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Synthesis of pyrazolone derivatives containing indole moiety bearing-4-oxazetidinone

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ABSTRACT

Schiff base synthesis of pyrazolone derivatives containing Indole moiety bearing-4-oxazetiding ring were synthesized by the condensation of 2-(3-(3chloro -1-(4-substitued phenyl)-4-oxozetiding -2-yl(1H-Indole –yl Aceto hydrazone with ethyl 2-(2-(4-substituted phenyl hydrazone)(-4,-4,-4 tri frouro-3-oxo butanoate) this reaction was subjected in schiff base reaction .The structure of these newly synthesized compounds were characterised by ^{1}H *NMR,*^{13}*CNMR ,Mass ,IR, and elemental analysis.*

Keywords: Azetidinones, Schiff base, β- Lactam, pyrazolones, indole

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INDRODUCTION

Hetero cyclic compounds represents an important class of biological molecules. The hetero cyclic molecules which posses indole, pyrazole and azetidine moieties exhibit wide range of biological activities. Indoles are one of the most important alkaloids molecules found extensively in biological systems, which play vital role in many of the biochemical process. Indole ring constitutes an important basic skelton and development of the drug. The classical indole drugs are indomethacin and indoxole. Indole derivatives found to posses high which includes, antibacterial, analgesic, antipyretic, antifungal, anti-inflammatory, anthelmintic, cardiovascular, anticonvulsant and selective COX-2 inhibitory activities, anticonvulsant and selective COX-2 inhibitory activities .

Pyrazole derivatives have been reported to possess diverse biological activities such as antimicrobial [1, 2], antibacterial [3,4], antifungal [5, 6], herbicidal [7], insecticidal [8], anti-inflammatory[9-11], anticonvulsant [12], antitumor [13], anti-oxidant [14,15].

Azetidinones are of great biological interest, especially as anti-tubercular [16], antibacterial[17],[18],[19],[20] The important and structural diversity of biologically active β -lactam antibiotics led to the development of many novel methods for the construction of appropriately substituted azetidine with attendant control of functional group and stereochemistry. Azetidinone derivatives are reported to show a variety of antimicrobial [21],[22], anticonvulsant [23], anti-inflammatory [24] and cardiovascular activities [25], antimycobacterial activity[26], antibacterial activity [27], antihypertensive activity [28].

MATERIALS AND METHODS

Melting points were determined on open capillaries using a cintex melting point apparatus .T.L.C. analysis were performed on precoated silicagel (E-Merck Kieselgel 60 F_{254}) plates and visualization was done by exposing to iodine vapour. Solvent were purified by standard procedures before use. Column chromatography was conducted by using Silica gel with different solvent systems as elutes .IR Spectra were recorded KBr on perkin –elmer spectrum BX series FTIR spectrometer.H^1-NMR spectrum were recorded on varian zemini 300MHz and 200MHz spectrometers using TMS as internal standard(chemical shifts in & ppm) C^{13}NMR spectra were recorded on a brucker 75MHz spectrometer. Mass spectra were scanned on a varian MATCH -7 and jeol JMSD-300 mass spectrometer at 70 ev. elemental analysis were carried out on carloerba 106 and perkin –analyser. All the chemicals used in the present investigation were purchased from Aldrich chemicals; U.S.A. indole- 3-carbaldehyde was prepared by a reported methods.

RESULTS AND DISCUSSION

indole-3-carbaldehyde(1) and chloro ethyl acetate were dissolved in dimethyl formamide solvent and to this reaction mixture anhydrous K_2CO_3 was added and the reaction mixture was stirred at room temperature(35^0C) for 8 hours. The yield -2-(3-formyl-1H-indol-1-yl)acetate. The compound on treatment with substituted aniline afford Ethyl 2-(3-phenyl imino)metbyl-1H-Indole-1-yl-acetate (A). The compound- (A) on reaction with chloro ethyl acetate and ETA, dioxane compound (1) is Ethyl 2-(3-(3-chloro-1-(4-substituted phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)acetate(5) formed. The compound (1) is condensed with hydrazine hydrate in presence of afford 2-(3-(3-chloro-1-(4-substituted phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)aceto hydrazide2(a-f).The compound (2) is condensed with Synthesis of ethyl 2-(2-(4-nitrophenyl)hydrazono)-4-4-4-trifluoro-3-oxobutanoate(3) in presence of acetic anhydrate in ethanol afford 1-(2-(3-(3-chloro-1-(4-substituted phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)acetyl)-4-(2-(4-substituted phenyl)hydrazono)-3-(trifluoromethyl)-1H-pyrazol-5(4H)-one4(a-f).These reactions are summarized in the scheme-1.Yields were moderate to affair(55-70%). The purity of the compounds was monitored by TLC.

