k (1.0 g) was refluxed for **4h** (10 h for **1k**). The solution was concentrated (5 mL) under vacuum and treated with 20 mL of ethanol (ethyl acetate for 1d). The separated solid from **1a-d** was collected by filtration and recrystallized (toluene/light petroleum) to give **4a-d.** The unchanged **1k** was removed by filtration and the mother liquor was evaporated and diluted with ethanol. The crud product was collected by filtration and recrystallized (chloroform/light petroleum) to afford **4k**.

1-Phenyl-5-(2-phenyl-2-oxoethyl)-4-oxo-2-thioxoimidazolidine (**4a**). 0.28 g (93%); mp 226-228°; ir: ν 3237-3040 br (N-H, =CH), 2964 (C-H), 1739, 1681 (C=O, aroyl and hetero ring), 1248(C=S), 760, 690 cm^{-1}. ^1H nmr (DMSO-d_6): δ 11.72 (s, 1H, NH), 7.60 (d, $2H_{arom,}$ J = 8.0 Hz), 7.07 - 7.44 (m, $8H_{arom}$) , 4.84 - 4.88 (m, 1H, H_A), 3.21 – 3.44 (m, 2H , H_M, H_X); ms: m/z. 310 (35), 205 (59), 77 (100). *Anal.* Calcd for $C_{17}H_{14}N_2O_2S$ (310): C, 65.80; H, 4.51; N, 9.03. Found: C, 65.78; H, 4.50; N, 9.00.

1-Phenyl-5-[2-(4-bromophenyl)-2-oxoethyl]-4-oxo-2-thioxoimidazolidine (4b). 1.10 g (95.0%); mp 247-249°; ir: ν 3226-3040 br (N-H, =CH), 2980 (C-H), 1741, 1681 (C=O, aroyl and hetero ring), 1225 (C=S), 807, 762, 695 cm^{-1}. ^1H-NMR: δ = 12.0 (1H, NH), 7.56, 7.48 each (d, 2H, H_{arom}, J = 6.6 Hz), 7.20-7.33 (m, 5H, C_6H_5), 4.94 (apt., 1H, H_A, J_{AM} = J_{AX} = 4.4 Hz), 343 (dd, 1H, H_M, J_{MX} = 18.2, J_{AM} = 4.4 Hz), 3.30 (dd, 1H, H_X, J_{MX} = 18.2, J_{AX} = 4.4 Hz); ms: m/z. 388 (27), 205 (100), 77 (39). *Anal.* Calcd for $C_{17}H_{13}BrN_2O_2S$ (388): C, 52.57; H, 3.35; N, 7.21. Found: C, 52.50; H, 3.32; N, 7.18

1-Phenyl-5-[2-(4-chlorophenyl)-2-oxoethyl]-4-oxo-2-thioxoimidazolidine (4c). 0.95 g (93.0%); mp 238-240°; ir: 3229-3040 br (N-H, =CH), 2928 (C-H), 1740, 1681 (C=O, aroyl and hetero ring), 1205 (C=S), 809, 760, 695 cm^{-1}. ^1H nmr: δ 12.23 (1H, NH), 7.84, 7.55 each (d, 2H, H_{arom}, J = 8.6 Hz), 7.39-7.28 (m, 5H, C_6H_5), 5.314 (apt., $1H_A$, J_{AM} = J_{AX} = 4.2 Hz), 3.66 (dd, $1H_M$, J_{MX} = 18.8, J_{AM} = 4.2 Hz), 3.40 (dd, $1H_X$, J_{MX} = 18.8, J_{AX} = 4.2 Hz); ms: m/z. 344 (7), 205 (100), 77 (48). *Anal.* Calcd for $C_{17}H_{13}ClN_2O_2S$ (344.5): C, 59.21; H, 3.77; N, 8.12. Found: C, 59.22; H, 3.70; N, 8.15.

1,3-Diphenyl-5-(2-phenyl-2-oxoethyl)-4-oxo-2-thioxoimidazolidine (**4d**). 1.1 g (90 %); mp 152-154°; ir: ν 3062 (=CH), 2918 (C-H), 1759, 1669 (C=O, aroyl and hetero ring), 1220 (C=S), 753, 691 cm^{-1}. ^1H nmr: δ 7.82 (d, 2H, H_{arom}, J = 8.4 Hz), 7.37 – 7.61 (m, 13H, H_{arom}) 4.98 – 5.02 (m,1H, H_A), 3.68 (dd, 1H, H_M, J_{MX} = 18.6, J_{AM} = 3.9 Hz), 3.54 (dd, 1H, H_X, J_{MX} = 18.6, J_{AX} = 3.6 Hz); ms: m/z 386 (39), 281 (100), 77 (69). .*Anal.* Calcd for $C_{23}H_{18}N_2O_2S$ (386): C, 71.5; H, 4.66; N, 7.25. Found: C, 71.35; H, 4.60; N, 7.33.

