J. Serb. Chem. Soc. 77 (1) 17–26 (2012) UDC 547.869+547.789+542.913:615.28–188
JSCS–4245 *Original scientific paper*

Synthesis and biological activity of 4-thiazolidinone derivatives of phenothiazine

RITU SHARMA*, PUSHKAL SAMADHIYA, SAVITRI D. SRIVASTAVA and SANTOSH K. SRIVASTAVA

Synthetic Organic Chemistry Laboratory, Department of Chemistry, Dr. H. S. Gour University (A Central University), Sagar-470003, India

(Received 24 September 2010, revised 24 April 2011)

Abstract: A new series of *N*-[3-(10*H*-phenothiazin-10-yl)propyl]-2-(substituted phenyl)-4-oxo-5-(substituted benzylidene)-3-thiazolidinecarboxamide, **5a**–**s** were synthesized. The reaction of thioglycolic acid with *N*-[3-(10*H*-phenothiazin-10-yl)propyl]-*N*'-[(substituted phenyl)methylidene]urea, **3a**–**s** in the presence of anhydrous $ZnCl_2$ afforded the new heterocyclic compounds *N*-[3-(10*H*-phenothiazin-10-yl)propyl]-2-(substituted phenyl)-4-oxo-3-thiazolidinecarboxamide, **4a**–**s**. The latter product on treatment with several selected substituted aromatic aldehydes in the presence of C_2H_5ONa underwent the Knoevenagel reaction to yield **5a**–**s**. The structure of compounds **1**, **2**, **3a**–**s**, **4a**–**s** and **5a**–**s** were confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and FAB mass spectroscopy and by chemical analysis. All the above compounds were screened for their antimicrobial activity against some selected bacteria and fungi and for their antituberculosis activity, the compounds were screened against the bacterium *Mycobacterium tuberculosis*.

Keywords: synthesis; phenothiazine; 4-oxothiazolidine; antimicrobial; antitubercular.

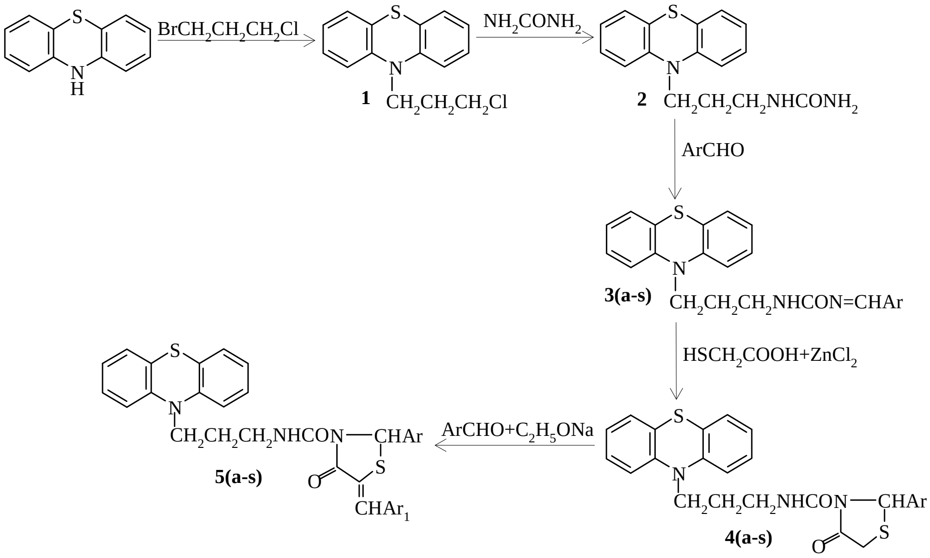
INTRODUCTION

Thiazolidines have been shown to possess various remarkable biological activities such as analgesic,[1] amoebicidal,[2] nematocidal,[3] anaesthetic,[4] mosquito-repellent,[5] anti-HIV, anticancer,[6] antibacterial,[7–12] antifungal,[13–14] antiinflammatory,[16–19] antitubercular,[20–22] EGFR and HER-2 kinase inhibitor,[23] antiproliferative,[24,25] *etc*. Phenothiazine is also a bioactive heterocyclic compound of pharmaceutical importance and possesses different biological activities *viz*. antibacterial,[26,27] antifungal,[28] antitubercular,[29] and anti-inflammatory.[30] In the present study, compounds **1**, **2**, **3a**–**s**, **4a**–**s** and **5a**–**s** were synthesized as shown in Scheme 1. The starting material, phenothiazine with 1-bromo-3-chloropropane un-

