VERSITA

Chemical Papers 68 (5) 719–724 (2014)
DOI: 10.2478/s11696-013-0496-4

## SHORT COMMUNICATION

# "Green synthesis" of benzothiazepine library of indeno analogues and their in vitro antimicrobial activity

[a]Ashok P. Acharya, [b]Rahul D. Kamble, [a] Snehalkumar D. Patil, [a]Shrikant V. Hese, [a]Omprakash S. Yemul, [b]Sudhakar G. Patil, [b]Shivshankar N. Halale, [a]Bhaskar S. Dawane*

[a]*School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Nanded (MS), India 431606*

[b]*Maharashtra Udayagiri Mahavidyalaya, Udgir (MS), India 413517*

Received 2 March 2013; Revised 7 August 2013; Accepted 19 August 2013

A novel series of indeno-benzothiazepine derivatives was synthesised via a "green" route. Synthesis of these compounds involves the treatment of dinucleophiles such as 2-aminobenzenethiols with $\alpha,\beta$-unsaturated ketones in poly(oxyethylene) (poly(ethylene glycol), PEG-400) catalysed by acetic acid. The synthone $\alpha,\beta$-unsaturated ketones were obtained by Claisen–Schmidt condensation of indan-1-one with substituted pyrazole-2-carbaldehydes prompted by bleaching earth (pH 12.5) as catalyst and PEG-400 as "green" reaction solvent. Screening of all the synthesised compounds for antimicrobial activity revealed that most of these compounds exhibited moderate to significant antimicrobial activity.


**Keywords:** indeno-benzothiazepine, PEG-400, bleaching earth, antimicrobial activity

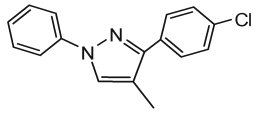
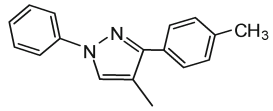
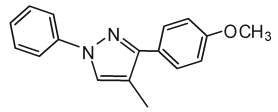
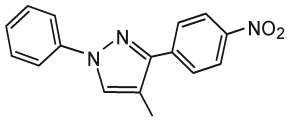
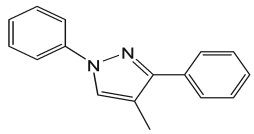
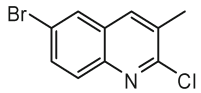
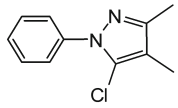
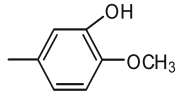
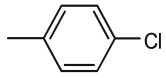
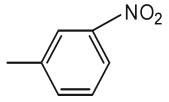
The seven-membered heterocycle 1,5-benzothiazepine is a versatile scaffold and it features in a number of well-known life-saving drugs such as CGP37157, Clonazepam and Diltiazem (Cox & Matlib, 1993) which have gained recognition for their multi-faceted pharmacological and medicinal applications. 1,5-Benzothiazepines are currently used as coronary vasodilators and as antidepressants. In addition, the 1,5-benzothiazepine moiety is a remarkable class of pharmacophore, as compounds bearing this structural unit possess a broad spectrum of biological activities such as antitubercular (Upadhyay et al., 2012), anticonvulsant (De Sarro et al., 1995), $Ca^{2+}$ channel antagonist (Kurokawa et al., 1997), antianginal (Miyata et al., 1997), anti-HIV (Grandolini et al., 1999), squalene synthase inhibitor (Yang et al., 2000), $V_2$-arginine vasopressin receptor antagonist (Urbanski et al., 2003), and HIV-1 reverse transcriptase inhibitor (Di Santo & Costi, 2005).

The importance of 1,5-benzothiazepine derivatives in the field of pharmacological and medicinal chemistry has stimulated interest in developing new methodologies for their synthesis. In this respect, numerous strategies have been reported including one-pot to multi-step approaches using various catalysts (Baag et al., 2007; El-Bayouki, 2013; Jain et al., 2011; Prakash et al., 2005; Rao et al., 1995; Sindler-Kulyk & Neckers, 1982; Yadav et al., 2002; Zhong et al., 2000). However, some of these methods have one or more drawbacks such as long reaction time, use of expensive reagents, low yields, harsh reaction conditions, effluent pollution, and tedious preparation procedure. The most convenient method for the synthesis of these compounds involves the treatment of dinucleophiles such as 2-aminobenzenethiols with $\alpha,\beta$-unsaturated ketones in PEG-400.

