International Journal of Innovative Technology and Exploring Engineering (IJITEE)
ISSN: 2278-3075 (Online), Volume-3 Issue-10, March 2014

Synthesis, 2DNMR and Crystal Structure Analysis of Piperidin - 4 - one Derivatives

Ramani Devi R, Kathirvel R, Seeni Mubarak M, Mohamed Rabeek S, Fazal Mohamed M.I.

Abstract - The compounds 3-chloro-3-methyl-2,6 diphenyl piperidine-4-one(1) and 3-chloro-2,6-bis-(4-methoxy-phenyl)-3-methyl-piperidin-4-one(2) have been newly synthesized and characterized by elemental analysis, IR, 1H NMR, 13C NMR and 2D NMR. X-ray crystal structure analysis has been carried out to determine the composition and molecular structures of the two compounds. The crystal packing exhibits bond lengths and bond angles.

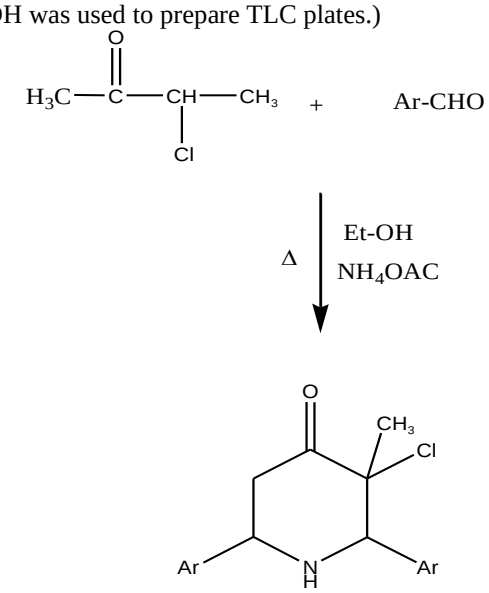
Keywords - 3-chloro-3-methyl-2,6-diphenylpiperidin-4-one, 3-chloro-2,6-bis-(4-methoxy-phenyl)-3-methyl-piperidin-4-one: IR, 1H NMR,13C NMR, 2D NMR and XRD studies.

I. INTRODUCTION

Heterocyclic compounds gain importance owing to their pharmacological, agro-chemical and in brief, biological activities. The piperidin-4-one units are present in a variety of alkaloids which are occurring naturally.[1-2] They find wide applications as drugs. Further, the stereochemical studies of piperidinone chemistry are thought provoking and quiet interesting. These aspects prompted us to take an indepth study on the heteranes, particularly on piperidinone chemistry.[3-4] Literature reports show that a wide range of 2,6-as well as 3,5-disubstituted piperidin-4-ones have been prepared, the substituents being alkyl, aryl and chloro groups.[5-8] There has been no report so for, on the disubstitution consisting of chloro and methyl groups in any of these positions[9-12]. Keeping in view of this, it has been prepared a chloro and methyl disubstituted piperidin-4-one at the 3-position.[13] The compounds (1and2) reported in this work are new to the literature. The formations of these compounds have been revealed by the measurement of analytical data and spectroscopic analyses such as IR, ^{1}HNMR and ^{13}CNMR techniques.[14] The compounds have been subjected to single crystal X-ray diffraction analysis so that their supramolecular structures could be studied in terms of possible intermolecular interactions. The compounds have been analysed for their structural features, stereochemistry, biological activity etc.

II. MATERIALS AND METHODS

3-Chloro-2-butanone (6ml; 0.1mol), ammonium acetate (4gm; 0.1mol) benzaldehyde (12.3ml; 0.2mol), in a RB flask containing ethanol (10ml). The mixture is refluxed at 60-70^{0} C in a water bath with occasional shaking until the colour changes into red orange. The solution is cooled, and then ether (50ml) is added. The filtered solution is transferred into conical flask, con.HCl (5ml) is added. A white precipitate is formed. The precipitate is washed with 5:1 ethanol:ether mixture and dried. Acetone (10ml), liquid ammonia (5ml), and excess of coldwater are added. The precipitate formed is filtered and dried. Then the product is recrystallised with ethanol and the crystal form of product obtained is dried. The melting point is 120^{0}C for compound (1). The same procedure is followed for the preparation compound (2) in which 4-methoxy benzaldehyde (12ml; 0.2mol) is used instead of benzaldehyde. The melting point is 125^{0}C for compound (2). (3-Chloro-2-butanone and ammonium acetate supplied by E.merk were used as such. Benzaldehyde and 4-methoxy benzaldehyde were supplied by BDH. Ethanol was distilled twice to get maximum alcohol content. Silica gel.G supplied by BDH was used to prepare TLC plates.)