Synthesis of 2-(3-formyl-1H-indol-1-yl)acetate

An equimolar mixture of indole-3-carbaldehyde and chloro ethyl acetate were dissolved in dimethyl formamide solvent and to this reaction mixture anhydrous K_2CO_3 was added and the reaction mixture was stirred at room temperature(35^0C) for 8 hours and the progress of the reaction was monitored by TLC using cyclohexane and ethylacetate solvent mixture (7:3) as eluent the reaction mixture was kept overnight. After completion of the reaction the solvent was evaporated on rota-evaporater. The gummy solid was separated and it was recrystallized from -2-propanol-petrolium ether(80^0c)solvent mixture. The crystalline solid was found to be -2-(3-formyl-1H-indol-1-yl)acetate. with a yield of 75% and mp 143-145^0C.The indole-3-carbaldehyde used in the present studies was purchased from aldrich company and was used without any further purification. Yield 75%,m.p.:143-145^0C.

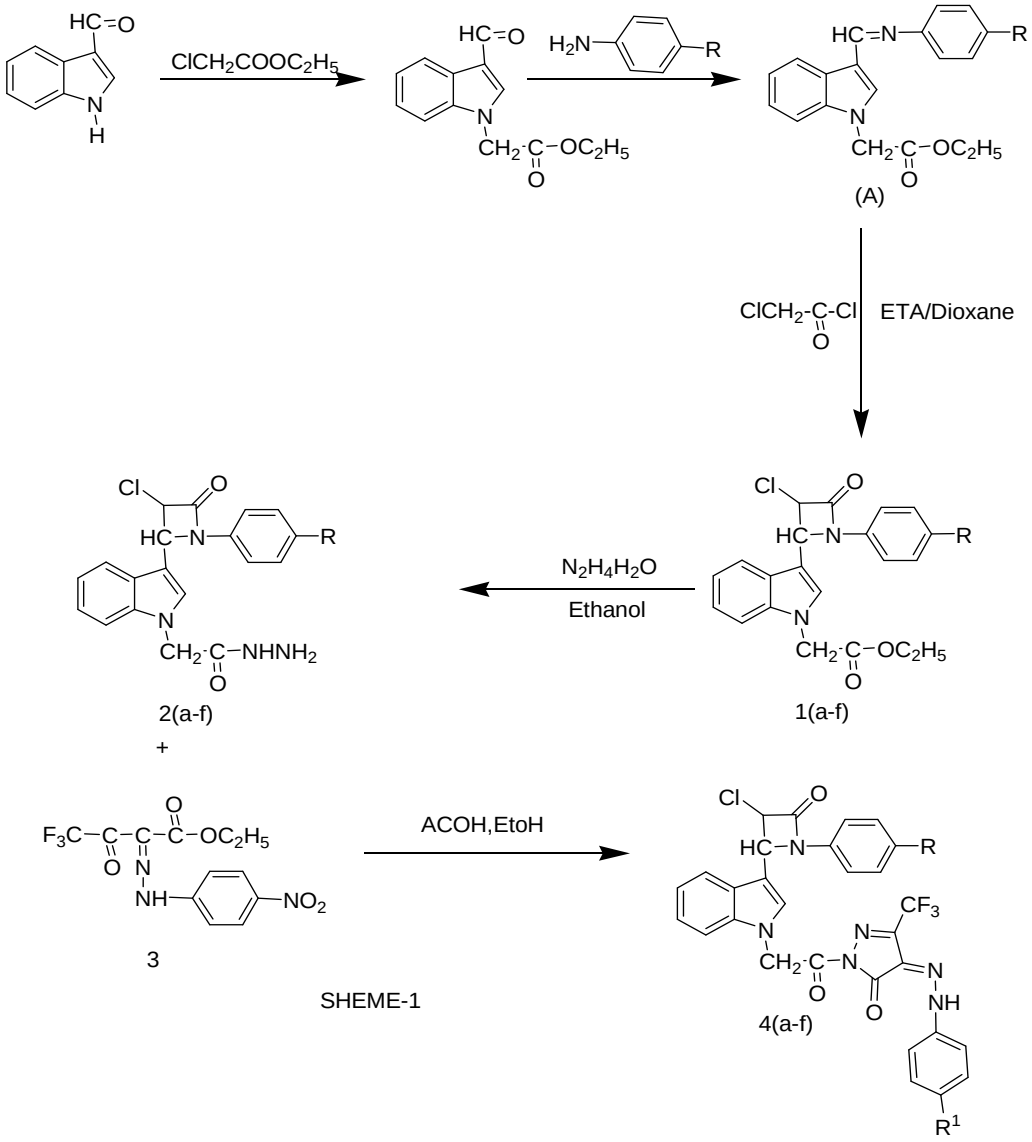
The IR(KBr) spectrum of 2-(3- formyl-1H-indol-1-yl) acetate(2) was recorded in the range 4000-667cm^{-1} and the absorption signals where found at 3032(√-Ar-H)**,** 2980 and 2960 (√ aliphatic CH_2 andCH_3), 1760 (√ CO of ester group), and 1182(√ C-O-C of ester group).

