Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(14):67-72
(http://derpharmachemica.com/archive.html)

Synthesis and Biological evaluation of novel (4-chlorophenyl) ((1R, 3r, 5S)-3-(phenyl amino)-8-aza-bicyclo [3.2.1] octan-8-yl) methanone derivatives

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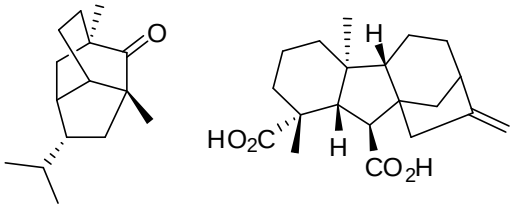
ABSTRACT

In the present study, we have carried out the synthesis of novel (4-chlorophenyl) ((1R, 3r, 5S)-3-(phenyl amino)-8-aza-bicyclo [3.2.1] octan-8-yl) methanone derivatives. The structure of the newly synthesized compounds was elucidated by IR, ^{1}HNMR, ^{13}CNMR, ^{19}FNMR, Mass spectral data and CHN elemental analysis. Further all the novel derivatives were investigated for their invitro antibacterial activity.

Keywords: Aza-bicyclo 4-chlorophenyl methanone derivatives, Antibacterial activity, Reductive aminations, Ciprofloxacin, Chloro benzoyl chloride.

INTRODUCTION

Natural products are ideal starting points for drug design because of their structural complexity, tridimensional architecture and useful biological activities. Diversity oriented synthesis (DOS) provide quick access to molecular diversity and complexity in natural products like libraries. Within the enormous diversity of carbon skeleton found in nature, the abundant bicyclic systems are of special interest. In particular, the bicyclo [3.2.1] octane system is present in many families of biologically active natural products and is also important because of its versatile reactivity, making it a very useful building block with an important impact in modern organic synthesis. Some representative examples of natural products containing a bicyclo [3.2.1] octane core are Pupukeanone and Gibberelline A12 **(Fig. 1)**.



Pupukeanone **Gibberelline A12**

Fig. 1

The 8-azabicyclo [3.2.1] octane ring is a central structural element in a number of neuroactive compounds, including Cocaine and Atropine [1]. Because of their importance in synthetic and medicinal chemistry and in peptide research, conformationally rigid, alicyclic *β*-amino acids have been subject to considerable interest during the past 20 years [2]. N-Heterocyclic *β*-amino acids have also attracted attention in view of their biological properties and their applications in peptide synthesis [3]. Bicyclic *α* or *β*-amino acids in which the *N* atom of the aminoacid functions

part of the ring system is a class of compounds of appreciable importance. Thus, bicyclic *α*-amino acids with the *N* atom in the ring system, such as 7-azabicyclo[2.2.1]heptane-1-carboxylic acid, its derivatives and compounds with an 8-azabicyclo[3.2.1]octane skeleton are conformationally restricted analogs of proline, hydroxyprolines and related proline derivatives [4,5]. 7-Azabicyclo[2.2.1]heptane-2-carboxylic acid *β*-amino acids are key compounds in novel *β*-peptide syntheses [6] were recently reported to behave as conformationally restricted proline analogs and also acting as efficient catalysts in organocatalytic aldol processes [7]. More-over, both bicyclic *α*- and *β*-amino acids with the *N* atom in the ring system serve as key precursors for the synthesis of medicinally valuable alkaloids such as Anatoxin-a,[8] Epibatidine, Epiboxidine etc [9]. A number of pharmacologically active 3-azabicyclo [3.2.1]octanes have been reported as bioactive molecules [10], the most important of them probably being those with an amino or carboxyl function in their structure. 3-Azabicyclo[3.2.1]octane *α*-amino acids were recently synthetized in enantiomerically pure form [11]. Because of the importance of the conformationally constrained alicyclic or heterocyclic β-aminoacids, our work was directed toward the synthesis of novel[3-(4-substitutedphenylamino)-8-azabicyclo[3.2.1]oct-8yl]-phenyl-methanone derivatives.

