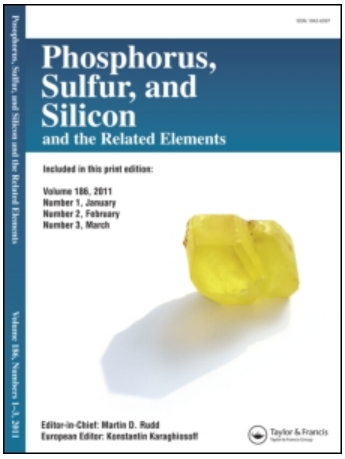

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Studies on 2,4-Dithioxo and 2-Thioxoimidazolidene Derivatives

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Studies on 2,4-Dithioxo and 2-Thioxoimidazolidene Derivatives

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*5,5-Dimethylimidazolidine-2,4-dithione (**1**) undergoes a Mannich reaction to give 5,5-dimethyl-3-(4-morpholinomethyl)imidazolidine-2,4-dithione (**2**), which on treatment with (2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)bromide (ABG) afforded 5,5-dimethyl-3(4-morpholinomethyl)-2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-thioglucopyranosyl)-4-thiohydantoin (**3**). Oxidation of **3** with $KMnO_4$ furnished the corresponding sulfone **4**. Deblocking of **3** with sodium ethoxide afforded **1**. Reaction of **1** with ABG gave the N-glucoside **5**. Deblocking of **5** afforded 5,5-dimethyl-3-N-(3,4,5-trihydroxy-6-hydroxy-methyltetrahydropyran-2-yl)imidazolidine-2,4-dithione (**6**). Oxidation of **5** yielded 5,5-dimethyl-imidazolidine-3-N-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-2-oxo,4-thione (**7**). Reaction of **1** with phenacyl chloride afforded **8**, which on thiation with P_4S_{10} gave **9**. 5-Benzylidene-2-thioxoimidazolidin-4-one (**10**) reacted with some halo compounds and afforded **11** and **12**. Treatment of **10** with 2,4-dinitro-1-chlorobenzene afforded N,N-dimethyl-2,4-dinitrobenzamide (**13**) and 2-benzylidene-6-nitro-2H-benzo[d]imidazo[2,1-b]thiazol-3-one (**14**). Refluxing **12** with semicarbazides gave **15** and **16**. Boiling **12** with 4-aminoacetophenone furnished **18**, which on treatment with hydrazine gave 5-benzylidene-2-[4-(1-hydrazonoethyl)phenylimino]imidazolidin-4-one (**19**). Conden- sation of **18** with benzaldehyde yielded 5-benzylidene-2-[4-(3-phenylacryoyl)phenylimino]-imidazolidin-4-one (**20**).*

Keywords Alkylation; glucoside; hydrazide; HIV; microbial activity; imidazolidines; mannich bases

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INTRODUCTION

For many years, our research group has been interested in the chemistry of hydantoins and their derivatives[1–6] due to their use in medicine, where they have mainly been described as anticonvulsant agents.[7] Some acyclic nucleoside analogues have achieved considerable success as antiviral agents[8] due to their low toxicity towards normal cells, while displaying inhibitory activity against herpes simplex virus (HSV),[9] and their nucleosides show potent activity against the human immunodeficiency virus (HIV).[10] Because of their resemblance with natural nucleosides, there is obvious interest in glycosylated hydantoin derivatives.[11–14] For these reasons, we are interested in continuing our work in this area to produce new derivatives for testing their activity against HIV and antimicrobial.

