Synthesis, Spectral investigation (^{1}H, ^{13}C) and Anti-microbial Screening of benzophenone imines

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Abstract: New series of benzophenone imines with general formula Ph_2-C=NR; R = Benzyl, 4-Fluorobenzyl, Naphthyl, Phenyl, 4-Nitrophenyl were synthesized by condensation of dichlorodiphenylmethane and different aromatic primary amines (1:1) Those imines were characterized by different physiochemical and spectroscopic techniques like melting point, elemental analysis, FT-IR, multinuclear NMR (^{1}H, ^{13}C). After characterization, imines were subjected to anti-microbial activities. All compounds showed promising activity against different bacterial strains like *Escherichia coli, Bacillussubtilis, Pasturellam ultocida* and *Staphylococcus aureus* as well as fungal strains like *Alternata alternaria, Ganoderma lucidium, Penicillium notatum* and *Trichoderma harzianum* using Amoxicillin and Flucanazole as a standard drugs respectively.

Keywords: Imines, Schiff base, Amoxicillin, Flucanazole.

INTRODUCTION

During the last few years there has been intense investigation and significant interest in the chemistry of imines because many of which are found to be pharmacologically active. Imines have a broad spectrum of biological activities such as lipoxygenase inhibition, anti-inflammatory (Hadjipavlou-litina *et al.,* 1996) and anti-cancer behavior (Vicini *et al.,* 2003). Furthermore, they are used as versatile components in synthesis of optically active *α*-alkyl aldehydes (Bergbreiter *et al.*, 1983), secondary amines by hydrogenation (Schellenberg, 1963), nucleophilic addition with organometallics reagent and in cycloaddition reactions (Tsuge *et al.,* 1989). Moreover, imines have attracted much attention in the fields of electronics and photonics (Wang *et al*, 2001; Li *et al,* 2004; Kiriy *et al,* 2004). Imines are also used as an important class of ligands that can be used for variety of applications including clinical, biological, industrial and analytical in addition to their important roles in organic synthesis and catalysis. By process of reductive amination, imine derivatives also play a vital role in the production of mixture of amines, primary, secondary and tertiary (Petrisko *et al.,* 2005). Imines are considered as most important ligand for the preparation of Cyclometallated compounds. In recent years, interests in the cyclometallation reaction renewed due to incorporation of imine in catalytic cycles that transform C-H bonds of hetero-substituted organic molecules into carbon-halogen bonds (Albert *et al.,* 2007). In pharmaceutical research imines are most extensively used (Carey *et al.,* 2006) and much efforts have been devoted to their synthesis. In spite of these efforts, the selective synthesis of highly substituted aromatic imines continues to be a significant challenge in the synthesis (Colby *et al.,* 2008). Conventional methods for synthesis imines involve the condensation of amines and 4-hydroxybenzaldehyde (Duggineni *et al.,* 2006; Beke *et al.,* 2002; Hutchins *et al*., 1996; Cutter *et al.,* 2000; Mohamed *et al.,* 2005). In the present study, new derivatives of aryl imines were synthesized by a convenient route in which condensation of primary aryl amines and dichlorodiphenylmethane taken place. The structures of such imines were characterized by elemental analysis, IR, multinuclear NMR (^{1}H, ^{13}C). Furthermore their antimicrobial activity was examined against different microbes.

MATERIALS AND METHODS

Materials

Chemicals like benzylamine, naphthylamine, aniline, 4-fluorobenzylamine, dichlorodi-phenylmethane, 4-nitroaniline, were purchased from Aldrich, Fluka and E-Merk. All solvents were dried before use according to standard methods given in literature (Armarego *et al.,* 2003).

Measurements

Melting points were determined by using electrothermal digital melting point apparatus (Model Stuart-SMP3, UK) and are uncorrected. Infrared absorption spectra were recorded using KBr disc on Bio-Rad Excalibur FT-IR Model FTS 3000 MX (4000-400 cm^{-1}). The NMR (^{1}H, ^{13}C) spectra were recorded on Varian Mercury 300

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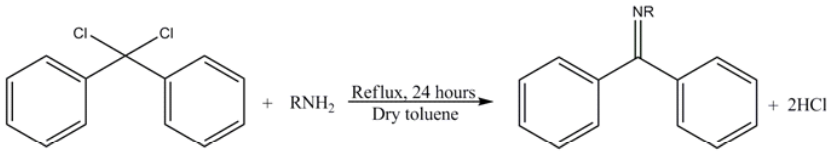

R = Benzyl (compound-1), 4-Fluorobenzyl (compound-2), Naphthyl (compound-3), Phenyl (compound-4), 4-Nitrophenyl (compound-5)

Spectrometer using deutrated solvent and TMS as a reference operating at 300 and 75.5 MHz respectively.

