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Original Research Article

Synthesis and antibacterial activities of novel 1-bromo-2-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl) ethanone and 1-bromo-2-(5-bromo-1,2,3-trihydrocyclopenta[b]indole-1-yl) ethanone

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ABSTRACT

Nitrogen containing hetero cyclic compounds constitute the interior structure of a number of biologically attracted compounds against bacteria and fungi. The synthesis of carbazole derivatives have been desire due to their importance in medicinal field. Enhanced approach of Fischer's synthesis followed by bromoacetylation have been used to synthesis four different carbazole derivatives, namely 1-bromo-2-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl) ethanone, 1-bromo-2-(5-bromo-1,2,3-trihydrocyclopenta[b]indole-1-yl) ethanone. The synthesized compounds were identified and confirmed using spectral techniques *Viz*, FTIR, ^1H NMR, ^{13}C NMR, MASS Spectroscopy. Antibacterial evaluation of synthesized compounds found to have pronozed antibacterial activity.

Keywords: Acetic acid, Bromoacetyl bromide, Ciprofloxacin, 1-bromo-2-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl) ethanone.

Introduction

Heterocyclic compounds participate an imperative role in the metabolism of living cell. A number of the heterocyclic compounds have microbial activity and medicinal uses. The chemistry of heterocyclic compounds have desire to study of long time. Especially nitrogen containing heterocyclic compounds have received unique attention in pharmaceutical chemistry due to their varied medicinal potential [1]. Heterocyclic compounds containing nitrogen, sulphur and oxygen moieties compose the nucleus structure of a number of biologically interested compounds, against bacteria and fungi [2]. Structurally unique and functionality enriched heterocyclic systems are of great significances in chemically and biologically related research areas [3]. Heterocyclic compounds are widely distributed in nature and occupy a prominent place in medicinal chemistry as pharmaceuticals and drug intermediates.

Tetrahydrocarbazole was nitrogen containing heterocyclic compound and it's found to be a starting material for the synthesis of larger number of pharmacophores [4]. Nitrogen containing heterocyclic such as indole or carbazole are probably the most widely spread nitrogen heterocycles in nature[5]. A survey of the pertinent literature revealed that carbazole have been found to possess a wide spectrum of biological activity such as antibacterial [6], anti-rheumatoid arthritis [7], anti-tubercular [8], anti-viral [9], anti-epileptic [10], anti-inflammatory [11], and anti-cancer [12-13] activities. Also, carbazole is a large and interesting group of organic compounds active, among which one can find dyes stuffs [14], and plastics [15], carbazole constitute an important class of naturally occurring heterocycles with interesting biological activities including their special affinity towards DNA [16]. The aim of present work is to synthesis bridged carbazole derivatives an enhanced Fischer's synthesis and antibacterial evaluation.

Experimental

Materials and Methods

The chemicals used to synthesis the derivatives of carbazole have been purchased from Avra synthesis, Merck and sigma Aldrich. The Melting points of synthesized compounds were determined using an X-5A Melting point apparatus and were uncorrected. IR Spectra were recorded on a Alpha Bruker FTIR Spectrometer by KBr pellets. The ^1H NMR Spectra were measured on a Bruker proton NMR-Avance 400 MHz with chemical shift articulated in ppm downfield from TMS as internal standard in DMSO (d-6). The ^{13}C NMR Spectra were

determined at 400 MHz by a Bruker Avance Spectrometer. Mass Spectra were recorded on GC-MASS Spectrometer in methanol.

Synthesis of 1-bromo-2-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl) ethanone

Equimolar quantities of 6-bromo-1,2,3,4-tetrahydrocarbazole **6** (1.7 g, 10 mmol) and bromo acetyl bromide (0.86 ml, 10 mmol) in dry dimethylformamide were taken in round bottom flask fitted with condenser with catalytic amount of potassium carbonate. The content was refluxed for overnight with constant stirring. After the completion of reaction using thin layer chromatography, the reaction mixture poured into ice cold water. The obtained product was filtered and recrystallized using ethanol. The synthesized compound **1** is shown in **Scheme 1**.

Yield :90%, Melting point 112-114°C. FTIR (KBr): 3389 cm^{-1} (N-H), 3023 cm^{-1} (C-H aromatic), 2940 and 2829 cm^{-1} (C-H aliphatic) , 1573 cm^{-1} (C=C). ^1H NMR(DMSO d_6 , ppm) :10.8(S, N-H), 7.0-7.4 (aromatic protons, m) , 3.35 (S, 2H), 2.50-2.58 (m, H) ,1.80-1.83(m, 2H), 1.77-1.79 (t, 2H). Mass spectrum : m/z ratio 372.9.

