Synthesis of novel 2,3-disubstituted indene derivatives and their anti bacterial activity

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Abstract: A series of novel 2,3-disubstituted indene derivatives (8a-8g) have been synthesized from (S)-phenylalanine (1) and evaluated their anti bacterial activity. The key steps involved in this process was internal Friedel-Crafts acylation of (S)-2-((1R,4R)-4-isopropylcyclohexane carboxamido)-3-phenylpropanoic acid (4) to give (1R,4S)-4-isopropyl-N-((S)-1-oxo-2,3-dihydro-1H-inden-2-yl)cyclohexanecarboxamide (5) and further Horner-Wadsworth-Emmons reaction of 5 in presence of cyanomethyl phosphonate and NaH furnished (1R,4R)-N-(3-(cyanomethyl)-1H-inden-2-yl)-4-isopropylcyclohexanecarboxamide (6), which upon catalytic reduction with Ra-Ni resulted (1S,4S)-N-(3-(2-aminoethyl)-1H-inden-2-yl)-4-isopropylcyclohexanecarboxamide (7). The resulting 7 coupled with various hetero aryl carboxylic acids and the obtained derivatives were subjected for anti bacterial activity.

Introduction

Indene framework is found in a large number of biological and pharmacological activities,[1-5] such as antipsychotic,[6,7] antidepressants,[8,9] anti inflammatory,[10] melatonin receptor agonist,[11,12] antihistaminic[13] and selective estrogen receptor modulation,[14,15] and it is also having other applications in chemical industry.[16-18] As a result, to a great extent attention has been paid to the synthesis of indene derivatives. According to Ishiguro et al, EP 0618182 extensively studies the anti microbial activity such as Bacillus subtilis, Saccharomyces cerevisiae, Aspergillus niger by using indene derivatives. Inspired by the better results on the indene systems, our investigations were focused on applications of indene reactions and generated indene derivatives and further subjected to anti bacterial activity.

Results and Discussion
A series of indene derivatives (Table-1) were synthesized according to the scheme-1. In our process compound 4 which is used for the treatment of type 2 diabetes (Nateglinide) was prepared from commercially available (S)-phenylalanine (1) according to the available reported process by Hisashi Shinkai\cite{19} with minor modifications.

Acid moiety of compound 4 reacted with SOCl\textsubscript{2} and furnished acyl chloride of 4 which upon internal Friedel-Crafts acylation with AlCl\textsubscript{3} afforded 5. During the synthesis of 5, this reaction was carried out using different reagents such as phosphorous oxy chloride\cite{20} and poly phosphoric acid\cite{21} observed that there is no product formation and by using thionyl chloride and AlCl\textsubscript{3} quite product formation was noticed and further stabilized the process by changing the conditions. During cyclisation with AlCl\textsubscript{3}, initially we observed lesser yield by using 1.0 equiv of reagent and better yield was achieved with 3.0 equiv of AlCl\textsubscript{3},\cite{22} beyond 3.0 equiv decomposition of 5 leads to change in description of product was noticed. To avoid two stages direct conversion of 4 to 5 was performed using fused sodium tetrachloroaluminate (AlCl\textsubscript{3}·NaCl)\cite{23} at 160 °C and observed product formation along with the considerable amount of decomposed product.

Compound 5 was confirmed by following spectral data, mass spectra of 5 showed protonated molecular ion peak at \(m/z\) 300 (M\textsuperscript{+}+1). In IR spectra observed bands at 1732 cm\(^{-1}\) corresponding to carbonyl group and 1644 cm\(^{-1}\) for amide stretching. \(^1\)H NMR revealed four proton signals at \(\delta\) 7.65-7.20 ppm and absence of acid proton indicated that compound 4 was cyclized and it was further confirmed by \(^{13}\)C NMR, signals at \(\delta\) 203.5 corresponding to carbonyl group. Based on the above spectral data structure was confirmed as 5.

Compound 5 was further subjected to a Horner-Wadsworth-Emmons reaction using diethyl cyanomethyl phosphonate (CMP) in the presence of sodium hydride at room temperature to gave the mixture compounds 6. None of the purification technique was found to be positive to isolate pure compound 6 and further the mixture of compound 6 were separated by silica gel column, surprisingly we noticed that these compounds are two isomers of 6 i.e exo 6 and endo 6 (Scheme-2).