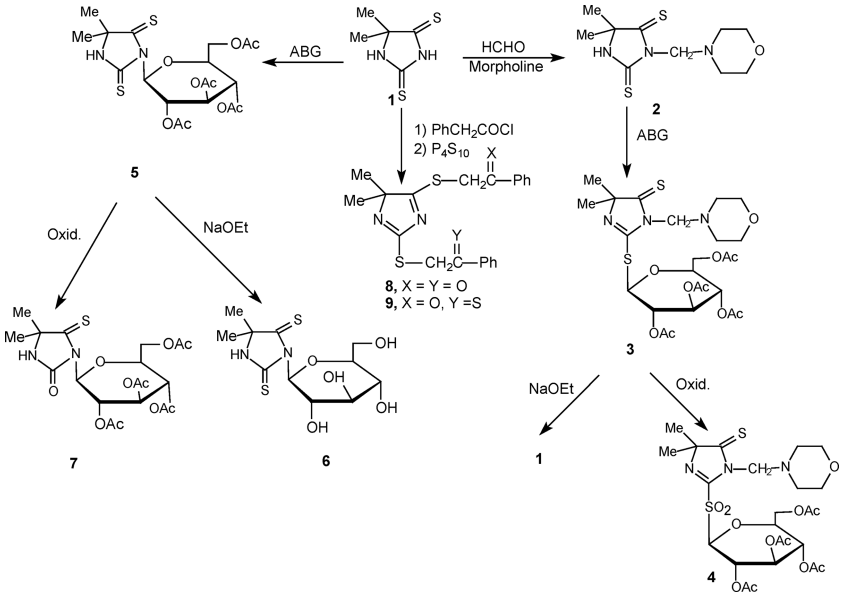
RESULTS AND DISCUSSION

In our earlier work,[6] we synthesized 5,5-dimethyl-3-(4-morpholinomethyl)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-*D*-thioglucopyranosyl)-4-thiohydantoin (**3**) via the reaction of **1** with formaldehyde and morpholine followed by treatment with (2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)bromide (ABG). Oxidation of **3** with potassium permanganate in glacial acetic acid at r.t. afforded the corresponding sulphone **4**, while deblocking of **3** with sodium ethoxide at r.t. afforded the starting aglycone **1**.[15]

Compounds **4–7** and **9** were characterized by their elemental analyses IR, ^{1}H-NMR, ^{13}C-NMR and MS data (see Experimental). For example, the IR spectrum of **4** showed two absorption bands due to SO_2 at 1040 and 1223 cm^{-1}. Reacting **1** with ABG in aqueous potassium hydroxide at 25°C afforded 5,5-dimethylimidazolidine-3-N-(2′,3′,4′,6′-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-2,4-dithione (**5**). The IR spectrum of **5** showed the C=O at 1720 cm^{-1}. Its ^{1}H-NMR spectrum showed peaks at 1.84–2.10 (4s, 12H, CH_3CO) ppm. Its ^{13}C-NMR spectrum showed 209.79 (C=S).

Deblocking of **5** with sodium ethoxide at 25°C gave 5,5-dimethyl-3-N-(3,4,5-trihydroxy-6-hydroxymethyltetrahydropyran-2-yl)imidazolidine-2,4-dithione (**6**). Its IR spectrum showed the OH groups at 3427 cm^{-1}. Oxidation of **5** with potassium permanganate at 25°C furnished 5,5-dimethylimidazolidine-3-N-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-oxo,4-thione (**7**), whose IR spectrum showed the hydantoin C=O at 1655 cm^{-1}. Its ^{13}C-NMR spectrum showed the C=O at 160.89 ppm.

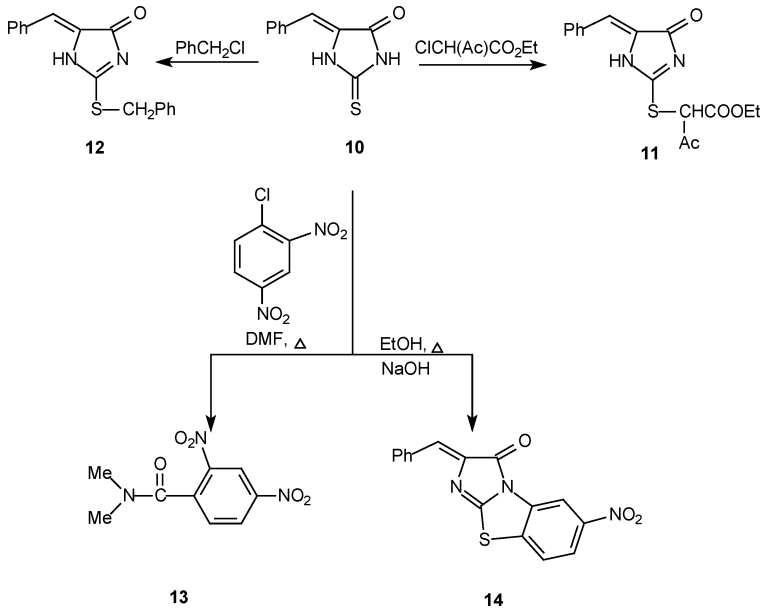
Earlier,[6] we had synthesized 5,5-dimethyl-2,4-dibenzoylmethylthiohydantoin (**8**) via the reaction of **1** with phenacyl chloride in alkaline medium. Thiation of **8** with P_4S_{10} in boiling xylene afforded 2-[5,5-Dimethyl-2-(3-propenyl-2-thioxohexa-3,5-diphenylsulfanyl)-5H-imidazol-4-ylsulfanyl]-1-phenylethanone (**9**). The ^{13}C-NMR spectrum of **9** showed C=S at 220.58 ppm (Scheme 1).



