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SYNTHESIS, ANTIMICROBIAL AND ANTIMALARIAL ACTIVITIES OF SOME CARBAZOLE DERIVATIVES

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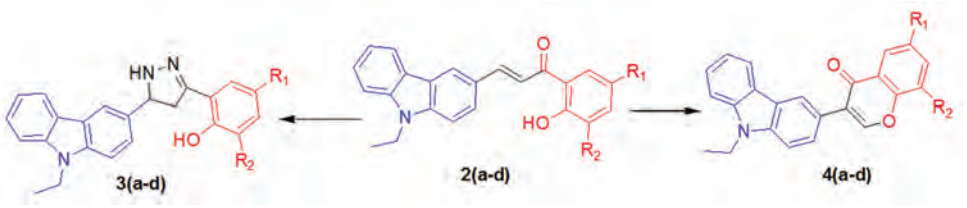
ABSTRACT A series of novel carbazole-tethered pyrazolines and chromone derivatives was synthesized from 9-ethyl-9*H*-carbazole-3-carbaldehyde. The structures of newly synthesized compounds were confirmed by their infrared, nuclear magnetic resonance and mass spectral data. All the synthesized compounds were screened for their *in vitro* antibacterial, antifungal, and antimalarial activity. Some of the synthesized compounds showed comparable or even better antibacterial, antifungal, and antimalarial activities than the reference drugs ampicillin, griseofulvin, and quinine, respectively.



KEYWORDS 9-Ethyl-9*H*-carbazole-3-carbaldehyde, Pyrazolines, Chromones, Antimicrobial, Antimalarial.

INTRODUCTION

Carbazole derivatives are important class of natural alkaloids isolated from different resources such as some genera of higher plants, blue-green algae, and filamentous fungi. Distinguishable interest of synthetic organic chemists has been created considerable attention to these structures due to their capability to accommodate the substituents around the carbazole frame,[1] biological activities, and potential application as pharmacological agents.[2] A large number of natural and synthetic carbazole derivatives have been reported to exhibit various biologically activities such as antimicrobial,[3-7] antitumor,[8-10] antiviral,[11] anti-inflammatory,[12] antimalarial,[13] antidiarrheal,[14] and antioxidant.[15,16]

Pyrazolines and a number of its derivatives have been reported to possess biological properties such as anti-inflammatory,[17] antioxidant,[18] antimicrobial,[19,20] and antimalarial.[21-23] Furthermore, chromone and its derivatives are the most important heterocyclic compounds, which is a common and integral feature of a variety of natural products and pharmacological importance.[24] Chromone derivatives exhibit various biological activities including antimycobacterial, antifungal, anticonvalescent, antimicrobial mushroom tyrosinase inhibition activities,[25-29] and antimalarial.[30] Therefore, pyrazolines and chromones are proved to be a useful starting material for physiologically or pharmacologically important product. In the recent years, studies have shown that carbazole incorporated with some nitrogen-containing heterocyclic moieties such as pyrazolines reported to possess broad spectrum of biological activities such as anti-inflammatory and antioxidant.[31] In light of these finding, it is supposed that the introduction of carbazole moiety to pyrazolines and chromones may

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produce derivatives with considerable antimicrobial and antimalarial activity.

