

Article

Synthesis of Schiff and Mannich Bases of Isatin Derivatives with 4-Amino-4,5-Dihydro-1H-1,2,4-Triazole-5-Ones

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Received: 15 August 2008; in revised form: 28 August 2008 / Accepted: 1 September 2008 / Published: 10 September 2008

Abstract: Ethyl imidate hydrochlorides **1** were prepared by passing HCl gas through solutions of substituted benzyl cyanides and absolute ethanol. Ethoxycarbonylhydrazones **2** were synthesized from the reaction of compounds **1** with ethyl carbazate. Treatment of **2** with hydrazine hydrate leads to the formation of substituted 4-amino-4,5-dihydro-1H-1,2,4-triazole-5-ones **3**. Isatin and 5-chloroisatin were added to **3** to form Schiff bases **4** and *N*-Mannich bases **5** of these compounds were synthesized by reacting with formaldehyde and piperidine. Their chemical structures were confirmed by means of IR, ¹H- and ¹³C-NMR data and by elemental analysis.

Keywords: Ethyl imidate hydrochloride; ethoxycarbonyl hydrazones; 4-amino-1,2,4-triazole-5-one; isatin; Schiff bases; Mannich bases.

Introduction

Schiff bases are used as substrates in the preparation of a number of industrial and biologically active compounds via ring closure, cycloaddition and replacement reactions [1]. Moreover, Schiff bases derived from various heterocycles have been reported to possess cytotoxic [2], anticonvulsant [3], antiproliferative [4], antimicrobial [5], anticancer [6], and antifungal activities [7]. Mannich bases

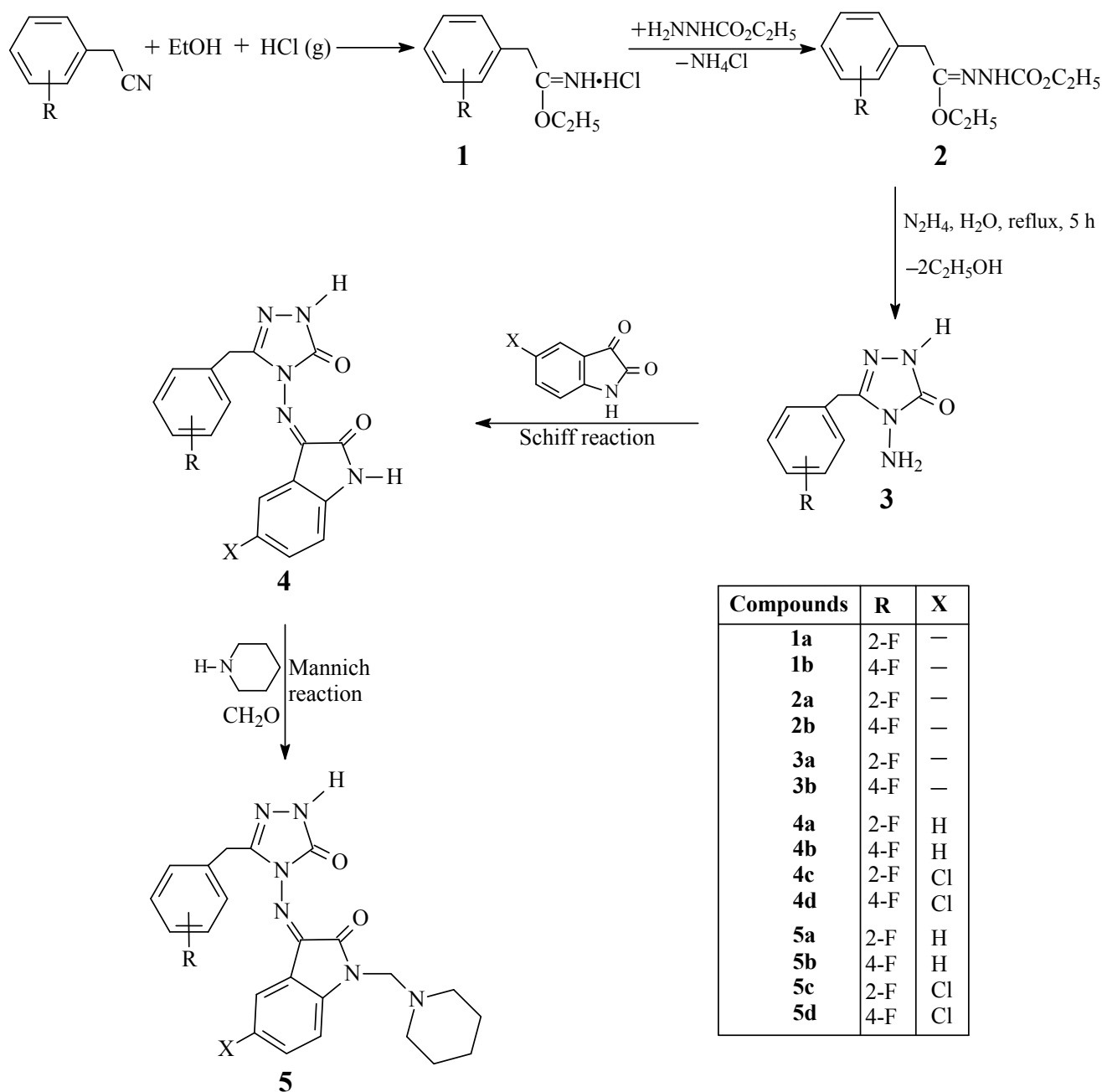
have gained importance due to their application in pharmaceutical chemistry. They have been encountered with antibacterial [8], anticancer [9], analgesic and anti-inflammatory [10], anticonvulsant [11], antimalarial [12], antiviral [13], and CNS depressant activities [14]. Isatin, chemically known as 1*H*-indole-2,3-dione, has become a popular topic due to its various uses. The chemistry of isatin and its derivatives is particularly interesting because of their potential application in medicinal chemistry. Isatins are very important compounds due to their antifungal properties [15]. Schiff and Mannich bases of isatin derivatives are reported to show variety of biological activities like antibacterial [16], antifungal [17], anticonvulsant [18], anti HIV [19], antidepressant [20], and antiinflammatory [21] activities. Similarly, 1,2,4-triazoles and their derivatives play important roles in medicinal, agricultural and industrial fields [22-25]. *N*-bridged heterocyclic derivatives derived from 1,2,4-triazoles show varied biological activities such as antimicrobial [26], anticonvulsant [27], anticancer [28], analgesic [29], anti HIV [30], and anti-inflammatory properties [31].

