ISSN 2395-3411 Available online at www.ijpacr.com 338-347

Research Article

Synthetic and spectral studies on piperidine derived phenylacetamides

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ABSTRACT

A variety of piperidine containing substituted phenylacetamide derivatives were synthesized by the reaction of phenylacetic acids and piperidines substituted with different functional groups in presence of 1, 1'-carbonyl diimidazole (CDI). The spectral analysis of the purified amides showed unique patterns in their NMR spectra while characteristic fragmentation pattern was observed in their mass spectra.

Keywords: Phenylacetamides, Piperidine, CDI, Spectral analysis.

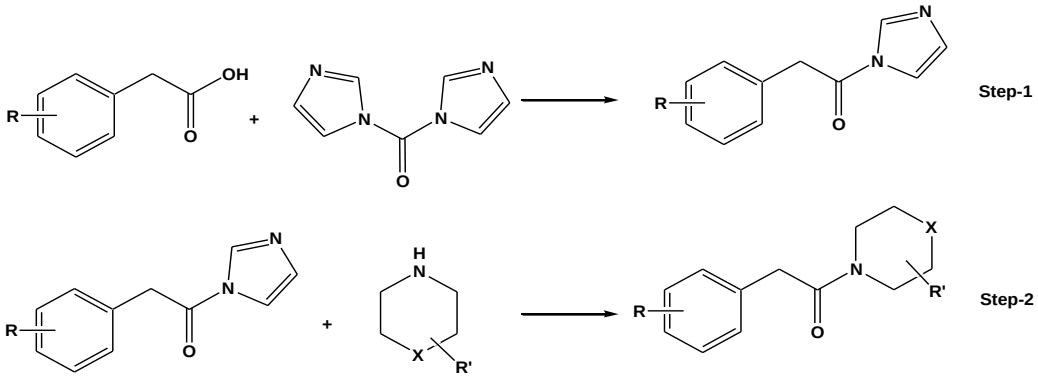
INTRODUCTION

Amides constitute a large group of organic molecules which show a wide range of biological activities. Chemically, the amide functional group represents a basic building block of proteins and is prone to build secondary bonds inside and outside the molecule. Due to its ability of making secondary chemical bonds, the amide groups along with other functional groups present in the molecule significantly affect the chemical properties of the molecules and hence their biological activity. Among different types of amides, phenylacetamides constitute a special class of amides. They have found numerous applications as human, veterinary and plant medicines and play an important role in daily life. The phenylacetamide derivatives have been reported to possess analgesic[1], anti-microbial[2], anti-convulsant[3], anti-arrhythmic[4], anti-tuberculosis[5], anti-tumor activities[6] and mosquito repellent activities. The compound N, N'-diethylphenylacetamide (DEPA) is a classical and representative example of mosquito repelling phenylacetamides. It has been formulated in commercial preparation by the Defence Research and Development Establishment [DRDE], Gwalior and is available in Indian market in the form of lotion, cream and spray formulations. It has been granted approval by the Drug Controller of India for use on humans[7]. Different formulations as well as fabrics impregnated with DEPA are effective for personnel protection from mosquito bites. However, in spite of the fact that systematic information on the chemistry, safety and efficacy of DEPA is available, there is still the need to find out a non-toxic and more efficient multi-insect repellent and to carry out further discoveries of newer mosquito repellents as the mosquito may develop resistance to the existing repellents. As piperidine has been found as a pharmacophore in a variety of drugs, it was envisaged that by replacing diethylamino group of DEPA molecule by a piperidine ring may lead to the favorable changes in terms of toxicity and repellency properties of the DEPA molecule. Recently, Akanksha *et al*[8] has synthesized a series of DEPA analogs at Defence R & D Establishment, Gwalior and as an extension to this work, we have synthsized some novel piperidine derived phenylacetamide derivatives which can be used an alternate to DEPA as a mosquito repellent. In this paper, we describe our work on the synthesis and spectral analysis of piperidine and morpholine derived phenylacetamide derivatives.

RESULTS AND DISCUSSION

During the present course of work, different substituted phenylacetic acids were coupled with a variety of (un)substituted piperidines in the presence of 1, 1'-Carbonyldiimidazole (CDI) (Scheme 1). The reaction was supposed

to take place in two steps. In the first step, reaction between the carboxylic acid with CDI in situ generates the corresponding imidazolide which, in the next step, reacts with the amine to get the desired amide.



Scheme 1: Conversion of phenylacetic acid to corresponding amides in presence of CDI

Based on this mechanism, the phenylacetic acids were reacted with piperidines in presence of 1, 1'-Carbonyldiimidazole (CDI) in THF and complete within half an hour for all the phenylacetic acids. After the completion of initial coupling reaction, the amine is added to the reaction mixture and reaction is continued till complete consumption of intermediate imidazolide. A comparison of the results indicated that the optimum reaction conditions for the preparation of amides by coupling of carboxylic acid and an amine in presence of CDI involves reacting acid, amine and CDI in 1:1.1:1.1 ratio at room temperature in Tetrahydrofuran (THF). With these optimized parameters, different amides were prepared by the treating various phenylacetic acids and piperidines (Table 1). It was further found that for most of the substrates, the reaction was quite fast and completed in two to five hours. The reaction speed was found to be slightly dependent on the steric crowding on the participating substrates and hence, reaction took more time with substrates having substitutions in the ring. After completion of the reaction, aqueous workup of the reaction mixture yielded the desired amide in crude form. The final compound is obtained in the pure form after passing through silica plug or after flash chromatography. A comparison of the product yields indicates that this reaction protocol gave excellent yield of the desired products.

Table 1: Synthesis of N-phenylacyl piperidines and morpholines

No	Amide	Time (Hrs)	Yield (%)
1	N-Phenylacetylpiperidine	2.0	90
2	N-(2-Methylphenylacetyl)piperidine	3.0	85
3	N-(3-Methylphenylacetyl)piperidine	3.5	87
4	N-(4-Methylphenylacetyl)piperidine	3.0	84
5	N-(2-Methoxyphenylacetyl)piperidine	2.5	85
6	N-(3-Methoxyphenylacetyl)piperidine	3.0	83
7	N-(4-Methoxyphenylacetyl)piperidine	2.5	87
8	N-(2-Fluorophenylacetyl) piperidine	4.0	80
9	N-(3-Fluorophenylacetyl) piperidine	4.5	78
10	N-(4-Fluorophenylacetyl) piperidine	3.5	81
11	N-(4-Chlorophenylacetyl) piperidine	4.0	84
12	N-Phenylacetyl-2-methylpiperidine	5.5	83
13	N-Phenylacetyl-3-methylpiperidine	5.0	83
14	N-Phenylacetyl-4-methylpiperidine	4.5	81
15	N-(2-Methylphenylacetyl)-2-methylpiperidine	5.5	83
16	N-(2-Methylphenylacetyl)-3-methylpiperidine	5.0	79
17	N-(2-Methylphenylacetyl)-4-methylpiperidine	3.5	78
18	N-(3-Methylphenylacetyl)-2-methylpiperidine	4.0	81
19	N-(3-Methylphenylacetyl)-3-methylpiperidine	5.0	81
20	N-(3-Methylphenylacetyl)-4-methylpiperidine	4.5	84
21	N-(4-Methylphenylacetyl)-2-methylpiperidine	5.0	85
22	N-(4-Methylphenylacetyl)-3-methylpiperidine	4.5	87
23	N-(4-Methylphenylacetyl)-4-methylpiperidine	3.0	88

Characterization of the synthesized compounds was performed by their spectral analysis involving Infrared (IR), ^{1}H and ^{13}C NMR and Electron Ionization-Mass spectral (EI-MS) analyses.