Liquid polymers or low melting polymers have recently emerged as alternative "green" solvent systems with unique properties such as thermal stability, commercial availability, non-volatility, immiscibil-

*Corresponding author, e-mail: bhaskardawane@rediffmail.com; rdkamble143@gmail.com

**Table 1.** Characterisation data of compounds *IIIa–IIIj* prepared by using PEG-400

| Compound | R | Time/min | Yield/% | M.p./℃ |
|---|---|---|---|---|
| *IIIa* |  | 130 | 93 | 204–206 |
| *IIIb* |  | 145 | 88 | 192–194 |
| *IIIc* |  | 135 | 91 | 196–198 |
| *IIId* |  | 120 | 95 | 210–212 |
| *IIIe* |  | 162 | 90 | 180–182 |
| *IIIf* |  | 155 | 85 | 170–173 |
| *IIIg* |  | 125 | 93 | 164–166 |
| *IIIh* |  | 140 | 92 | 152–154 |
| *IIIi* |  | 180 | 86 | 142–144 |
| *IIIj* |  | 170 | 90 | 156–158 |

ity with a number of organic solvents and recyclability. Poly(ethylene glycol) (PEG) (Dawane et al., 2010a, 2010b) is one of the "green" solvents and, as included in an environmentally benign protocol, it was applied in many reactions (Chen et al., 2005; Chobe et al., 2012, 2013; Konda et al., 2011). Keeping these observations in view and within the framework of "Green Chemistry", PEG-400-prompted reactions (Chandrasekhar et al., 2002, 2003; Heldebrant & Jessop, 2003) have attracted attention of organic chemists due to the versatile advantages of these reactions such as solvating ability, aptitude to act as a phase-transfer catalyst, negligible vapour pressure, easy recyclability, eco-friendly nature and easy work-up of the reaction mixture.

Recently, bleaching earth (known also as bleaching clay) was found to exhibit unique physical and chemical properties such as shape selectivity, acidic and basic nature and thermal stability; it was used as a catalyst in some reactions (Ballini et al., 2001).

Prompted by these versatile applications, a novel series of indeno-benzothiazepine viz. 11-[substituted-phenyl)-1-phenyl-1*H*-pyrazol-4-yl]-12*H*-10-thia-5-aza-dibenzo[*a*,*g*]azulenes (*IIIa–IIIj*) derivatives was synthesised using PEG-400 as a "green" solvent and bleaching earth as a catalyst (pH 12.5).

Melting points were determined in an open capillary tube and are uncorrected. The chemical solvents used were purified prior to use. Bleaching earth was a gift from Supreme Silicones (Pune, India). Completion of the reaction was monitored by thin layer chromatography (TLC) on a pre-coated sheet of silica gel G using iodine vapour for detection. IR spectra (in KBr pellets) were recorded on a Shimadzu FTIR 8401 spectrophotometer. $^1$H NMR spectra (400 MHz) of compounds dissolved in dimethyl sulphoxide (DMSO-

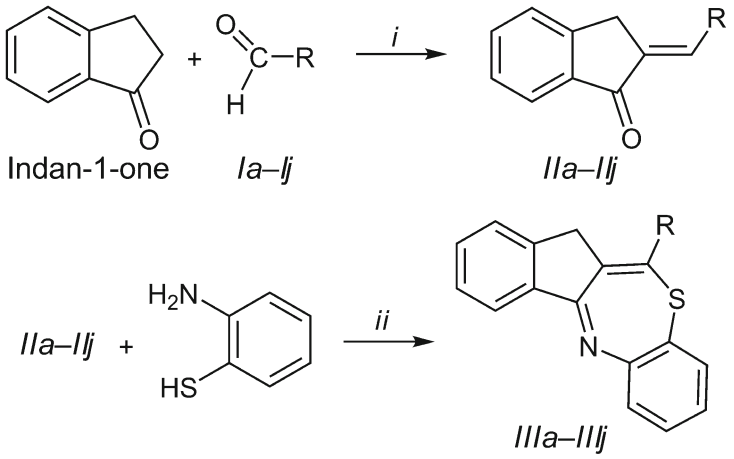



**Fig. 1.** Two-step synthesis of indeno-benzothiazepine derivatives *IIIa–IIIj*. Reaction conditions: *i*) PEG-400, bleaching earth (pH 12.5), 60–80 °C, 1–2 h; *ii*) PEG-400, AcOH, 60–80 °C, 2–3 h; for hetaryl or aryl substituent R, see Table 1.

$d_6$) were recorded using a Bruker Avance spectrometer and tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on a GC–MS Shimadzu QP2010 Plus spectrometer (EI mode). Elemental analyses were performed on a Carlo Erba 106 Perkin–Elmer 240 analyser.

The antimicrobial activities of compounds *IIIa–IIIj* against *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus* and *Bacillus subtilis* (bacteria) and *Aspergillus niger*, *Aspergillus flavus* and *Penicillium chrysogenum* (fungi) (all obtained from the Institute of Microbial Technology (IMTech), Chandigarh, India) were determined using the agar-well diffusion method. Penicillin (25 μg $mL^{-1}$) and nystatin (25 μg $mL^{-1}$) were used as reference drugs for antibacterial and antifungal activity, respectively. DMSO (1 vol. %) was used as a control.