1. Ar = C_6H5
2. Ar = p-*OMe*-C_6H_5

Scheme-I

Table –I: Single Crystal X-ray diffraction data and structure refinement for (1).

Empirical formula	C_{18} H_{18} Cl N O
Formula weight	299.78
Temperature	293(2) K
Wavelength	0.71073 A

Manuscript published on 30 March 2014.
*Correspondence Author(s)
R. Ramani Devi, Research Scholar, PG and Research Department of Chemistry, Jamal Mohamed College (Autonomous), Affiliated to the Bharathidasan University, Tiruchirappalli-.Tamil Nadu,India
R. Kathirvel, Research Scholar, PG and Research Department of Chemistry, Jamal Mohamed College (Autonomous), Affiliated to the Bharathidasan University, Tiruchirappalli-Tamil Nadu, India.
Dr. M.Seeni Mubarak, Associate Professor, PG and Research Department of Chemistry, Jamal Mohamed College (Autonomous), Tiruchirappalli-Tamil Nadu, India.

Crystal system, space group	Triclinic, p-1
Unit cell dimensions a = 6.7048(2) A alpha = 72.0890deg.b=11.0070(4)A beta = 79.5420(10) deg c = 11.2699(3)A gamma = 77.118(2) deg.	
Volume	765.75(4) A^3
Z, Calculated density	2, 1.300 Mg/m^3
Absorption coefficient	0.248 mm^-1
F(000)	316
Crystal size	0.35 x 0.30 x 0.10 mm
Theta range for data collection	1.91 to 23.55 deg.
Limiting indices	-7<=h<=7, -12<=k<=12, -12<=l<=12
Reflections collected/unique	10632/2231[R(int) = 0.0426]
Completeness to theta =23.99	97.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9945 and 0.9065
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2231 / 1 / 194
Goodness-of-fit on F^2	1.078
Final R indices[I>2sigma(I)]	R1 = 0.0514, wR2 = 0.1496
R indices (all data)	R1 = 0.0668, wR2 = 0.1496
Largest diff. peak and hole	0.448 and -0.287 e.A^-3

Table–II Single Crystal X-ray diffraction data and structure refinement for (2).

Empirical formula	C_{20} H_{22} Cl N O_3
Formula	359.84
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P21/c
Unit cell dimensions a=13.430(3) Aalpha = 90 deg. b = 7.7945(15) Abeta = 108.550(6) deg. c = 18.162(4) A gamma = 90 deg.	
Volume	1802.5(6) A^3
Z, Calculated density	4, 1.326 Mg/m^3
Absorption coefficient	0.231 mm^-1
Crystal size	0.30 x 0.20 x 0.20 mm
Theta range for data collection	2.37 to 24.99 deg.
Limiting indices	-15<=h<=14, -9<=k<=9,-21<=l<=21
Reflections collected / unique	14412 / 14412 [R(int) = 0.0000]
Completeness to theta =24.99	99.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9865 and 0.9025
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	14412 / 2 / 239
Goodness-of-fit on F^2	1.070
Final R indices [I>2sigma(I)]	R1 = 0.0723,wR2 = 0.2152
R indices (all data)	R1 = 0.1079, wR2 = 0.2466
Largest diff. peak and hole	0.468 and -0.387 e.A^-3

A. Crystal growth

In order to grow the crystal, the compound was dissolved in ethanol medium, and allowed to stand for 7 days. The colourless needle like crystals were obtained.

B. Single crystal X-ray diffractometry

High resolution single crystal X-ray diffraction data were collected at 293(2)K on a Bruker SMART APEX II CCD diffractometer, equipped with a graphite monochromator and a fine- focus sealed tube [λ(Mo-K_α) = 0.71073 A^0]. The large 62mm square 4k CCD collect single crystal data.[15-18] The single crystal was mounted in a Lindmann capillary and 2400 Frames were recorded with scanning angle ω of 0.3º, each for 5 sec exposure with 0.5mm Collimated x-ray. The crystal to detector distance was kept 62mm. The structure was solved by direct methods using SHELXS-97 and the refinement was carried out against F^2 using SHELXL-97.[19-20] The molecular-packing diagram was generated by Hg of CCDC.[21-23]

