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SYNTHESIS AND ANTIMICROBIAL ASSESSMENT OF EFFICACIOUS CARBAZOLE DERIVATIVES

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ABSTRACT

Rooted in invigorating pharmacological applications of carbazole, herein a successful synthesis of some novel and highly potent carbazole derivatives by economically viable means using casual laboratory agents and robust synthetic strategies is detailed. A short linear sequence has been followed to furnish the desired effectual molecules (2-8) having promising anti-microbial activities. All new analogues have been characterized by UV-Vis, FTIR, ^{1}H and ^{13}C NMR, MS and elemental analysis data. The novel chemical moieties have been tested for their bactericidal activity against Methicillin-resistant *Staphylococcus aureus, Escherichia coli* and for fungicidal property against *Aspergillus flavus* using agar well diffusion assay showing remarkable antimicrobial potential.

KEYWORDS: Carbazole derivatives, Synthesis, Antibacterial activity, Fungicidal property

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1. INTRODUCTION

Carbazoles represent one of the most valuable ring systems in the modern synthetic chemistry, because of their widely recognized versatility as significant intermediates for the synthesis of compounds with biological and pharmacological activities such as anti-microbial[1] and anti-cancer[2]. Efficient synthetic avenues have been developed for structurally adapted analogues[3] which are well documented since its first isolation.[4] Since then, a variety of methods have been introduced for the synthesis of functionalized carbazoles particularly at positions 3, 6 and 9 has become one of the most useful strategies to this class of compounds.[5-7] The prevalence of this compound in medicinal field has always inspired academic researchers to carry on working on this potent molecule.[8] Recently, different carbazole derivatives have been used in photodynamic therapy[9] . Due to these properties, the synthetic interest to functionalize the core structure of carbazole has re-emerged adding enormous value to the biological activities of this compound. These include the reported synthesis of its thiazole, thiazolidine, azetidinone[10], pyrimido[11] and pyrido[12] derivatives. Keeping these findings in our close observation, we aimed to synthesize novel and potent carbazole derivatives having diversely important substitutions. This derivatization will potentially lead to further modification of this pharmacological imperative molecule into prospective drug candidates like carbazomycin class - well known antibiotic agents containing carbazole motif.[13] Moreover, Vetprofen[14], Ondansetron[15] and Carvedilol[16] are renown therapeutics having this skeleton as a core structural unit (Figure 1).

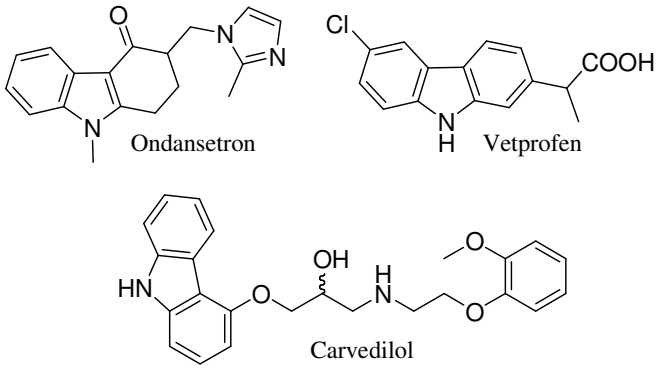


FIGURE 1
Some medicinally important carbazole derivatives

2. MATERIALS AND METHODS

All the chemical reagents and solvents used for this experimental section were of AR grade. Analytical TLC was carried out on silica gel pre-coated Aluminum based sheets (Merck 60 F_{254}, 0.2 mm thick) using different solvents. Spots were observed under UV light at 254/365 nm (CAMAG scientific Inc). Melting points were determined by open capillary method and are uncorrected. U-2800 Hitachi, UV-visible spectrophotometer was used for finding $\lambda_{max.}$ KBr disks were used to record FTIR spectra on Midac Corporation FTIR spectrophotometer and values were reported in cm^{-1}. Proton and carbon NMR spectra were measured on Bruker AXS 300 MHz spectrometer using TMS as an internal standard and DMSO-d_6 as solvent (chemical shift in δ, ppm). Mass spectra were recorded by GCMS-QP2010S Shimadzu Scientific Instruments, Inc. and elemental

analysis on Perkin Elmer 2400 CHN elemental analyzer.