5-[2-(4-Bromophenyl)-2-oxoethyl]-4-oxo-2-thioxoimidazolidine (**4k**). 0.10 g (10%); mp 206- 208° (EtOH); ir: 3190 (br, N-H), 3089 (=CH), 2574 (S-H), 1734, (C=O, aroyl and hetero ring), 1680 (C=N), 819 cm^{-1}; ms: m/z 312 (28), 129 (100), 183 (24). *Anal.* Calcd for $C_{11}H_9BrN_2O_2S$ (312): C, 42.3; H, 2.88; N, 8.97. Found: C, 42.53; H, 2.80; N, 8.93.

Synthesis of 1-phenyl and 1,3-diphenyl-5-(benzoylmethylene)-4-oxo-2-thioxoimidazolidines 5a and 5d: (Method A): A solution of glacial acetic acid (10 mL) containing 1-phenyl [18] (0.38 g, 2 mmol) and/or 1,3-diphenyl-4-oxo-2-thioxoimidazolidine [19] (0.53 g, 2 mmol) was refluxed for 20 min with phenylglyoxal (0.27 g, 2 mmol) and fused CH_3COONa (0.5 g, 6 mmol). The reaction mixtures were concentrated (3 mL), poured onto water (50 mL) and extracted twice with $CHCl_3$ (50 mL). The organic solutions were combined, dried ($CaCl_2$ anhydrous) and evaporated. The residue was chromatographed silica gel- (diethyl ether/light petroleum 5:1 v/v) to give 5a, b.

(Method B): A solution of glacial acetic acid (15 mL) containing **4a** (0.3 g, 1mmol) and/or **4d** (0.38 g, 1mmol) was treated with bromine (0.5 mL, 1 mmol). The mixture was stirred for 10 min, and then warmed till HBr ceased to evolve. The reaction mixture of **4a** was concentrated and the precipitated solid was collected by filtration dried, and reystallized from acetic acid to give **5a**. The reaction mixture of **4d** was worked out as described in method A to afford **5b**.

1-Phenyl-5-(benzoylmethylene)-4-oxo-2-thioxoimidazolidine (5a). 0.28 g (36 %, method A), 0.20 g (56 %, method B); mp 154-156°C (light petroleum/ chloroform); ir: ν 3238-3030 br (N-H, =CH), 1739, 1681 (C=O, aroyl and hetero ring), 1222 (C=S), 750, 690 cm^{-1}. ^1H nmr: δ 9.45 (s, 1 H, NH) 7.05 – 7.628 (m,6 H, H_{arom}), *E*-isomer (42 %): 7.9 (d, 2H, H_{arom} , J = 7.8 Hz), 6.2 (s, 1 H, =CH), *Z*-isomer (58 %), 7.07 (d, 2H, H_{arom}, J = 7.8 Hz), 6.835 (s, 1H, =CH); ms: m/z. 308 (47.2),105 (80.9) 77 (100). *Anal.* Calcd for $C_{17}H_{12}N_2O_2S$ (308): C, 66.22; H, 3.92; N, 9.08. Found: C, 66.26; H, 3.93; N, 9.12.

1,3-Diphenyl-5-(benzoylmethylene)-4-oxo-2-thioxoimidazolidine (**5d**). 0.28 g (36 %, method A) , 0.20 g (56%, method B); mp 155-157° (light petroleum/ chloroform); ir: ν 3058 (=CH), 1749, 1666 (C=O, aroyl and hetero ring), 1230(C=S),

760, 690 cm^{-1}. ^{1}H nmr: δ 7.14- 7.61 (m, 13H, H_{arom}), *E*-isomer (29%): 7.93 (d, 2H, H_{arom}, J = 7.0 Hz), 6.12 (s, 1 H, =CH), *Z*-isomer (71%) , 7,66 (d, 2H, H_{arom}, J = 8.0 Hz), 6.85 (s,1H, =CH); ms: m/z. 384 (11), 105 (100), 77 (91). *Anal*. Calcd for $C_{23}H_{16}N_2O_2S$ (384): C, 71.87; H, 4.16; N, 7.29. Found: C, 71.82; H, 4.11; N, 7.33.

Synthesis of 5-aryl-2,3-dihydro-2-phenyliminothieno[2,3-*d*]-thiazoles 6a-c. A mixture **1a, b** and/or **c** (0.5 g; 1.5 mmol) and Lawesson's reagent [18] (0.7 g; 1.7 mmol) was refluxed in xylene/ dioxane solution (50 mL; 5/2 v/v) for 4 h. The mixture was concentrated (15 mL), treated with light petroleum and left to cool. The product was collected by filtration, washed with hot water, dried and recrystallized from toluene – dioxane to afford **6a-c**.