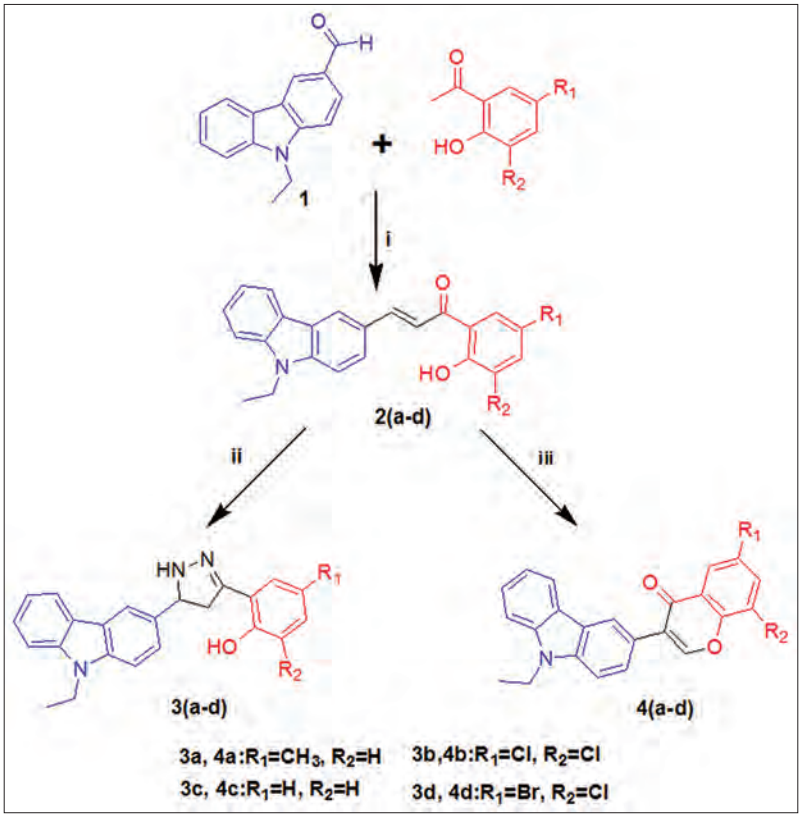
RESULTS AND DISCUSSION

Carbazole-based pyrazolines and chromones were synthesized from carbazole (**1**), which on treatment with substituted *o*-hydroxyacetophenones produces the chalcones **2(a-d)** with the yields of 60-65% in the presence of potassium hydroxide in ethanol. Carbazole chalcones **2(a-d)** reacted with hydrazine hydrate, acetic acid in ethanol give **3(a-d)** with the yields of 45-54%. Finally, **2(a-d)** on treatment with catalytic amount of I_2 in dimethyl sulfoxide (DMSO) solvent produces carbazole chromones **4(a-d)** yield ranging from 48% to 55%. The chemistry of target compounds is quoted in **Scheme 1.**

The infrared (IR) spectrum of representative compound **2b** showed observed characteristic peak at 1651/cm due to the presence of a conjugated carbonyl group -C=O. In ^{1}H nuclear magnetic resonance (NMR) spectrum of 2**B**, the Cα-H and Cβ-H protons appear significantly shifted downfield at 7.27δ and 7.49δ, respectively. These protons can be notable for those of the aromatic ring. Again, the formation of compound **2b** was confirmed by high-resolution mass spectrometry (HRMS). The calculated (M^++H) for compound **2b** is 410.0710 and observed (M^++H) in HRMS at 410.0709. Carbazole pyrazolines **3(a-d)** have been prepared from the compounds **2** by treatment with hydrazine hydrate in ethanol and acetic acid; the reaction most likely takes place through the intervention of an appropriate α, β unsaturated hydrazone, which instantly cyclizes to give a pyrazoline ring, at reflux temperature cyclizing agent is acetic acid. IR spectra δ of the compounds **3(a-d)** revealed a characteristic strong intensity band due to –NH stretching at ~3340^{-1}cm while the pyrazoline -CH band was observed around 2930-3000^{-1}cm. The ^{1}H NMR spectrum of these compounds, exhibited an ABX pattern for the presence of two diastereotopic protons at C-4 and one single proton at the C-5 positions. Asymmetric -CH proton displayed as a triplet, whereas the prochiral methylene (-CH_2) protons appeared as two characteristic doublet of a doublet indicating the magnetic non-equivalence of the two protons. According to the HRMS of representative compound **3b** calculated (M^++H) is 424.0981 and observed (M^++H) in HRMS at 424.0978. Finally, carbazole chromones **4(a-d)** has been synthesized from compound **2** which on treatment with a catalytic amount of I_2 in DMSO at reflux temperature undergoes cyclodehydration reaction to give the target compounds, **4(a-d)**. In the IR spectrum of these compounds the -O-H stretching band disappeared and a new peak ~1615/cm due to chromone -C=O group appeared. Representative compound **4b,** ^{1}H NMR spectrum displayed multiplet at 6.99δ for the C-2 proton of the chromone ring. The calculated (M^++H) for compound **4b** is 408.0478 and observed (M^++H) in HRMS at 408.0475.