MATERIALS AND METHODS

All reagents were purchased from Sigma-Aldrich, Alfa, Lancaster, AVRA laboratory, Spectrochem and were used without further purification. All chemistry reactions were performed under nitrogen atmosphere using standard techniques. All nuclear magnetic resonance (NMR) spectra were measured using a Bruker Spectrospin advance DPX400 Ultrashield (400, 300 and 100 MHz) instrument with 5-mm Sigma 528-PP-8 tubes. ^{1}H and ^{13}C NMR, $^{19}FNMR$ spectras were recorded for approximately 0.03-0.04 M solutions in d_6-dimethyl sulfoxide (DMSO-d_6), $CDCl_3$ with tetramethyl silane (TMS) as internal reference. Infrared (IR) spectra were recorded on a Perkin–Elmer FT-IR 240-c spectrophotometer using KBr optics. Liquid chromatography-mass spectroscopy (LC-MS) was carried out using an Agilent 1200 series LC and Micromass ZQ spectrometer. Flash column chromatography was performed using silica gel (230-400 mesh). Melting points were determined on a Buchi R-535 apparatus with open capillary method and are uncorrected. Reactions were carried out under CATA-4R microwave at 490 Watts. Combustion analysis was performed on a Costech Elemental Combustion System CHN elemental analyzer.

General procedure for synthesis of compounds 4(a-j):

Tert-Butyl (1R, 5S)-3-oxo-8-azabicyclo [3.2.1] octane-8-carboxylate 1 (5g, 0.021 mol) was dissolved in 4M hydrochloric acid in 1,4-Dioxane (10 mL), stirred for 30 minutes. After completion of the reaction, reaction mixture was concentrated under reduced pressure to afford (1R, 5S)-8-azabicyclo[3.2.1]octan-3-one hydrochloride **(2)** as an off white solid. The compound was pure enough to go to the next step.

The compound **2** (2g, 0.016 mol) was dissolved in dry DCM (30 mL), was added pyridine (3.79 g, 0.0479 mol) under nitrogen atmosphere, stirred for 15 minutes. Then, 4-chloro benzoyl chloride (2.39 g, 0.019 mol) was added at 0 ^{o}C, stirred for 2h. After completion of the reaction, reacion mixture was quenched with ice water, extracted with dichloromethane (DCM), washed with sat $NaHCO_3$ solution, dried over Na_2SO_4 and concentrated under reduced pressure to give crude compound (1R, 5S)-8-(4-chlorobenzoyl)-8-azabicyclo[3.2.1]octan-3-one **(3)**. The crude compound was purified by flash column chromatography (FCC) method using 0-20% Ethyl acetate in hexane as eluent.

Compound **3** (0.1 g, 0.00003 mol), R-NH_2 (0.042 g, 0.00004) in Ethanol (5 ml), was added catalytic acetic acid (3 drops), stirred for 30 mins. Then $NaBH_3CN$ (0.072 g, 0.00009) was added, stirred for 6h. After completion of the reaction, quenched with ice water, extracted with ethyl acetate, washed with saturated $NaHCO_3$, dried over Na_2SO_4, concentrate to give crude compound. The crude compound was purified by FCC method using 0-20% ethyl acetate in hexane to get pure compound **4(a-j)**. The same reactions were performed under microwave irradiation mehod using CATA-4R microwave at 490 watts to get more yields (79-86%) than conventional method as shown in **Table 1**.