Synthesis of benzophenone imines

Stoichiometric amounts of primary aryl amines and dichlorodiphenylmethane (1:1) were taken in dried toluene (50mL). The reaction mixture was refluxed for 24 hours and was cooled at room temperature, filtered. Toluene was removed under reduced pressure. The crude product was purified by column chromatography using n-Hexane and ethyl acetate (4:1). After few days thick residue was re-crystallized in chloroform to get pure product (Seno *et al.,* 1978).

Biological screening

Antibacterial activity

Antibacterial activity of synthesized benzophenone imines were investigated by agar well diffusion method against different bacterial strains, *Escherichia coli, Pasturellamultocida, Bacillus subtilis* and *Staphylococcus aureus* (Rehman *et al.,* 2001). Amoxycillin was used as a standard drug. The 24- hours-old culture containing approximately 104-106 colony forming unit (CFU) was spread over Muller Hinton Agar (MHA) plates. In the medium wells were created with the help of a sterilized metallic borer and different concentrations of test samples were added in respective wells. Experimental plates were incubated at 37ºC for 24 hrs and zones of inhibition (%) were measured and compared with standard, Amoxicillin.

Antifungal activity

Antifungal activity of the benzophenone imines against various fungal strains such as *Alternaria alternata, Ganoderma lucidium, Penicillium notatum* and *Trichoderma harzianum were determined* by agar tube dilution protocol (Rehman*et al.,* 2001). *Flucanazole* was used as a standard drug. The Sabarod's agar media ($15cm^3$) kept at 45ºC was poured in the Petri-dishes and allowed to solidify. Test fungal cultures were inoculated on the slant, and growth inhibition (%) was measured after an incubation period of seven days.

RESULTS

Compound (1) *[N-(diphenylmethylene)-1-(phenylmethanamine)]*

Off white solid, yield: 88%; m.p. 235ºC; Anal. Calc. for $C_{20}H_{17}N$: C, 88.56; H, 6.27; N, 5.16. Found: C, 88.49; H, 6.31; N, 5.18. IR (cm^{-1}) $(C\text{-}H)_{aromatic}$3001, (C=N) 1589, $(C=C)_{aromatic}$ 1685, ^1H NMR (dmso-d_6, δ ppm): δ (Ar–H) = 7.53^m, 7.40^m, δ ($–CH_2–$) =3.99^s; ^{13}C NMR (dmso-d_6, δ ppm): 161.0, 134.60, 129.44, 128.98, 128.80, 42.55.

Compound (2) [*N-(diphenylmethylene)-1-(4-fluorophenyl)methanamine]*

Light yellow solid, yield: 71%; m.p. 210ºC, Anal. Calc. for $C_{20}H_{16}NF$: C, 83.04; H, 5.53; N, 4.84; F, 6.57. Found: C, 82.97; H, 5.57; N, 4.79; F, 6.55. IR (cm^{-1}) $(C\text{-}H)_{aromatic}$ 3007, (C=N) 1598, $(C=C)_{aromatic}$ 1664, ^1H NMR (dmso-d_6, δ ppm): δ (Ar–H) =7.72^m, 7.58^m, δ (-CH_2-) = 3.99^s; ^{13}C NMR (dmso-d_6, δ ppm): 164.15, 160.91, 143.74, 137.43, 133.17, 131.90, 131.79, 130.85, 115.70, 41.81.

Compound (3)*[(N-(diphenylmethylene)naphthalen-1-amine)]*

Reddish black solid: yield: 85%, m.p. 112ºC, Anal. Calc. for $C_{23}H_{17}N$: C, 89.90; H, 5.53; N, 4.56. Found: C, 89.89; H, 5.54; N, 4.53. IR (cm^{-1}) $(C\text{-}H)_{aromatic}$ 3060, (C=N) 1568, $(C=C)_{aromatic}$ 1652, ^1H NMR (dmso-d_6, δ ppm): δ (Ar–H) = 7.67^m, 7.45^m, 6.57^m; ^{13}C NMR (dmso-d_6, δ ppm): 168.83, 147.94, 136.72, 133.74, 131.61, 130.07, 129.38, 128.41, 128.27, 128.05, 126.79, 126.59, 126.13, 123.36.

