ORIGINAL ARTICLE

A C G publications

Org. Commun. 4:2 (2011) 42-51

organic communications

Synthesis and biological activity of 2-oxo-azetidine derivatives of phenothiazine

Sharma Ritu*, Samadhiya Pushkal, Srivastava S. D. and Srivastava S. K.

Synthetic Organic Chemistry Laboratory, Department of Chemistry, Dr. H.S. Gour University, Sagar, M.P. India 470003

(Received May 7, 2011; Revised June 15, 2011; Accepted June 20, 2011)

Abstract: We have synthesized of *N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(phenyl)-3-chloro-2-oxo-1-iminoazetidine **4(a-m)**. The structures of all the newly synthesized compounds were confirmed by IR, ^{1}H NMR, ^{13}C NMR and FAB-Mass and chemical methods. All synthesized compounds were evaluated for their antibacterial, antifungal and antitubercular activity which displayed acceptable results.

Keywords: Synthesis; biological activity; 2-azetidinone, phenothiazine.

1. Introduction

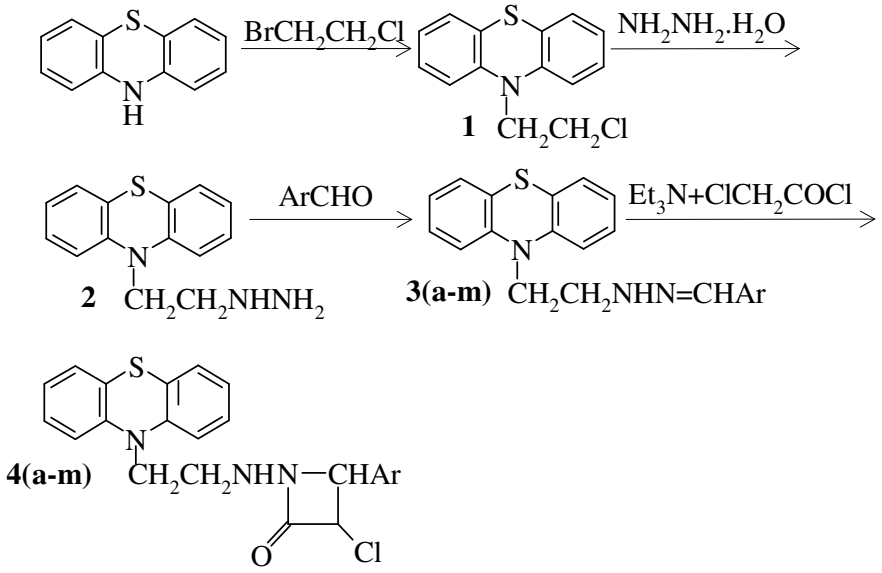
Phenothiazines are amongst the most frequently encountered heterocycles in compounds of biological interest. They have been shown to possess a broad spectrum of biological activity depending on their particular structure. Infect**,** its constitute the largest group of psychoactive clinically used compounds, phenothiazine derivatives possess several other biological activities including antibacterial[1,2], antifungal, antiproliferative[3], antipsychotic[4,5], anti-inflammatory[6,7] and antiparkinsonian activities[8]. Tuberculosis is the leading infectious disease among adults and youth, one third of the world population infected with mycobacterium tuberculosis[9]. Recent studies have shown the synthesis of some new phenothiazine candidates as antitubercular agents[10,11]. 2-Azetidinone skeleton is well established as the pharmacophore of β-lactam antibiotics. β-lactam antibiotics are the most widely employed class of antibiotics[12]. The important and structural diversity of biologically active β-lactam antibiotics led to the development of many novel methods for the construction of appropriately substituted azetidine with attendant control of functional group and stereochemistry. Azetidine derivatives are reported to show a variety of antimicrobial[13-15], antitubercular[16], anticonvulsant[17], antiinflammatory[18] and cardiovascular activities[19]. These all activities showed that the minor change in the substitution pattern activities of azetidine derivatives have enhanced dramatically so our research group decide to synthesized a new series azetidine derivatives with several substitutions.

* Corresponding author: E-mail: ritusharmaic@rediffmail.com

The article was published by Academy of Chemistry of Globe Publications
www.acgpubs.org/OC/index.htm © Published 06/20/2011 EISSN:1307-6175

2. Results and discussion

We have synthesized of *N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(phenyl)-3-chloro-2-oxo-1-iminoazetidine compounds **4(a-m)** as shown in scheme 1. Phenothiazine on reaction with $Cl(CH_2)_2Br$ at room temperature gave 1-(2-chloroethyl)-10*H*-phenothiazine, compound **1**. The compound **1** on the reaction with hydrazine hydrate at room temperature, yielded *N*-[2-(10*H*-phenothiazinyl)ethyl]-hydrazine, compound **2**. The compound **2** on further reaction with several substituted aromatic aldehydes produced *N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(phenyl)methylidene]-hydrazine, compounds **3(a-m)**. The compounds **3(a-m)** on treatment with $ClCH_2COCl$ in the presence of Et_3N furnished final products compounds **4(a-m)**. The structures of all the newly synthesized compounds were confirmed by IR, ^1H NMR, ^{13}C NMR and FAB-Mass and chemical methods. All synthesized compounds were evaluated for their antibacterial, antifungal and antitubercular activity which displayed acceptable activity in Table 1 and 2.



Ar= substituted phenyl ring

Scheme 1: Synthesis of compounds **1, 2, 3(a-m)** and **4(a-m).**

2.1. Spectral data

2.1.1. Infrared spectral analysis

The appearance of an absorption band in the IR spectrum of the compound **1** for (N-CH_2) and (C-Cl) at 1262 and 771 cm^{-1} respectively have been found and NH proton of phenothiazine has been disappeared (at 3462cm^{-1}). The appearance of absorption band in IR spectrum of compound **2** were appeared for (NH) and (NH_2) at 3348 and 3430 cm^{-1} respectively. Appearance of absorption band in the spectra of compounds **3(a-m)** for (N=C) was found in range of 1542.-1585 cm^{-1} which was a strong evidence for the synthesis of compounds **3(a-m**). In the IR spectra of compounds **4(a-m),** appearances of absorption peak for (CO cyclic) was found in range of 1732-1753 cm^{-1} which was suggesting the cyclization. This fact also supported by the disappearance of the peak of (N=CH) in the compounds **3(a-m**).