2.1 Experimental procedures for the compounds (2-8)

(i) Synthesis of 3-Methyl carbazole (2)

The solution of carbazole **1** (0.167 g, 1 mmol) in CCl_4 (5 mL) was added CH_3I (0.170 g, 1.2 mmol) and refluxed for 5 hours. The neutral pink contents were allowed to ice cool and filtered with suction. The off-white crude product was washed with MeOH and recrystallized from acetone to afford pure 3-methyl carbazole 2 (0.156 g, 0.86 mmol, 87%).

State: White crystals; M.p. 234 ˚C.

UV λ_{max} (MeOH): 257, 332, 338 nm.

IR (KBr, v_{max}, cm^{-1}): 690 and 746 (benzenoid pattern), 1580 (C=C), 2860 (C-H), 3014 (C-H), 3417 (NH).

^{1}H-NMR (DMSO-d_6, ppm) δ: 2.34 (s, 3H, CH_3), 6.89 (d, J = 7.7 Hz, 1H, H-2), 7.01 (dd, J = 7.7, 8.0 Hz, 1H, H-6), 7.10 (dd, J = 7.7, 7.9 Hz, 1H, H-7), 7.29 (d, J = 7.3 Hz, 1H, H-1), 7.33 (s, 1H, H-4), 7.39 (d, J = 7.8 Hz, 1H, H-8), 7.53 (d, J = 7.4 Hz, 1H, H-5), 9.9 (s, 1H, NH).

^{13}C-NMR (DMSO-d_6) δ: 25.1, 106, 110, 110.2, 118.2, 119.3, 119.8, 119.9, 122.4, 124.3, 128.5, 131.2, 132.3.

MS (ES^+): 181.12 (MH^+); Anal. calcd for $C_{13}H_{11}N$ (Found): C 86.20 (86.23), H 6.07 (6.05), N 7.75 (7.71).

(ii) Oxidation of 2 to carbazole-3-carboxylic acid (3)

The freshly prepared saturated solution of $K_3[Fe(CN)_6]$ in NaOH (20 mL) was slowly added 3-methylcarbazole (1.81 g, 10 mmol) at reflux point having temperature 220-240 ˚C. At this homogenized stage, pyridine (0.5 mL) was added as catalyst. After 4.5 hours, the flask contents were allowed to cool in ice bath. The crude yellow precipitates turned to bluish green color after acidification with concentrated HCl (2.5 mL). Precipitates were filtered, dried and recrystallized from acetone to achieve product **3** (1.9 g, 9 mmol, 90%).

State: Blue amorphous powder; M.p. decomposes.

UV λ_{max} (MeOH): 275, 287, 315 nm.

IR (KBr, v_{max}, cm^{-1}): 690, 746, 1237 (C-O), 1580, 1638 (C=O), 3014, 3417, 3424 (OH of COOH); ^{1}H-NMR (DMSO-d_6, ppm) δ: 7.01 (dd, J = 7.7, 8.0 Hz, 1H), 7.10 (dd, J = 7.7, 7.9 Hz, 1H), 7.29 (d, J = 7.3 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 7.4 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H, H-2), 8.43 (s, 1H, H-4), 9.9 (s, 1H), 10.70 (s, 1H, COOH).

^{13}C-NMR (DMSO-d_6) δ: 106.3, 110.2, 110.5, 114.2, 119.2, 120.5, 121.8, 122.5, 123.5, 124.3, 132.2, 140.3, 168.5.

MS (ES^+): 211.09 (MH^+); Anal. calcd for $C_{13}H_9NO_2$ (Found): C 73.95 (73.94), H 4.25 (4.27), N 6.66 (6.63), O 15.13 (15.15).

(iii)Synthesis of 4-allyl-2-methoxyphenyl 9H-carbazole-3-carboxylate (4):

The carboxylic acid **3** (2.11 g, 10 mmol) in dry DMF (25 mL) was mixed with eugenol (4.92 g, 30 mmol) and stirred at room temperature for 10 min. After the addition of conc. H_2SO_4 (2 mL, 37 mmol), it was refluxed for 2 hours. The blackish blue reaction mixture was allowed to cool to room temperature and neutralized with $NaHCO_3$ (30 mL). From this, ester was quenched with DCM (50 mL) and the organic layer was dried to get product 4 (2.96 g, 8.29 mmol, 83%).