Infrared (IR) Spectral Analysis

The infrared (IR) spectra of all the synthesized amides showed characteristic absorption band corresponding to C=O and C-N stretching vibrations. The amide band due to the C=O stretching vibration is often referred to as the Amide I band which has appeared in the region of 1650-1630 cm^{-1} for all the synthesized compounds. Being tertiary amides, all the synthesized compounds do not show any N-H stretching bands, generally called as Amide II band which is commonly observed in the IR spectra of primary and secondary amides. In addition to it, all the amides have broad bands of medium-to-strong intensity in the region of 695-550 cm^{-1} which are probably due to the bending motion of the O=C-N groups.

NMR Spectral Analysis

The ^{1}H and ^{13}C NMR spectra of the synthesized compounds were fully commensurate with their structures. The synthesized piperidine derived phenylacetamide derivatives were divided into two groups: first in which the phenyl ring is substituted with different substituents and in the second group of amides, both the phenyl and piperidine rings are substituted. Amides belonging to each group showed almost similar splitting pattern in their NMR spectra. However, they differ significantly with that of other group.

In ^{1}H NMR spectra of phenyl ring substituted amides (Table 2), the benzylic protons appeared at their usual chemical shift positions (3.66-3.78). The position of these methylene protons was found to differ in the ^{1}H NMR spectra of different amides and was difficult to correlate with the nature of substituent. The, H-3', 4' and 5' methylene protons of the piperidine ring appeared at their usual positions as two sets of multiplet due to the complex interaction between the axial and equatorial protons of the piperidine ring. On the other hand, H-2' and H-6' protons of the piperidine ring were displayed as triplets at 3.33-3.42 and 3.55-3.60. Additionally, depending upon the nature and position of the substituents attached to phenyl ring, the aromatic protons showed different signals in the ^{1}H NMR spectra. For ortho substituted amides, the aromatic protons were showed as a multiplet, integrated for four protons, in the aromatic region. On the other hand, in the ^{1}H NMR spectra of para substituted amide, two sets of doublets, each integrated for two protons in observed due to the aromatic protons. In case of *meta*-substituted amides, splitting pattern characteristic of *meta*-substituted aromatic compounds (triplet, broad singlet and multiplet) was observed in their ^{1}H NMR spectrum.

While unsubstituted piperidine amides show uncomplicated patterns in their NMR spectra, substitution in piperidine ring adds a considerable complexity to the corresponding ^{1}H NMR spectra (Table 3). Because of the symmetrical structures in the piperidine rings and unhindered rotation around C-N bond, the symmetrical piperidine amides are observed as single rotamers at room temperature. On the other hand, the proton spectra of the piperidine amides with substitution in piperidine ring encounter a hindered rotation about the N–C=O bond on the NMR time scale. Due to the partial double bond character of C–N bonds, these unsymmetrical amides exist as mixtures of two rotamers in almost equal proportions at room temperature. Detailed variable temperature NMR spectra of such compounds have been reported to give $\Delta G‡$ values of 16.2 ± 0.3 $kcal.mol^{-1}$ for inter conversion of the rotamers, corresponding to a first order rate constant of ~30 s^{-1} at ambient temperature[117]. Because of this reason, all the protons of the compounds revealed two sets of signal for every proton present in the amides at room temperature leading to very complex NMR spectra. For example, in case of piperidine amides with methyl groups at piperidine ring exhibit two sets of signals for the CH_3 protons at room temperature. At the same time, the adjacent protons of the piperidine ring also have different chemical shifts due to differing environments and give rise to different splitting patterns in their ^{1}H NMR spectra.

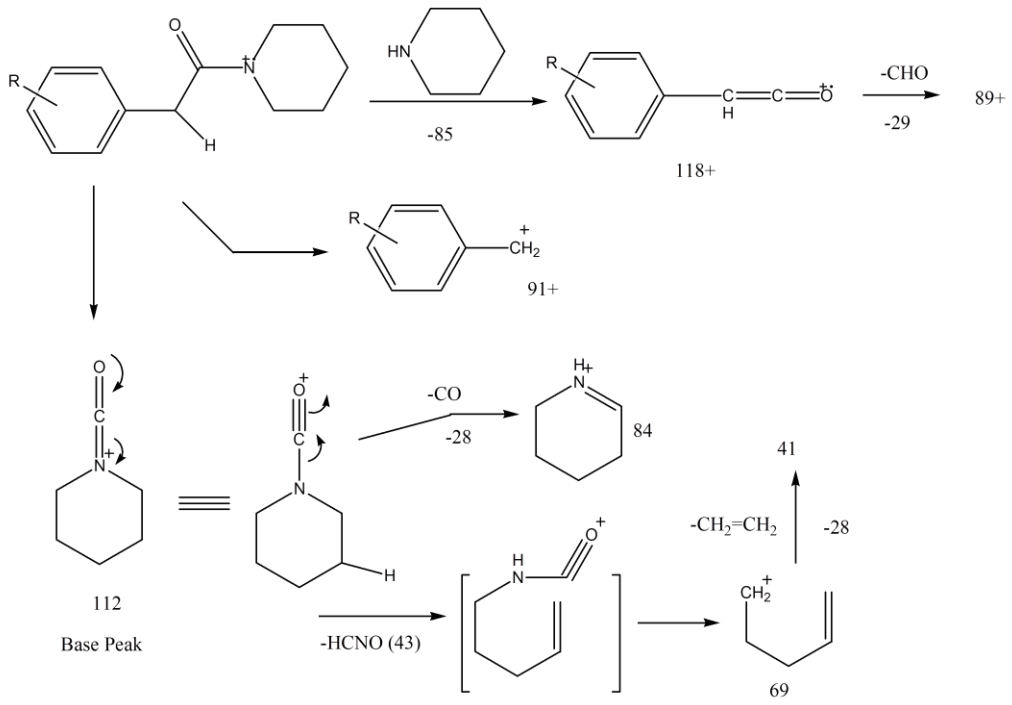
Mass Spectral Analysis

The fragmentation pattern in the mass spectra of these amides was found to be dependent on the substitutions on both the phenyl ring and on the amine components of the amides. The amides with unstubstituted piperidine ring exhibited prominent molecular ion peak and a characteristic fragmentation pattern is observed in their mass spectrum. The main fragmentation pathway in the mass spectra of such compounds can be described by two major events including *α*-cleavages at the carbonyl functions at C-C and C-N bonds which, depending upon the retention of charge, produce fragment ions characteristics

