Research Article

A Synthesis, Characterization and Antibacterial Studies of Bis-(3-amino-2-chloro-phenyl)-phenyl-methanol and its [Polinuclear complex with Fe III]

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ABSTRACT

In present paper, we report the organic syntheses of three compounds from 2-Chloro-phenylamine and describe the results of antibacterial activity of purified compounds. Compounds Bis-(3-amino-2-chloro-phenyl)-chloro-methanol (1a), Bis-(3-amino-2-chloro-phenyl)-phenyl-methanol (2a), Bis-(3-amino-2-chloro-phenyl)-phenyl-methanol [Polinuclear complex Fe III] (3a) , have been synthesized and characterized using melting points, IR spectra, ^{1}H-NMR and ^{13}C-NMR spectra. The antibacterial activity of synthesized compounds and streptomycin and Cephalexin at concentrations of 2mg/ml, 3mg/ml and 5mg/ml, have been evaluated against three strains of bacterial culture; Staphylococcus aureus, E.coli and Bacillus cereus. The compounds show bacteriostatic and bactericidal activity.

Keywords: 2-Chloro-phenylamine, Antibacterial activity, IR, ^{1}H-NM, ^{13}C-NMR, Streptomycin.

INTRODUCTION

Starting from 2-Chloro-phenylamine (a); derivatives (1a, 2a, 3a) are synthesized. 2-Chloro-phenylamine derivatives synthesized with Benzene and Trichloro-methanol with alcilyc reaction (Fridel-Crafts), they are large group of chemical compound (specifically, a benzo derivatives) found in many plants[1,2,4] notably in high concentration in the tonka bean (Dipteryx odorata), vanilla grass (Anthoxanthum odoratum), woodruff (Galium odoratum) , mullein (Verbascum spp), and sweet grass (Hierochloe odorata).

2-Chloro-phenylamine and their derivatives have shown various biological activities. Their fame has come mainly from their anti thrombic, anti inflammatory, vasodilatory, and antiviral activities. Other several 2-Chloro-phenylamine derivatives have antimicrobial properties[5,6] (Sanghyun et al., 1996; Mohareb et al 2007; Nofal et al 2000[6,8]), with reflux and condensation we have synthesize some new coumarin derivatives and to investigate their antibacterial activity against Staphylococcus aureus, E.coli and Bacillus cereus. The antibacterial activity of synthesized compounds is compared with antibacterial activity of Cefalexine and Streptomycine.

Experimental Section

Experimental Chemistry

Compounds Bis-(3-amino-2-chloro-phenyl)-chloro-methanol (1a), Bis-(3-amino-2-chloro-phenyl)-phenyl-methanol (2a), Bis-(3-amino-2-chloro-phenyl)-phenyl-methanol [Polinuclear complex Fe III] (3a) are synthesized.

Measurement

The identification of derivatives (1a, 2a, 3a,), is made by using melting point, IR, ^{1}H NMR, ^{13}C NMR spectra and elemental analysis. Melting point was determinated on a Electro thermal apparatus (Fisher Scientific 2555) in a open capillary tube and are uncorrected. Infrared spectra were recorded in cm-1 for KBr pellets on a FT-IR Shimadzu 8400S spectrophotometer with resolution 4 cm-^{1}. ^{1}H NMR spectra were recorded on a Bruker UNITY plus-500 'NMR 1' spectrometer using DMSO-d6 as the solvent and TMS as the internal references standard (σ = 0,00 ppm). Chemical shifts are expressed in δ ppm. Mass spectra were taken on a LKB 9000 mass spectrometer. Element analyze was performed on a Perikin-Elmer 240 BCHN analyzer. The purity of the compounds (synthesized) was routinely checked by TLC using Merck Kieselgel-60 (F-254) and benzene, toluene, glacial acetic acid (80:10:10) as mobile phase. The spots were exposed in iodine vapor for visualization.

Preparation of Bis-(3-amino-2-chloro-phenyl)-chloro-methanol (1a)

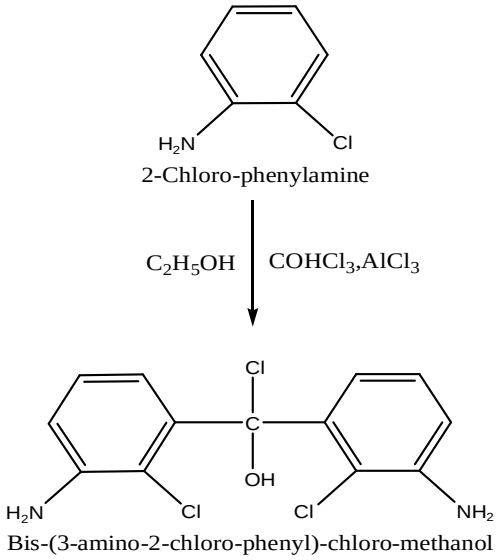
For this synthesis is used as substrate 2-Chloro-phenylamine in a 100 ml flask mixed 5ml C_2H_5OH, Trichloro-methanol , $AlCl_3$.