These biological data prompted us to synthesize new isatin derivatives bearing 1,2,4-triazole ring and the newly synthesized compounds were characterized by elemental analysis, IR, ¹H- and ¹³C-NMR spectral data.

Results and Discussion

In the present study, ethyl imidate hydrochlorides **1** were prepared by passing HCl gas through solutions of *o*- or *p*-fluorobenzyl cyanide in absolute ethanol, followed by precipitation with ether. Ester ethoxycarbonyl hydrazones **2** were synthesized by the reactions of alkyl imidate hydrochlorides **1** with ethyl carbazate. Treatment of compounds **2** with hydrazine hydrate in water resulted in the formation of 3-*o*-fluorobenzyl-4-amino-4,5-dihydro-1*H*-1,2,4-triazole-5-one (**3a**) and 3-*p*-fluorobenzyl-4-amino-4,5-dihydro-1*H*-1,2,4-triazole-5-one (**3b**), respectively. The substituted 4-amino-4,5-dihydro-1*H*-1,2,4-triazoles **3** were condensed with isatin derivatives in the presence of a few drops of glacial acetic acid as a catalyst to produce Schiff bases **4** in rather good yields. Mannich base formation can take place at both the isatin and triazole NH protons, but it is known that the isatin NH proton is more active than the triazole one [32]. In addition, after the Mannich reactions, the ¹H-NMR spectra of compounds **5** show NH proton signals at around δ 11.00 ppm, which correspond to a triazole NH, so we conclude that in the current study, Mannich bases were formed by condensing the acidic imino group of isatin with formaldehyde and piperidine, instead of the triazole NH proton (Scheme 1).