2.1.2. ^1H NMR spectral analysis

In the ^1H NMR spectrum of the compound **1,** a new signal appeared for N-CH_2 at (δ) 4.77 ppm. In the ^1H NMR spectrum of the compound **2** showed two signals for NH and NH_2 at (δ) 7.61 and 5.69 ppm respectively. Presence of signals of NH and NH_2 confirm the synthesis of compound **2**. In the

compounds **3(a-m),** the ^{1}H NMR spectra showed a singlet for N=CH in the range of (δ) 7.68-8.08 ppm which provide a strong evidence for presence of benzylidine type proton and also supported by disappearance of NH_2 proton in the 1H NMR spectrum of compound **2**. In the ^{1}H NMR spectra of compounds **4(a-m)** showed a strong signals for (CH-Cl) and (N-CH) of azetidine ring in the range of (δ) 4.20-4.49 and 4.68-4.98 ppm respectively and fact also supported by disappearance of N=CH signal in the compounds **3(a-m).**

2.1.3. ^{13}C NMR spectral analysis

^{13}C NMR spectra of the compound **1** showed a strong signal of N-CH_2 at (δ) 54.8 ppm. The signal for N=CH appeared in the range of (δ) 152.6-158.8 ppm in the ^{13}C NMR spectra of compounds **3(a-m)** which confirm the presence of carbon which is doubly bonded to nitrogen. In the spectra of compounds **4(a-m)** three new characteristic signals were found for (CH-Cl), (N-CH) and cyclic CO in the range of (δ) 47.6-58.6, 57.7-67.7 and 169.5-177.6 ppm respectively. It is strong evidence of the cyclization and also supported by disappearance of N=CH signal of ^{13}C NMR spectra of the compound **3(a-m)**.

2.1.4. FAB mass spectral analysis

FAB-Mass spectra of compounds **1, 2, 3(a-m)** and **4(a-m)** were showed appropriate parent ion peaks corresponding to their molecular formula weight respectively.

2.2 Biological activities

Compounds **4(a-m)** were prepared and screened for their antimicrobial and antitubercular activities data (as shown in Table 1 and 2) revealed that all the synthesized compounds **4(a-m)** have a structure activity relationship (SAR) because activity of compounds varies with substitution. Nitro group containing compounds **(4h, 4i** and **4j)** showed higher activity than chloro **(4c, 4d),** or bromo group containing compounds **(4e, 4f).** Chloro and bromo derivatives also have higher activity than other rested compounds**.** On the basis of SAR, concluded that the activity of compounds depends on electron withdrawing nature of the substituted groups. The sequence of the activity is following

$$NO_2 > Cl > Br > OH > OCH_3 > CH_3$$

Table 1. Antifungal and antibacterial activities of compounds **4(a-m)** with MIC value (μg/mL).

	Antibacterial activity				Antifungal activity			
Comp.	*B. subtilis*	*E. coli*	*S. aureus*	*K. pneumoniae*	*A. niger*	*A. flavus*	*F. oxisporium*	*C. albicans*
4a	12.5	>6.25	12.5	6.25	>25	>25	>25	>25
4b	>3.25	6.25	3.25	>3.25	>25	>12.5	>25	>25
4c	6.25	>3.25	6.25	3.25	>12.5	25	>12.5	>12.5
4d	>3.25	6.25	3.25	6.25	>12.5	>25	>12.5	>12.5
4e	6.25	>3.25	3.25	>3.25	>12.5	25	25	>25
4f	6.25	3.25	6.25	>3.25	>12.5	>12.5	>12.5	>12.5
4g	>3.25	>6.25	>3.25	6.25	25	>12.5	>12.5	25
4h	3.25	>3.25	3.25	3.25	25	>12.5	>12.5	>25
4i	3.25	3.25	6.25	3.25	>12.5	>12.5	>12.5	>12.5
4j	3.25	>3.25	3.25	3.25	>12.5	>12.5	>12.5	>12.5
4k	>12.5	6.25	>12.5	6.25	25	25	>25	>25
4l	>12.5	>12.5	>12.5	>12.5	>25	>25	>25	>25
4m	>3.25	>3.25	>6.25	>6.25	>25	25	>12.5	>12.5
Strept.	1.25	2.75	2.25	3.25	-	-	-	-
Griso.	-	-	-	-	8.5	12.5	6.25	9.25

strept.= streptomycin standard for all bacteria strain and griso. = griseofulvin standard for all fungi strain.

The investigation of antimicrobial (antibacterial, antifungal and antitubercular) data revealed that the compounds **(4c), (4d), (4e), (4f), (4h), (4i)** and **(4j)** displayed high activity in the series, the compounds **(4b), (4g)** and **(4m)** showed moderate activity and rest compounds showed less activity against all the strains compared with standard drugs.

Table 2. Antitubercular activity of compounds **4(a-m)** with MIC value (µg/mL)**.**

Comp.	Conc.	Comp.	Conc.	Comp.	Conc.	Comp.	Conc.	Comp.	Conc.
4a	>12.5	4d	2.50	4g	6.25	4j	>2.50	4m	6.25
4b	>2.50	4e	>2.50	4h	2.50	4k	12.5	-	-
4c	>2.50	4f	>2.50	4i	2.50	4l	>12.5	-	

comp. = compound, conc. = concentration (µg/ml). isoniazid and rifampicin were used as standards, mic values 1.25, 2.50 µg/ml respectively for m. *tuberculosis.*

3. Conclusion

Compounds **4(a-m)** were synthesized by an efficient route and screened for their antibacterial, antifungal and antitubercular activity against selected microorganisms. The investigation of antimicrobial data revealed that the compounds **(4c), (4d), (4e), (4f), (4h), (4i)** and **(4j)** displayed highly active in the series, compounds **(4b), (4g)** and **(4m)** showed moderate activity and rest compounds showed less activity against all the strains compared with standard drugs.

4. Experimental

Melting points were taken in open capillaries and are uncorrected. Progress of reaction was monitored by silica gel-G coated TLC plates using MeOH:$CHCl_3$ system (1:9). The spot was visualized by exposing dry plate at iodine vapours chamber. IR spectra were recorded in KBr disc on a Schimadzu 8201 PC, FTIR spectrophotometer (ν_{max} in cm^{-1}) and ^1H NMR and ^{13}C NMR spectra were measured on a Brucker DRX-300 spectrometer in $CDCl_3$ at 300 and 75 MHz respectively using TMS as an internal standard. All chemical shifts were reported on δ scale. The FAB mass spectra were recorded on a Jeol SX–102 mass spectrometer. Elemental analyses were performed on a Carlo Erba–1108 analyzerThe analytical data of all the compounds were highly satisfactory. For column chromatographic purification of the products, Merck silica Gel 60 (230-400 Mesh) was used. The reagent grade chemicals were purchased from the commercial sources and further purified before use.

