

## SYNTHESIS OF SOME NEW PYRIMIDINE DERIVATIVES INCORPORATED INTO OTHER HETEROCYCLES FOR BIOLOGICAL EVALUATION

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Chloroacetyl pyrimidine was synthesized and reacted with both aromatic amines and hydrazine hydrate. Hydrazone was reacted with  $\beta$ -dicarbonyl compounds and also with different acid anhydrides. 2-Amino-pyrimidine afforded new Schiff's bases which were cyclized with thioglycolic acid and thiolactic acid. Thiosemicarbazido derivatives were cyclized to give thiadiazole which gave Mannich bases. Some of the newly prepared compounds were biologically tested as antimicrobials.

**Key words:** Chloroacetyl, Pyrimidine, Thioglycolic acid, Thiolactic acid, Thiadiazole, Thiosemicarbazide.

### Introduction

Several publications [Laurent *et al* 1994 and Richard 1973] reports show that pyrimidine and its derivatives have biological properties [Gupta and Misra 1979] as, antitumor [Youssef *et al* 1994], antitubercular [Manhas *et al* 1979], bacteriostatic [Kuechler and Koch 1973], hypoglycemic [Kurihara *et al* 1971], diuretic [Thomae 1967], antiinflammatory [Centre d' Etudes 1973], herbicidal [Anderson *et al* 1994] and antifungal activities [Tokio *et al* 1994]. It was found of interest to investigate the chemical and biological properties of some new pyrimidine derivatives.

The synthesis of 5-membered ring heterocyclic compounds were found to possess multifarious biological activities. So, we report here the synthesis of thiazolidinones [Patolia *et al* 1994], thiadiazoles [Ahluwalia *et al* 1987], pyrazoles and pyrazolines [Omar 1997 and Zayed *et al* 1981] incorporated into pyrimidine ring.

These observations prompted us to synthesize the title compounds in which biologically active moieties were present, and to evaluate them and their intermediates for antibacterial and antifungal activities.

### Experimental

Melting points were determined on an electrothermal capillary apparatus and were not corrected. TLC was performed on silica gel 60F<sub>245</sub> plates purchased from E Merck and Co. Infrared spectral analysis were performed on a Shimadzu IR spectrophotometer 435 and Unicam SP 1000 infracord spectrophotometer using KBr discs. <sup>1</sup>H-NMR spectra were recorded on Jeol EX-270 MHz with TMS as an internal reference. The mass spectra were recorded on GC-MS-QP 1000 EX Shimadzu gas chromatography MS apparatus. Elemental microanalyses were performed by

micro analytical service laboratories, Faculty of Science, Cairo University.

**Synthesis of Compounds: 2-[N-(Chloroacetyl)] pyrimidine (I).** A mixture of 2-aminopyrimidine (0.1 mol) and chloroacetyl chloride (0.15 mol) in dry benzene (200 ml) was refluxed for 10 hrs. On evaporation of the solvent followed by addition of chloroform, the product was separated, washed with pet. ether (40-60) and crystallized (Table 1).

**2-[N-(Substituted arylamino)acetamido]pyrimidine (IIa-d).** General Method. A mixture of I (0.01 mol) and different aromatic and/or heterocyclic amines namely (p-aminoacetophenone, m-chloroaniline, o-aminothio-phenol and/or 2-aminopyrimidine) (0.01 mol) in absolute ethanol (30-40 ml) was refluxed for 10 hrs in the presence of (2-3 gm) anhydrous K<sub>2</sub>CO<sub>3</sub>. The contents were poured onto ice cold water and the resulting solid was dried and recrystallized (Table 1).

**2-[N-(Hydrazinoacetamido)]pyrimidine (III).** A mixture of compound I (0.008 mol) in absolute ethanol and hydrazine hydrate 98% (0.016 mol) was refluxed with stirring for 8 hrs. The solvent was concentrated and cooled, the product III was separated out by scratching with MeOH and recrystallized (Table 1).

**2-[N-(3',5'-Dimethylpyrazol-1'-yl) and (3'-methyl-5'-pyrazolon-1'-yl)-acetamido]pyrimidine (IVa,b).** A mixture of III (0.01 mol) and acetylacetone and/or ethyl acetoacetate (0.01 mol) was heated at 100°C for 8 hrs., then cooled, triturated with pet. ether (60-80), filtered off and recrystallized to give IVa,b, respectively (Table 1).

**2-[1'-N-(Acetamido)-3',4'-dihydro-3'-methyl-5'-pyrazolon-5'-yl]-pyrimidine (IVc).** A solution of III (0.01 mol) and ethyl-3-bromopropionate (0.01 mol) in absolute ethanol (25 ml) was refluxed for 10 hrs. The solvent was evaporated and the residue was washed with ether to give IVc, (Table 1).