Synthesis of 1-bromo-2-(5-bromo-1,2,3-trihydrocyclopenta[b]indole-1-yl) ethanone

Equimolar quantities of 5-bromo-1,2,3-trihydrocyclopenta[b] indole (1.5 g, 10 mmol) and bromo acetyl bromide (0.86 ml, 10 mmol) in dry dimethylformamide were taken in round bottom flask with catalytic amount of potassium carbonate. The content was refluxed for overnight with constant stirring. After the completion of reaction, the reaction mixture poured into ice cold water. The obtained product was filtered and recrystallized using ethanol. The synthesized compound **2** is shown in **Scheme 2**.

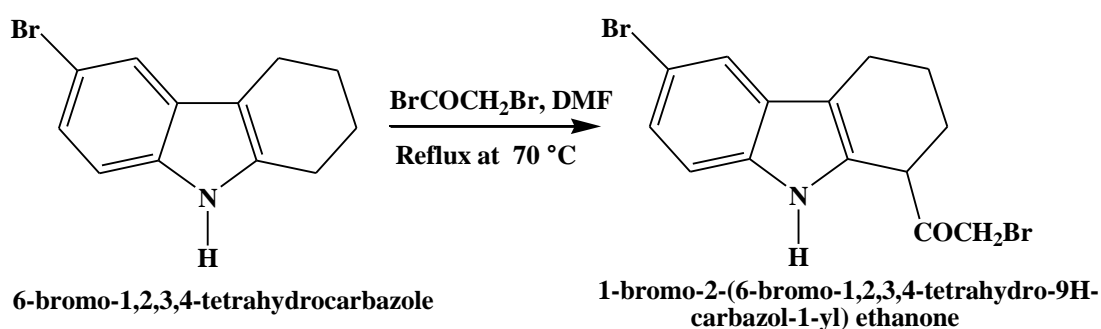
Yield :95% ,Melting point 106-108°C, FTIR (KBr):3387 cm^{-1} (N-H), 3026 cm^{-1} (C-H aromatic), 2925 cm^{-1} and 2828 cm^{-1} (C-H aliphatic) , 1699 cm^{-1} (C=C). ^1H NMR(DMSO d_6 , ppm) : 11.05(S, N-H), 7.0-8.5 (aromatic protons, m), 4.63 (S, 2H), 3.1-3.4 (m, H), 2.7-2.8 (m, 2H), 2.50-2.55 (t, 2H).. Mass spectrum : m/z ratio 358.08.

Bacterial cultures and evaluation of antimicrobial activities

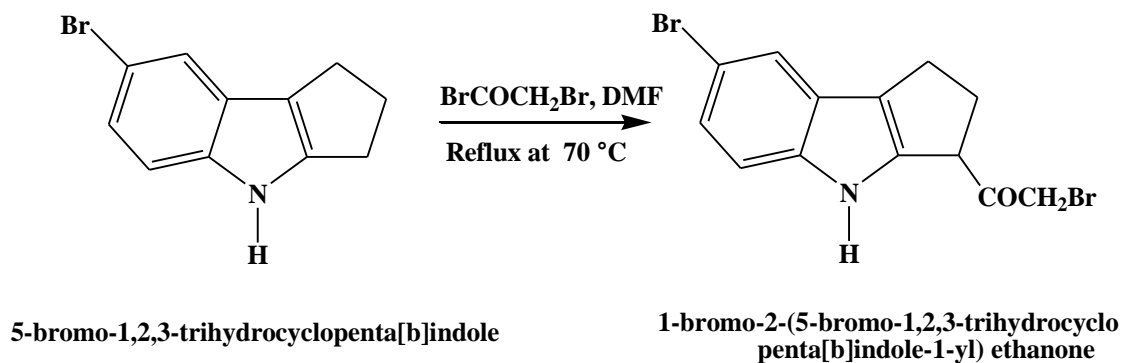
Agar well diffusion method

Antimicrobial analysis was followed via standard agar well diffusion method to examine the antibacterial activity of compounds. Each bacterial isolate was suspended in Brain Heart Infusion (BHI) broth and diluted to approximately 10⁵ colony forming unit

(CFU) per ml. The test organisms were flood-inoculated onto the surface of BHI agar and dried. Five-millimetre diameter wells were cut from the agar using a sterile cork-borer and 30 μ L (50 μ g compound in 1 ml of solvent-Ethanol) of the sample solution were poured into the wells. The plates were incubated for 18 hours at 37 $^{\circ}$ C for bacteria. Antibacterial activity was evaluated by measuring the diameter of the zone inhibition in mm against the test microorganisms. DMSO was used as solvent control. Ciprofloxacin was used as reference antibacterial agent. The tests were carried out in triplicate.