$\alpha,\beta$-Unsaturated ketones (*IIa–IIj*) were prepared as follows: a mixture of indan-1-one (1 mmol), substituted hetaryl- or aryl-aldehyde (1 mmol), and a catalytic amount of bleaching earth (10 mole %, pH 12.5) in PEG-400 (20 mL) was stirred at 60–80 °C for 1–2 h. After completion of the reaction (monitored by TLC), the mixture was filtered to separate the catalyst and the filtrate was poured into a beaker containing ice-cold water (100 mL) under stirring. The solid product thus obtained was filtered, washed with water (2 × 20 mL), dried and recrystallised from ethanol to afford the corresponding $\alpha,\beta$-unsaturated ketone (*IIa–IIj*).

11-[(Substituted-phenyl)-1-phenyl-1*H*-pyrazol-4-yl]-12*H*-10-thia-5-aza-dibenzo[*a*,*g*]azulenes (*IIIa–IIIj*) were prepared as follows: a mixture of $\alpha,\beta$-unsaturated ketones (*IIa–IIf*) (1 mmol), 2-aminothiophenol (1 mmol), PEG-400 (20 mL), and acetic acid (3–4 drops) was heated at 60–80 °C for 2–3 h (see Table 1 for specific reaction time). After completion of the reaction (monitored by TLC), the reaction mixture was cooled and poured into ice-cold water (100 mL). The solid product thus obtained was filtered, washed with water (2 × 5 mL), and recrystallised from aqueous acetic acid to afford a pure product (*IIIa–IIIj*). The PEG-400 was recovered from water by direct distillation and re-used for a second run by charging the same substrates.

A new series of 11-[(substituted-phenyl)-1-phenyl-1*H*-pyrazol-4-yl]-12*H*-10-thia-5-aza-dibenzo[*a*,*g*]azulenes (*IIIa–IIIj*) (indeno-benzothiazepine derivatives) was synthesised in two steps. Thus, $\alpha,\beta$-unsaturated ketones *IIa–IIj* were prepared by Claisen–Schmidt condensation of indan-1-one with various hetaryl- or aryl-aldehydes *Ia–Ij* in the presence of a catalytic amount of bleaching earth (10 mass %, pH 12.5) and PEG-400 as a "green" reaction solvent. It is assumed that bleaching earth abstracts one proton in the C-2 position of indan-1-one to produce a carbanion which serves as nucleophile in the subsequent reaction with an aldehyde, followed by dehydration to afford $\alpha,\beta$-unsaturated ketone (known mechanism of Claisen–Schmidt condensation). The ubsequent reaction of *IIa–IIj* with 2-aminothiophenol (addition of a thiol group to the double bond of $\alpha,\beta$-unsaturated ketone and the subsequent intramolecular cyclocondensation of amine with ketone) in PEG-400 as a "green" reaction solvent and a catalytic amount (a few drops) of acetic acid afforded the desired *IIIa–IIIj* (Fig. 1).

The chemical structures of the newly synthesised compounds were confirmed by IR, $^1$H NMR and mass spectral data (Table 2). The IR spectra exhibited the relevant bands in the region of 3350–3440 $cm^{-1}$ (O—H stretching vibrations) and 1610–1650 $cm^{-1}$ (C═N). The absence of bands corresponding to C═O stretching vibrations at 1660–1695 $cm^{-1}$ indicates the intramolecular cyclisation of $\alpha,\beta$-unsaturated ketone with 2-aminothiophenol to afford a seven-membered indeno-benzothiazepine ring. The presence of $\alpha,\beta$-unsaturated sulphide bond in the 1,5-benzothiazepine ring is confirmed by the signals at $\delta = 149$ and $\delta = 152$

