Synthesis, characterisation and biological study of pyrazolino and isoxazolo cycloocta[b]indole derivatives

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An efficient route for the synthesis and study of biological activity of eight membered indole fused compounds has been found by employing methyl-benzaldehyde to condense with a precursor cycloocta[b]indole derivative to give condensed product namely, 2-(4'-methyl-benzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole 3. Using 3, further compounds have been prepared namely, pyrazolincycloocta[b]indole and isoxazolocycloocta[b]indole derivatives by allowing the condensed product to react with hydrazine hydrate and hydroxylamine hydrochloride, which results in the formation of 3-(4'-methyl-phenyl)-4,5,6,7-tetrahydro-2H-pyrazolino[4',5':7,8]cycloocta[b]indoles 4 and 3-(4'-methyl-phenyl)-4,5,6,7-tetrahydroisoxazolo[4',3':7,8]cycloocta[b]indoles 5. Their biological activities have been studied against bacterial and fungal strains.

Keywords: Cycloocta[b]indole, methyl-benzaldehyde, pyrazolino, isoxazolo, biological activities

Diverse studies have been doing in indole, their fused moieties and relative compounds. In such class, some alicyclic rings are made to be occupied in fusion to indole moiety; those are recognized in possessing enhanced activities viz., biological, catalyt, etc. Various synthetic routes for synthesis of such novel compounds are being adopted, as this region provides wide range of prospect to researchers. For instance, basic carbazole analogues and indole fused analogue compounds with, notable activities are occurring naturally such as Olivacine4, homoarcyriaflavin5, etc., (Figure 1 and Figure 2). The widespread use of azole antimicrobial drugs led numerous efforts to develop azole derivatives as new antimicrobial agents. Adding to the account heteroatom containing molecules can be seen in the natural products with large applications and possible reactions. The fused alicyclic and indole moiety are believed to bring the inspiration due to the promising applications may possessed by them, because usually such large sized molecule are not easier to construct, but those building blocks can be attained by certain sequence of reactions. In addition they are tested for their application, and are noted as the important part of research. They may be bi-aryl coupling, catalyzed reaction, cyclization, etc. Some are involved in quinoline, quinoxaline, fusion to bring their intended product. Synthetically chemists are interested to bring a crenulated molecule with the higher potency about any biological activity that may be prepared by characteristic method, which is comfortable in all level. The cycloocta[b]indole skeleton has been a recently an adaptation for biology-oriented synthesis (BIOS)6. Their analogues are hopeful in developing a novel group of (MptpB) Mycobacterium protein tyrosine phosphatase B, inhibitors against Mycobacterium tuberculosis7. For the development of biologically improved compounds the varied biological activities of above alkaloids pave the way towards the cycloocta[b]indole derivatives (Figure 3) as a promising one. Antidepressant, anti
inflammatory, etc., can be seen for the cycloocta[\textit{b}]indole derivatives\textsuperscript{8,9}. Some fused indole derivatives display few important and reliable therapeutic properties, anti diabetic property, etc. Therefore with the literature survey relevant to the various synthetic routes available for the carbazole, the indole heterocyclic nucleus fused with six or five or seven member ring are acting well and so it is fascinated with eight membered ring cycloalkane[\textit{b}]indole as cyclooct[\textit{b}]indole derivatives.

More descriptions and information are presented in various reports about alicyclic compounds of five and seven member, with indole moiety and their derivatives. But in the eight-member a few reports are there and they describe about the synthetic methods and activity in different studies. It is interesting to report here about a consistent class of compounds with the trustworthy synthetic method and credible biological activities. Mainly it is intended to bring a convenient synthesis of target compounds using the eight member ring is to know about the reactivity and stability of larger ring, that brings a large hetero annulated structure. In addition to synthesis, discovery of potency in biological region is the further plan. Pyrazolino and Isoxazolo compounds of cyclooct[\textit{b}]indole derivatives are the content of this report with simple strategies of preparation, characterization to identify their structure and activities. The pyrazine ring and pyrido ring are a part of many polycyclic compounds of industrial significance and biological studies namely, antimicrobial and antifungal activities\textsuperscript{10,11} and this property has been recognized to the following compounds in this manuscript.