2-[(*N*-Malimido;*N*-succinimido;*N*-phthalimido)acetamido] pyrimidine (*Va-c*): General method: A mixture of III (0.01 mol) and the appropriate acid anhydride, namely, maleic, succinic and/or phthalic anhydride (0.01 mol) in glacial acetic acid (10 ml) was heated under reflux for 10 hrs. The solvent was concentrated and the residue was poured onto crushed ice, the formed precipitate was filtered off and recrystallized to give *Va-c*, (Table 1).

2-[(*p*-Substituted benzylidene)amino] pyrimidine (*Vla-d*). General method. A mixture of 2-aminopyrimidine (0.01 mol) and different aromatic aldehydes, namely, *p*-chlorobenzaldehyde, *p*-nitrobenzaldehyde, *p*-dimethyl-aminobenzaldehyde and/or *p*-anisaldehyde (0.01 mol) in methanol and few drops of acetic acid was refluxed for 8-10 hrs. The excess of solvent was distilled off and the residue was poured onto ice cold water. The solid separated out was filtered and recrystallized to give (*Vla-d*), respectively. (Table 2).

2-[(2'-Thienylidene)amino]pyrimidine (*Vle*). A mixture of 2-aminopyrimidine (0.01 mol) and 2-thiophene-carboxaldehyde (0.01 mol) in acetic acid was refluxed for 10 hrs. Excess

solvent was distilled off and the residue was poured onto ice cold water. The separated solid was filtered off and recrystallized to give (*Vle*) (Table 2).

2-[2'-(*p*-Substituted phenyl)-4'-thiazolidinon-3'-yl] pyrimidine (*VIIa-d*). General method. Substituted benzylidenes *Vla-d* (0.01 mol) was dissolved in dry benzene, thioglycolic acid (0.01 mol) was added and the mixture was refluxed on water bath for 6-10 hrs, the solvent was evaporated under reduced pressure, the separated solid was filtered off, washed with sodium bicarbonate solution and recrystallized to give *VIIa-d*, respectively. (Table 2).

2-[2'-(2-Thienyl)-4'-thiazolidinon-3'-yl]pyrimidine (*VIIe*). Thioglycolic acid (0.01 mol) was added to *Vle* (0.01 mol) in dry benzene and refluxed on water bath for 7 hrs. The solvent was concentrated and the separated solid was filtered off, washed with sodium bicarbonate solution and recrystallized to give *VIIe*. (Table 2).

2-[2'-(*p*-Substituted phenyl)-5'-methyl-4'-thiazolidinon-3'-yl]-pyrimidine (*VIIIa-d*). A mixture of thiolactic acid (0.01 mol)

**Table 1**  
Physical and analytical data of the prepared compounds

Comp. No.	M.P.[°C] Solvent	Yield %	Formula (M. Wt)	Analysis % Calculated/Found		
				C	H	N
<i>I</i>	182	51	C <sub>6</sub> H <sub>6</sub> ClN <sub>3</sub> O	42.00	3.53	24.49
	EtOH		171.59	42.43	3.25	24.69
<i>IIa</i>	323	51	C <sub>14</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub>	62.21	5.22	20.73
	DMF/EtOH		270.29	62.43	4.99	20.55
<i>IIb</i>	>300	50	C <sub>12</sub> H <sub>11</sub> ClN <sub>4</sub> O	54.86	4.22	21.33
	DMF/H <sub>2</sub> O		262.70	55.00	4.30	21.55
<i>IIc</i>	256	50	C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> OS	55.36	4.65	21.52
	DMF/Ether		260.32	55.60	4.40	21.22
<i>IId</i>	>300	52	C <sub>10</sub> H <sub>10</sub> N <sub>6</sub> O	52.17	4.38	36.51
	DMF/H <sub>2</sub> O		230.23	52.55	4.25	36.35
<i>III</i>	288	89	C <sub>6</sub> H <sub>9</sub> N <sub>5</sub> O	43.11	5.43	41.90
	EtOH		167.17	43.55	5.29	42.03
<i>IVa</i>	200	45	C <sub>11</sub> H <sub>13</sub> N <sub>5</sub> O	57.12	5.67	30.28
	EtOH		231.27	57.48	5.34	30.00
<i>IVb</i>	>300	52	C <sub>10</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub>	51.49	4.75	30.03
	DMF/H <sub>2</sub> O		233.23	51.95	4.57	29.88
<i>IVc</i>	>300	60	C <sub>9</sub> H <sub>11</sub> N <sub>5</sub> O <sub>2</sub>	48.86	5.01	31.66
	DMF/H <sub>2</sub> O		221.22	49.02	4.88	31.44
<i>Va</i>	252	50	C <sub>10</sub> H <sub>9</sub> N <sub>5</sub> O <sub>3</sub>	48.58	3.67	28.33
	AcOH		247.21	49.00	3.47	28.06
<i>Vb</i>	205	30	C <sub>10</sub> H <sub>11</sub> N <sub>5</sub> O <sub>3</sub>	48.19	4.45	28.10
	AcOH/H <sub>2</sub> O		249.23	48.60	4.33	27.96
<i>Vc</i>	298	45	C <sub>14</sub> H <sub>11</sub> N <sub>5</sub> O <sub>3</sub>	56.56	3.73	23.56
	AcOH		297.27	56.99	3.54	23.23

and substituted benzylidenes *Vla-d* was refluxed for 12-15 hrs. at 110-120°C in sand bath. Sodium bicarbonate solution was added for removal of excess of thiolactic acid. The products were isolated and recrystallized to give *VIIa-d*. (Table 2).