SCHEME 1

Reacting 5-benzylidene-2-thioxoimidazolidin-4-one (**10**) with ethyl chloroacetoacetate or benzyl chloride gave 2-(4-benzylidene-5-oxo-4,5-dihydro-1*H*-imidazol-2-ylsulfanyl)-3-oxobutyric acid ethyl ester (**11**) and 5-benzylidene-2-benzylsulfanyl imidazolidin-4-one (**12**), respectively.

Refluxing **10** with 2,4-dinitro-1-chlorobenzene in DMF afforded N,N-dimethyl-2,4-dinitro-benzamide (**13**) as the sole product (tlc), whereas refluxing **10** with the same reagent in ethanol and sodium hydroxide furnished 2-benzylidene-6-nitro-2*H*-benzo[d]imidazo[2,1-b]thiazol-3-one (**14**) through the elimination of nitrous and hydrochloric acids. This is in accordance with earlier findings.[16,17] The IR spectrum of **13** showed NO_2 at 1502 and a strong band for C=O at 1625 cm^{-1}. Its ^{1}H-NMR spectrum showed a signal (s, 6H, $2CH_3$) at 2.98 ppm. Its ^{13}C-NMR spectrum showed $2CH_3$ at 42.10, and C=O at 148.76 ppm. The mass spectrum of **13** showed M^+-CO (base peak) at (EI) m/z (211.06, 100 %,



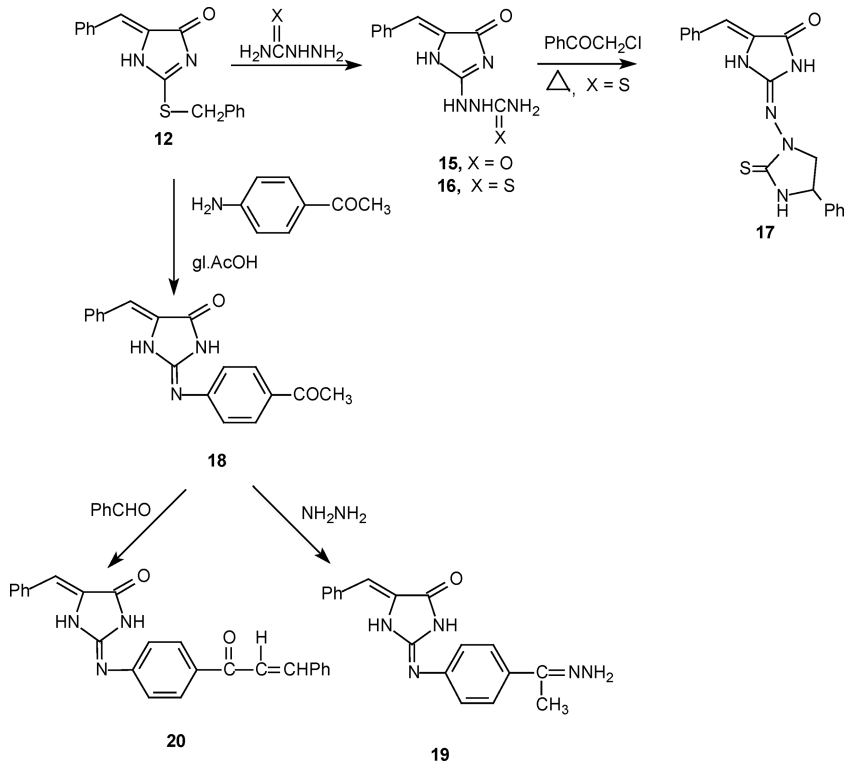
SCHEME 2

$C_8H_9N_3O_4$). The IR spectrum of **14** showed the NO_2 group at 1525 cm^{-1} (Scheme 2).

Compounds **11–14** were characterized by their elemental analyses IR, ^{1}H-NMR, ^{13}C-NMR and MS data (see Experimental section). Refluxing of compound **12** with semicarbazide or thiosemicarbazide in ethanol afforded 1-(4-benzylidene-5-oxo-4,5-dihydro-1*H*-imidazol-2-yl) semicarbazide (**15**) or 1-(4-benzylidene-4,5-dihydro-1*H*-imidazol-2-yl)thiosemicarbazide (**16**), respectively. Boiling compound **16** with phenacyl chloride in glacial acetic acid afforded 5′-benzylidene-4-phenyl-2-thioxo-2,3,4,5,1′,5′-hexahydro-[1,2′]biimidazolyl-4′-one (**17**).