4.1. Procedure for the synthesis of compound 1.

A mixture of phenothiazine and 1-bromo-2-chloroethane (1:1 mole) was dissolved in acetone at room temperature. The reaction mixture was continuously stirred on a magnetic stirrer for about 8 h. The product was filtered and purified over a column chromatography using solvent system acetone : chloroform (8 : 2) as eluent. The purified product was recrystallized from ethanol at room temperature to yield compound **1.**

1-(2-chloroethyl)-10*H*-phenothiazine (1). Yield: 60%; mp 160-165 ºC; Anal. Calcd for $C_{14}H_{12}NSCl$: C,64.23, H,4.62, N,5.35%; found C,64.20, H,4.53, N,5.31%; IR (cm^{-1}): 3034, 2936 (CH), 1552 (C=C), 1262 (N-CH_2), 771 (C-Cl), 681 (C-S-C), ^1H NMR ($CDCl_3$, 300 MHz) δ: 3.48 (t, 2H, *J* = 7.42 Hz, $\underline{CH_2}$-Cl), 3.77 (t, 2H, *J* = 7.42 Hz, N-$\underline{CH_2}$), 6.91-8.21 (m, 8H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 54.8 (N-$\underline{CH_2}$), 46.3 ($\underline{CH_2}$-Cl), 117.7, 121.7, 126.5, 127.7, 146.7, 148.8 (Ar); Mass (FAB): $262M^+$.

4.2. Procedure for the synthesis of compound 2.

A mixture of compound **1** and hydrazine hydrate (1:1 mole) was dissolved in acetone at room temperature. The reaction mixture was continuously stirred on a magnetic stirrer for about 6 h. The product was filtered and purified over a column chromatography ethanol : chloroform (6 : 4) as eluent. The purified product was recrystallized from ethanol at room temperature to yield compound **2.**

***N*-[2-(10*H*-phenothiazinyl)ethyl]-hydrazine (2).** Yield: 71%; mp 145-150 ºC; Anal. Calcd for $C_{14}H_{15}N_3SCl$: C,57.42, H,5.16, N,14.35%; found C,57.36, H,5.12, N,14.31%; IR: 1236 (C-N), 3348 (NH), 3430 (NH_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.41 (m, 2H, $\underline{CH_2}$-NH), 3.93 (t, 2H, *J* = 7.44 Hz, N-$\underline{CH_2}$), 5.69 (s, 2H, NH_2), 7.61 (s, 1H, NH), 6.88-8.05 (m, 8H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 44.6 ($\underline{CH_2}$-NH), 56.6 (N-$\underline{CH_2}$), 114.0, 120.1, 125.2, 128.6, 145.3, 147.4 (Ar); Mass (FAB): 299M^+.

4.3. General procedure for synthesis of compounds 3(a-m).

A mixture of compound **2** and several substituted benzaldehydes (1:1 mole) was dissolved in acetone at room temperature and allow to reaction. The reaction mixture was first continuously stirred on a magnetic stirrer for about 2-4 h then kept on a steam bath for about 2.3-5 h. The products were filtered and cooled at room temperature. The filtered products were purified over a column chromatography acetone : chloroform (7 : 7) as eluent and recrystallized from ethanol at room temperature to yield compounds **3(a-m).**

