SYNTHESIS OF SOME NEW HETEROCYCLIC COMPOUNDS CONTAINING INDOLE MOIETY

Mostafa Sayed\textsuperscript{[b]}, Adel M. Kamal El-Dean\textsuperscript{[a]}, Mostafa Ahmed\textsuperscript{[b]*} and Reda Hassanien\textsuperscript{[b]}

**Keywords:** chloroacetic acid; anthranilic acid; Schiff bases; lactams.

3-Chloro-1H-indole-2-carbaldehyde (4) was synthesized and converted into Schiff base derivatives (5a-5c). Compounds 5a-5c were reacted with chloroacetyl chloride to give 2-azetidinone derivatives (6a-6c). Compound 4 reacts with active methylene group containing compounds, hydrazine and phenylhydrazine derivatives undergoing a condensation reaction. Compound 4 was reacted with ethyl chloroacetate derivatives to give N-alkylated indole Schiff bases which undergoing cyclization reaction using chloroacetyl chloride to afford azetidinone derivatives.

*Corresponding Authors
E-Mail: drmostafa@scinv.au.edu.eg
[a] Chemistry Department, Faculty of Science, Assiut University, Assiut 71516, Egypt
[b] Chemistry Department, New Valley Faculty of Science, Assiut University, El Kharja 72511, Egypt

**Introduction**

Indoles are found in abundance in biologically active compounds such as pharmaceuticals, agrochemicals, and alkaloids. Therefore Indole derivatives have captured the attention of organic synthetic chemists. Furthermore, indole and its analogs possess a wide spectrum of biological activities such as anti-inflammatory,\textsuperscript{1,2} anti-microbial,\textsuperscript{3,5} anti-bacterial,\textsuperscript{5,7} anticonvulsant\textsuperscript{8,11} and cardiovascular\textsuperscript{12,13} effect. Indole is a popular component of fragrances and the precursors of many pharmaceuticals. Fluoro-substituted indole derivatives have received wide attention from either synthetic or pharmaceutical viewpoint for a long time due to their wide potential bioactivities.\textsuperscript{14-17}

**Result and Discussion**

3-Chloro-1H-indole-2-carbaldehyde (4) was synthesized via Vilsmeier-Hack reaction of 2-(carboxymethylamino)-benzoic acid (3) prepared by the reaction of chloroacetic acid (1) and anthranilic acid (2) in the presence of sodium carbonate, then reaction of compound 4 with different aromatic amines in ethanol and piperidine gave the corresponding Schiff bases (5a-5c).

Reaction of these Schiff bases with chloroacetyl chloride in the presence of catalytic amount of triethylamine in dioxane gave the corresponding 2-azetidinones (5a-5c), on the other hand the reaction of chloroaldehyde 4 with hydroxylamine hydrochloride in the presence of sodium acetate gives the corresponding oxime (7). The oxime 7 can be dehydrated using acetic anhydride to give 3-chloro-1-acetyl-indole-2-carbonitrile (8) which its deacylation with hydrazine hydrate gives the compound 9 (Scheme 1.)

Compound 4 can be reacted with different active methylene group containing compounds such as malononitrile and ethyl acetocetate in ethanol and piperidine to give compounds (10,11) (Scheme 2). Compound 4 also upon refluxing with acetylacetone in ethanol according to Knoevenagel condensation affording derivatives 12.
Compound 16 can be prepared directly also by oxidation of compound 4 by potassium permanganate in acidic medium, compounds (13, 14, 15) were obtained from compound 4 by reacting it with hydrazine derivatives as hydrazine hydrate, phenylhydrazine, and benzoic acid hydrazide (Scheme 2).

The reaction of compound 4 with ethyl chloroacetate in the presence of DMF as base and solvent give the N-alkylated indole (17) which upon the reaction with aromatic amines showed the corresponding Schiff bases (18a-18c).

Scheme 2. Synthesis of 3-chloro-2-substituted indoles

These Schiff bases when react with chloroacetyl chloride in the presence of TEA and dioxane gave the β-lactam derivatives (19a-19c). These compounds when subjected to reaction with hydrazine hydrate in ethanol gave N-carboxyhydrazide derivatives (20a-20c).

