# SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITIES OF N, N-DICYCLOHEXYLBENZYLAMINE AND ITS COMPLEXES WITH ZINC(II), CADMIUM(II) AND MERCURY(II)

***Hafiz Muhammad Farooq**
Institute of Chemistry, University of the Punjab, Lahore-54590. (Pakistan).
(Present address: Government Islamia College Railway Road, Lahore.)
*Contact:* farooqchem@yahoo.com

***ABSTRACT:*** *N,N-dicyclohexylbenzylamine and its complexes with Zn(II), Cd(II) and Hg(II) are reported. The compounds were characterized on the basis of spectroscopic and analytical techniques such as UV, IR, AAS and XRD. Antibacterial and antifungal activities of N,N-dicyclohexylbenzylamine and its complexes were investigated against some species of bacteria such as Bacillus subtilis (B.S), Eschericha coli (E.c), Micrococcus luteus (M.I) and staphylococcus aureus (S.a) and a fungus Aspergillus flavus by diffusion plate method.*

**Key words:** N, N-dicyclohexylbenzylamine, tertiary arylamine, antimicrobial activities.

## INTRODUCTION

Cassebaum and his coworkers [1] synthesized N (o-nitrobenzyl) – N-methyl cyclohexylamine hydrochloride and separated from the mixture of its meta and para isomers and non-nitroanalog by condensation with N-methyl cyclohexylbenzylamine. Ubaidulaev and his coworkers reported alkyl aromatic amine from alkyl benzene. They converted alkyl benzene into alkyl benzylamine by chloramethylation and subsequent reaction with gaseous $NH_3$. The resulting alkylbenzylamines were converted into alkyl, N,N-dimethylbenzylamine by reaction with HCHO-$HCO_2$ to yield $phCH_2NMe_2$ has been reported [3]. $PhNHCH_2ph$ and its derivatives (substitutents = alkyl, alkoxy, halo, $–NO_2$, –OH or $–CO_2H$ groups) were prepared by Suzuki and his coworkers [4].

Nara and his coworkers synthesized alkyl, aryl amine by the reaction of aromatic sulphonates (Sodium benzene, toluene and naphthalene sulphonates) with three mole of $NaNH_2$ in excess $RNH_2$ (R = Me, Et. N-propyl, 2-propyl, n-butyl, iso-butyl and cyclohexyl) at 140-170$^{O}$C [5]. Alkyl aryl amine and aromatic secondary amines were obtained. They also prepared dialkylamine by the use of excess amount of $NaNH_2$. Weland and his coworkers [**6]** synthesized sterically hindered tertiary amines by reaction of iminium salts. Yamada and coworkers [**7]** synthesized amino benzylamine derivatives and their acid adducts were prepared by reaction of o-$NH_2C_6H_4OH$ with N-methyl or N-ethylcyclohexylamine in the presence of fatty acid. Schoenwald and his coworkers [8] synthesized N-cyclohexyl-N-ethylbenzylamine by refluxing N-ethyl cyclohexylamine benzylchloride and 4-methyl-2-pentanone.

## MATERIALS AND METHODS:

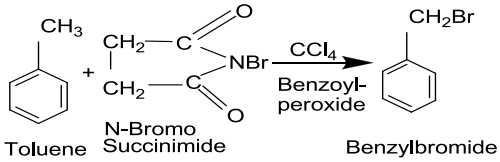
N-bromosuccinimide, $NaHCO_3$ and $CdCl_2$ were taken from E. Merck. $ZnCl_2$, $CCl_4$ and toluene were purchased from Reidel de Haen. All chemicals were used without further purification. Solvents were of reagent quality and dried before use. N, N-dicyclohexylbenzylamine was prepared starting from toluene and N-bromosuccinimide in $CCl_4$ using benzoylperoxide as catalyst followed by the addition of dicyclohexylamine under reflux.

The metal complexes of N, N-dicyclohexylbenzylamine with II-B metals were synthesized in alcohol: water mixture (4:1) under reflux. The products, after evaporating the solvent, were filtered off, washed with distilled water, ethanol and finally within hexane. Purity of the ligand was checked on T.L.C. plates coated with kiesel gel 60G. Ethanol: n-hexane (4:1) was used as mobile phase. λmax of the ligand was taken (in ethanol) on Hitachi UV-Visible spectrophotometer, Model U-2000. Melting/decomposition point of the ligand and complexes were taken on Gallen Kamp M.P. Apparatus and reported uncorrected. Infrared spectra of the ligand and metal complexes were recorded on Hitachi Infrared Spcetrophotometer, model 270-30 in nujol mulls in the spectral range of 4000-400cm$^{-1}$. Metal content in the complexes was estimated on Atomic Absorption Spectrophotometer, Model AA-1275. Estimation of nitrogen was done by Kjeldahl's process and halogen by Stepanow method [**9]**. XRD analysis was performed qualitatively using a Siemen Diffractometer, model D 5000.