Compound **12** was reacted with 4-aminoacetophenone in refluxing acetic acid to give 2-(4-acetylphenylimino)-5-benzylideneimidazolidin-4-one (**18**) which on treatment with hydrazine hydrate in refluxing anhydrous DMF afforded 5-benzylidene-2-[4-(1-hydrazonoethyl)phenylimino]imidazo- lidin-4-one (**19**). Condensation of **18** with benzaldehyde in refluxing methanol afforded 5-benzylidene-2-[4-(3-phenylacryloyl)phenylimino]imidazolidin-4-one (**20**) (Scheme 3).

Compounds **15–20** were characterized by their elemental analyses IR, ^{1}H-NMR, ^{13}C-NMR, and MS (see Experimental section).



SCHEME 3

BIOLOGICAL ACTIVITY

All the compounds were tested against HIV-1. The test was performed in MT4 cell cultures infected with wild type HIV-1 (strain IIIB) using the assay as previously described.[18] The compounds were inactive at 100 uM or inactive at subtoxic concentrations. None of the tested compounds showed any significant antiviral activity at 100 μM against HIV-1. In addition, the new products were tested as acaricides (*Tetranychus urticae*, Koch), fungicides (*Rhizoctonia solani, Fusarium oxysporium, Fusarium solani, Verticillium dahliae* and *Verticillium sulphurellium*), and bactericides (*Pseudomonas solaniserum, Erwinia carotovora* and *Ralstonia salanceanum*), at concentration of 10–100 ppm. None of them showed any activity.

EXPERIMENTAL

All melting points were uncorrected and performed by the open capillary melting point apparatus. Microanalyses performed by Microanalysis Unit, Faculty of Science, Cairo University, Egypt and Microanalysis Unit, Central Laboratory, Tanta University, Egypt. IR spectra recorded with a Perkin-Elmer 1720 spectrometer. The NMR spectra were recorded on a Bruker AC 250 FT NMR spectrometer at 250 MHz for ^{1}H and 62.9 MHz for ^{13}C, Varian UNITY 500 NMR spectrometer at 500 MHz for ^{1}H, or 125.7 MHz for ^{13}C, Bruker 200 MHz And Bruker 90 MHz spectrometer using TMS as an internal standard DMSO as a solvent. Chemical shifts (δ) are reported in parts per million (ppm) and signals are expressed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad). Mass spectra (MS) were recorded using electron ionization (E.I.) on a Varian Mat 311A spectrometer and using fast atom bombardment (FAB) on a Kratos MS 50 spectrometer. The silica gel (0.040–0.063 mm) was used for the column chromatography and was purchased from Merck.

Reaction of 5,5-Dimethylimidazolidine-2,4-dithione (1) and Its 3-Morpholinomethyl Derivative (2) with (2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosyl) Bromide (ABG)

A solution of compound **1** or **2** (0.01 mol) was dissolved in a mixture of acetone (30 mL) and potassium hydroxide (0.56 g, 0.01 mol) and added to a solution of ABG (0.011 mol). The reaction mixture was stirred at r.t. for 3 h to completion (tlc). The reaction mixture poured onto cooled water, the solid formed was filtered off, washed with water, dried, and crystallized from ethanol to afford **3** and **5**, respectively.

5,5-Dimethyl-3(4-morpholinomethyl)-2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-thioglucopyranosyl)-4-thiohydantoin (3)

Yield: 3.4 g (82%); m.p., 100–102°C.[6]

5,5-Dimethylimidazolidine-3-N-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-2,4-dithione (5)

Yield: 3.5 g (71%); m.p., 182–184°C; IR (KBr): υ (cm^{-1}): 1776 (acetyl CO), 3342 (NH); ^{1}H-NMR (DMSO-d_6): δ 1.35–1.42 (s, 6H, 2CH$_3$), 1.84–2.10 (4s,12H, 4CH$_3$CO), 5.49–4.21 (m, 5H, sugar protons), 6.44–6.56 (d, 1H, anomeric proton, $J = 10.67$ Hz); ^{13}C-NMR (DMSO-d_6): δ 20.31, 20.47 (2 CH$_3$ at C-5), 27.16, 27.54, 27.62, and 27.80 (4 *C*H$_3$CO), 81.98, 72.65,

71.88, 67.01, 66.39, and 61.17 (C′1, C′5, C′3, C′2, C′4 and C′6), 168.87–169.78 (4 C=O, acetyl), 178.25 (C_4=S), 209.79 (C_2=S) ppm; Anal. Calcd. for $C_{19}H_{26}N_2O_9S_2$ (490.54): C, 46.52 ; H, 5.34; N, 5.71. Found: C, 45.51; H, 4.37; N, 5.82.