Results and Discussion

Chemistry

Earlier synthetic routes towards the alicyclic of hetero annulated compounds are done by ring closure method\textsuperscript{15}. Due to the activities of the above said compounds are being prepared by various techniques including one pot synthesis\textsuperscript{16} and are the recent advancement as well as efforts made such as benzannulation\textsuperscript{17}, Fischer indolization\textsuperscript{18}, modified Nenitzescu reaction\textsuperscript{19}, cycloaddition reaction\textsuperscript{20}, cycloaromatisation\textsuperscript{21}, coupling reactions\textsuperscript{22}, or radical reactions\textsuperscript{23} and most recently annulations based on cycloaddition reactions\textsuperscript{24}.

A simple method of organic compound synthesis is adopted here which yields significant quantity, which is also reduced effort and uncomplicated steps in synthesis. Using the reported method, the precursor 1 is prepared and the reagent 4-methyl benzaldehyde (2), is used for the synthesis of condensed product, which is commercially available.

8-Methyl-2-(4'-methyl-benzylidene)-1-oxo-1,2,3,4,5, 6-hexahydrocycloocta[\textit{b}]indole (3) is prepared by the condensation of 4-methyl benzaldehyde with 8-methyl-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[\textit{b}] indole (1a) in the alkaline condition (KOH in ethanol) can be seen in the reaction (Scheme 1). The product is yellow amorphous that has melting point of 142°C where as the yield is achieved above 70%. The IR spectrum for (3a) shows a strong band at 3331 cm\textsuperscript{-1} a typical band for −\textit{NH} group where as for (C=O) band appears at 1690 cm\textsuperscript{-1}. A weak band at 3023 cm\textsuperscript{-1} is assigned to the (=\textit{CH}−) group. Compound (3a) can be justified with \textsuperscript{1}H NMR (\textit{δ} values in ppm) spectrum which gives particulars as follow; a four proton multiplet resonates in the region \textit{δ} 1.57-1.69 assigned for \textit{C}×\textit{H}2 and \textit{C}2-H2. Two singlets for three proton appear in the region of \textit{δ} 2.31 and 2.38 assigned for \textit{C}7-\textit{CH}2 and \textit{C}8-CH\textit{H}; a four proton multiplet for \textit{C}3-H\textit{2} and \textit{C}6- H\textit{2} is present at \textit{δ} 2.78-3.00; \textit{δ} 6.91 is a peak of benzylic \textit{NH} which is singlet; the aromatic prostons of benzylidine and indole moieties shows a signal at \textit{δ} 7.09-7.71 as a multiplet \textit{C}7, \textit{C}9, \textit{C}10, \textit{C}2, \textit{C}3, \textit{C}5, and \textit{C}6 - 7\textit{H}, a less intense peak at \textit{δ} 8.82 a singlet is for indole \textit{NH}. Hence the condensation product (3a) can be assigned with molecular formula in accordance with the elemental analysis (C\textsubscript{23}H\textsubscript{23}NO) and their calculated value and found value are matching in finely. 3b, 3c and 3d compounds have been prepared respectively, by using appropriate 1b, 1c and 1d for

![Figure 3](image-url)
the reaction with 4-methyl-benzylidene with yield 75-90% and their spectra are associated to their structure.