By using 1.2 equiv of both CMP, NaH found mixture of products along with starting material. As the NaH mole ratio increased significant conversion of starting material, finally major endo 6 product formation was observed.

Mass of the compound 6 exhibited \(m/z\) 323.2, IR spectra showed band at 2252 cm\(^{-1}\) corresponding to nitrile and stretching at 1680 cm\(^{-1}\) for amide. In \(^1\)H NMR spectrum of CH\textsubscript{2} attached to nitrile function was observed at \(\delta\) 3.53 ppm as a singlet, however, further confirmed by \(^{13}\)C NMR and DEPT spectrum appeared in the alkane region at \(\delta\) 13.5 ppm as a methylene carbon. The nitrile function was also observed at \(\delta\) 117.4 ppm and in addition to it does not shown a carbonyl function. Based on the above spectral data and fragmentation pattern structure was confirmed as 6.

Compound 6 (endo) was converted to 7 with catalytic hydrogenation over Raney-nickel\cite{23} in methanol and used catalytic amount of aq. ammonia to enhance the reaction. However, other solvents such as ethanol, isopropyl alcohol, 1-propanol and THF medium observed the reaction was slow.
Mass spectra of 7 showed protonated molecular ion at m/z 327.2 (M⁺+H), IR spectrum showed amide N-H band at 3216 cm⁻¹, amide carbonyl stretching at 1670 cm⁻¹ and absence of nitrile functional group. In ¹H NMR spectrum of CH₂ attached to amine was observed at δ 2.99 ppm as a broad singlet and it was further confirmed by ¹³C NMR and DEPT spectrum appeared in region of δ 43.3 ppm, the nitrile carbon was not observed at their chemical shift range. Based on the above spectral data structure was confirmed as a 7.

Indene derivatives (8a-8g) were prepared from 7 by coupling with various aryl and heteroaryl carboxylic acids using the well known dicyclohexylcarbodiimide (DCC) in presence of catalytic amount of DMAP. This reaction was carried out in DCM at rt for 2 h and pure compound was isolated by silica gel column. The transformation was simple, rapid and efficient, alternatively SOCl₂ have also been used for the conversion but moderate yields were observed. Various aryl and heteroaryl carboxylic acids such as pyrazine carboxylic acid, pyridine carboxylic acids and fluoro benzoic acids reacted with 7 gave the desired products in better yield. Complete conversion was not observed using others solvents such as CH₃CN, THF, 1,4 dioxane and DMSO. The structures of compounds 8a-8g were confirmed on the basis of their IR, ¹H NMR and mass spectral analysis.

Conclusions

An effective approach to the synthesis of new 2,3-disubstituted indene derivatives and their anti bacterial activity has been developed. An internal Friedel-Crafts cyclization and Horner-Wadsworth-Emmons reactions provided the endo 6 main framework of the molecule, Raney-nickel reagent has provided a simple, highly effective catalytic hydrogenation of the 6, further conversion of 7 to an indene derivatives (8a-8g) afforded by coupling procedure using DCC gave better yields. This scheme provided an overall effective and efficient approach to this important class of derivatives.

Experimental Section

The ¹H NMR and ¹³C NMR spectra were recorded in DMSO-d₆ & CDCl₃, on a Varian Gemini 2000 FT-NMR spectrometer. Chemical shifts were reported in δ ppm relative to TMS. FT-IR spectra were recorded in the solid state as KBr dispersion using Perkin-Elmer 1650 FT-IR spectrometer. Mass spectra (70 eV) were recorded on HP-5989 A LC-MS spectrometer. Melting points were determined by using the capillary method on POLMON (Model MP-96) melting point apparatus.
(S)-Methyl 2-amino-3-phenylpropanoate (2). To a stirred solution of (S)-phenylalanine (1) (20.0 g, 121 mmol) in DMF (1 mL), methanol (140 mL) was added drop wise thionyl chloride (16.5 g, 139.2 mmol) at room temperature and mixture was maintained at 55 °C for 8 h. After completion of the reaction concentrated the mass under vacuum and the obtained residue was triturated in 2-propanol, collected the solid by filtration and dried gave 2 as a white crystalline solid. (17.4 g, 80% yield), MS (m/z): 166.2 (100% intensity) [M + + H]; IR (KBr, cm⁻¹): 3477 (N–H), 3090 (Ar-H), 2934, 2846 (C-H), 1747 (C =O), 1240 (C-O) 1084 (C-N); ¹H NMR (400 MHz, CDCl₃) in ppm: δ 8.76 (s, br, 2H), 7.22-7.34 (m, 5H), 4.234 (q, 1H), 3.53 (s, 3H), 3.19-3.24 (m, 1H,), 3.15-3.08 (m, 1H,).