Compounds **2** showed absorption bands at around 3277, 1720, and 1659 cm⁻¹ regions, resulting from the NH, C=O, and C=N functions, respectively. Compounds **3** showed two peaks at around 3220 and 3165 cm⁻¹ due to asymmetric and symmetric vibrations of the primary amino group. Compounds **4** and **5** showed two separate bands belonging to triazole indole C=O functions in the 1733-1750 and 1698-1710 cm⁻¹ regions, and C=N stretching vibrations at around 1650 cm⁻¹. In the IR spectra of **5**, triazole NH stretching vibrations were around 3200 cm⁻¹. The characteristic NH protons of compounds **2** were detected around δ 9.00 ppm. The characteristic NH₂ protons of compounds **3** were detected around δ 5.00 ppm. The ¹H-NMR spectra of **4** displayed the NH protons of the triazole moiety (δ 11.07-11.17 ppm) and the indole NH proton (δ 12.09-12.53) as two separate singlets. Compounds **5** displayed characteristic >N-CH₂-N< signals at around δ 4.36 ppm (s, 2H, CH₂).

Scheme 1. Synthetic pathway for preparation of compounds **1** and **5**.

In the ^{13}C -NMR spectra of compounds **2a-b** characteristic C=O signals appeared at around δ 171.00 ppm. The triazole C-3 and triazole C-5 signals of compounds **3a-b** were recorded at δ 149.38 ppm (C-3) and δ 156.33 ppm (C-5). Characteristic triazole and indole C=O and the C=N carbon signals of compounds **4a-d** were recorded at around δ 150 ppm, δ 165 ppm, and δ 150 ppm, respectively. In the ^{13}C -NMR spectra of compounds **5a-d** characteristic $>\text{N}-\text{CH}_2-\text{N}<$ signals belonging to the Mannich bases were observed at around δ 171.00 ppm.

Conclusions

It is known that the heterocycle compounds containing both 1,2,4-triazole and isatin rings have diverse pharmacologic properties [15-20, 25-31, 33]. A general and convenient method was established for the synthesis of new heterocyclic compounds bearing these two rings. Thus, two new ester ethoxycarbonyl hydrazones **2**, two new amino compounds **3**, and eight new Schiff and Mannich bases of isatin and 5-chloro isatin with substituted 4-amino-4,5-dihydro-1H-1,2,4-triazole-5-ones **4-5** were synthesized in good yields. Compounds **4-5** are expected to exhibit biological activities.

Experimental

General

Melting points were determined on a Barnstead Electrothermal melting point apparatus and are uncorrected. ^1H -NMR and ^{13}C -NMR spectra (δ , ppm) were recorded in DMSO- d_6 solutions on a Varian-Mercury 200 MHz spectrometer using tetramethylsilane as the internal reference. The IR spectra (ν , cm^{-1}) were obtained with a Perkin-Elmer 1600 FTIR spectrometer in KBr pellets. Elemental analyses were performed on a ECS 4010 Elemental Combustion System. The starting compounds, alkyl imidate hydrochlorides **1a-b**, were synthesized by previously reported routes [34, 35]. The necessary chemicals were purchased from Merck and Fluka companies.

Synthesis of Ethoxycarbonyl Hydrazones **2a-b**

The corresponding ethyl imidate hydrochlorides (**1a-b**, 0.01 mol) was dissolved in absolute ethanol (50 mL) with ice-bath cooling, and ethyl carbazate (0.01 mol) dissolved in absolute ethanol (50 mL) was then added to this solution. After stirring for 6 h at 0-5 °C, the precipitate was filtered to remove the ammonium chloride which separated from the solution and the filtrate was evaporated at 30-35 °C under reduced pressure. The solid residue, after drying in a dessicator, was recrystallized from petroleum ether to yield compounds **2a-b**.

Ethyl o-fluorophenylacetate ethoxycarbonyl hydrazone (2a): Yield 82%, m.p. 48-49 °C; IR ν (cm^{-1}): 3277 (NH), 1720 (C=O), 1650 (C=N), 758 (1,2-disubstituted phenyl); ^1H -NMR δ (ppm): 1.10-1.20 (m, 6H, 2CH₃), 3.74 (s, 2H, benzyl CH₂), 3.96-4.09 (m, 4H, 2CH₂), 7.11-7.29 (m, 4H, Ar-H), 9.37 (s, 1H, NH); ^{13}C -NMR δ (ppm): 15.70 (O=COCH₂CH₃), 16.38 (OCH₂CH₃), 29.55 (benzyl CH₂), 61.96 (O=COCH₂CH₃), 63.59 (OCH₂CH₃), Ar-C: [115.58, 124.35, 125.00, 126.32, 130.79, 156.19], 163.11 (C=N), 171.92 (C=O); Calculated (%) for C₁₃H₁₇FN₂O₃ (268.29); C: 58.20, H: 6.39, N: 10.44, found (%): C: 58.18, H: 6.40, N: 10.45.