**Table 2.** Spectral data of newly prepared compounds

| Compound | Spectral data |
|---|---|
| *IIa* | IR, $\tilde{\nu}$/cm$^{-1}$): 1230 (C—N), 1500–1542 (C═C$_{aryl}$), 1692 (C═O), 2924 (C—H), 3059 (H—C$_{aryl}$)<br>$^1$H NMR (400 MHz, DMSO-$d_6$), $\delta$: 3.51 (s, 3H, OCH$_3$) 4.32 (s, 2H, CH$_2$), 6.93 (d, 1H, H$_{aryl}$), 7.05 (d, 6H, H$_{aryl}$), 7.11 (t, 4H, H$_{aryl}$), 7.32 (t, 1H, H$_{aryl}$), 7.51 (d, 2H, H$_{aryl}$), 8.41 (s, 1H, C═CH)<br>$^{13}$C NMR (400 MHz, DMSO-$d_6$), $\delta$: 34 (CH$_2$), 58 (OCH$_3$), 130, 138, 142 (C$_{pyrazole}$), 130–155 (C$_{aryl}$) 190 (C═O)<br>MS, $m/z$: 392 (M$^+$)<br>For $C_{26}H_{20}N_2O_2$ ($M_r$ = 392.45) $w_i$/mass % calculated: C, 79.57; H, 5.14; N, 7.14; O, 8.15; found: C, 79.58; H, 5.16; N,7.12; O, 8.16 |
| *IIIa* | IR, $\tilde{\nu}$/cm$^{-1}$: 736 (C—Cl), 1250 (C—S), 1501–1600 (C═C$_{aryl}$), 1610 (C═N$_{thiazepine}$), 3061 (H—C$_{aryl}$)<br>$^1$H NMR (DMSO-$d_6$), $\delta$: 5.43 (s, 2H, CH$_2$), 6.77 (d, 2H, H$_{aryl}$), 6.91–7.26 (m, 6H, H$_{aryl}$), 7.32 (t, 4H, H$_{aryl}$), 7.43 (t, 2H, H$_{aryl}$), 7.51 (d, 2H, H$_{aryl}$), 7.55 (s, 1H, H$_{pyrazole}$), 8.23 (s, 2H, H$_{aryl}$)<br>$^{13}$C NMR (400 MHz, DMSO-$d_6$), $\delta$: 114 (═C—S), 124 (C═N), 128–148 (C$_{aryl}$), 130, 138, 142 (C$_{pyrazole}$), 148–156 (C$_{thiazepine}$)<br>MS, $m/z$: 502 (M$^+$)<br>For $C_{31}H_{20}ClN_3S$ ($M_r$ = 502.03) $w_i$/mass % calculated: C, 74.17; H, 4.02; Cl, 7.06; N, 8.37; S, 6.39; found: C, 74.14; H, 4.05; Cl, 7.02; N, 8.36; S, 6.41 |
| *IIIb* | IR, $\tilde{\nu}$/cm$^{-1}$: 1240 (C—S), 1580–1600 (C═C$_{aryl}$), 1632 (C═N$_{thiazepine}$), 2935 (C—H), 3095 (H—C$_{aryl}$)<br>$^1$H NMR (400 MHz, DMSO-$d_6$), $\delta$: 1.07 (s, 3H, CH$_3$) 5.31(s, 2H, CH$_2$), 6.57 (d, 2H, H$_{aryl}$), 6.73–7.08 (m, 6H, H$_{aryl}$), 7.22 (t, 4H, H$_{aryl}$), 7.34 (t, 2H, H$_{aryl}$), 7.58 (s, 1H, H$_{pyrazole}$), 7.63 (d, 2H, H$_{aryl}$), 8.14 (s, 2H, H$_{aryl}$)<br>$^{13}$C NMR(400 MHz, DMSO-$d_6$) $\delta$: 22 (CH$_3$), 118 (═C—S), 125 (C═N), 130, 138, 142 (C$_{pyrazole}$), 130–155 (C$_{aryl}$), 148–156(C$_{thiazepine}$)<br>EIMS, $m/z$: 482 (M$^+$)<br>For $C_{32}H_{23}N_3S$ ($M_r$ = 481.61) $w_i$/mass % calculated: C, 79.80; H, 4.81; N, 8.72; S, 6.66; found: C, 79.76; H, 4.82; N, 8.70; S, 6.63 |
| *IIIc* | IR, $\tilde{\nu}$/cm$^{-1}$: 1240 (C—S), 1581–1600 (C═C$_{aryl}$), 1610 (C═N$_{thiazepine}$), 3061 (H—C$_{aryl}$)<br>$^1$H NMR (400 MHz, DMSO-$d_6$), $\delta$: 3.73 (s, 3H, OCH$_3$), 5.30 (s, 2H, CH$_2$), 6.47 (d, 2H, H$_{aryl}$), 6.71–7.01 (m, 6H, H$_{aryl}$), 7.22 (t, 4H, H$_{aryl}$), 7.47 (t, 2H, H$_{aryl}$), 7.53(d, 2H, H$_{aryl}$), 7.58 (s, 1H, H$_{pyrazole}$), 8.43 (s, 2H, H$_{aryl}$)<br>$^{13}$C NMR (400 MHz, DMSO-$d_6$), $\delta$: 53 (OCH$_3$), 117 (═C—S), 123 (C═N), 132, 135, 140 (C$_{pyrazole}$), 138–151 (C$_{aryl}$), 149–158 (C$_{thiazepine}$)<br>EIMS, $m/z$: 482 (M$^+$)<br>For $C_{31}H_{20}N_3OS$ ($M_r$ = 482.58) $w_i$/mass % calculated: C, 77.16; H, 4.18; N, 8.71; O, 3.32; S, 6.64; found: C, 77.05; H, 4.20; N, 8.73; O, 3.33; S, 6.60 |