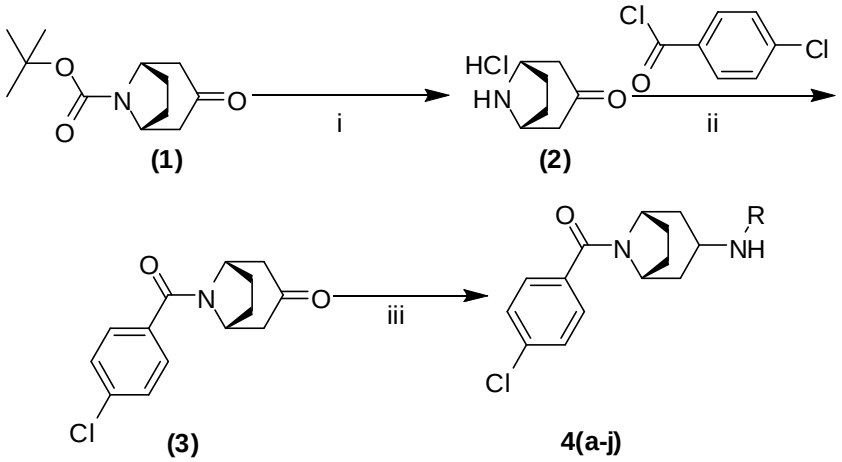
Microwave irradiation method was adapted to synthesize all the tile compounds with high yields **4(a-j).**

Table 1: comparable studies of reductive amination

Compd.	Time		Yield (%)	
	Conventional method (h)	Microwave method (min)	Conventional method	Microwave method
4a	6.00	40	62	75
4b	6.10	42	65	79
4c	4.30	27	60	69
4d	5.00	30	66	79
4e	5.30	34	48	59
4f	4.30	25	45	49
4g	5.00	31	67	73
4h	6.00	40	62	69
4i	5.00	28	50	58
4j	5.00	28	74	86

RESULTS AND DISCUSSION

In biochemical systems, one pot reductive amination of aldehydes and ketones is an important transformation, which allows the direct conversion of carbonyl compounds into amines using simple operations [12]. In this study, the reductive aminations are successfully carried out under conventional and microwave irradiation by reaction with $NaBH_3CN$ using five-fold excess of amine at pH 6-8 [13].



R=C_6H_5, 2-FC_6H_4, 3-FC_6H_4, 4-FC_6H_4, 2-CH_3-C_6H_4, 3-CH_3-C_6H_4, 4-CH_3-C_6H_4, 2-NO_2-C_6H_4, 3-NO_2-C_6H_4, 4-NO_2-C_6H_4

Scheme-1: Synthetic path way of 4(a-j), Reagents and Conditions: (i) 4M Dioxane.HCl, 30 min (ii) pyridine, DCM,0 ^oC, 2h. (iii) R-NH_2, AcOH, $NaBH_3CN$, Ethanol, MWI, 40min

The synthetic pathway employed to prepare the title compounds is outlined in ***Scheme 1.*** (4-chlorophenyl) ((1R, 3R, 5S)-3-(phenyl amino)-8-aza-bicyclo [3.2.1] octan-8-yl) methanone derivatives were synthesized by the reaction of *tert*-Butyl (1R, 5S)-3-oxo-8-azabicyclo [3.2.1] octane-8-carboxylate with 4M hydrochloric acid in 1,4-Dioxane gives Compound **2** as an off white Solid. The HCl salt of Compound **2** was dissolved in dry dichloromethane was added pyridine under nitrogen atmosphere and stirred for 15 minutes at room temperature. After 15 minutes 4-chloro benzoyl chloride was added at 0 ^oC, the reaction mixture was stirred for 2h to get compound **3**. Reductive amination of compound **3** with various aryl amines in ethanol carried the reaction under microwave and conventional conditions with $NaBH_3CN$ and catalytic amount of AcOH gives title compounds **4(a-j)**. We observed high yields with in short time in microwave irradiation method compare to conventional method. So we adapted microwave method for the synthesis of all title compounds.