Ethyl p-fluorophenylacetate ethoxycarbonyl hydrazone (2b): Yield 80%, m.p. 58-59 °C; IR ν (cm^{-1}): 3226 (NH), 1724 (C=O), 1659 (C=N), 837 (1,4-disubstituted phenyl); ^1H -NMR δ (ppm): 1.11-1.18 (m, 6H, 2CH₃), 3.45 (s, 2H, benzyl CH₂), 4.00-4.06 (m, 4H, 2CH₂), 7.07 (d, 2H, J= 8.80 Hz, Ar-H), 7.21 (d, 2H, J= 8.80 Hz, Ar-H), 9.08 (s, 1H, NH); ^{13}C -NMR δ (ppm): 14.72 (O=COCH₂CH₃), 15.22

(OCH₂CH₃), 21.39 (benzyl CH₂), 60.44 (O=COCH₂CH₃), 60.93 (OCH₂CH₃), Ar-C: [115.55 (2C), 130.85 (2C), 133.19, 160.39], 162.79 (C=N), 171.87 (C=O); Calculated (%) for C₁₃H₁₇FN₂O₃ (268.29); C: 58.20, H: 6.39, N: 10.44, found (%); C: 58.22, H: 6.40, N: 10.47.

Synthesis of Amino Compounds **3a-b**

Compounds **2** (0.01 mol) were added to a solution of hydrazine hydrate (0.01 mol) in water (50 mL) and the mixture was refluxed for 5 h. On cooling, a precipitate was formed. This product was filtered and, after drying, was recrystallized from an appropriate solvent to give compounds **3a-b**.

3-o-Fluorobenzyl-4-Amino-4,5-dihydro-1H-1,2,4-triazole-5-one (3a): Recrystallized from water; Yield 87%; m.p. 158-159 °C; IR ν (cm⁻¹): 3316 (NH), 3220-3164 (NH₂), 1726 (C=O), 1652 (C=N), 764 (1,2-disubstituted phenyl); ¹H-NMR δ = 3.91 (s, 2H, benzyl CH₂), 5.21 (s, 2H, NH₂), 7.11-7.36 (m, 4H, Ar-H), 11.44 (s, 1H, NH); ¹³C-NMR δ = 25.87 (benzyl CH₂), Ar-C: [116.68, 124.65, 121.11, 130.50, 132.92, 164.60], 149.38 (triazole C-3), 156.35 (triazole C-5); Calculated (%) for C₉H₉FN₄O (208.20); C: 51.92, H: 4.36, N: 26.91, found (%); C: 51.82, H: 4.36, N: 26.96.

3-p-Fluorobenzyl-4-Amino-4,5-dihydro-1H-1,2,4-triazole-5-one (3b): Recrystallized from ethanol-water (1:2); Yield 82%; m.p. 182-183 °C; IR ν (cm⁻¹): 3318 (NH), 3223-3165 (NH₂), 1729 (C=O), 1644 (C=N), 844 (1,4-disubstituted phenyl); ¹H-NMR δ = 3.86 (s, 2H, benzyl CH₂), 4.60 (s, 2H, NH₂), 7.13 (d, 2H, J= 6.4 Hz, Ar-H), 7.32 (d, 2H, J= 6.4 Hz, Ar-H), 11.43 (s, 1H, NH); ¹³C-NMR δ = 31.61 (benzyl CH₂), Ar-C: [116.60 (2C), 132.31 (2C), 134.01, 165.27], 149.38 (triazole C-3), 156.33 (triazole C-5); Calculated (%) for C₉H₉FN₄O (208.20); C: 51.92, H: 4.36, N: 26.91, found (%); C: 51.90, H: 4.35, N: 26.94.