(S)-Methyl 2-(4-isopropylcyclohexane carboxamido)-3-phenylpropanoate (3). To a stirred solution of 2 (15.0 g, 83.6 mmol) in DCM (30 mL) was added trans cyclohexane carboxylic acid (15.6 g, 92 mmol), DMAP (2.0 g, 16.2 mmol) and stirred for 5 min. Then added solution of DCC (21.4 g, 104 mmol) in DCM (90 mL) over a period of 30 min and maintained at room temperature for 5 h. After completion of the reaction filtered the unwanted solid and filtrate was washed with water (50.0 mL), brine and dried over anhydrous Na₂SO₄. The obtained organic layer was concentrated under vacuum and the pure compound was isolated from IPA-water (1:1) gave 3 as white colored solid. (22.3 g, 84% yield) MS (m/z): 332.4 (100% intensity) [M⁺ + H]; IR (KBr, cm⁻¹): 3317 (N–H amide), 3064. 3030 (N–H amide), 3064. 3030 (Ar-H), 2939 (C-H stretch), 1740 (C=O), 1644 (amide C=O), 1540 (C=C), 1176 (C-N). ¹H NMR (400 MHz, CDCl₃) in ppm: δ 7.17-7.24 (m, 3H), 7.06 (t, J = 6.4 Hz, 2H,), 5.99 (d, J = 4.0 Hz, 1H,), 4.77-4.81 (m, 1H), 3.15-3.20 (dd, J = 5.6, 8.4 Hz, 1H), 3.04-3.09 (dd, J = 5.7, 8.0 Hz, 1H), 1.91-1.99 (m, 1H), 1.67-1.82 (m, 4H), 1.23-1.34 (m, 3H), 0.89-0.97 (m, 3H), 0.86 (d, J = 6.8 Hz, 6H).

N-(2,3-Dihydro-1-oxo-1H-inden-2-yl)-4-isopropylcyclohexanecarboxamide (5). To a stirred solution of 4 (30 g, 94.5 mmol) in DMF (2.0 mL), DCM (30 mL) was added SOCl₂ (12.9 g, 108.5 mmol) over a period of 30 min at 0 °C and temperature raised to rt and maintained for 2 h. Further AlCl₃ (37.8 g, 284.2 mmol) was added in 8.0 equal portions at 5 °C, and temperature raised to rt and maintained for 2 h. After completion of the reaction added ethylacetate (100 mL) and stirred for 10 min then poured into ice cold water. Separated aq. layer was extracted with ethylacetate (50 mL) and the combined organic layer was washed with brine, dried over anhydrous magnesium
sulfate. Finally distill off organic layer under vacuum afforded crude 5. Pure compound was isolated by silica gel column [hexane/ethylacetate (9:1)]. White colored crystalline solid. (17 g, 60% yield). MS (m/z): 300.2 (100% intensity) [M+ + H]; IR (KBr, cm⁻¹): 3289 (N–H amide), 3068 (Ar-H), 2934 (C-H), 1732 (C=O), 1644 (amide C=O); ¹H NMR (400 MHz, CDCl₃) in ppm: δ 7.65 (d, J = 7.5 Hz, 1H), 7.50-7.54 (m, 1H), 7.20-7.36 (m, 2H), 6.36 (d, J = 5.6 Hz, 1H, 1H), 4.35-4.40 (m, 1H), 3.59-3.65 (m, 1H, 1H), 2.84-2.89 (m, 1H, 1H), 2.00-2.08 (m, 1H), 1.85-1.92 (m, 2H), 1.70-1.73 (m, 2H), 1.30-1.43 (m, 3H), 0.89-1.00 (m, 3H), 0.77 (d, J = 6.8 Hz, 6H,). ¹³C NMR (100 MHz, CDCl₃) in ppm: 203.5, 176.9, 151.5, 135.6, 134.8, 127.6, 126.7, 124.1, 56.2, 45.2, 43.2, 34.9, 32.8, 29.8, 29.0, 19.7.