ANTIMICROBIAL AND ANTIMALARIAL EVALUATION

All synthesized compounds were studied for their *in vitro* antibacterial activities against Gram-positive bacteria such as



Scheme 1: Reagents and conditions: (i) KOH, ethanol, rt, 24 h. (ii) $NH_2NH_2.H_2O$, acetic acid, ethanol, reflux 6 h (iii) dimethyl sulfoxide, I_2, 140°C, 3 h

Staphylococcus aureus, *Streptococcus pyogenes* and Gram-negative bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa*, and antifungal activity against *Candida albicans*, *Aspergillus niger*. The antimicrobial activity was assessed in terms of minimum inhibitory concentration by a modified microdilution method.[32] The antimalarial activity was evaluated *in vitro* on *P. falciparum* by microassay protocol with minor modification.[33,34]

The obtained data (**Table 1**) showed that the tested compounds **3** and **4** showed good to moderate antibacterial and antifungal activities against *E. coli*, *P. aeruginosa*, *S. aureus*, *S. pyogenes* bacterial, and *A. niger*, *C. albicans* fungal species. Among the synthesized compounds, carbazole-based pyrazolines **3(a-d) 3c** was found to be equipotent against *E. coli* and *S. aureus* bacterial strains. Carbazole-based pyrazolines containing chlorine group **3b** showed an excellent antibacterial and an antifungal spectrum against *E. coli* and *C. albicans* as compared with standard drug ampicillin and griseofulvin, respectively. On the other hand, synthesized carbazole derivatives chromones **4(a-d), 4b,** and **4c** showed promising activity against *E. coli* and *S. pyogenes* bacterial strains. Carbazole-based chromones containing chlorine **4b** showed excellent antibacterial activity with *E. coli*, *S. aureus*, and *S. pyogenes* bacterial strains as compared with standard drug ampicillin. Concerning the antifungal activity of the tested compounds carrying chlorine **4b** and bromine **4d** showed considerable antifungal activity against griseofulvin as a broad-spectrum antifungal agent while remaining compounds showed moderate to very less activity against standard antibacterial and antifungal agents.

The study of antimalarial evaluation data **1** showed that all the tested compounds of **3** and **4** showed satisfactorily activities against *Plasmodium falciparum* using chloroquine and quinine as standard drug. Compound **3b** (0.56 µg/mL) was found moderate antimalarial activity against standard quinine (0.268 µg/mL). Compounds contain chromones moiety **4c** (0.46 µg/mL) and **4d** (0.80 µg/mL) showed promising activity against quinine (0.268 µg/mL) while remaining compounds showed moderate to very less activity against quinine (0.268 µg/mL).

EXPERIMENTAL

The progress of each reaction was monitored by thin layer chromatography (TLC) by n-hexane:ethyl acetate solvent system. Starting compound 9-ethyl-9*H*-carbazole is of Sigma-Aldrich make. Melting points were uncorrected taken in an open capillary tube on a Stuart melting point apparatus. The IR spectra of the compounds were recorded on Shimadzu FTIR spectrometer with KBr pellets. PMR spectrum was recorded on Bruker Avance 400 MHz NMR spectrometer. Chemical shifts (δ) value is denoted in parts per million (ppm) using tetramethylsilane (TMS) as an internal standard. Bruker Daltonics Micro TOF-Q-II attach with electron spray ionization (ESI) was used for HRMS data.