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(phenyl)methylidene]-hydrazine (3a).** Yield: 58%; mp 150-153 ºC; Anal. Calcd for $C_{21}H_{19}N_3S$: C,73.01, H,5.54, N,12.16%; found C,72.95, H,5.50, N,12.11%; IR: 1545 (N=CH), 3362 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.45 (m, 2H, $\underline{CH_2}$-NH), 3.95 (t, 2H, *J* = 7.51 Hz, N-$\underline{CH_2}$), 7.78 (s, 1H, NH), 7.86 (s, 1H, N=CH), 6.49-8.22 (m, 13H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 46.8 ($\underline{CH_2}$-NH), 52.6 (N-$\underline{CH_2}$), 153.7 (N=CH), 117.4, 120.7, 122.6, 125.8, 127.3, 128.1, 129.0, 137.6, 145.4, 146.8, (Ar); Mass (FAB): 345M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(4-chlorophenyl)methylidene]-hydrazine (3b).** Yield: 66%; mp 165-168 ºC; Anal. Calcd for $C_{21}H_{18}N_3SCl$: C,66.39, H,4.77, N,11.06%; found C,66.35, H,4.72, N,11.01%; IR: 736 (C-Cl), 1574 (N=CH), 3372 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.49 (m, 2H, $\underline{CH_2}$-NH), 3.98 (t, 2H, *J* = 7.69 Hz, N-$\underline{CH_2}$), 7.90 (s, 1H, NH), 7.98 (s, 1H, N=CH), 6.45-7.99 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 45.6 ($\underline{CH_2}$-NH), 56.3 (N-$\underline{CH_2}$), 156.8 (N=CH), 115.7, 121.2, 124.6, 126.9, 127.7, 127.8, 129.8, 138.6, 145.8, 147.7 (Ar); Mass (FAB): 380M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(3-chlorophenyl)methylidene]-hydrazine (3c).** Yield: 67%; mp 160-162 ºC; Anal. Calcd for $C_{21}H_{18}N_3SCl$: C,66.39, H,4.77, N,11.06%; found C,66.32, H,4.74, N,11.02%; IR: 734 (C-Cl), 1572 (N=CH), 3364 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 4.57 (m, 2H, $\underline{CH_2}$-NH), 5.06 (t, 2H, *J* = 7.64 Hz, N-$\underline{CH_2}$), 8.01 (s, 1H, NH), 8.08 (s, 1H, N=CH), 6.44-7.92 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 46.7 ($\underline{CH_2}$-NH), 56.8 (N-$\underline{CH_2}$), 158.7 (N=CH), 114.8, 116.2, 119.7, 122.0, 124.9, 125.3, 127.1,129.4, 130.9, 134.2, 144.6, 147.2 (Ar); Mass (FAB): 380M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(2-chlorophenyl)methylidene]-hydrazine (3d).** Yield: 74%; mp 158-161 ºC; Anal. Calcd for $C_{21}H_{18}N_3SCl$: C,66.39, H,4.77, N,11.06%; found C,66.37, H,4.71, N,11.00%; IR: 744 (C-Cl), 1584 (N=CH) 3374 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.52 (m, 2H, $\underline{CH_2}$-NH), 4.01 (t, 2H, *J* = 7.65 Hz, N-$\underline{CH_2}$), 8.06 (s, 1H, NH), 8.11 (s, 1H, N=CH), 6.41-7.88 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 45.2 ($\underline{CH_2}$-NH), 56.3 (N-$\underline{CH_2}$), 157.6 (N=CH), 116.8, 122.9, 123.7, 124.8, 125.7, 126.8, 127.8, 128.9, 130.7, 135.5, 146.4, 149.4 (Ar); Mass (FAB): 380M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(4-bromophenyl)methylidene]-hydrazine (3e).** Yield: 65%; mp 149-154 ºC; Anal. Calcd for $C_{21}H_{18}N_3SBr$: C,59.43, H,4.27, N,9.90%; found C,59.38, H,4.21, N,9.87%; IR: 639 (C-Br), 1571 (N=CH), 3378 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.47 (m, 2H, $\underline{CH_2}$-NH), 3.92 (t, 2H, *J* = 7.61 Hz, N-$\underline{CH_2}$), 7.97 (s, 1H, NH), 8.09 (s, 1H, N=CH), 6.39-7.96 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 47.6 ($\underline{CH_2}$-NH), 58.2 (N-$\underline{CH_2}$), 158.8 (N=CH), 116.9, 120.8, 122.9, 126.8, 127.8, 128.8, 132.4, 138.7, 148.4, 150.9 (Ar); Mass (FAB): 424M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(3-bromophenyl)methylidene]-hydrazine (3f).** Yield: 64%; mp 151-154 ºC; Yield: Anal. Calcd for $C_{21}H_{18}N_3SBr$: C,59.43, H,4.27, N,9.90%; found C,59.34, H,4.17, N,9.81%; IR: 647 (C-Br), 1572 (N=CH), 3371 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.39 (m, 2H, $\underline{CH_2}$-NH), 3.94 (t, 2H, *J* = 7.60 Hz, N-$\underline{CH_2}$), 7.99 (s, 1H, NH), 8.10 (s, 1H, N=CH), 6.37-7.92 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 47.6 ($\underline{CH_2}$-NH), 60.6 (N-$\underline{CH_2}$), 157.8 (N=CH), 116.1, 122.4, 124.4, 125.7, 126.8, 127.3, 128.9, 129.4, 135.8, 139.2, 145.4, 152.4 (Ar); Mass (FAB): 424M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(2-bromophenyl)methylidene]-hydrazine (3g).