Oxidation of 3 and/or 5

To a solution of **3** and/or **5** (0.002 mol) in glacial acetic acid (25 mL), a solution of potassium permanganate (0.06 g, 0.004 mol) in water (10 mL) was added gradually with stirring for 30 min. Stirring was continued for 5 h at r.t., and the mixture was then poured onto crushed ice. The resulting solid was collected and recrystallized from ethanol to afford **4** and **7**, respectively.

5,5-Dimethyl-3-N-(4-morpholinomethyl)-2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl-sulfonyl)-4-thiohydantoin (4)

Yield 1.2 g (56 %); m.p., 65–67°C; IR (KBr): υ (cm^{-1}) 1040–1223 (SO_2), 1652 (cyclic, C=O), 2932 (CH_2), 3375 (NH); ^{1}H-NMR (DMSO-d_6): δ 1.50 (s, 6H, 2 CH_3 at C-5), 1.91 (s, 3H, CH_3—CO at C-6′), 1.98 (s, 3H, CH_3—CO at C-4′), 2.06 (s, 3H, CH_3—CO at C-2′), 2.12 (s, 3H, CH_3—CO at C-3′), 2.89 (s, 2H, N—CH_2—N), 3.68 (t, 4H, 2CH_2—N), 3.89 (t, 4H, 2CH_2—O), 4.19–4.45 (m, 2H, C-6′), 4.34–4.38 (t, 1H, CH-4′), 4.46–4.47 (t, 1H, CH-2′), 5.24–5.27 (m, 1H, CH-3′), 6.33–6.34 (t, 1H, CH-5′), 6.63–6.64 (d, 1H, CH-1′, J = 10.17 Hz, β-configuration); ^{13}C-NMR (DMSO—d_6): δ 14.98 (2CH_3), 20.21, 20.32, 20.41, and 20.53 (4$\underline{CH_3}$CO), 50.24 (CH_2), 62.19, 65.92, 68.85, 72.78, 75.33, and 80.45 (C-6′, C-4′, C-2′, C-3′, C-5′, and C-1′anomeric), 169.28–169.88 (Ac, 4C=O) ppm; Anal. Calcd. for $C_{24}H_{35}N_3O_{12}S_2$ (621.65): C, 46.32; H, 5.63; N, 6.75. Found: C, 46.61; H, 5.72; N, 6.90.

5,5-Dimethylimidazolidine-3-N-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyl)-2-oxo-4-thione (7)

Yield 0.7 g (77%); m.p., 130–132°C; IR (KBr): υ (cm^{-1}) 1655 (cyclic, C=O), 1767 (acetyl, C=O), 2945 (CH_3), 3315 (NH); ^{1}H-NMR (DMSO-d_6): δ 1.25–1.29 (s, 6H, 2CH_3), 1.86–2.12 (4s, 12H, 4CH_3CO), 4.01–4.32 (t, 1H, CH-2′), 5.04–5.10 (t, 1H, CH-3′), 5.45–5.53 (t, 1H, CH-5′), 6.44–6.56 (d, 1H, anomeric proton, J = 9.75 Hz); ^{13}C-NMR (DMSO-d_6): δ 20.28, 26.55 (2CH_3), 27.39, 27.61, 27. 67 and 27. 87 (4 $\underline{CH_3}$CO), 61.23, 66.48, 67.07, 72.25, 72.73, and 82.07 (C′6, C′4, C′2, C′3, C′5, and C′1 anomeric), 160.89 (C-2), 169.29, 169.43 169.88, and 169.97 (4 C=O, acetyl), 178.88 (C-4) ppm.

Deblocking of 3 and/or 5

Compound **3** or **5** (0.001 mol) was dissolved in methanol (15 mL) and few drops of sodium methoxide in methanol (0.001 N) were added. The reaction mixture was stirred at r.t. for 4 h (tlc). The solvent was evaporated under vacuum and the residual solid was dissolved in water, neutralized with dil. HCl. The solid formed was filtered off, washed with water, dried, recrystallized from ethanol to give the starting material **1** (m.p. and mixed m.p.)[15] and **6**.

5,5-Dimethyl-3-N-(3,4,5-trihydroxy-6-hydroxymethyl-tetrahydropyran-2-yl)imidazolidine-2′,4-dithione (6)

The structure of **6** was confirmed by its IR spectrum, it showed the absence of C=O (acetyl) at 1767 cm^{-1}, while OH groups appeared at 3427 cm^{-1}.