State: Black gummy; M.p. -.

UV λ_{max} (MeOH): 243, 276, 352 nm.

IR (KBr, v_{max}, cm^{-1}): 690, 746, 790, 920, 1237, 1580, 1644 (C=C), 1700 (O=C-O), 2734 (CH_2), 3014, 3417, 3485 (NH).

^{1}H-NMR (DMSO-d_6, ppm) δ: 3.21 (d, J = 7.7 Hz, 2H), 3.73 (s, 3H, OCH_3), 4.93 (m, 1H), 4.95 (m, 1H), 6.31 (m, 1H), 6.63 (s, 1H), 6.85 (d, J = 7.5 Hz, 1H), 6.94 (d, J = 7.4 Hz, 1H), 7.01 (dd, J = 7.7, 8.0 Hz, 1H), 7.10 (dd, J = 7.7, 7.9 Hz, 1H), 7.29 (d, J = 7.3 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 7.4 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H), 8.43 (s, 1H), 9.9 (s, 1H).

^{13}C-NMR (DMSO-d_6) δ: 48.5, 55.9, 110.3, 110.4, 106.1, 113.2, 114.2, 117.3, 119.0, 120.4, 121.9, 121.9, 122.2, 122.3, 123.3, 124.1, 132.1, 135.6, 135.8, 136.2, 140.5, 157.1, 165.5.

MS (ES^+): 357.14 (MH^+); Anal. calcd for $C_{23}H_{19}NO_3$ (Found): C 77.29 (77.30), H 5.35 (5.34), N 3.96 (3.98), O 13.41 (13.38).

(iv) Synthesis of quinolin-8-yl 9H-carbazol-3-carboxylate (5)

Compound **3** (0.211g, 1 mmol) in anhydrous DMF (5 mL) was allowed to mix with 8-hydroxyquinoline (0.435 g, 3 mmol) in small portions followed by concentrated H_2SO_4 (0.3 mL) with stirring at room temperature for a while and then converted to reflux for 2 hours. The reaction mixture was cooled to 30 ˚C, treated with $NaHCO_3$ (15 mL) and quenched with EtOAc (25 mL). The organic phase was separated, dried (Na_2SO_4), filtered and concentrated on rotary evaporator to get rude precipitates. Purification by recrystallization (MeOH) afforded the title ester 5 as grey precipitates (0.30 g, 0.88 mmol, 89%).

State: Greyish crystals; M.p. 260 ˚C.

UV λ_{max} (MeOH): 244, 274, 352 nm.

IR (KBr, v_{max}, cm^{-1}): 1236 (C-O), 1399 (C-N), 1580, 1640 (aromatic), 1675 (C=N), 1745 (C=O), 3014, 3412 (NH), 3417.

^{1}H-NMR (DMSO-*d_6*, ppm) δ: 6.83 (d, J = 7.01 Hz, 1H), 7.01 (dd, J = 7.7, 8.0 Hz, 1H), 7.10 (dd, J = 7.7, 7.9 Hz, 1H), 7.26 (dd, J = 7.5, 8.2 Hz, 1H), 7.29 (d, J = 7.3 Hz, 1H), 7.30 (dd, J = 7.6, 8.2 Hz, 1H),7.31 (d, J = 7.51 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 7.4 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H), 8.04 (d, J = 7.11 Hz, 1H), 8.43 (s, 1H), 8.89 (d, J = 7.09 Hz, 1H), 9.9 (s, 1H).

^{13}C-NMR (DMSO-*d_6*) δ: 106.1, 110.6, 110.7, 112.2, 114.3, 119.2, 120.3, 121.4, 121.9, 122.2, 122.3, 123.7, 124.2, 127, 129.4, 131.2, 136.1, 137.9, 140.7, 150.2, 152.5, 165.1.

MS (ES^+): 338.15 (MH^+); Anal. calcd for $C_{22}H_{14}N_2O_2$ (Found): C 78.05 (77.09), H 4.22 (4.21), N 8.25 (8.23), O 9.47 (9.51).

