ISSN: 2319-8753

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 3, Issue 6, June 2014

Synthesis and Evaluation of Novel 1, 5-Benzothiazepine Derivatives as Anti-Inflammatory Agents

Ganesh R. Mhaske[1], ShivdasS. Bajod[2], DamodharM. Ambhore[2] and Sharad N. Shelke[1]

Research Center, Department of Chemistry, S.S.G.M. College, Kopargaon, Dist-Ahmednagar (MS) 423601, India[1].

Department of Chemistry, JijamataMahavidyalaya, Buldhana (MS) 443001, India[2].

ABSTRACT:Novel 1, 5-benzothiazepine derivatives were synthesized and characterized by spectral studies. The newly synthesized compounds (**4a–g**) were screened for in vivo anti-inflammatory activity at a dose of 10 mg/kg BW. Among those tested, compounds **4c**, **4d** and **4g** exhibited significant anti-inflammatory activity in models of acute inflammation such as rat paw edema, while compounds 4c and 4g showed considerable activity compared with diclofenac as a standard drug.

KEYWORDS:Benzothiazepine, chalcone, pyrazole, anti-inflammatory activity.

I. INTRODUCTION

Organic synthetic chemistry is now a fast growing research field in chemistry. Among the various organic compounds, heterocyclic compounds have been associated with various biologically activities. Due to bioactivity connected with heterocycle and ease of preparation, a number of researchers are takings keen interested into the study of this.

N- and S- containing heterocycle, such as thiazepine and its derivatives, exhibit a broad spectrum of biological activity[1,2]. Thiazepine fused with a benzene ring is known as benzothiazepine, and it is associated with antibacterial, antifungal[3], antimicrobial[4], anticonvulsant[5], and anti-breast cancer activity[6], acting as a central nervous system depressant[7].

Pyrimido[4,5-b]-1,4-Benzothiazepine draws considerable attention because it is used as an inhibitor of the epidermal growth receptor tyrosine kinase[8] and is applicable for stabilization of the skeletal muscle ryanodine receptor ion channel-FKBP12 complex[9]. In the last decade, a series of monocyclic thiazepine inhibitors of the interleukin-1β converting enzyme (ICE) were synthesized[10] and also exhibited neuroprotective properties[11].

As 1,5-benzothiazepine plays an important role in the pharmacological and medicinal field, various researchers are interested in its synthesis[12] and characteristics[13, 14]. Recently, synthesis and a biological evaluation of thiazepine from chalcone and 2-aminoethanethiol has been investigated[15], and a written survey revealed that different synthetic routes of thiazepine had been reported[16, 17].

Encouraged by the significance of benzothiazepine cited in literature and the movement of our work in the bioorganic field[18–20], we have studied its anti-inflammatory activity. In this current investigation, we report the synthesis, biological evaluation and preliminary structure activity relationship (SAR) of benzothiazepine derivatives.

II. RESULT AND DISCUSSION

Chemistry

The synthetic route used to synthesize the target compound **4a–g** is outlined in Scheme 1. 1-(4-chlorophenyl)-1*H*-pyrazole-4-carbaldehyde **1** was prepared by Vilsemeier-Haack reaction of the acetaldehyde N-(4-chlorophenyl)hydrazone[21].