All the synthesized compounds were characterized by FT-IR, ^{1}HNMR, ^{13}CNMR, ^{19}FNMR and Mass spectroscopic analysis. The IR spectral data of all compounds showed characteristic peaks of NH stretching at 3340-3385 cm^{-1}, aliphatic tertiary C-N stretching at 1340-1352 cm^{-1} indicating the presence of -OH and -NO_2 groups respectively were also observed in the corresponding synthesized compounds.

Table 2. Antibacterial activity (MIC) of the newly synthesized compounds 4(a-j)

Compd.	*S.a*	*E.c*	*S.a*	*S.f*	*P.a*
4a	++	++	++	++	+++
4b	++	++	++	++	++
4c	+++	++++	+++	++	+
4d	++	+++	+++	++	+
4e	++++	++	+	+	+
4f	+++	++	++	++	++
4g	+++	++	+++	++	+++
4h	++	++	+	++	++
4i	++++	++	++	++	+++
4j	++	++	++	++	+++
Ciprofloxacin Cloxacillin Gentamycin	++++	++++	++++	++++	++++

50 µgm/mL = ++++, 100 µgm/mL = +++, 150 µgm/mL = ++, 200 µgm/mL = +, Not active up to 200 µgm/mL = Ciprofloxacin, Cloxacillin & Gentamycin is (++++) at 50 µgm/mL S.a = Staphylococcus aureus, S.P = salmonella paratyphi, E.c = Escherichia coli, S.f = Shingella flexneri, P.a = Pseudomonas auregenosa.

Antibacterial activity

The minimum inhibition concentration (MIC) was determined using the streak plate and cup plate method by measuring the zone of inhibition according to standard procedure. All the synthesized compounds were screened *in vitro* for their antibacterial activity against a variety of bacterial strains such as *Staphylococcus aureus, salmonella paratyphi, Escherichia coli, Shingella flexneri, Pseudomonas auregenosa* (**Table 1**). The MIC of the compounds was defined, as lowest concentration at which there was 80% inhibition of growth compared with the growth for a drug free controle.[15] standard inhibition of zone size for Ciprofloxin, Cloxacillinand for Gentamycin [15] is (++++) at 50 µgm/mL against all microbes.

Among the synthesized compounds **4c** have shown better activity against all bacterial strains. Compounds **4e** and **4i** have exhibited potent activity against *Staphylococcus aureus*. Whereas, **4d** and **4e** compounds have posseses moderate activity against *salmonella paratyphi* bacterial strains. Compounds **4a**, **4g**, **4i** and **4j** have shown moderate activity against *Pseudomonas auregenosa*.

(4-Chlorophenyl)((1R,5S)-3-(phenylamino)-8-aza-bicyclo[3.2.1]octan-8-yl)methanone (4a):

Yellow solid: yield: 75%; Rf-0.42; IR (KBr, ν/cm^{-1}: 3326, 3284, 3056, 2954, 2885, 1720, 1648, 1592, 1325, 1142, 662: ^{1}H NMR ($CDCl^3$, 300 MHz): δ 8.06-6.88 (m, 9H, Ar-H), 4.59 (brs, 1H, NH), 3.95 (m, 1H, CH), 2.56 (d, J = 6.8 MHz, 4H, CH^2), 2.17 (t, J = 6.4, 6.8 MHz, 4H, CH^2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.7, 149.5, 144.9, 132.3, 131.7, 129.3, 127.0, 121.2, 115.7, 52.6, 49.1, 43.0, 28.7; MS (ESI): m/z 342.4 (M+). Anal. Calculated for $C_{20}H_{21}ClN_2O$: C, 70.48; H, 6.21; Cl, 10.40; N, 8.22; O, 4.69 found: C, 70.39; H, 6.28; N, 8.34.