The structure of the new compounds prepared was confirmed by elemental and spectral analysis. The IR spectrum of compound 17 showed peaks at 1739 (C=O, ester), 1663 (C=O, aldehyde) cm⁻¹ and the NH peak observed in the spectrum of compound 4 had been disappeared. The NMR spectrum showed signals at δ=1.37(t, 3H CH₃), 4.14(q, 2H, CH₂), 5.08 (s, 2H, CH₂) ppm.

The IR spectrum of compounds 18a-18c showed peaks at 1735 and 1607 cm⁻¹ (C=O, ester) and CH=N bonds. The NMR spectra of the compounds showed signals at δ=1.34(t, 3H CH₃), 4.19(q, 2H, CH₂), 5.23(s, 2H, CH₂), 5.43(s, 1H, CH), 5.72(dd, 1H, CH).

The IR spectra of the compounds 19a-19c was confirmed by IR spectral bands at 1750 and 1666 cm⁻¹ (C=O, ester and C=O, lactam, respectively). The NMR spectra of the compounds showed signals at δ=1.39(t, 3H CH₃), 4.19(q, 2H, CH₂), 5.12(s, 2H, CH₂), 5.44(dd, 1H, CH), 5.72(dd, 1H, CH).

The IR spectra of the compounds 20a-20c showed peaks at 1656 (C=O, hydrazide, 1650 (C=O, lactam), and 3182, 3292, 3320 (NH, NH₂) cm⁻¹. The 1H-NMR spectra of the compounds showed signals at δ=2.04 (s, 2H, NH₂), 5.06(s, 2H, CH₂), 5.42(dd, 1H, CH), 5.44(dd, 1H, CH), 6.03(s, 1H, NH), 4.19(q, 2H, CH₂), 5.12(s, 2H, CH₂), 5.44(dd, 1H, CH), 5.76(dd, 1H, CH) which confirm theirs structure.
Experimental

All melting points given were uncorrected. IR spectra were recorded (KBr discs) with a Perkin-Elmer 1400 Spectrophotometer. 1H NMR spectra and 13C NMR were obtained on a BRUKER (400 MHz) spectrometer in CDCl3 and DMSO-d6 using TMS as an internal standard, and chemical shifts are expressed as δ ppm. Mass spectra were obtained on a Jeol-JMS 600 spectrometer. Analytical data were obtained on elemental analysis system GmbH-Vario EL V.3 micro analyzer in the central lab of Assiut University. Compounds 3 and 4 were prepared according to the literature procedure.18

General procedure to prepare the Schiff base derivatives (5a-5e).

All the Schiff base derivatives were synthesized by refluxing an ethanolic solution of the compound 4 (2.78 mmol, 0.5 g) with the corresponding amines namely aniline, p-chloroaniline and p-nitroaniline (2.78 mmol) in 1:1 stoichiometric ratio for 5 h in the presence of catalytic amount of piperidine. The precipitate obtained after cooling and concentration of the reaction mixture were filtered off, dried and was recrystallized from ethanol to give the desired compounds.

3-Chloro-1H-2-(phenyliminomethyl)indole (5a)

The product was obtained as pale yellow crystals and recrystallized from ethanol (0.6 g, 85 %). m.p.110-112 °C. IR (KBr): υ (cm-1): 3063 (CH aromatic), 1613 (C=O), 1599, 1526, 1298 (C=O), 1515, 1193 (NH), 8.94 (s, 1H, CH), 10.54 (s,1H, NH). Anal.: Calcd. for C12H11ClN2O: C 60.11; H 3.36; Cl 11.83; N 9.31 %; Found: C 60.39; H 3.38; Cl 11.88; N 9.30 %.

3-Chloro-1H-2-(4-nitrophenyliminomethyl)indole (5b)

This compound was obtained as yellow crystals (83 %). m.p. 219-220 °C. IR (KBr) υ (cm-1): 3050 (C=H aromatic), 3376(NH), 1608 (CH=N), 755 (C=C), 1H NMR (DMSO-d6) δ=7.25-7.84 (m, 8H, Ar-H), 8.53(S,1H, CH), 10.54 (S,1H, NH). ppm. MS: m/z (M+): 3106 (CH aromatic), 2942 (CH aliphatic), 1663(C=O), 3291(NH). 1H NMR(DMSO-d6) δ= 7.26-8.22(m, 8H, Ar-H), 10.53(s, 1H, NH). Anal.: Calcd. for C21H12Cl2N2O3: C 59.90; H 3.41; Cl 11.95; N 9.31 %.