ISSN: 2319-8753

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

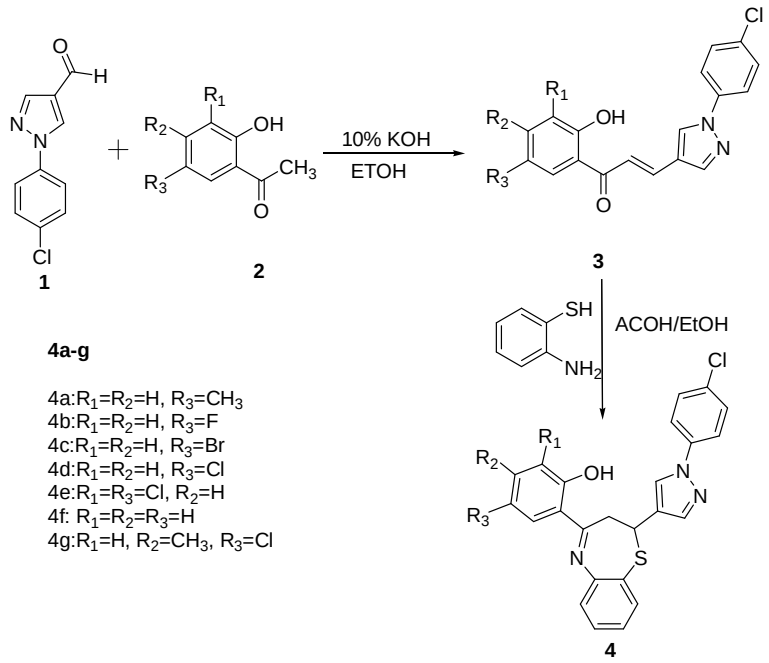
Vol. 3, Issue 6, June 2014

Chalcones 3a–g were prepared by the Claisen–Schmidt condensation reaction of 1-(4-chlorophenyl)-1*H*-pyrazole-4-carbaldehyde **1** and variously substituted *o*-hydroxyacetophenones**2** in the basic medium. The target compounds 4a–g were synthesized by Michael addition of *o*-amino thiophenol to chalcones**3** in acetic acid/ethanol.

The purity of the synthesized compounds was checked by TLC. The proposed structure of the synthesized compound has been confirmed by spectral studies.

In general, three thiazepine protons of known benzothiazepines**4a–g** showed similar patterns of signals in ^{1}H NMR. They displayed doublet of doublet (dd) for two protons and triplet (t) for one proton. The methine proton of the thiazepine nucleus resonates at around δ 2.96 as a triplet with coupling constants of nearly 12.8 Hz. This signal is observed as a triplet instead of a doublet of a doublet (dd) because two J-values accidentally are the same and two inner lines of the quartet occur at the same point, appearing as a single line of double the intensity[22]. The two methylene protons displayed two signals: a doublet of doublet at around δ 3.40 with coupling constants of nearly 13.8 Hz and 4.8 Hz and a doublet of doublet at around δ 5.16 with coupling constants of nearly 10 or 10.4 Hz and 5.2 Hz.

Scheme 1



Scheme-1: Synthesis of benzothiazepine 4a–g.

III. BIOLOGICAL EVALUATION

In vivo anti-inflammatory activity

All the newly synthesized benzothiazepines (4a–g) were screened for their in vivo anti-inflammatory activity by paw edema method. Wister rats were used in the study were fed in house diet and water adlibitum and maintained at 12-12h dark light cycle, 25 C. Animals were administered Diclofenac 10 mg/kg, or test compound 10 mg/kg

ISSN: 2319-8753

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 3, Issue 6, June 2014

p.o., (n=3) two hours prior to injection of 0.1% formaldehyde in the paw. The anti-inflammatory was then calculated 120 minutes after induction and presented in **Table–1** as the mean paw dimension in addition to the percentage inhibition. Paw dimension was measured by digital vernier calliper (Mitutoya, Japan.)

Table–1: Anti-inflammatory activity of the compounds 4a–g

Compound	**Animal**	**Paw volume (mm)**		**% Inhibition**
		Uninduced	Induced	
4a	1	6.2	7.7	1.52
	2	6.2	8.3	
	3	6.1	8.1	
4b	1	6.3	8.2	3.80
	2	6.2	8.0	
	3	6.2	7.6	
4c	1	6.4	8.2	6.52
	2	6.2	8.1	
	3	6.1	8.5	
4d	1	6.3	8.0	10.89
	2	6.4	8.6	
	3	6.1	7.9	
4e	1	6.3	8.2	2.21
	2	6.1	8.1	
	3	6.2	8.6	
4f	1	6.3	7.9	6.14
	2	6.2	7.8	
	3	6.1	7.4	
4g	1	6.1	8.2	0.51
	2	6.4	8.1	
	3	6.2	8.3	
Untreated	1	6.2	8.1	0.00
	2	6.1	8.3	
	3	6.3	8.2	
Diclofenac	1	6.3	7.2	14.21
	2	6.2	7.1	
	3	6.0	6.7	

Out of the seven compounds tested, three compounds (**4c, 4d and 4g**) showed significant anti-inflammatory activity. Among these compounds, the compound 4d (R_3=-Cl) was found to be highly active with 10.89 % inhibition activity, while 4c and 4g with –Br and –H groups were also found have a respective inhibition rate of 6.52 % and 6.14 %.