** Yield: 62%; mp 153-157 ºC; Anal. Calcd for $C_{21}H_{18}N_3SBr$: C,59.43, H,4.27, N,9.90%; found C,59.40, H,4.21, N,9.84%; IR: 630 (C-Br), 1585 (N=CH), 3364 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.48 (m, 2H, $\underline{CH_2}$-NH), 4.00 (t, 2H, *J* = 7.62 Hz, N-$\underline{CH_2}$), 8.04 (s, 1H, NH), 8.18 (s, 1H, N=CH) 6.41-7.88 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 46.8 ($\underline{CH_2}$-NH), 59.7 (N-$\underline{CH_2}$), 157.2 (N=CH), 115.1, 122.6, 123.7, 125.0, 126.4, 127.5, 128.4, 130.1, 134.2, 138.2, 144.2, 147.4 (Ar); Mass (FAB): 424M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(4-nitrophenyl)methylidene]-hydrazine (3h).** Yield: 66%; mp 165-168 ºC; Anal. Calcd for $C_{21}H_{18}N_4SO_2$: C,64.59, H,4.64, N,14.34%; found C,64.52, H,4.60, N,14.32%; IR: 849 (C-N), 1535 (N=O), 1561 (N=CH), 3364 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.38 (m, 2H, $\underline{CH_2}$-NH), 3.98 (t, 2H, *J* = 7.69 Hz, N-$\underline{CH_2}$), 8.06 (s, 1H, NH), 8.12 (s, 1H, N=CH), 6.36-7.91 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 47.9 ($\underline{CH_2}$-NH), 56.7 (N-$\underline{CH_2}$), 156.8 (N=CH), 116.1, 122.1, 124.4, 126.8, 127.8, 129.4, 135.8, 138.2, 145.4, 149.0 (Ar); Mass (FAB): 390M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(3-nitrophenyl)methylidene]-hydrazine (3i).** Yield: 63%; mp 162-166 ºC; Ana l. Calcd for $C_{21}H_{18}N_4SO_2$: C,64.59, H,4.64, N,14.34%; found C,64.53, H,4.62, N,14.28%; IR: 848 (C-N), 1529 (N=O), 1562 (N=CH), 3360 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.40 (m, 2H, $\underline{CH_2}$-NH), 3.92 (t, 2H, *J* = 7.64 Hz, N-$\underline{CH}$), 8.02 (s, 1H, NH), 8.17 (s, 1H, N=CH) 6.39-7.96 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 46.5 ($\underline{CH_2}$-NH), 56.8 (N-$\underline{CH_2}$), 155.3 (N=CH), 115.0, 118.5, 120.1, 124.2, 126.7, 128.9, 129.4, 135.8, 138.2, 145.4, 147.4, 149.2 (Ar); Mass (FAB): 390M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(2-nitrophenyl)methylidene]-hydrazine (3j).** Yield: 62%; mp 160-164 ºC; Anal. Calcd for $C_{21}H_{18}N_4SO_2$: C,64.59, H,4.64, N,14.34%; found C,64.55, H,4.58, N,14.30%; IR: 848 (C-N), 1534 (N=O), 1557 (N=CH), 3358 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.35 (m, 2H, $\underline{CH_2}$-NH), 4.01 (t, 2H, *J* = 7.63 Hz, N-$\underline{CH_2}$), 7.96 (s, 1H, NH), 8.07 (s, 1H, N=CH), 6.36-7.91 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 47.9 ($\underline{CH_2}$-NH), 58.8 (N-$\underline{CH_2}$), 155.8 (N=CH), 116.1, 121.4, 124.4, 125.7, 127.8, 128.4, 129.4, 131.8, 135.3, 139.6, 144.7, 148.2 (Ar); Mass (FAB): 390M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(4-methoxyphenyl)methylidene]-hydrazine (3k).** Yield: 61%; mp 147-150 ºC; Anal. Calcd for $C_{22}H_{21}N_3SO$: C,70.37, H,5.63, N,11.19%; found C,70.32, H,5.60, N,11.12%; IR: 1559 (N=CH), 2950 (OCH_3), 3358 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 4.21 (s, 3H, OCH_3), 3.31 (m, 2H, $\underline{CH_2}$-NH), 3.85 (t, 2H, *J* = 7.56 Hz, N-$\underline{CH_2}$), 7.79 (s, 1H, NH), 7.78 (s, 1H, N=CH), 6.54-7.85 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 45.9 ($\underline{CH_2}$-NH), 54.2 (N-$\underline{CH_2}$), 55.9 (OCH_3), 154.6 (N=CH), 118.4, 121.5, 125.7, 126.4, 130.8, 135.1, 138.6, 142.2, 149.3, 158.9 (Ar); Mass (FAB): 375M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(4-methylphenyl)methylidene]-hydrazine (3l).** Yield: 60%; mp 142-146 ºC; Anal. Calcd for $C_{22}H_{21}N_3S$: C,73.50, H,5.88, N,11.58%; found C,73.42, H,5.81, N,11.52%; IR: 1542 (N=CH), 2924 (CH_3), 3348 (NH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.39 (s, 3H, CH_3), 3.19 (t m, 2H, $\underline{CH_2}$-NH), 3.71 (t, 2H, *J* = 7.51 Hz, N-$\underline{CH_2}$), 7.84 (s, 1H, NH), 7.98 (s, 1H, N=CH), 6.52-8.03 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 27.6 (CH_3), 46.3 ($\underline{CH_2}$-NH), 54.6 (N-$\underline{CH_2}$), 152.6 (N=CH), 117.2, 123.5, 124.7, 126.2, 127.8, 129.6, 136.0, 138.1, 143.5, 149.8 (Ar); Mass (FAB): 359M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-*N*'-[(4-hydroxyphenyl)methylidene]-hydrazine (3m).** Yield: 64%; mp 140-143 ºC; Anal. Calcd for $C_{21}H_{19}N_3SO$: C,69.77, H,5.29, N,11.62%; found C,69.72, H,5.21, N,11.60%; IR: 1557 (N=CH), 3362 (NH), 3464 (OH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.38 (m, 2H, $\underline{CH_2}$-NH), 3.94 (t, 2H, *J* = 7.46 Hz, N-$\underline{CH_2}$), 4.24 (s, 1H, OH), 7.98 (s, 1H, NH), 8.05 (s, 1H, N=CH), 6.49-7.72 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 47.5 ($\underline{CH_2}$-NH), 58.2 (N-$\underline{CH_2}$), 157.9 (N=CH), 115.7, 122.6, 124.9, 125.7, 127.8, 128.7, 137.3, 139.7, 145.8, 156.6 (Ar); Mass (FAB): 403M^+.