General procedure Synthesis of 9-Ethyl-9*H*-carbazole-3-carbaldehyde (1)

Phosphorus oxychloride (0.008 mol) was added dropwise to dry DMF (0.008 mol) at –10°C. Then, 9-ethyl-9*H*-carbazole (0.002 mol) was added to the Vilsmeier-Haack complex and the reaction mixture heated at 75°C for 3 h. After neutralization with 10% aq $NaHCO_3$, the precipitate was filtered and recrystallized from alcohol.

Table 1: *In vitro* antibacterial, antifungal, and antimalarial activities as MIC (µg/mL) for compounds 3(a-d) and 4(a-d)

Compound	MIC values in µg/mL						MIC µg/mL
	Bacterial strain				Fungal strains		Malarial strain
	E. coli (MTCC443)	*P. aeruginosa* (MTCC1688)	*S. aureus* (MTCC96)	*S. pyogenes* (MTCC 442)	*C. albicans* (MTCC227)	*A. niger* (MTCC282)	*P. falciparum*
3a	250	100	200	125	1000	>1000	1.20
3b	62.5	250	250	250	500	500	0.56
3c	100	125	250	100	>1000	500	0.88
3d	250	100	250	250	500	>1000	1.45
4a	200	200	250	125	>1000	1000	1.40
4b	62.5	125	100	100	500	>1000	1.20
4c	100	125	250	62.5	>1000	250	0.46
4d	250	200	200	200	250	500	0.80
Ampicillin[a]	100	---	250	100	---	---	---
Chloramphenicol[b]	50	50	50	50	---	---	---
Griseofulvin[c]	---	---	---	---	500	100	---
Chloroquine[d]	---	---	---	---	---	---	0.020 µg/mL
Quinined	---	---	---	---	---	---	0.268 µg/mL

[a]Ampicillin (standard broad-spectrum antibiotic), [b]chloramphenicol (standard broad-spectrum antibiotic), [c]griseofulvin (standard broad-spectrum antifungal agent), [d]standards taken for antimalarial activity, *E. coli: Escherichia coli*, *P. aeruginosa: Pseudomonas aeruginosa*, *S. aureus: Staphylococcus aureus*, *S. pyogenes: Streptococcus pyogenes*, MIC: Minimum inhibitory concentration

General procedure for the synthesis of (9-ethyl-9*H*-carbazole-6-yl)-1-(2-hydroxy-substituted) Prop-2-en-1-one, 2(a-d)

9-Ethyl-9*H*-carbazole-3-carbaldehyde (0.005 mol), substituted *o*-hydroxy acetophenones (0.005 mol), and 2 gm KOH were dissolved in 15 mL ethanol, at room temperature reaction mixture was stirred for 24 h. Completion of the reaction was identified by TLC. Finally, the reaction mixture was poured with crushed ice, acidified with concentrated HCl and the solid obtained was filtered and recrystalized from ethanol afford the target compounds **2(a-d)**.

3-(9-Ethyl-9H-carbazol-6-yl)-1-(2-hydroxy-5-methylphenyl)prop-2-en-1-one (2a)

Yellow solid; m.p 182-183°C; Yield 65%; IR (KBr) ν_{max} (cm^{-1}): 3590 (OH), 1660 (C=O), 1602 (C=C), 1209 (C-O). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.38 (t, 3H, J=7.1Hz, CH_2CH_3); 2.39 (s, 3H, Ar-CH_3); 4.44 (q, 2H, J=7.1Hz, N-CH_2); 6.86 (m, 1H, Cα-H); 7.25 (m, 1H, Cβ-H); 7.33-7.48 (m, 2H, Ar-H); 7.57-7.63 (m, 2H, Ar-H); 7.99-8.11 (m, 4H, Ar-H); 8.18 (m, 1H, Ar-H); 8.69 (m, 1H, Ar-H) and 12.84 (s, 1H, Ar-OH). HRMS (M^++H) 356.1643, found 356.1645.