However, the compounds **4a** and **4g** with methyl groups were found to be less active, with 1.52 and 0.51 % inhibition, respectively. The **4d** with chloro group displayed considerable potent anti-inflammatory activity (10.89 % inhibition) comparable with diclofenac (14.21 % inhibition). However, none was found to be superior to the reference drug.

ISSN: 2319-8753

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 3, Issue 6, June 2014

IV. CONCLUSION

In conclusion, the present investigation reports the synthesis of 1, 5 benzothiazepine derivatives and the evaluation of their anti-inflammatory activity (Figure 1).

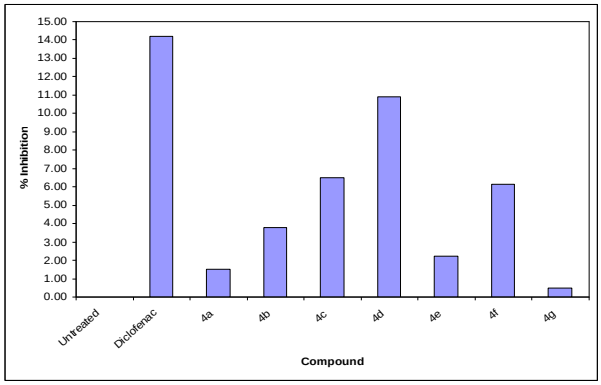


Figure-1: Percentage inhibition of paw edema with the test compounds

The submission pattern of the 1, 5 benzothiazepine was rationalized to be correlated to the aryl heterocyclic template. Among all tested compounds, chloro-substituted benzothiazepine derivative 4d showed the highest anti-inflammatory activity (10.89 % inhibition) that was comparable to diclofenac (14.21 % inhibition), while compounds 4c and 4g displayed good anti-inflammatory activity (6.52% and 6.14 % inhibition), respectively). However, none of the newly synthesized compounds were found to be superior to the reference drug.

V. EXPERIMENTAL

All the recorded melting points (^{o}C) were determined in the m.p. apparatus (Model: KI-11 [MP-D]), Make: Kumar Sales Corporation, Mumbai, India). IR spectra were recorded on a Perkin–Elmer FTIR spectrophotometer on a KBr disc. 1H NMR spectra were recorded on a Bruker ARX spectrometer with peak values shown in δ ppm using $SiMe_4$ as the internal standard when measured in $CDCl_3$ or DMSO-d_6. Signal multiplicities are represented by s (singlet), d (doublet), t (triplet), m (multiplet), and q (quartet). Mass spectra were obtained by the Finnigan mass spectrometer. Substituted phenols and required chemicals for preparation of precursors were purchased from a commercial chemical company. TLC was performed on pre-coated silica gel glass plates (Kieselgel 60, 254, E. Merck, Germany)

General procedure for the preparation of chalcone (**3a–g**)

A 100 mL of conical flask was charged with an equivalent quantity of 1-(4-chlorophenyl)-1H-pyrazole-4-carbaldehyde 1 (0.01 mol) and with o-hydroxyacetophenones 2a–e (0.01 mol) in EtOH as a solvent. A solution of 40% KOH (5 mL) solution was added and the resulting mixture allowed remaining for 24 hours at room temperature. The progress of the reaction was monitored by TLC. After completion, the resulting mixture was poured into ice water and then neutralized with ACOH. The solid was obtained by filtration, dried and purified by recrystallization from ethanol, and column chromatography was applied to create the products **3a–g**.

