

## Synthesis, Characterization and Antibacterial Activity of O-Cyano-N, N-Dipropylbenzylamine and its Complexes with Iron(II), Nickel(II) and Cobalt(II)

<sup>1</sup>F. MAZHAR AND <sup>2</sup>M. Z. IQBAL

<sup>1</sup>Chemistry Department

Lahore College for Women University, Lahore, Pakistan

<sup>2</sup>Institute of Chemistry, University of the Punjab  
Quaid-e-Azam Campus, Lahore, Pakistan

(Received 26<sup>th</sup> September, 2003, revised 12<sup>th</sup> January, 2004)

**Summary:** O-Cyano-N,N-dipropylbenzylamine and its complexes with iron (II), nickel (II) and cobalt (II) are reported. Physical properties of the ligand i.e; boiling point, miscibility, relative density, refractive index,  $\lambda_{max}$ , viscosity and surface tension are given. Evaluation of complexes was carried out on the basis of infrared spectra and analytical data. Antibacterial activity of O-cyano-N,N-dipropylbenzylamine and its metal complexes are reported against some pathogenic bacteria by diffusion plate method.

### Introduction

Research on complex compounds expanded rapidly after 1945. A tremendous amount of work has been carried out in this field [1].

N, N-Dimethylbenzylamine reacts with potassium tetrachloroplatinate (II) and palladium chloride to give di- $\mu$ -chloro-bis (N, N-dimethylbenzyl-amine-2-C-N) diplatinum (II) and dipalladium (II), respectively. These stable complexes possess both ortho-metalated covalent metal-carbon bonding and metal-nitrogen coordinate bonding to the benzyl-amine [2].

Schoenwald and his co-workers synthesized N-cyclohexyl-N-ethylbenzylamine by refluxing N-ethylcyclohexylamine benzylchloride and 4-methyl-2-pentanone [3].

Irradiation of benzylamine  $\text{PhCH}_2\text{NR}_1\text{R}_2$  ( $\text{R}_1 = \text{H}$ ,  $\text{R}_2 = \text{Me}$ , H, octyl,  $\text{CH}_2\text{CH}_2\text{Ph}$ , Ph;  $\text{R}_1 = \text{R}_2 = \text{Me}$ ) complexed with trialkyl aluminium  $\text{R}_3\text{Al}$  ( $\text{R} = \text{Me}$ , Et) in benzene gave PhMe and  $\text{PhCH}_2\text{R}$  and amines [4].

Some new chelates have been prepared by 3-azo-(P-benzene sulfonamido)-bipyridyls and their biological activity tested against a number of bacteria. These metal chelates have shown higher antimicrobial activities than the ligand [5].

Compounds of O-Amino-N-ethyl-N-phenylbenzylamine and O-Carboxy-N,N-dibutylbenzylamine with group II-B metals have also been investi-

gated for their antimicrobial activity against some specific pathogenic bacteria. [6,7].

### Results and Discussion

Physical data of O-cyano-N,N-dipropylbenzylamine is given in table-1. The Infrared spectra are given in table-2. Infrared spectrum of O-cyano-N, N-dipropylbenzylamine indicates C-H stretching frequency for methyl and methylene groups at 2925, 2872 and 2810  $\text{cm}^{-1}$ . The aromatic C-H stretching vibration is indicated at 3050  $\text{cm}^{-1}$ . Characteristic frequency of C N bond is depicted at 2224  $\text{cm}^{-1}$ . C-H bending for methyl appears at 1443, 1365  $\text{cm}^{-1}$  due to asymmetrical and symmetrical vibrations, respectively. The aromatic C—C stretching is indicated at 1620 and 1599  $\text{cm}^{-1}$ . The absorption bands observed at 1185, 1151, and 1065  $\text{cm}^{-1}$  are due to in-plane bending of aromatic C-H and the bands at 970, 840 and 747  $\text{cm}^{-1}$  are due to out of plane bending. In case of metal complexes some new bands appeared below 600  $\text{cm}^{-1}$  which may be assigned to M-N bond. The

Table-1: Physical Properties of O-Cyano-N,N-dipropylbenzylamine

Colour	Orange yellow oily liquid
Solubility	Soluble in almost all organic solvents
Yield	42.8%
Relative density	1.34 gm/ml at 23 °C
$\lambda_{max}$	316.5 nm
Boiling point	130 °C
Refractive index	1.562 at 23 °C
Viscosity	31.26 g/cm/sec at 23 °C
Surface tension	32.52 dynes/cm at 23 °C