3-Chloro-1H-2-(4-chlorophenyliminomethyl)indole (5e)

This compound was obtained as a yellow crystalline mass (78 %), m.p. 145-147 °C. IR (KBr): υ (cm-1): 3080, 3049 (C=H aromatic), 3415 (NH), 1604 (CH=N), 737 (C=C), 1H NMR (DMSO-d6) δ= 6.90-8.03 (m, 8H, Ar-H), 9.80(S, 1H, NH), 8.35 (S,1H, CH), 13C NMR (DMSO-d6): 112.24 (C3), 119.52 (C7), 121.07 (C4), 121.07 (C4), 121.30 (C5), 121.35 (C6), 124.60 (C2), 129.09 (C2' and C6'), 130.16 (C3a), 136.43(C3' and C5'), 151.01(C1'), 156.66(C8), MS m/z (M+, 289) Anal.: Calcd. for C13H10Cl2N2: 289.15 (M+); Found: C 62.30; H 3.49; Cl 24.52; N 9.29. Found: M 62.01; H 3.54; Cl 24.41; N 9.31 %.

Synthesis of 2-azetidinones (6a-6c): General procedure

A mixture of the Schiff base (0.002 mol) and triethylamine (3 mL) was dissolved in 1,4-dioxane (30 mL), cooled and stirred. To this well-stirred solution (0.004 mol) chloroacetyl chloride was added dropwise in a period of 15 min. The reaction mixture was then stirred for an additional 3 h and left at room temperature for 24 h. The resultant mixture was concentrated, cooled, poured onto ice-cold water, filtered and then dried. The product obtained was recrystallized from ethanol.

3-Chloro-1H-2-(3-chloro-1-phenylazetidin-2-one-4-yl)-indole (6a)

This compound was obtained as yellow crystals (85 %). M.p. 178-180 °C. IR: υ (cm-1): 3050 (CH aromatic), 1665.07 (C=O), 3292.45(NH) cm-1. 1H NMR(DMSO-d6) δ=7.19-7.86 (m, 9H, Ar-H), 10.49(s, 1H, NH), 5.16(d, 1H, CH-Cl), 5.44(d, 1H, CH-N)pmm. MS: (M+, 330). Anal.: Calcd. for C17H13Cl2N2O3 (330.9) C 61.65; H 3.65; Cl 21.41; N 8.64 % Found: C 61.33; H 3.70; Cl 21.60; N 8.43 %.

3-Chloro-1H-2-(3-chloro-1-(4-nitrophenyl)azetidin-2-one-4-yl)-indole (6b)

The crude product recrystallized from ethanol as yellow crystals (66 %). M.p. 182-184 °C. IR: υ (cm-1): 3106 (CH aromatic), 2942 (CH aliphatic) 1666(C=O), 3291(NH). 1H NMR(DMSO-d6) δ= 7.26-8.22(m, 8H, Ar-H), 10.53(s, 1H, NH), 5.16(d, 1H, CH-Cl), 5.22(d, 1H, CH-N). Anal.: Calcd. for C22H14Cl3N2O5 (381.61) C 54.28; H 2.95; Cl 18.85; N 11.17 %. Found: C 54.01; H 2.99; Cl 18.69; N 11.22 %.

3-Chloro-1H-2-(3-chloro-1-(4-chlorophenyl)azetidin-2-one-4-yl)-indole (6c)

The crude product was recrystallized from ethanol as yellow crystals (65 %). M.p. 184-186 °C. IR: υ (cm-1): 3131, 3084 (CH aromatic), 1663(C=O), 3291(NH). 1H NMR(DMSO-d6) δ= 7.14-7.84 (m, 8H, Ar-H), 5.16(d, 1H, CH-Cl), 5.44(d, 1H, CH-N) ppm. MS m/z (335.6). Anal.: Calcd. for C17H13Cl2N2O: C 55.84; H; 3.03; Cl 29.09; N 7.66 %; Found: C 55.64; H 3.13; Cl 29.11; N 7.60 %.