III. RESULTS AND DISCUSSION

A. Spectral characterization

Compound-I

IR (KBr): 3334 (υ_{N-H}), 3065, 2936 (υ_{C-H}), 1718 ($\upsilon_{C=O}$), 1545, 1448 ($\upsilon_{C=C}$), 749 (υ_{C-Cl})cm^{-1}, ^{1}H NMR (400MHz, $CDCl_3$): δ7.493-7.336 (m, 10H, ArH), 4.065-4.027 (d, 1H, Benzylic-H), 3.935 (s, 1H, Benzylic-H), 3.458-3.394 (t, 2H, CH2), 2.545-2.503 (d, 1H, NH), 1.698 (s, 3H, CH3).^{13}CNMR ($CDCl_3$, 100MHz): δ201.73, 143.07, 140.43, (129.02-126.87), 85.43, 65.42, 60.53, 45.25, 21.93.

2D NMR SPECTRAL DATA

Coupling between adjacent protons are well explained with the help of 2D NMR rather than 1D NMR. Some of the observations not observed in 1D NMR are well explained using 2D NMR of which the most important interaction is spatial interaction between protons. A peak on the diagonal appearing at the δ value 7.3 corresponds to the aromatic proton of phenyl attached at C_2 and C_6.The cross peak δ=4.2 suggests that there is an interaction between the protons of C_5 and C_6. A peak appearing at δ=4 on the diagonal corresponds to the benzyclic protons. The diagonal peak appearing at δ=3.2 is assigned to the protons at C_5. The diagonal peak appearing at δ=2.3 corresponds to the N-H of amide proton. The value at δ=1.3 correspond to the methyl protons at carbon C_3.

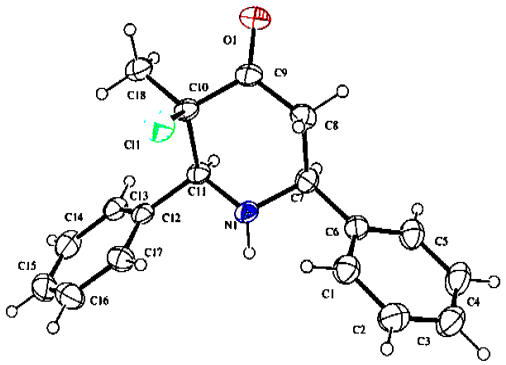


Figure 1- Thermal ellipsoidal plots with 50% probability for non-H atoms

Published By:
Blue Eyes Intelligence Engineering and Sciences Publication (BEIESP)

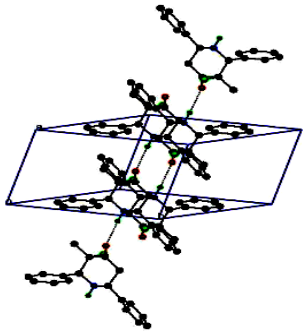


Figure 2- Crystal packing structure of compound (1).

Compound-II

IR (KBr): 3333 (υ_{N-H}), 3023, 2926 (υ_{C-H}), 1718 ($\upsilon_{C=O}$), 1543, 1448 ($\upsilon_{C=C}$), 758 (υ_{C-Cl}) cm^{-1}, ^{1}HNMR (400MHz, $CDCl_3$): δ7.268-7.209 (d, 4H, ArH), 6.998-6.926 (d,4H, ArH), 4.065-4.027 (d, 1H, Benzylic H), 3.935(s,1H, Benzylic-H), 3.857 (s, 6H, methoxyprotons), 3.458-3.394 (t, 2H, CH_2), 2.545-2.503 (d,1H,NH), 1.698 (s,3H,CH_3). ^{13}C NMR ($CDCl_3$, 100MHz): δ 201.7, 159.6, 158.7, 136.2, 133.7, (128.4 & 128.1), 115.6, 114.9, 85.4, 65.4, 60.5, 56.6, 45.2, 21.9.