3-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)-1-(2-hydroxy-5-methylphenyl)prop-2-en-1-one (**3a**)

ISSN: 2319-8753

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 3, Issue 6, June 2014

Yield 76%; m.p. 164–166 °C; FT-IR (KBr) v/max (cm^{-1}): 3431, 3020, 2412, 1646, 1584, 1215, 756; ^{1}H NMR (400 MHz, $CDCl_3$): 2.35 (3H, s, CH_3), 6.91 (1H, d, J = 8.44 Hz), 7.30 (1H, d, J = 8.52 Hz), 7.44–8.16 (9H, m, ArH), 12.67 (1H, s, -OH); ^{13}C NMR (100 MHz, DMSO-d_6): 20.04, 117.60, 119.98, 120.11, 120.23, 120.76, 127.82, 129.61, 129.95, 131.10, 135.40, 137.13, 137.84, 141.7, 116.06, 193.33; MS, ES+1 mode (m/z): 339.08 (M+1).

3-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)-1-(5-fluoro-2-hydroxyphenyl)prop-2-en-1-one (**3b**)

Yield 69%; m.p. 200–202 °C; FT-IR (KBr) v/max (cm^{-1}): 3130, 2468, 1638, 1573, 833, 793; ^{1}H NMR (400 MHz, DMSO-D_6): 7.10 (1H, d, J = 8.52 Hz), 7.50 (1H, d, J = 8.58 Hz), 7.81–-9.22 (9H, m, ArH), 12.79 (1H, s, -OH); MS, ES+1 mode (m/z): 343.06 (M+1).

1-(5-bromo-2-hydroxyphenyl)-3-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)prop-2-en-1-one (**3c**)

Yield 72%; m.p. 176–178 °C; FT-IR (KBr) v/max (cm^{-1}): 3439, 1676, 1556, 834; ^{1}H NMR (400 MHz, DMSO-D^6): 6.95 (1H, d, J = 8.4 Hz), 7.08 (1H, d, J =8.8 Hz), 7.56–8.52 (9H, m, ArH), 13.2 (1H, s, -OH); MS, ES+1 mode (m/z): 402.98 (M+1).

1-(5-chloro-2-hydroxyphenyl)-3-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)prop-2-en-1-one (**3d**)

Yield 75%; m.p. 175–178 °C; FT-IR (KBr) v/max (cm^{-1}): 3150, 2351, 1682, 1567, 822; ^{1}H NMR (400 MHz, DMSO-D_6): 6.99 (1H, d, J = 8.44 Hz), 7.32 (1H, d, J = 8.52 Hz), 7.54–9.2 (9H, m, ArH), 12.40 (1H, s, -OH); MS, ES+1 mode (m/z): 359.03 (M+1).

1-(3, 5-dichloro-2-hydroxyphenyl)-3-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)prop-2-en-1-one (**3e**)

Yield 71%; m.p. 260–261 °C; FT-IR (KBr) v/max (cm^{-1}): 3435, 1676, 1596, 772; ^{1}H NMR (400 MHz, DMSO-D_6): 7.00 (1H, d, J = 8.44 Hz), 7.34 (1H, d, J = 8.52 Hz), 7.52–9.02 (8H, m, ArH), 13.02 (1H, s, -OH); MS, ES+1 mode (m/z): 392.99 (M+1).

3-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)-1-(2-hydroxyphenyl) prop-2-en-1-one (**3f**)

Yield 62%; m.p. 168–171 °C; FT-IR (KBr) v/max (cm^{-1}): 3373, 2401, 1640, 1590, 772; ^{1}H NMR (400 MHz, DMSO-D_6): 7.01 (1H, d, J = 8.44 Hz), 7.30 (1H, d, J = 8.52 Hz), 7.61–9.12 (10H, m, ArH), 12.99 (1H, s, -OH); MS, ES+1 mode (m/z): 325.07 (M+1).

1-(3-chloro-2-hydroxy-5-methylphenyl)-3-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)prop-2-en-1-one (**3g**)

Yield 74%; m.p. 258–260 °C; FT-IR (KBr) v/max (cm^{-1}): 3338, 3001, 2352, 1678, 1573, 834; ^{1}H NMR (400 MHz, DMSO-D_6): 2.52 (3H, s, CH_3), 6.86 (1H, d, J = 8.44 Hz), 7.01 (1H, d, J = 8.52 Hz), 7.60–9.13 (8H, m, ArH), 12.61 (1H, s, -OH); MS, ES+1 mode (m/z): 373.04 (M+1).