Table-2: Infrared Spectra of Compounds

Compounds	Infrared Absorption Bands ( $\nu$ $\text{cm}^{-1}$ )
O-Cyano-N,N-dipropylbenzylamine [ I ]	3050 (w), 2925 (s), 2872 (s), 2810 (s), 2224 (s), 1620 (m), 1599 (s), 1443 (s), 1365 (s), 1275 (s), 1185 (s), 1161 (s), 1065 (s), 970 (m), 840 (w), 747 (s).
Complex of O-Cyano-N, N-dipropyl-Benzylamine with cobalt chloride [ II ]	3380(w), 3080(w), 2900 (s), 2390 (w), 2210 (w), 1850 (w), 1650(m), 1560 (w), 1450 (w), 1390(m), 1210(m), 1150(w), 1080 (s), 838 (s), 718 (s), 610 (w), 560 (w), 416 (s).
Complex of O-Cyano-N,N-dipropyl-benzylamine with nickle chloride[ III ]	3300(w), 2910(s), 2850 (m), 2250 (m), 1780 (m), 1600(w), 1550 (w), 1390 (s), 1110 (w), 1050 (m), 898 (w), 540 (w), 512 (s).
Complex of O-Cyano-N,N-dipropyl-Benzylamine with ferrous sulphate [ IV ]	3370 (w), 2900 (w), 2840(w), 2220(w), 1870(w), 1720 (w), 1650 (w), 1580 (m), 1490 (m), 1150 (m), 980 (w), 840(w), 620 (m), 580 (m), 480 (m).

lowering in position of bands also depicts the formation of complexes [8].

The atomic absorption data for metal analysis is given in table-3 and estimation of nitrogen by Kjeldahl's method indicated the formation of metal ligand complexes in the ratio of M: L=1:1.

Antibacterial activity of the ligand and its complexes was investigated against some bacteria such as *Escherichia coli* (E.c), *Pseudomonas*, *Bacillus subtilis* (B.s) and *Staphylococcus aureus* (S.a) by diffusion plate method. Ligand shows least activity. Data is given in Table-4.

Table-3: Physical Properties, Estimation of Nitrogen and Metal

Com-pound	Colour	Melting point/Decomposition point °C	% Yield	% Metal	% Nitrogen
II	Purple	Above 300	24.4	15.6 (17)*	7.0 (8.0)*
III	Light green	Above 300	30.5	15.4 (16.8)*	7.2 (8.1)*
IV	Brown	Above 300	35.7	13.8 (15.0)*	6.7 (7.6)*

\*Theoretical values are given in parenthesis.

Table-4: Antibacterial Activity

Compounds	Concen Trations mg/mL	Inhibition Zone (mm)			
		E.c	Pseudo	B.s	S.a
I		10	9	9	10
II	10 mg/mL	*	10	*	9
	25 mg/mL	10	13	12	10
	50 mg/mL	14	19	16	13
III	10 mg/mL	*	10	9	*
	25 mg/mL	10	15	13	11
	50 mg/mL	15	20	18	15
IV	10 mg/mL	*	9	*	*
	25 mg/mL	*	9	11	*
	50 mg/mL	9	10	12	10

\* No activity

The antibacterial activity trend of the complexes is in the following order.

Ni (II) Complex > Co (II) Complex > Fe (II) Complex.

### Experimental

N-Bromosuccinimide,  $\text{CCl}_4$ , benzoyl peroxide, sodium bicarbonate, O-tolunitril, ferrous sulphate, nickel chloride and cobalt chloride were purchased from E.Merk. Dipropylamine was obtained from Fluka. All chemicals were used without further purification. Solvents were purified through distillation.

Melting/Decomposition points of the complexes were taken on Gallenkamp M.P. device and are uncorrected. Viscosity of ligand was determined by using technico VS250 viscometer size No. B.S/1P/RF. Water was used as a reference solvent. The surface tension of the ligand was determined by stalagmometer and refractive index was taken on Abbe's refractometer.

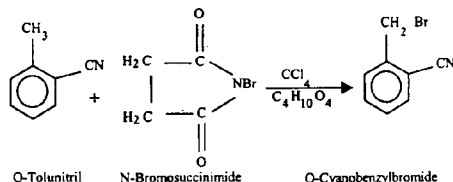
Infrared spectra of the ligand and complexes were recorded in thin film and KBr disc, respectively, in the spectral range of  $4000\text{-}400\text{ cm}^{-1}$  on Hitachi infrared spectrophotometer, Model 270-30.  $\lambda_{\text{max}}$  of ligand was taken in  $\text{CCl}_4$  on Hitachi UV-visible spectrophotometer, Model U-2000. Estimation of metal was carried out on Hitachi atomic absorption spectrophotometer, Model Z-8000 and nitrogen was estimated by Kjeldahl's method.

### Synthesis of O-Cyano-N, N-Dipropylbenzylamine

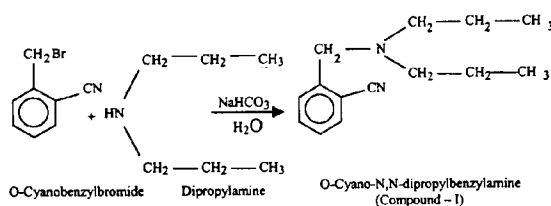
#### a) Bromination of O-Tolunitril:

O-Tolunitril (64.3 mL, 0.5 mol), N-bromo-succinimide (88.9 g, 0.5 mol) and benzoyl peroxide (1.0 g) in  $\text{CCl}_4$  (250 mL) were charged in a quickfit

flask equipped with water condenser and reaction mixture was heated under reflux for 6-8 hours, 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 O-cyanobenzyl bromide.