The ^{1}HNMR spectra of 2-(3- formyl-1H-indol-1-yl) acetate(2) was recorded in DMSO-d6 solvent. The NMR signal of 2-(3- formyl-1H-indol-1-yl) acetate(2) was found at $\delta_{PPm,}$ 1.29 (t,3H, J=13.2Hz, CH_3 of ethyl group), 4.13 (q, 2H, J=13.2Hz, CH_2 of ethyl group), 4.78(s, 2H, N-CH_2 group) and 6.92 , 7.58 (m, 10H, C_8H_5N indole nucleus).

Synthesis of Ethyl 2-(3-phenyl imino)metbyl-1H-Indole-1-yl-acetate (A)

Equimolar quantity of aniline(3) and ethyl-2-(-3-formyl-1H-indol-1-yl)acetate(2) were dissolved in absolute alcohol, to this three drops of acetic acid is added then heated on a steam bath for 5-6hrs at 100^0C. After standing for 24hrs at room temperature, the product was dried and recrystallized from warm absolute alcohol. The separated solid was identified as ethyl 2-(-3-(((-4-nitro phenyl)imino)methyl)-1H-indol-1-yl)acetate. Yield 75%,m.p.:154-156^0C

IR (KBr) spectrum of ethyl 2-(3-phenyl imino)metbyl-1H-Indole-1-yl-acetate 1(a)was recorded in the range 4000-667cm^{-1} and IR absorption signals were found at 3032 (√ Ar-H), 2980 and 2960 (√ aliphatic CH_2 and CH_3), 1760 (√ CO of ester group), 1610(√ C=N group) and 1182(√ C-O-C of ester group).



SHEME-1

compound	4a	4b	4c	4d	4e	4f
R	H	CH_3	OCH_3	Br	NO_2	CF_3
R^1	H	H	H	H	H	H

^{1}H NMR Spectra ethyl 2-(3-phenyl imino)metbyl-1H-Indole-1-yl-acetate 1(a)was recorded in DMSO-d6 solvent. The NMR signal of ethyl 2-(3-phenyl imino)metbyl-1H-Indole-1-yl-acetate(A) was found at $\delta_{PPm,}$ 1.29(t,3H, J=13.2Hz, CH_3 of ethyl group), 4.13 (q, 2H, J=13.2Hz, CH_2 of ethyl group), 4.78(s, 2H, N-CH_2 group) and 6.92 , 7.58 (m, 10H, C_8H_5N indole nucleus and C_6H_5 phenyl nucleus) and 8.44(s, 1H, N=CH group).