3-Chloro-1H-indole-2-carboxaldehyde oxime (7)

A mixture of 3-chloro-1H-indole-2-carboxaldehyde (2g, 0.01 mol) and hydroxylamine hydrochloride (1 g, 0.015 mol) and fused sodium acetate (1.2 g, 0.015 mmol) in ethanol (20 ml) are refluxed for 2 hours. The reaction mixture is cooled, poured onto ice-water to give white precipitate and recrystallized from ethanol to give desired compound.
1-Acetyl-3-chloro-1H-indole-2-carbonitrile (8)

A mixture of oxime (5 g, 0.025 mol) and acetic anhydride (50 ml, 0.33 mol) was refluxed for 6 hrs. The reaction mixture was poured into ice-water mixture and well stirred for about 1 hour. The solid product was filtered off, dried and recrystallized from dilute ethanol as pale brown crystals (4.46g, 89 %), m.p. 120-122 °C. IR: ν (cm⁻¹): 3040 (CH aromatic), 2910, 2850 (CH aliphatic), 1730 (C=O), 2230 (CN). ¹H NMR(DMSO-d₆) δ = 7.60-7.80 (m, 4H ArH), 2.878(s, 3H CH₃), 3.70(m, 8H CH₂), 4.23; 7.95 (m, 5H Ar). ¹³C NMR: 29.10, 111.42 (C3), 117.03 (C10), 122.77 (C7), 125.64 (C5), 126.24 (C2 and C1), 128.69 (C3a), 139.97 (C7a), 167.76(C8 C=O) MS: m/z (M⁺, 218). Anal. Calcd. for: C₉H₁₅CIN₂O (218.64) C 60.43; H 3.23; Cl 16.22; N 12.81; O 7.29 % Found: C 60.20; H 2.95; Cl 20.30; N 15.90; O 7.29 %.

3-Chloro-1H-indole-2-carbonitrile (9)

A mixture of compound 8 (1 g, 4 mmol) and hydrazine hydrate (2 ml, 4 mmol) was refluxed in ethanol for 4 hours after which the reaction mixture was poured into ice-water. The solid product was filtered off, dried and recrystallized from dilute ethanol to give the title compound (4.46 g, 89 %). M.p.120-122°C. IR: ν (cm⁻¹): 3040 (CH aromatic), 2910, 2850 (CH aliphatic), 2230 (CN), 3307 (NH). ¹H NMR(DMSO-d₆) δ = 7.31-7.82(m, 4H ArH), 11.60(s, 1H, NH) MS: m/z (M⁺, 177). Anal. Calcd. for: C₉H₈ClN₂O (177) C 55.54; H 3.63; Cl 18.22; N 14.39 %. Found: C 55.22; H 3.70; Cl 18.29; N 14.35 %.

Ethyl-2-((3-chloro-1H-indol-2-yl)methylene)-3-oxobutanoate (10)

A mixture of the compound 4 (1 g, 5.5 mmol) and ethyl acetocetate (0.715 g, 5.5 mol) was refluxed in ethanol for 3 hour in the presence of catalytic amount of piperidine. The solid product formed was recrystallized from ethanol to give yellow crystals (1.3 g, 85.5 %). M.p. 202-203 °C. IR: ν (cm⁻¹): 3058 (CH aromatic), 1715, 1730(C=O), 2980(CH aliphatic), 3349 (NH), 1703(C=O). ¹H NMR(DMSO-d₆) δ =1.2(t, 3H, CH₃), 2.66(s, 2H, CH₂), 4.14(q, 2H, CH₂), 7.01-7.76(m, 4H ArH), 8.58(s, 1H, CH), 11.73(s, 1H, NH indole) ppm. MS: m/z (M⁺, 291). Anal. Calcd. for: C₁₄H₁₅ClN₂O (291.73) C 61.76; H 4.84; Cl 12.15; N 8.40% Found: C 61.93; H 4.23; Cl 12.97; N 10.25 %.

2-((3-Chloro-1H-indol-2-yl)methylene)malononitrile (11)

A mixture of the compound 4 (1 g, 5.55 mmol) and malononitrile (0.366 g, 5.55 mol) was refluxed in ethanol for 1 hour in the presence of catalytic amount of piperidine. The solid product formed was recrystallized from ethanol to give brown crystals (1.0 g, 80 %). M.p.195-200 °C. IR: ν (cm⁻¹): 3015 (CH aromatic), 2221, 2223 (2 CN), 3328 (NH). ¹H NMR(DMSO-d₆) δ =7.29-7.93(m, 4H ArH), 9.00(s, 1H, CH), 12.51(s, 1H, NH) ppm. MS: m/z (M⁺, 227). Anal. Calcd. for: C₁₃H₁₁ClN₂ (227.65) C 63.31; H 2.66; Cl 15.57; N 18.46 %. Found: C 62.95; H 2.73; Cl 15.63; N 18.39 %.

