Solvent Free Green Synthesis of Schiff Bases and Studies of their Anti Microbial Activities

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The condensation between an aldehyde and an amine leading to a formation of Schiff base described by Hugo Schiff in 1864.The chemistry of the carbon-nitrogen double bond plays key role in the progress of chemical science.Schiff base comprise a group of both cyclic and acyclic chemical compounds containing azomethine moieties (-C=N-R). This azomethine linkage acts as donor site. These ligands are capable to coordinate with metal ions through imine nitrogen and other donor groups present in substituted aldehyde. They are termed as 'privileged ligands', being active, well designed and easy to prepare through the aldehyde-amine condensation. Schiff bases have been studied extensively because of their high potential chemical permutation. Magnetic susceptibility, absorption spectra, elemental analysis, molecular weight determination, conductivity, thermal analysis of many Schiff bases and their complexes has been reported. Schiff bases are important intermediates for the synthesis of some bioactive compounds such as β-lactums .Several workers also studied their biological properties, such as antibacterial, antifungal, etc. It is reported that the rapidly developing field of bioinorganic chemistry is centered on the presence of coordination compounds in living systems.

Schiff Bases and their metal complexes have diverse range of applications in various fields. Schiff bases form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that include antibacterial, antifungaland antitumor activity. Furthermore, they are reported to show a variety of interesting biological actions, including anti mouse hepatitis virus (MHV),inhibition of herpes simplex virus type 1 (HSV-1) and adenovirus type 5 (Ad 5), anticancer, anti mosquito larvae and herbicidal activities. They have been extensively studied as a class of ligands which confirms their applicability in inorganic chemistry.

Application of many new analytical devices requires the presence of organic reagents as essential compounds of the measuring system. They are used, in optical & electrochemical sensors, as well as in various chromatographic methods, to enable detection of enhance selectivity and sensitivity

SYNTHESIS OF SCHIFF BASES(As per method mentioned in reference 1)

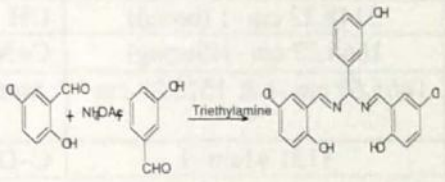
Materials and Methods

All reagents used were obtained from Sigma Aldrich, and are chemically pure or analytical reagent grade. Purity of organic compounds was checked by TLC.

Infrared spectra of samples were measured in KBr pellets on a FTIR Jasco 4100 type A Serial No. C193161016. The purity confirmation and reaction monitoring by TLC on silica gel plates prepared on glass slides.

Synthesis of 2,2'-{[(3-hydroxyphenyl) methanediyl] bis [nitrilo(E) methylylidene]}bis(4-chlorophenol) a Schiff base from 5-Chloro salicylaldehyde– Scheme A

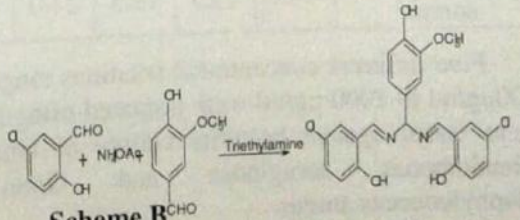
To the mixture of 0.469gm 5-Chloro salicylaldehyde (3mmole) & 0.183 gm 3-hydroxy benzaldehyde (1.5mmole) 0.25gm ammonium acetate (3.27mmole) was added in presence of base triethylaimne. The mixture was stirred with magnetic stirrer. Reaction was monitor by TLC. Reaction mixture was poured in ice cold water then precipitate formed was filtered and purified by recrystalisation from ethyl alcohol.



Scheme A

Synthesis of 2,2'-{[(4-hydroxy-3-methoxyphenyl) methanediyl] bis [nitrilo (E) methylylidene]} bis(4-chlorophenol) a Schiff base from 5-Chloro salicylaldehydeSheme B

To the mixture of 0.469gm 5-Chloro salicylaldehyde (3mmole) & 0.229gm vaniline (1.5mmole) 0.25gm ammonium acetate (3.27mmole) was added in presence of base triethylaimne. The mixture was stirred with magnetic stirrer. Reaction was monitor by TLC. Reaction mixture was poured in ice cold water then precipitate formed was filtered and purified by recrystalisation from ethyl alcohol.