(4-Chlorophenyl)((1R,5S)-3-(2-fluorophenylamino)-8-aza-bicyclo[3.2.1]octan-8-yl)methanone (4b):

Pale yellow solid: yield: 79%; Rf: 0.45; IR (KBr, υ/cm^{-1}): 3346, 3281, 3010, 2940, 2845, 1220, 1651, 1567, 1343, 1124, 668; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.00-6.95 (m, 8H, Ar-H), 4.65 (brs, 1H, NH), 3.84 (m, 1H, CH), 2.76 (d, J = 6.2 MHz, 4H, CH_2), 2.13 (t, J = 6.0, 6.4 MHz 2H, CH_2), 1.86 (m, 4H, CH_2); ^{13}C NMR (CDCl3, 75 MHz): δ 172.3, 148.4, 144.2, 131.3, 130.4, 128.3, 127.0, 121.2, 114.7, 52.2, 49.1, 43.0, 28.7; ^{19}FNMR($CDCl_3$, 376 MHz): δ (ppm)-73.41; MS (ESI): m/z 360.2 (M+). Anal. Calculated for $C_{20}H_{20}ClFN_2O$ C, 66.94; H, 5.62; Cl, 9.88; F, 5.29; N, 7.81; O, 4.46 found: C, 66.89; H, 5.48; N, 7.78.

(4-Chlorophenyl)((1R,5S)-3-(3-fluorophenylamino)-8-aza-bicyclo[3.2.1]octan-8-yl)methanone(4c):

White solid, Mp: 138-141 ^{o}C; yield: 69%; Rf: 0.47; IR (KBr, υ/cm^{-1}): 3358, 3289, 3022, 2961, 2852, 1728, 1650, 1589, 1342, 1145, 669; ^{1}HNMR ($CDCl_3$, 300 MHz): δ 8.05-6.82 (m, 8H, Ar-H), 4.69 (brs, 1H, NH), 3.82 (m, 1H, 2CH), 2.82 (d, J = 6.6 MHz, 4H, CH_2), 2.18 (t, J = 6.2, 6.8 MHz, 2H, CH_2), 1.76 (m, 4H, CH_2); ^{13}CNMR ($CDCl_3$, 75 MHz): δ 174.1, 147.9, 143.9, 131.7, 130.7, 129.0, 127.6, 122.2, 114.6, 51.5, 47.1, 44.8, 27.4; ^{19}FNMR($CDCl_3$, 376 MHz): δ (ppm)-71.41; MS (ESI): m/z 360.2 (M+). Anal. Calculated for $C_{20}H_{20}ClFN_2O$ C, 66.94; H, 5.62; Cl, 9.88; F, 5.29; N, 7.81; O, 4.46 found: C, 66.84; H, 5.58; N, 7.84.

(4-Chlorophenyl)((1R,5S)-3-(4-fluorophenylamino)-8-aza-bicyclo[3.2.1]octan-8-yl)methanone(4d):

yellow solid, Mp: 192- 194 ^{o}C; yield: 79%; Rf: 0.45; IR (KBr, υ/cm^{-1}): 3363, 3294, 3018, 2963, 2859, 1733, 1652, 1580, 1348, 1147, 653; ^{1}HNMR ($CDCl_3$, 300 MHz): δ 8.00-6.75 (m, 9H, Ar-H), 4.59 (brs, 1H, NH), 3.89 (m, 1H, 2CH), 2.85 (d, J = 6.4 MHz, 4H, CH_2), 2.25 (t, J = 6.1, 6.6 MHz, 2H, CH_2), 1.8 (m, 4H, CH_2); ^{13}CNMR ($CDCl_3$, 75 MHz): δ 174.3, 147.0, 143.9, 132.0, 130.9, 129.2, 127.7, 122.3, 114.8, 51.0, 47.8, 44.5, 26.9; ^{19}FNMR($CDCl_3$, 376 MHz): δ (ppm)-72.41; MS (ESI): m/z 360.4 (M+). Anal. Calculated for $C_{20}H_{20}ClFN_2O$ C, 66.94; H, 5.62; Cl, 9.88; F, 5.29; N, 7.81; O, 4.46 found: C, 66.80; H, 5.78; N, 7.94.