2-[2'-(2-Thienyl)-5'-methyl-4'-thiazolidinon-3'-yl]pyrimidine (*VIIIe*). A mixture of thiolactic acid (0.01 mol) and thienylidene *VIe* (0.01 mol) was refluxed for 15 hrs. at 110-120°C in sand bath. Sodium bicarbonate solution was added for removal of excess acid. The product was isolated and recrystallized to give *VIIIe* (Table 2).

2-(Thiosemicarbazido)pyrimidine (*IX*). To a solution of 2-aminopyrimidine (0.01 mol) in DMF (10 ml) sodium hydroxide (0.01 mol) and carbon disulphide (0.75 ml) were added, stirred at 15-20°C for 1 hr. Then hydrazine hydrate (0.01 mol) was

added and stirred at 60°C for 5 hrs more. On adding water, a solid was separated out, filtered off, washed with water and recrystallized to give *IX*. (Table 3).

2-(2'-Mercapto-1',3',4'-thiadiazol-5'-yl)aminopyrimidine (*X*). Compound *IX* (0.01 mol) and carbon disulphide (0.01 mol) in DMF (10 ml) were stirred and heated at 95-100°C in the presence of TEA (2 ml) for 15 hr., and carbon disulphide was distilled off. The solid obtained on adding crushed ice and acetic acid was filtered off, washed with water and recrystallized to give *X*. (Table 3).

2-[3'-[(Diethylamino), (piperidino), (morpholino) and/or (N-methyl-piperazino)methyl]-2'-thio-1',3',4'-thiadiazol-5'-yl]aminopyrimidine (*XIa-d*). A mixture of paraformaldehyde (0.01 mol) and the appropriate secondary amines (0.02 mol),

**Table 2**  
Physical and analytical data of the prepared compounds

Comp. No.	M.P.[°C] Solvent	Yield %	Form (M. Wt)	Analysis %Calculated/Found		
				C	H	N
<i>Vla</i>	173	68	C <sub>11</sub> H <sub>8</sub> ClN <sub>3</sub>	60.70	3.70	19.31
	EtOH		217.65	60.40	4.00	18.95
<i>Vlb</i>	171	74	C <sub>11</sub> H <sub>8</sub> N <sub>4</sub> O <sub>2</sub>	57.89	3.53	24.55
	EtOH		228.20	57.60	3.90	24.35
<i>Vlc</i>	143	84	C <sub>13</sub> H <sub>14</sub> N <sub>4</sub>	69.00	6.24	24.76
	EtOH		226.28	69.40	5.90	24.70
<i>Vld</i>	175	84	C <sub>12</sub> H <sub>11</sub> N <sub>3</sub> O	67.59	5.20	19.71
	EtOH		213.23	67.60	5.00	19.40
<i>Vle</i>	175	63	C <sub>9</sub> H <sub>7</sub> N <sub>3</sub> S	57.12	3.73	22.21
	EtOH		189.23	57.30	4.00	21.95
<i>VIIa</i>	120	60	C <sub>13</sub> H <sub>10</sub> ClN <sub>3</sub> OS	53.51	3.45	14.40
	EtOH		291.76	53.75	3.35	14.17
<i>VIIb</i>	162	75	C <sub>13</sub> H <sub>10</sub> N <sub>4</sub> O <sub>3</sub> S	51.65	3.33	18.53
	EtOH		302.31	52.00	3.20	18.35
<i>VIIc</i>	122	77	C <sub>15</sub> H <sub>16</sub> N <sub>4</sub> OS	59.97	5.37	18.65
	EtOH		300.38	60.30	5.22	18.55
<i>VIIId</i>	129	67	C <sub>14</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S	58.52	4.56	14.62
	EtOH		287.33	58.85	4.35	14.33
<i>VIIe</i>	95	60	C <sub>11</sub> H <sub>9</sub> N <sub>3</sub> OS <sub>2</sub>	50.17	3.44	15.96
	EtOH		263.33	49.99	3.23	15.75
<i>VIIIa</i>	210	57	C <sub>14</sub> H <sub>12</sub> ClN <sub>3</sub> OS	54.98	3.96	13.74
	MeOH		305.79	55.15	4.16	13.44
<i>VIIIb</i>	242	57	C <sub>14</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub> S	53.15	4.82	17.71
	DMF/H <sub>2</sub> O		316.33	53.50	4.02	17.50
<i>VIIIc</i>	238	57	C <sub>16</sub> H <sub>18</sub> N <sub>4</sub> OS	61.12	5.78	17.82
	EtOH		314.42	61.00	5.50	17.55
<i>VIIIId</i>	268	64	C <sub>15</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub> S	59.78	5.02	13.94
	DMF/EtOH		301.37	60.03	4.87	13.78
<i>VIIIe</i>	276	55	C <sub>12</sub> H <sub>11</sub> N <sub>3</sub> OS <sub>2</sub>	51.96	4.00	15.15
	DMF/EtOH		277.36	52.15	3.87	14.96