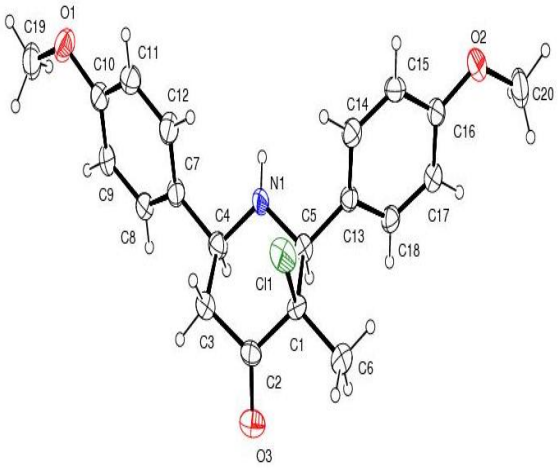


Figure 3- Thermal ellipsoidal plot with 50% probability for non-H atoms

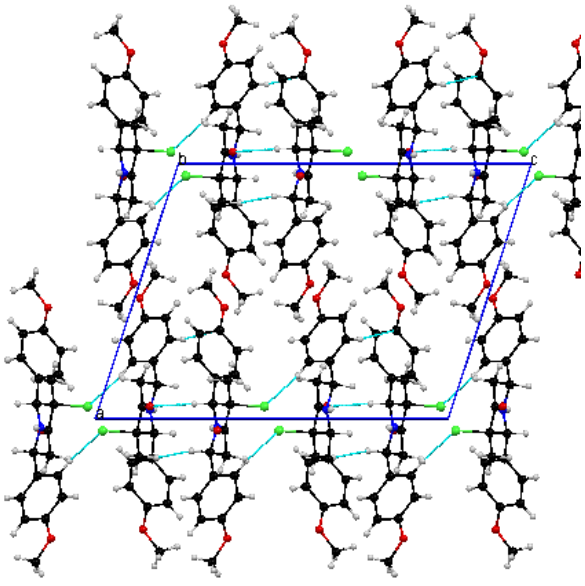


Figure 4- Crystal packing structure of compound(2).

Description of the crystal structure

The structure of the compound (1and2) are shown in figure 1and2.The unit cell parameters are listed in Table I and II. The crystal system is triclinic P-1 and monoclinic P21/c space group with all atoms located at general positions (Figure 2 and 4) and such molecules in the unit cell (Z=2,Z=4).The analysis of bond lengths and bond angles as given in table III and IV.

Table III-Bond lengths [Å] and angles [deg] compound (1)

Bond lengths	
C(1)-C(6)	1.378(4)
C(1)-H(1)	0.9300
C(2)-C(3)	1.373(5)
C(7)-N(1)	1.454(4)
C(7)-C(8)	1.528(4)
C(7)-H(7)	0.9800
C(8)-C(9)	1.498(4)
C(8)-H(8A)	0.9700
C(9)-O(1)	1.209(3)
C(9)-C(10)	1.515(4)
C(10)-C(18)	1.496(4)
C(10)-C(11)	1.550(4)
C(10)-Cl(1)	1.811(3)
C(11)-N(1)	1.448(3)
N(1)-H(1A)	0.951(10)
Bond angles	
C(2)-C(3)-H(3)	119.9
C(5)-C(4)-H(4)	120.0
C(4)-C(5)-C(6)	121.1(3)
C(4)-C(5)-H(5)	119.4
N(1)-C(7)-C(6)	109.6(2)
O(1)-C(9)-C(8)	122.6(3)
O(1)-C(9)-C(10)	121.0(3)
N(1)-C(11)-C(12)	110.3(2)
N(1)-C(11)-H(11)	107.2
C(10)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(11)-N(1)-C(7)	114.3(2)
C(11)-N(1)-H(1A)	110.7(18)
C(7)-N(1)-H(1A)	110.6(17)

Table IV-Bond lengths [Å] and angles [deg] compound (2)

Bond lengths	
C(1)-Cl(1)	1.822(3)
C(14)-C(15)	1.383(4)
C(14)-H(14)	0.9300
C(15)-C(16)	1.378(4)
C(15)-H(15)	0.9300
C(16)-O(2)	1.376(3)
C(16)-C(17)	1.386(4)
C(17)-C(18)	1.385(4)
C(17)-H(17)	0.9300
C(18)-H(18)	0.9300
C(19)-O(1)	1.414(4)
C(19)-H(19A)	0.9600
N(1)-H(1A)	0.902(16)

Published By:
Blue Eyes Intelligence Engineering
and Sciences Publication (BEIESP)

Bond angles

C(2)-C(1)-Cl(1)	106.00(16)
C(6)-C(1)-Cl(1)	106.9(2)
C(5)-C(1)-Cl(1)	109.69(18)
C(4)-C(3)-H(3A)	109.7
N(1)-C(4)-C(7)	110.2(2)
N(1)-C(4)-C(3)	108.7(2)
C(7)-C(4)-C(3)	111.5(2)
N(1)-C(4)-H(4)	106.5(15)
N(1)-C(5)-C(1)	109.8(2)
C(10)-C(9)-H(9)	120.4
C(8)-C(9)-H(9)	120.4
O(1)-C(10)-C(11)	115.3(3)
O(1)-C(10)-C(9)	124.6(3)
C(11)-C(10)-C(9)	120.1(3)
C(10)-C(11)-C(12)	120.3(3)
C(14)-C(15)-H(15)	119.6
O(2)-C(16)-C(15)	15.4(2)
O(2)-C(16)-C(17)	125.5(3)
O(1)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
O(1)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(5)-N(1)-C(4)	113.9(2)
C(5)-N(1)-H(1A)	121.3(15)
C(4)-N(1)-H(1A)	110.6(15)
C(10)-O(1)-C(19)	118.6(2)
C(16)-O(2)-C(20)	117.6(2)