The compound (A) was converted into azetidine-2-one on treatment with chloro acetyl chloride. The formation compound was confirmed by IR, NMR data.

^{1}HNMR spectra; 1.29(t, 3H, CH_3 of C_2H_5), 4.78(s, 2H, N-CH_2-C=O), 4.13(q, 2H, -O-CH_2 of OC_2H_5), 6.92-7.58(m, 10H, Ar-H, 8.44(N=CH).

IR spectra; 1610(C=N), 1760 (ester –C=O), 3032(Ar-H), 1182(-C-O-C).

^{1}HNMR spectra; 1.29(t, 3H, CH_3 of C_2H_5), 4.78(s, 2H, N-CH_2-C=O), 4.13(q, 2H, -O-CH_2 of OC_2H_5), 6.92-7.58(m, 10H, Ar-H, 8.44(N=CH). Table: 2.2 ^{1}H NMR spectra of ethyl 2-(3-phenyl imino)methyl-1H-Indole-1-yl-acetate (A)

Synthesis of ethyl 2-(3-(3-chloro-1-(4-substituted phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)acetate 1(a)
Equimolar quantities of ethyl 2-(3-(((phenyl) imino)methyl)1-1H-Indol -1yl) acetate (A) was converted into azetidine- 2-one on treatment with chloro acetyl chloride Yield 75%,m.p.:155-150^{0}C. This general procedure was extended to substituted indoles to synthesis azetidin -2-one derivative 5(a-f) the structure of 1 (a-f) were established by IR and H^1 NMR data

Ethyl 2-(3-(3-chloro -1-(4-substituted phenyl)-4-oxaezetidine -2-yl) -1H - Indol -1-yl)acetate 1(a)
1.30 (t, 3H, CH_3 of C_2H_5), 4.75 (s, 2H, N-CH_2-C =O), 4.15 (q, 2H, -O-CH_2 of OC_2H_5), 5.16(d, 1H, -CH of azetidine attached to phenyl ring), 5.44(d, 1H, -CH of azetidine attached to -Cl), 6.94-7.59 (m, 10H, Ar-H). IR(KBr) spectra; The compound 1(a) shows signals at, 1578(C=N), 1177(-C-O-C-), 1765(-C=O), 826(CCl) are due to stretching vibrations of –C=O, C=N, C-O-C, C-Cl respectively. *Anal*. Cacld. for (382); C, 67.02; H, 5.05; N, 7.44 found(%); C:65.88, H:5.00, N:7.32

Ethyl 2-(3-(3-chloro -1-(4-methyl phenyl) -4 oxaezetidine -2-yl) -1H - Indol -1-yl)acetate 1(b)
1.33 (t, 3H, CH_3 of C_2H_5), 4.78 (s, 2H, N-CH_2-C =O), 4.18 (q, 2H, O-CH_2 of OC_2H_5), 5.18 (d, 1H, -CH of azetidine attached to phenyl ring), 5.48 (d, 1H, -CH of azetidine attached to -Cl), 6.94-7.60 (m, 9H, Ar-H), 2.23(s, 3H, CH_3 attached to phenyl ring). IR(KBr) spectra; The compound 1(a) shows signals at, 1565(C=N), 1175(-C-O-C-), 1760(-C=O), 820(CCl) are due to stretching vibrations of –C=O, C=N, C-O-C, CCl respectively. Yield 70%, m.p 140-150^{0}C *Anal*. Cacld. for (396); C, 67.69; H, 5.38; N, 7.17 found(%); C:66.58, H:5.33, N:7.06

Ethyl 2-(3-(3-chloro -1-(4-methoxyphenyl) -4 oxaezetidine -2-yl) -1H - Indol -1-yl)acetate 1(c)
1.34 (t, 3H, CH_3 of C_2H_5), 4.79 (s, 2H, N-CH_2-C=O), 4.19 (q, 2H, -O-CH_2 of OC_2H_5), 5.20 (d, 1H, -CH of azetidine attached to phenyl ring), 5.46 (d, 1H, -CH of azetidine attached to -Cl), 6.96-7.62 (m, 9H, Ar-H), 2.26 (s, 3H, OCH_3 attached to phenyl ring). IR(KBr) spectra; The compound 1(c) shows signals at, 1560(C=N), 1170 (-C-O-C-), 1755(-C=O), 815(CCl) are due to stretching vibrations of –C=O, C=N, C-O-C, CCl respectively. Yield 65%, m.p.: 130-140^{0}C *Anal*. Cacld. for (412); C, 64.07; H, 5.09; N, 6.85 found(%); C:64.00, H:5.13, N:6.79

