INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH & DEVELOPMENT

ISSN: 2278 – 0211 (Online)

Synthesis And Biological Activity Of Aniline Derivative Schiff Bases

A. V. G. S. Prasad
R& D Department, Chiral Biosciences Ltd., Hyderabad, A.P., India
K. Trinagaraju
R& D Department, Chiral Biosciences Ltd., Hyderabad, A.P., India
Boyina Gopala Rao
R& D Department, Chiral Biosciences Ltd., Hyderabad, A.P., India
Y. Usha
Microbiology Lab K. N. Biosciences Pvt. Ltd., Hyderabad, A.P., India
P. Sudha Reddy
Microbiology Lab K. N. Biosciences Pvt. Ltd., Hyderabad, A.P., India
P. Venkateswara Rao
Department Of Chemistry, Nizam College (Autonomous), Hyderabad, A.P., India

Abstract:
In the present study new Schiff base compounds derived from amine derivative 1-(2-amino-5-chlorophenyl) -2,2,2, -trifluroethane-1,1-diol hydrochloride with aldehydes such as Isovanillin, Pyridine 2-Carboxyaldehyde , 2-Carboxybenzaldehyde and 3 hydroxy 4 methyl benzaldehyde. The Schiff base compounds were characterized by IR, and 1H NMR spectroscopy. The Schiff base ligands have also been tested in vitro for their antibacterial and anti fungal activity. The experimental results suggest that Schiff base ligands are more potent in anti bacterial and anti fungal activities.

Key words: *Schiff bases, amine derivative and aldehydes and Antibacterial activity; Antifungal activity.*

1.Introduction

In organic synthesis, Schiff base reactions are useful in making carbon nitrogen bonds compounds containing azomethine group (-CH=N-).

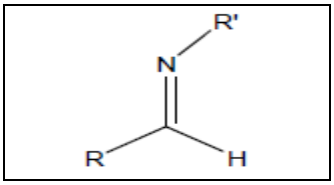

Figure 1

The possibility of having a lone pair of electrons in either π or sp2 hybridized orbital or trigonally hybridized nitrogen in the C=N group is of the fundamental chemical and biological importance.

Heterocyclic systems containing mainly nitrogen, sulphur and oxygen atom constitute a large class of compounds of biological and medicinal interest [1]. Recent literature has explored the biological importance of various structural derivatives of heterocyclic compounds. Since 1886 [2] up now, Schiff bases have become increasingly important mainly due to their stability, ease of preparation, structural variability and variety of applications. On the other hand, Schiff's bases, the condensed products of aromatic amines with aromatic aldehydes, have been known to possess a wide variety of biological applications like antibacterial, antifungal, antitumor, analgesic and anti-inflammatory activities [3, 4]. It has been observed that several Schiff bases show fungicidal [5], anti-inflammatory [6], antibacterial [7], antiviral [8], antioxidant [9], anticancer [10], antibacterial, [11 antifungal, [12].

Schiff's bases containing heterocyclic scaffolds have been known to possess a wide range of biological and pharmacological activities for a long time. In recent years, they have gained significant interest in the area of drug research and development owing to their broad bioactivities such as antibacterial, antifungal, anti-inflammatory, anticonvulsant, antiviral and anticancer activities. In this paper, biologically relevant Schiff's bases derived from a diverse group of heterocyclic scaffolds have been intensively investigated.

It is strongly believed that the specific -C=N grouping (azomethine) is an important structural requirement for the bioactivity of Schiff's bases. In this review, the pharmacological potential of several heterocyclic scaffolds (pharmacophores) and their combined biological effect with an active moiety i.e., imino (-CH=N-) have been extensively studied.

Nowadays, the research field dealing with Schiff base coordination chemistry has expanded enormously. The importance of Schiff base complexes of bioinorganic chemistry, biomedical applications, supramolecular chemistry, catalysis and material sciences, separation and encapsulation processes, and formation of compounds with unusual properties and structures has been well recognized and reviewed.

The present aim of the work is to synthesize a Schiff base derived from amine derivative 1-(2-amino-5-chlorophenyl) -2,2,2, -trifluroethane-1,1-diol hydrochloride with aldehydes such as Isovanillin, Pyridine 2-Carboxyaldehyde , 2-Carboxybenzaldehyde and 3 hydroxy 4 methyl benzaldehyde. And to characterize them and study their antibacterial and anti fungal activities.