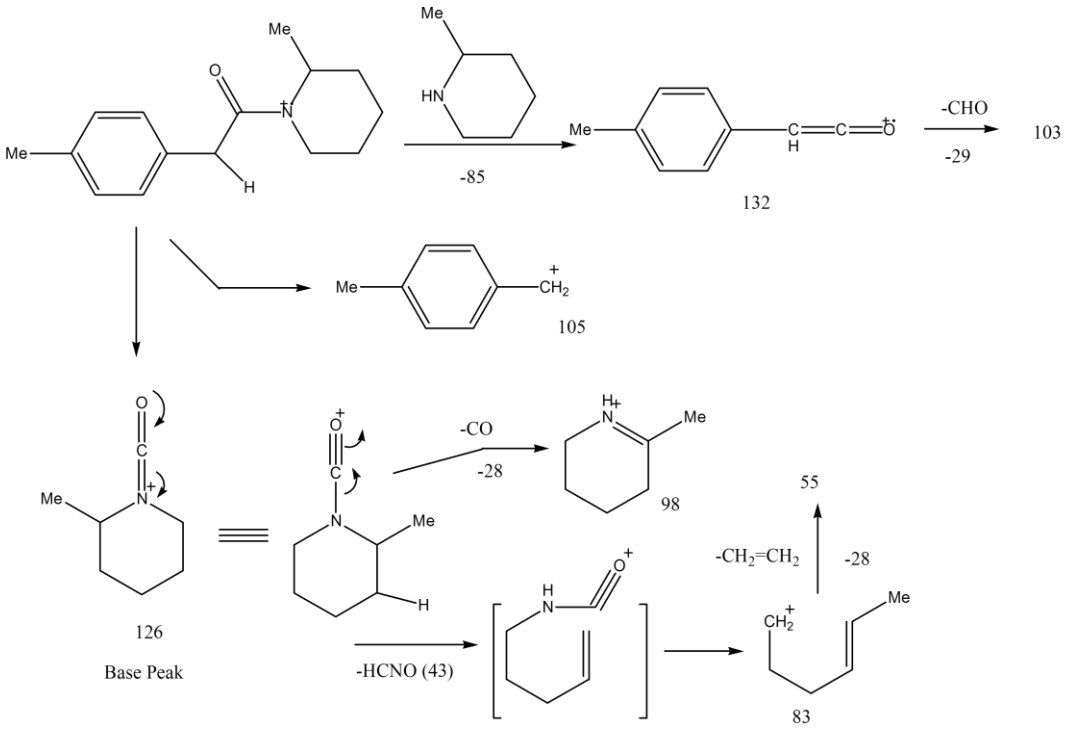
of the acid and amine components of the amide respectively.

In the mass spectra of piperidine derived phenylacetamides, the most important pathway involves □-cleavage leading to carboxamide ion $[CONR_2]^+$ to give rise to a base peak at *m/z* 112. The major fragmentation pathway in the carboxamide ion involves the ring opening followed by expulsion of HCNO molecule which leads to a prominent peak at m/z 69. The later also fragments with the loss of ethylene molecule to give peak at m/z 41. An alternate fragmentation involves CO-N cleavage with hydrogen transfer to nitrogen leading to less abundant peak at m/z 84 corresponding to $[HNR_2]^+$ ion. It can be considered as a result of methylene hydrogen transfer to carboxamide nitrogen, subsequent homolytic cleavage with charge retention on nitrogen and expulsion of a CO molecule. These fragment ions were observed in all the mass spectra and are characteristic of the presence of intact piperidine nucleus. On the other hand, rest of the ions is characteristics of the substituents present on the phenyl ring of the acetic acid moiety. In all the cases, the molecular ion peak was quite strong and prominent. A peak, although very weak, at M-1 was also observed in mass spectra of all the molecules. However, the most abundant ion resulting from the cleavage of bond □ to the CO group (CO-N bond) leads to the fragment ion at m/z 118 in case of unsubstituted phenyl acetic acid while in substituted amides, the corresponding ion was observed at its respective position depending upon the mass of substituents present of the phenyl ring. On the other hand, cleavage of another □-CO bond leads to the formation of ion at m/s 91 and corresponding ions in the mass spectra of other substituted amides. Loss of substituent from the phenyl ring of the amides was also observed with some of the amides but not with all the amides. For example, a very faint peak at M-1 was observed in the mass spectra of 2- and 3-methyl and methoxy substituted amides and that of 4-fluoro amide only (Scheme 3).

In case of halogenated phenylacetylpiperidine amide with halogen at ortho position in the phenyl ring, fragment ion resulting from the expulsion of ortho substituent, i. e., fluorine, directly from the molecular ion is also observed at M-X position. However, such fragmentation is not observable in case of meta- and para- substituted amides.



Scheme 3: Mass Spectral Fragmentation Pattern of Phenyl Substituted N-Phenylacetylpiperidine Amides



Scheme 4: Mass Spectral Fragmentation Pattern of Amine Substituted N-Phenylacetylpiperidine Amides

In case of amides differing in the nature of amine also, similar trend of fragmentation was followed. The fragment ions characteristics of the parent carboxylic acid moiety, i.e., ions at 132, 105 and 103 were observed consistently in mass spectra of all these amides. On the other hand, other ions appeared in the mass spectra contained the amine component and observed at different m/z values in amides of different amines (Scheme 4).

Table 4: Mass Spectral Fragment Ions appearing in the mass spectra of Phenyl ring substituted Piperidine derived Phenylacetamides

No	Amide	M Wt	Fragment Ions m/z (Intensity)
1	N-Phenylacetylpiperidine	203	203 [M] (48), 118 (3), 112 (100), 91 (20), 89 (3), 84 (10), 69 (42), 41 (10), 56 (6)
2	N-(2-Methylphenylacetyl) piperidine	217	217 [M] (68), 216 (2), 202 (9), 132 (2), 112 (100), 105 (22), 91 (2), 103 (7), 84 (9), 69 (36), 41 (11), 77 (11), 56 (4)
3	N-(3-Methylphenylacetyl) piperidine	217	217 [M] (63), 216 (8), 202 (2), 132 (3), 112 (100), 105 (22), 91 (7), 103 (9), 84 (12), 69 (48), 41 (14), 77 (12), 56 (7)
4	N-(4-Methylphenylacetyl) piperidine	217	217 [M] (55), 216 (7), 132 (4), 112 (100), 105 (22), 91 (2), 103 (7), 84 (9), 69 (44), 41 (11), 77 (11), 56 (7)
5	N-(2-Methoxyphenylacetyl) piperidine	233	233 [M] (98), 232 (1), 202 (38), 148 (7), 132 (5), 112 (100), 121 (24), 91 (55), 119 (3), 84 (12), 69 (67), 41 (15), 77 (8), 56 (6)
6	N-(3-Methoxyphenylacetyl) piperidine	233	233 [M] (77), 232 (12), 218 (2), 148 (4), 112 (100), 121 (17), 91 (12), 119 (2), 84 (10), 69 (39), 41 (9), 78 (8), 56 (6)
7	N-(4-Methoxyphenylacetyl) piperidine	233	233 [M] (98), 232 (4), 148 (6), 132 (1), 112 (100), 121 (94), 91 (9), 119 (4), 84 (7), 69 (64), 41 (14), 78 (14), 56 (7)
8	N-(2-Fluorophenylacetyl)piperidine	221	221 [M] (42), 220 (3), 202 (3), 136 (3), 112 (100), 109 (39), 107 (5), 84 (10), 69 (42), 41 (11), 83 (11), 56 (6)
9	N-(3-Fluorophenylacetyl)piperidine	221	221 [M] (29), 220 (7), 136 (3), 112 (100), 109 (37), 107 (3), 84 (12), 69 (43), 41 (12), 83 (10), 56 (7)