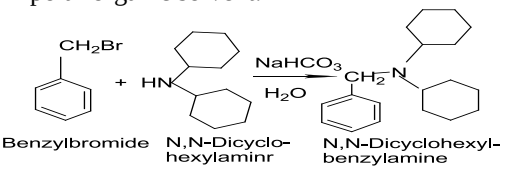
Antibacterial and antifungal activities of N,N-dicyclohexylbenzylamine and IIB metal complexes were investigated by diffusion plate method. The bioassay medium consisted of (g/L): beef extract 1.0, yeast extract 2.0, peptone 5.0, NaCl 5.0, agar 15.0, and water 1000 mL. pH of the medium was adjusted to 7 before the addition of agar. The medium was then dispensed in 250 mL Erlenmeyer flask and sterilized at 15psi pressure for 30 minutes. The petriplates were washed and sterilized in the oven at 120$^{O}$C overnight. 20 mL of the molten bio-assay medium was poured in the sterile plates and allowed to set. 4.0 mL of the molten assay medium incubated with predetermined concentrations of the microorganisms and spread uniformly over the first layer. After setting the second layer, four wells of 0.8 cm were made in the plates aseptically using stainless borer. An emulsion of the sample (0.1% salt complex) in Gumacacia was used for testing its antimicrobial activities. 1-2 drops of tween 80 (an emulsifier) was also used during preparation of emulsion. 0.12 mL of the emulsion was added to a hole incubated at 37$^{O}$C for 24 hours. Clear zones of inhibition were developed and the diameter of the zones of inhibition were measured in mm. The blank has no antimicrobial activity.

## SYNTHESIS OF N,N-DICYLCOHEXYLBENZYLAMINE

**Step-I**: Toluene (53.0 mL, 0.5 mole), N-bromosuccinimide (88.5 g, 0.5 mole) in CCl4 (250 mL) and benzoylperoxide (1.0 g) were charged in a quickfit flask equipped with water condenser and reaction mixture was heated under reflux for 6-8h, until all the solid started floating on the liquid surface. The mixture was allowed to cool down to room temperature and regenerated succinimide was filtered off. The filtrate was evaporated to give benzylbromide.




**Step-II**: Benzylbromide, $NaHCO_3$ (42.0 g, 0.5 mole) and distilled water (100 mL) were taken in quickfit flask equipped with water condenser. Dicyclohexylamine (25.0 mL, 0.5 mole) was added to the reaction mixture through condenser with the help of separating funnel drop wise. White crystals were formed which were recrystallized in ethanol to get pure compound (compound-I) λmax = 200.9, soluble in polar organic solvent.




## REACTION OF N, N-DICYCLOHEXYLBENZYLAMINE WITH:

**i). Zinc(II) Chloride:** N, N-dicyclohexylbenzylamine (1.076 g, 4.0 mol) was dissolved in ethanol (20 mL) by warming and stirring and then filtered off. Clear solution of $ZnCl_2$ (0.273 g, 2.0 mmol) was prepared in distilled water (10 mL). Both the solutions were mixed and refluxed for 2-3h. The solution was concentrated on water bath. The white solid obtained which was washed with n-hexane and dried to get the compound-II.

**ii) Cadmium (II) Chloride:** N, N-dicyclohexylbenzylamine (1.076 g, 4.0 mmol) was dissolved in ethanol (20 mL) by warming and stirring and then filtered off. Clear solution of CdCl2 (0.402 g, 2.0 mmol) was prepared in distilled water (10 mL). Both the solutions were mixed and refluxed for 2-3h. The solution was concentrated on water bath. The off-while solid obtained which was washed with n-hexane and dried to get the compound-III.

**Table-I: Physical Properties And Estimation* of Nitrogen, Halogen And Metal**

| Compound | Colour | m.p/d.p | % Yield | %N | %M | %Cl |
|---|---|---|---|---|---|---|
| **I** | White | 260$^oC$ | 33.5 | 5.1 (5.2) | -- | -- |
| **II** | White | 250$^oC$ | 45.0 | 3.6 (3.8) | 17.3 (17.0) | 9.3 (9.5) |
| **III** | Off-white | 155$^oC$ | 29.5 | 3.0 (3.3) | 26.2 (26.9) | 8.4 (8.5) |
| **IV** | Light Green | 152$^oC$ | 41.0 | 2.6 (2.8) | 24.3 (23.9) | 6.8 (7.0) |