(3,5-Dichloro-2-hydroxyphenyl)-3-(9-ethyl-9H-carbazol-6-yl)prop-2-en-1-one (2b)

Yellow solid; m.p 202-203°C; Yield 63%; IR (KBr) ν_{max} (cm^{-1}): 3600 (OH), 1651 (C=O), 1610 (C=C), 1190 (C-O), 1085 (C-Cl). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.39 (t, 3H, J=7.2 Hz, CH_2CH_3); 4.46 (q, 2H, J=7.2 Hz, N-CH_2); 7.27 (m, 1H, Cα-H); 7.49 (m, 1H, Cβ-H); 7.58-7.74 (m, 3H, Ar-H); 8.01-8.23 (m, 4H, Ar-H); 8.46 (m, 1H, Ar-H); 8.76 (m, 1H, Ar-H) and 13.85 (s, 1H, Ar-OH). HRMS (M^++H) 410.0710, found 410.0709.

3-(9-Ethyl-9H-carbazol-6-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one (2c)

Yellow solid; m.p 252-253°C; Yield: 60%; IR (KBr) ν_{max} (cm^{-1}): 3585 (-OH), 1654 (-C=O), 1609 (C=C), 1215 (-C-O). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.35 (t, 3H, J=7.1Hz, CH_2-CH_3); 4.25 (q, 2H, J=7.1Hz, N-CH_2); 6.90 (m, 1H, Cα-H); 7.50 (m, 1H, Cβ-H); 7.40-7.49 (m, 3H, Ar-H); 7.80-7.90 (m, 4H, Ar-H); 8.0-8.11(m, 4H, Ar-H) and 10.06 (s, 1H, Ar-OH). HRMS (M^++H) 342.1416, found 342.1414.

1-(5-Bromo-3-chloro-2-hydroxyphenyl)-3-(9-ethyl-9H-carbazol-6-yl)prop-2-en-1-one (2d)

Yellow solid; m.p 246-247°C; Yield 63 %; IR (KBr) ν_{max} (cm^{-1}): 3595 (OH), 1653 (C=O), 1608 (C=C), 1205 (C-O), 885 (C-Br). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.40 (t, 3H, J=7.4 Hz, CH_2-CH_3); 4.57 (q, 2H, J=7.4 Hz, N-CH_2); 7.48 (m, 1H, Cα-H); 7.56 (m, 1H, Cβ-H); 7.93-8.20 (m, 4H, Ar-H); 8.25-8.38 (m, 3H, Ar-H); 8.40-8.58 (m, 3H, Ar-H) and 12.01 (s, 1H, Ar-OH). HRMS (M^++H) 420.0521, found 420.0520.

General procedure for the synthesis of 2-(5-(9-ethyl-9*H*-carbazol-6-yl)-4,5-dihydro-1H-pyrazol-3-yl) substituted phenols, 3(a-d)

To a solution of chalcone (2a-d, 0.005 mol) in 15 mL of ethanol, was added 0.5 mL hydrazine hydrate and 0.2 mL acetic acid. The reaction mixture was heated at reflux temperature for 6 h. Completion of reaction (monitored by TLC, ethyl acetate:hexane solvent) and the reaction mixture was cooled to room temperature. Then, slowly add 15 mL cold water to the flask, the solid was obtained wash with cold water, recrystallized by ethyl alcohol to afford the target compounds **3(a-d)**.

2-(5-(9-Ethyl-9H-carbazol-6-yl)-4,5-dihydro-1H-pyrazol-3-yl)-4-methylphenol (3a)

White solid; m.p 119-120°C; Yield 54%; IR (KBr) ν_{max} (cm^{-1}): 3335 (NH), 2930 (CH), 1685 (C=N), 1585 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.37 (t, 3H, J=7.6 Hz, CH_2-CH_3); 1.94 (s, 3H, Ar-CH_3); 3.25 (dd, 1H, J=10.7 & 5.9 Hz, pyrazoline ring); 3.50 (dd, 1H, 1H, J=10.7 & 5.9 Hz, pyrazoline ring); 4.25 (q, 2H, J=7.6 Hz, N-CH_2); 5.15 (t, 1H, 1H, J=10.7Hz, pyrazoline ring); 7.26-7.45 (m, 4H, Ar-H); 7.50-7.69 (m, 3H, Ar-H); 7.75-7.88 (m, 3H, Ar-H); 8.10(m, 1H, N-H) and 12.26 (s, 1H, Ar-OH). HRMS (M^++H) 370.1914, found 370.1914.