Ethyl 2-(3-(3-chloro -1-(4-bromo phenyl) -4 oxaezetidine -2-yl) -1H - Indol -1-yl)acetate 1(d)
1.37 (t, 3H, CH_3 of C_2H_5), 4.82 (s, 2H, N-CH_2-C =O), 4.21 (q, 2H,-O-CH_2 of OC_2H_5), 5.23 (d, 1H, -CH of azetidine attached to phenyl ring), 5.48 (d, 1H, -CH of azetidine attached to -Cl), 6.98-7.65 (m, 9H, Ar-H). IR(KBr) spectra; The compound 1(d) shows signals at, 1563(C=N), 1173(-C-O-C-), 1763(-C=O), 818(CCl) are due to stretching vibrations of –C=O, C=N, C-O-C, CCl respectively. Yield 66%, m.p.: 170-180^{0}C *Anal*. Cacld. for (460); C, 54.78; H, 3.91; N, 6.08 found(%); C:54.63, H:3.93, N:6.07

Ethyl 2-(3-(3-chloro -1-(4-nitro phenyl) -4 oxaezetidine -2-yl) -1H - Indol -1-yl)acetate 1(e)
1.39 (t, 3H, CH_3 of C_2H_5), 4.85 (s, 2H, N-CH_2-C =O), 4.23 (q, 2H, -O-CH_2 of OC_2H_5), 5.25 (d, 1H, -CH of azetidine attached to phenyl ring), 5.50 (d, 1H, -CH of azetidine attached to -Cl), 6.99-7.67 (m, 9H, Ar-H). IR(KBr) spectra; The compound 1(e) shows signals at, 1555(C=N), 1160(-C-O-C-), 1745(-C=O), 814(CCl) are due to stretching vibrations of –C=O, C=N, C-O-C, CCl respectively. Yield 70%, m.p.: 185-190^{0}C *Anal*. Cacld. for (427); C, 59.01; H, 4.21; N, 9.83 found(%); C:58.95, H:4.24, N:9.82

Ethyl 2-(3-(3-chloro -1-(4-nitro phenyl) -4 oxaezetidine -2-yl) -1H - Indol -1-yl)acetate 1(f)
1.40 (t, 3H, CH_3 of C_2H_5), 4.90 (s, 2H, N-CH_2-C =O), 4.25 (q, 2H, -O-CH_2 of OC_2H_5), 5.28 (d, 1H, -CH of azetidine attached to phenyl ring), 5.52 (d, 1H, -CH of azetidine attached to -Cl), 7.2-7.70 (m, 9H, Ar-H). IR(KBr) spectra; The compound 1(f) shows signals at, 1580(C=N), 1180(-C-O-C-), 1770(-C=O), 830(CCl) are due to stretching vibrations of –C=O, C=N, C-O-C, CCl respectively. Yield 71%, m.p.: 180-185^{0}C *Anal*. Cacld. for (705); C, 56.00; H, 4.21; N, 6.22 found(%); C:58.61, H:4.02, N:6.21.

Synthesis of 2-(3-(3-chloro-1-(4-substituted phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)aceto hydrazide(2).
A solution of (5a) (0.01mol) and hydrazine hydrate (0.015mol) in ethanol(20ml) was refluxed for 5hrs. The reaction mixture was cooled and poured in to ice cold water with stirring. The separated solid was filtered, washed with water and recrystallized from ethanol to afford 2-(3-(3-chloro-1-(4-substituted phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)aceto hydrazide(6).