Compound (4)*[(N-(diphenylmethylene)aniline)]*

Orange solid: yield. 78%: m.p. 104ºC, Anal. Calc. for $C_{19}H_{15}N$: C, 88.71; H, 5.83; N, 5.44. Found: C, 88.68; H, 5.85; N, 5.41. IR (cm^{-1}) $(C\text{-}H)_{aromatic}$ 3053, (C=N) 1591, $(C=C)_{aromatic}$ 1654, ^1H NMR (dmso, δ ppm): δ (Ar–H) = 7.76^m, 7.27^m, 6.75^m; ^{13}C NMR ($CDCl_3$, δ ppm): 168.28, 130.72, 129.53, 129.33, 128.56, 128.47, 128.20, 127.89, 120.94.

Compound (5)*[N-(diphenylmethylene)-4-nitroaniline]*

Yellow solid: yield 87%: m.p. 190ºC, Anal. Calc. for $C_{19}H_{14}N_2O_2$: C, 75.49; H, 4.63; N, 9.27; O, 10.59. Found: C, 75.47; H, 4.64; N, 9.25; O, 10.57. IR (cm^{-1}), (C=N) 1519, $(C=C)_{aromatic}$ 1634, (NO_2) 1492_{sym}, 737_{asym}, , ^1H NMR (dmso-d_6, δ ppm): δ (Ar–H) =7.93^m, 7.56^m; ^{13}C NMR (dmso-d_6, δ ppm): 155.65, 136.35, 126.81, 113.23.

DISCUSSION

The synthesized compounds have sharp melting points and were soluble in common organic solvents. The solubility was investigated as 0.01g of sample in 2mL of solvent.

IR Spectroscopy

The infrared spectra of imine derivatives were recorded in the range of 4000-400 cm^{-1} by using KBr pallets. The intensity of bands in compounds has been assigned on the basis of earlier literature values (Shebl, 2008). Important IR bands are *ν*C=N, aromatic *ν*C-H, aromatic *ν*C=C and *ν*N=O and appearing at 3001-3060 cm^{-1} (Aromatic C-H stretching), 1519-1598 cm^{-1} (C=N imine stretching), 1634-1685 cm^{-1} (Aromatic C=C stretching) and 1492_{sym}, 737_{asym} cm^{-1} (Aromatic NO). Most important bands in all the aromatic imine derivatives were shifted significantly which indicates the formation of new compounds.

NMR Spectroscopy

The following multinuclear techniques (^1H, ^{13}C NMR) were used for the identification of aromatic imines derivatives.

^1H NMR

Three important Informations are generally obtained from this technique. The chemical shift of peak gives information about the environment of proton involved, the intensity of each peak corresponds to the number of protons and multiplicity tells about the number of neighboring protons. The ^1H NMR spectra of the compounds in deutrated solvents showed the absence of chemical shifts for amino protons confirming the formation of final products after removal of two protons from $-NH_2$ group of the amino reactant (Albert *et al.,* 2007). Further, evidence for the product formation was provided by the presence of two kinds of aromatic signals in each case, one group of signals appeared for the diphenylmethane portion and the other for the substituted aromatic amino proton (Chen *et al.,* 2004). The numbers of protons obtained by the integration of peaks were found to obey the proposed structures. The methylene protons in compounds 1 and 2 showed the absorbance of peak at the same position (3.99 ppm) indicating uniform behavior of $-CH_2$ protons in both cases (Albert *et al.,* 2003).

^{13}C NMR

The ^{13}C NMR spectroscopy is an important technique used for structure determination of pure organic compounds. The ^{13}C NMR studies provide Informations to assign the magnetically non-equivalent carbon atoms (methyl, methylen, aromatic and imine etc.) that may present in compounds (Mohamed *et al.,* 2005). The ^{13}C NMR spectrum of synthesized imine derivatives was recorded in deutrated DMSO for compounds1-3, 5 and chloroform for compound 4. The chemical shifts for imine carbons observed at 168.83-155.65ppm (Benito *et al.,* 2000). The highest value was observed for the C=N carbon in compound 3 where the naphthyl group caused downfield shift, the compound 5 showed up field shift for imine carbon. Different signals were observed for aromatic carbons of diphenylmethane portion in each case, the values are in complete agreement with those reported in earlier literature (Bosque *et al.,* 1999). The introduction of flouro group caused significant upfield and downfield shifts for methylene and δ carbons as compared to the non-fluorinated derivative. The NMR data confirmed the signals for naphthalene in compound 3. It was found that the nitro group caused significant upfield absorption for δ′ carbon in compounds.