* Corresponding author. E-mail: ritusharmaic@rediffmail.com
doi: 10.2298/JSC100924152S

Available online at www.shd.org.rs/JSCS/

2012 Copyright (CC) SCS



Ar= substituted phenyl ring

Compound	Ar = Ar_1	Compound	Ar = Ar_1	Compound	Ar = Ar_1
3a, **4a**, **5a**	C_6H_5	**3h**, **4h**, **5h**	4-$NO_2C_6H_4$	**3o**, **4o**, **5o**	3-$CH_3OC_6H_4$
3b, **4b**, **5b**	4-ClC_6H_4	**3i**, **4i**, **5i**	3-$NO_2C_6H_4$	**3p**, **4p**, **5p**	2-$CH_3OC_6H_4$
3c, **4c**, **5c**	3-ClC_6H_4	**3j**, **4j**, **5j**	2-$NO_2C_6H_4$	**3q**, **4q**, **5q**	4-HOC_6H_4
3d, **4d**, **5d**	2-ClC_6H_4	**3k**, **4k**, **5k**	4-$CH_3OC_6H_4$	**3r**, **4r**, **5r**	3-HOC_6H_4
3e, **4e**, **5e**	4-BrC_6H_4	**3l**, **4l**, **5l**	3-$CH_3OC_6H_4$	**3s**, **4s**, **5s**	2-HOC_6H_4
3f, **4f**, **5f**	3-BrC_6H_4	**3m**, **4m**, **5m**	2-$CH_3OC_6H_4$		
3g, **4g**, **5g**	2-BrC_6H_4	**3n**, **4n**, **5n**	4-$CH_3C_6H_4$		

Scheme 1. Reaction scheme for synthesis of compounds **1**–**5**.

derwent an nucleophilic substitution reaction yielding 10-(3-chloropropyl)-10*H*-phenothiazine, compound **1**. Compound **1** on reaction with urea afforded *N*-[3-(10*H*-phenothiazin-10-yl)propyl]urea, compound **2**. Compound **2** on reaction with several selected substituted benzaldehydes underwent a condensation reaction to afford *N*-[3-(10*H*-phenothiazin-10-yl)propyl]-*N*'-[(substituted phenyl)-methylidene]urea, compounds **3a**–**s**. The reaction of thioglycolic acid with compounds **3a**–**s** in the presence of anhydrous $ZnCl_2$ gave new heterocyclic compounds *N*-[3-(10*H*-phenothiazin-10-yl)propyl]-2-(substituted phenyl)-4-oxo-3--thiazolidinecarboxamide, compounds **4a**–**s**. Compounds **4a**–**s** on treatment with various selected substituted benzaldehydes in the presence of C_2H_5ONa underwent a Knoevenagel condensation reaction to yield the final products *N*-[3-(10*H*--phenothiazin-10-yl)propyl]-2-(substituted phenyl)-4-oxo-5-(substituted benzylidene)-3-thiazolidine-carboxamide, compounds **5a**–**s**. The structures of all the newly synthesized compounds **1**, **2**, **3a**–**s**, **4a**–**s** and **5a**–**s** were confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and FAB mass spectroscopy and by chemical analysis. All

Available online at www.shd.org.rs/JSCS/

2012 Copyright (CC) SCS

the above compounds were screened for their antimicrobial activity against some selected bacteria and fungi and antituberculosis activity against *Mycobacterium tuberculosis*.

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. The progress of the reactions was monitored on silica gel-G coated TLC plates using MeOH : $CHCl_3$ (1:9). The spot was visualized by exposing the dry plate to iodine vapour. The IR spectra were recorded in KBr discs on a Shimadzu 8201 PC FTIR spectrophotometer (ν_{max} in cm^{-1}) and the ^{1}H- and ^{13}C-NMR spectra were measured on a Bruker DRX-300 spectrometer in $CDCl_3$ at 300 and 75 MHz, respectively, using TMS as an internal standard. All chemical shifts are reported on δ scales. The FAB mass spectra were recorded on a Jeol SX–102 mass spectrometer. Elemental analyses were realised on a Carlo Erba-1108 analyzer. The 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 employed reagent grade chemicals were purchased from commercial sources and further purified before use.