2.Experimental

Reagents And Apparatus

All the chemicals used were of AnalaR grade and procured from Sigma-Aldrich and Fluka. The IR spectra were recorded on Jusco 300 instruments in KBr pellets. 1H NMR spectra of ligands in DMSO solution were recorded on a Bruker DT- 400MHz spectrometer, and chemical shifts are indicated in ppm relative to tetramethylsilane. Mass spectra were recorded using a KRATOS MS50TC spectrometer.

SCHIFF BASE 1: 1-(2-(3-hydroxy-4-methoxybenzylideneamino) -5-chlorophenyl) -2,2,2-trifluoroethanone.

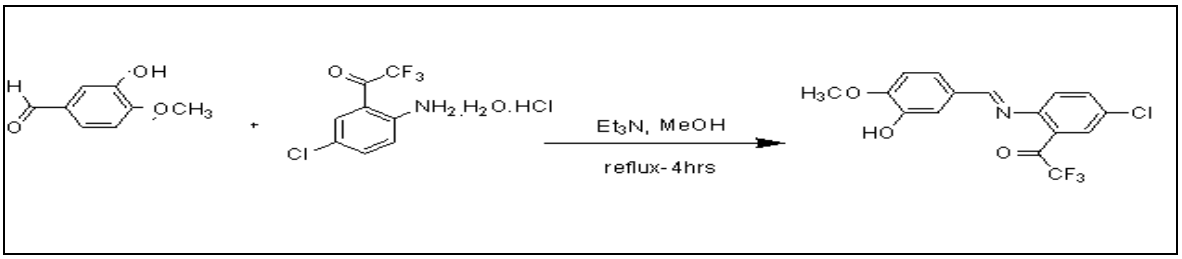

Figure 2

Isovanillin (1.52g, 10 mmol), 1-(2-amino-5-chlorophenyl)-2,2,2,-trifluroethane-1,1-diol hydrochloride (2.76g, 10 mmol) and triethylamine (1 ml, 10 mmol) were mixed in 50 ml ethanol in a round flask. The mixture was refluxed with agitation for 4 h at 60^0C to give a yellow precipitate. After filtration and washing the precipitate with ethanol, a pure Schiff base 1-(2-(3-hydroxy-4-methoxybenzylideneamino) -5-chlorophenyl) -2,2,2-trifluoroethanone. Yield: 2.02 g, was obtained.

Analytical Data Of Compound

Mol. Forula : $C_{18}H_{16}ClF_3NO_3$

Melting point : 138-142°c

Spectral data;

IR (KBr) cm^{-1}

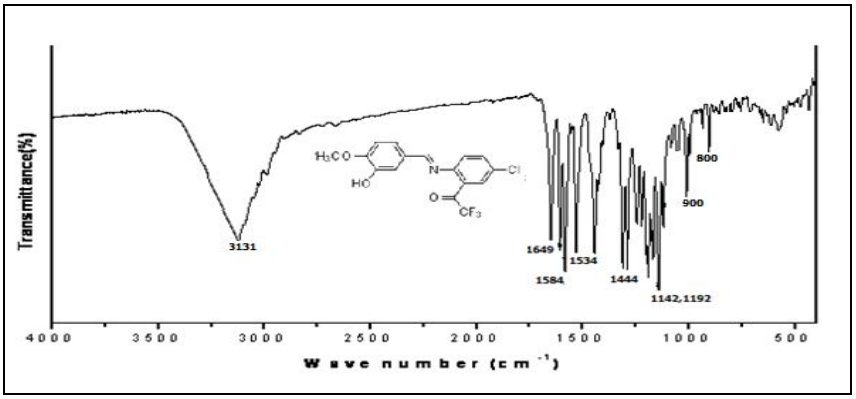

Figure 3

^{1}H.NMR. (300MHz, DMSO)