namely, diethylamine, piperidi, morpholine and/or N-methylpiperazine was refluxed for 30 min., in absolute ethanol. Compound **X** (0.01 mol) in (10 ml) absolute ethanol was added to the reaction mixture and refluxed for 8-12 hrs. On evaporation of ethanol and scratching the residue with ethyl acetate, the resulting solid was filtered off and recrystallized to give *XIa-d*. (Table 3).

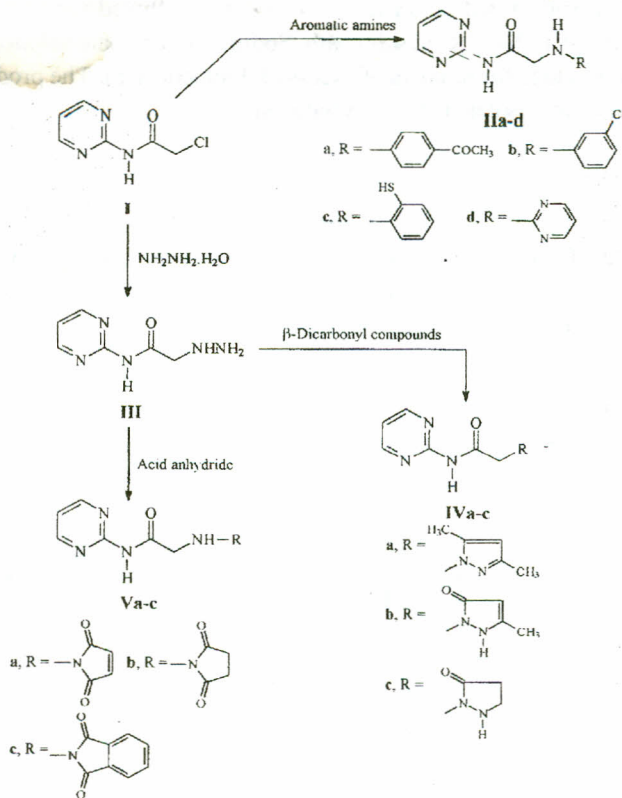
## Results and Discussion

**Synthesis and Characterization:** The present investigation deals with the synthesis and antimicrobial evaluation of a series of the new heterocyclic compounds incorporated into pyrimidine moiety.

2-Aminopyrimidine was chloroacetylated [Jani *et al* 1990 and Nabih *et al* 1986] with chloroacetyl chloride in dry benzene to get 2-[N-chloroacetyl]pyrimidine (**I**). IR spectrum of **I** showed peaks at 3180 (NH), 2920 (CH-aliphatic), 1650 (C=O), 1560 (C=N), 730 (C-Cl).

Condensation of **I** with various aromatic amines yielded compounds *Ila-d*. [Jani *et al* 1990] (Scheme 1) which were confirmed by the spectral data. IR (KBr,  $\text{cm}^{-1}$ ) of *Ila*: 3300 (NH), 1690 (C=O), 1640 (C=O), 1630 (C=N), 1580 (C=C). Ms,  $m/z$  (%) of *Ila*: 270 (6), 135 (69), 120 (100) and 92 (20). Ms,  $m/z$  (%) of *Ilc*: 249 (18), 248 (100), 125 (4), 124 (35) and 80 (6).

It has been reported that, [Nabeta *et al* 1972] various compounds bearing hydrazide moiety showed pharmacological activities. This urged the preparation of hydrazinoacetamido pyrimidine **III** via the reaction of 98% hydrazine hydrate with **I** (Scheme 1). The spectral data showed IR (KBr,  $\text{cm}^{-1}$ ) of **III**: 3420, 3300 (NH,  $\text{NH}_2$ ), 1710 (C=O), 1620 (C=N), 1600 (C=C).  $^1\text{H}$ -



NMR (DMSO) of **III**:  $\delta$  4.2 (2H, s,  $\text{NH}_2$ ), 4.4 (2H, s,  $\text{NCH}_2$ ), 7.0-7.5 (3H, m, pyrimidine), 8.6 and 9.4 (2H, 2s, 2NH). Ms,  $m/z$  (%): 167,  $\text{M}^+$  (10), 162 (100), 134 (11), 106 (30), 93 (14) and 79 (31).