*Theoretical values are given in parenthesis

**Table-II: Infrared Spectra of Compounds**

| Compound | Infrared Absorption Bands ($cm^{-1}$) |
|---|---|
| I. | 3100w, 3025w, 2925vw, 2900m, 2825vw, 2725w, 1700s, 1625s, 1580m, 1530vs, 1460m, 1350vs, 1310vs, 1100m, 1040w, 830vw, 810vs, 755s, 730vw, 690w. |
| II. | 3380 broad, 3080w, 2900s, 2730s, 1620w, 1585s, 1322s, 1280w, 1170w, 1070s, 1050s, 982m, 942w, 920m, 880m, 750s, 600m, 570m, 500m |
| III. | 3370w, 2995m, 2895vs, 1585w, 1325m, 1268w, 1178w, 1050m, 970m, 948w, 920w, 870w, 805w, 750w, 540. |
| IV. | 3355 broad 3060m, 2900s, 2825s, 1610w, 1590m, 1558s, 1465vs, 1390s, 1275m, 1320s, 1175m, 1050s, 990m, 970m, 940m, 860w, 750m. |

**Table-III: XRD Data of N, N-dicylcohexylbenzylamine**

| No. | 2 Theta | d | Rel. I. |
|---|---|---|---|
| 1. | 8.940 | 9.885 | 100.00 |
| 2. | 19.403 | 4.572 | 22.26 |
| 3. | 23.683 | 3.754 | 14.96 |
| 4. | 19.589 | 4.529 | 14.43 |
| 5. | 8.538 | 10.349 | 13.25 |
| 6. | 17.155 | 5.165 | 13.09 |
| 7. | 60.384 | 1.532 | 12.36 |
| 8. | 15.299 | 5.787 | 9.619 |
| 9. | 30.840 | 2.897 | 9.24 |
| 10. | 24.526 | 3.627 | 9.12 |
| 11. | 26.940 | 3.307 | 7.66 |
| 12. | 60.554 | 1.528 | 7.44 |
| 13. | 22.474 | 3.953 | 6.26 |
| 14. | 27.093 | 3.289 | 5.70 |
| 15. | 35.084 | 2.556 | 4.83 |
| 16. | 28.077 | 3.176 | 4.49 |
| 17. | 28.204 | 3.162 | 3.60 |
| 18. | 20.610 | 4.306 | 3.57 |
| 19. | 43.018 | 2.101 | 3.32 |
| 20. | 43.852 | 2.063 | 3.18 |
| 21. | 31.673 | 2.823 | 3.14 |
| 22. | 45.130 | 2.008 | 3.06 |
| 23. | 25.098 | 3.546 | 2.69 |
| 24. | 56.316 | 1.632 | 2.55 |
| 25. | 28.522 | 3.127 | 2.52 |
| 26. | 31.206 | 2.864 | 2.44 |
| 27. | 26.175 | 3.402 | 2.38 |
| 28. | 25.849 | 3.444 | 2.30 |
| 29. | 17.948 | 4.939 | 2.07 |

**Table-IV: Antibacterial Activities of Ligands And II-B Metal Complexes**

| Compound | Inhibition Zone Diameter (mm) | | | |
|---|---|---|---|---|
| | E.c | B.s | S.a | M.l |
| Compound-I | 18.0 | 17.0 | 20.0 | 20.0 |
| Compound-II | 20.0 | 16.0 | 16.0 | 14 |
| Compound-III | 18.0 | 24.0 | 21.0 | 20.0 |
| Compound-IV | 18.0 | 23.0 | 22.0 | 20.0 |

**Table-V: Activity of Ligands And II-B Metal Complexes Activity of Compounds**

| Complex | Inhibition Zone Diameter (mm) |
|---|---|
| Compound-I | 14 |
| Compound-II | 18 |
| Compound-III | 30 |
| Compound-IV | 29 |

**iii) Mercury (II) Chloride:** =N, N-dicyclohexylbenzylamine (1.076 g, 4.0 mmol) was dissolved in ethanol (20 mL) by warming and stirring and then filtered off. Clear solution of HgCl2 (0.542 g, 2.0 mmol) was prepared in distilled water (10 mL). Both the solutions were mixed and stirred for 24h. The solution was concentrated on water bath. The light apple green solid obtained which was washed with n-hexane and dried to get the compound-IV.