Antibacterial activity

The synthesized compounds were tested for their antibacterial activity against bacterial strains like *Escherichia coli, Bacillus subtilis, Pasturella multocida,* and *Staphylococcus* aureus (Ferrari *et al.,* 1999; Jayabalakrishnan *et al.,* 2000; Jeeworth, *et al.,* 2000; Dharmaraj *et al.,* 2001). The highest activity was shown against *E. coli and P. multocida* with zone 24±1.0 mm and 22.6±0.57 mm, respectively because of the presence of imine group with substituent of high molecular aromatic aryl groups. The activity against *B. subtilis and S. aureus* were average with zones 20.3±1.52 mm and 16.3±0.57 mm, respectively (table 1).

Antifungal activity

Anti-fungal activity of synthesized compounds was tested against various fungal strains using disc diffusion method. The anti-fungal activity was performed against *Alternaria alternata, Ganoderma lucidium, Penicillium notatum* and *Trichoderma harzianum* (Dharmaraj *et al*., 2001). The activity against *Alternata alternaria and Ganoderma lucidium* was highest with zone 22.3±0.57 mm and 21.6±1.15 mm, respectively. The average activity was shown by two fungus strains, *Penicillium notatum* and *Trichoderma harzianum* with zones 19.3±1.52 mm and 13.6±1.52 mm, respectively. The greater activity of compounds is due to the presence of fluorine in the imines compound, which itself anti-microbial. Halogens have high anti-microbial activity and are antiseptic to most of the microbial strains (Sonboli *et al.,* 2006; Khosa *et al.,* 2007) table 2.

CONCLUSION

The synthesized benzophenone imines were prepared and confirmed by using different physicochemical and spectroscopic techniques like M.P, solubility, IR and multinuclear nmr (^1H, ^{13}C) analysis. The presence of N=C peak indicated the formation of imines derivatives. After confirmation of formation of imine derivatives, anti-microbial activity was investigated. The compound (2) showed highest antibacterial and anti-fungal activity against different strains. In compound (3) and (5), moderate activity against different bacterial and fungal strains was observed. Compound (4) showed the minimum activity against all the anti-microbial strains.

Table 1: Antibacterial activity of the synthesized benzophenone imine

Compound No.	*Escherichia Coli*	*Pasturella Multocida*	*Bacillus subtilis*	*Staphylococcus aureus*
(1)	$13.6^{bc}\pm1.5$	$16.3^{bc}\pm 1.15$	$12.6^{bc}\pm 1.15$	$11.6^{bc}\pm 1.15$
(2)	$24^{ab}\pm 1.0$	$22.6^{ab}\pm 0.57$	$19.6^{bc}\pm 0.57$	$16.3^{bc}\pm 0.57$
(3)	$17.6^{bc}\pm 0.57$	$18.3^{bc}\pm 0.57$	$14.6^{bc}\pm 1.15$	$12.6^{bc}\pm 1.15$
(4)	$13.3^{c}\pm 1.15$	$11.6^{c}\pm 1.15$	$10.3^{c}\pm 0.57$	$11.3^{c}\pm 1.52$
(5)	$20.6^{bc}\pm 1.52$	$17.6^{bc}\pm 0.57$	$20.3^{bc}\pm 1.52$	$15.6^{bc}\pm 0.57$
Amoxycillin	$31.5^{a}\pm 1.0$	$30.2^{a}\pm 1.1$	$30.8^{a}\pm 1.0$	$32.1^{a}\pm 1.0$

[a]Values are mean ± SD of three independent repeats. [b]Concentration = 1mg/ml in DMSO. [c]Standard = Amoxycillin
[c]0 = No activity, 5-10 = Activity present, 11-25 = Moderate activity, 26-40 = Strong activity
[d]Different letters in superscrips indicate significant differences.