(v) Synthesis of 3-Nitro carbazole (6)

Carbazole **1** (0.48 g, 2.85 mmol) in glacial CH_3COOH (5 mL) was added 65% conc. HNO_3 (2 mL, 47.9 mmol) at laboratory temperature. The reaction mixture as dirty green precipitates was stirred for 5 hours. After this, the flask contents were cooled to 5 ˚C to ensure complete precipitation and filtered through suction. The crude product was washed with cold distilled water and recrystallized from acetone to furnish 3-nitro carbazole (0.56 g, 4.7 mmol, 93%).

State: Yellow brown crystals; M.p. 360 ˚C.

UV λ_{max} (MeOH): 217, 263, 313 nm.

IR (KBr, v_{max}, cm^{-1}): 710, 735, 1335 (NO_2), 1580, 3014, 3460 (NH).

^{1}H-NMR (DMSO-*d_6*, ppm) δ: 7.09 (dd, J = 7.7, 7.9 Hz, 1H), 7.10 (dd, J = 7.7, 8.0 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 7.3 Hz, 1H), 7.65 (d, J = 7.7 Hz, 1H), 8.05 (d, J = 7.4 Hz, 1H), 8.45 (s, 1H), 9.80 (s, 1H).

^{13}C-NMR (DMSO-*d_6*) δ: 106.1, 111.2, 112.2, 114.9, 115.3, 119.3, 119.9, 122.2, 124.2, 132, 141.5, 141.9.

MS (ES^+): 212.05 (MH^+); Anal. calcd for $C_{12}H_8N_2O_2$ (Found): C 67.95 (67.92), H 3.81 (3.85), N 13.24 (13.27), O 15.03 (15.01).

(vi) Reduction of 6 to 3-Amino carbazole (7)

To the well stirred mixture of compound **6** (0.425 g, 2.0 mmol) and $SnCl_2$ (0.758 g, 4.0 mmol) was gradually added conc. HCl (1.5 mL, 61.2 mmol) at room temperature and then converted to reflux on water bath for 1 hour. Precipitates appeared after cooling were basified with strong alkaline solution (6 mL), indicted by pH paper. The crude mass was filtered, washed with distilled water (15 mL) and recrystallized from MeOH to get product **7** as pure precipitates (0.34 g, 1.86 mmol, 93%).

State: Brown crystals; M.p. 380 ˚C.

UV λ_{max} (MeOH): 217, 255, 376 nm.

IR (KBr, v_{max}, cm^{-1}): 695, 740, 1250 (C-N), 1580, 3014, 3324 (NH_2), 3430 (NH).

^{1}H-NMR (DMSO-*d_6*, ppm) δ: 6.25 (d, J = 7.4 Hz, 1H,H-2), 6.73 (s, 1H, H-4), 7.03 (s, 2H, NH_2), 7.09 (dd, J = 7.7, 7.9 Hz, 1H), 7.10 (dd, J = 7.7, 8.0 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 7.3 Hz, 1H), 7.65 (d, J = 7.7 Hz, 1H), 9.80 (s, 1H).

^{13}C-NMR (DMSO-*d_6*) δ: 104.3, 105.6, 107.5, 111.3, 111.8, 119.2, 120.4, 122.1, 124.5, 125.9, 132.3, 143.5.

MS (ES^+): 182.05 (MH^+); Anal. calcd for $C_{12}H_{10}N_2$ (Found): C 79.15 (79.20), H 5.49 (5.50), N 15.31 (15.32).

(vii) Synthesis of (E)-N-((1H-Indol-3-yl)methylene)-9H-carbazoel-3-amine (8)

The compound **7** (0.182 g, 1 mmol) in MeOH (15 mL) was added solution of indole-3-carboxyaldehyde (0.174 g, 1.2 mmol) in MeOH (15 mL) and stirred at room temperature for 20

min. At this stage, conc. H_2SO_4 (1 mL, 18.8 mmol) was added that readily changed the brown color of reaction mixture to reddish tinge. The flask contents were refluxed for 3 hours and then concentrated *in vacuo* to afford the product 8 as gummy liquid (0.27 g, 0.87 mmol, 87%).

State: Dark red semi solid; M.p. -.

UV λ_{max} (MeOH): 227, 288, 354 nm.

IR (KBr, ν_{max}, cm^{-1}): 690, 735, 1585 (aromatic nucleus), 1685 (C=N), 3040, 3410 (NH).