*Synthesis of 10-(3-chloropropyl)-10*H*-phenothiazine, compound **1***

Phenothiazine (0.301 mol) and 1-bromo-3-chloropropane (0.301 mol) in ethanol (100 ml) were stirred on a magnetic stirrer for 5.0 h at room temperature. Completion of the reaction was monitored on silica gel-G coated TLC plates. The product was filtered and purified over a silica gel packed column chromatography using $CHCl_3$:CH_3OH (8:2 v/v) as the eluant (120 ml). The purified product was dried under vacuum and recrystallized from acetone to yield compound **1** (Fig. 1).

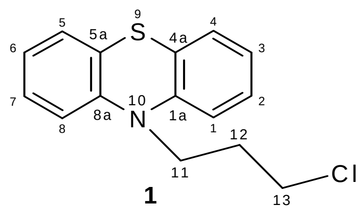


Fig. 1. Structure of compound **1**.

Synthesis of N*-[3-(10*H*-phenothiazin-10-yl)propyl]urea, compound **2***

Compound **1** (0.20 mol) and urea (0.20 mol) in ethanol (100 ml) were stirred on a magnetic stirrer for 4.0 h at room temperature. The completion of the reaction was monitored by silica gel-G coated TLC plates. The product was filtered and purified over a silica gel packed column chromatography using $CHCl_3$:CH_3OH (8:2 v/v) as eluant (120 ml). The purified product was dried under *vacuo* and recrystallized from ethanol to yield compound **2** (Fig. 2).

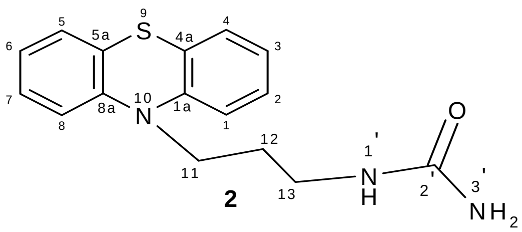


Fig. 2. Structure of compound **2**.

2012 Copyright (CC) SCS

Synthesis of N-*[3-(10*H-*phenothiazin-10-yl)propyl]*-N'-*(phenylmethylidene)urea, compound* ***3a***

Compound **2** (0.026 mol) and benzaldehyde (0.026 mol) in ethanol (100 ml) in the presence of 2–4 drops glacial acetic acid were first stirred on a magnetic stirrer for 2.0 h at room temperature followed by refluxing on a steam bath at 80–90 °C for 3.3 h. The completion of the reaction was monitored using silica gel-G coated TLC plates. The product was filtered, cooled and purified over a silica gel packed column chromatography using $CH_3OH:CHCl_3$ (7:3 v/v) as eluant (90 ml). The purified product was dried under vacuum and recrystallized from acetone at room temperature to furnish compound **3a** (Fig. 3).

Compounds **3b**–**s** (Fig. 3) were synthesized using a similar method.

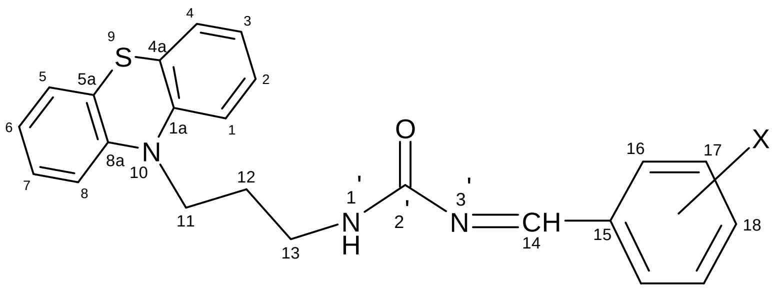


Fig. 3. Structure of compounds **3a**–**s**.

*Synthesis of 4-oxo-*N-*[3-(10*H-*phenothiazin-10-yl)propyl]-2-(phenyl)-3-thiazolidine-carboxamide, compound* ***4a***

Compound **3a** (0.0129 mol) and thioglycolic acid (0.0129 mol) in methanol (50 ml) in the presence of $ZnCl_2$ were first stirred on a magnetic stirrer for 2.0 h at room temperature followed by refluxing on a steam bath at 70–90 °C for 6.0 h. The completion of the reaction was monitored using silica gel-G coated TLC plates. The product was filtered, cooled and purified over a silica gel packed column chromatography using $CH_3OH:CHCl_3$ (7:3 v/v) as eluant (80 ml). The purified product was dried under vacuum and recrystallized from ethanol at room temperature to furnish compound **4a** (Fig. 4).