10	N-(4-Fluorophenylacetyl)piperidine	221	221 [M] (29), 220 (4), 136 (3), 112 (100), 109 (37), 107 (4), 84 (8), 69 (43), 41 (12), 83 (10), 56 (6)
11	N-(2-Chlorophenylacetyl)piperidine	237	239 [M] (8), 237 (30), 152 (7), 125 (40), 123 (10), 112 (100), 84 (10), 69 (50).
12	N-Phenylacetyl-2-methylpiperidine	217	217 [M], 132, 126 (100), 105, 103, 98, 83.
13	N-Phenylacetyl-3-methylpiperidine	217	217 [M], 132, 126 (100), 105, 103, 98, 83.
14	N-Phenylacetyl-4-methylpiperidine	217	217 [M] (54), 126 (100), 98 (6), 91 (33), 82 (17), 65 (8), 55 (25).
15	N-(2-Methylphenylacetyl)-2-methylpiperidine	231	231 [M] (6), 216 (3), 126 (100), 105 (30), 98 (13), 84 (25), 70 (5), 55 (23).
16	N-(2-Methylphenylacetyl)-3-methylpiperidine	231	231 [M] (84), 216 (12), 126 (100), 105 (27), 98 (14), 83 (25), 77 (14), 55 (27), 41 (10).
17	N-(2-Methylphenylacetyl)-4-methylpiperidine	231	231 [M] (66), 216 (10), 126 (100), 105 (26), 98 (7), 83 (20), 77 (10), 55 (26).
18	N-(3-Methylphenylacetyl)-2-methylpiperidine	231	231 [M] (69), 216 (3), 126 (100), 105 (28), 84 (30), 76 (9), 70 (5), 55 (18).
19	N-(3-Methylphenylacetyl)-3-methylpiperidine	231	231 [M] (65), 216 (3), 126 (100), 105 (25), 98 (13), 83 (20), 77 (10), 55 (25).
20	N-(3-Methylphenylacetyl)-4-methylpiperidine	231	231 [M], 126 (100), 105 (29), 98 (15), 91 (10), 83 (20), 55 (30).
21	N-(4-Methylphenylacetyl)-2-methylpiperidine	231	231 [M] (50), 216 (1), 132 (4), 126 (100), 112 (2), 105 (28), 98 (12), 91 (3), 84 (12), 70 (4), 55 (12).
22	N-(4-Methylphenylacetyl)-3-methylpiperidine	231	231 [M] (69), 216 (3), 132 (3), 126 (100), 105 (24), 103 (5), 98 (9), 91 (3), 83 (12), 70 (3), 55 (20).
23	N-(4-Methylphenylacetyl)-4-methylpiperidine	231	231 [M] (46), 132 (4), 126 (100), 105 (23), 103 (4), 98 (4), 91 (3), 83 (17), 55 (25).

EXPERIMENTAL

Chemicals

All the chemicals required for the synthesis of amides in the present work were purchased from Aldrich and were used as such without further purification. IR spectra were recorded as neat samples using a PerkinElmer spectrum BX FT-IR spectrophotometer. ^{1}H NMR spectra was recorded in $CDCl_3$ on a Bruker Advance (400 MHz) spectrometer using TMS as internal reference. Chemical shift values are recorded in δ (ppm). GC-MS was performed using a Agilent Technology 6890 N gas chromatograph equipped with a split/ split less injector and a capillary column (30 m x 0.32 mm i.d., 0.25 μm film thickness, BP-5 stationary phase, SGE) directly coupled to Agilent Technologies 5973 quadrupole mass spectral detector and integral data system. Ionization was done by electron impact at 70 eV and 230°C. Helium was used as the carrier gas.

Experimental procedure

The melting points of the compounds were determined in soft glass capillaries in an electro thermal melting point apparatus and are uncorrected. Silica gel (200-400 mesh, s d fine) was used as stationary phase for flash column chromatography. Thin layer chromatography experiments were conducted on TLC aluminum sheets Silica $60F_{254}$ (E. Merck). Iodine was used as the visualizing agent for TLC. Infrared spectra were recorded on Perkin Elmer 577 Infrared Spectrophotometer on KBr pellets (for solids) or as neat (for liquids) and the frequencies are reported in wave number (cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with tetramethylsilane (TMS) as internal standard on Bruker Avance 400 NMR Spectrometer. Chemical shifts (δ) were recorded in parts per million (ppm) from the internal standard (TMS=0.00). Mass spectra were recorded on Agilent 5973i Mass spectral Detector attached to Agilent 6890 Gas Chromatograph. All starting materials and other reagents were obtained from Sigma Aldrich and Acros and used as obtained.

General method for the synthesis of amides: In a three neck round bottom flask, 1, 1'-carbonyldiimidazole (1.2 eq) was added to a solution of carboxylic acid (1 eq.) in freshly distilled THF at RT. After complete consumption of carboxylic acid (TLC), amine (1.1 eq.) was added and the reaction continued at room temperature. After completion of the reaction, reaction mixture was diluted with ethyl acetate and treated with 10% aq. NaOH solution (100 ml). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic phase was washed successively with 2 N HCl (100 ml) and brine (100 ml), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Pure amide was then obtained after flash chromatography (hexane- ethyl acetate) and then characterized using spectral techniques.

Phenylacetylpiperidine (1): Oil, 90 %, IR (ν, KBr): 3050, 2983, 2855, 1634, 1443, 1267, 727 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]:

7.33-7.21 (m, 5 x Ar-H), 3.73 (s, 2H, $COCH_2$), 3.55 (t, J=5.6 Hz, 2H, NCH_2), 3.37 (t, J=5.6 Hz, 2H, NCH_2), 1.57-1.52 (m, 4H, 2 x CH_2), 1.34-1.32 (m, 2H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 24.34, 25.45, 26.11, 41.02, 42.85, 47.21, 126.57, 128.54, 128.58, 135.38, 169.29. EI-MS (m/z, %): 203 (48), 118 (3), 112 (100), 91 (20), 89 (3), 84 (10), 69 (42), 41 (10), 56 (6). Anal. Calc'd for $C_{13}H_{17}NO$ (M=203) 76.81 (C); 8.43 (H); 6.89 (N). Found: 76.80 (C); 8.44 (H); 6.88 (N).

N-(2-Methylphenylacetyl)piperidine (2): Oil, 85 %, IR (ν, KBr): 3020, 2936, 2855, 1725, 1641, 1443, 1256, 1220, 1136,1016, 852 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.16-7.11 (m, 4 x Ar-H), 3.66 (s, 2H, $COCH_2$), 3.60 (t, J=5.6 Hz, 2H, NCH_2), 3.33 (t, J=5.6 Hz, 2H, NCH_2), 2.27(s, 3H, $PhCH_3$), 1.63-1.55 (m, 4H, 2 x CH_2), 1.45-1.41 (m, 2H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 19.23, 24.00, 25.18, 25.82, 38.10, 42.47, 46.68, 125.67, 126.36, 128.22, 129.79, 133.57, 135.82, 169.00. EI-MS (m/z, %):217 (68), 216 (2), 202 (9), 132 (2), 112 (100), 105 (22), 91 (2), 103 (7), 84 (9), 69 (36), 41 (11), 77 (11), 56 (4). Anal. Calc'd for $C_{14}H_{19}NO$ (M=217) 77.38 (C); 8.81 (H); 6.45 (N). Found: 77.38 (C); 8.82 (H); 6.43 (N).