A typical reaction has been proceeded using the condensed product 8-methyl-2-(4'-methylbenzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole (3a) which reacts with hydrazine hydrate to give a pyrazolino compound 8-methyl-3-(4'-methyl phenyl)-4,5,6,7-tetrahydro-2H-pyrazolino[4',5':7,8]cycloocta[b]indole (4a). In the IR spectrum of (4a), stretching frequency of carbonyl group (C=O) has been disappeared, instead of that a new signal for C=N appeared at 1521 cm\(^{-1}\), and the NH gives a band at 3289 cm\(^{-1}\). The \(^1\)H NMR spectrum gives the particulars about the hydrogen atoms as follows, at \(\delta\) 1.25-1.80 multiplet for four protons of C\(_5\)-H\(_2\) and C\(_6\)-H\(_2\), a singlet at \(\delta\) 2.44 for methyl protons (C\(_7\)-CH\(_3\)), at \(\delta\) 2.87-3.07 which is multiplet due to the four protons of cyclooctanone at the position C\(_3\)-H\(_2\) and C\(_7\)-H\(_2\), while a multiplet at the range \(\delta\) 3.70-3.75 for the two protons at the position C\(_3\) and C\(_3\)\(_a\), another singlet signal for methyl protons emerges at \(\delta\) 3.84 for C\(_4\)-CH\(_3\), a range of aromatic multiplet signal \(\delta\) 6.50-7.40 for 7H of C\(_8\), C\(_{10}\), C\(_{11}\), C\(_2\), C\(_3\), C\(_5\) and C\(_6\)-H, where as the presence of signal for one proton at \(\delta\) 8.93 which is assignable for pyrazolino NH, and another singlet is there for one proton occurs in the region \(\delta\) 9.00 due to the indole NH. Likewise, 3b, 3c and 3d reacts with hydrazine hydrate to give respective products such as 4b, 4c and 4d with yield 75-90% (Scheme II) and their spectra are associated to their structure.

In the case of reaction with hydroxylamine hydrochloride, isoxazo derivatives are produced.

When the condensed product 8-methyl-2-(4'-methylbenzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole (3a) reacts with hydroxylamine hydrochloride in pyridine gives 9-methyl-3-(4'-methyl phenyl)-4,5,6,7-tetrahydroisoxazolo[4',3':7,8]cycloocta[b]indoles (5a) with 74% of yield which is a pale yellow amorphous solid with melting point of 102°C. IR spectrum augmented the result of formation pretended compound by the appearance of a signal (C=N) at 1521 cm\(^{-1}\) accompanied by the fading of carbonyl group signal (C=O) and another characteristic signal for indole NH at 3289 cm\(^{-1}\). It is enhanced through the \(^1\)H NMR spectrum since the multiplet at \(\delta\) 1.25-1.99 for four protons of C\(_5\) and C\(_6\); another multiplet for another four protons appears at \(\delta\) 2.87-3.07 for C\(_4\)-H\(_2\) and C\(_7\)-H\(_2\); a sharp singlet signal for \(\delta\) C\(_9\)-CH\(_3\) (methyl group) at \(\delta\) 3.08; a signal which is singlet \(\delta\) 3.13 is assignable for methyl group of C\(_4\)-CH\(_3\); a multiplet for 7H resonates in the aromatic regions at the range \(\delta\) 7.05-7.38 (C\(_8\), C\(_{10}\), C\(_{11}\), C\(_2\), C\(_3\), C\(_5\) and C\(_6\)-H); characteristically for indole NH a weak singlet appears at \(\delta\) 8.21. With hydroxylamine hydrochloride 3b, 3c and 3d compounds react and give the respective products 5b, 5c and 5d with yield about 60-75% (Scheme III). Their structure can be assignable most in fair manner as their spectral values are relatively appropriate.

**Biological activity of synthesized compound**

Indole alkaloids attract more researchers, with interest as synthetic targets, as many of their derivatives exhibit expansive range of probable
biological activities. Carbazole and other indole fused compounds represent new and interesting options. In the large number of indole alkaloids, several important drugs such as Murraya koenigii (Rutaceae) popularly known in India as the curry leaf plant has been found to be a wealthy and rewarding source. Various parts of the plant have been used in traditional or folk medicine for the treatment of various disorders and diseases. Not only the above, but other plants also possess the indole alkaloid properties. Some microorganisms are also useful in isolation of alkaloid. Hyellazole isolated from the blue-green algae, Hyella caespitosa, represent the first carbazole alkaloid of the marine origin. Carbazole alkaloids isolated from the leaves of this plant elicit anti-inflammatory, antioxidant, antimicrobial and topoisomerase I and topoisomerase II inhibition activities. Recently carbazole alkaloid, glycoborine, was isolated from the roots of glycosmis arborea.