((1R,5S)-3-(o-Toluidino)-8-aza-bicyclo[3.2.1]octan-8-yl)(4-chlorophenyl) methanone(4e):
Yellow powder; yield: 59%; IR (KBr, υ/cm^{-1}): 3397, 3268, 3060, 2950, 2862, 1721, 1651, 1590, 1326, 1145; 1H NMR ($CDCl_3$, 300 MHz): δ 8.00-6.67 (m, 8H, Ar-H), 4.48 (brs, 1H, NH), 3.63 (m, 1H, 2CH), 2.86 (s, 3H, CH_3), 2.54 (m, 4H, CH_2), 2.16 (t, J = 6.4 MHz, 2H, CH_2), 1.74 (m, 4H, CH_2); ^{13}CNMR ($CDCl_3$, 75 MHz): δ 172.1, 145.9, 142.0, 132.9, 131.2, 129.4, 127.5, 123.8, 114.0, 51.5, 47.8, 44.1, 27.0, 14.5; MS (ESI): m/z 356.2 (M+). Anal.Calculated for $C_{21}H_{23}ClN_2O$ C, 71.07; H, 6.53; Cl, 9.99; N, 7.89; O, 4.51 found: C, 71.15; H, 6.78; N, 7.94.

((1R,5S)-3-(m-Toluidino)-8-aza-bicyclo[3.2.1]octan-8-yl)(4-chlorophenyl) methanone(4f):
Brownish solid; yield: 49%; IR (KBr, υ/cm^{-1}): 3345, 3275, 3085, 2925, 2840, 1720, 1640, 1589, 1350, 1152; ^{1}HNMR ($CDCl_3$, 300 MHz): δ 8.05- 6.70 (m, 8H, Ar-H), 4.45 (brs, 1H, NH), 3.69 (m, 1H, 2CH), 2.81 (s, 3H, CH_3), 2.53 (m, 4H, CH_2), 2.12 (t, J = 6.4, 6.6 MHz, 2H, CH_2), 1.75 (m, 4H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.8, 145.2, 141.9, 133.0, 131.7, 129.3, 127.9, 124.0, 114.8, 52.8, 41.6, 44.8, 27.3, 13.9; MS (ESI): m/z 356.2 (M+). Anal.Calculated for $C_{21}H_{23}ClN_2O$ C, 71.07; H, 6.53; Cl, 9.99; N, 7.89; O, 4.51 found: C, 71.25; H, 6.72; N, 7.90.

((1R,5S)-3-(p-Toluidino)-8-aza-bicyclo[3.2.1]octan-8-yl)(4-chlorophenyl) methanone(4g):
Off white Solid; yield: 73%; IR (KBr, υ/cm^{-1}): 3358, 3269, 3081, 2927, 2842, 1717, 1648, 1587, 1353, 1153; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.01-6.74 (m, 9H, Ar-H), 4.48 (brs, 1H, NH), 3.60 (m, 1H, 2CH), 2.88 (s, 3H, CH_3), 2.54 (m, 4H, CH_2), 2.19 (t, J = 6.2, 6.8 MHz, 2H, CH_2), 1.70 (m, 4H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.0, 144.9, 142.0, 132.8, 131.4, 129.8, 128.9, 124.2, 115.1, 53.4, 42.8, 45.0, 27.7, 13.7; MS (ESI): m/z 356.2 (M+). Anal.Calculated for $C_{21}H_{23}ClN_2O$ C, 71.07; H, 6.53; Cl, 9.99; N, 7.89; O, 4.51 found: C, 71.20; H, 6.70; N, 7.94.