Compounds **4b**–**s** (Fig. 4) were synthesized using a similar method.

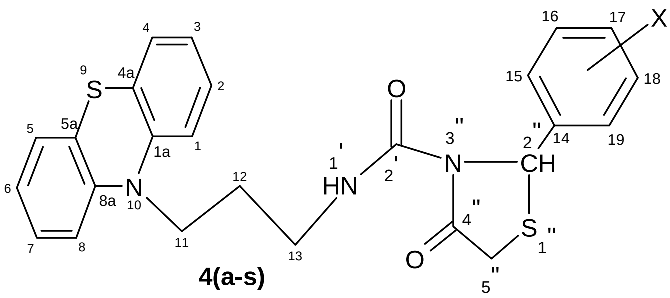


Fig. 4. Structure of compounds **4a**–**s**.

2012 Copyright (CC) SCS

*Synthesis of 4-oxo-*N*-[3-(10*H*-phenothiazin-10-yl)-propyl]-2-phenyl-5-(phenylmethylidene)--3-thiazolidinecarboxamide, compound **5a***

Compound **4a** (0.008 mol) and benzaldehyde (0.008 mol) in ethanol (50 ml) in the presence of CH_3CH_2ONa were first stirred on a magnetic stirrer for 2.0 h at room temperature followed by refluxing on a steam bath at 80–90 °C for 5.0 h. Completion of the reaction was monitored using silica gel-G coated TLC plates. The product was filtered, cooled and purified by a silica gel packed column chromatography using $CH_3OH:CHCl_3$ (7:3 v/v) as eluant (70 ml). The purified product was dried under vacuum and recrystallized from ethanol at room temperature to furnish compound **5a**.

Compounds **5b–s** were synthesized using a similar method.

Biological study

The antibacterial, antifungal and antitubercular activities of compounds **1**, **2**, **3a–s**, **4a–s** and **5a–s** were assayed *in vitro* against selected bacteria, *i.e.*, *Escherichia coli*, *Bacillus subtilis*, *Staphylococus aureus*, and selected fungi, *Aspergillus flavus*, *Aspergillus niger* and *Candida albicans* H37Rv strain. The inhibition zone (mm) of compounds **1**, **2**, **3a–s**, **4a–s** and **5a–s** were determined using the filter paper disc diffusion method[31] (antibacterial and antifungal activity) at two concentration of 50 and 100 ppm and the percentage activity of compounds **1**, **2**, **3a–s**, **4a–s** and **5a–s** were determined using the L. J. medium (conventional) method (antitubercular activity) at 25 and 50 μg mL^{-1} and lower concentrations. Streptomycin and griseofulvin were used as the standard for the antibacterial and antifungal activity, respectively, and for the antitubercular activity, isoniazid and rifampicin were taken as standards.

RESULTS AND DISCUSSION

The analytical and spectral data of the synthesized compounds are given in the Supplementary material to this paper.

The reaction of 1-bromo-3-chloropropane with phenothiazine was performed in ethanol as solvent to afford compound **1**. The spectroscopic analyses of compound **1** showed absorption peaks for N–CH, C–Cl and C–S–C at 1272, 774 and 687 cm^{-1} in the IR spectrum. The IR spectrum confirms the formation of compound **1**. This fact was also supported by the disappearance of NH absorption of the phenothiazine.

Compound **1** on reaction with urea under continuous stirring at room temperature yielded compound **2**. In the spectroscopic analyses of compound **2**, three absorption peaks were found in the IR spectrum for NH, NH_2 and CO at 3342, 3412 and 1655 cm^{-1}, respectively while the absorption of C–Cl found in the spectrum of **1** had disappeared. This clearly indicated that compound **1** underwent substitution reaction with urea. This fact was also supported by the ^{1}H- and ^{13}C-NMR spectra as two signals appeared in the ^{1}H-NMR spectrum for NH and NH_2 at δ 5.83 and 5.99 ppm, respectively. The formation of compound **2** was fully supported by the signal for the CO group at δ 163.4 ppm in the ^{13}C-NMR spectrum. All the facts together were strong evidence for the synthesis of compound **2**.