5-Phenyl-2,3-dihydro-2-phenyliminothieno[2,3-*d*]thiazole (**6a**) 0.4 g (80 %); mp 200- 202°; ir: ν 3176 (=NH), 1565 (C=N), 1269 (C-N), 3055 (=CH), 693, 750 cm^{-1}. ^{1}H nmr: δ 10.57 (s, 1H, NH) 7.62-7.74 (m, 4H, H_{arom}), 7.69 (s, 1H, H-6) 7.2565-7.469 (m,5H, H_{arom}), 7.02 (apt., 1 H, H_{arom}, J = 8.0 Hz); ms: m/z. 308 (100), 204 (6), 146 (2). *Anal*. Calcd for $C_{17}H_{12}N_2S_2$ (308): C, 66.23; H, 3.89; N, 9.09. Found: C, 66.26; H, 3.91; N, 9.12

5-(4-Bromophenyl)-2,3-dihydro-2-phenyliminothieno[2,3-*d*]-thiazole (**6b**). 0.42 g (84 %); mp 259- 261°C; ir: ν 3176 (=NH), 3044 (=CH), 1563 (C=N), 1267 (C-N),698, 752, 811 cm^{-1}. ^{1}H nmr: δ 10.558 (s, 1H, NH), 7.70 (s, 1H, H-6), 7.67 (d, 2H, H_{arom}, J = 7.2 Hz), 7.57- 7.58 (m, 4H, H_{arom}), 7.36 (apt., 2H, H_{arom} , J = 7.2 Hz), 7.11 (apt., 1 H, H_{arom} , J =7.2 Hz); ms: m/z. 387 (100), 386 (76), 282 (11), 224 (9). *Anal*. Calcd for $C_{17}H_{11}BrN_2S_2$ (386): C, 52.85; H, 2.85; N, 7.25. Found: C, 52.84; H, 2.80; N, 7.29.

5-(4-Chlorophenyl)-2,3-dihydro-2-phenyliminothieno[2,3-*d*]-thiazole (**6c**). 0.42 g (84 %); mp 216- 218°; ir: ν 3188 (=NH), 3044 (=CH), 1569 (C=N), 1272 (C-N), 693, 748, 810 cm^{-1}; ms: m/z. 342 (100), 238 (12.9), 180 (3.62). *Anal*. Calcd for $C_{17}H_{11}ClN_2S_2$ (342.5): C, 59.65; H, 3.21; N, 8.18. Found: C, 59.65; H, 3.22; N, 8.26.

Synthesis of 1-phenyl-5-aryl-2,3-dihydro-2-thioxothieno-[2,3-*d*]imidazoles 7a-c. A mixture **4a, b** and/or **c** (0.5 gm; 1.5 mmol) and Lawesson's reagent (0.7 gm; 1.7 mmol) was refluxed in xylene solution (50 mL) for 4h. The reaction mixture was concentrated (30 mL). After cooling, the crude precipitate was collected by filtration, washed with water then with dilute methanol, dried and recrystallized from the proper solvent with charcoalization to give **7a-c**.

1,5-Diphenyl-2,3-dihydro-2-thioxothieno[2,3-*d*]imidazole (**7a**). 0.41 g (82 %); mp 236-238°; ir: ν 3065 (=CH), 2668 (S-H), 682, 743 cm^{-1} ^{1}H nmr: δ 11.65 (brs, 1H, NH), 7.68 (d, 2H, H_{arom}, J = 8.0Hz), 7.58 (apt., 2H, H_{arom}, J = 8.0 Hz), 7.46- 7.54, 7.26- 7.37 each (m, 3H, H_{arom}), 6.89 (s, 1H, H-6); ms: m/z. 308 (100), 307 (25), 121 (28). *Anal*. Calcd for $C_{17}H_{12}N_2S_2$ (308): C, 66.23; H,3.89; N,9.09. Found: C,66.30;H,3.91; N, 9.10.

1-Phenyl-5-(4-bromophenyl)-2,3-dihydro-2-thioxothieno-[2,3-*d*]imidazole (**7b**). 0.37 g (74 %); mp 279- 281°; ir: ν 3065 (=CH), 2668 (S-H), 686, 733, 799 cm^{-1}. ^{1}H nmr: δ 7.95 (brs, 1H, NH), 7.42-7.68 (m, 9H, H_{arom}), 7.36 (s, 1H, H-6); ms: m/z. 386 (93.6), 307 (5.4), 308 (2.5). .*Anal*. Calcd for $C_{17}H_{11}BrN_2S_2$ (386): C, 52.85; H, 2.85; N, 7.25. Found: C, 52.86; H, 2.80; N, 7.31.

1-Phenyl-5-(4-chlorophenyl)-2,3-dihydro-2-thioxothieno-[2,3-*d*]imidazole (**7c**). 0.4 g (80 %); mp 222-224°; ir: ν 3065 (=CH), 2668 (S-H), 686, 799 cm^{-1}; ms: m/z. 342 (100) 307 (2.3), 265 (3). *Anal*. Calcd for $C_{17}H_{11}ClN_2S_2$ (342.5): C, 59.65; H, 3.21; N, 8.18. Found: C, 59.67; H, 3.20; N, 8.27.

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