The biological activity is studied and referred in the form of inhibition zones that were developed biologically, for the compounds (4) and (5) series and the concentration was inferred as moderate activity for both bacteria and fungi, which can be seen in Table I and Table II. According to that, the indole fused alicyclic compounds, 9-chloro-3-(4'-methyl-phenyl)-4,5,6,7-tetrahydro-[2H]-pyrazolino[4',5':7,8]cycloocta[b]indole (4d) and 9-chloro-3-(4'-methyl-phenyl)-4,5,6,7-tetrahydroisoxazolo [4',3':7,8]cycloocta[b]indole (5d) show more potency to counter the bacterial and fungal organisms. All compounds exhibit better activity against Aeromonas and Acinetobacter, than other bacterial strains, has been seen at higher concentration levels; and nearer activity is noted for fungal strains. In the case of comparison between two species, both pyrazolino and isoxazolo compounds shows reasonably more active against fungal strains than bacterial strains in lower concentrations too. Table I and Table II reveal the increasing action of compounds against micro organisms towards the increment of concentration that are assigned for the series (a-d). Commonly in opposition to micro organisms all the subjects compounds are showing moderate activity comparatively in the increasing concentration.

Experimental Section

General procedure for the synthesis of 2-(4'-methyl-benzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole, 3

An appropriate 1-oxo-1,2,3,4,5,6-hexahydrocycloocta [b]indole (1, 0.001 mol), was added to 10 mL of 5%
al. KOH (Potassium hydroxide in ethanol) and 4-methyl benzaldehyde (2, 0.001 mol). The mixture was allowed to stir for 24 h. At the end of the period the mixture was added to ice crush which gave a yellow solid mass. The precipitated product was filtered off, washed with distilled water and dried. Using petroleum ether:ethyl acetate (98:2) as eluent the yellow solid mass was purified by column chromatography over silica gel which yields the corresponding 2-(4'-methyl-benzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole 3.

8-Methyl-2-(4'-methyl-benzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole, 3a: Yellow solid. Yield 85%. m.p.142°C. IR (KBr): 3331 (N-H), 1690 (C=O), 3023 cm⁻¹ (=CH-); ¹H NMR (500 MHz, CDCl₃); δ 1.57-1.69 (m, 4H, C₆H₂ and C₅H₃); 2.31 (s, 3H, C₆H₃), 2.38 (s, 3H, C₆H₂), 2.78-3.00 (m, 4H, C₆H₂ and C₅H₃), 6.91 (s, 1H, benzylic NH), 7.09-7.17 (m, 7H, C₆H₂, C₆H₃, C₅H₆, C₅H₅, C₅H₆, and C₅H₇), 8.82 (s, 1H, Indole NH). Anal. Calcd for: C, 83.85; H, 07.03; N, 04.25. Found: C, 83.83; H, 07.07; N, 04.23%, which was compatible with the molecular formula C₂₃H₂₃NO.

10-Methyl-2-(4'-methyl-benzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole, 3b: Yellow solid. Yield 75%. m.p.138°C. IR (KBr): 3315 (N-H), 1632 (C=O), 3051 cm⁻¹ (=CH-); ¹H NMR (500 MHz, CDCl₃); δ 1.75-1.88 (m, 4H, C₆H₂ and C₅H₃); 2.39 (s, 3H, C₆H₃), 2.50 (s, 3H, C₆H₂), 3.01 (t, 2H, C₅H₃), 3.29 (t, 2H, C₅H₃), 6.91 (s, 1H, benzylic NH), 7.05-7.55 (m, 7H, C₇H₇, C₈H₈, C₉H₉, C₁₀H₁₀, C₁₁H₁₁, and C₁₂H₁₂), 8.93 (s, 1H, Indole NH). Anal. Calcd for: C, 83.85; H, 07.03; N, 04.25. Found: C, 83.87; H, 07.00; N, 04.28%, which was compatible with the molecular formula C₂₃H₂₃NO.