3-((3-Chloro-1H-indol-2-yl)methylene) pentane-2,4-dione (12)

A mixture of the compound 4 (1 g, 5.57 mmol) and acetylene (0.55 g, 5.57 mol) was refluxed in ethanol for 5 h and 2 drops of piperidine. The solution was cooled, the solid formed was filtered off, washed and recrystallized from ethanol. The yield of brown crystals was 1.1 g, 0.75 %. M.p. 181-183 °C. IR: ν (cm⁻¹): 3057 (CH aromatic), 2922 (CH aliphatic), 3307(14(NH)), 1708.59 and 1651.74(C=O). ¹H NMR(DMSO-d₆) δ =7.19-7.59(m, 4H, ArH), 9.97(s, 1H, CH), 11.00(s, 1H, NH), 2.36(s, 6H 2CH₃) ppm. Anal. Calcd. for: C₁₃H₁₁ClN₂O (261.06) C 64.25; H 4.62; Cl 13.55; N 5.35, 12.23 %. Found: C 64.39; H 4.55; Cl 13.50; N 5.30 %.

3-Chloro-2-(hydroxazomethyl)-1H-indole (13)

A mixture of the compound 4 (1 g, 5.57 mmol) and phenylhydrazine (3 ml, 27 mmol) was fused for 1 h then absolute ethanol (20 ml) was added dropwise. The reaction mixture was refluxed for additional 2 h. The solid product formed was recrystallized from ethanol to give pale yellow crystals (0.75g, 70 %), m.p. 195-198 °C. IR: ν (cm⁻¹): 3040 (CH aromatic), 1615(CH=N), 2922(CH aliphatic) 3219, 3391, 3359 (NH NH₂). ¹H NMR(DMSO-d₆) δ =7.72-7.84(m, 4H, ArH), 3.94(s, 2H, NH₂) ppm. MS: m/z (M⁺, 193). Anal. Calcd. for: C₁₃H₁₁ClN₃ (193.04) C 55.83; H 4.16; Cl 18.31; N 21.70 %. Found: C 55.32; H 4.31; Cl 18.40; N 21.65 %.

3-Chloro-2-(2-phenylhydrazonomethyl)-1H-indole (14)

A mixture of the compound 4 (1 g, 5.57 mmol) and phenylhydrazine(3 ml, 27 mmol) was fused for 1 h then absolute ethanol (20 ml) was added dropwise. The reaction mixture was refluxed for additional 2 h. The solid product formed was recrystallized from ethanol to give pale yellow crystals (0.75g, 70 %), M.p. 121-123 °C. IR: ν (cm⁻¹): 3050 (CH aromatic), 1615(CH=N), 2950(CH aliphatic) 3219, 3391(2NH). ¹H NMR(DMSO-d₆) δ =7.50-8.20(m, 9H, ArH), 8.63(s, 1H, CH), 9.79(s, 1H, NH), 11.02(s, 1H, NH indole) ppm. Anal. Calcd. for: C₁₃H₁₁ClN₃ (269.73) C 66.79; H 4.48; Cl 13.14; N 15.58 %. Found: C 66.02; H 4.31; Cl 12.82; N 15.75 %.

N′-(3-Chloro-1H-indol-2-yl)benzohydrazide (15)

An equimolecular mixture of compound 4 (0.5 g, 2.78 mmol) and benzoic acid hydrazide (0.375 g, 2.78 mmol) in absolute ethanol was heated under reflux for 2 h. The precipitate formed after cooling was filtered off, washed with cold ethanol, dried and recrystallized from ethanol to give the title compound as yellow crystals (0.3 g, 83.3 %). M.p. 250-252 °C. IR: ν (cm⁻¹): 3059 (CH aromatic), 3282, 3310(NH). ¹H NMR(DMSO-d₆) δ = 6.88 (s, 1H, CH), 7.05-8.01 (m, 9H ArH), 10.38(s, 1H, NH), 11.37(s, 1H, NH)
indole) ppm. MS: m/z (297). Anal.: Calcd. for C_{18}H_{23}ClN_{3}O (297.74) C 64.54; H 4.06; Cl 11.91; N 14.11; % Found C 64.89; H 3.66; Cl 11.67; N 13.98.57 %.