Scheme 1. Synthesis of 1-bromo-2-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl) ethanone



Scheme 2. Synthesis of 1-bromo-2-(5-bromo-1,2,3-trihydrocyclopenta[b]indole-1-yl) ethanone

Results and Discussion

1-bromo-2-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl) ethanone

The FTIR spectrum of the 2-bromo-1-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl)ethanone have presented in **Fig 1**. The sharp intense band at 3389 and 1265 cm^{-1} owing to the N-H stretching and bending vibration. The band at 3023 and 750 cm^{-1} were associated with the aromatic =C-H stretching and bending vibration respectively. The frequency at 1716 cm^{-1} devoted to the C=O stretching frequency. The stretching frequency appeared at 2940 and 2829 cm^{-1} associated with aliphatic C-H stretching vibration. **Fig 2** illustrates the ^1H NMR spectrum of 2-bromo-1-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl)ethanone. A singlet peak appeared at 10.8 δ ppm due to N-H proton. The chemical shift value 1.77-1.79 δ ppm corresponds to triplet of two protons. The multiplet of two protons signal appeared at 1.80-1.83 δ ppm. The two proton multiplet signal appeared at 2.50-2.58 δ ppm. The one proton triplet appeared at 2.60-2.71 δ ppm. A singlet at 3.35 δ ppm owing to acetyl proton and aromatic multiplet signal appeared at 7.0-7.4 δ ppm. The ^{13}C NMR spectrum of 2-bromo-1-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl)ethanone shows the spectral peaks at 20-23 and 69 δ ppm related to the alicyclic carbon atoms in **Fig 3**. The aromatic carbon atoms exhibited the spectral value around 108 to 129 δ ppm. The peak appeared at 136 and 182 δ ppm owing to the carbon atoms present neighbouring to the nitrogen atom followed by carbonyl carbon. **Fig 4** represented the mass spectrum of 2-bromo-1-(6-bromo-1,2,3,4-tetrahydro-9H-carbazol-1-yl)ethanone shows the molecular ion peak at m/z ratio 372.9.

1-bromo-2-(5-bromo-1,2,3-trihydrocyclopenta[b]indole-1-yl) ethanone

FTIR spectrum of 2-bromo-1-(6-Bromo-1,2,3,4-tetrahydrocyclopenta [b]indole -1-yl) ethanone is shown in **Fig 5**. The intensity band at 3387 and 1260 cm^{-1} observed due to the N-H stretching as well as bending vibration. The medium at 3026, 790 cm^{-1} were designated to the aromatic =C-H stretching and bending vibration respectively. The band appeared at 2925, 2828 cm^{-1} associated the aliphatic C-H stretching vibration. The stretching frequency at 1699 cm^{-1} was related to C=O stretching vibration. The ^1H NMR spectrum of 2-bromo-1-(6-Bromo-1,2,3,4-tetrahydrocyclopenta[b] indole-1-yl)ethanone illustrated in **Fig 6**. The chemical shift at 11.05 δ ppm was associated with N-H proton. The two triplets of three protons appeared at 2.50-2.55 and 3.1 -3.4 δ ppm. The multiplet appeared at 2.7- 2.8 δ ppm corresponds to two alicyclic proton. The signal observed has singlet at 4.63 δ ppm. The multiplet for three protons signal appeared 7.0- 8.5 δ ppm. The compound **2** have also

confirmed by using ^{13}C NMR spectrum in **Fig 7**. The aliphatic carbon atoms have shown the spectral peak at 24, 29 & 64 δ ppm. The aromatic carbon atoms have the spectral value at 114, 123, 129 and 132 δ ppm. The peak appeared at 139 & 168 δ ppm corresponds to the and carbon atom present near to the nitrogen atom followed by carbonyl carbon. **Fig 8** represented the mass spectrum of 2-bromo-1-(6-Bromo-1,2,3,4-tetrahydrocyclopenta[b]indole-1-yl) ethanone shows the molecular ion peak at m/z ratio 358.08.

Antibacterial Activity

The results of antibacterial activity for synthesized compounds A & B have shown in Table 1. The zone of inhibition was indicated the nature of antibacterial activity. The synthesized compounds were subjected to *staphylococcus aureus* and *Escherichia coli*. Compound B shows good antibacterial activity than A compound.

Based on the literature survey bromo ethanone carbazole derivatives found to have good antibacterial activity. Here in the carbazole synthesized from cyclohexanone would have been converted to bromoacetylation. So, the bromoacetyl derivative of carbazole found to have excellent antibacterial activity against gram positive and gram negative bacteria's.

4. CONCLUSION

The expected carbazole derivatives were synthesized and identified using thin layer chromatography. All the synthesized compounds have been characterized various spectral techniques viz UV-visible, FTIR, ^1H NMR, ^{13}C NMR, ^{31}P NMR and Mass spectroscopy. The synthesized compounds were subjected to antibacterial activity. The synthesized compounds A & B found to have excellent bacterial activity.

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