(b) O-Cyanobenzyl bromide, sodium bicarbonate (42.0 g, 0.5 mol) and distilled water (100 mL) were taken in a quickfit flask (500 mL) equipped with water condenser. Dipropylamine (69.0 mL, 0.5 mol) was added and mixture was again refluxed for 4 hours. The mixture was transferred to a separating funnel where two layers were formed. The organic layer was collected and passed through a column packed with silica gel No.60 (70-230 mesh ASTM). The n-hexane: ether (3:1) eluted a yellow fraction which on evaporation gave orange yellow oily liquid (compound-I), soluble in almost all organic solvents. It was used without further purification.



*Reaction of O-Cyano- N, N-Dipropylbenzylamine with Cobalt (II) Chloride:*

O-Cyano-N,N-dipropylbenzylamine (1.0 mL, 6.0 mol) dissolved in ethanol (60 mL) was added to cobalt (II) chloride (0.71 g, 3.0 m. mol) in distilled water (15ml) followed by the addition of 3-4 drops of liquid NH<sub>3</sub>. The reaction mixture was heated in water bath till ammonia ceased to evolve (checked by HCl on rod). Purple solid settled which was filtered and washed with distilled water, ethanol and n-hexane, dried and further purified by refluxing it with ethanol and THF, then washed with petroleum ether and n-hexane and dried to get compound (II) as purple solid (yield 24.4%).

*Reaction of O-Cyano- N, N-Dipropylbenzylamine with Nickel (II) Chloride:*

O-Cyano-N,N- dipropylbenzylamine (1.0 mL, 6.0 m. mol) dissolved in ethanol (60 mL) was added to nickel (II) chloride (0.71 g, 3.0 m. mol) in distilled water (15 mL) followed by the addition of 3-4 drops of liquid NH<sub>3</sub>. The reaction mixture was heated in water bath till ammonia ceased to evolve (checked by HCl on rod). A light green solid settled which was filtered and washed with distilled water, ethanol and n-hexane, dried and further purified by refluxing it with ethanol and THF, then washed with petroleum ether and n-hexane and dried to get compound (III) as light green solid (yield 30.5%).

*Reaction of O-Cyano- N, N-Dipropylbenzylamine with Ferrous (II) Sulphate:*

O-Cyano-N,N-dipropylbenzylamine (1.0 mL, 6.0 m. mol) was dissolved in ethanol (60 mL). Clear solution of ferrous (II) sulphate (0.77 g, 3.0 m. mol) was prepared in distilled water (15 mL) by warming. Both the solutions were mixed and stirred for 3-4 hours. A brown solid settled which was filtered and washed with warm distilled water, ethanol and n-hexane, dried and further purified by refluxing it with ethanol and THF, then washed with petroleum ether and n-hexane and dried to get compound (IV) as brown solid (yield 35.7%).

*Preparation of Plates*

Antibacterial activity of ligand and their complexes was investigated by agar diffusion method [9] against *Pseudomonas*, *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus*. Assay medium was adjusted before the addition of agar. The nutrient agar was also used for the bioassay. 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 before the addition of agar. The medium was then dispersed in 250 mL Erlenmeyer flask and sterilized at 15 Psi pressure for 30 minutes.

The petri-plates were washed and sterilized in oven at 120°C overnight. 20 mL of the molten bioassay medium poured in the sterile plates was allowed to set. 4.0 mL of molten assay medium was incubated with predetermined concentrations of the microorganisms and spread uniformly over the first layer and was allowed to set. Then four wells of 0.8 cm were made in the plates aseptically using stainless steel borer. An emulsion of sample (0.1%) in

gumacacia was used for testing its antibacterial activity. 0.12 mL of the emulsion was added to a hole incubated at 37°C for 24 hours. Clear zones of inhibition were developed and the diameters of the zones of inhibition were measured in mm.

#### References

1. Charkberk and Marellel, "Organic Sequestering Agent", P-1 (1967).
2. A.C. Cope and E.C. Friedrich, *J. Am. Soc.*, **90**, 909 (1968).
3. D.Shoenwald Ronald, Barfknecht, F.Charles, E.Newton Roger. *PCT. Inst. Appl. WO* **92**, 10,449(1992).
4. Omura, Kanji, Furukawa and Junji, *Chem. Lett.*, **10**, 1633 (1982).
5. Awad, *Synth. React. Inorg. Met. Org.*, **21** (1991).
6. H. M. Farooq, M.Z. Iqbal, F. Mazher and B.B. Ali, *Acta Sci.*, **9**, 163 (1999).
7. H. M. Farooq. M.Z. Iqbal, N. Nadir and I. Hussaini, *Acta Sci.*, **10**, 59 (2000).
8. D.W. Brown, A.J. Floyd and M. Sainsbury, "Organic Spectroscopy", John Wiley and Sons, Chichester, New York, Brisbane, Toronto, Singapore, pp 32 (1988).
9. B. Arret, D.P. Jonson and Kishbaam, *J. Pharmaceutical Sciences*, **60**: 373 (1999).