IV. CONCLUSIONS

The crystal system of 3-chloro-3methyl-2, 6-diphnylpiperidin-4-one is triclinic and that of 3-chloro-2,6-bis-(4-methoxy-phenyl)-3-methyl-piperidin-4-one is monoclinic. These crystal packing exhibits bond lengths and bond angles. Single crystal X-ray diffraction studies confirm that the structure arrival in crystalline state.

ACKNOWLEDGEMENTS

We thank National Single Crystal Diffractometer Facility, Indian Institute of Technology, Chennai, for X-ray crystallographic studies.

REFERENCES

1. O. P. Agarwal, “Chemistry of Organic Natural Products”.,Goel Publishing House Meerut., Vol 1, 2002.
2. I. L. Finer, “Organic Chemistry” ELBS., Vol 2, 1975.
3. V. Baliah, V. Gopalakrishnan, R. Jeyaraman, Indian. J.Chem, Soc.,Sec.B, 6B, 1978, 1065.
4. V. Baliah, R. Jeyaraman. Indian.J.Chem., 15B, 1977, 1207.
5. Baliah, V.;Jeyaraman, R. Indian.J.Chem., 9, 1971, 1020.
6. M. I. Fazal Mohamed, M. Krishnapillay, Indian J.Chem., 70, 1993, 258.
7. C. Noller, V. Baliah, J.Am.Chem. Soc., 70, 1948, 3853.
8. V. Baliah, A. Ekambaram, T. S. Govindarajan, Curr. Sci., 23, 1954, 264.
9. V. Baliah, T. S. Govindarajan, Curri. Sci., 23, 1954, 91.
10. V. Baliah, A. Ekambaram, J.Indian. Chem. Soc., 33, 1955, 274.
11. V. Baliah, V. Gopalakrishnan, J.Indian. Chem. Soc., 31, 1954, 250.
12. M. I. Fazal Mohamed, M. Krishna Pillay,Indian. J. Chem.,36B, 1997,50.
13. M. I. Fazal Mohamed, M. Krishna Pillay, Indian. J. Heterocyclic chem., 9, 2000, 209.
14. M. Seeni Mubarak, et al., Oriental J. Chem., 27(1), 2011, 333.
15. V. Baliah, R. Jeyaraman, Indian.J.Chem., 9, 1971,1020.
16. D.B. Lovejoi, D.R. Richardson, Blood., 100(2), 2002, 666.
17. M. Hong, H. Yill, D. Wang, Z. Gao, Acta Cryst., E 61, 2005,m801.
18. B. Sireesha, B. Krishna Rao, Sarala Devi Ch, P. Raghavaiah, Indian J.Chem, 47B, 2008, 592.
19. Refat EI-Sayed, Indian J.Chem., 45(A), 2006, 738.
20. Thomas Steiner, J. Molec Struct., 39, 1998, 447.
21. C. Katika, D. Vesna , K. Vlado, G. M. Dora, B. Aleksandra, Molecules., 6, 2001, 815.
22. A. Padmaja, Aliya Begum, P. Ragavaiah, Indian J.Chem., 50B, 2011,326-329.
23. Afshan Banu, D. E. Vasundhara, S. Ravi, Lamani, J.Saudi Chem Soc.,17,2013,211-217.

R. Ramani Devi, Research Scholar, PG and Research Department of Chemistry, Jamal Mohamed College (Autonomous), Affiliated to the Bharathidasan University, Tiruchirappalli-.Tamil Nadu,India

R. Kathirvel, Research Scholar, PG and Research Department of Chemistry, Jamal Mohamed College (Autonomous), Affiliated to the Bharathidasan University, Tiruchirappalli-Tamil Nadu, India.

Dr. M.Seeni Mubarak, Associate Professor, PG and Research Department of Chemistry, Jamal Mohamed College (Autonomous), Tiruchirappalli-Tamil Nadu, India.