Endo-(1R,4R)-N-(3-(cyanomethyl)-1H-inden-2-yl)-4-isopropylcyclohexanecarboxamide (6) To a stirred solution of 5 in (10.0 g, 33.3 mmol) in THF (60.0 mL) was added diethyl cyanomethylphosphonate (8.85 g, 50 mmol) and followed 60% sodium hydride in mineral oil (3.33 g, 83 mmol) and maintained for 4 h at rt. After completion of the reaction slowly added water and stirred for 15 min, extracted the compound with ethylacetate (2 x 50 mL). The extract was washed with brine and dried over anhydrous magnesium sulfate, the obtained organic layer was distill off under vacuum afforded 6 in crude form and pure compound was isolated by silica gel column [hexane/EtOAc (9:1)]. (7.45 g, 65% yield). White colored solid. m.p: 116-117 °C; MS (m/z): 327.2 (100% intensity) [M+ + H]; IR (KBr, cm⁻¹): 3216 (N–H amide), 3068 (Ar-H), 1670 (amide C=O); ¹H NMR (400 MHz, CDCl₃) in ppm: δ 9.92 (s, 1H), 8.15 (s, br, 2H), 7.30-7.35 (m, 2H), 7.21 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 8.0 Hz, 1H), 3.82 (s, 2H), 2.99 (s, 4H), 2.61-2.67 (m, 1H), 1.86 ( br, 2H), 1.70 ( br, 2H), 1.36-1.39 (dd, J = 4.8, 5.6 Hz, 3H), 1.00 (d, J = 12 Hz, 3H), 0.85 (d, J = 6.8 Hz, 6H) ¹³C NMR (100 MHz, CDCl₃) in ppm: δ 174.9, 144.2, 141.6, 139.4, 126.6, 123.7, 123.6, 118.1, 118.0, 44.4, 43.3, 37.9, 32.8, 29.8, 28.9, 20.5.

To a stirred solution of 6 (10.0 g, 31.01 mmol) in MeOH (60 mL) was added aq. ammonia (2 mL) and Raney nickel (3 g). Applied 60 psi hydrogen pressure and maintained at rt for 2 h. After completion of the reaction catalyst was filtered and filtrate was distilled off completely under vacuum afforded 7. Hydrochloride salt of 7 was prepared with NH₄Cl in methanol. White colored crystalline solid. (8.1 g, 80.0% yield). MS (m/z): 327.2 (100% intensity) [M+ + H]; IR (KBr, cm⁻¹): 3216 (N–H amide), 3068 (Ar-H), 1670 (amide C=O); ¹H NMR (400 MHz, CDCl₃) in ppm: δ 9.92 (s, 1H), 8.15 (s, br, 2H), 7.30-7.35 (m, 2H), 7.21 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 8.0 Hz, 1H), 3.82 (s, 2H), 2.99 (s, 4H), 2.61-2.67 (m, 1H), 1.86 ( br, 2H), 1.70 ( br, 2H), 1.36-1.39 (dd, J = 4.8, 5.6 Hz, 3H), 1.00 (d, J = 12 Hz, 3H), 0.85 (d, J = 6.8 Hz, 6H) ¹³C NMR (100 MHz, CDCl₃) in ppm: δ 174.9, 144.2, 141.6, 139.4, 126.6, 123.7, 123.6, 118.1, 118.0, 44.4, 43.3, 37.9, 32.8, 29.8, 28.9, 20.5.

General method for preparation of 8a-8g: To a stirred solution of 7 in DCM (18 mL) was added aryl or hetero aryl benzoic acid (10.56 mmol), DMAP (0.91 mmol) followed by DCC (10.56 mmol) and the reaction mixture was stirred at rt for 5 h. After completion of the reaction filtered the unwanted solid and the filtrate was washed with 1M NaOH solution, followed by water (50.0 mL). Separated organic layer was distilled off under vacuum afforded crude compound and further pure compound was
isolated by silica gel column (ethylacetate : Hexane).