Table 2: Antifungal activity of the synthesized benzophenone imine

Compound No.	*Alternata alternaria*	*Ganoderma lucidium*	Penicillium notatum	*Trichoderma harzianum*
(1)	$21.6^{bc} + 0.57$	$20.6^{bc} + 1.52$	$20^{bc} + 1$	---
(2)	$22.3^{bc} + 0.57$	$21.6^{bc} + 1.15$	$18.6^{bc} + 1.15$	$13.6^{bc} + 1.52$
(3)	$20.6^{bc} + 1.52$	$19.6^{bc} + 1.15$	$19.3^{bc} + 1.52$	$12.3^{c} + 1.52$
(4)	$14.6^{c} + 1.52$	$16.0^{c} + 1$	$13.6^{c} + 1.52$	---
(5)	$20.3^{bc} + 1.52$	$21.6^{bc} + 1.57$	$18.3^{bc} + 0.57$	---
Flucanazole	$37.1^{a} + 1$	$39.6^{a} + 1.15$	$28^{a} + 1.6$	$18.5^{a} + 1$

[a]Values are mean ± SD of three independent repeats. [b]Concentration = 1mg/ml in DMSO. [c]Standard = Flucanazole
[c]0 = No activity, 5-10 = Activity present, 11-25 = Moderate activity, 26-40 = Strong activity
[d]Different letters in superscripts indicate significant differences.

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REFERENCES

Albert J, Andrea LD, Granell J, Tavera R, Bardia MF and Solans X (2007). Synthesis and reactivity towards carbon monoxide of an optically active endo five membered ortho-cyclopalladatedimine: X-ray molecular structure of trans-(μ-Cl)$_2$[Pd(κ^2-C,N-(R)-C$_6$H$_4$-CH{double bond, long}N-CHMe-Ph)]$_2$. *J. Organomet. Chem.*, **692**(14): 3070-3080.

Albert J, Granell J and Tavera R (2003). The cyclopalladation reaction of benzylamine revisted. *Polyhed.*, **22**: 287-291.

Armarego WLF and Chai CLL (2003). *Purification of Laboratory Chemicals*, 5th Edition, Pergamon Press, Oxford U.K. pp56.

Beke G, Szabo LF and Podanyi BJ (2002). Investigation of Pictet-Spengler type reactions of secologanin with histamine and its benzyl derivative. *J. Nat.. Prod.,* **65**(5): 649-655.

Benito M, Lopez C, Morvan X, Solans X and Bardia MF (2000). A comparative study of the reactivity of the σ(Pd–C$_{sp^2,\ ferrocene}$) and σ(Pd–C$_{sp^2,\ biphenyl}$) bonds in cyclopalladated complexes derived from [Fe(η^5-C$_5$H$_5$)(η^5-C$_5$H$_4$CH**251658240=**NC$_6$H$_4$C$_6$H$_5$-2)]. *Dalt. Trans.*, **65**: 4470-4479.

Bergbreiter DEM and Newcombe M (1983). *Asymmetric Synthesis*, *Vol. 2A*, J. D. Morrison (Ed.), Academic Press, Orlando, F. L. p. 243.

Bosque R, Lopez C, Solans X and Bardia FM (1999). Heterodi- and hetero trimetallic compounds containing five-membered rings and *δ*(Pd-Csp$_2$, ferrocene) bonds. X-ray crystal structure of the *meso*-form of [Pd$_2${Fe[(□$_5$-C$_5$H$_3$)-C(CH$_3$)=N-C$_6$H$_5$]}$_2$Cl$_2$(PPh$_3$)$_2$]. *Organomet.*, **18**: 1267-1274.

Carey JS, Laffan D, Thomson C and Williams MT (2006). Analysis of the reactions used for the preparation of drug candidate molecules. *Org. Biomol. Chem.,***4**: 2337-2347.

Chen CL, Liu YH, Peng SM and Liu ST (2004). Substituent effect on cyclopalladation of arylimines. *J. Organomet. Chem.,* **689**: 1806-1815.

Colby DA, Bergman RG and Ellman JA (2008). Synthesis of dihydropyridines and pyridines from Imines and alkynes via C-H activation. *J. Am. Chem. Soc.,* **130**: 3645-3651.

Cutter PS, Miller RB and Schore NE (2000). Synthesis of proto-berberinesusinga silyl-directed Pictet–spengler-cyclization. *Tetrahed.*, **58**: 1471-1478.

Dharmaraj N, Viswanathamurthi P and Natarajan K (2001). Ruthenium (II) complexes containingbidentate Schiff bases and their antifungal activity. *Trans. Met. Chem.*, **26**: 105-108.

