

## Substituted 1,2,4-triazoles and thiazolidinones from fatty acids: Spectral characterization and antimicrobial activity

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Received 5 August 2008; accepted (revised) 5 October 2008

The compounds (Z)-5-(alk-9/8-en-1-yl)-4-phenyl-1,2,4-triazole-3-thiones, (Z)-5-(8/11-hydroxyalk-11/8-en-1-yl)-4-phenyl-1,2,4-triazole-3-thiones, (Z)-N-[2-(phenylimino)-3-yl]-alk-9-enamide-4-thiazolidinone and (Z)-9/12-hydroxy-N-[2-(phenylimino)-3-yl]alk-12/9-enamide-4-thiazolidinone have been synthesized from different fatty acid hydrazides. The structural elucidation of these compounds is based on IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, mass spectral data and elemental analysis. These compounds have been tested for their antibacterial activity against *Escherchia coli*, *Enterobacter aerogenes*, *Staphylococcus aureus* and *Salmonella typhi* by cup-plate method.

**Keywords:** Triazoles, thiazolidinones, IR, NMR, MS, antimicrobial activity

The therapeutic effects of 1,2,4-triazole ring has been studied for a number of pathological conditions which include anti-inflammatory<sup>1,2</sup>, ulcerogenic<sup>3</sup>, antibacterial<sup>4</sup>, antifungal<sup>5,6</sup> and anticancer agents<sup>7</sup>. The scientific literature reveals that these activities are due to presence of -NH-C(S)-NH- function in a molecule and change in activity depends on nature of the substituents<sup>8</sup>. Thiazolidinone derivatives have been found to possess antibacterial<sup>5</sup>, anti-*Toxoplasma gondii*<sup>9</sup> and antitubercular activities<sup>10</sup>. Screening the literature reveals that thiazolidinones also exhibit antinociceptive<sup>11</sup>, anti-inflammatory<sup>12</sup> anticancer and HIV-1 RT inhibitor activities<sup>13</sup>.

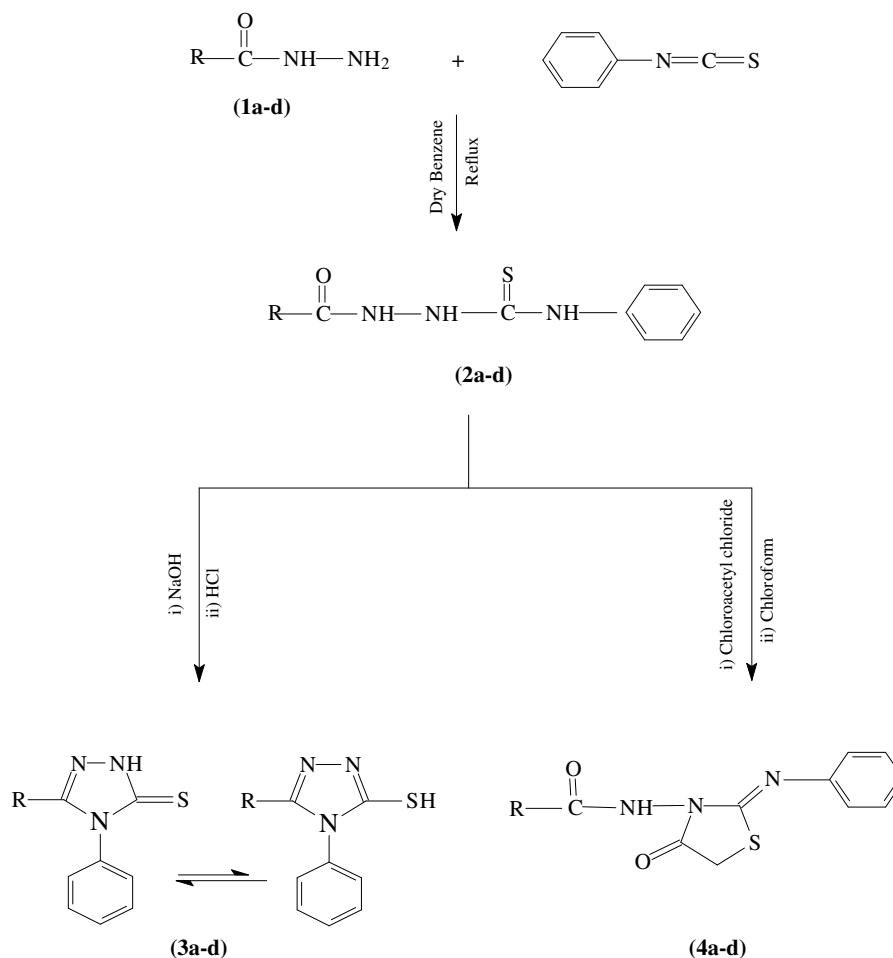
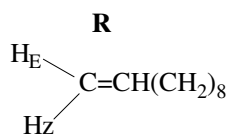
Many seed oils, fatty acids and their derivatives are known for their antimicrobial<sup>14,15</sup> antifungal<sup>16</sup>, pesticidal<sup>17</sup> and anticancer activities<sup>18</sup>. Thus fatty acids on derivatization to these heterocyclic compounds can be used as valuable oleo-chemicals. Therefore in view to explore such possibilities different 1,2,4-triazoles and thiazolidinones were synthesized from fatty acid hydrazides (**Scheme I**). These compounds have been also screened for their antibacterial activity.