3-Chloro-1H-indole-2-carboxylic acid (16)

A solution of the compound 4 (1 g, 5.57 mmol) in acetic acid and potassium permanganate solution in sulfuric acid (0.88 mL, 5.77 mmol) were stirred at room temperature for 2 hours. The solid product formed after dilution with water was filtered and recrystallized from acq. ethanol to give dark yellow crystals (1.4 g, 90 %). M.p.190-192 °C IR: ν (cm⁻¹): 3040 (CH, aromatic), 1715 (C=O), 3295 (NH). ¹H NMR (DMSO-d₆) δ=7.01-8.05 (m, 4H, ArH), 11.81(s, 1H, NH), 13.9(s, 1H, OH exchange with D₂O) ppm. Anal.: Calcd. for: C₉H₆ClNO (195.60) C 55.26; H 3.09; Cl 18.12; N 7.16 %. Found: C 55.05; H 3.55; Cl 18.22; N 6.98 %.

1-(Ethyl ethanoate-2-yl)-3-chloro-indole-2-carbaldehyde (17)

A mixture of the compound 4 (1 g, 5.57 mmol) and ethyl chloroacetate (0.6 mL, 6 mmol) in DMF(10 mL) was stirred at room temp for 8 hours, the reaction mixture was added with good stirring to 200 g of ice cold water till the solid product was separated, the solid was filtered off, washed and recrystallized from ethanol to give the title compound (1 g, 90 %). M.p. 203-205 °C. IR: ν (cm⁻¹): 3055(CH, aromatic), 2985(CH, aliphatic), 1739(C=O, ester), 1663(C=O, aldehyde). ¹H NMR (DMSO-d₆) δ=1.37(t, 3H, CH₃), 4.14(q, 2H, CH₂), 5.08(s, 2H, CH₂), 7.29-7.84 (m, 4H, ArH), 9.70(s, 1H, CH aldehydic) ppm. MS: m/z (M⁺, 265). Anal.: Calcd. for: C_{11}H_{12}ClNO (265.15) C 58.77; H 4.55; Cl 13.34; N 5.27 %. Found: C 58.52; H 4.59; Cl 13.40; N 5.20 %.

General procedure for the synthesis of the Schiff base (18a-c)

All the Schiff base derivatives were synthesized by refluxing an ethanolic solution of N-alkyl indole carbaldehyde (1.3 g, 5 mmol) with corresponding amines (6 mmol) for 5 hrs in the presence of catalytic amount of piperidine. The precipitate obtained after concentration of the reaction mixture were filtered off, dried and recrystallized from ethanol.

1-(Ethyl ethanoate-2-yl)-3-chloro-2-(phenylimino methyl)indole (18a)

The compound obtained as pale yellow crystals (1.5 g, 88 %). M.p. 153-157 °C. IR: ν (cm⁻¹): 3050 (CH aromatic), 2982(CH, aliphatic), 1735(C=O, ester), 1607(CH=N). ¹H NMR (DMSO-d₆) δ=1.34(t, 3H, CH₃), 4.17(q, 2H, CH₂), 5.23(s, 2H, CH₂), 7.22-7.83 (m, 9H, ArH), 8.54(s, 1H, CH=N) ppm. MS: m/z (M⁺, 340). Anal.: Calcd. for: C_{18}H_{21}ClN_{3}O (340.81): C 66.96; H 5.03; Cl 10.40; N 8.22 %. Found: C 66.90; H 5.15; Cl 10.43; N 8.15 %.

1-(Ethyl ethanoate-2-yl)-3-chloro-2-(4-chlorophenylimino methyl)indole (18b)

The compound obtained as pale yellow crystals (1 g, 60 %). m.p 145-147 °C. IR: ν (cm⁻¹): 3050 (CH aromatic), 2982(CH aliphatic), 1753(C=O ester), 1607(CH=N). ¹H NMR (DMSO-d₆) δ=1.34(t, 3H, CH₃), 4.17(q, 2H, CH₂ of ester), 5.23(s, 2H, CH₂), 7.22-7.83 (m, 9H, ArH), 8.54(s, 1H, CH=N) ppm. Anal.: Calcd. for: C_{20}H_{16}ClN₂O₂ (375.25) C 68.81; H 4.30; Cl 18.90; N 7.47 %. Found: C 66.90; H 4.25; Cl 18.85; N 7.40 %.