General procedure for the preparation of benzothiazepine derivatives (**4a–g**)

To a solution of chalcone (0.01 mol) (3a–e) in 10 mL of ethanol, 0.01 mol of o-amino thiophenol and 2–3 drops of glacial acetic acid were added. The reaction mixture was refluxed by heating for 6 hours, and the progress of the reaction was monitored by TLC. After completion of the reaction, the resulting solution was cooled and transferred into crushed ice. The solid product was filtered and recrystallized from EtOH to enable benzodiazepine derivatives 4a–e.

2-(-2-(1-(4-chlorophenyl)-1*H*-pyrazol-4-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)-4-methylphenol (**4a**)

ISSN: 2319-8753

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 3, Issue 6, June 2014

Yield 71%; m.p. 220–222 ^{o}C; FT-IR (KBr) v/max (cm^{-1}): 3400, 3020, 1575, 1467, 771; ^{1}H NMR (400 MHz, DMSO-d_6)3,5: 2.24 (3H, s, CH_3), 2.96 (1H, t, J=12.8 Hz thiazepine ring), 3.40 (1H, dd, J=12.8 Hz, 4.8 Hz thiazepine ring), 5.16 (1H, dd, J=10.0 Hz, 4.8 Hz thiazepine ring), 6.97–7.79 (13H, m, ArH), 14.24 (1H, s, -OH exchangeable); ^{13}C NMR (100 MHz, DMSO-d_6): 20.09, 35.57, 50.62, 117.48, 117.80, 119.72, 122.87, 125.06, 125.26, 126.35, 126.76, 127.38, 129.45, 129.63, 130.25, 130.43, 134.63, 135.28, 138.33, 139.59, 148.74, 159.46, 174.28; MS, ES+1 mode (m/z): 446.10 (M+1).

2-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl)-4-fluorophenol (**4b**)

Yield 67%; m.p. 168–171 ^{o}C; FT-IR (KBr) v/max (cm^{-1}): 3400, 3420, 1416, 771; ^{1}H NMR (400 MHz, DMSO-d_6): 2.87 (1H, t, J=13 Hz thiazepine ring), 3.65 (1H, dd, J=13.2 Hz, 5.2 Hz thiazepine ring), 5.4 (1H, dd, J=12.3 Hz, 5.3 Hz thiazepine ring), 7.01–8.80 (13H, m, ArH), 13.98 (1H, s, -OH exchangeable); MS, ES+1 mode (m/z): 450.08 (M+1).

4-bromo-2-(2-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl)phenol (**4c**)

Yield 69%; m.p. 158–160 ^{o}C; FT-IR (KBr) v/max (cm^{-1}): 3483, 1476, 1215, 668; ^{1}H NMR (400 MHz, $CDCl_3$): 2.97 (1H, t, J=11.48 Hz thiazepine ring), 3.39 (1H, d, J=12.92 Hz thiazepine ring), 5.19 (1H, d, J=5.16 Hz thiazepine ring), 7.09–7.80 (13H, m, ArH), 12.93 (1H, s, -OH exchangeable); MS, ES+1 mode (m/z): 510.00 (M+1).

4-chloro-2-(2-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)-2,3-dihydrobenzo[b][1,4] Thiazepin-4-yl)phenol(**4d**)

Yield 72%; m.p. 165–168 ^{o}C; FT-IR (KBr) v/max (cm^{-1}): 3387, 1476, 755, 669; ^{1}H NMR (400 MHz, $CDCl_3$): 2.80 (1H, t, J=12.8 Hz thiazepine ring), 3.76 (1H, dd, J=12.9 Hz, 5.0 Hz thiazepine ring), 5.6 (1H, dd, J=12.6 Hz, 5.2 Hz thiazepine ring), 6.91–8.82 (13H, m, ArH), 14.10 (1H, s, -OH exchangeable); MS, ES+1 mode (m/z): 466.00 (M+1).