N-(3-Methylphenylacetyl)piperidine (3): Oil, 87 %, IR (ν, KBr): 3035, 2936, 2858, 1636, 1444, 1266, 1123, 1022, 957, 855, 766 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]:7.18 (t, J=7.6 Hz, 1 x Ar-H), 7.07 (sbr, 1 x Ar-H), 7.03 (d, J=7.6 Hz, 2H), 3.69 (s, 2H, $COCH_2$), 3.57 (t, J=5.6 Hz, 2H, NCH_2), 3.37 (t, J=5.6 Hz, 2H, NCH_2), 2.32 (s, 3H, $PhCH_3$), 1.59-1.51 (m, 4H, 2 x CH_2), 1.37-1.34 (m, 2H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 21.35, 24.41, 25.50, 26.17, 41.01, 42.91, 47.27, 125.58, 127.37, 128.49, 129.27, 135.24, 138.22, 169.50. EI-MS (m/z, %): 217 (63), 216 (8), 202 (2), 132 (3), 112 (100), 105 (22), 91 (7), 103 (9), 84 (12), 69 (48), 41 (14), 77 (12), 56 (7). Anal. Calc'd for $C_{14}H_{19}NO$ (M=217) 77.38 (C); 8.81 (H); 6.45 (N). Found: 77.37 (C); 8.82 (H); 6.43 (N).

N-(4-Methylphenylacetyl)piperidine (4): Oil, 84 %, IR (ν, KBr): 3012, 2938, 2855, 2363, 1631, 1446, 1259, 1123, 1024, 779 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.13 (d, J=8.4 Hz, 2 x Ar-H), 7.10 (d, J=8.4 Hz, 2 x Ar-H), 3.69 (s, 2H, $COCH_2$), 3.55 (t, J=5.6 Hz, 2H, NCH_2), 3.35 (t, J=5.6 Hz, 2H, NCH_2), 2.31 (s, 3H, $PhCH_3$), 1.57-1.54 (m, 4H, 2 x CH_2), 1.36-1.32 (m, 2H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 21.00, 24.42, 25.49, 26.17, 40.71, 42.86, 47.23, 128.41, 129.30, 132.30, 136.08, 169.51. EI-MS (m/z, %): 217 (55), 216 (7), 132 (4), 112 (100), 105 (22), 91 (2), 103 (7), 84 (9), 69 (44), 41 (11), 77 (11), 56 (7). Anal. Calc'd for $C_{14}H_{19}NO$ (M=217) 77.38 (C); 8.81 (H); 6.45 (N). Found: 77.35 (C); 8.84 (H); 6.43 (N).

N-(2-Methoxyphenylacetyl)piperidine (5): Oil, 85 %, IR (ν, KBr): 3012, 2936, 2855, 1722, 1644, 1496, 1446, 1326, 1246, 1181, 1139, 1029, 957, 855, 753 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.25-7.19 (m, 2 x Ar-H), 6.92-6.84 (m, 2 x Ar-H), 3.81 (s, 3H, OCH_3), 3.69 (s, 2H, $COCH_2$), 3.57 (t, J=5.6 Hz, 2H, NCH_2), 3.36 (t, J=5.6 Hz, 2H, NCH_2), 1.60-1.48 (m, 4H, 2 x CH_2), 1.39-1.34 (m, 2H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 24.50, 25.57, 26.23, 34.64, 42.90, 47.07, 55.39, 110.38, 120.65, 124.02, 127.95, 129.79, 156.65, 169.92. EI-MS (m/z, %): 233 (98), 232 (1), 202 (38), 148 (7), 132 (5), 112 (100), 121 (24), 91 (55), 119 (3), 84 (12), 69 (67), 41 (15), 77 (8), 56 (6). Anal. Calc'd for $C_{14}H_{19}NO_2$ (M=233) 72.07 (C); 8.21 (H); 6.00 (N). Found: 72.05 (C); 8.20 (H); 5.98 (N).

N-(3-Methoxyphenylacetyl)piperidine (6): Oil, 83 %, IR (ν, KBr): 3010, 2938, 2855, 1634, 1493, 1446, 1264, 1150, 1050, 954, 855, 769 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.22 (t, J=8.0 Hz, 1 x Ar-H), 6.84 (sbr, 1 x Ar-H), 6.81-6.77 (m, 2 x Ar-H), 3.79 (s, 3H, OCH_3), 3.70 (s, 2H, $COCH_2$), 3.57 (t, J=5.6 Hz, 2H, NCH_2), 3.37 (t, J=5.6 Hz, 2H, NCH_2), 1.58-1.52 (m, 4H, 2 x CH_2), 1. 37 -1.34 (m, 2H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 24.36, 25.48, 26.14, 41.05, 42.82, 47.21, 55.09, 112.19, 114.11, 120.90, 129.53, 136.92, 159.82, 169.80. EI-MS (m/z, %): 233 (77), 232 (12), 218 (2), 148 (4), , 112 (100), 121 (17), 91 (12), 119 (2), 84 (10), 69 (39), 41 (9), 78 (8), 56 (6). Anal. Calc'd for $C_{14}H_{19}NO_2$ (M=233) 72.07 (C); 8.21 (H); 6.00 (N). Found: 72.05 (C); 8.25 (H); 6.02 (N).

N-(4-Methoxyphenylacetyl)piperidine (7): Oil, 87 %, IR (ν, KBr): 3010, 2935, 2850, 2370, 1635, 1448, 1260, 1135, 1024, 950, 856, 779 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.16 (d, J=8.8 Hz, 2 x Ar-H), 6.85 (d, J=8.8 Hz, 2 x Ar-H), 3.79 (s, 3H, OCH_3), 3.78 (s, 2H, $COCH_2$), 3.56 (t, J=5.6 Hz, 2H, NCH_2), 3.37 (t, J=5.6 Hz, 2H, NCH_2), 1.59-1.48 (m, 4H, 2 x CH_2), 1. 38 - 1.33 (m, 2H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 24.38, 25.48, 26.17, 40.06, 42.82, 47.17, 55.13, 114.11, 127.41, 129.57, 158.33, 169.58. EI-MS (m/z, %): 233 (98), 232 (4), 148 (6), 132 (1), 112 (100), 121 (94), 91 (9), 119 (4), 84 (7), 69 (64), 41 (14), 78 (14), 56 (7). Anal. Calc'd for $C_{14}H_{19}NO_2$

(M=233) 72.07 (C); 8.21 (H); 6.00 (N). Found: 72.05 (C); 8.23 (H); 5.98 (N).

N-(2-Fluorophenylacetyl)piperidine (8): Oil, 80 %, IR (ν, KBr): 3009, 2925, 2370, 1632, 1450, 1230, 1130, 1021, 947, 850, 785 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.32-7.01 (m, 4 x Ar-H), 3.72 (s, 2H, $COCH_2$), 3.58 (t, J=5.6 Hz, 2H, NCH_2), 3.41 (t, J=5.6 Hz, 2H, NCH_2), 1.62-1.45 (m, 6H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 25.12, 25.91, 26.83, 46.2, 116.00, 122.97, 124.62, 129.05, 131.44, 163.4, 172.71. EI-MS (m/z, %):221 (42), 220 (3), 202 (3), 136 (3), 112 (100), 109 (39), 107 (5), 84 (10), 69 (42), 41 (11), 83 (11), 56 (6). Anal. Calc'd for $C_{13}H_{16}FNO$ (M=221) 70.56 (C); 7.29 (H); 6.33 (N). Found: 70.58 (C); 7.25 (H); 6.35 (N).