4.36 (s, 2H, N-CH_2-C=O), 4.95 (s, 1H, -N-NH), 5.20 (d, 1H, -CH of azetidine attached to phenyl ring), 6.9-8.3(m, 14H, due to 5H of indole C_6H_6, C_6H_4 of phenyl ring), 5.49 (d, 1H, –CH of azetidine attached to –Cl). IR(KBr) spectra; The compound 1(f) shows signals at 3494(-NH), 3330(Ar-H), 2920(-CH- of aliphatic), 1680(C=O, amide), 3494(-NH_2), 820(CCl). Yield 65%, m.p.:175-185^{0}C.

Synthesis of 1-(2-(3-(3-chloro-1-(4-substituted phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)acetyl)-4-(2-(4-substituted phenyl)hydrazono)-3-(trifluoromethyl)-1H-pyrazol-5(4H)-one(4)

In a solution of 6(a-f) in (0.01 mol),(10ml) ethanol , and(0.01) ethyl acetoacetate were added and the mixture was refluxed for 12hrs in presence of catalytical amount glacial acetic acid. Excess of ethanol was removed by distillation and crystalline residue obtained was filtered, washed with ethanol, dried and recrystallized to get the compounds 8(a-f) in good yields.

1-(2-(3-(3-Chloro-1-(4-substituted phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl) acetyl)-4-(2-(4-substituted phenyl)hydrazono)-3-(trifluoromethyl)-1H-pyrazol-5(4H)-one4(a)

4.36 (s, 2H, N-CH_2-C=O), 4.95 (s, 1H, -N-NH), 5.20 (d, 1H, -CH of azetidine attached to phenyl ring), 6.94-8.34(m, 14H, due to 5H of indole C_6H_6, C_6H_4 of phenyl ring 5.49 (d, 1H –CH of azetidine attached to –Cl). IR(KBr) spectra; The compound 4(a) shows signals at 3158(-NH-), 1780(-C=O), 2,260(C=N), 580(CCl), 1770(-C=O), 750(C-F). The ^{13}C spectrum of ($CDCl_3$) shown δ:138.4-C_1, 121.9- C_2, 117.2- C_3, 149.2- C_4(nitro phenyl), 63.1-C_5, 59.6-C_6, 162.2-C_7(azetidine ring), 121.6-C_8, 141.7-C_9, 129.0-C_{10}, 124.4.0-C_{11} (phenyl ring),116.5- C_{12}, 126.5-C_{13}, 127.8-C_{14}, 119.0-C_{15}, 122.2-C_{16}, 120.7-C_{17}, 111.8-C_{18}, 137.6-C_{19}(indole ring), 41.0-C_{20}, 171.0- C_{21}, 155.0-C_{22}, 122.0-C_{23}, 128.6-C_{24}, 162.5-C_{25}(pyrazolone ring), Yield 57%, m.p.: 150-160^{0}C *Anal.* Cacld. for (637); C, 54.63; H, 2.98; N, 15.38 found(%); C:54.60, H:3.00, N:15.37

1-(2-(3-(3-Chloro-1-(4-methyl phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)acetyl)-4-(2-(4-substituted phenyl) hydrazono)-3-(trifluoromethyl)-1H-pyrazol-5(4H)-one4(b)

4.37 (s, 2H, N-CH_2-C=O), 4.95 (s, 1H, -N-NH), 5.21 (d, 1H, -CH of azetidine attached to phenyl ring), 6.95-8.35(m, 14H, due to 5H of indole C_6H_6, C_6H_4 of two phenyl rings), 5.50 (d, 1H –CH of azetidine attached to –Cl), 2.23(s, 3H, CH_3, attached to phenyl ring) IR(KBr) spectra; The compound 4(b) shows signals at 3150(-NH-), 1775(-C=O), 2255(C=N), 578(CCl), 1765(-C=O), 745(C-F). The ^{13}C spectrum of ($CDCl_3$) shown δ: 138.4-C_1, 121.9-C_2, 117.2-C_3,149.2-C_4(nitro phenyl), 63.1-C_5, 59.6-C_6, 162.2-C_7(azetidine ring), 121.5-C_8, 138.7-C_9, 129.3-C_{10}, 134.0-C_{11}, 24.3-C_{12}(tollyl group),116.5-C_{13}, 126.5-C_{14}, 127.8-C_{15}, 119.0-C_{16}, 122.2-C_{17}, 120.1-C_{18}, 111.8-C_{19}, 137.6-C_{20}(indole ring), 41.0-C_{21}, 171.0-C_{22}, 155.0-C_{23}, 122.0-C_{24}, 128.6-C_{25}, 162.5-C_{26},(pyrazolone ring). Yield 55%, m.p.: 143-150^{0}C *Anal.* Cacld. for (651); C, 55.29; H, 3.22; N, 15.05 found(%); C:55.27, H:3.25, N:15.04