2,4-dichloro-6-(2-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl)phenol (**4e**)

Yield 70%; m.p. 180–182 ^{o}C; FT-IR (KBr) v/max (cm^{-1}): 3393, 1582, 775, 669; ^{1}H NMR (400 MHz, $CDCl_3$): 2.85 (1H, t, J=12.4 Hz thiazepine ring), 3.75 (1H, dd, J=13.08 Hz, 4.72 Hz thiazepine ring), 5.36 (1H, dd, J=11.72 Hz, 5.0 Hz thiazepine ring), 6.41–8.77 (12H, m, ArH), 15.79 (1H, s, -OH exchangeable); MS, ES+1 mode (m/z): 500.01 (M+1).

2-(-2-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)-2,3-dihydrobenzo[b][1,4]thiazepin-4-yl)phenol (**4f**)

Yield 61%; m.p. 141–143 ^{o}C; FT-IR (KBr) v/max (cm^{-1}): 3393, 1599, 769, 669; ^{1}H NMR (400 MHz, $CDCl_3$): 2.83 (1H, t, J=12.2 Hz thiazepine ring), 3.65 (1H, dd, J=12.68 Hz, 4.62 Hz thiazepine ring), 4.99 (1H, dd, J=12.74 Hz, 4.8 Hz thiazepine ring), 6.40–9.00 (14H, m, ArH), 14.67 (1H, s, -OH exchangeable); MS, ES+1 mode (m/z): 432.09 (M+1).

4-chloro-2-(2-(1-(4-chlorophenyl)-1H-pyrazol-4-yl)-2,3-dihydrobenzo[b][1,4] thiazepin-4-yl)-6-methylphenol (**4g**)

Yield 73%; m.p. 186–188 ^{o}C; FT-IR (KBr) v/max (cm^{-1}): 3444, 3002, 1455, 794, 681; ^{1}H NMR (400 MHz, DMSO-d_6): 2.09 (3H, s, CH_3), 2.92 (1H, t, J=12.4 Hz thiazepine ring), 3.40 (1H, dd, J=13.2 Hz, 5.2 Hz thiazepine ring), 5.14 (1H, dd, J=10.4 Hz, 5.2 Hz thiazepine ring), 6.92–7.95 (12H, m, ArH), 14.33 (1H, s, -OH exchangeable); MS, ES+1 mode (m/z): 480.06 (M+1).

Pharmacological Assay

Male Wistar rats were used for this study. They were fed an in-house diet and water and kept at a 12–12 hour dark/light cycle, 25C. Food was withdrawn 12 hours before and during experimental hours. The animals were arbitrarily divided into sets, each consisting of three rats. One group of three rats was kept as a control group. Such rats were administered

ISSN: 2319-8753

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 3, Issue 6, June 2014

Diclofenac 10 mg/kg, or test compound 10 mg/kg p.o., (n=3) two hours prior to injection of 0.1% formaldehyde in the paw. Paw dimensions were measured by digital vernier callipers (Mitutoto, Japan).

ACKNOWLEDGEMENTS

One of the authors (Sharad N. Shelke) is thanks to University Grant Commission for financial assistance. The authors would like to thank the director of the Deshpande Laboratory (Bhopal, India) for the tests of anti-inflammatory activity. We are also grateful to Dr. A. B. Nikumbh, Head, Dept. of Chemistry, S.S.G.M. College, Kopargaon, Ahmednagar (MH) for providing research facilities and constant encouragement.

REFERENCES

[1] Struga M., Kossakowski J., Koziol A. E., Kedzierska E., Fidecka S., Colla P. L., Ibba C., Collu G., Sanna G., Secc B. andLoddod R.,"Synthesis, pharmacological and antiviral activity of 1,3-thiazepine derivatives", Eur. J. Med. Chem.,Vol. 44, pp.4960–4969, 2009.

[2] Campiani G., Butini S., Fattorusso C., Trotta F., Gemma S., Catalanotti B., Nacci V., Fiorini I., Cagnotto A., Mereghetti I., Mennini T., Minetti P., Di Cesare M. A., Stasi M. A., Di Serio S., Ghirardi O., Tinti O. andCarminati P.,"Novel Atypical Antipsychotic Agents: Rational Design, an Efficient Palladium-Catalyzed Route, and Pharmacological Studies", J. Med. Chem. Vol.,48, pp. 1705–1708, 2005.