Further, the hydrazide derivative **III** was allowed to react with acetylacetone, ethyl acetoacetate and/or ethyl-3-bromopropionate to give pyrazole and pyrazolone derivatives *IVa-c*

**Table 3**  
Physical and analytical data of the prepared compounds

Comp. No.	M.P. [°C] Solvent	Yield %	Formula (M.wt)	Analysis % Calculated/Found		
				C	H	N
<i>IX</i>	172	90	$\text{C}_5\text{H}_7\text{N}_5\text{S}$	35.49	4.17	41.39
	DMF		169.22	35.70	4.20	41.17
<i>X</i>	150	92	$\text{C}_6\text{H}_5\text{N}_5\text{S}_2$	34.11	2.38	33.15
	EtOH		211.26	34.45	2.52	32.98
<i>XIa</i>	160	63	$\text{C}_{11}\text{H}_{16}\text{N}_6\text{S}_2$	44.57	5.44	28.35
	EtOH		296.42	44.99	5.23	28.15
<i>XIb</i>	175	43	$\text{C}_{12}\text{H}_{16}\text{N}_6\text{S}_2$	46.73	5.23	27.25
	MeOH		308.43	47.12	5.02	26.90
<i>XIc</i>	309	50	$\text{C}_{11}\text{H}_{14}\text{N}_6\text{OS}_2$	42.56	4.55	27.08
	AcOH		310.40	43.00	4.67	27.28
<i>XId</i>	>300	50	$\text{C}_{12}\text{H}_{17}\text{N}_7\text{S}_2$	44.56	5.30	30.32
	AcOH		323.46	44.18	4.90	29.90

(Omar 1997 ; Zayed *et al.*, 1981) (Scheme 1), which were confirmed by the spectral data. IR (KBr,  $\text{cm}^{-1}$ ) of *IVb*: 3400 (NH), 1720, 1700 (2 C=O), 1620 (C=N), 1600 (C=C).  $^1\text{H-NMR}$  (DMSO) of *IVb*:  $\delta$  2.2 (3H, s,  $\text{CH}_3$ ), 4.4 (2H, s,  $\text{NCH}_2$ ), 5.3 (1H, s, CH, pyrazole), 7.0-7.5 (3H, m, pyrimidine), 8.4 and 8.6 (2H, 2s, 2 NH). Ms,  $m/z$  (%): 233,  $\text{M}^+$  (14), 218 (8), 135 (29), 121 (11), 98 (67), 95 (100) and 79 (11).

Also, the hydrazide derivative *III* was reacted with maleic anhydride, succinic anhydride phthalic anhydride to afford the corresponding substituted imido derivatives *Va-c* [Nofal *et al.*, 1997] (Scheme 1), IR (KBr,  $\text{cm}^{-1}$ ) of *Vb*: 3350 (NH), 1775, 1710 (2 C=O), 1690 (C=O), 1620 (C=N), 1600 (C=C).  $^1\text{H-NMR}$  (DMSO) of *Vc*:  $\delta$  4.4 (2H, s,  $\text{NCH}_2$ ), 7.2-8.0 (7H, m, aromatic protons) and 8.4, 8.6 (2H, 2s, 2 NH).

Schiff's bases [Kassem *et al.*, 1995] have gained prominent anti-microbial activities. Therefore it is of interest to synthesize some new Schiff's bases incorporated into the pyrimidine moiety. Reaction of 2-aminopyrimidine with different aromatic heterocyclic aldehydes led to the formation of the respective Schiff's bases *VIa-e* (Scheme 2).

Spectral analysis of prepared compounds showed the IR of *VIa*: 2810-2850 ( $\text{OCH}_3$ ), 1620 (C=N), 1600 (C=C) and of *VIe*: 1620 (C=N), 1600 (C=C) and 660 (C-S-C).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) of *VIa*:  $\delta$  3.8 (3H, s,  $\text{OCH}_3$ ), 5.4 (1H, s, CH) and 7.0-7.5 (7H, m, aromatic protons). Ms,  $m/z$  (%) of *VIa*: 217,  $\text{M}^+$  (32), 218 (100), 182 (7), 106 (18) and 79 (54).