Available online at www.shd.org.rs/JSCS/

2012 Copyright (CC) SCS

Substituted benzaldehydes underwent condensation reaction with compound **2**, resulting in the formation of Schiff bases N=CH, which was confirmed by the IR, ^{1}H-NMR and ^{13}C-NMR spectra of compounds **3a**–**s**. In the IR spectra, an absorption was found in the range 1531–1584 cm^{-1}, while a strong signal appeared in the range of δ 7.84–8.34 and 143–158.4 ppm in the ^{1}H-NMR and ^{13}C-NMR spectra of compounds **3a**–**s**, respectively. These facts were also supported by the disappearance of the signal for NH_2 present in the ^{1}H-NMR spectrum of compound **2**.

Compounds **3a**–**s** on reaction with an equimolar amount of thioglycolic acid in the presence of $ZnCl_2$ underwent a reaction whereby a five-membered thiazolidinone ring was formed, compounds **4a**–**s**. Compounds **4a**–**s** showed a characteristic absorption for a cyclic carbonyl group in the range 1725–1758 cm^{-1} in the IR spectra. The ^{1}H-NMR spectra of compounds **4a**–**s** clearly indicated the presence of the active methylene group in the thiazolidine ring by exhibiting a signal in the range δ 3.26–3.68 ppm. The ^{13}C-NMR spectra of compounds **4a**–**s** also supported the fact that a cyclic carbonyl group was present by the signal that appeared in the range δ 160.4–178.8 ppm. These facts were supported by a) the disappearance of the N=CH proton and b) the appearance of a N–CH proton in the range of δ 5.23–5.82 ppm in the ^{1}H-NMR spectra of compounds **4a**–**s**.

Compounds **4a**–**s** underwent a Knoevenagel condensation reaction with substituted benzaldehydes in the presence of alkali metal alkoxide (C_2H_5ONa) to afford compounds **5a**–**s**. In the ^{1}H-NMR spectra of compounds **5a**–**s**, the two methylene protons of compounds **4a**–**s** were absent and a new signal for C=CH appeared in the range δ 6.32–6.77 ppm and in the ^{13}C-NMR spectra of compounds **5a**–**s**, two new signals for C=**C**H and **C**=CH appeared in the δ range 134.6–143.2 and 140.1–149.2 ppm, respectively. All these facts clearly confirmed the synthesis of all the final products.

Biological study

The results of the antimicrobial (antibacterial, antifungal and antitubercular) activities are summarized in Table I. All the compounds **1**, **2**, **3a**–**s**, **4a**–**s** and **5a**–**s** were screened for their antimicrobial activity against selected strains of bacteria and fungi and antitubercular activity against *M*. *tuberculosis* (H37Rv strain). The investigation of antimicrobial data revealed that compounds **5c**, **5d**, **5e**, **5f**, **5h**, **5i** and **5j** displayed high activity, compounds **4h**, **4j**, **5b**, **5g** and **5q** showed moderate activity and the other compounds showed less activity against all the strains compared with standard drugs.

The compounds exhibited a structure–activity relationship (SAR) because the activity of compounds varies with substitution. The nitro group-containing compounds **5h**, **5i** and **5j** showed higher activity than the chloro group- (**5c** and **5d**) or the bromo group-containing compounds (**5e** and **5f**). In addition, the

Available online at www.shd.org.rs/JSCS/

2012 Copyright (CC) SCS

chloro- and bromo-derivatives also had a higher activity than the other tested compounds. Based on the SAR, it could be concluded that the activity of compounds depended on the electron withdrawing nature of the substituent groups. The sequence of the activity is following:

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

TABLE I. Antibacterial, antifungal (inhibition zone in mm) and antitubercular activity of compounds **1**, **2**, **3a–s**, **4a–s** and **5a–s**