Synthesis of Schiff Bases **4a-d**

Equimolar quantities (0.01 mol) of isatin or 5-chloroisatin and the corresponding amino compound **3a-b** were dissolved in warm ethanol (50 mL) containing glacial acetic acid (0.5 mL). The reaction mixture was refluxed for 4 h and then kept at room temperature overnight. The resultant solid was washed with dilute ethanol, dried and recrystallized from ethanol-water (1:2) mixture to afford compounds **4a-d**.

3-[3-(o-Fluorobenzyl)-5-oxo-4,5-dihydro-1,2,4-triazol-1-yl]-iminoisatin (4a): Yield 78%; obtained as yellowish crystals; m.p. 278-279 °C; IR ν (cm⁻¹): 3182, 3087 (NH), 1750 (triazole C=O), 1709 (isatin C=O), 754 (1,2-disubstituted phenyl); ¹H-NMR δ = 4.02 (s, 2H, benzyl CH₂), Ar-H: [6.88-6.99 (m, 1H), 7.02-7.15 (m, 4H), 7.20-7.36 (m, 2H), 7.43-7.50 (m, 1H)], 11.07 (s, 1H, triazole NH), 12.11 (s, 1H, isatin NH) ppm; ¹³C-NMR δ = 27.03 (benzyl CH₂), Ar-C: [116.72, 123.4, 123.73, 126.07, 130.98, 159.75], indole-C: [112.92, 117.56, 124.12, 131.04, 133.21, 137.27 (C=N), 146.66, 165.00 (C=O)], 147.96 (triazole C-3), 150.94 (triazole C-5) ppm; Calculated (%) for C₁₇H₁₂FN₅O₂ (337.31); C: 60.53, H: 3.59, N: 20.76, found (%); C: 60.54, H: 3.81, N: 20.64.

3-[3-(p-Fluorobenzyl)-5-oxo-4,5-dihydro-1,2,4-triazol-1-yl]-iminoisatin (4b): Yield 82%; obtained as yellow-orange crystals; m.p. 253-254 °C; IR ν (cm⁻¹): 3175, 3089 (NH), 1733 (triazole C=O), 1710 (isatin C=O), 842 (1,4-disubstituted phenyl); ¹H-NMR δ = 4.00 (s, 2H, benzyl CH₂), Ar-H: [6.90-7.09 (m, 5H), 7.25-7.32 (m, 2H), 7.42-7.50 (m, 1H)], 11.15 (s, 1H, triazole NH), 12.20 (s, 1H, isatin NH) ppm; ¹³C-NMR δ = 32.51 (benzyl CH₂), Ar-C: [116.61 (2C), 132.52 (2C), 132.99, 159.27], indole-C: [112.91, 117.03, 124.11, 129.71, 132.46, 137.26 (C=N), 147.65, 165.01 (C=O)], 147.91(triazole C-3), 150.73 (triazole C-5) ppm; Calculated (%) for C₁₇H₁₂FN₅O₂ (337.31); C: 60.53, H: 3.59, N: 20.76, found (%);C: 60.54, H: 3.58, N: 20.74.

3-[3-(o-Fluorobenzyl)-5-oxo-4,5-dihydro-1,2,4-triazol-1-yl]-imino-5-chloro-isatin (4c): Yield 85%; obtained as orange crystals; m.p. 302-303 °C; IR ν (cm⁻¹): 3203, 3080 (NH), 1747 (triazole C=O), 1701 (isatin C=O), 755 (1,2-disubstituted phenyl); ¹H-NMR δ = 4.04 (s, 2H, benzyl CH₂), Ar-H: [6.93-6.96 (m, 1H), 7.10-7.27 (m, 2H), 7.29-7.37 (m, 2H), 7.54-7.64 (m, 2H)], 11.17 (s, 1H, triazole NH), 12.09 (s, 1H, isatin NH) ppm; ¹³C-NMR δ = 26.95 (benzyl CH₂), Ar-C: [116.73, 123.47, 124.29, 126.07, 130.99, 159.99], indole-C: [114.56, 122.30, 128.38, 131.07, 133.11, 136.36 (C=N), 145.46, 162.87 (C=O)], 145.94 (triazole C-3), 150.46 (triazole C-5) ppm; Calculated (%) for C₁₇H₁₁ClFN₅O₂ (371.76); C: 54.92, H: 2.98, N: 18.84, found (%);C: 54.94, H: 2.98, N:18.80.