^{1}H-NMR (DMSO-d_6, ppm) δ: 7.02 (dd, J = 7.8, 7.9 Hz, 1H), 7.09 (dd, J = 7.7, 7.9 Hz, 1H), 7.10 (dd, J = 7.7, 8.0 Hz, 1H), 7.30 (s, 1H), 7.30 (d, J = 7.6 Hz, 1H, H-2), 7.41 (d, J = 7.5 Hz, 1H), 7.44 (dd, J = 7.8, 7.9 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.51 (s, 1H), 7.52 (d, J = 7.5 Hz, 1H), 7.56 (s, 1H, H-4), 7.56 (d, J = 7.3 Hz, 1H), 7.65 (d, J = 7.7 Hz, 1H), 9.90 (s, 1H), 10.02 (s, 1H).

^{13}C-NMR (DMSO-d_6) δ: 103.4, 105.8, 110.8, 111.3, 112.5, 112.8, 119.2, 119.5, 120.2, 120.6, 122.1, 122.4, 124.2, 124.9, 126.3, 130.9, 132.9, 134.4, 135.9, 142.1, 159.5.

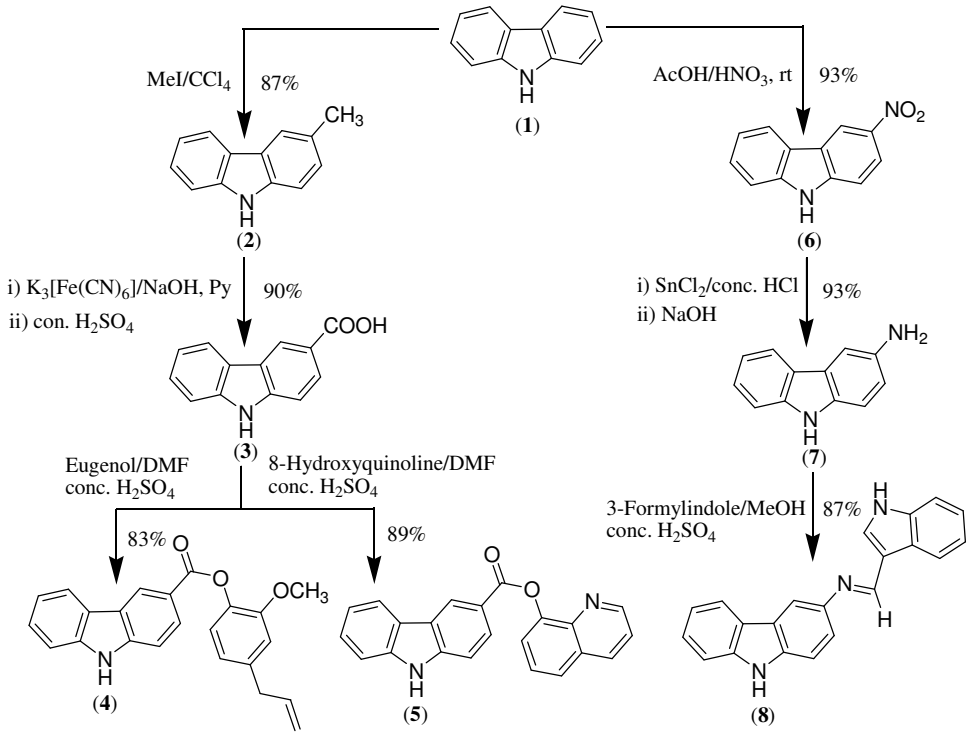
MS (ES^+): 309.10 (MH^+); Anal. calcd for $C_{21}H_{15}N_3$ (Found): C 81.55 (81.53), H 4.85 (4.89), N 13.60 (13.59).

2.2 Antimicrobial Assay

The instruments used in this study include Muller Hinton agar (Scharlau Chemie, 1-136), Potato dextrose agar (Oxoid Ltd., England), Laminar flow cabinet (Local made by Technico scientific supplier (blower, fluorescent and UV light), Incubator (Ehret, BK4444), Autoclave (Hirayama, HVA-110, Maximum pressure = 4 bar), Refrigerator (Capacity 14CFt, Model 9188 MDS, Dawlance), Microwave oven (Capacity 43 liter, Model 55-APB-9, Orient).