| *IIId* | IR, $\tilde{\nu}$/cm$^{-1}$: 1305 (C—S), 1535 (N—O), 1506–1602 (C═C$_{aryl}$), 1608 (C═N$_{diazepine}$), 3083 (H—C$_{aryl}$)<br>$^1$H NMR (400 MHz, DMSO-$d_6$), $\delta$: 5.42 (s, 2H, CH$_2$), 6.52 (d, 2H, H$_{aryl}$), 6.61–7.01 (m, 7H, H$_{aryl}$), 7.32 (t, 4H, H$_{aryl}$), 7.47 (t, 2H, H$_{aryl}$), 7.51 (d, 2H, H$_{aryl}$), 7.63 (s, 1H, H$_{pyrazole}$), 8.43 (s, 2H, H$_{aryl}$)<br>$^{13}$C NMR (400 MHz, DMSO-$d_6$), $\delta$: 115 (═C—S), 122 (C═N), 128, 135, 141 (C$_{pyrazole}$), 142–150 (C$_{aryl}$), 152–160 (C$_{thiazepine}$)<br>EIMS, $m/z$: 512 (M$^+$)<br>For $C_{31}H_{20}N_4O_2S$ ($M_r$ = 512.58) $w_i$/mass % calculated: C, 75.14; H, 4.27; N, 14.13; O, 6.46; found: C, 75.18; H, 4.30; N, 14.15; O, 6.44 |
| *IIIe* | IR, $\tilde{\nu}$/cm$^{-1}$: 1235 (C—S), 1570–1602 (C═C$_{aryl}$), 1610 (C═N$_{thiazepine}$), 3080 (H—C$_{aryl}$)<br>$^1$H NMR (400 MHz, DMSO-$d_6$), $\delta$: 5.41 (s, 2H, CH$_2$), 6.22–7.56 (m, 10H, H$_{aryl}$), 8.32 (s, 1H, NH ), 9.71 (s, 1H, OH)<br>EIMS, $m/z$: 354 (M$^+$)<br>For $C_{23}H_{18}N_2O_2$ ($M_r$ = 354.40) $w_i$/mass % calculated: C, 77.95; H, 5.12; N, 7.90; O, 9.03; found: C, 77.96; H, 5.10; N, 7.80; O, 9.20 |
| *IIIg* | IR, $\tilde{\nu}$/cm$^{-1}$: 1245 (C—S), 1581–1600 (C═C$_{aryl}$), 1610 (C═N$_{thiazepine}$), 3061 (H—C$_{aryl}$), 3380 (OH)<br>$^1$H NMR (400 MHz, DMSO-$d_6$), $\delta$: 1.71 (s, 3H, CH$_3$), 5.40 (s, 2H, CH$_2$), 6.28–6.61 (m, 5H, H$_{aryl}$), 6.71–7.80 (m, 8H, H$_{aryl}$), 9.90 (s, 1H, OH)<br>$^{13}$C NMR (400 MHz, DMSO-$d_6$), $\delta$: 18 (CH3), 21 (CH$_3$), 116 (═C—S), 124 (C═N), 131, 135, 140 (C$_{pyrazole}$), 136–159 (C$_{aryl}$), 158–165 (C$_{thiazepine}$)<br>EIMS, $m/z$: 371 (M$^+$)<br>For $C_{23}H_{17}NO_2S$ ($M_r$ = 371.45) $w_i$/mass % calculated: C, 74.37; H, 4.61; N, 3.77; O, 8.61; S, 8.63; found: C, 74.35; H, 4.62; N, 3.73; O, 8.63; S, 8.60 |
| *IIIh* | IR, $\tilde{\nu}$/cm$^{-1}$: 732 (C—Cl), 1580–1600 (C═C$_{aryl}$), 1608 (C═N$_{thiazepine}$), 3085 (H—C$_{aryl}$)<br>$^1$H NMR (400 MHz, DMSO-$d_6$), $\delta$: 3.83 (s, 3H, OCH$_3$), 5.45 (s, 2H, CH$_2$), 6.63 (d, 1H, H$_{aryl}$), 6.78 (s, 1H, H$_{aryl}$), 6.83(d, 1H, H$_{aryl}$), 6.96 (t, 1H, H$_{aryl}$), 7.06 (m, 2H, H$_{aryl}$), 7.12–7.25 (m, 5H, H$_{aryl}$) 9.82 (s, 1H, OH)<br>EIMS, $m/z$: 359 (M$^+$)<br>For $C_{22}H_{14}ClNS$ ($M_r$ = 358.12) $w_i$/mass % calculated: C, 73.42; H, 3.92; Cl, 9.85; N, 3.89; S, 8.91; found: C, 73.45; H, 3.93; Cl, 9.94; N, 3.91; S, 8.90 |