2-[5,5-Dimethyl-2-(3-propenyl-2-thioxohexa-3,5-diphenyl-sulfanyl)-5H-imidazol-4-ylsulfanyl]-1-phenylethanone (9)

A mixture of compound **8** (1 g, 0.002 mol) and phosphorus pentasulphide (0.9 g, 0.002 mol) was added to dioxane (30 mL). The reaction mixture was refluxed for 1 hr (tlc). The reaction mixture poured onto cooled water and the solid formed was filtered off, washed with water, dried, and recrystallized from aqueous methanol to afford **9**. Yield 0.3 g (36%); m.p., 212–214°C; IR (KBr): υ (cm^{-1}) 1215 (C=S), 1675 (cyclic, C=O), 1772 (C=OPh), 2842 (CH_2 at C2), 2981 (CH_2 at C4); ^{1}H-NMR (DMSO-d_6): δ 1.45 (s, 6H, 2 CH_3), 4.75 (s, 2H, CH_2C=S), 5.15 (s, 2H, CH_2C=O), 7.50–8.10 (m, 10H, H_{arom}); ^{13}C-NMR (DMSO-d_6): δ 24.80 ($2CH_3$), 56.20 ($2CH_2$), 82.12 (C-5, cyclic), 128.15, 128.24, 128.74 128.67, 133.47, 133.70, 135.24, 135.50, (C_{arom}), 168.84 (C_4=N), 192.24 (C_2=N), 193.25 (C=O), 220.58 (C=S) ppm. Anal. Calcd. for $C_{12}H_{20}N_2OS_3$ (412.57): C, 61.08; H, 4.84; N. 6.78. Found: C, 60.94; H, 5.01; N, 6.89.

2-(4-Benzylidene-5-oxo-4,5-dihydro-1H-imidazol-2-ylsulfanyl)-3-oxobutyric Acid Ethyl Ester (11)

To a solution of compound **10** (2 g, 0.01 mol) in ethanol (15 mL) and potassium hydroxide (0.56 g, 0.01 mol), ethyl chloroacetoacetate (1.5 mL, 0.01 mol) was added. The reaction mixture was stirred at r.t. for 6 h (tlc). The solid product that formed was recrystallized from ethanol to give **11**. Yield 2.7 g (84%); m.p., 200–202°C; IR (KBr): υ (cm^{-1}) 1648 (CONH), 1699 (Ac, C=O), 1731 (ester, CO), 2929 (CH), 3430 (NH); ^{1}H-NMR (DMSO-d_6): δ 1.22 (t, 3H, $\underline{CH}_3CH_2$), 2.25 (s, 3H, CH_3CO), 4.12 (q,

2H, $\underline{CH_2}CH_3$), 6.55 (s, 1H, CH=), 7.45–7.65 (m, 6H, H_{arrom}., SCH), 10.85 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ 14.25 ($\underline{CH_3}CH_2$), 28.99 (CH_3), 60.20 ($\underline{C}H_2CH_3$), 68.94 (CH=), 126.89 (SCH), 128.50, 128.66, 129.28, 129.74, 133.29 (C_{arrom})., 156.14 (C=N), 164.08 (cyclic, C=O), 167.99 (ester, CO), 195.03 ($\underline{CO}CH_3$) ppm. Anal. Calcd. for $C_{16}H_{16}N_2O_4S$ (332.08): C, 57.82, H, 4.85, N, 8.43. Found: C, 58.70, H, 5.08, N, 8.43.

5-Benzylidene-2-benzylsulfanyl imidazolidin-4-one (12)

To a solution of compound **10** (10 g, 0.05 mol) in ethanol (50 mL), sodium hydroxide (2 g, 0.05 mol), and benzylchloride (6.3 mL, 0.05 mol) was added, and the reaction mixture was stirred for 4 h (tlc). The solid product was filtered off, recrystallized from petroleum ether (80–100°C), and dried to afford **12**, yield 12 g (82 %); m.p., 170–172°C; IR(KBr): υ (cm^{-1}) 1630 (cyclic, C=O), 2620 (CH_2), 2910 (CH), 3425 (NH); ^{1}H-NMR (DMSO-d_6): δ 4.52 (s, 2H, CH_2), 6.65 (s, 1H, CH=), 7.45–8.20 (m, 10H, H_{arom}); ^{13}C-NMR (DMSO-d_6): δ 33.32 (CH_2), 120.88 (CH=), 128.40, 128.50, 128.96, 129.47, 131.26, 134.18, 137.09, 139.12, (C_{arom}), 163.68 (C=N), 170.49 (C=O) ppm. Anal. Calcd. for $C_{17}H_{14}N_2OS$ (294.37): C, 69.36; H, 4.79; N, 9.52. Found: C, 69.29; H, 4.68; N, 9.42.