Compound	Antibacterial activity						Antifungal activity						Antitubercular activity, %	
	B. subtilis		*E. coli*		*S. aureus*		*A. niger*		*A. flavus*		*C. albicans*		*M. tuberculosis* H37Rv strain	
	c / ppm												*c* / µg mL^{-1}	
	50	100	50	100	50	100	50	100	50	100	50	100	25	50
1	–	7	–	5	4	7	–	8	4	6	–	5	13	20
2	2	9	–	7	2	6	5	8	4	7	3	6	10	18
3a	7	12	10	14	11	13	9	12	10	15	9	13	18	22
3b	10	20	11	18	13	19	10	17	13	17	11	14	25	32
3c	12	19	12	16	10	16	11	17	13	17	11	14	27	34
3d	10	13	14	17	12	19	13	20	14	20	13	17	30	35
3e	8	21	9	22	10	21	9	18	8	15	8	16	28	40
3f	9	20	10	21	11	20	8	14	6	13	6	17	27	50
3g	10	24	7	21	9	20	6	13	8	12	9	14	25	52
3h	13	26	10	24	13	27	10	18	12	25	14	22	32	65
3i	11	23	9	20	10	25	10	17	11	26	12	23	35	68
3j	13	27	10	24	12	26	10	18	10	24	11	22	38	66
3k	7	10	6	10	8	12	7	13	6	13	8	14	25	40
3l	8	12	6	13	7	13	6	14	7	13	7	12	28	42
3m	8	13	7	14	6	12	7	12	6	14	6	10	23	43
3n	4	10	5	12	4	11	6	13	5	9	4	10	20	38
3o	5	7	6	8	6	10	5	12	6	11	7	10	24	35
3p	5	8	5	9	4	7	6	10	5	9	6	11	25	38
3q	9	14	8	13	8	15	7	13	6	14	8	14	28	50
3r	10	16	9	14	8	13	7	12	7	15	9	14	30	52
3s	9	13	10	15	7	14	9	13	8	15	10	14	32	55
4a	15	20	13	19	14	20	10	15	12	20	10	14	20	35
4b	14	23	10	21	13	21	10	17	11	17	12	18	25	55
4c	10	27	10	28	12	27	11	20	10	19	11	21	30	60
4d	12	26	11	27	12	29	11	20	8	17	12	19	30	60
4e	10	29	10	27	10	28	9	21	8	17	10	19	30	68
4f	10	28	11	30	13	30	12	24	13	20	13	21	32	70
4g	17	30	8	31	10	30	7	20	8	21	10	22	30	75
4h	18	30	15	28	10	30	11	24	9	20	8	22	30	70
4i	10	22	13	24	12	28	10	12	9	19	8	20	32	68
4j	12	24	15	30	13	27	12	28	10	22	9	24	35	70

Available online at www.shd.org.rs/JSCS/

2012 Copyright (CC) SCS

TABLE I. Continued

Compound	Antibacterial activity						Antifungal activity						Antitubercular activity, %	
	B. subtilis		*E. coli*		*S. aureus*		*A. niger*		*A. flavus*		*C. albicans*		*M. tuberculosis* H37Rv strain	
	c / ppm												*c* / μg mL^{-1}	
	50	100	50	100	50	100	50	100	50	100	50	100	25	50
4k	10	14	9	22	10	20	8	21	9	17	7	21	30	50
4l	11	15	8	20	10	21	8	20	8	15	6	15	32	53
4m	9	14	10	16	8	18	8	15	7	14	7	13	30	50
4n	8	10	8	12	8	14	7	13	9	13	7	13	29	41
4o	9	13	8	14	7	13	7	13	8	12	8	10	28	42
4p	8	14	9	17	8	15	7	16	7	13	8	14	30	45
4q	16	26	18	30	14	29	14	25	12	22	13	25	33	70
4r	17	24	15	30	15	27	13	24	13	21	10	21	34	70
4s	12	20	11	22	10	21	11	23	10	18	10	22	33	65
5a	18	25	07	22	10	23	07	15	07	12	10	14	22	45
5b	15	29	10	30	15	29	12	20	10	20	14	21	32	74
5c	13	34	12	32	14	31	15	24	17	25	14	23	36	80
5d	15	32	10	31	13	32	11	23	10	21	13	22	32	80
5e	12	33	12	31	15	31	10	22	12	23	15	23	30	78
5f	11	31	11	31	14	32	11	22	11	21	14	23	30	79
5g	20	27	10	28	10	28	10	19	10	20	10	20	29	76
5h	22	35	19	33	12	34	18	24	09	24	12	25	32	82
5i	20	34	10	32	12	35	12	25	10	23	12	24	27	83
5j	24	36	11	33	10	33	13	25	11	22	10	24	28	81
5k	08	28	09	21	08	27	11	18	10	14	11	17	28	60
5l	11	26	12	23	12	25	10	16	12	15	12	16	30	63
5m	13	27	15	25	14	26	13	15	13	15	12	12	31	65
5n	14	18	14	17	16	22	10	15	10	13	10	14	22	45
5o	12	19	14	15	15	20	09	14	09	12	11	15	18	49
5p	14	20	15	18	14	19	08	12	10	18	09	15	20	47
5q	12	29	13	28	12	30	14	20	13	16	12	21	24	76
5r	13	28	14	24	13	27	13	18	13	17	13	20	27	70
5s	11	30	12	21	11	29	12	18	10	15	11	19	25	65
Standard	28	37	26	34	27	35	20	26	18	25	19	26	100	100
	Streptomycin						Griseofulvin						Standards[a]	