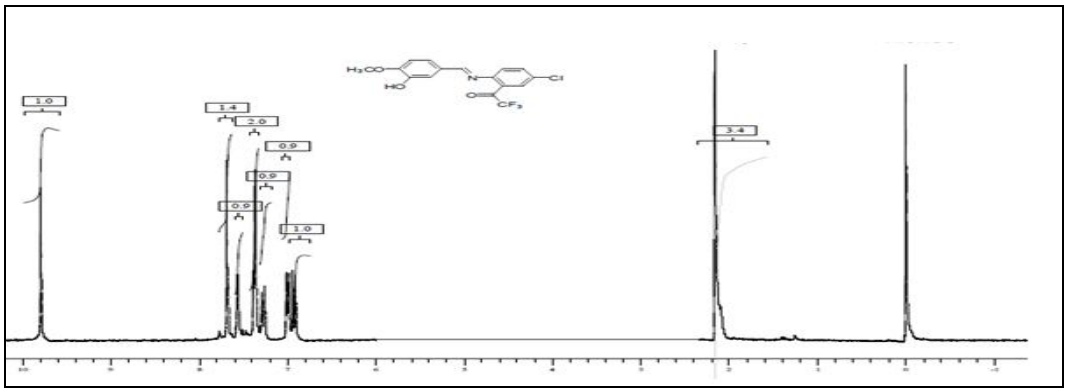

Figure 4

ESI-MS for $C_{18}H_{16}ClF_3NO3$: m/z 386 $[M]^+$
SCHIFF BASE 2:1-(5-chloro-2-(pyridin-2-ylmethyleneamino) phenyl) -2,2,2-trifluoroethanone

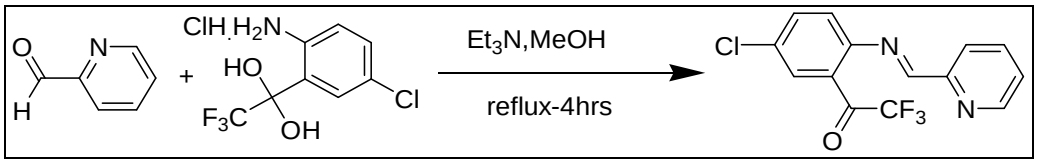

Figure 5

Pyridine 2-Carboxyaldehyde (1.07g, 10 mmol), 1-(2-amino-5-chlorophenyl 2, 2, 2, trifluroethane 1,1-diol hydrochloride, triethylamine (1 ml, 10 mmol) were mixed in 50 ml ethanol in a round flask. The mixture was refluxed with agitation for 4 h at 323 K to give a yellow precipitate. After filtration and washing the precipitate with ethanol, a pure Schiff base ligand, 1-(5-chloro-2-(pyridin-2-ylmethyleneamino)phenyl)-2,2,2-trifluoroethanone (yield: 2.0 g) was obtained.

Analytical data of compound

Mol.Forula :$C_{16}H_{13}ClF_3N_2O$
Melting point :176-180°C
Spectral data;
IR (KBr) cm^{-1}

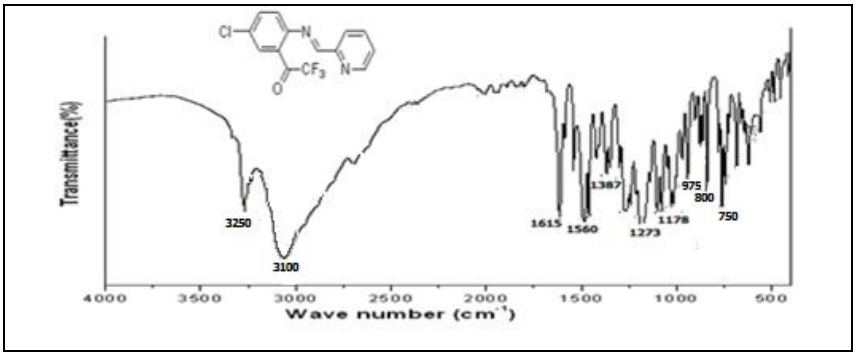

Figure 6

^{1}HNMR(300MHz,DMSO)

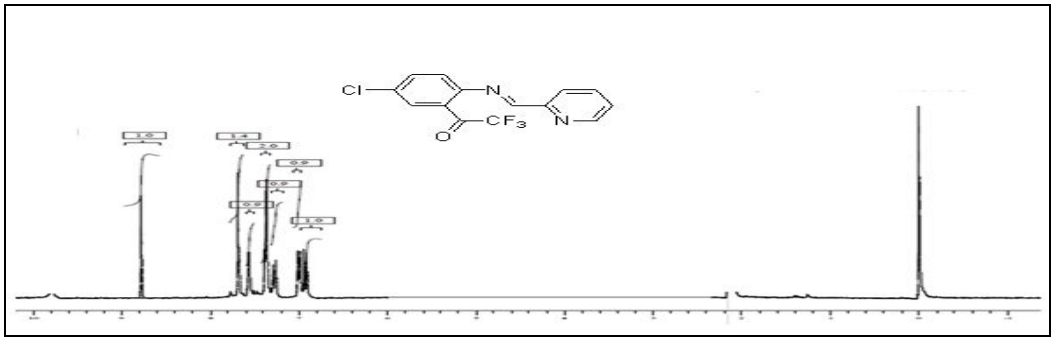

Figure 7

ESI-MS for $C_{16}H_{13}ClF_3N_2O$: m/z 341 $[M]^+$.