N,N-Dimethyl-2,4-dinitrobenzamide (13)

A mixture of compound **10** (2 g., 0.01 mol) and 2,4-dinitro-1-chlorobenzene (2 gm, 0.01 mol) in dry DMF (10 ml.) was refluxed for 3 h (tlc). The excess solvent was evaporated in vaccum until dried. The residual solid product, crystallized from diethyl ether and dried to afford **13**. Yield 1.5 g (71%); m.p., 60–62 °C; IR (KBr): υ (cm^{-1}) 1502 (NO_2), 1625 s (C=O); ^{1}H-NMR (DMSO-d_6): δ 2.98 (s, 6H, $2CH_3$), 7.25 (d, 1H, $J = 9.00$ Hz, H-6), 8.17 (d, 1H, $J = 30.00$ Hz, H-5), 8.55 (s, 1H, H-3); ^{13}C-NMR (DMSO-d_6): δ 42.10 ($2CH_3$), 117.49, 123.66, 127.44, 134.98, (C_{arom}), 148.76 (C=O) ppm. MS (EI) m/z 211(M^+-CO, $C_8H_9N_3O_4$, 100 %).

2-Benzylidene-6-nitro-2H-benzo[d]imidazo[2,1-b]thiazol-3-one (14)

Compound **10** (1.5 g, 0.01 mol) was refluxed with 2,4-dinitro-1-chlorobenzene (1.63 gm, 0.01 mol) in a mixture of ethanol (20 mL) and sodium hydroxide (0.8 gm, 0.02 mol) for 11 h (tlc). After cooling, the solid that separated was recrystallized from ethanol, filtered, and dried to give **14**. Yield 2.1 g (66%); m.p., 160–162°C; IR (KBr): υ (cm^{-1}) 1525

(NO_2), 1634 (hydantoin C=O). Anal. Calcd. for $C_{16}H_9N_3O_3S$ (323.27): C, 59.44; H, 2.78; N, 13.00. Found: C, 58.97, H, 2.81, N, 12.85.

1-(4-Benzylidene-5-oxo-4,5-dihydro-1H-imidazol-2-yl)semi- or (thiosemi)-carbazide (15) and (16)

A mixture of compound **12** (2 g, 0.01 mol) and semi- or (thiosemi)-carbazide hydrochloride (0.01 mol) in ethanol (20 mL) was refluxed for 4 to 6 h in the presence of anhydrous sodium acetate (0.85 g, 0.01 mol) (tlc). The solid product that formed was filtered off, recrystallized from acetic acid, and dried to afford **15** and**16,** respectively.

Compound **15**, yield 1.8 g (72%); m.p., 175–177°C; Calc. for $C_{11}H_{11}N_5O_2$ (240.09): 53.87% C, 4.52% H, 28.56% N. Found: 53.62% C, 4.67% H, 28.73% N; IR (KBr): υ (cm^{-1}) 1583 (HNCONH), 1632 ($CONH_2$), 2829 (CH), 3355 (NH_2); ^{1}H-NMR (DMSO-d_6): δ 6.15 (s, 2H, NH_2), 6.40 (s, 1H, CH=), 7.67–7.35 (m, 5H, H_{arom}), 9.10 (s, 1H, NHCO), 10.95 (br, 2H, 2NH); ^{13}C-NMR (DMSO-d_6): δ 106.55 (CH), 127.25, 127.99, 128.11, 128.60, 129,03 (C_{arom})., 157.71 (C=ONH_2), 158.16 (cyclic, C=O) ppm.

Compound **16**, yield 2.1 g (81%); m.p., 240–242°C; IR (KBr): υ (cm^{-1}) 758 (C=S), 1649 (cyclic, C=O), 3237 (NH_2), 3398 (NH); ^{1}H-NMR (DMSO-d_6): δ 6.41 (s, 2H, NH_2), 6.95 (s, 1H, CH=), 7.62–8.11 (H_{arrom})., 10.06 (s, 1H, NH at N-1), 10.46 (s, 1H, NHC=S), 11.37 (s, 1H, NH, at N-3); ^{13}C-NMR (DMSO-d_6): δ 105.43 (CH), 127.58–133.51 (C_{arom} and C-5)., 139.92 (C-2), 164.18 (C-4), 176.02 (C=S) ppm. Anal. Calcd. for $C_{11}H_{11}N_5OS$ (261.30): C, 50.56; H, 4.24; N, 26.80. Found: C, 49.42; H, 4.69; N, 25.37.