3. RESULTS AND DISCUSSION

As part of our research plan directed to the use of substitution methodology, we envisaged to synthesize mono substituted derivatives followed by further structural modifications leading to a range of novel bioactive moieties. Knowing the fact that the C-3 and C-6 of the tricyclic ring of carbazole is susceptible to substitution, interesting synthetic strategies were designed to construct a library of potent mono substituted carbazole derivatives. Among all the seven synthesized compounds, five compounds (2, 3, 4, 5 and 8) are novel structures while compounds 6 and 7 were prepared *via* new synthetic routes (Scheme 1). All compounds were fully characterized by UV-visible, FTIR, ^{1}H and ^{13}C-NMR, MS and CHN analysis techniques to confirm their structures. A facile approach of methylation was adopted using methyl iodide under reflux conditions in a ratio of 1.2:1 with carbazole. R_f value of product 2 was same as observed for compound 1



Scheme 1
Synthetic strategy for carbazole analogues (2-8)

However, the product had comparatively more fluorescence intensity under UV light. We believe that this substitution at position 3 is favored due to the heterocyclic amine which activates the ring towards electrophilic substitution as compared to inactivated phenyl ring even in the absence of catalyst. The reaction conditions were optimized using different solvents and reaction times as shown in table 1.

Table 1
Reaction conditions for the synthesis of 2

Solvent	Yield (%)	Time (h)
CCl_4/N_2	87	1.25
CCl_4	87	5.00
C_2H_5OH	49	5.45
CH_2Cl_2	35	6.50

Carbon tetrachloride was found to be the best choice of solvent in terms of yield and the reaction time. This may be due to polarity of ethanol for this reaction giving 49% yield, while the low boiling point of dichloromethane is probably not sufficient for the reaction activation affording only 35% yield. The same solvents when tried under inert condition, using nitrogen, the reaction time greatly reduced to one fourth without affecting the yield of the reaction appreciably. The pH of the reaction was also monitored using NaOH solution. It was found that the basic reaction conditions also had no or very little effect on the reaction outcome. This methylation is very significant because it allows further structural modification such as oxidation to carboxylic acid derivative 3. Pure crystals of compound 2 were oxidized under reflux conditions using a mild oxidizing agent; potassium ferricyanide in 0.5 M NaOH to afford compound 3. No product was observed when the concentration of sodium hydroxide was doubled. The corresponding acid 3 was successfully treated with eugenol in DMF using conc. sulfuric acid as a catalyst to yield ester 4. The crude reaction mixture was treated with

$NaHCO_3$ to dissolve unreacted acid and the product was extracted with CH_2Cl_2. Treatment of acid 3 with 8-hydroxyquinoline afforded another novel analogue 5 using the same procedure applied to the synthesis of ester 4, the reaction activation affording only 35% yield.

Solvent free nitration of carbazole was successfully carried out in an acidic condition at ambient temperature. Using 65% conc. HNO_3, 3-nitrocarbazole (6) was formed predominantly along with 3, 6-dinitro- and 1-nitro derivative of the corresponding molecule as side products. It is observed that when the reaction time was increased, the 1-nitro derivative might be diminished due to intramolecular migration of nitro group from position 1 to position 3.[17] The strength of nitrating agent and the reaction time are the key factors to control the nitration on this nucleus. It is also reported that the stoichiometric ratio of nitric and acetic acid solution yields 1- and 3-nitrocarbazole in 3:7 ratio approximately. The desire product may form by an intramolecular rearrangement of nitro group from position 9 to 1 and then further migration at position 3 of carbazole.[18] Here the rearrangement reaction is responsible for nitro substitution on heterocyclic ring instead to follow electrophilic substitution pathway.[18] Reduction of nitro compound 6 afforded its amino derivative 7 in an excellent yield. Amine functional group in the carbazole ring is prone to further functional group modifications such as amide and imine formation, coordination complexes, diazotization *etc*. For the synthesis of the compound 8, amine derivative 7 was refluxed with 3-formyl indole in methanol. This reaction was also performed in ethanol to evaluate the diversity of the reaction. This change of solvent resulted in lowering the reaction yield, hence not favorable. The rate of the reaction was enhanced by the use of conc. H_2SO_4 as a catalyst while in the presence catalyst (NaOH), no product was achieved. The product remains in semi-solid form even after azeotropic removal of the solvent.