### Results and Discussion

Fatty acid hydrazides, **1a-d** which are the required starting materials were prepared from fatty alkenoates following the literature method<sup>19</sup>. Reacting fatty acid hydrazides with phenyl isothiocyanate in dry benzene for 4 hr under reflux and removing excess solvent under reduced pressure gave thiosemicarbazide **2a-d**.

Although the compounds **2a** and **2b** are reported in literature<sup>20</sup>, they have been not characterized fully. Thiosemicarbazide **2a** showed IR bands at 3226 (NH), 1667 (C=O) and 1238  $\text{cm}^{-1}$  (C=S).  $^1\text{H}$  NMR was more informative, characteristic peaks were observed at  $\delta$  8.92 (2H, br. s, CO-NH-NH-CS), 8.42 (1H, s, CS-NH-Ar) and 7.37-7.07 (5H, m, Ar-H). In  $^{13}\text{C}$  NMR peaks at  $\delta$  165.4 (C=O), 160.8 (C=S) were observed. Similarly compounds **2b-d** were confirmed from their spectral data (given in experimental section).

Thiosemicarbazides **2a-d** were subjected to intermolecular cyclization in alkaline medium (2M, NaOH) followed by acidification with HCl to give 1,2,4-triazoles **3a-d**. Since 1,2,4-triazole-3-thione may exist in thiol-thione tautomeric forms<sup>2,21</sup>, our investigations showed that in this case thione structure dominates in solid state. Structure of triazole **3a** and **3b** appeared in literature<sup>22</sup>, without spectral data. Triazole **3a** gave diagnostic IR bands at 3181 (NH), 1541 (C=N) and 1243  $\text{cm}^{-1}$  (C=S) and no peak was observed around 2600-2550  $\text{cm}^{-1}$  indicator of thiol form. The  $^1\text{H}$  NMR was more informative in assigning the structure. In addition to peaks of fatty acid chain other characteristic peaks were observed at  $\delta$  11.39 (1H, s, NH), 7.55-7.31 (5H, m, Ar-H). In  $^{13}\text{C}$  NMR peaks at  $\delta$  168.2 (C=S), 153.0 (C=N) were observed. Mass spectra showed  $[\text{M}+1]^+$  ion peak at  $m/z$  316. Similar types of spectral data were observed for **3b-d**.

**Compound****1a-4a****1b-4b****1c-4c****1d-4d****Scheme I** — Synthesis of triazoles

Cyclization of thiosemicarbazide **2a-d** with chloroacetylchloride in chloroform gave thiazolidinone **4a-d** (**Scheme I**). The IR spectra of compound **4a** showed absorption bands at 3226 (NH), 1660 (C=O), 1496 (C=N) and 666  $\text{cm}^{-1}$  (C-S-C). The  $^1\text{H}$  NMR

characteristic peaks were observed at  $\delta$  8.65 (1H, s, NH), 7.39-7.07 (5H, m, Ar-H) and 2.93 (2H, s,  $\text{CH}_2$  ring). In  $^{13}\text{C}$  NMR peaks at  $\delta$  174.3 (C=O, ring), 164.1 (C=O) and 153.4 (C=N) were observed. Mass spectra showed  $[\text{M}+1]^+$  ion peak at  $m/z$  374. Similar

types of spectral data were observed for compounds **4b-d**.