The mixture was refluxed at 80^{o}C for ca. 60 min. The obtained crystals yellow are filtered and rinsed with ethanol and dried at room temperature. Recrystallization form absolute ethanol gave a yellow product of 80% yield, melting point 210^{o}C.

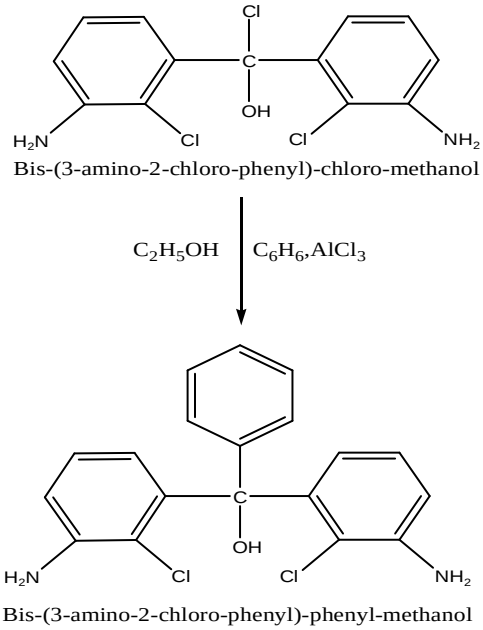
Preparation of Bis-(3-amino-2-chloro-phenyl)-phenyl-methanol (2a)

In a 100 ml flask were mixed 2g Bis-(3-amino-2-chloro-phenyl)-chloro-methanol with 5ml C_2H_5OH, 1ml C_6H_6, $AlCl_3$. The mixture was refluxed at 60°C for ca. 2 hrs.

The obtained red crystals are filtered and dried at room temperature. Re-crystallization form C_2H_5OH gave red crystals product of 70 % yield, melting point, 225°C.



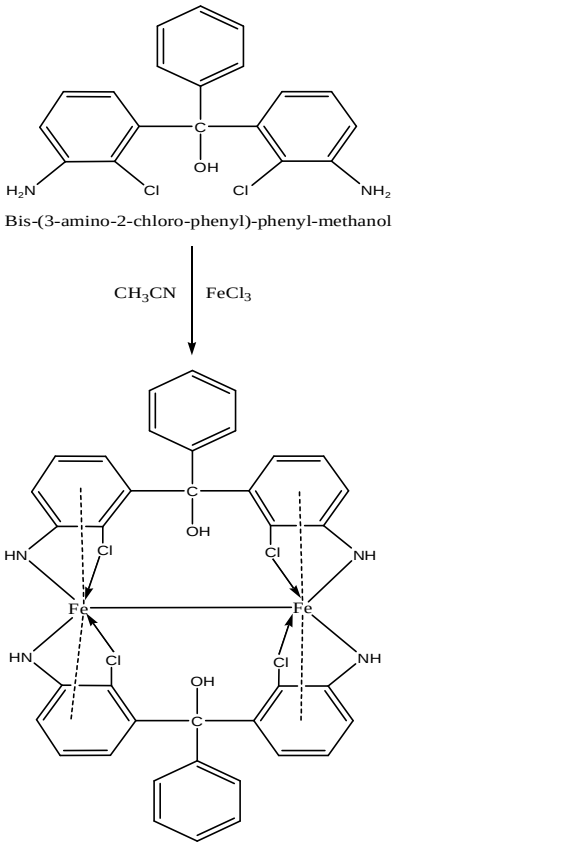
Scheme 1



Scheme 2

Preparation of Bis-(3-amino-2-chloro-phenyl)-phenyl-methanol [Polinuclear complex Fe III] (3a)

In a 100 ml flask were mixed 2g of Bis-(3-amino-2-chloro-phenyl)-phenyl-methanol, with 8 ml C_2H_5OH, 1.5g $FeCl_3$ and 0,2 ml Et_3N as catalyze. The mixture was refluxed at 95°C in water bath for ca 8 h. The flask was placed in an ice bath for 1h until yellow crystalline precipitate was formed. After filtration the product was recrystallized from C_2H_5OH. The re-crystallization gave a red product at 70% yield, melting point 170°C.



Scheme 3

Antibacterial activity

The purified synthesized compounds (1a, 2a, 3a) was subjected to test in vitro its antibacterial activity against three bacterial cultures; Staphylococcus aureus, E.Coli and B.cereus. Antibacterial activity of compounds was investigated applying the Kirby-Bayer method or disc method (d=5.5 mm max. capacity 10 µg)

RESULTS AND DISCUSSION

By reacting equimolar amounts of 2-Chloro-phenylamine and corresponding reagents (according scheme 1) under reflux reaction conditions product 1a is synthesized in 80 % yield.

By reacting equimolar amounts of Bis-(3-amino-2-chloro-phenyl)-chloro-methanol and corresponding reagents (according scheme 2) under reflux reaction conditions product 2a is synthesized in 70 % yield.

By reacting equimolar amounts of Bis-(3-amino-2-chloro-phenyl)-phenyl-methanol and corresponding reagents (according scheme 3) under reflux reaction conditions product 3a is synthesized in 70% yield.