1-(2-(3-(3-Chloro-1-(4-methoxy phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)acetyl)-4-(2-(4-substituted phenyl) hydrazono)-3-(trifluoromethyl)-1H-pyrazol-5(4H)-one4(c))

3.24(s, 3H, OCH_3 attached to phenyl ring), 4.37 (s, 2H, N-CH_2-C=O), 4.95 (s, 1H, -N-NH), 5.22 (d, 1H, -CH of azetidine attached to phenyl ring), 6.96-8.33(m, 14H, due to 5H of indole C_6H_6, C_6H_4 of two phenyl rings), 5.51, (d, 1H –CH of azetidine attached to –Cl), 2.23(s, 3H, CH_3 attached to phenyl ring). IR(KBr) spectra; The compound 4(c) shows signals at 3145(-NH-), 1770(-C=O), 2250(C=N), 576(CCl), 1740(-C=O), 750(C-F). The ^{13}C spectrum of ($CDCl_3$) shown δ: 138.4-C_1, 21.9-C_2, 117.2-C_3, 149.2-C_4(nitro phenyl), 63.1-C_5, 59.6-C_6, 162.2-C_7(azetidine ring), 121.5-C_8, 138.7-C_9, 129.3-C_{10}, 134.0-C_{11}, 55.9-C_{12}(methoxy phenyl group), 116.5-C_{13}, 126.5-C_{14}, 127.8-C_{15}, 119.0-C_{16}, 122.2-C_{17}, 120.1-C_{18}, 111.8-C_{19}, 137.6-C_{20}(indole ring), 41.0-C_{21}, 171.0-C_{22}, 155.0- C_{23}, 122.0-C_{24}, 128.6-C_{25}, 162.5-C_{26}(pyrazolone ring). Yield 54%, m.p.: 135-145^{0}C *Anal.* Cacld. For (667); C, 53.97; H, 3.14; N, 14.69 found(%); C:53.94, H:3.17, N:14.68

1-(2-(3-(3-Chloro-1-(4-bromo phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)acetyl)-4-(2-(4-substituted phenyl) hydrazono)-3(trifluoromethyl)-1H-pyrazol-5(4H)-one4(d))

4.40 (s, 2H, N-CH_2-C=O), 4.98 (s, 1H,-N-NH), 5.24 (d, 1H, -CH of azetidine attached to phenyl ring), 6.96-8.46 (m, 14H, due to 5H of indole C_6H_6, C_6H_4 of two phenyl rings), 5.53 (d, 1H, –CH of azetidine attached to –Cl) IR(KBr) spectra; The compound 4(d) shows signals at 3152(-NH-), 1774(-C=O), 2254(C=N), 574(CCl), 1755(-C=O), 750(C-F). The ^{13}C spectrum of ($CDCl_3$) shown δ:138.4-C_1, 121.9-C_2, 117.2-C_3, 149.2-C_4(nitro phenyl), 63.1-C_5, 59.6-C_6, 162.2-C_7(azetidine ring), 123.8-C_8, 140.7-C_9, 131.9-C_{10}, 118.0-C_{11} (halo phenyl ring), 116.5-C_{12}, 126.5-C_{13}, 127.8-C_{14}, 119.0-C_{15}, 122.2-C_{16}, 120.7-C_{17}, 111.8-C_{18}, 137.6-C_{19}(indole ring), 41.0-C_{20}, 171.0-C_{21}, 155.0-C_{22}, 122.0-C_{23}, 128.6-C_{24}, 162.5-C_{25}(pyrazolone ring), Yield 56%, m.p.: 160-170^{0}C *Anal.* Cacld. for (460); C, 54.78; H, 3.91; N, 6.08 found(%); C:54.63, H:3.93, N:6.07