Earlier works<sup>10,13</sup>, show that thiazolidinone were prepared from different substituted thiosemicarbazides (other than fatty thiosemicarbazides) by reacting them with chloroacetic acid and anhydrous sodium acetate under drastic conditions like high temperature, more reaction time and use of high boiling point solvents e.g. acetic acid. In present study chloroacetylchloride was used to overcome all these lachrymatory conditions.

The antimicrobial activity of compounds **3a-d** and **4a-d** was investigated against four bacterial strains. From **Table I**, it may be seen that triazole **3a**, **3b** and **3d** showed moderate activity against *E. coli* and *E. aerogenes* where as triazole **3b** was moderately active against *S. typhi*. None of the triazoles was found active against *S. aureus*. Compounds **4a** and **4c** showed good activity against *E. coli*. Compound **4a** showed moderate activity against *E. aerogenes* and **4b** showed moderate activity against *E. coli* and *S. aureus*. While as compound **4d** was moderately active against all the strains of bacteria. It may be noticed that compounds **3c**, **4a** and **4c** showed promising results against *E. coli*.

### Experimental Section

Undec-10-enic (purity 98%) and (9Z)-octadec-9-enoic (97%) acids were purchased from Fluka Chemicals (Bucks, Switzerland). (9Z)-12-hydroxyoctadec-9-enoic (ricinolic acid, 98%) and (12Z)-9-hydroxyoctadec-12-enoic (isoricinolic acid, 98%) were isolated from *Ricinus communis* and *Wrightia tinctoria* seed oils respectively following Gunstone's partition procedure<sup>23</sup>. Phenyl isothiocyanate was purchased from Merck, Mumbai, India. Chloroacetylchloride and hydrazine hydrate (80%) were purchased from S-D Fine-Chem (Mumbai, India). Thin layer chromatography was done on glass plates (20 × 5 cm) with a layer of silica gel G (Merck, Mumbai, India, 0.5 mm thickness). Mixture of petroleum ether-ethyl acetate-acetic acid (80:20:1 v/v) were used as developing solvents. Column chromatography was carried out on silica gel (Merck, Mumbai, India, 60-120 mesh). <sup>1</sup>H NMR was recorded with Bruker DRX 300 spectrometer at 300 MHz and <sup>13</sup>C NMR was recorded at 75 MHz in CDCl<sub>3</sub>. Chemical shifts (δ) are quoted in ppm. The FAB mass spectra were recorded on a JEOL-SX 102/DA-600 mass spectrometer. Melting points were taken in open capillary and are uncorrected.

**Table I** — Response of various micro-organisms to newly synthesized compounds

Compd	Diameter of zone of inhibition			
	<i>E. coli</i>	<i>S. aureus</i>	<i>E. aerogenes</i>	<i>S. typhi</i>
<b>3a</b>	++	-	++	-
<b>3b</b>	++	-	++	++
<b>3c</b>	+++	-	-	-
<b>3d</b>	++	-	++	-
<b>4a</b>	+++	-	++	-
<b>4b</b>	++	++	-	-
<b>4c</b>	+++	-	-	-
<b>4d</b>	++	++	++	++
Chloro-mycetin	++++	++++	++++	++++

DMF used as control

Concentration used= 100µg/mL of DMF

Low activity (1-5mm) (+), moderate activity (6-10mm) (+ +), high activity (11-15mm) (+ + +), very high activity (16-20mm) (+ + + +), no activity (-)

### General procedure for synthesis of 4-phenyl-1-(alkenoyl)-thiosemicarbazide, **2a-d**

Fatty acid hydrazide (0.02 mole) and phenyl isothiocyanate (0.02 mole) were refluxed in dry benzene (30 mL) for 5 hr. The resulting solution was then concentrated by removing the excess solvent by distillation under reduced pressure. The solid thus separated was filtered, dried and recrystallized from mixture of benzene-chloroform and identified from spectral data.