**Table 2.** (continued)

| Compound | Spectral data |
|---|---|
| *IIIi* | IR, $\tilde{\nu}$/cm$^{-1}$: 1230 (C—S), 1570–1605 (C═C$_{aryl}$), 1620 (C═N$_{thiazepine}$), 3025 (H—C$_{aryl}$), 3415 (OH)<br>$^1$H NMR (400 MHz, DMSO-$d_6$), $\delta$: 5.3 (s, 2H, CH$_2$), 6.46–6.88 (m, 4H, H$_{aryl}$), 7.04–7.12 (m, 4H, H$_{aryl}$), 9.83 (s, 1H, OH)<br>EIMS, $m/z$: 341 (M$^+$)<br>For $C_{22}H_{15}NOS$ ($M_r$ = 340.23) $w_i$/mass % calculated: C, 77.39; H, 4.43; N, 4.10; O, 4.69; S, 9.39; found: C, 77.4; H, 4.41; N, 4.11; O, 4.67; S, 9.40 |
| *IIIj* | IR, $\tilde{\nu}$/cm$^{-1}$: 1244 (C—S), 1530 (N—O), 1520–1600 (C═C$_{aryl}$), 1636 (C═N$_{thiazepine}$), 3046 (H—C$_{aryl}$)<br>$^1$H NMR (400 MHz, DMSO-$d_6$), $\delta$: 5.26 (s, 2H, CH$_2$), 7.39–7.61 (m, 12H, H$_{aryl}$)<br>EIMS, $m/z$: 370 (M$^+$)<br>For $C_{22}H_{14}N_2O_2S$ ($M_r$ = 369.01) $w_i$/mass % calculated: C, 71.33; H, 3.81; N, 7.56; O, 8.64; S, 8.66; found: C, 71.30; H, 3.82; N, 7.55; O, 8.63; S, 8.67 |

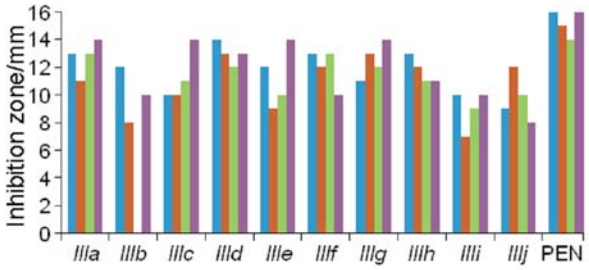



**Fig. 2.** Antibacterial activity of compounds *IIIa–IIIj*. Coloured column (left to right): *Escherichia coli* (blue), *Staphylococcus aureus* (brown), *Bacillus subtilis* (green), *Salmonella typhi* (violet); PEN = penicillin.

(C-2 and C-3 atoms of 1,5-benzothiazepine moiety) in $^{13}$C NMR spectra. In addition, the corresponding molecular ion peak (M$^+$) was observed in the mass spectra for all compounds *IIIa–IIIj*, thus supporting their proposed structure.

The results of antimicrobial testing are summarised in Fig. 2. In comparison with antibacterial penicillin as a standard, compounds *IIIa*, *IIIb*, *IIId–IIIf*, and *IIIh* were found to be active against *Escherichia coli*. Compounds *IIId* and *IIIf–IIIh* also exhibited activity against *Salmonella typhi*. Compounds *IIIa*, *IIId*, *IIIf*, and *IIIg* showed comparatively good activity against *Bacillus subtilis*, while *IIIa*, *IIIc–IIIe*, and *IIIg* were active against *Staphylococcus aureus*. Regarding antifungal activity, some reduction in the growth of *Aspergillus niger* (compounds *IIIc*, *IIIe*, *IIIf*, *IIIi*, and *IIIj*) and *Aspergillus flavus* (compounds *IIIb*, *IIIe*, *IIIg*, and *IIIh*) was observed in comparison with the standard nystatin. By contrast, compounds *IIIa*, *IIIe*, *IIIg* and *IIIh* were inactive against *Penicillium chrysogenum*.

*Acknowledgements. The authors wish to express their thanks to UGC SAP Award no. (F.3-36/2011 (SAP-II) and to UGC for the teacher fellowship under the FDP scheme. RDK and SDP wish to express their thanks to CSIR, New Delhi for JRF. The authors are grateful to the Director, School of Chemical Sciences, SRTMU, IICT and Vishnu Chemicals, Hyderabad for the spectral analysis.*

## References

Ballini, R., Bosica, G., Maggi, R., Ricciutelli, M., Righi, P., Sartori, G., & Sartorio, R. (2001). Clay-catalysed solventless synthesis of *trans*-chalcones. *Green Chemistry*, *3*, 178–180. DOI: 10.1039/b101355f.