SCHIFF BASE 3: 2-((4-chloro-2-(2,2,2-trifluoroacetyl)phenylimino)methyl)benzoic acid 2-Carboxybenzaldehyde (1.5g, 10 mmol), 1-(2-amino-5-chlorophenyl 2,2,2,trifluroethane-1,1 diol hydrochloride, triethylamine (1 ml, 10 mmol) were mixed in 50 ml ethanol in a round flask. The mixture was refluxed with agitation for 4 h at 323 K to give a yellow precipitate. After filtration and washing the precipitate with ethanol, a pure Schiff base ligand, 2-((4-chloro-2-(2,2,2-trifluoroacetyl)phenylimino)methyl)benzoic acid (yield: 2.02 g was obtained.

Analytical data of compound

Mol.Forula : $C_{18}H_{14}ClF_3NO_3$

Melting point :160-162°C

Spectral data;

IR (KBr) cm^{-1}

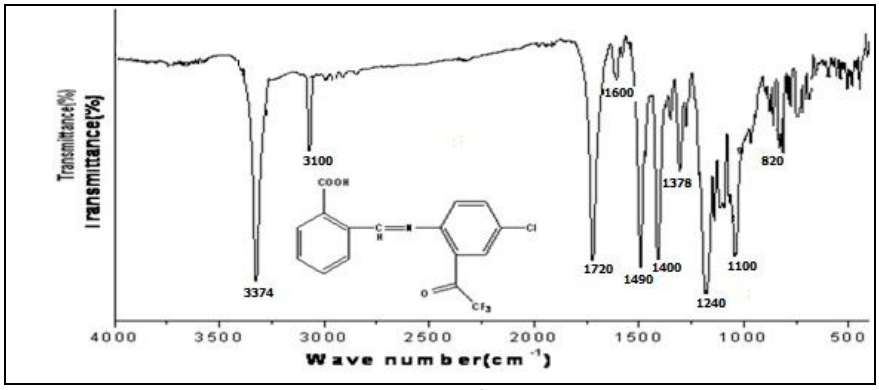

Figure 8

^{1}H NMR(300 MHz , DMSO)

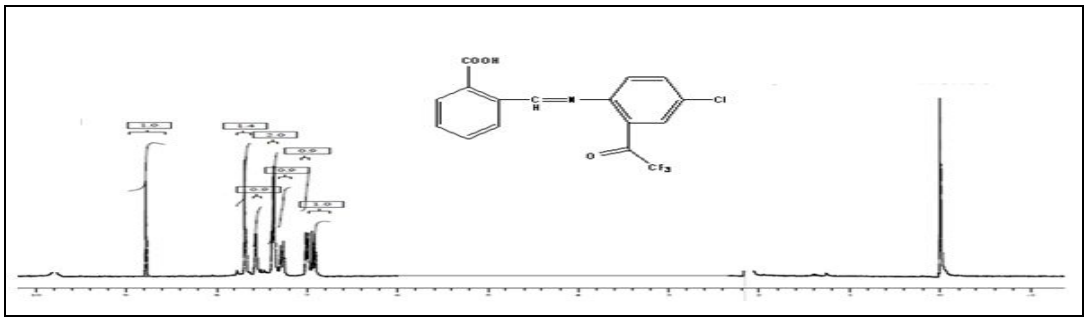

Figure 9

ESI-MS for $C_{18}H_{14}ClF_3NO_3$: m/z 384 $[M]^+$.

SCHIFF BASE 4: 1-(2-(3-hydroxy-4-methylbenzylideneamino)-5-chlorophenyl)-2,2,2-trifluoroethanone

3 hydroxy 4 methyl benzaldehyde (1.36g, 10 mmol), 1-(2-amino-5-chlorophenyl 2,2,2, trifluro ethane- 1,1-diol hydrochloride, triethylamine (1 ml, 10 mmol) were mixed in 50 ml ethanol in a round flask. The mixture was refluxed with agitation for 4 h at 323 K to give a yellow precipitate. After filtration and washing the precipitate with ethanol, a pure Schiff base ligand, 1-(2-(3-hydroxy-4-methylbenzylideneamino)-5-chlorophenyl)-2,2,2-trifluoroethanone (yield: 2.1 g was obtained.