N-(3-Fluorophenylacetyl)piperidine (9): Oil, 78 %, IR (ν, KBr): 3015, 2930, 2365, 1630, 1455, 1231, 1125, 1028, 945, 855, 790 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.17 (t, J=7.6 Hz,, 1 x Ar-H), 6.92 (sbr, 1 x Ar-H), 6.89 (d, J=8.0 Hz, 1 x Ar-H), 6.75 (d, J=8.0 Hz, 1 x Ar-H), 3.68 (s, 2H, $COCH_2$), 3.59 (t, J=5.6 Hz, 2H, NCH_2), 3.45 (t, J=5.6 Hz, 2H, NCH_2), 1.28-1.11 (m, 6H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 25.11, 25.92, 37.65, 46.27, 114.46, 125.48, 130.62, 137.53, 162.51, 172.79. EI-MS (m/z, %):221 (29), 220 (7), 136 (3), 112 (100), 109 (37), 107 (3), 84 (12), 69 (43), 41 (12), 83 (10), 56 (7). Anal. Calc'd for $C_{13}H_{16}FNO$ (M=221) 70.56 (C); 7.29 (H); 6.33 (N). Found: 70.53 (C); 7.26 (H); 6.35 (N).

N-(4-Fluorophenylacetyl)piperidine (10): Oil, 81 %, IR (ν, KBr): 3010, 2987, 2365, 1635, 1455, 1225, 1127, 1022, 946, 849, 786 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.25 (d, J=7.2 Hz, 2 x Ar-H), 7.16 (d, J=7.2 Hz, 2 x Ar-H), 3.67 (s, 2H, $COCH_2$), 3.55 (t, J=5.6 Hz, 2H, NCH_2), 3.42 (t, J=5.6 Hz, 2H, NCH_2), 1.63-1.45 (m, 6H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 24.22, 26.33, 38.79, 46.50, 116.00, 131.38, 133.45, 161.39, 180.12. EI-MS (m/z, %): 221 (29), 220 (4), 136 (3), 112 (100), 109 (37), 107 (4), 84 (8), 69 (43), 41 (12), 83 (10), 56 (6). Anal. Calc'd for $C_{13}H_{16}FNO$ (M=221) 70.56 (C); 7.29 (H); 6.33 (N). Found: 70.55 (C); 7.25 (H); 6.30 (N).

N-(4-Chlorophenylacetyl)piperidine (11): Oil, 84 %, IR (ν, KBr): 3012, 2937, 2375, 1635, 1447, 1135, 1095, 946, 846, 783 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.27 (d, J=6.4 Hz, 2 x Ar-H), 7.17 (d, J=6.4 Hz, 2 x Ar-H), 3.66 (s, 2H, $COCH_2$), 3.57 (t, J=5.6 Hz, 2H, NCH_2), 3.36 (t, J=5.6 Hz, 2H, NCH_2), 1.62-1.20 (m, 6H, CH_2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 23.19, 26.18, 39.00, 52.55, 129.43, 132.05, 134.75, 140.43, 181.35. EI-MS (m/z, %): 239 (8), 237 (30), 152 (7), 125 (40), 123 (10), 112 (100), 84 (10), 69 (50). Anal. Calc'd for $C_{13}H_{16}ClNO$ (M=237) 65.68 (C); 6.78 (H); 5.89 (N). Found: 65.59 (C); 6.78 (H); 5.89 (N).

N-(Phenylacetyl)-2-methylpiperidine (12): Oil, 83 % (Mixture of Rotamers), IR (ν, KBr): 3025, 2982, 2851, 1633, 1442, 1257, 727 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.32-7.20 (m, 10 x Ar-H), 4.95 (sbr, 1H, H-6_{ax}), 4.53 (d, J=12.8 Hz, 1H, H-6_{ax}), 4.14-4.10 (m, 1H, H-2_{ax}), 3.72 (s, 4H, $COCH_2$), 3.60 (d, J=12.8 Hz, 1H, H-2_{ax}), 3.00 (t, J= 12.8 Hz, 1H, H-6_{eq}), 2.65 (t, J=12.8 Hz, 1H, H-6_{eq}), 1.66-1.32 (m, 12 H, H-3, 4, 5), 1.11 (dd, J=6.4 Hz, 6 H, Me-2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 17.75, 18.75, 21.24, 22.14, 25.40, 27.45, 33.15, 35.13, 37.84, 38.49, 44.25, 45.25, 48.25, 49.48, 127.40, 128.39, 129.95, 136.91, 180.22. EI-MS (m/z, %): 217, 132, 126 (100), 105, 103, 98, 83. Anal. Calc'd for $C_{14}H_{19}NO$ (M=217) 77.38 (C); 8.81 (H); 6.45 (N). Found: 77.37 (C); 8.85 (H); 6.43 (N).

N-(Phenylacetyl)-3-methylpiperidine (13): Oil, 83 % (Mixture of two rotamers), IR (ν, KBr): 3022, 2981, 2850, 1633, 1442, 1260, 725 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.30-7.21 (m, 10 x Ar-H), 4.47-4.42 (m, 2H, H-2_{ax}), 3.77-3.67 (m, 6H, $COCH_2$, H-6_{ax}), 2.89 (dt, J=12.8, 2.8 Hz, 2H, H-2_{eq}), 2.58 (dt, J=12.8, 2.8 Hz, 2H, H-6_{eq}), 2.26 (q, J=13.2 Hz, 2H, H-3_{ax}), 1.80-1.05 (m, 8H, H-4, 5), 0.85 (dd, J=6.8 Hz, 6H, Me-3). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 16.50, 17.57, 21.23, 22.00, 26.80, 27.86, 32.33, 33.25, 37.49, 38.49, 43.52, 46.43, 53.45, 54.29, 126.27, 127.29, 129.95, 136.91 179.72. EI-MS (m/z, %): 217, 132, 126 (100), 105, 103, 98, 83. Anal. Calc'd for $C_{14}H_{19}NO$ (M=217) 77.38 (C); 8.81 (H); 6.45 (N). Found: 77.35 (C); 8.84 (H); 6.43 (N).

N-(Phenylacetyl)-4-methylpiperidine (14): Oil, 81 %, IR (ν, KBr): 3025, 2983, 2852, 1634, 1441, 1260, 1100, 725 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.32-7.10 (m, 5 x Ar-H), 4.60 (d, J= 12.0 Hz, 1H, H-2_{ax}), 3.82 (d, 1H, J=12.0 Hz, H-6_{ax}), 3.70 (s, 2H, $COCH_2$), 2.95 (dt, J=12.8, 2.8 Hz, 1H, H-2_{eq}), 2.60 (dt, J=12.8, 2.8 Hz, 1H, H-6_{eq}), 1.60-1.47 (m, 3H, H-3, 5), 1.10 (m, 1H, H-5), 0.90-0.80 (m, 4H, H-4, Me-4). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 17.20, 27.80, 32.15, 37.15, 43.43, 125.27, 129.29, 130.80, 137.29, 181.11. EI-MS (m/z, %):217[M] (54), 126 (100), 98 (6), 91 (33), 82 (17), 65 (8), 55 (25). Anal. Calc'd for

$C_{14}H_{19}NO$ (M=217) 77.38 (C); 8.81 (H); 6.45 (N). Found: 77.40 (C); 8.83 (H); 6.46 (N).