Baag, M. M., Sahoo, M. K., Puranik, V. G., & Argade, N. P. (2007). Reactions of *o*-aminothiophenol and *o*-aminophenyl disulfide with itaconic anhydride and (–)-dimenthyl itaconate: Access to enantiomerically pure 1,5-benzothiazepines and benzothiazolyl-2-methylacrylic acid. *Synthesis*, *2007*, 457–463. DOI: 10.1055/s-2006-958977.

Chandrasekhar, S., Narsihmulu, C., Sultana, S. S., & Reddy, N. R. (2002). Poly(ethylene glycol) (PEG) as a reusable solvent medium for organic synthesis. Application in the Heck reaction. *Organic Letters*, *4*, 4399–4401. DOI: 10.1021/ol0266976.

Chandrasekhar, S., Narsihmulu, C., Sultana, S. S., & Reddy, N. R. (2003). Osmium tetroxide in poly(ethylene glycol) (PEG): a recyclable reaction medium for rapid asymmetric dihydroxylation under Sharpless conditions. *Chemical Communication*, *2003*, 1716–1717. DOI: 10.1039/b305154b.

Chen, J., Spear, S. K., Huddleston, J. G., & Rogers, R. D. (2005). Polyethylene glycol and solutions of polyethylene glycol as green reaction media. *Green Chemistry*, *7*, 64–82. DOI: 10.1039/b413546f.

Chobe, S. S., Dawane, B. S., Tumbi, K. M., Nandekar, P. P., & Sangamwar, A. T. (2012). An ecofriendly synthesis and DNA binding interaction study of some pyrazolo[1,5-*a*]pyrimidines derivatives. *Bioorganic & Medicinal Chemistry Letters*, *22*, 7566–7572. DOI: 10.1016/j.bmcl.2012.10.027.

Chobe, S. S., Kamble, R. D., Patil, S. D., Acharya, A. P., Hese, S. V., Yemul, O. S., & Dawane, B. S. (2013). Green approach towards synthesis of substituted pyrazole-1,4-dihydro,9-oxa,1,2,6,8-tetrazacyclopentano[*b*]naphthalene-5-one derivatives as antimycobacterial agents. *Medicinal Chemistry Research*, *22*, 5197–5203. DOI: 10.1007/s00044-013-0487-6.

Cox, D. A., & Matlib, M. A. (1993). Modulation of intramitochondrial free $Ca^{2+}$ concentration by antagonists of $Na^+$-$Ca^{2+}$ exchange. *Trends in Pharmacological Sciences*, *14*, 408–413. DOI: 10.1016/0165-6147(93)90063-p.

Dawane, B. S., Konda, S. G., Mandawad, G. G., & Shaikh, B. M. (2010a). Poly(ethylene glycol) (PEG-400) as an alternative reaction solvent for the synthesis of some new 1-(4-(4′-chlorophenyl-2-thiazolyl)-3-aryl-5-(2-butyl-4-chloro-1*H*-imidazol-5-yl)-2-pyrazolines and their *in vitro* antimicrobial evaluation. *European Journal of Medicinal Chemistry*, *45*, 387–392. DOI: 10.1016/j.ejmech.2009.10.015.

Dawane, B. S., Shaikh, B. M., Khandare, N. T., Kamble, V. T., Chobe, S. S., & Konda, S. G. (2010b). Eco-friendly

polyethylene glycol-400: a rapid and efficient recyclable reaction medium for the synthesis of thiazole derivatives. *Green Chemistry Letters and Reviews*, *3*, 205–208. DOI: 10.1080/17518251003709506.

De Sarro, G., Chimirri, A., De Sarro, A., Gitto, R., Grasso, S., & Zappalà, M. (1995). 5*H*[1,2,4]Oxadiazolo[5,4-*d*][1,5]benzothiazepines as anticonvulsant agents in DBA/2 mice. *European Journal of Medicinal Chemistry*, *30*, 925–929. DOI: 10.1016/0223-5234(96)88311-5.

Di Santo, R., & Costi, R. (2005). 2*H*-Pyrrolo[3,4-*b*][1,5]benzothiazepine derivatives as potential inhibitors of HIV-1 reverse transcriptase. *II Farmaco*, *60*, 385–392. DOI: 10.1016/j.farmac.2005.03.006.

El-Bayouki, K. A. M. (2013). Benzo[1,5]thiazepine: Synthesis, reactions, spectroscopy, and applications. *Organic Chemistry International*, *2013*, 210474. DOI: 10.1155/2013/210474.