[a]Standards for the antitubercular activity, isoniazid and rifampicin, showed 100 % activity at both tested concentrations

CONCLUSIONS

The present research study reports the successful synthesis of all the newly synthesized compounds **1**, **2**, **3a**–**s**, **4a**–**s** and **5a**–**s**. Some of the synthesized compounds displayed good biological activities while the others showed lower antimicrobial and antitubercular activities.

Available online at www.shd.org.rs/JSCS/

2012 Copyright (CC) SCS

SUPPLEMENTARY MATERIAL

Analytical and spectral data of synthesized compounds are available electronically from http://www.shd.org.rs/JSCS/, or from the corresponding author on request.

Acknowledgements. The authors are thankful to SAIF, Central Drugs Research Institute, Lucknow (India) for providing the spectral and analytical data of the compounds. We are thankful to the Head, Department of Biotechnology, Dr. H. S. Gour University (A Central University), Sagar (India) for the antimicrobial (antibacterial and antifungal) results and the Microcare Laboratory and Tuberculosis Research Centre, Surat, Gujarat (India) for the anti-tuberculosis activity results. We are also thankful to the Head, Department of Chemistry, Dr. H. S. Gour University (A Central University), Sagar (India) for providing the facilities for the realisation oft the work.

И З В О Д

СИНТЕЗА И БИОЛОШКА АКТИВНОСТ 4-ТИАЗОЛИДИНОНСКИХ ДЕРИВАТА ФЕНОТИАЗИНА

RITU SHARMA, PUSHKAL SAMADHIYA, SAVITRI D. SRIVASTAVA и SANTOSH K. SRIVASTAVA

Synthetic Organic Chemistry Laboratory, Department of Chemistry, Dr. H.S. Gour University (A Central University), Sagar-470003, India

Синтетисана је серија нових деривата *N*-[3-(10*H*-фенотиазин-10-ил)-пропил]-2-(супституисани фенил)-4-оксо-5-(супституисани бензилиден)-3-тиазолидин-карбоксамида **5a**–**s**. Реакција тиогликолне киселине и *N*-[3-(10*H*-фенотиазин-10-ил)-пропил]-*N*'-[(супституисани фенил)-метилиден]-уреа **3a–s**, у присуству анхидрованог $ZnCl_2$ даје нова хетероциклична једињења *N*-[3-(10*H*-фенотиазин-10-ил)-пропил]-2-(супституисани фенил)-4-оксо-3-тиазолидин-карбоксамиде, **4a**–**s**. Добијени производи у реакцији са одабраним супституисаним ароматични алдехидима, у присуству C_2H_5ONa подлежу Кневенагеловој реакцији и дају једињења **5a**–**s**. Једињења **1**, **2**, **3a–s**, **4a**–**s** и **5a**–**s** потвргнуте су IR, ^{1}H-NMR, ^{13}C-NMR, FAB MS инструменталним анализама и елементалној анализи. Испитана је антибактеријска, антифунгална и антитуберкулозна активност према *M. tuberculosis* синтетисаних једињења.

(Примљено 24. септембра 2010, ревидирано 24. априла 2011)