Analytical data of compound

Mol.Forula : $C_{18}H_{16}ClF_3NO_2$

Melting point :142-144°C

Spectral data;

IR (KBr) cm^{-1}

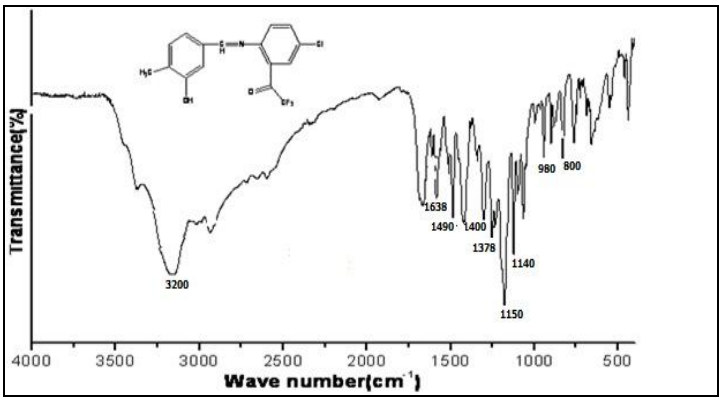

Figure 10

^{1}H NMR(300 MHz , DMSO) :

3.Biological Activity

3.1.Antibacterial

The in vitro biological screening effects of the investigated compounds were tested against the bacteria E. Coli. Paper discs of Whatman filter paper no. 1 were cut and sterilized in an autoclave. The paper discs were saturated with 10 µl of the compounds dissolved in DMSO solution or DMSO as negative control and was placed aseptically in the Petri dishes containing Nutrient agar media inoculated with the above mentioned two bacteria separately. The petridishes were incubated at 37^0C and the inhibition zones were recorded after 24 h of incubation.

3.2.Antifungal

The Schiff base complexes were screened for their antifungal activity against fungi viz. candida. Filter paper discs of 5 mm in size, prepared by using Whatman filter paper no. 1 (sterilized in an autoclave) was saturated with 10 µl of the compounds dissolved in DMSO solution . The fungal culture plates were inoculated and incubated at 25± 2^0C for 48 h. The plates were then observed and the diameters of the inhibition zones (in mm) were measured and tabulated.