**4-Phenyl-1-(undec-10-enoyl)-thiosemicarbazide, 2a:** White powder; yield 78%; m.p. 115-17°C; IR (KBr, cm<sup>-1</sup>): 3226 (NH), 1667 (C=O), 1238 (C=S); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 8.92 (2H, br. s, CO-NHNH-CS), 8.42 (1H, s, CS-NH-Ar), 7.37-7.07 (5H, m, Ar-H), 5.81 (tdd, 1H,  $J_{H-^9CH_2} = 6.6$  Hz,  $J_{H-H_Z} = 10.2$  Hz,  $J_{H-H_E} = 17.2$  Hz, CH<sub>2</sub>=CH-), 5.01 (1H, dd,  $J_{H_Z-H} = 10.2$  Hz,  $J_{H_Z-H_E} = 2.1$  Hz, H<sub>Z</sub>C=CH), 4.92 (1H, dd,  $J_{H_E-H} = 17.2$  Hz,  $J_{H_E-H_Z} = 2.1$  Hz, H<sub>E</sub>C=CH-), 2.35 (2H, t,  $J = 7.5$  Hz, CH<sub>2</sub>-CO), 2.02 (2H, m, CH<sub>2</sub>=CH-CH<sub>2</sub>), 1.72 (2H, m, CH<sub>2</sub>CH<sub>2</sub>-CO), 1.26 (10H, br. s, (CH<sub>2</sub>)<sub>5</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 165.4, 160.8, 139.2, 133.2, 131.3, 128.9, 128.6, 114.2, 33.8, 29.9, 29.6, 29.3, 29.2, 29.1, 29.0, 28.9. Anal. Found: C, 64.79; H, 8.04; N, 12.63. C<sub>18</sub>H<sub>27</sub>N<sub>3</sub>OS requires C, 64.87; H, 8.10; N, 12.60; S, 9.62%.

**(9Z)-4-Phenyl-1-(octadec-9-enoyl)-thiosemicarbazide, 2b:** White crystals; yield 85%; m.p. 114-17°C; IR (KBr, cm<sup>-1</sup>): 3213 (NH), 1661 (C=O), 1242 (C=S); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 8.65 (2H, br. s, CO-

NHNH-CS), 8.40 (1H, s, CS-NH-Ar), 7.34-7.17 (5H, m, Ar-H), 5.31 (2H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 2.32 (2H, t,  $J = 7.5$  Hz, CH<sub>2</sub>-CO), 2.01 (4H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 1.68 (2H, m, CH<sub>2</sub>-CH<sub>2</sub>-CO), 1.26 (20H, br. s, (CH<sub>2</sub>)<sub>10</sub>), 0.88 (3H, dist. t, terminus CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  165.4, 160.8, 139.2, 137.3, 133.2, 131.3, 128.8, 128.6, 31.9, 29.9, 29.8, 29.7, 29.5, 29.4 "three signals are hidden", 29.3 "two signals are hidden", 29.1, 22.7, 14.2. Anal. Found: C, 69.56; H, 9.41; N, 9.77. C<sub>25</sub>H<sub>41</sub>N<sub>3</sub>OS requires C, 69.61; H, 9.50; N, 9.37; S, 7.43%.

**(9Z)-4-Phenyl-1-(12-hydroxy-octadec-9-enoyl)-thiosemicarbazide, 2c:** White powder; yield 73%; m.p. 151-52°C; IR (KBr, cm<sup>-1</sup>): 3293 (OH), 3222 (NH), 1661 (C=O), 1236 (C=S); <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.94 (2H, br. s, CO-NHNH-CS), 8.65 (1H, s, CS-NH-Ar), 7.55-7.29 (5H, m, Ar-H), 5.51-5.43 (2H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 3.59 (1H, m, CH-OH), 2.31 (2H, t,  $J = 7.5$  Hz, CH<sub>2</sub>-CO), 2.21 (1H, br. s, CH-OH), 2.00 (4H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 1.72 (2H, m, CH<sub>2</sub>-CH<sub>2</sub>-CO), 1.25 (18H, br. s, (CH<sub>2</sub>)<sub>9</sub>), 0.87 (3H, dist. t, terminus CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  163.2, 159.9, 138.7 "one signal hidden", 132.2, 128.1, 128.0, 127.0, 70.7, 40.1, 39.9, 39.7, 39.5, 39.3, 31.3, 30.4, 29.1, 29.0, 28.8, 28.6, 25.1, 22.0, 13.6. Anal. Found: C, 67.04; H, 9.04; N, 9.43. C<sub>25</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub>S requires C, 67.12; H, 9.16; N, 9.38; S, 7.16%.