2,4-Dichloro-6-(5-(9-ethyl-9H-carbazol-6-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenol (3b)

white solid; m.p 135-136°C; Yield 43%; IR (KBr) ν_{max} (cm^{-1}): 3332 (NH), 2935 (CH), 1688 (C=N), 1590 (C=C), 1095 (C-Cl). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.35 (t, 3H, J=7.5Hz, CH_2-CH_3); 3.13 (dd, 1H, J=10.6 & 5.8 Hz, pyrazoline ring); 3.63 (dd, 1H, J=10.6 & 5.8 Hz, pyrazoline ring); 4.38 (q, 2H, J=7.5 Hz, N-CH_2); 5.10 (t, 1H, J=10.6 Hz, pyrazoline ring); 7.16-7.33 (m, 3H, Ar-H); 7.41-7.50 (m, 4H, Ar-H); 8.01 (m, 2H, Ar-H); 8.13 (m, 1H, N-H) and 12.01 (s, 1H, Ar-OH). HRMS (M^++H) 424.0981, found 424.0978.

2-(5-(9-Ethyl-9H-carbazol-6-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenol (3c)

White solid; m.p 158-159°C; Yield 45%; IR (KBr) ν_{max} (cm^{-1}): 3340 (NH), 3000 (CH), 1680 (C=N), 1579 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.38 (t, 3H, J=7.8 Hz, CH_2-CH_3); 3.52 (dd, 1H, J=10.9 & 5.8 Hz, pyrazoline ring); 3.60 (dd, 1H, J=10.9 & 5.8 Hz, pyrazoline ring); 4.36 (q, 2H, J=7.8 Hz, N-CH_2); 4.90 (t, 1H, pyrazoline ring); 6.90-7.80 (m, 7H, Ar-H); 7.88-8.05 (m, 3H, Ar-H); 8.25 (m, 1H, N-H) and 11.72 (s,1H, Ar-OH). HRMS (M^++H) 356.1685, found 356.1683.

4-Bromo-2-chloro-6-(5-(9-ethyl-9H-carbazol-6-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenol (3d)

White solid; m.p 255-256°C; Yield 48 %; IR (KBr) ν_{max} (cm^{-1}): 3335 (NH), 2932 (CH), 1681 (C=N), 1581 (C=C), 890 (C-Br). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.36 (t, 3H, J= 7.8 Hz, CH_2-CH_3); 3.23 (dd, 1H, J=10.8 & 5.8 Hz, pyrazoline ring); 3.36 (m, 1H, J=10.8 & 5.8 Hz, pyrazoline ring); 4.30 (q, 2H, J=7.8 Hz, N-CH_2); 4.86 (m, 1H, pyrazoline ring); 7.15-7.65 (m, 4H, Ar-H); 7.75-8.10 (m, 6H, Ar-H); 8.36 (m, 1H, N-H) and 11.80 (s, 1H,). HRMS (M^++H) 434.0792, found 434.0790.