2-(4'-Methyl-benzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole, 3c: Yellow solid. Yield 90%. m.p.141°C. IR (KBr): 3322 (N-H), 1622 (C=O), 3050 cm⁻¹ (=CH-); ¹H NMR (500 MHz, CDCl₃); δ 1.74-1.88 (m, 4H, C₆H₂ and C₅H₃); 2.39 (s, 3H, C₆H₃), 2.99 (t, 2H, C₆H₃), 3.31 (m, 2H, C₅H₉), 6.90 (s, 1H, benzylic NH), 7.12-7.71 (m, 7H, C₇H₇, C₈H₈, C₉H₉, C₁₀H₁₀, C₁₁H₁₁, C₁₂H₁₂, C₁₃H₁₃, and C₁₄H₁₄ - H), 9.00 (s, 1H, Indole NH). Anal. Calcd for: C, 83.77; H, 06.71; N, 04.44. Found: C, 83.75; H, 06.68; N, 04.49%, which was compatible with the molecular formula C₂₃H₂₃NOCl.

General procedure for the synthesis of 3-(4'-methyl-phenyl)-4,5,6,7-tetrahydro-2H-pyrazolino[4',5',7,8]cycloocta[b]indoles, 4:

A mixture of 2-(4'-methyl-benzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole (3, 0.001 mol) was dissolved in absolute ethanol (20 mL) and 0.5 mL of hydrazine hydrate was added and refluxed for 1 h. Reaction was monitored by TLC. The excess solvent was evaporated, and the crude reaction mixture was poured into crushed ice. The white precipitate formed was filtered, washed with water and dried. The crude sample was purified by column chromatography with eluent (petroleum ether:ethyl acetate, 90:10) to yield 3-(4'-methyl-phenyl)-4,5,6,11-tetrahydro-2H-pyrazolino[4',3',5',7,8]cycloocta[b]indole 4.
9-Methyl-3-(4'-methyl-phenyl)-4,5,6,7-tetrahydro-2H-pyrazolino[4',5':7,8]cycloocta[b]indole, 4a: White amorphous solid. Yield 71%. m.p.220°C. IR (KBr): 3345 (N-H), 1518 cm⁻¹ (C≡N); ¹H NMR (500 MHz, CDCl₃): δ 1.25-1.80 (m, 4H, C₅-H₂ and C₆-H₂), 2.44 (s, 3H, C₃-C₅H₃), 2.87-3.07 (m, 4H, C₄-H₂ and C₅-H₂), 3.70-3.75 (m, 2H, C₁₃-H and C₃₃H₃), 3.84 (s, 3H, C₆-C₆H₃), 6.50-7.40 (m, 7H, C₈, C₁₀, C₁₁, C₂, C₃, C₅ and C₆-H), 8.93 (s, 1H, pyrazolino NH), 9.00 (s, 1H, indole NH). Anal. Calcd for: C, 80.67; H, 06.47; N, 08.20%. Found: C, 80.65; H, 06.50; N, 08.20%, which was well-matched with the molecular formula C₂₂H₂₈N₃O.