Duggineni S, Sawant D, Saha B and Kundu B (2006). Application of modified Pictet-spengler reaction for the synthesis of thiazolo- and pyrazolo-quinolines. *Tetrahed.*, **62**: 3228-3241.

Ferrari MB, Capacchi S, Pelosi G, Reffo G, Tarasconi P, Albertini R, Pinelli S and Lunghi P (1999). Synthesis, structural characterization and biological activity of helicinthiosemicarbazone monohydrate and a copper (II) complex of salicylaldehyde thiosemicarbazone. *Inorg. Chim. Acta*, **286**: 134-141.

Hadjipavlou-litina DJ and Geronikaki AA (1996). Thiazolyland benzothiazolyl schiff base as novel possible lipoxygenase inhibitors and anti-inflammatory agents. Synthesis and biological evaluation. *Drug Design and Discov.,* **15**: 199-206.

Hutchins SM and Chapman KT (1996). Solid phase synthesisof tetrahydroisoquinolines & tetrahydro-imidazopyridines. *Tetrahed. Let.***37**: 4865-4868.

Jayabalakrishnan C and Natarjan K (2000). Synthesis, characterization and biological activities of ruthenium (I) carbonyl complexes containing bifunctional tridentate Schiff bases. *Syn. React. Inorg. Metal-Org. Nano-Met. Chem.,* **31**: 983-995.

Jeeworth T, Wah HLK, Bhowon MG, Ghoorhoo D and Babooram K (2000). Synthesis and anti-bacterial/ catalytic properties of Schiff bases and Schiff base metal complexes derived from 2, 3-diaminopyridine. *Syn. React. Inorg. Metal-Org. Nano-Met. Chem.,,* **30**: 1023-1038.

Khosa MK, Mazhar M, Ali S, Dastgir S, Parvez M and Malik A (2007). Synthesis, Spectral (FT-IR, ^{1}H, ^{13}C, ^{119}Sn) and Biological studies of bimetallic trimethyltin (IV) germapropionates: X-Ray structure of $(CH_3)_3Sn(C_{22}H_{21}O_2Ge)$. *Syn. React. Inorg. Metal-Org. Nano-Met. Chem.,* **37**: 165-173.

Mohamed GG and El-Wahab ZHA (2005). Mixed ligand complexes of bis (phenylimine) Schiff base ligands incorporating pyridinium moiety.Synthesis characterization and biological activity. *Spectrochim. Act.*, **61**(6): 1059-1068.

Petrisko M and Krupka J (2005). Isomerization of an imine intermediate in a reductive amination reaction over metal catalysts. *Res. Chem. Intermed.*, **31**(9): 769-778.

Rehman A, Choudhary MI and Thomsen WJ (2001). *Bioassay Techniques for Drug Development,* Harvard Academy Press: Amsterdam. Schellenberg, KA. (1963). Thesynthesis of secondary and tertiary amines by borohydride reduction. *J. Organic Chem.*, **28**: 3259-3261.

Seno M, Shiraishi S, Suzuki z and Asahara T (1978). A Synthetic route to 3, 3-diphenyl-2-indolinone derivatives. *Bull. Chem. Soc. Japan*, **51**: 1413-1417.

Shebl M (2008). Synthesis and spectroscopic studies of binuclear metal complexes of a tetradentate N_2O_2 Schiff base ligand derived from 4,6-diacetylresorcinol and benzylamine. *Spectrochim. Act.,* **70**: 850-859.

Sonboli A, Babakhani B and Mehrabian AR, (2006). Anti-microbial activity of six constituents of essential oil from *Salvia*. *J. Essenent. oil Res.,* **61**: 160-164.

Tabatabaee M, Heravi MM, Sharif M and Esfandiyari, F. (2011). Fast and efficient method forimination of *N*-aminorhodanineusing inorganic solid support under microwave irradiation and classical heating. *E- J. Chem.*, **8**(2): 535-540.

Tsuge O and KanemasaR (1989).Recent advances in azomethineylidechemistry. *Ad. Heterocycl. Chem.,* **45**: 231-236.

Vicini P, Geronikaki A, Incerti M, Busonera B, Poni G, Cabras CA and Colla PL (2003). Synthesis and biological evaluation of benzoisothiazole, benzothiazole and thiazole Schiff bases. *Bioorg. Med. Chem.*, **11**: 4785-4789.