## RESULTS AND DISCUSSION

N, N-dicyclohexylbenzylamine was prepared starting from toluene and N-bromosuccinimide (a brominating agent) in CCl4 using benzoylperoxide as catalyst. Benzylbromide was formed which reacted with dicyclohexylamine to give N, N-dicyclohexylbenzylamine in 33.5% yield. The metal complexes of N, N-dicyclohexylbenzylamine melt / decompose in the temperature range of 152-250$^{o}$C and they show decreasing order down the group. The complexes are found to be hardly soluble in number of polar and non-polar solvents indicating their dimeric or polymeric nature.

Infrared spectrum indicated aromatic C–H stretching frequency at 3100 and 3025 $cm^{-1}$. The bands around 2925 and 2825 $cm^{-1}$ were due to C – H stretching frequency for methylene groups. C–H bending for methylene rocking was indicated at 1350$cm^{-1}$. The bands which appeared at 1625 and 1460 $cm^{-1}$ were due to ring stretching vibrations. The absorption bands observed at 1040$cm^{-1}$ and 755 and 730 cm–1 were due to in characteristic frequency of C–N bond of the type $(R)_2N–CH_2–$(R = $C_6H_{11}$) was indicated 1350-1310$cm^{-1}$ region of the spectrum. In case of metal complexes (II-IV), the bands appeared around 600 and below which may be assigned to M-N bonds [**11-13]**.

Estimation of nitrogen and metal in the complexes indicated 1 : 1 L : M ratio.

XRD study of ligand indicated 2 theta values, d values and relative intensity of the peaks (Table - III). X-ray diffractograph of the ligand showed that peaks belong to starting material were absent which indicated the formation of new compound. The diffractograph showed large number of peaks which argued that unit cell is of lower symmetry.

The antibacterial activity exhibited by the ligand (Compound-I) and its Zn(II), Cd(II) and Hg(II) complexes (Complexes II-IV) was investigated against four bacteria Becillus subtilis (B.S), eschericha coli (E.c), Micrococcus luteus (M.l) and Staphylococcus aureus (S.a) and results are reported in Table-IV. zn(II) complex maximum antibacterial activity against Eschericha coli (E.c). Cd (II) Complex showed maximum activity against Bacillus subtilis (B.s), In case of Staphylococcus aureus (S.a), maximum activity exhibited by Hg(II) complex. Ligand, Cd(II) and Hg(II) complexes showed equal activity against Micrococcus luteus (M.l).

The over antibacterial activity exhibited by Compounds I-IV is as under:-

Cd (II) complex = Hg (II) Complex > Ligand > Zn(II) Complex

The antifungal activity exhibited by the ligand and its complexes (Compound I-IV) was investigated against Aspergilus flavus Table IV. The increasing order of antifungal activity as observed from the table is:

Cd(II) Complex > Hg(II) Complex > Zn(II) Complex > Ligand

## REFERENCES


1. Cassebaum H., Hilger H. G. DD 204, 913 (ClCO7C **87**/36), *Appl.* 235, 942, 1981, 19 pp (1983).
2. Ubaidulaev S., Makhmudov T.M., Akhmedov K.S., *Dokl Akad Nauk Uzb.,* 29 (9), 33-4(1972).
3. Pinzon A. Jorge Balamco H. Puis, (1993) *Rev. Colomb. Quim*, **12(1)**, 43-9.
4. Suzuki Seiji, (1976) Japan Kokai 26, 125, 331 (ClCO7C85/08), *Appl.* **75**/36, 362, 5pp, (1975).
5. Nara Kenichi, Mana be Osamu, *Nippon Kagaku Kaishi* (9), 1704-7(1974).
6. Weland Gerhard and Sim Chen Gerhard, *Japan Kokai* **75**, 83, 348 (Cl CO7C87/52), (1973) *Appl.* **74**/127, 667, 7pp(1985)
7. Yamada Yoshitsuge, Kurdoda Setsuo, *Japan Kokai **75***, 83, 348 (Cl CO7C87/52), (1973) *Appl.* 74/127, 667, 7pp(1975).
8. Shoenwald Ronald D. Barfkneeht, Carhles F., Neuttton Roger E. PCT. *Inst. Appt.* WO 92, 10,449(1992).
9. Vogel A. I., *Elemental Practical Organic Chemistry*, p. 653(1965).
10. Silverstein R.M., Bassler G.C. and Morill T.C., *"Spectrophotometric Identification or Organic Compounds",* 5th Ed, (1991).
11. Barrow G.M., Krugar R.H. and Basolo F., J. *Inorganic and Nuclear Chemistry*, 2, 340(1956).
12. Bertin E.P., Nakagawa I., Miszushima S., Lane T.J. and Quagliano J.V., *J. Am. Chem. Soc.*, 80, 525(1958).
13. Nakagawa I., Penland R.B., Miszushima S., Lane T.J. and Quagliano J.V., *Spectrochim Acta*, 9, 199(1957).