4.4. General procedure for the synthesis of compounds 4(a-m).

A mixture of compounds **3(a-m)** and chloroacetyl chloride in the presence of Et_3N (1:1 mole) was dissolved in acetone at room temperature and allow to reaction. The reaction mixture was first continuously stirred on a magnetic stirrer for about 2-3. h then kept on a steam bath for about 2.3-4.2 h. The products were filtered and cooled at room temperature. The filtered products were purified over a column chromatography acetone : chloroform (7 : 3) as eluent and recrystallized from ethanol at room temperature to yield compounds **4(a-m).**

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(phenyl)-3-chloro-2-oxo-1-iminoazetidine (4a).** Yield: 68%; mp 142-145 ºC; Anal. Calcd for $C_{23}H_{20}N_3SO$: C,71.47, H,5.21, N,10.47%; found C,71.41, H,5.18, N,10.41%; IR: 1334 (C-N), 1732 (C=O cyclic), 2927 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.30 (m, 2H, $\underline{CH_2}$-NH), 3.90 (t, 2H, *J* = 7.40 Hz, N-$\underline{CH_2}$), 4.34 (d, 1H, *J* = 5.0 Hz, CH-Cl), 4.81 (d, 1H, *J* = 5.0 Hz, N-CH), 6.52-7.84 (m, 13H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 42.1 ($\underline{CH_2}$-NH), 53.0 (N-$\underline{CH_2}$), 47.6 (CH-Cl), 57.9 (N-CH), 171.5 (CO cyclic), 114.5, 118.9, 123.5, 126.7, 128.5, 129.1, 130.7, 136.2, 145.8, 149.7 (Ar); Mass (FAB): 386M$^+$.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(4-chlorophenyl)-3-chloro-2-oxo-1-iminoazetidine (4b).** Yield: 64%; mp 144-146 ºC; Anal. Calcd for $C_{23}H_{19}N_3SOCl_2$: C,60.52, H,419, N,9.20%; found C,60.48, H,4.12, N,9.16%; IR: 769 (C-Cl), 1336 (C-N), 1748 (CO cyclic), 2920 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.32 (m, 2H, $\underline{CH_2}$-NH), 3.98 (t, 2H, *J* = 7.45 Hz, N-$\underline{CH_2}$), 4.41 (d, 1H, *J* = 5.10 Hz, CH-Cl), 4.98 (d, 1H, *J* = 5.10 Hz, N-CH), 6.51-8.12 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 41.3 ($\underline{CH_2}$-NH), 55.2 (N-$\underline{CH_2}$), 53.9 (CH-Cl), 65.6 (N-CH), 177.6 (CO cyclic), 117.5, 122.8, 124.9, 126.7, 127.7, 129.9, 130.8, 138.8, 146.3, 149.4 (Ar); Mass (FAB): 456M$^+$.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(3-chlorophenyl)-3-chloro-2-oxo-1-iminoazetidine (4c).** Yield: 64%; mp 140-142 ºC; Anal. Calcd for $C_{23}H_{19}N_3SOCl_2$: C,60.52, H,419, N,9.20%; found C,60.44, H,4.13, N,9.14%; IR: 774 (C-Cl), 1342 (C-N), 1750 (CO cyclic), 2929 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.35 (m, 2H, $\underline{CH_2}$-NH), 3.88 (t, 2H, *J* = 7.45 Hz, N-$\underline{CH_2}$), 4.43 (d, 1H, *J* =5.10 Hz, CH-Cl), 4.91 (d, 1H, *J* = 5.10 Hz, N-CH), 6.53-8.05 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 44.9 ($\underline{CH_2}$-NH), 52.6 (N-$\underline{CH_2}$), 55.7 (CH-Cl), 64.8 (N-CH), 177.5 (CO cyclic), 115.8, 124.2, 125.8, 127.7, 129.3, 130.9, 131.6, 135.1, 135.8, 141.6, 145.7, 148.8 (Ar); Mass (FAB): 456M$^+$.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(2-chlorophenyl)-3-chloro-2-oxo-1-iminoazetidine (4d).** Yield: 64%; mp 138-141 ºC; Anal. Calcd for $C_{23}H_{19}N_3SOCl_2$: C,60.52, H,419, N,9.20%; found C,60.41, H,4.11, N,9.18%; IR: 774 (C-Cl), 1339 (C-N), 1742 (C=O cyclic), 2922 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.30 (m, 2H, $\underline{CH_2}$-NH), 3.92 (t, 2H, *J* = 7.40 Hz, N-$\underline{CH_2}$), 4.39 (d, 1H, *J* = 5.15 Hz, CH-Cl), 4.96 (d, 1H, *J* = 5.15 Hz, N-CH), 6.46-8.01 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 43.7 ($\underline{CH_2}$-NH), 55.4 (N-$\underline{CH_2}$), 57.8 (CH-Cl), 64.5 (N-CH), 177.6 (CO cyclic), 114.8, 119.0, 123.5, 125.8, 126.7, 128.7, 130.8, 136.7, 138.8, 145.8, 148.3, 150.4, (Ar); Mass (FAB): 456M$^+$.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(4-bromophenyl)-3-chloro-2-oxo-1-iminoazetidine (4e).** Yield: 61%; mp 151-154 ºC; Anal. Calcd for $C_{23}H_{19}N_3SOBrCl$: C,55.15, H,3.82, N,8.38%; found C,55.11, H,3.78, N,8.34%; IR: 572 (C-Br), 1338 (C-N), 1742 (CO cyclic), 2892 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.31 (m, 2H, $\underline{CH_2}$-NH), 3.91 (t, 2H, *J* = 7.46 Hz, N-$\underline{CH_2}$), 4.39 (d, 1H, *J* = 5.05 Hz, CH-Cl), 4.88 (d, 1H, *J* = 5.05 Hz, N-CH), 6.48-7.89 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 40.9 ($\underline{CH_2}$-NH), 53.4 (N-$\underline{CH_2}$), 52.6 (CH-Cl), 62.3 (N-CH), 176 (CO cyclic), 115.8, 120.8, 124.3, 126.7, 127.3, 128.3, 133.2, 137.6, 141.3, 148.4 (Ar); Mass (FAB):): 501M$^+$.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(3-bromophenyl)-3-chloro-2-oxo-1-iminoazetidine (4f).** Yield: 64; mp 153-155 ºC; Anal. Calcd for $C_{23}H_{19}N_3SOBrCl$: C,55.15, H,3.82, N,8.38%; found C,55.10, H,3.80, N,8.31%; IR: 593 (C-Br), 1338 (C-N), 1746 (CO cyclic), 2890 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.35 (m, 2H, $\underline{CH_2}$-NH), 3.87 (t, 2H, *J* = 7.50 Hz, N-$\underline{CH_2}$), 4.32 (d, 1H, *J* = 5.15 Hz, CH-Cl), 4.86 (d, 1H, *J* = 5.15 Hz, N-CH), 6.43-7.87 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 46.1 ($\underline{CH_2}$-