The structure of 2-Chloro-phenylamine derivatives (1a, 2a, 3a) were determined from their IR, ^{1}H NMR, ^{13}C NMR spectra and their melting points as follows.

For (1a); IR bands (KBr, cm-1) 3500cm^{-1} (OH), 3400-3000 cm^{-1} (NH), 3040-3000 cm^{-1} (C-H arom), 1600-1520 cm^{-}

^{1}(C=C arom), 1600-1500 cm^{-1} (N-H bend), 1470-1420 cm^{-1} (C-H bend), 800-700 cm^{-1} (C-Cl)

^{1}H NMR (DMSO-d6) δppm, 2.0ppm s(H,OH); 4.0ppm d(4H,2NH_2) ; 6.33,6.49,6.82, ppm (6H .arom)

^{13}C NMR (DMSO) δppm 86ppm (C,C-OH); 114ppm 127ppm 119ppm 144ppm (8C aromatic) 120ppm (C,C-Cl); 147.6ppm (C,C-N).

Table 1: Analytical data

Compound	Yield %	m.p	M.F	Elemental analysis, Calculate (calc %)					
				C	H	O	N	Cl	Fe
1a	80	210°C	$C_{13}H_{11}Cl_3N_2O$	49.16 49.14	3.49 3.57	5.04 5.00	8.82 8.78	33.49 33.46	——
2a	70	225°C	$C_{19}H_{16}Cl_2N_2O$	63.52 63.50	4.49 4.46	4.45 4.43	7.80 7.77	19.74 19.71	——
3a	80	320°C	$Fe_2[C_{42}H_{40}Cl_4N_4O_2]$	56.92 56.89	4.55 4.53	3.61 3.60	6.32 6.30	16.00 15.97	12.60 12.59

Table 2: Antibacterial activity-Staphylococcus aureus

Compound	Inhibition zone (mm)		
	2mg/ml	3mg /ml	5mg/ml
1a	12	16	20
2a	13	16	19
3a	14	17	21
Cefalexine	9	9	9 10 µg
Streptomycine	20	20	20 10 µg

Table 3: Antibacterial activity – E.Coli

Compound	Inhibition zone (mm)		
	2mg/ml	3mg /ml	5mg/ml
1a	9	14	22
2a	10	16	20
3a	11	17	21
Cephalexin	9	9	9 10 µg
Streptomycine	23	23	23 10 µg

Table 4: Antibacterial activity – Bacillus cereus

Compound	Inhibition zone (mm)		
	2mg/ml	3mg /ml	5mg/ml
1a	11	15	22
2a	9	14	20
3a	12	18	23
Cephalexin	9	9	9 10 µg
Streptomycine	23	23	23 10 µg

For (2a) IR bands (KBr,cm -1) 3500-33450 cm^{-1} (OH);3400-3330 cm^{-1} (N-H)'3030-3010 cm^{-1} (C-H arom); 1580-1500 cm^{-1} (C=C arom); 1480-1442 cm^{-1} (C-H bend) ; 842-720 cm^{-1} (C-H arom)

^{1}H NMR (DMSO-d6) δppm; 2.0ppm s(H-OH); 4.0ppm (H,NH); 4.0p (4H,2NH_2),6.33ppm,6.49ppm,6.82ppm,7.19ppm m(11H arom) ^{13}C NMR (DMSO) δppm ;69.9ppm (C,C-OH); 114,119,127,126,129,143,142ppm (14 C arom), 120.3ppm (C-Cl) 147.6ppm (,C,C-NH)

For (3a) IR bands (KBr,cm -1) 3400-3300 cm^{-1} (N-H); 3050-3010 cm^{-1} (C-H arom); 1600-1500cm^{-1} (C=C arom); 1480 cm^{-1} (N-H bend); 1460-1410 cm^{-1} (C-H bend); 1250-1200cm^{-1} (C-O); 840-720 cm^{-1} (C-H arom); 530-510cm^{-1}(M-O); 440-420cm^{-1}(M-N) ^{1}H NMR (DMSO-d6) δppm ; 4.0ppm d(H,NH_2), 6.33ppm, 6.49ppm, 6.82ppm, 7.19ppm m(22H arom); ^{13}CNMR (DMSO) δppm ; 47ppm (C,C-O); 114ppm, 119.8ppm, 126ppm, 127.9ppm, 126ppm, 129ppm, 143ppm, 128.4ppm (328 C arom), 147.6ppm(2C,C-N), 120.3ppm (C,C-Cl)

CONCLUSION

From the results the following conclusion where drawn: The study provides the first evidence that compounds (1a, 2a, 3a) obviously inhibit the growth of S.auerus, E.coli and B.cereus.

The compounds (1a, 2a, 3a) compared with the antibacterial activity of Streptomycin in S.aureus, E.coli and B.cereus.

This study provided the first evidence that these compounds 1a, 2a, 3a showed a significant antibacterial effect against S.aureus, E.coli and B.cereus.

The chemical structures of synthesized compounds were determined according to extensive NMR experiments and published data.

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