\( \text{N-(2-(2-((1R,4R)-4-isopropylcyclohexanecarboxamido)-1H-inden-3-yl)ethyl)pyrazine-2-carboxamide (8a)} \): Yield: 75%; m.p: 159-161 °C; ESI (+)-HRMS calcd for C\(_{26}\)H\(_{32}\)N\(_4\)O\(_2\) [M+H]+: 3335, 3264 (N–H amide), 3020 (Ar-H), 2935 (C-H aliphatic), 1681, 1647 (amide C=O), 1587, 1532 (C=C). \(^1\)H NMR (400 MHz, CDCl\(_3\)) in ppm: 9.42 (s, 1H), 9.18 (s, 1H), 9.05 (t, 1H), 8.85 (s, 1H), 8.50 (s, 1H), 8.30 (s, 2H), 8.24-8.30 (m, 1H), 8.50 (s, 1H), 7.55-7.59 (m, 4H), 7.70-7.75 (m, 2H), 7.21 (t, 1H), 3.82 (s, 2H), 3.49-3.55 (q, 1H, 8.0 Hz, 2H), 2.89 (t, 1H), 2.61-2.74 (m, 1H), 1.80-1.86 (m, 2H), 1.60-1.68 (m, 2H), 1.33-1.39 (m, 3H), 1.00-1.15 (m, 3H), 0.85 (d, 1H).

\( \text{N-(2-(2-((1R,4R)-4-isopropylcyclohexanecarboxamido)-1H-inden-3-yl)ethyl)nicotinamide (8c)} \): Yield: 77%; m.p: 142-145 °C; ESI (+)-HRMS calcd for C\(_{26}\)H\(_{32}\)N\(_4\)O\(_2\) [M+H]+: 3260 (N–H amide), 3020 (Ar-H), 2925 (C-H aliphatic), 1661, 1642 (amide C=O), 1587, 1532 (C=C). \(^1\)H NMR (400 MHz, CDCl\(_3\)) in ppm: 9.00 (d, 1H), 8.80-8.72 (m, 1H), 8.50 (s, 1H), 8.24-8.30 (m, 1H), 7.55-7.59 (m, 2H), 7.21 (t, 1H), 6.79 (s, 1H), 3.82 (s, 2H), 3.49-3.55 (q, 1H, 8.0 Hz, 2H), 2.89 (t, 1H), 2.61-2.74 (m, 1H), 1.80-1.86 (m, 2H), 1.60-1.68 (m, 2H), 1.33-1.39 (m, 3H), 1.00-1.15 (m, 3H), 0.85 (d, 1H).

\( \text{N-(2-(2-((1R,4R)-4-isopropylcyclohexanecarboxamido)-1H-inden-3-yl)ethyl)isonicotinamide (8d)} \): Yield: 75%; m.p: 148-151 °C; ESI (+)-HRMS calcd for C\(_{26}\)H\(_{32}\)N\(_4\)O\(_2\) [M+H]+: 3260 (N–H amide), 3020 (Ar-H), 2925 (C-H aliphatic), 1661, 1642 (amide C=O), 1587, 1532 (C=C). \(^1\)H NMR (400 MHz, CDCl\(_3\)) in ppm: 8.66 (d, 1H), 7.36 (d, 1H), 7.30-7.35 (m, 2H), 7.18-7.15 (m, 2H), 3.99 (s, 2H), 3.49-3.54 (q, 1H, 8.0 Hz, 2H), 2.97 (t, 1H), 2.61-2.74 (m, 1H), 1.80-1.86 (m, 2H), 1.60-1.68 (m, 2H), 1.33-1.39 (m, 3H), 1.00-1.15 (m, 3H), 0.85 (d, 1H).

\( \text{2,6-difluoro-N-(2-(2-((1R,4R)-4-isopropylcyclohexanecarboxamido)-1H-inden-3-yl)ethyl)benzamide (8e)} \): Yield: 75.0%; m.p: 143-146 °C; ESI (+)-HRMS calcd for C\(_{26}\)H\(_{28}\)F\(_2\)N\(_4\)O\(_2\) [M+H]+: 3260 (N–H amide), 3020 (Ar-H), 2925 (C-H aliphatic), 1661, 1642 (amide C=O), 1587, 1532 (C=C). \(^1\)H NMR (400 MHz, CDCl\(_3\)) in ppm: 8.60 (s, 1H), 8.04-8.10 (m, 1H), 7.31 (d, 1H), 7.13-7.18 (m, 2H), 7.02-7.06 (m, 2H), 6.92-6.97 (m, 1H), 6.77-6.83 (m, 1H), 3.94 (s, 2H), 3.49-3.54 (q, 1H, 8.0 Hz, 2H), 2.83 (t, 1H), 1.71 (br, 2H), 1.40-1.49 (m, 2H), 1.29-1.37 (m, 1H), 0.99-1.20 (m, 3H), 0.87 (d, 1H).