[3] Khan A. J., Baseer M. A., Dhole J. M. and Shah S. N., "Synthesis, Experimental Studies of the Antimicrobial Potential of Some Novel 1, 5-Benzo Thiazepine Derivatives", Int. J. Pharma. Sci. Res.,Vol. 2, No. 10, pp. 2619–2622, 2011.

[4] Wang L., Zhang P., Zhang X., Zhang Y., Li Y. and WangY.,"Synthesis and biological evaluation of a novel series of 1, 5-benzothiazepine derivatives as potential antimicrobial agents", Eur. J. Med. Chem.,Vol. 44, pp. 2815–2821, 2009.

[5] Garg N., Chandra T., Jain A. B. and Kumar A., "Synthesis and evaluation of some new substituted benzothiazepine and benzoxazepine derivatives as anticonvulsant agents", Eur. J. Med. Chem.,Vol. 45, pp. 1529–1535, 2010.

[6] Ameta K. L.,Rathore, N. S. and Kumar B., "Synthesis and in vitro anti-breast cancer activity of some novel 1, 5-benzothiazepine derivatives", J. Serb. Chem. Soc.,Vol. 77, No. 6, pp. 725–731, 2012.

[7] Nikalje A. P. andVyawahare, D., "Facile green synthesis of 2, 4-substituted -2, 3- dihydro-1, 5 Benzothiazepine derivatives as novel anticonvulsant and central nervous system (CNS) depressant agents", African J. Pure Appl. Chem.,Vol. 5, No. 12, pp. 422–428, 2011.

[8] Smith L., Wong W. C., Kiselyov A. S., Wizemann S. B., Mao Y., Xu Y., Duncton M. A. J., Kim K., Piatnitski E. L., Doody J. F., Wang Y., Rosler R. L., Milligan D., Columbus J., Balagtas C., Lee S. P., Konovalova A. andHadari Y. R.,"Novel tricyclic azepine derivatives: Biological evaluation of pyrimido[4,5-b]-1,4-benzoxazepines, thiazepines, and diazepines as inhibitors of the epidermal growth factor receptor tyrosine kinase",Bioorg. Med. Chem. Lett.,Vol. 16, pp. 5102–5106, 2006.

[9] Mei Y., Xu L., Kramer H. F., Tomberlin G. H., Townsend C. and Meissner G., "Stabilization of the Skeletal Muscle Ryanodine Receptor Ion Channel-FKBP12 Complex by the 1,4-Benzothiazepine Derivative S107", PLOS ONE.,Vol. 8, No. 1, pp. 1–12, 2013.

[10] Ellis C. D., Oppong K. A., Laufersweiler M. C., O'Neil S. V., Soper D. L., Wang Y., Wos J. A., Fancher A. N., Lu W., Suchanek M. K., Wang R. L., De B. and Demuth T. P., "Synthesis and evaluation of thiazepines as interleukin-1b converting enzyme (ICE) inhibitors",Bioorg. Med. Chem. Lett.,Vol. 16, pp. 4728–4732, 2006.

[11] Lafuente L. G., Egea J., Leon R., Martínez-Sanz F. J., Monjas L., Perez C., Merino C., Garcia-De Diego A. M. andRodríguez-Franco M. I., "Benzothiazepine CGP37157 and Its Isosteric 2′ -Methyl Analogue Provide Neuroprotection and Block Cell Calcium Entry", Chem. Neurosci.,vol. 3, 519–529, 2012.

[12] Tamura Y., Takebe Y., Bayomi S. M. M., Mukai C., Ikeda M., Murase M. andKise M., "Conversions of Thiochroman-4-ones into 1 ,Z-Benzothiazepine, Benzo-[b] thiophen, and 1,2-Benzisothiarole Systems via Sulphimide Intermediates", J. Chem. Soc. Perkin Trans.1, pp. 1037–1040, 1981.

[13] Incerti M., Acquotti D., Sandor P., Vicini P., "Synthesis and NMR spectral assignments of novel 1,4-benzothiazepine- 5-one derivatives", Tetrahedron, Vol. 65, pp. 7487–7490, 2009.