11-Methyl-3-(4'-methyl-phenyl)-4,5,6,7-tetrahydro-2H-pyrazolino[4',5':7,8]cycloocta[b]indole, 4b: Dirty White solid. Yield 63%. m.p. 165°C. IR (KBr): 3313 (N-H), 1528 cm⁻¹ (C≡N); ¹H NMR (500 MHz, CDCl₃): δ 1.73-1.87 (m, 4H, C₅-H₂ and C₆-H₂), 2.37 (s, 3H, C₃-C₅H₃), 2.43 (s, 3H, C₁₁-C₁₆H₃), 2.52-2.56 (m, 2H, C₁₂-H₂ and C₃₃H₃), 3.00-3.03 (t, 2H, C₁₃-H), 3.27-3.31 (t, 2H, C₁₇-H₂), 7.05-7.56 (m, 7H, C₈, C₉, C₁₀, C₂, C₃, C₅ and C₆-H), 7.56 (s, 1H, pyrazolino NH), 8.93 (s, 1H, indole NH). Anal. Calcd for: C, 80.43; H, 07.34; N, 12.23. Found: C, 83.80; H, 07.35; N, 12.25%, which was well-matched with the molecular formula C₂₂H₂₈N₃.

3-(4'-Methyl-phenyl)-4,5,6,7-tetrahydro-2H-pyrazolino[4',5':7,8]cycloocta[b]indole, 4c: Yellowish white, amorphous solid. Yield 80%. m.p. 123°C. IR (KBr): 3316 (N-H), 1529 cm⁻¹ (C≡N); ¹H NMR (500 MHz, CDCl₃): δ 1.75-1.88 (m, 4H, C₅-H₂ and C₆-H₂), 2.50 (s, 3H, C₃-C₅H₃) 3.00-3.04 (t, 2H, C₁₃-H), 3.27-3.31 (m, 4H, C₁₄-H₂, C₃-H and C₃₃H₃), 7.05-7.56 (m, 8H, C₈, C₉, C₁₀, C₁₁, C₁₂, C₂, C₃, C₅ and C₆-H), 7.71 (s, 1H, pyrazolino NH), 8.92 (s, 1H, indole NH). Anal. Calcd for: C, 80.22; H, 07.03; N, 12.75. Found: C, 80.24; H, 07.00; N, 12.76%, which was well-matched with the molecular formula C₂₂H₂₈N₃.

General procedure for the synthesis of 3-(4'-methyl-phenyl)-4,5,6,7-tetrahydroisoxazolo[4',3':7,8]cycloocta[b]indoles, 5

The intended product was obtained, when appropriate 2-(4'-methyl-benzylidene)-1-oxo-1,2,3,4,5,6-hexahydrocycloocta[b]indole (3, 0.001 mol) and hydroxylamine hydrochloride (0.27 g) in pyridine (5 mL) were refluxed at 120°C for 1 h. The completion of reaction was monitored through TLC. After the completion of reaction, the reaction mixture was cooled and poured into crushed ice, followed by dilute hydrochloric acid. The solid thus separated out was filtered, washed with water, dried and purified by column chromatography (petroleum ether:ethyl acetate, 90:10) and so it yielded the respective 3-(4'-methyl-phenyl)-4,5,6,7-tetrahydroisoxazolo [4',3':7,8]cycloocta[b]indole 5.

9-Methyl-3-(4'-methyl-phenyl)-4,5,6,7-tetrahydroisoxazolo[4',3':7,8]cycloocta[b]indoles, 5a: Dirty White, amorphous solid. Yield 74%. m.p.102°C. IR (KBr): 3289 (N-H), 1521 cm⁻¹ (C≡N); ¹H NMR (500 MHz, CDCl₃): δ 1.25-1.99 (m, 4H, C₅-H₂ and C₆-H₂), 2.87-3.07 (m, 4H, C₁₂-H₂ and C₁₇-H₂), 3.08 (s, 3H, C₃₃H₃), 3.13 (s, 3H, C₂-C₃H₃), 7.05-7.38 (m, 7H, C₈, C₁₀, C₁₁, C₁₂, C₂, C₃, C₅ and C₆-H), 8.21 (s, 1H, indole NH). Anal. Calcd for: C, 80.67; H, 06.47; N, 08.18. Found: C, 80.60; H, 06.43; N, 08.20%, which was well-matched with the molecular formula C₂₄H₂₆N₄O.