General procedure for the synthesis of 3-(9-ethyl-9H-carbazol-6-yl)-substituted-4H-chromen-4-ones 4(a-d)

To a solution of chalcone (2a-d, 0.005 mol) in 10 ml of DMSO was added catalytic amount of I_2 (50 mg). The

reaction mixture was reflux at 140°C for 3h, progress of the reaction was monitored by TLC using ethyl acetate: hexane as the solvent system. Reaction mixture was cooled to room temperature, and 10 mL cold water was slowly added. The formed precipitate was filtered off recrystallized by ethanol, afford the target compounds **4(a-d).**

3-(9-Ethyl-9H-carbazol-6-yl)-6-methyl-4H-chromen-4-one (4a)

Brown solid; m.p 149-150°C; Yield 49%; IR (KBr) ν_{max} (cm^{-1}): 2885 (C=CH), 1610 (C=O), 1578 (C=C), 1180 (C-O). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.39 (t, 3H, J=7.8 Hz, CH_2-CH_3); 2.39 (s, 3H, Ar-CH_3); 4.40 (q, 2H, J=7.8 Hz, N-CH_2); 6.85 (m, 1H, chromone ring); 7.50 -7.80 (m, 4H, Ar-H); 8.15-8.60 (m, 3H, Ar-H) and 8.75-9.0 (m, 3H, Ar-H). HRMS (M^++H): 354.1418, found 354.1417.

6,8-Dichloro-3-(9-ethyl-9H-carbazol-6-yl)-4H-chromen-4-one (4b)

Brown solid; m.p 158-160°C; Yield 55 %; IR (KBr) ν_{max} (cm^{-1}): 2880 (-C=CH), 1615 (C=O), 1581 (C=C), 1190 (C-O), 1075 (C-Cl). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.37 (t, 3H, J=7.9 Hz, CH_2-CH_3); 4.47 (q, 2H, J=7.9 Hz, N-CH_2); 6.99 (m, 1H, chromone ring); 7.46 -7.81 (m, 4H, Ar-H) and 8.01-8.94 (m, 5H, Ar-H). HRMS (M^++H): 408.0478, found 408.0475.

3-(9-Ethyl-9H-carbazol-6-yl)-4H-chromen-4-one (4c)

Brown solid; m.p 170-171°C; Yield 52%; IR (KBr) ν_{max} (cm^{-1}): 2875 (C=CH), 1618 (C=O), 1575 (C=C), 1185 (C-O). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.42 (t, 3H, J=7.8 Hz, CH_2-CH_3); 4.29 (q, 2H, J=7.8 Hz, N-CH_2); 6.88 (m, 1H, chromone ring); 7.75-8.35 (m, 8 H, Ar-H) and 8.55 (m, 3H, Ar-H). HRMS (M^++H): 340.1260, found 340.1259.

6-Bromo-8-chloro-3-(9-ethyl-9H-carbazol-6-yl)-4H-chromen-4-one (4d)

Brown solid; m.p185-186°C; Yield 48 %; IR (KBr) ν_{max} (cm^{-1}): 2888 (C=CH), 1614 (C=O), 1581 (C=C), 1178 (C-O), 878 (C-Br). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.45 (t, 3H, J=7.5 Hz, CH_2-CH_3); 4.15 (q, 2H, J=7.5 Hz, N-CH_2); 6.80 (m, 1H, chromone ring); 7.56-7.80 (m, 7H, Ar-H) and 8.10-8.86 (m, 3H, Ar-H). HRMS (M^++H): 418.0362, found 418.0361.

CONCLUSION

We have synthesized and evaluated the biological potential of some new carbazole pyrazolines and chromones. All novel synthesized compounds show moderate to promising antimicrobial activity against a moderate range of bacterial and fungal strains as compared with standard drug ampicillin, chloramphenicol and griseofulvin, respectively. Among the compound tested, **3b, 3c, 4b,** and **4c** exhibited pronounced antibacterial activities, and **4d** was created attention of its two-fold more antifungal activity against *C. albicans* comparable to positive control. Concerning the antimalarial activity of tested compounds **3b, 4c,** and **4d** were able to exhibit good antimalarial potency. As structure-activity relationship, study of all compounds (**2,3**) was taken into account; it was observed that compounds having electron withdrawing groups such as chloro and bromo showed excellent potential of antimicrobial and antimalarial activity. Furthermore, compounds containing moderate electron releasing group methyl was able to produce moderate growth inhibitory activity against *S. aureus* bacterial strain.

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