[14] Bruno G., Chimirri A., Gitto R., Grasso S., Nicolò F., Scopelliti R. andZappalà M., "Synthesis and structural characteristics of novel 5H-thiazolo[2,3-d][1,5]benzothiazepine derivatives", J. Chem. Soc. Perkin Trans.1, pp. 2211–2215, 1997.

[15] Drewe J., Kasibhatla S., Tseng B., Shelton E., Sperandio D., Yee R. M., Litvak J., Sendzik M., Spencer J. R. andCaid S. X., "Discovery of 5-(4-hydroxy-6-methyl-2-oxo-2H-pyran-3-yl)-7-phenyl-(E)-2,3,6,7-tetrahydro-1,4-thiazepines as a new series of apoptosis inducers using a cell- and caspase-based HTS assay",Bioorg. Med. Chem. Lett.,Vol. 17, pp. 4987–4990, 2007.

[16] Calvo L. A., Gonzalez-Ortega A., Marcos R., Perez R. M. andSanudo M. C., "Synthesis of 2, 3, 4, 7-tetrahydro[1,4]thiazepines from thiazolidines and β-enaminonitriles", Tetrahedron,Vol. 64, pp. 3691–3700, 2008.

[17] Fu R., Xu X., Dang Q. nadBaiX.,"Synthesis of Novel Tricyclic Pyrimido[4,5-b][1,4]benzothiazepines via Bischler-Napieralski-Type Reactions" J. Org. Chem. Vol. 70, pp. 10810–10816, 2005.

[18] Shelke S. N., Mhaske G. R., Bonifácio V. D. B. andGawande M. B., "Green synthesis and anti-infective activities of fluorinated pyrazoline derivatives",Bioorg. Med. Chem. Lett.,Vol. 22, No. 17, pp. 5727–5730, 2012.

[19] Shelke S., Mhaske G., Gadakh S. and Gill C., "Green synthesis and biological evaluation of some novel azoles as antimicrobial agents",Bioorg. Med. Chem. Lett.,Vol. 20,No. 24, pp. 7200–7204, 2010.

[20] Shelke S., Salunkhe N., Mhaske G., Jadhav R. andKarale B., "Synthesis and Antimicrobial Screening of Some Fluorinated Azoles Containing (2-(6-Methyl-2-P-Tolyl-lH-Imidazo[1,2-a]Pyridin-3-yl) Nucleus", J. Korean Chem. Soc., Vol. 54, pp. 59–64, 2010.

ISSN: 2319-8753

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 3, Issue 6, June 2014

[21] Chornous V. A., Bratenko M. K. andVovk, M. V., "Synthesis of 1-aryl-4-formylpyrazoles from acetaldehyde N-aryl-hydrazones by the Vilsmeier-Haack method. Chemistry of Heterocyclic Compounds", New York. United States, Vol. 42, No. 9, pp.1242-1243, 2006.

[22] Kalsi, P. S., An introduction to more complex ^{1}H NMR spectra and spin-spin splitting. In The Spectroscopy of Organic Compounds, 6th ed.; New Age International Publishers: New Delhi. pp. 282, 2010.

BIOGRAPHY

Dr. Sharad N. Shelke received his Ph.D. degree in Chemistry in 2007 from Research Centre, Department of Chemistry, RayatShikshanSanstha's, S.S.G.M. College, Kopargaon, Dist: Ahmednagar (MS), India (Recognized Research Centre, Affiliated to University of Pune), under the supervision of Prof. C. H. Gill. Presently, he is working at S.S.G.M. College, Kopargaon as an Assistant Professor. He is recognized Ph.D. guide of University of Pune and number of research students registered under his guidance. He has investigated various bioactive heterocycles and green methods, which is applicable in organic synthesis. In 2005, he received the "Teacher Fellowship" from UGC. He has completed number of projects received from various funding agencies. His research interests are investigation of bioactive heterocyclic compound and designation of green chemical reactions and their applications in organic synthesis. He has published over 20, scientific articles, including research articles and patent.Among these,one publicationhave high impact factor 20.833 (Acc. Chem. Res. 2014, 47, 1338−1348).
He was presented the proposal for "PG Diploma in Green Chemistry" under the UGC Innovative Programme before Experts Committee and college received 48.5 lacks funds to his credits.