4-Thiazolidinones and pyrimidines are associated with various biological activities. With an intention to prepare more

active drugs, we have synthesized 4-thiazolidinone derivatives [Patolia *et al.* 1994] having pyrimidine moiety *VIIa-e* and *VIIIa-e* by the action of thioglycolic acid and thiolactic acid on Schiff's bases (Scheme 2). These compounds were established by the IR (KBr,  $\text{cm}^{-1}$ ) of *VIIa,b*: 1700 (C=O), 1620 (C=N), 1600 (C=C) and 660 (C-S-C).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) of *VIIa*:  $\delta$  3.6 (2H, s,  $\text{CH}_2$  thiazolidinone), 5.6 (1H, s, CH thiazolidinone) and 6.6-7.8 (7H, m, aromatic protons).  $^1\text{H-NMR}$  (DMSO) of *VIIc*:  $\delta$  2.8 (2H, s,  $\text{CH}_2$  thiazolidinone), 3.1 (6H, s, 2  $\text{CH}_3$ ), 5.2 (1H, s, CH thiazolidinone) and 6.9-7.4 (7H, m, aromatic protons).  $^1\text{H-NMR}$  (DMSO) of *VIIId*:  $\delta$  3.6 (3H, s,  $\text{OCH}_3$ ), 3.8 (2H, s,  $\text{CH}_2$  thiazolidinone), 5.2 (1H, s, CH thiazolidinone) and 6.5-7.3 (7H, m, aromatic protons). Ms,  $m/z$  (%) of *VIIb*: 302,  $\text{M}^+$  (11), 181 (17), 180 (5), 106 (5), 93 (7), 80 (100) and 79 (49).

IR (KBr,  $\text{cm}^{-1}$ ) of *VIIIa*: 2940 (CH), 1710 (C=O), 1610 (C=N), 1580 (C=C) and 740 (C-Cl).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) of *VIIIa*:  $\delta$  1.4 (3H, s,  $\text{CH}_3$  thiazolidinone), 3.4 (1H, s, CH of thiazolidinone at  $\text{C}_3$ ), 5.6 (1H, s, CH of thiazolidinone at  $\text{C}_2$ ) and 6.9-7.4 (7H, m, aromatic protons).

1,3,4-Thiadiazoles have been reported to possess antimicrobial, fungicidal, herbicidal and antiviral activities [Ahluwalia *et al.* 1987]. So, compound X have been synthesized by the condensation of 2-amino-pyrimidine with  $\text{CS}_2$  and hydrazine hydrate followed by the cyclization of the intermediate thiosemicarbazide IX with  $\text{CS}_2$  in presence of TEA [Ahluwalia *et al.*, 1987] (Scheme 3).

IR (KBr,  $\text{cm}^{-1}$ ) of IX: 3400, 3300, 3200 (NH, NH,  $\text{NH}_2$ ), 1620 (C=N), 1600 (C=C) and 1100 (C=S). IR of X: 3100 (NH), 2700 (SH), 1630 (C=N), 1600 (C=C) and 1120 (C=S).

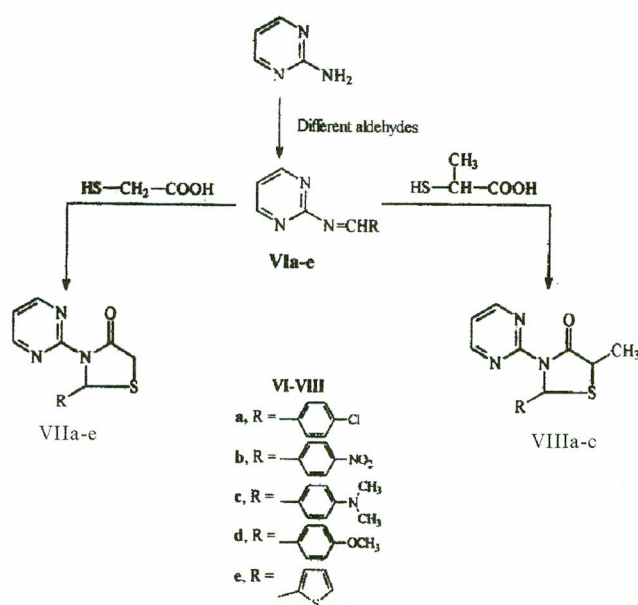
Applying the Mannich reaction conditions on compound X yielded the corresponding Mannich bases *XIa-d* [Kassem and El-Masry, 1995] (Scheme 3).

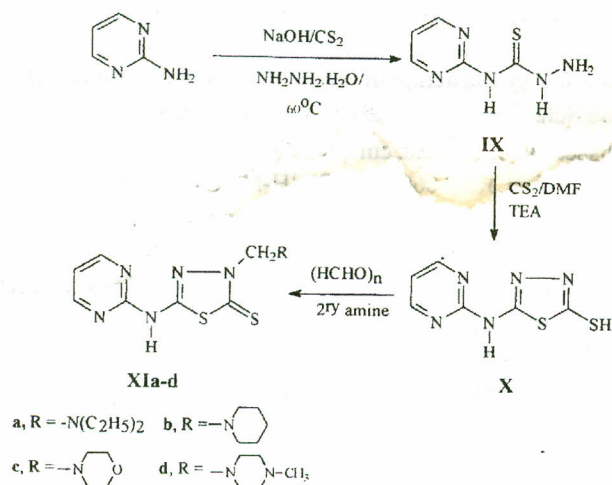
IR spectrum of *XIa* showed bands at: 3300 (NH), 1620 (C=N), 1600 (C=C), 1100 (C=S) and 620 (C-S-C).