NH), 53.2 (N-$\underline{CH_2}$), 54.4 (CH-Cl), 63.4 (N-CH), 177.4 (CO cyclic), 115.8, 121.8, 124.3, 125.7, 126.4, 126.7, 127.5, 128.9, 131.4, 135.2, 145.8, 148.4 (Ar); Mass (FAB): 501M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(2-bromophenyl)-3-chloro-2-oxo-1-iminoazetidine (4g).** Yield: 65%; mp 149-151 ºC; Anal. Calcd for $C_{23}H_{19}N_3SOBrCl$: C,55.15, H,3.82, N,8.38%; found C,55.14, H,3.76, N,8.32%; IR: 589 (C-Br), 1339 (C-N), 1752 (C=O cyclic), 2873 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.30 (m, 2H, $\underline{CH_2}$-NH), 3.92 (t, 2H, *J* = 7.46 Hz, N-$\underline{CH_2}$), 4.34 (d, 1H, *J* = 5.15 Hz, CH-Cl), 4.85 (d, 1H, *J* = 5.15 Hz, N-CH), 6.41-7.93 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 43.3 ($\underline{CH_2}$-NH), 52.7 (N-$\underline{CH_2}$), 55.5 (CH-Cl), 61.4 (N-CH), 175.2 (CO cyclic), 115.8, 119.2, 124.3, 125.7, 127.5, 128.1, 128.7, 132.9, 134.3, 137.8, 140.8, 146.1 (Ar); Mass (FAB): 501M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(4-nitrophenyl)-3-chloro-2-oxo-1-iminoazetidine (4h).** Yield: 63%; mp 157-160 ºC; Anal. Calcd for $C_{23}H_{19}N_4SO_3Cl$: C,59.16, H,4.10, N,11.99%; found C,59.12, H,4.04, N,11.92%; IR: 868 (C-NO), 1352 (C-N), 1540 (NO_2), 1741 (CO cyclic), 2927 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.35 (m, 2H, $\underline{CH_2}$-NH), 3.87 (t, 2H, *J* = 7.50 Hz, N-$\underline{CH_2}$), 4.37 (d, 1H, *J* = 5.0 Hz, CH-Cl), 4.91 (d, 1H, *J* = 5.0 Hz, N-CH), 6.37-7.79 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 43.7 ($\underline{CH_2}$-NH), 54.2 (N-$\underline{CH_2}$), 58.6 (CH-Cl), 62.8 (N-CH), 174.9 (CO cyclic), 118.8, 123.5, 126.7, 127.5, 128.3, 129.4, 135.2, 138.8, 145.3, 147.4 (Ar); Mass (FAB): 497M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(3-nitrophenyl)-3-chloro-2-oxo-1-iminoazetidine (4i).** Yield: 64%; mp 155-157 ºC; Anal. Calcd for $C_{23}H_{19}N_4SO_3Cl$: C,59.16, H,4.10, N,11.99%; found C,59.11, H,4.05, N,11.96%; IR: 867 (C-NO), 1347 (C-N), 1548 (NO_2), 1742 (CO cyclic), 2923 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.41 (m, 2H, $\underline{CH_2}$-NH), 3.98 (t, 2H, *J* = 7.50 Hz, N-$\underline{CH_2}$), 4.32 (d, 1H, *J* = 4.95 Hz, CH-Cl), 4.78 (d, 1H, *J* = 4.95 Hz, N-CH), 6.26-7.89 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 46.0 ($\underline{CH_2}$-NH), 55.2 (N-$\underline{CH_2}$), 51.5 (CH-Cl), 62.8 (N-CH), 173.8 (CO cyclic), 116.1, 119.8, 122.6, 124.4, 125.7, 128.9, 132.3, 137.8, 138.2, 141.4, 150.4, 156.2 (Ar); Mass (FAB): 497M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(2-nitrophenyl)-3-chloro-2-oxo-1-iminoazetidine (4j).** Yield: 62%; mp 152-154 ºC; Anal. Calcd for $C_{23}H_{19}N_4SO_3Cl$: C,59.16, H,4.10, N,11.99%; found C,59.12, H,4.04, N,11.94%; IR: 879 (C-NO), 1548 (NO_2), 1347 (C-N), 1741 (CO cyclic), 2929 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.40 (m, 2H, $\underline{CH_2}$-NH), 5.0 (t, 2H, *J* = 7.50 Hz, N-$\underline{CH_2}$), 4.25 (d, 1H, *J* = 5.10 Hz, CH-Cl), 4.81 (d, 1H, *J* = 5.10 Hz, N-CH), 6.32-7.82 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 42.7 ($\underline{CH_2}$-NH), 53.2 (N-$\underline{CH_2}$), 54.7 (CH-Cl), 63.4 (N-CH), 172.8 (CO cyclic), 116.4, 124.1, 126.7, 127.8, 128.4, 128.9, 129.4, 131.3, 136.2, 140.8, 147.4, 158.0 (Ar); Mass (FAB): 497M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(4-methoyphenyl)-3-chloro-2-oxo-1-iminoazetidine (4k).** Yield: 65%; mp 135-137 ºC; Anal. Calcd for $C_{24}H_{22}N_3SO_2Cl$: C,63.77, H,4.90, N,9.29%; found C,63.74, H,4.87, N,9.22%; IR: 1150 (C-O), 1338 (N-C), 1736 (CO cyclic), 2891 (CH-Cl); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.28 (m, 2H, $\underline{CH_2}$-NH), 3.63 (s, 3H, OCH_3), 3.84 (t, 2H, *J* = 7.45 Hz, N-$\underline{CH_2}$), 4.28 (d, 1H, *J* = 5.0 Hz, CH-Cl), 4.87 (d, 1H, *J* = 5.0 Hz, N-CH), 6.26-7.92 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 41.9 ($\underline{CH_2}$-NH), 50.2 (N-$\underline{CH_2}$), 51.6 (CH-Cl), 55.6 (OCH_3), 65.4 (N-CH), 174.5 (CO, cyclic), 117.9, 122.4, 125.9, 128.7, 130.8, 136.5, 137.8, 139.8, 148.7, 155.9 (Ar); Mass (FAB): 452M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(4-methylphenyl)-3-chloro-2-oxo-1-iminoazetidine (4l).** Yield: 62%; mp 133-136 ºC; Anal. Calcd for $C_{24}H_{22}N_3SOCl$: C,66.11, H,5.08, N,9.63%; found C,66.05, H,5.02, N,9.60%; IR: 1332 (C-N), 1732 (CO cyclic), 2887 (CH-Cl), 2932 (CH_3); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.69 (s, 3H, CH_3), 3.25 (m, 2H, $\underline{CH_2}$-NH), 3.80 (t, 2H, *J* = 7.45 Hz, N-$\underline{CH_2}$), 4.20 (d, 1H, *J* = 4.90 Hz, CH-Cl), 4.68 (d, 1H, *J* = 4.90 Hz, N-CH), 6.28-7.98 (m, 12H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 27.7 (CH_3), 40.9 ($\underline{CH_2}$-NH), 51.3 (N-$\underline{CH_2}$), 55.4 (CH-Cl), 63.8 (N-CH), 169.5 (CO cyclic), 115.8, 122.8, 122.9, 124.8, 125.7, 127.7, 129.9, 135.9, 143.6, 149.8 (Ar); Mass (FAB): 436M^+.

***N*-[2-(10*H*-phenothiazinyl)ethyl]-4-(4-hydroxyphenyl)-3-chloro-2-oxo-1-iminoazetidine (4m).** Yield: 60%; mp 132-135 ºC; Anal. Calcd for $C_{23}H_{20}N_3SO_2Cl$: C,63.07, H,4.60, N,9.59%; found C,63.01, H,4.53, N,9.51%; IR: 1177 (C-O), 1357 (C-N), 1753 (CO cyclic), 2927 (CH-Cl), 3469 (OH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.30 (m, 2H, $\underline{CH_2}$-NH), 3.90 (t, 2H, *J* = 7.45 Hz, N-$\underline{CH_2}$), 4.24 (s, 1H, OH), 4.49 (d, 1H, *J* = 4.85 Hz, CH-Cl), 4.98 (d, 1H, *J* = 4.85 Hz, N-CH), 7.09-8.1 (m, 12H, Ar-H); ^{13}C

NMR ($CDCl_3$, 75 MHz) δ: 44.1 ($\underline{CH_2}$-NH), 51.7 (N-$\underline{CH_2}$), 56.9 (CH-Cl), 67.7 (N-CH), 176.5 (CO cyclic), 115.3, 124.4, 126.8, 129.7, 130.8, 135.8, 138.9, 146.4, 148.4, 158.3 (Ar); Mass (FAB): $438M^+$.

4.5. Biological study

The antibacterial, antifungal and antitubercular activities of compounds **4(a-m)** has been assayed *in vitro* against selected Gram positive bacteria, *Bacillus subtilis, Staphylococcus aureus* and Gram negative bacteria*, Escherichia coli, Klebsiella pneumoniae* fungi, *Aspergillus niger, Aspergillus flavus, Candida albicans Fusarium oxisporium* and *Mycobacterium tuberculosis* H37Rv strain MIC values of compounds **4(a-m)** were determined using filter paper disc diffusion method (antibacterial and antifungal activities) and L.J. medium (Conventional) method[20] (antitubercular activity). Streptomycin and Griseofulvin used as standard for antibacterial and antifungal activity showed MIC range for all bacterial strain 1.25-6.25 μg/mL and for all fungal strain 6.25-12.5 μg/mL respectively and for antitubercular activity, Isoniazid and Rifampicin taken as standards. All standards also screened under the similar condition for comparison. Results of all given activities of above compounds were given in Table 1 and 2.