Grandolini, G., Perioli, L., & Ambrogi, V. (1999). Synthesis of some new 1,4-benzothiazine and 1,5-benzothiazepine tricyclic derivatives with structural analogy with TIBO and their screening for anti-HIV activity. *European Journal of Medicinal Chemistry*, *34*, 701–709. DOI: 10.1016/s0223-5234(99)00223-8.

Heldebrant, D. T., & Jessop, P. G. (2003). Liquid poly(ethylene glycol) and supercritical carbon dioxide: a benign biphasic solvent system for use and recycling of homogeneous catalysts. *Journal of the American Chemical Society*, *125*, 5600–5601. DOI: 10.1021/ja029131l.

Jain, R., Yadav, T., Kumar, M., & Yadav, A. K. (2011). Facile ionic liquid-mediated protocol for the regioselective synthesis of 1,5-benzothiazepines. *Synthetic Communications*, *41*, 1889–1900. DOI: 10.1080/00397911.2010.493626.

Konda, S. G., Humne, V. T., & Lokhande, P. D. (2011). Rapid and selective deallylation of allyl ethers and esters using iodine in polyethylene glycol-400. *Green Chemistry*, *13*, 2354–2358. DOI: 10.1039/c1gc15153c.

Kurokawa, J., Adachi-Akahane, S., & Nagao, T. (1997). Effects of a novel, potent benzothia-zepine $Ca^{2+}$ channel antagonist, DTZ323, on guinea-pig ventricular myocytes. *European Journal of Pharmacology*, *325*, 229–236. DOI: 10.1016/s0014-2999(97)00119-2.

Miyata, O., Hinada, T., Ninomiya, I., & Naito, T. (1997). Asymmetric construction of two contiguous stereocenters by diastereoface differentiating addition reaction of thiols to chiral imides: Formal synthesis of (+)-diltiazem. *Tetrahedron*, *53*, 2421–2438. DOI: 10.1016/s0040-4020(96)01191-x.

Prakash, O., Kumar, A. Sadana, A., Prakash, R., Singh, S. P., Claramunt, R. M., Sanz, D., Alkorta, I., & Elguero, J. (2005). Study of the reaction of chalcone analogs of dehydroacetic acid and o-aminothiophenol: synthesis and structure of 1,5-benzothiazepines and 1,4-benzothiazines. *Tetrahedron*, *61*, 6642–6651. DOI: 10.1016/j.tet.2005.03.035.

Rao, D. M., Giridhar, T., Reddy, R. B., & Mouli, G. V. P. C. (1995). A novel synthesis of benzothiazepines. *Indian Journal of Heterocyclic Chemistry*, *5*, 145–148.

Sindler-Kulyk, M., & Neckers, D. C. (1982). Photochemistry of 2-phenylbenzothiazole with ethoxyacetylene and ethoxypropyne. Synthesis of 1,5-benzothiazepines *The Journal of Organic Chemistry*, *47*, 4914–4919. DOI: 10.1021/jo00146a018.

Upadhyay, K. Manvar, A., Rawal, K., Joshi, S., Trivedi, J., Chaniyara, R., & Shah, A. (2012). Evaluation of structurally diverse benzoazepines clubbed with coumarins as *Mycobacterium tuberculosis* agents. *Chemical Biology & Drug Design*, *80*, 1003–1008. DOI: 10.1111/j.1747-0285.2012.01436.x.

Urbanski, M. J., Chen, R. H., Demarest, K. T., Gunnet, J., Look, R., Ericson, E., Murray, W. V., Rybczynski, P. J., & Zhang, X. (2003). 2,5-Disubstituted 3,4-dihydro-2*H*-benzo[*b*][1,4]thiazepines as potent and selective $V_2$ arginine vasopressin receptor antagonists. *Bioorganic & Medicinal Chemistry Letters*, *13*, 4031–4034. DOI: 10.1016/j.bmcl.2003.08.051.

Yadav, J. S., Reddy, B. V. S., Eshwaraiah, B., & Anuradha, K. (2002). Amberlyst-15®: a novel and recyclable reagent for the synthesis of 1,5-benzodiazepines in ionic liquids. *Green Chemistry*, *4*, 592–594. DOI: 10.1039/b206558b.

Yang, X., Buzon, L., Hamanaka, E., & Liu, K. K. C. (2000). Enzymatic resolution of benzothiazepine for the preparation of squalene synthetase inhibitors. *Tetrahedron Asymmetry*, *11*, 4447–4450. DOI: 10.1016/s0957-4166(00)00458-4.

Zhong, W., Chen, X., & Zhang, Y. (2000). Low-valent titanium induced simultaneous reduction of nitro group and S-S bond in nitrodisulfides: A novel method for the synthesis of benzothiazoline, benzothiazoles and 2,3-dihydro-1,5-benzothiazepines. *Synthetic Communications*, *30*, 4451–4460. DOI: 10.1080/00397910008087072.