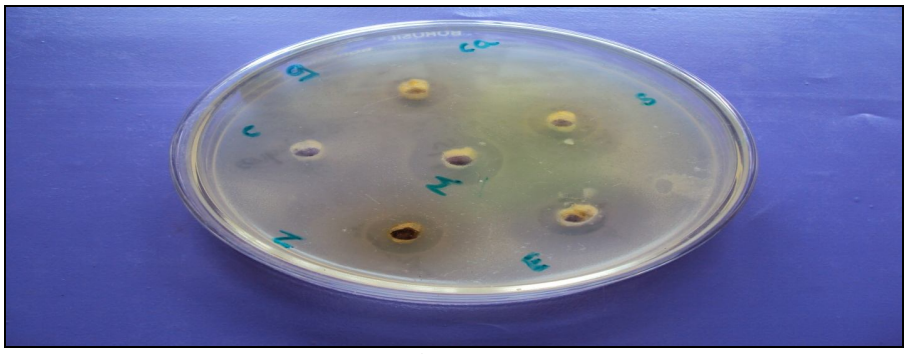

Figure 11

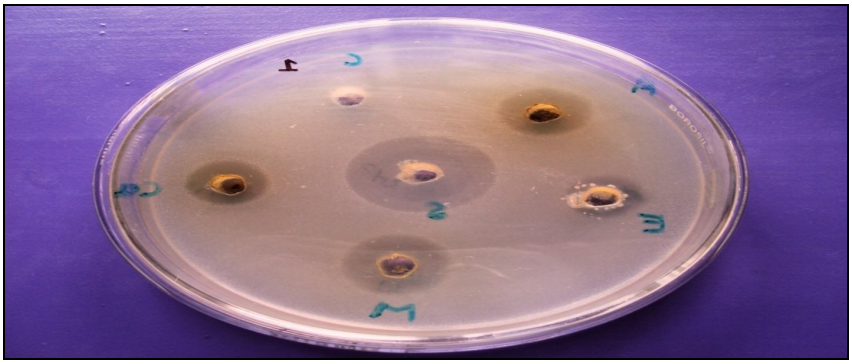

Figure 12

4.Results And Discussion

- Structures of compounds have been elucidated by IR, Proton NMR and Mass Spectral measurements. Schiff bases show IR absorption peak at 1615-1530 cm-1 (C=N stretching). All the compounds show NMR signals for different kinds of protons at their respective positions.
- The synthesized all four Schiff bases were found to be more active than standard antibacterial drug against E. Coli. The synthesized compound 1-(2-(3-hydroxy-4-methoxybenzylideneamino) -5-chlorophenyl) -2,2,2-trifluoroethanone showed more active against Bacillus subtilis compared to other Schiff bases.
- The synthesized compound 1-(2-(3-hydroxy-4-methoxybenzylideneamino) -5-chlorophenyl) -2,2,2-trifluoroethanone. M) showed more active than standard drug amoxicillin.
- The synthesized all four Schiff bases were found to be more active than standard antifungal drug against Candida. The synthesized Schiff base 1-(2-(3-hydroxy-4-methoxybenzylideneamino) -5-chlorophenyl) -2, 2, 2-trifluoroethanone S) showed more active against Candida compared to other Schiff bases.

5.Conclusion

Hence, further study of a synthesized Schiff base compound 1-(2-(3-hydroxy-4-methoxybenzylideneamino) -5-chlorophenyl) -2,2,2-trifluoroethanone in antimicrobial and anti fungal activities may become fruitful.

6.References

1. Young DW. Heterocyclic Chemistry.1st ed. London: Longman group Ltd.; 1975.
2. Schiff, H. 1864. Eine neue Reihe Organischer Basen, Liebigs. Ann. Chem. 131:118-119.
3. Kumar S, Niranjan MS, Chaluvaraju KC, Jamakhandi CM, Dayanand K. Synthesis and Antimicrobial Study of Some Schiff Bases of Sulfonamides. J Curr Pharm Res. 2010;01:39-42.
4. Mistry KM, Desai KR. Synthesis of Novel Heterocyclic 4-Thiazolidinone Derivatives and their Antibacterial Activity. E-J Chem. 2004;1(4):189-193.
5. Pandey, V.K., Yadava, S., Chandra, K., Joshi, M.N. and Bajpai, S.K. 1999. Antiviral studies of 7-arylamido/imidoalkyl-2,3 dihydro-2, 3- diphenyl-1, 3 benzoxazine-4-ones. Indian Drugs, 36:532-534.
6. Vazzanaa, I. Terranovaa, E. Mattiolib, F. and Sparatorea, F. 2004. Aromatic Schiff Bases and 2.3-disubstituted-1.3-thiazolidin-4-one Derivatives as Antiinflammatory Agents, Arkivoc (v): 364-374.
7. Nair, V. R. Soni, M. Baluja, S. 2004, Synthesis, Structural Determination and Anti bakterial Activity of compounds derived from vanillin and 4-aminoantipyrine, J. Serb. Chem. Soc. 69 :991-998
8. Garg, H. G. Kaur, M. 1972. Synthesis of N`-substituted Arylsulfonylpyrazoles, their anthelmintic Activity, and the Cytotoxicity of some Hydrazides, J. Med. Chem. 15(5) :554-555
9. Ambroziak, K. Rozwadowski, Z Dziembowska, T. and Bieg, B. 2002. Synthesis and spectroscopic Study of Schiff bases derived from trans-1,2-diaminocyclohexane. Deuterium isotope shift ob 13C chemical shift, J. Mol. Struct., 615:105-120.
10. Desai, S. B., Desai, P. B. & Desai, K. R. 2001. Synthesis of some Schiff Bases,Thiazolidones, and Azetidinones derived from 2.6-diaminobenzo[1.2-d.4,5-d`]bisthiazole and their Anticancer Activities, Heterocycl. Commun,7(1):83-90.
11. Samadhiya, S., Halve, A. 2001. Synthetic Utility of Schiff Bases as potential herbicidal Agents, Orient. J. Chem. 17:119-122.
12. More, P. G., Bhalvankar, R. B. & Pattar, S. C., 2001. Synthesis and biological activity of schiff bases of aminothiazoles, J. Indian Chem. Soc.,78:474-475.