Acknowledgments

The authors are thankful to SAIF, Central Drugs Research Institute, Lucknow (India) for providing spectral and analytical data of the compounds. We are also thankful to Head, Department of Chemistry, Dr. H. S. Gour, University (A Central University), Sagar (India) for giving the facilities to carryout the work.

References

[1] Swarnkar, P. K.; Kriplani, P.; Gupta, G. N.; Ojha, K.G. Synthesis and Antibacterial Activity of Some New Phenothiazine Derivatives. *E-J. Chem.* **2007,** *4,* 14-20.

[2] Havaldar, F.H.; Khatri, N.K. Synthesis of 2-trifluoromethyl-phenothiazinoazetidin-2-ones as antibacterial and antifungal agents. *Indian J. Heterocyclic Chem*., **2006**, *16,* 87-88.

[3] Tandon, V. K.; Maurya, H. K.; Tripathi, A.; ShivaKeshava, G.B.; Shukla, P. K.; Srivastava, P.; Panda, D. 2,3-Disubstituted-1,4-naphthoquinones, 12H-benzo[b]phenothiazine-6, 11-diones and related compounds: Synthesis and Biological evaluation as potential antiproliferative and antifungal agents. *Eur. J. Med. Chem.* **2009,** *44,* 1086-1092.

[4] Mohamed, F.A.; Mohamed, H. A.; Hussein, S. A.; Ahmed, S. A. A validated spectrofluorimetric method for determination of some psychoactive drugs. *J. Pharm. Biomed. Analysis* **2005,** *39,* 139–146.

[5] Wen, B.; Zhou, M. Metabolic activation of the phenothiazine antipsychotics chlorpromazine and thioridazine to electrophilic iminoquinone species in human liver microsomes and recombinant P450s. *Chemico-Biol. Interact.* **2009**, *181,* 220–226.

[6] Sadanandam, Y.S.; Shetty, M. M.; Rao, A. B.; Rambabu, Y. 10H-Phenothiazines: A new class of enzyme inhibitors for inflammatory diseases. *Eur. J. Med. Chem.* **2009,** *44,* 197-202.

[7] Rajasekaran, A.; Thampi, P. P. Synthesis and anti-inflammatory activity of some 10-[(1-acyl-1h-tetrazol-5-yl)ethyl-10-phenothiazine. *Acta Pharm. Turcica,* **2003,** *45,* 227-232.

[8] Khanna, R.; Palit, G.; Srivastava, V.K.; Shanker, K. Newer heterocycles of phenothiazine and their antiparkinsonian activity. *Indian J. Chem.*, **1990**, *29B*, 556-560.

[9] WHO Report 2005—Global Tuberculosis Control; Surveillance, Planning, Financing; World Health Organization: Geneva, 2005.

[10] Trivedi, A. R.; Siddiqui, A. B.; Shah, V. H. Design, synthesis, characterization and antitubercular activity of some 2-heterocycle-substituted phenothiazines. *Arkivoc,* **2008**, *2,* 210-217.

[11] Madrid, P. B.; Polgar, W. E.; Toll, L.; Tanga, M. J. Synthesis and antitubercular activity of phenothiazines with reduced binding to dopamine and serotonin receptors. *Bioorg. Med. Chem. Let.* **2007,** *17,* 3014–3017.

[12] Delpiccolo, C. M. L.; Fraga, M. A.; Mata, E. G. An Efficient, Stereoselective Solid-Phase Synthesis of β-Lactams Using Mukaiyama's Salt for the Staudinger Reaction. *J. Comb. Chem.* **2003**, *5*, 208-210.

[13] Srivastava, S.K.; Dua, R.; Srivastava, S.D. Synthesis and antimicrobial activity of [N1-(N-substituted-arylidene-hydrazino)-acetyl]-2-methyl-imidazoles and [N1-(4-substituted aryl-3-chloro-2-oxo-1-azetidinyl-amino)-acetyl]-2-methyl-imidazoles. *Proc. Nat. Acad. Sci. India, Sec. A: Phys. Sci.* **2010**, *80*, 117-121.

[14] Trivedi, P.B.; Undavia, N.K.; Dave, A.M.; Bhatt, K.N.; Desai, N.C., Synthesis and antimicrobial activity of 4-oxothiazolidines, 4-oxoazetidines, malonanilic acid hydrazines and pyrazoline derivatives of phenothiazine. *Indian J. Chem.,* **1993**, *32B (7),* 760-765.

[15] Panwar, H.; Verma, R.S.; Srivastava, V. K.; Kumar, A. Synthesis of some substituted Azetidinonyl and thiazolidinonyl-1,3,4-thiadiazino[6,5-b]indoles as prospective antimicrobial agents. *Indian J. Chem.,* **2006,** *45B,* 2099-2104.

[16] Patel, R.B.; Desai, P.S.; Desai, K.R.; Chikhalia, K.H. Synthesis of pyrimidine based thiazolidinones and azetidinones: antimicrobial and antitubercular agents. *Indian J. Chem,* **2006,** *45B,* 773-778.

[17] Siddiqui, N; Rana, A; Khan, S. A.; Haque, S. E.; Alam, M. S.; Ahsan W; Arshada, M. F.; Anticonvulsant and Toxicity Evaluation of Newly Synthesized 1-2-(3,4-disubstitutedphenyl)-3-chloro-4-oxoazetidin-1-yl-3-(6-substituted-1,3-benzothiazol-2-yl)ureas. *Acta Chim. Slov.* **2009,** *56,* 462–469.

[18] Srivastava, S.K.; Srivastava, S.L.; Srivastava, S.D. Synthesis of new 2-chloro phenothiadiazol-2-oxo-azetidines- antimicrobial and anti-inflammatory agents. *Indian J. Chem,* **2000,** *39B,* 464-467.

[19] Kumar, A.; Gurtu, S.; Agarwal, J.C.; Sinha, J.N.; Bhargava, K.P.; Shanker, K., Synthesis and cardiovascular activity of substituted 4-azetidinones. *J. Indian Chem. Soc*., **1983**, *60(6)*, 608-610.

[20] Dubey, A.; Srivastava, S.K.; Srivastava, S.D., Conventional and microwave assisted synthesis of 2-oxo-4-substituted aryl-azetidine derivatives of benzotriazole: A new class of biological compounds. *Bioorg. Med. Chem. Lett.*, **2011,** *21*, 569-573.

A C G
publications