\( \text{N-(2-(2-((1R,4R)-4-isopropylcyclohexanecarboxamido)-1H-inden-3-yl)ethyl)isonicotinamide (8d)} \): Yield: 75%; m.p: 148-151 °C; ESI (+)-HRMS calcd for C\(_{26}\)H\(_{32}\)N\(_4\)O\(_2\) [M+H]+: 3260 (N–H amide), 3020 (Ar-H), 2925 (C-H aliphatic), 1661, 1642 (amide C=O), 1587, 1532 (C=C). \(^1\)H NMR (400 MHz, CDCl\(_3\)) in ppm: 8.60 (s, 1H), 8.04-8.10 (m, 1H), 7.31 (d, 1H), 7.13-7.18 (m, 2H), 7.02-7.06 (m, 2H), 6.92-6.97 (m, 1H), 6.77-6.83 (m, 1H), 3.94 (s, 2H), 3.49-3.54 (q, 1H, 8.0 Hz, 2H), 2.83 (t, 1H), 1.71 (br, 2H), 1.60-1.63 (m, 1H), 1.47-1.49 (m, 1H), 1.34-1.41(m, 2H), 1.20-1.27
(m, 1H), 0.97-1.18 (m, 3H), 0.81 (d, J = 6.8 Hz, 6H).

**2-Fluoro-N-(2-((1R,4R)-4-isopropylcyclohexanecarboxamido)-1H-inden-3-yl)ethyl benzamide (8f)**: Yield: 70%; m.p: 149-151 °C; MS (m/z): 449.3 (100% intensity) [M+H]+; IR (KBr, cm⁻¹): 3253 (N–H amide), 3058 (Ar-H), 2946 (C-H Aliphatic), 1665, 1634 (amide C=O), 1492, 1450 (C=C), 1190 (C-F); ¹H NMR (400 MHz, CDCl₃) in ppm: δ 8.50 (s, 1H), 8.10 (s, 1H), 7.38-7.28 (m, 2H), 7.15-7.20 (m, 4H), 6.94-6.98 (m, 1H), 6.75-6.83 (m, 1H), 3.94 (s, 2H), 3.47-3.55 (q, J = 6.8 Hz, 2H), 2.80 (t, J = 7.2 Hz, 2H), 2.20-2.27 (m, 1H), 1.71-1.75 (m, 2H), 1.55-1.63 (m, 2H), 1.34-1.41 (m, 3H), 0.97-1.18 (m, 4H), 0.73 (d, J = 6.8 Hz, 6H).

**4-Fluoro-N-(2-((1R,4R)-4-isopropylcyclohexanecarboxamido)-1H-inden-3-yl)ethyl benzamide (8g)**: Yield: 78%; m.p: 141-143 °C; MS (m/z): 449.2 (100% intensity) [M+H]+; IR (KBr, cm⁻¹): 3289 (N–H amide), 3068 (Ar-H), 2934 (C-H Aliphatic), 1660, 1644 (amide C=O), 1580, 1550 (C=C), 1250 (C-F); ¹H NMR (400 MHz, CDCl₃) in ppm: δ 8.50 (s, 1H), 8.10 (s, 1H), 7.37-7.28 (m, 2H), 7.20-7.27 (m, 2H), 7.09-7.16 (m, 2H), 6.99-7.05 (m, 1H), 6.88-6.96 (m, 1H), 3.97 (s, 2H), 3.49-3.53 (q, J = 6.8 Hz, 2H), 2.82 (t, J = 7.2 Hz, 2H), 2.22-2.29 (m, 1H), 1.68-1.77 (m, 2H), 1.45-1.63 (m, 2H), 1.34-1.41 (m, 3H), 0.97-1.18 (m, 4H), 0.77 (d, J = 6.8 Hz, 6H).

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**Scheme 1**: Synthetic scheme for preparation of 7.

Table-1: Synthesis of indene derivatives from 7.
Table 2: The reproducible anti bacterial activity of indene derivatives (8a-8g) by cup plate diffusion method

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* Ciprofloxacin

References