N-(2-Methylphenylacetyl)-2-methylpiperidine (15): Oil, 83 % (Mixture of Rotamers), IR (ν, KBr): 3011, 2935, 2857, 1723, 1643, 1434, 1260, 1221, 1137, 1011, 849 cm^{-1}. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.26-7.15 (m, 8 x Ar-H), 4.99 (sbr, 1H, H-6_{ax}), 4.59 (d, J=12.8 Hz, 1H, H-6_{ax}), 4.14 (m, 1H, H-2_{ax}), 3.62 (s, 4H, $COCH_2$), 3.49 (m, 1H, H-2_{ax}), 3.06 (t, J= 12.8 Hz, 1H, H-6_{eq}), 2.70 (t, J=12.8 Hz, 1H, H-6_{eq}), 2.27 (s, 6 H, Ar-Me), 1.64-1.40 (m, 12 H, H-3, 4, 5), 1.18 (dd, J=6.4 Hz, 6H, Me-2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 11.25, 12.65, 17.84, 18.14, 23.39, 24.46, 26.27, 27.27, 32.46, 34.26, 36.70, 37.60, 42.43, 43.50, 46.20, 47.28, 126.47, 128.39, 133.45, 137.53, 142.37, 178.58. EI-MS (m/z, %): 231 [M] (6), 216 (3), 126 (100), 105 (30), 98 (13), 84 (25), 70 (5), 55 (23). Anal. Calc'd for $C_{15}H_{21}NO$ (M=231) 77.88 (C); 9.15 (H); 6.05 (N). Found: 77.89 (C); 9.16 (H); 6.03 (N).

N-(3-Methylphenylacetyl)-2-methylpiperidine (16): Oil, 79 % (Mixture of Rotamers), IR (ν, KBr): 3015, 2933, 2865, 1731, 1641, 1433, 1261, 1221, 1143, 1015, 860 cm^{-1}. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.18 (t, J=7.6 Hz, 2 x Ar-H), 7.07-7.02 (m, 6 x Ar-H), 4.95 (sbr, 1H, H-6_{ax}), 4.54 (d, J=12.0 Hz, 1H, H-6_{ax}), 4.14 (m, 1H, H-2_{ax}), 3.69 (s, 4H, $COCH_2$), 3.60 (m, 1H, H-2_{ax}), 3.00 (t, J= 13.2 Hz, 1H, H-6_{eq}), 2.66 (t, J=13.2 Hz, 1H, H-6_{eq}), 2.32 (s, 6H, Ar-Me), 1.56-1.36 (m, 12 H, H-3, 4, 5), 1.12 (dd, J=6.4 Hz, 6H, Me-2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 15.14, 17.15, 19.20, 20.43, 23.68, 24.38, 28.95, 29.39, 31.47, 32.55, 38.20, 39.25, 42.14, 43.26, 46.70, 47.58, 125.55, 126.43, 129.32, 134.43, 136.98, 137.95, 175.27. EI-MS (m/z, %): 231 [M] (69), 216 (3), 126 (100), 105 (28), 84 (30), 76 (9), 70 (5), 55 (18). Anal. Calc'd for $C_{15}H_{21}NO$ (M=231) 77.88 (C); 9.15 (H); 6.05 (N). Found: 77.88 (C); 9.10 (H); 6.03 (N).

N-(4-Methylphenylacetyl)-2-methylpiperidine (17): Oil, 78 % (Mixture of Rotamers), IR (ν, KBr): 3013, 2935, 2874, 1735, 1640, 1433, 1252, 1225, 1140, 1016, 850 cm^{-1}. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.28-7.11 (m, 8 x Ar-H), 4.95 (sbr, 1H, H-6_{ax}), 4.53 (d, J=12.0 Hz, 1H, H-6_{ax}), 4.13 (m, 1H, J=12.0 Hz, H-2_{ax}), 3.68 (s, 4H, $COCH_2$), 3.58 (m, 1H, H-2_{ax}), 2.98 (t, J= 13.6 Hz, 1H, H-6_{eq}), 2.65 (t, J=13.6 Hz, 1H, H-6_{eq}), 2.31 (s, 6H, Ar-Me), 1.55-1.21 (m, 12 H, H-3, 4, 5), 1.09 (dd, J=6.4 Hz, 6H, Me-2). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 16.95, 18.24, 20.53, 21.20, 24.59, 25.29, 27.36, 28.23, 33.44, 34.89, 37.90, 39.56, 41.25, 42.22, 48.65, 49.32, 125.79, 128.99, 131.92, 138.66, 179.72. EI-MS (m/z, %): 231 (50), 216 (1), 132 (4), 126 (100), 112 (2), 105 (28), 103 (6), 98 (12), 83/84 (12), 55 (12), 91 (3), 70 (4). Anal. Calc'd for $C_{15}H_{21}NO$ (M=231) 77.88 (C); 9.15 (H); 6.05 (N). Found: 77.89 (C); 9.12 (H); 6.06 (N).

N-(2-Methylphenylacetyl)-3-methylpiperidine (18): Oil, 81 % (MIxture of Rotamers), IR (ν, KBr): 3008, 2933, 2860, 1725, 1641, 1435, 1259, 1222, 1140, 1020, 859 cm^{-1}. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.27-7.13 (m, 8 x Ar-H), 4.49 (d, J=13.8 Hz, 2H, H-2_{ax}), 3.67-3.59 (m, 6H, $COCH_2$, H-6_{ax}), 2.89 (dt, J=12.8, 2.8 Hz, 1H, H-2_{eq}), 2.62 (dt, J=12.8, 2.8 Hz, 2H, H-6_{eq}), 2.32-2.26 (m, 7H, Ar-Me, H-2_{eq}), 1.85-1.10 (m, 10H, H-3_{ax}, 4, 5), 0.85 (dd, J=6.8 Hz, 6H, Me-3). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 9.95, 11.40, 13.99, 15.27, 20.49, 21.62, 24.57, 25.86, 26.33, 31.10, 31.99, 33.00, 33.82, 45.56, 46.63, 52.13, 54.03, 125.60, 126.37, 129.70, 139.66, 142.09, 181.72. EI-MS (m/z, %): 231 [M] (84), 216 (12), 126 (100), 105 (27), 98 (14), 83 (25), 77 (14), 55 (27), 41 (10). Anal. Calc'd for $C_{15}H_{21}NO$ (M=231) 77.88 (C); 9.15 (H); 6.05 (N). Found: 77.89 (C); 9.16 (H); 6.07 (N).