5′-Benzylidene-4-phenyl-2-thioxo-2,3,4,5,1′,5′-hexahydro-[1,2′]biimidazolyl-4′-one (17)

A mixture of compound **16** (1 g, 0.003 mol) and phenacyl chloride (0.5 g, 0.003 mol) in glacial acetic acid (20 mL), in the presence of fused sodium acetate (0.85 g, 0.003 mol) was refluxed for 5 h (tlc). The solid product that formed was filtered off, recrystallized from ethanol, and dried to afford **17**. Yield 0.8 g (74); m.p., 193–195°C; IR (KBr): υ (cm^{-1}) 771 (C=S), 1630 (cyclic, C=O), 2950 (CH_2), 3442 (NH); ^{1}H-NMR (DMSO-d_6): δ 3.45 (s, 2H, CH_2), 7.22–7.95 (m, 10H, H_{arom}), 9.45 (NHC=O), 10.25 (NHC=N); ^{13}C-NMR (DMSO-d_6): δ 20.63 (CH_2), 102.96 (CH=), 125.60–134.75 (C_{arom}), 150.68 (C=N), 169.35 (C=O), 172.64 (C=S) ppm. Anal. Calcd. for $C_{19}H_{15}N_5OS$ (361.42): C, 63.14; H, 4.18; N, 19.37. Found: C, 62.98; H, 4.68; N, 19.70.

2-(4-Acetylphenylimino)-5-benzylidene imidazolidin-4-one (18)

A mixture of compound **12** (3 g, 0.01 mol) and 4-aminoacetophenone (1.35 g, 0.01 mol) in gl. acetic acid (20 mL) was refluxed for 2 h (tlc). The solid product that formed was recrystallized from DMF and dried to afford **18**. Yield 3.5 g (78%); m.p., 340–342°C; IR (KBr): υ (cm^{-1}) 1560 (CONH), 1692 (acetyl, C=O), 2978(CH),3347 (NH). ^{1}H-NMR (DMSO-d_6): δ 2.95 (s, 3H, CH_3), 7.00 (s, H, CH=), 7.50–8.50 (m, 9H, H_{arrom})., 10.52 (s, 1H, NH, at N-1), 11.33 (s, 1H, NH at N-3); ^{13}C-NMR (DMSO-d_6): δ 26.48 (CH_3), 118.55 (CH), 128.25, 128.60, 129.64, 130.42, 131.18, 135.10, (C_{arom}), 168.02(C=O), 196.45 (C=OCH_3) ppm. Anal. Calcd. for $C_{18}H_{15}N_3O_2$ (305.34): C, 70.81; H, 4.95; N, 13.76. Found: C, 70.90; H, 5.00; N, 13.97.

5-Benzylidene-2-[4-(1-hydrazinoethyl)phenylimino]-imidazolidin-4-one (19)

To a solution of compound **18** (3 g, 0.01 mol) in anhy. DMF (15 mL), hydrazine hydrate (1.5 mL, 0.03 mol) was added. The reaction mixture was refluxed for 3 h (tlc). The solid product that formed was filtered off, washed with hot DMF and dried to give **19**. Yield 2.8 g (87%); m.p., 355–357°C; IR (KBr): υ (cm^{-1}) 1695 (C=O), 2976 (CH), 3425 (NH_2). Anal. Calcd. for $C_{18}H_{17}N_5O$ (319.14); C, 69.95; H, 4.92; N, 18.48. Found: C, 70.00; H, 4.81; N, 18.67.

5-Benzylidene-2-[4-(phenylacryloyl)phenylimino]imidazolidin-4-one (20)

A mixture of compound **18** (4 g, 0.01 mol) in methanol (30 mL) and benzaldehyde (1.05 mL, 0.01 mol) was refluxed for 8 h (tlc). The solid product that formed was filtered off, recrystallized from DMF and dried to give **20**. Yield 2.8 g (90%); m.p., 310–312°C; IR (KBr): υ (cm^{-1}) 1601 (C=ONH), 1657 (C=O–CH), 2845 (CH=CH), 3296 (NH); ^{1}H-NMR (DMSO-d_6): δ 6.50 (s, 1H, CHPh), 6.55 (s, 1H, PhCH=C), 6.85–7.54 (14H_{arom},), 8.12 (d, 1H, CHPh), 8.43 (d, 1H, CH=CO), 10.65 (br, 2H, 2NH); ^{13}C-NMR (DMSO-d_6): δ 119.33 (<u>C</u>HPh), 121.35 (CH=<u>C</u>O)., 122.52, 129.46, 130.30, 130.94, 135.39, 135.68 (C_{arom}), 143.65 (C=N), 188.15 (COCH) ppm. Anal. Calcd. for $C_{25}H_{19}N_3O_2$ (393.44); C, 76.32; H, 4.87; N, 10.68. Found: C, 76.21; H, 4.79; N, 10.93.

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