**Biological Part. Antimicrobial Activity.** The test was performed according to the cup-plate method [Abou-Zeid *et al.*, 1969] adopted with some modifications for the prepared compounds using chloramphenicol as reference (500  $\mu\text{/disk}$ ).

The prepared compounds were tested against three strains of Gram -ve bacteria (*E. coli*, *P. aeruginosa* and *K. pneumoniae*), one strain of Gram +ve bacteria (*B. subtilis*) and one strain of fungi (*A. niger*) (500  $\mu\text{/disk}$ ).

From the data obtained (Table 4), it is clear that compounds *IIC*, *VIa,e*, *VIIa* and *X* possess moderate activity towards *K. pneumoniae*. Also, compound *III*, *VIa* and *VIIa* possess moderate activity against *B. subtilis*, but compound *I* possesses moderate activity against *P. aeruginosa*, where some of the





Scheme 3

Table 4

Antimicrobial activity of the tested compounds

Comp. No.	1	2	3	4	5
2-aminopyrimidine	-	+	+	++	+
Chloramphenicol	+++	++	+	+++	+++
I	+	++	+	+	+
IIc	+	+	++	+	+
III	+	+	+	++	+
IVb	+	+	+	+	+
Vc	+	+	+	+	+
VIa	+	-	++	++	+
VIe	-	+	++	+	+
VIIa	+	-	++	++	+
VIIIe	+	-	+	+	+
X	+	+	++	+	+
XI	-	+	+	+	+

- *Escherichia coli*                      - *Bacillus subtilis*  
 - *Pseudomonas aeruginosa*       - *Aspergillus niger*  
 - *Klebsiella pneumonia*

Reference used was chloramphenicol (500 µ/disk).

+++ = Highly active (inhibition zone 12-15 mm)

++ = Moderately active (inhibition zone 9-12 mm)

+ = Moderately active (inhibition zone 6-9 mm)

- = not active

tested compounds show slight activity against all the tested organisms. Compounds VIe and XIa are not active against *E. coli* and compounds VIa, VIIa and VIIIe are not active against *P. aeruginosa*.

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the fact that the magnesium carbonate component of dolomite decomposes at temperatures below 750°C (normally between 500 - 600°C). The partial calcining process proceeds according to the equation 1; hydration (equation 2) and recarbonation (equation 3) then follows:



The process is studied by three methods, differential thermal analysis (DTA), x-ray diffraction (XRD), and infrared spectroscopy (Ghosh *et al* 1976).

*Application in glass.* Dolomite is introduced in the glass composition (Rafique *et al* 1971) where it is desired to have both calcium and magnesium as in the case of sheet glass, container glass, electric light bulbs glass and also in tungsten sealing glasses. The oxide compositions and properties of these glasses are given in Table 1 (Charan 1956; Patric and Bowden 1962)

The low iron glass grade local dolomite is found suitable for use in the above compositions when blended with good quality glass making raw materials silica sand, soda ash and feldspar, produced good quality glass of the required specifications.

*Application in refractory.* The process of magnesia-silica bricks of over-burned lime involves separating a fraction consisting mainly of particles of 106 microns from calcined dolomite. This fraction is then slaked to substantially complete hydration of magnesium oxide and the remaining calcium oxide. The separation of this fraction can be done by sieving or by using an air classifier, whereby gritty particles are rejected. The gritty particles consisted mainly of magnesium oxide and 106 micron fraction consisted half the original amount of magnesium oxide. In this way the two allotropic forms of magnesium oxide L-form and B-form are separated. Although both the forms have the same chemical composition but they differ in several important respects: (i) the A-variety is soluble in acid while the B-variety is very resistant to this action, (ii) A-form is amorphous while B-form is crystalline, B-form or 106 micron fraction is desirable as a refractory material on accounts of its constancy of volume at different temperatures. It is surprising that no phosphate agents were used in this application in the light of their desirable effect. It is anticipated that the use of such additives will improve the quality of magnesia-silica bricks.

While forming bricks, the moisture to be maintained is: 12 - 20 % of 4 - 6 mm grains, 25 - 34 % of 1 - 4 mm grains, and 28 - 34 % of 1 - 4 mm grains. The raw dolomite brick is dried in tunnel driers at 90 - 180°C for 12 - 15 h.

The dried brick must have a compressive strength not less than 100 kg/cm<sup>3</sup> and contain not more than 0.8 % uncombined moisture. The firing is done in tunnel kilns with

a holding period of 6 - 10 hr at 1550°C or in batch kiln for 24 - 40 hr at 1450°C (Prescott 1980).