N-(3-Methylphenylacetyl)-3-methylpiperidine (19): Oil, 81 % (Mixture of Rotamers), IR (ν, KBr): 3009, 2945, 2856, 1637, 1445, 1267, 1125, 1025, 960, 857, 767 cm^{-1}. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.18 (t, J= 7.6 Hz, 2 x Ar-H), 7.08-7.02 (m, 6 x Ar-H), 4.60 (d, J=13.8 Hz, 2H, H-2_{ax}), 3.77-3.65 (m, 6H, $COCH_2$, H-6_{ax}), 2.90 (dt, J=12.8, 2.8 Hz, 1H, H-2_{eq}), 2.60 (dt, J=12.8, 2.8 Hz, 2H, H-6_{eq}), 2.32 (s, 6H, Ar-Me), 2.26-2.16 (m, 1H, H-2_{eq}), 1.77-1.23 (m, 10H, H-3_{ax}, 4, 5), 0.85 (dd, J=6.8 Hz, 6H, Me-3). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 12.27, 13.25, 20.00, 20.21, 21.62, 22.37, 24.97, 25.86, 31.82, 33.13, 36.97, 34.57, 45.65, 46.56, 53.13, 55.10, 125.86, 127.81, 129.98, 131.05, 134.85, 137.28, 182.27. EI-MS (m/z, %): 231 [M] (65), 216 (3), 126 (100), 105 (25), 98 (13), 83 (20), 77 (10), 55 (25). Anal. Calc'd for $C_{15}H_{21}NO$ (M=231) 77.88 (C); 9.15 (H); 6.05 (N). Found: 77.86 (C); 9.15 (H); 6.07 (N).

N-(4-Methylphenylacetyl)-3-methylpiperidine (20): Oil, 84 % (Mixture of Rotamers), IR (ν, KBr): 3015, 2936, 2875, 1736, 1645, 1436, 1258, 1230, 1142, 1019, 851 cm^{-1}. ^1H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.28-7.09 (m, 8 x Ar-H), 4.45 (d, J=13.8 Hz, 2H, H-2_{ax}), 3.76-3.69 (m, 6H, $COCH_2$, H-6_{ax}), 2.88 (dt, J=12.8, 2.8 Hz, 1H, H-2_{eq}), 2.57 (dt, J=12.8, 2.8 Hz, 2H, H-6_{eq}), 2.31-2.02 (m,

7H,Ar-Me, H-2_{eq}), 1.76-1.05 (m, 10H, H-3_{ax}, 4, 5), 0.80 (dd, J=6.8 Hz, 6H, Me-3). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]:15.27, 16.00, 21.90, 22.53, 24.59, 25.26, 25.86, 27.13, 31.82, 31.91, 36.67, 38.11, 45.56, 46.55, 52.13, 53.15, 128.79, 130.80, 133.92, 138.66, 180.62. EI-MS (m/z, %): 231 (69), 216 (3), 132 (3), 126 (100), 105 (24), 103 (5), 98 (9), 83 (12), 55 (20), 91 (3), 70 (3). Anal. Calc'd for $C_{15}H_{21}NO$ (M=231) 77.88 (C); 9.15 (H); 6.05 (N). Found: 77.90 (C); 9.13 (H); 6.05 (N).

N-(2-Methylphenylacetyl)-4-methylpiperidine (21): Oil, 85 %, IR (ν, KBr): 3012, 2935, 2861, 1730, 1643, 1436, 1260, 1225, 1138, 1017, 860 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.17-7.10 (m, 4 x Ar-H), 4.63 (d, J= 13.2 Hz, 1H, H-2_{ax}), 3.73 (d, 1H, J=11.6 Hz, H-6_{ax}), 3.67 (s, 2H, $COCH_2$), 3.00 (dt, J=13.2, 2.4 Hz, 1H, H-2_{eq}), 2.60 (dt, J=13.2, 2.4 Hz, 1H, H-6_{eq}), 2.27 (s, 3H, Ar-Me), 1.70-1.09 (m, 4H, H-3, 5), 0.90-0.85 (m, 4H, H-4, Me-4). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]:11.54, 18.59, 26.67, 31.02, 49.73, 125.60, 128.37, 129.89, 132.33, 137.67, 140.29, 173.27. EI-MS (m/z, %): 231 [M] (66), 216 (10), 126 (100), 105 (26), 98 (7), 83 (20), 77 (10), 55 (26). Anal. Calc'd for $C_{15}H_{21}NO$ (M=231) 77.88 (C); 9.15 (H); 6.05 (N). Found: 77.85 (C); 9.13 (H); 6.06 (N).

N-(3-Methylphenylacetyl)-4-methylpiperidine (22): Oil, 87 %, IR (ν, KBr): 3010, 2946, 2857, 1640, 1446, 1270, 1127, 1030, 985, 860, 770 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.18 (t, J=7.6 Hz, 1 x Ar-H), 7.07-7.01 (m, 3 x Ar-H), 4.58 (dt, J=9.6, 3.4 Hz, 1H, H-2_{ax}), 3.80 (dt, J=13.2, 2.0 Hz, 1H, H-6_{ax}), 3.68 (s, 2H, $COCH_2$), 2.90 (dt, J=12.0, 1.6 Hz, 1H, H-2_{eq}), 2.55 (dt, J=13.2, 2.8 Hz, 1H, H-6_{eq}), 2.30 (s, 3H, Ar-Me), 1.65-1.05 (m, 4H, H-3, 5), 0.90 -0.80 (m, 4H, H-4, Me-4). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 15.59, 20.21, 25.76, 29.20, 35.97, 48.37, 125.86, 129.18, 129.89, 131.50, 136.55, 140.28, 180.49. EI-MS (m/z, %): 231, 126 (100), 105 (29), 98 (15), 83 (20), 55 (30), 91 (10). Anal. Calc'd for $C_{15}H_{21}NO$ (M=231) 77.88 (C); 9.15 (H); 6.05 (N). Found: 77.86 (C); 9.13 (H); 6.07 (N).

N-(4-Methylphenylacetyl)-4-methylpiperidine (23): Oil, 88 %, IR (ν, KBr): 3006, 2937, 2871, 1733, 1641, 1435, 1251, 1230, 1141, 1018, 849 cm^{-1}. ^{1}H NMR [400 MHz, $CDCl_3$, δ(ppm)]: 7.14-7.09 (m, 4 x Ar-H), 4.59 (d, J=13.2 Hz, 1H, H-2_{ax}), 3.80 (d, J=13.2 Hz, 1H, H-6_{ax}), 3.68 (s, 2H, $COCH_2$), 2.90 (dt, J=13.2, 2.4 Hz, 1H, H-2_{eq}), 2.57 (dt, J=13.2, 2.4 Hz, 1H, H-6_{eq}), 2.32 (s, 3H, Ar-Me), 1.60-1.00 (m, 4H, H-3, 5), 0.95 -0.80 (m, 4H, H-4, Me-4). ^{13}C NMR [100 MHz, $CDCl_3$, δ(ppm)]: 12.95, 19.20, 27.60, 31.56, 38.67, 45.93, 129.76, 130.88, 131.83, 131.83, 137.93, 140.78, 175.79. EI-MS (m/z, %): 231 (46), 132 (4), 126 (100), 105 (23), 103 (4), 98 (4), 83 (17), 55 (25), 91 (3), 70 (4). Anal. Calc'd for $C_{15}H_{21}NO$ (M=231) 77.88 (C); 9.15 (H); 6.05 (N). Found: 77.90 (C); 9.14 (H); 6.05 (N).

ACKNOWLEDGEMENTS

The authors thank Director, DRDE for his keen support and encouragement.

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