(4-Chlorophenyl)((1R,5S)-3-(3-nitrophenylamino)-8-aza-bicyclo[3.2.1]octan-8-yl)methanone (4h):
Yellow powder; yield: 69%; IR (KBr, υ/cm^{-1}): 3428, 3358, 3296, 3117, 2952, 2864, 1729, 1663, 1587, 1358, 1149; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.16-6.95 (m, 8H, Ar-H), 4.75 (brs, 1H, NH), 3.95 (m, 1H, 2CH), 2.88 (m, 4H, CH_2), 2.23 (t, J = 6.4, 6.9 MHz, 2H, CH_2), 1.85 (m, 4H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.9, 145.4, 143.7, 142.8, 133.4, 132.0, 130.8, 128.1, 126.7, 118.4, 54.5, 43.7, 41.6, 28.2.$C_{20}H_{21}N_3O_3$: MS (ESI): m/z 387.1 (M+). Anal.Calculated for $C_{20}H_{20}ClN_3O_3$ C, 62.26; H, 5.22; Cl, 9.19; N, 10.89; O, 12.44 found: C, 62.37; H, 6.70; N, 7.94.

(4-Chlorophenyl)((1R,5S)-3-(4-nitrophenylamino)-8-aza-bicyclo[3.2.1]octan-8-yl)methanone (4i):
Dark brown powder; yield: 58%; IR (KBr, υ/cm^{-1}): 3415, 3386, 3245, 3110, 2955, 2860, 1735, 1663, 1584, 1354, 1146; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.10-6.99 (m, 9H, Ar-H), 4.78 (brs, 1H, NH), 3.99 (m, 1H, 2CH), 2.82 (m, 4H, CH_2), 2.35 (t, J = 5.8, 6.2 MHz, 2H, CH_2), 1.46 (m, 4H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.2, 145.2, 142.6, 141.9, 133.5, 132.2, 130.8, 128.6, 126.7, 118.4, 54.7, 43.2, 41.5, 28.5; $C_{20}H_{21}N_3O_3$: MS (ESI): m/z 387.1 (M+). Anal.Calculated for $C_{20}H_{20}ClN_3O_3$ C, 62.26; H, 5.22; Cl, 9.19; N, 10.89; O, 12.44 found: C, 62.47; H, 6.80; N, 7.84.

(4-Chlorophenyl)((1R,5S)-3-(4-nitrophenylamino)-8-aza-bicyclo[3.2.1]octan-8-yl)methanone (4j):
Oil; yield: 86%; IR (KBr, υ/ cm^{-1}): 3415, 3359, 3284, 3118, 2951, 2869, 1730, 1664, 1582, 1358, 1143; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.15- 6.94 (m, 9H, Ar-H), 4.72 (brs, 1H, NH), 3.97 (m, 1H, 2CH), 2.84 (m, 4H, CH_2), 2.30 (t, J = 6.4, 6.6 MHz, 2H, CH_2), 1.51 (m, 4H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.7, 145.2, 142.7, 140.4, 133.6, 132.8, 130.2, 128.4, 126.4, 117.9, 53.9, 43.4, 41.8, 28.4; $C_{20}H_{21}N_3O_3$: MS (ESI): m/z 387.1 (M+). Anal.Calculated for $C_{20}H_{20}ClN_3O_3$ C, 62.26; H, 5.22; Cl, 9.19; N, 10.89; O, 12.44 found: C, 62.37; H, 5.40; N, 10.84.

CONCLUSION

In the present study we have synthesized a new series of novel (4-chlorophenyl) ((1R, 3R, 5S)-3-(phenyl amino)-8-aza-bicyclo [3,2,1] octan-8-yl) methanone derivatives with very good yields. All the synthesized compounds screened for their antibacterial activity against various microorganisms. Among the all synthesized compounds **4c**, **4g**, **4i** confer the highest antibacterial activity against all tested bacterial strains in both 50 µg, 100 µg and 200 µg concentrations. Hence **4c**, **4g** and **4i** are identified as the most potent antibacterial agents in the present series and deserve further investigation in order to clarify the mode of action at molecular level responsible for the activity observed.

Acknowledgements
The authors are thankful to the Geehanjali Institute of Scienece and Technology, Department of Chemistry, Nellore for their financial and support.

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