In vitro antimicrobial screening of all the compounds (2-8) was performed against *Escherichia coli* (*E. coli*), Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Aspergillus flavus* (*A. flavus*) through agar well diffusion method.[19] MRSA is widely believed to cause human infections in soft tissues, abscess, skin, bones, joints, respiratory track and heart valves, resulting in high mortality rate worldwide.[20] *E. coli* is chiefly responsible for food poisoning, severe diarrhea, urinary infections and cramps.[21] *A. flavus* causes lungs aspergillosis, nasoorbital, otomycotic infections and aflatoxins.[22]

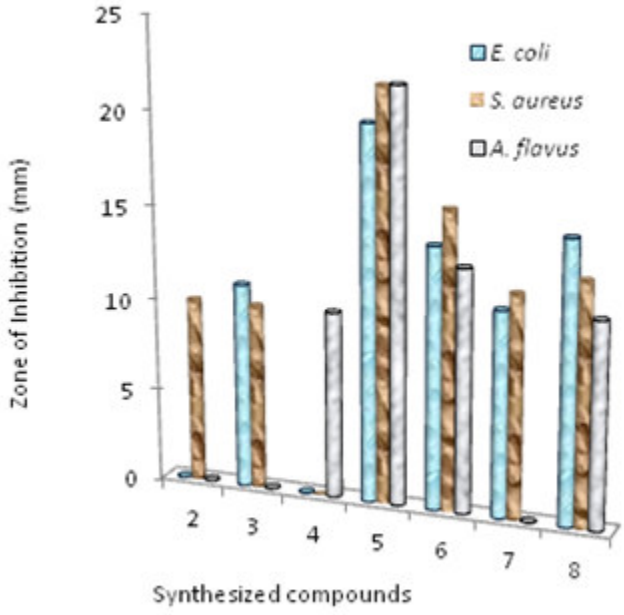
All synthesized compounds (2-8) showed moderate to excellent bioactivity against above mentioned pathogenic strains at different concentrations as shown below in table 2 and a comparative graph in figure 2. Ester 4 had significant fungicidal activity as compared to the bactericidal properties. Compounds 6-8 demonstrated moderate to good antimicrobial activity while the ester 5 showed an exceptionally excellent potency against all tested microbial strains. Nitro moiety was found more effective than the amino functional group. Carbazole imine 8 exhibited good bactericidal activity as compared to the fungicidal one. Keeping these results in our consideration, we can conclude that methyl and carboxylic functionalities do not possess good antimicrobial activity however, these can be used as building scaffolds for further structural modifications.

Table 2
Antimicrobial statistical data of compounds (2-8)

Compound	*In vitro* Inhibitory Zone (mm)					
	E. coli		*S. aureus*		*A. flavus*	
	Concentration (mg/mL)					
	50	1.56	50	1.56	50	1.56
2	-	-	-	+	-	-
3	-	+	-	+	-	-
4	-	-	+	-	++	+
5	+++++	++	+++++	+++	+++++	+++
6	++	+	++	++	+++	+
7	+	+	+	+	+	-
8	+	++	+	+	-	+

Inhibition zone diameter (mm): -,no zone; +,10-15; ++,16-20; +++,21-25; ++++,26-30; +++++,31-35.

Figure 2
Biological screening comparison of compounds 2-8



2. CONCLUSION

In the present study, derivatization of carbazole was achieved in an excellent yield by applying simple but interesting synthetic strategies. These functionally diverse novel moieties showed moderate to remarkable antibacterial and antifungal activities. Our effort is an effective contribution encouraging to establish a library of diversified potent carbazole analogues. Antibiotic resistant bacterial strains are a great challenge to developed and

developing nations. Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the common examples which is highly resistant to many drugs. Therefore, there is an urgent need to design novel antibiotics that have broad spectrum of bioactivities and effective against resistant pathogenic strains. Moreover, discovery paradigm for drugs is now based on "one-drug-multi-diseases" philosophy. These newly synthesized reported carbazole derivatives represent such diversity for further structural modifications leading to the discovery of novel leads and drug candidates. Also, the effectiveness of our approach can be enhanced when used in combination with efflux pump inhibitors or photosensitizes.

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