1-(Ethyl ethanoate-2-yl)-3-chloro-2-(4-nitrophenylimino methyl)indole (18c)

The compound obtained as pale yellow crystals (1.3 g, 77 %). M.p. 160-162 °C. IR: ν (cm⁻¹): 3050 (CH, aromatic), 2994(CH, aliphatic), 1746(C=O, ester), 1610(CH=N). ¹H NMR (DMSO-d₆) δ= 6.80-8.20 (m, ArH) ppm. Anal.: Calcd. for: C₂₀H₁₆ClN₂O₂ (385.80) C 59.15; H 4.18; Cl 9.19; N 10.89; O 16.59 %. Found: C 59.30; H 4.15; Cl 9.13; N 10.92; O 16.55 %.

1-(Ethyl ethanoate-2-yl)-3-chloro-2-(3-chloro-1-(4-nitrophenyl)azetidin-2-one-4-yl)indole (19c)

A mixture of the Schiff base 18c (2 g, 5 mmol) and triethylene (3 mL) was dissolved in 1,4-dioxane (30 mL), cooled and stirred. To this well-stirred cooled solution (0.56 mL, 5 mmol) chloroacetyl chloride was added dropwise within a period of 15 min. The reaction mixture was then stirred for an additional 3 h and left at room temperature for 24 h. The resultant mixture was concentrated, cooled, poured onto ice-cold water, filter and then dried. The product thus obtained was recrystallized from ethanol. The compound obtained as pale yellow crystals (2 g, 84 %). M. p. 210-212 °C. IR: ν (cm⁻¹): 3059 (CH, aromatic), 2983(CH, aliphatic), 1750(C=O, ester), 1666(C=O, lactam). ¹H NMR (DMSO-d₆) δ=1.39(t, 3H, CH₃), 4.19(q, 2H, CH₂), 5.12(s, 2H, CH₂), 5.44(dd, 1H, CH), 7.57-7.83 (m, 8H, ArH) ppm. MS: m/z (M⁺,461) Anal.: Calcd. for C_{21}H_{17}Cl₂N₂O₅ (461.05) C 54.56; H 3.71; Cl 15.34; N 9.09 %. Found: C 54.60; H 3.75; Cl 15.30; N 9.13%.

1-(Acetohydrazide-2-yl)-3-chloro-2-(3-chloro-1-(4-nitrophenyl)azetidin-2-one-4-yl)indole (20c)

A mixture of the lactam derivative 19c (0.9 g, 2 mmol) and hydrazine hydrate (2 mL, 40 mmol) in ethanol (10 mL) was gentle refluxed for 1 h. The precipitate formed was collected by filtration, dried and recrystallized from dioxane as pale yellow crystals (0.7 g, 90 %). M.p.190-192 °C. IR: ν (cm⁻¹): 3059 (CH, aromatic), 2983(CH, aliphatic), 1656 (C=O, hydrazide), 1650(C=O, lactam), 3182, 3292, 3320(NH, NH₂). ¹H NMR (DMSO-d₆) δ=2.04 (s, 2H, NH₂), 5.06(s, 2H, CH₂), 5.42(dd, 1H, CH), 5.44(dd, 1H, CH), 6.03(s, 1H, NH)
4.19(q, 2H, CH₂). 5.12(s, 2H, CH₂). 5.44(dd, 1H, CH). 5.7.62(dd, 1H, CH) 7.22-7.80 (m, 8H, ArH) ppm. MS: m/z (M⁺, 448). Anal.: Calcd. for C₉H₇Cl₂N₃O₄ (448.26) C 50.91; H 3.37; Cl 15.82 %; N 15.62 %. Found: C 50.65; H 3.75; Cl 15.90; N 15.70 %.

Acknowledgements

We thank Prof. Dr. Ahmed Abdo Geies President of Assiut University and Professor of Organic Chemistry.

References


Received: 28.04.2017. Accepted: 25.05.2017.