3-[3-(p-Fluorobenzyl)-5-oxo-4,5-dihydro-1,2,4-triazol-1-yl]-imino-5-chloro-isatin (4d): Yield 80%; obtained as orange crystals; m.p. 194-195 °C; IR ν (cm⁻¹): 3193, 3078 (NH), 1750 (triazole C=O), 1698 (isatin C=O), 841 (1,4-disubstituted phenyl); ¹H-NMR δ = 3.96 (s, 2H, benzyl CH₂), Ar-H: [6.93-7.13 (m, 3H), 7.28-7.35 (m, 2H), 7.56-7.66 (m, 2H)], 11.15 (s, 1H, triazole NH), 12.53 (s, 1H, isatin NH) ppm; ¹³C-NMR δ = 31.61 (benzyl CH₂), Ar-C: [115.61 (2C), 132.48 (2C), 133.87, 155.32], indole-C: [117.03, 120.92, 125.92, 128.04, 132.33, 134.09 (C=N), 139.10, 160.92 (C=O)], 149.38 (triazole C-3), 150.93 (triazole C-5) ppm; Calculated (%) for C₁₇H₁₁ClFN₅O₂ (371.76); C: 54.92, H: 2.98, N: 18.84, found (%);C: 54.96, H: 2.66, N:18.72.

Synthesis of Mannich Bases **5a-d**

The corresponding Schiff bases **4a-d** (0.002 mol) were dissolved in absolute ethanol (100 mL). Then formaldehyde (37%, 0.5 mL) and piperidine (0.002 mol) were added dropwise with vigorous stirring. After combining all reagents, the reaction mixture was stirred at room temperature for 12 h. The mixture was cooled, the solid product was filtered and washed with petroleum ether. The solid that separated was recrystallized from ethanol-dioxane (1:2) to yield the title compounds **5a-d**.

1-Piperidinomethyl-3-[3-(o-fluorobenzyl)-5-oxo-4,5-dihydro-1,2,4-triazol-1-yl]-iminoisatin (5a): Yield 72%; obtained as yellow crystals; m.p. 115-116 °C; IR ν (cm⁻¹): 3247 (NH), 2936 (aliphatic CH₂), 1745 (triazole C=O), 1709 (isatin C=O), 757 (1,2-disubstituted phenyl); ¹H-NMR δ = 1.45 (br, s, 6H, piperidine 3CH₂), 2.51 (br, s, 4H, piperidine 2CH₂), 4.01 (s, 2H, benzyl CH₂), 4.36 (s, 2H, N-CH₂-N), 6.91-7.11 (m, 3H, Ar-H), 7.26-7.30 (m, 2H, Ar-H), 7.50-7.70 (m, 3H, Ar-H), 11.16 (s, 1H, triazole NH) ppm; ¹³C-NMR δ = 25.40 (piperidine C), 27.12 (piperidine 2C), 31.28 (benzyl CH₂), 52.93 (piperidine 2C), 69.32 (N-CH₂-N), Ar-C: [115.65, 125.40, 125.99, 127.74, 128.63, 161.00], indole-C:

[117.20, 120.98, 126.04, 129.41, 130.99, 139.07 (C=N), 146.88, 164.54 (C=O)], 147.27 (triazole C-3), 151.04 (triazole C-5) ppm; Calculated (%) for $C_{23}H_{23}FN_6O_2$ (434.47); C: 63.58, H: 5.34, N: 19.34, found (%); C: 63.19, H: 5.33, N: 19.54.

1-Piperidinomethyl-3-[3-(p-fluorobenzyl)-5-oxo-4,5-dihydro-1,2,4-triazol-1-yl]-iminoisatin (**5b**): Yield 65%; obtained as yellow crystals; m.p. 141–142 °C; IR ν (cm^{-1}): 3236 (NH), 2936 (aliphatic CH_2), 1740 (triazole C=O), 1705 (isatin C=O), 856 (1,4-disubstituted phenyl); 1H -NMR δ = 1.46 (br, s, 6H, piperidine $3CH_2$), 2.50 (br, s, 4H, piperidine $2CH_2$), 4.00 (s, 2H, benzyl CH_2), 4.59 (s, 2H, N- CH_2 -N), 6.93–7.07 (m, 5H, Ar-H), 7.23–7.30 (m, 2H, Ar-H), 7.42–7.50 (m, 1H, Ar-H), 11.11 (s, 1H, triazole NH) ppm; ^{13}C -NMR δ = 25.39 (piperidine C), 27.33 (piperidine 2C), 32.40 (benzyl CH_2), 52.75 (piperidine 2C), 69.37 (N- CH_2 -N), Ar-C: [116.62 (2C), 129.99 (2C), 132.36, 159.77], indole-C: [117.09, 123.91, 124.45, 129.37, 132.53, 137.52 (C=N), 148.09, 164.46 (C=O)], 149.55 (triazole C-3), 154.90 (triazole C-5) ppm; Calculated (%) for $C_{23}H_{23}FN_6O_2$ (434.47); C: 63.58, H: 5.34, N: 19.34, found (%); C: 63.58, H: 5.36, N: 19.36.