Scheme B

Spectral Analysis:

Schiff bases formation were characterized by FT-IR Spectrometric Techniques. The Results are discussed below

The IR Spectrum of compound of Scheme A shows a broad band around 3064.33 cm^{-1} due to phenolic OH. IR spectra did not observe any C=O stretching band generally observed between 1680cm^{-1}– 1720 cm^{-1}but showed strong band at 1620.88 cm^{-1}which is a characteristic C = N stretching of azomethine. This confirmed that entire aldehyde is converted into azomethine (CH=N) linkage and Schiff base is successfully formed.

1	3064.33 cm^{-1} (broad)	OH
2	1620.88 cm^{-1}(Strong)	C=N
3	1426.10 cm^{-1}& 1547.59 cm^{-1}	Aromatic C=C
4	1115.62 cm^{-1}	C~O

The IR Spectrum of compound Scheme B shows a broad band around 3148.22 cm-1 due to phenolic OH. IR spectra did not observe any C=O stretching band generally observed between 1680cm^{-1}–1720cm^{-1}but showed strong band at 1664.27cm^{-1} which is a characteristic C = N stretching of azomethine. This confirmed that entire aldehyde is converted into azomethine (CH=N) linkage and Schiff base is successfully formed.

1	3148.22 cm -1 (broad)	OH
2	1664.27 cm -1(Strong)	C=N
3	1465.63 cm -1 & 1512.88 cm^{-1}	Aromatic C=C
4	1121.41cm -1	C~O

STUDY OF BIOLOGICAL ACTIVITY

Compound of Scheme A

Stock concentration: - 1.0 mg/ml
Concentration range: - 0.2 mg/ml to 1.0 mg/ml
Diluents used: - DMF (Di Methyl Formamide)
Test Culture: - 1) Pseudomonas aeruginosa
2) Staphylococcus aureus

Test culture	Diameter of inhibition Zone (mm)					
Concentration (mg/ml)	0.2	0.4	0.6	0.8	1.0	DMF
Pseudomonas aeruginosa	00	00	00	00	00	00
Staphylococcus aureus	14.5	15.5	19.5	24.0	ND	00

Five different concentrated solutions ranging between 200µg/ml to 1000 µg/ml were prepared using DMF. These were tested against bacterial culture of Gram negative Pseudomonas aeruginosa and Gram positive Staphylococcus aureus.

The test compounds of scheme Ais water insoluble and hence solutions were prepared by dissolving them in DMF solvent to find their anti bacterial activity. The solvent DMF itself does not have anti bacterial activity which was also confirmed by maintaining a solvent control during the experiment.

The observations revealed that the test compound of scheme A is found to effective in inhibiting Gram positive bacteria test culture of Staphylococcus aureus. MIC (Minimum Inhibitory Concentration) for of scheme A was 200µg/ml.

The test compounds of scheme A was failed to inhibiting Gram negative test bacteria culture of Pseudomonas aeruginosa.

Compound of Scheme B

Stock concentration: - 1.0 mg/ml
Concentration range: - 0.2 mg/ml to 1.0 mg/ml
Diluents used: - DMF (Di Methyl Formamide)
Test Culture: - 1) Pseudomonas aeruginosa
2) Staphylococcus aureus

Test culture	Diameter of inhibition Zone (mm)					
Concentration (mg/ml)	0.4	0.8	1.2	1.6	2.0	DMF
Pseudomonas aeruginosa	00	11.0	14.0	16.5	16.5	00
Staphylococcus aureus	11.0	13.5	13.5	13.5	13.5	00

Five different concentrated solutions ranging between 400 µg/ml to 2000 µg/ml were prepared using DMF. These were tested against bacterial culture of Gram negative Pseudomonas aeruginosa and Gram positive Staphylococcus aureus.

The test compounds of Scheme B is water insoluble and hence solutions were prepared by dissolving them in DMF solvent to find their anti bacterial activity. The solvent DMF itself does not have anti bacterial activity which was also confirmed by maintaining a solvent control during the experiment.

The observations revealed that the test compound Scheme B is found to effective in inhibiting Gram positive bacteria test culture of Staphylococcus aureus. MIC (Minimum Inhibitory Concentration) for of scheme B was 400µg/ml.

The test compounds of scheme B is found to effective in inhibiting Gram positive bacteria test culture of Staphylococcus aureus. MIC (Minimum Inhibitory Concentration) for of scheme B was 1200µg/ml.

CONCLUSION

Both Schiff bases of scheme A and of scheme B can be synthesized under solvent free condition at room temperature and exhibit antimicrobial activity. Both are

inhibiting gram positive bacteria whereas of scheme A fails to inhibit gram negative bacteria.

ACKNOWLEDGMENT

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