1-(2-(3-(3-Chloro-1-(4-nitro phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)acetyl)-4-(2-(4-substituted phenyl) hydrazono)-3--(trifluoromethyl)-1H-pyrazol-5(4H)-one4(e)

4.44 (s, 2H, N-CH_2-C =O), 5.15(s, 1H, -N-NH), 5.28 (d, 1H, -CH of azetidine attached to phenyl ring), 6.98-8.45 (m, 14H, due to 5H of indole C_6H_6, C_6H_4 of two phenyl rings), 5.58 (d, 1H –CH of azetidine attached to –Cl), IR(KBr) spectra; The compound 4(e) shows signals at 3150(-NH-), 1760(-C=O), 2252(C=N), 572(CCl), 1762(-C=O), 755(C-F). The ^{13}C spectrum of ($CDCl_3$) shown δ: 138.4-C_1, 121.9-C_2, 117.2-C_3, 149.2- C_4 (nitro phenyl), 63.1-C_5, 59.6-C_6, 162.2-C_7 (azetidine ring), 122.5-C_8, 147.8-C_9, 121.3-C_{10}, 144.0-C_{11} (azetidine attached to nitro phenyl ring), 116.5-C_{12}, 126.5-C_{13}, 127.8-C_{14}, 119.0-C_{15}, 122.2-C_{16}, 120.7-C_{17}, 111.8-C_{18}, 137.6- C_{19}(indole ring), 41.0-C_{20}, 171.0-C_{21}, 155.0-C_{22}, 122.0-C_{23}, 128.6-C_{24}, 162.5-C_{25} (pyrazolone ring), Yield 60%, m.p.: 180-190^{0}C, *Anal.* Cacld. for (682); C, 51.02; H, 2.63; N, 16.42 found(%); C:51.00, H: 2.66, N: 16.41

1-(2-(3-(3-Chloro-1-(4-trifluoro methyl phenyl)-4-oxoazetidine-2-yl)-1H-indol-1-yl)acetyl)-4-(2-(4-substituted phenyl)hydrazono)-3-(trifluoromethyl)-1H-pyrazol-5(4H)-one 4(f)

4.38 (s, 2H, N-CH_2-C =O), 4.96(s, 1H, -N-NH), 5.22 (d, 1H, -CH of azetidine attached to phenyl ring), 6.95-8.39 (m, 14H, due to 5H of indole C_6H_6, C_6H_4 of two phenyl rings), 5.51 (d, 1H, –CH of azetidine attached to –Cl), IR(KBr) spectra; The compound 4(f) shows signals at 3105(-NH-), 1785(-C=O), 2300(C=N), 585(CCl), 1775(-C=O), 765(C-F). The ^{13}C spectrum of ($CDCl_3$) shown δ: 138.4-C_1, 121.9- C_2, 117.2- C_3, 149.2-C_4(nitro phenyl), 63.1-C_5, 59.6-C_6, 162.2-C_7(azetidine ring), 121.5-C_8, 138.7-C_9, 129.3-C_{10}, 134.0- C_{11}, 55.9-C_{12}(trifluoro tollyl group), 116.5-C_{13}, 126.5- C_{14}, 127.8- C_{15}, 119.0-C_{16}, 122.2-C_{17}, 120.1C_{18}, 111.8- C_{19}, 137.6-C_{20}(indole ring), 41.0-C_{21},171.0-C_{22}, 155.0-C_{23}, 122.0-C_{24}, 128.6-C_{25}, 162.5-C_{26}, (pyrazolone ring), Yield 58%, m.p.: 175-185^{0}C, *Anal.* Cacld. for (705); C, 51.06; H, 2.55; N, 13.90 found (%); C: 51.04, H: 2.57, N: 13.89.

CONCLUSION

The substitution with phenyl group having a chloro group at p-position showed better activities. The azeditine showed better anti-inflammatory and analgesic activities. Pyrazolone and its derivatives were found to play an important role in medicinal chemistry as herbicidal, fungicidal, bacterial, anti-inflammatory.

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