11-Methyl-3-(4'-methyl-phenyl)-4,5,6,7-tetrahydroisoxazolo[4',3':7,8]cycloocta[b]indoles, 5b: Dirty White solid. Yield 63%. m.p. 98°C. IR (KBr): 3429 (N-H), 1509 cm⁻¹ (C≡N); ¹H NMR (500 MHz, CDCl₃): δ 1.74-1.88 (m, 4H, C₅-H₂ and C₆-H₂), 2.43 (s, 3H, C₁₁-C₃H₃), 2.47 (s, 3H, C₂-C₃H₃), 3.13-3.20 (t, 4H, C₁₂-H₂ and C₁₇-H₂), 7.02-7.45 (m, 7H, C₈, C₉, C₁₀, C₁₂, C₂, C₃, C₅ and C₆-H), 9.38 (s, 1H, indole NH). Anal. Calcd for: C, 80.67; H, 06.47; N, 8.018. Found: C, 80.65; H, 06.50; N, 08.20%, which was well-matched with the molecular formula C₂₄H₂₆N₄O.

3-(4'-Methyl-phenyl)-4,5,6,7-tetrahydroisoxazolo [4',3':7,8]cycloocta[b]indoles, 5c: Pale yellow, amorphous solid. Yield 72%. m.p. 90°C. IR (KBr): 3409 (N-H), 1518 cm⁻¹ (C≡N); ¹H NMR (500 MHz, CDCl₃): δ 1.74-1.85 (m, 4H, C₅-H₂ and C₆-H₂), 2.36 (s, 3H, C₂-C₃H₃), 3.10-3.19 (m, 4H, C₁₂-H₂ and C₁₇-H₂), 7.07-7.59 (m, 8H, C₈, C₉, C₁₀, C₁₁, C₂, C₃, C₅ and C₆-H), 9.02 (s, 1H, indole NH). Anal. Calcd for: C, 80.45; H, 06.13; N, 08.53. Found: C, 80.49; H, 06.17; N, 08.50%, which was well-matched with the molecular formula C₂₂H₂₈N₂O.
9-Chloro-3-(4'-methyl-phenyl)-4,5,6,7-tetrahydroisoxazolo[4',3':7,8]cycloocta[b]indole, 5d: Pale yellow, amorphous solid. Yield 70%. m.p. 138°C. IR (KBr): 3306 (N-H), 1496 cm⁻¹ (C=N); 1H NMR (500 MHz, CDCl₃): δ 1.73-1.97 (m, 4H, C₅-H₂ and C₆-H₂), 2.43 (s, 3H, C₆-CH₃) 2.89-3.26 (m, 4H, C₄-H₂ and C₇-H₂), 7.13-7.67 (m, 7H, C₅, C₁₀, C₁₁, C₂, C₃, C₄ and C₆-H), 8.74 (s, 1H, indole NH). Anal. Calc'd for: C, 72.82; H, 05.24; N, 7.72. Found: C, 72.90; H, 05.24; N, 07.71%, which was well-matched with the molecular formula C₂₂H₁₉N₃OCl.

Biological Study
To view the activity of our compounds they were subjected to the microbial studies. All the bacterial cultures were subjected to analysis of their susceptibility / resistance pattern to test samples by disc diffusion method (Bauer et al., 1996), using Mueller Hinton Agar medium (Cat. No. M1084, Himedia, India) for bacteria and Sabrouds Dextrose Agar medium for fungi. Sterile medium was dispensed into sterile petri dishes. Broth cultures were subjected to analyses. Using sterile cotton swab the test cultures were subjected to analysis. All the bacterial cultures were axenically carried out, namely, pyrazolincycloocta[b]indole and isoxazolocycloocta[b]indole derivatives. By employing methyl-benzaldehyde to condense with cycloocta[b]indole derivatives, the primary step was to create a favourable condition for the formation of the compounds. The procedure is simple and yield is fair at about 60% and above. Moreover, the biological results show a remarkable action towards microorganisms and it could be assigned to the functional group such as carbonitriles or five member heterocyclic ring annulations.

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References