REFERENCES

1. J. Fraga-Dubrevil, J. P. Bazureau, *Tetrahedron* **59** (2003) 6121
2. A. Rao, A. Carbone, A. Chimirri, E. D. Clercq, A. M., Monforte, P. Monforte, C. Pannecouque, M. Zappala, *Farmaco* **57** (2002) 747
3. A. Rao, J. Balzarini, A. Carbone, A. Chimirri, E. D. Clercq, A. M. Monforte, M. Zappala, *Antiviral Res.* **63** (2004) 79
4. M. L. Barreca, A. Chimirri, L. D. Luca, A.-M. Monforte, P. Monforte, A. Rao, M. Zappalà, J. Balzarini, E. D. Clercq, C. Pannecouque, M. Witvrouw, *Bioorg. Med. Chem. Lett.* **11** (2001) 1793
5. N. B. Allens, A. S. Anderson, B. Fauber, A. Allen, L. E. Burgess, *Bioorg. Med. Chem. Lett.* **14** (2004) 1619
6. Y. S. Prabhaker, V. R. Solomon, R. K. Rawat, M. K. Gupta, S. B. Katti, *QSAR Comb. Sci.* **23** (2004) 234
7. S. K. Sonwane, S. D. Srivastava, *Proc. Nat. Acad. Sci. India* **78** (2008) 129

Available online at www.shd.org.rs/JSCS/

2012 Copyright (CC) SCS

8. K. M. Mistry, K. R. Desai, *E-J. Chem*. **1** (2004) 189
9. M. Sayyed, S. Mokle, M. Bokhare, A. Mankar, S. Bhusare, Y. Vibhute, *Arkivoc* (2006) 187
10. P. Kohli, S. D. Srivastava, S. K. Srivastava, *J. Chin. Chem. Soc*. **54** (2007) 1003
11. V. V. Mulwad, A. M. Abid, *J. Korean Chem. Soc*. **52** (2008) 649
12. V. J. Sattigeri, A. Soni, S. Singhal, S. Khan, M. Pandya, P. Bhateja, T. Mathur, A. Rattan, J. M. Khanna, A. Mehta, *Arkivoc* (2005) 46
13. S. K. Sonwane, S.D. Srivastava, S.K. Srivastava, *J. Indian Counc. Chem*. **25** (2008) 15
14. H.-L. Liu, Z. Li, T. Anthonsen, *Molecules* **5** (2000) 1055
15. R. Yadav, S. D. Srivastava S. K. Srivastava, *Indian J. Chem., B* **44** (2005) 1262
16. R. Ottana, R. Maccari, M. L. Barreca,; G. Bruno, A. Rotondo, A. Rossi, G. Chiricosta, R. Di Paola, L. Sautebin, S. Cuzzocrea, M. G. Vigorita, *Bioorg. Med. Chem.* **13** (2005) 4243
17. P. Venkatesh, S. N. Pandeya, *E-J. Chem*. **6** (2009) 495
18. I. Vazzana, E. Terranova, F. Mattioli, F. Sparatore, *Arkivoc* (2004) 364
19. R. B. Patel, P. S. Desai, K. R. Desai, K. H. Chikhalia, *Indian J. Chem., B* **45** (2006) 773
20. T. Shrivastava, A. K. Gaikwad, W. Haq, S. Sinha, S. Katti, *Arkivoc* (2005) 120
21. A. S. Narute, P. B. Khedekar, K. P. Bhusari, *Indian J. Chem., B* **47** (2008) 586
22. P.-C. Lv, C.-F. Zhou, J. Chen, P.-G. Liu, K.-R. Wang, W.-J. Mao, H.-Q. Li, Y. Yang, J. Xiong, H.-L. Zhu, *Bioorg. Med. Chem*. **18** (2010) 314
23. R. Ottana, S. Carotti, R. Maccari, I. Landini, G. Chiricosta, B. Caciagli, M. G. Vigorita, E. Mini, *Bioorg. Med. Chem. Lett.* **15** (2005) 3930
24. J. P. Raval, K. R. Desai, *Arkivoc* (2005) 21
25. S. D. Srivastava, P. Kohli, *Proc. Natl. Acad. India* **77** (2007) 199
26. T. R. Rawat, S. D. Srivastava, *Indian J. Chem., B* **37** (1998) 91
27. A. R. Trivedi, A. B. Siddiqui, V. H. Shah, *Arkivoc* (2008) 210
28. F. Weng, J. Tan, *Acta Pharmacol. Sin.* **24** (2003) 1001
29. A. Rajasekaran, P. P. Tripathi, *Acta Pharm. Turc.* **45** (2003) 235
30. S. Kasmi-Mir, A. Djafri, L. Paquin, J. Hamelin, M. Rahmouni, *Molecules* **11** (2006) 597
31. R. Sharma, P. Samadhiya, S. D. Srivastava, S. K. Srivastava, *Acta Chim. Slov.* **58** (2011) 110.

Available online at www.shd.org.rs/JSCS/

2012 Copyright (CC) SCS