1-Piperidinomethyl-3-[3-(o-fluorobenzyl)-5-oxo-4,5-dihydro-1,2,4-triazol-1-yl]-imino-5-chloroisatin (**5c**): Yield 64%; obtained as reddish-orange crystals; m.p. 155–156 °C; IR ν (cm^{-1}): 3224 (NH), 2935 (aliphatic CH_2), 1748 (triazole C=O), 1708 (isatin C=O), 756 (1,2-disubstituted phenyl); 1H -NMR δ = 1.22 (br, s, 6H, piperidine $3CH_2$), 2.26 (br, s, 4H, piperidine $2CH_2$), 3.82 (s, 2H, benzyl CH_2), 4.35 (s, 2H, N- CH_2 -N), 6.99–7.04 (m, 5H, Ar-H), 7.28–7.34 (m, 2H, Ar-H), 11.13 (s, 1H, triazole NH) ppm; ^{13}C -NMR δ = 25.30 (piperidine C), 27.40 (piperidine 2C), 31.24 (benzyl CH_2), 52.50 (piperidine 2C), 69.67 (N- CH_2 -N), Ar-C: [116.57, 124.06, 124.16, 125.98, 130.64, 159.66], indole-C: [117.09, 123.75, 130.49, 132.94, 133.00, 139.73 (C=N), 146.26, 164.55 (C=O)], 146.33 (triazole C-3), 154.54 (triazole C-5) ppm; Calculated (%) for $C_{23}H_{22}ClFN_6O_2$ (468.92); C: 58.91, H: 4.73, N: 17.92, found (%); C: 58.64, H: 4.70, N: 17.86.

1-Piperidinomethyl-3-[3-(p-fluorobenzyl)-5-oxo-4,5-dihydro-1,2,4-triazol-1-yl]-imino-5-chloroisatin (**5d**): Yield 67%; obtained as reddish-orange crystals; m.p. 126–127 °C; IR ν (cm^{-1}): 3251 (NH), 2937 (aliphatic CH_2), 1748 (triazole C=O), 1708 (isatin C=O), 846 (1,4-disubstituted phenyl); 1H -NMR δ = 1.46 (br, s, 6H, piperidine $3CH_2$), 2.51 (br, s, 4H, piperidine $2CH_2$), 4.02 (s, 2H, benzyl CH_2), 4.36 (s, 2H, N- CH_2 -N), 6.91–7.11 (m, 3H, Ar-H), 7.26–7.30 (m, 2H, Ar-H), 7.50–7.70 (m, 2H, Ar-H), 11.16 (s, 1H, triazole NH) ppm; ^{13}C -NMR δ = 25.40 (piperidine C), 27.26 (piperidine 2C), 32.11 (benzyl CH_2), 52.69 (piperidine 2C), 69.45 (N- CH_2 -N), Ar-C: [115.59 (2C), 125.97 (2C), 132.66, 160.99], indole-C: [117.10, 120.87, 125.40, 128.55, 132.45, 139.67 (C=N), 146.85, 164.87 (C=O)], 149.17 (triazole C-3), 151.07 (triazole C-5); Calculated (%) for $C_{23}H_{22}ClFN_6O_2$ (468.92); C: 58.91, H: 4.73, N: 17.92, found (%); C: 58.95, H: 4.71, N: 17.95.

Acknowledgements

This work was supported by Karadeniz Technical University Research Fund (Project No: 2004.122.002.01).

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Sample Availability: Samples of the compounds are available from authors

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