## Results and Discussion

Dolomite is used as a partial replacement of lime stone when it is desired to have magnesium in glass composition as in the case of flat glasses and particularly in container glass. Partial lime stone replacement by dolomite introduces magnesia which improves workability and reduces the likelihood of devitrification. In the flat glass process, molten glass is held at one stage at very low temperature, and the possibility of devitrification is high, so the presence of magnesia is extremely valuable. Dolomite is also used for tableware or pressed ware where enhanced workability is a benefit.

In view of the mounting price of soda ash, the glass manufacturer should look hard at the use of dolomite in the batch composition of glass. It will be advantageous, at least, in two respects: (1) it will improve the quality of the finished product enhancing its strength and reducing brittleness, (ii) soda ash as a proportion of batch weight will decrease from about 15 % to 11 %. There are two routes to cut down the cost of soda ash in the glass batch: (i) to increase alumina level, (ii) to introduce magnesia. The former is ruled out through the economics of supply and demand while the latter is viable subject to the availability of good quality dolomite, no scarcity in Pakistan, is a significant factor in the decision to change to magnesia (low soda composition). Adoption of dolomite by glass maker means not only a reduction in soda ash requirement, but an incidental decrease in lime stone needs.

**Table 1**  
Dolomite containing glass compositions

Oxide %	Sheet glass	Fibre glass	Electric bulb glass	Tungsten seal glass	Container glass	White neutral glass
SiO <sub>2</sub>	73.0	59.0	73.6	58.5	73.6	67.0
Al <sub>2</sub> O <sub>3</sub>	0.5	4.5	----	22.5	2.0	8.5
CaO	8.0	16.0	5.4	6.3	9.0	4.0
NaO	15.5	11.0	17.2	----	17.8	8.7
K <sub>2</sub> O <sub>2</sub>	----	0.5	----	0.8	1.1	4.0
B <sub>2</sub> O <sub>3</sub>	----	3.5	----	3.0	2.5	----

**Table 2**  
Chemical composition of glasses

Article	SiO <sub>2</sub> %	Al <sub>2</sub> O <sub>3</sub> %	Fe <sub>2</sub> O <sub>3</sub> %	Mn <sub>2</sub> O <sub>3</sub> %	CaO %	MgO %	B <sub>2</sub> O <sub>3</sub> %
Dolomite burned	16.52	1.19	2.67	0.76	46.05	30.05	1.18
Dolomite unburned	16.50	1.21	2.71	0.72	46.00	30.10	1.15
Dolomite with free lime	2.03	2.0	2.77	----	53.5	39.7	0.05

**Table 3**  
Properties of glasses

Article	Bulk density g/c.c	Cold crushing Kg/cm <sup>2</sup>	Refractoriness	Excess shrinkage	Temperature in Co of deformation under load of 2 Kg/cm <sup>2</sup>		
					Deformation begining of T <sup>1</sup>	Deformation 2% T <sup>2</sup>	Deformation 3.2% T <sup>3</sup>
Dolomite	2.8	1080	1770	1.37	1550	1630	1680
Burned	2.9	1335	1780		1610	1680	1690
Dolomite	2.7	116	1780	----	-----	-----	-----
Unburned	2.78	160					
Dolomite with free lime	3.04 3.12	1680	----	0.5	1670	1820	1820

Free MgO and free CaO are the most valuable in burned dolomite and in articles made of them. The maximum content of free CaO is associated with the minimum content of SiO<sub>2</sub> which combines with it to form 3CaO SiO<sub>2</sub>, and with a limited content of sesquioxides (Al<sub>2</sub>O<sub>3</sub> + Fe<sub>2</sub>O<sub>3</sub> + Mn<sub>3</sub>O<sub>4</sub>) which have had effects on product quality, and it is particularly important that their content be low. The sintering temperature varies with the grain size of the rock. Thus the sintering temperature of uncrushed dolomite is 1600 - 1650°C, the granular dolomite (5 - 16 mm) is above 1700°C, the coarse crushed dolomite (30 - 40 mm) is 1600 - 1650°C and that of the lumps dolomite (30 - 120 mm) is 1450 - 1550°C. The sintering temperature of uncrushed dolomite increases with grain size and with decreasing sesquioxide content. The alkalis contained in mica, as well as silica or gypsum, adversely affects sintering.

The dolomite lumps must be from 2 to 20 mm in size, fraction under 2 mm not over 3%, fraction 2 - 4 mm, not over 15 %, lumps over 20 mm, not more than 5%. Lumps dolomite prepared from hard-to-sinter raw rock, even after burning at 1700°C slakes very rapidly in air and disintegrates as early as the 16th day. Wet ground dolomite without additions resists slaking fairly well after burning at 1500°C and keeps rather long in air. Decreasing free lime from 45 % to 15 - 30 % considerably slows slaking.

Dolomite is the most valuable industrial mineral and its application in glass and refractory is beneficial and advantageous. Since this mineral, from glass grade to refractory grade, is found in Pakistan in huge quantities, its industrial exploitation is badly needed. To increase our knowledge

about the material, the promotion of research is of vital importance.

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