**(12Z)-4-Phenyl-1-(9-hydroxy-octadec-12-enoyl)-thiosemicarbazide, 2d:** White powder; yield 75%; m.p. 152-53°C; IR (KBr, cm<sup>-1</sup>): 3287 (OH), 3180 (NH), 1668 (C=O), 1228 (C=S); <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.76 (2H, br. s, CO-NHNH-CS), 8.12 (1H, s, CS-NH-Ar), 7.56-7.35 (5H, m, Ar-H), 5.37-5.14 (2H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 3.54 (1H, m, CH-OH), 2.38 (2H, t,  $J = 7.5$  Hz, CH<sub>2</sub>-CO), 2.11 (1H, br. s, CH-OH), 2.02 (4H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 1.67 (2H, m, CH<sub>2</sub>-CH<sub>2</sub>-CO), 1.26 (18H, br. s, (CH<sub>2</sub>)<sub>9</sub>), 0.86 (3H, dist. t, terminus CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  163.2, 159.0, 138.4, 137.6, 131.2, 128.7, 128.3, 125.5, 70.56, 40.1, 39.9, 36.3, 24.8, 31.3, 29.1, 29.0, 28.9, 28.8, 28.5, 28.4, 25.1, 22.3, 14.01. Anal. Found: C, 67.00; H, 9.07; N, 9.45. C<sub>25</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub>S requires C, 67.12; H, 9.16; N, 9.38; S, 7.16%.

#### General procedure for synthesis of 5-(alkenyl)-4-phenyl-1,2,4-triazole-3-thion, 3a-d

Thiosemicarbazide **2a-d** (0.01 mole) was dissolved in 30 mL of 2M NaOH solution and heated under reflux for 6 hr. After cooling, the solution was acidified with HCl. Crude product was precipitated, filtered and washed with distilled water. The solid

thus separated was dried and recrystallized in chloroform and petroleum ether. These compounds were identified from their spectral data of IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, MS and elemental analysis.

**5-(Dec-9-en-1-yl)-4-phenyl-1, 2, 4-triazole-3-thion, 3a:** White powder; yield 76%; m.p. 85-87°C; IR (KBr, cm<sup>-1</sup>): 3181 (NH), 1541 (C=N), 1243 (C=S); <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  11.39 (1H, s, NH), 7.55-7.31 (5H, m, Ar-H), 5.81 (tdd, 1H,  $J_{H-8CH_2} = 6.8$  Hz,

$J_{H-H_Z} = 10.2$  Hz,  $J_{H-H_E} = 17.8$  Hz, CH<sub>2</sub>=CH-), 5.00 (1H, dd,  $J_{H_Z-H} = 10.2$  Hz,  $J_{H_Z-H_E} = 2.2$  Hz, H<sub>Z</sub>C=CH), 4.92 (1H, dd,  $J_{H_E-H} = 17.8$  Hz,  $J_{H_E-H_Z} = 2.2$  Hz, H<sub>E</sub>C=CH-), 2.43 (2H, t,  $J = 7.5$  Hz, CH<sub>2</sub>-  $\alpha$  to ring), 2.03 (2H, m, CH<sub>2</sub>=CH-CH<sub>2</sub>), 1.64 (2H, m, CH<sub>2</sub>-  $\beta$  to ring), 1.27 (10H, br. s, (CH<sub>2</sub>)<sub>5</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  168.2, 153.0, 139.1, 133.4, 130.0, 129.8, 127.9, 114.2, 33.7, 31.9, 29.1, 28.9 "one signal hidden", 28.8, 28.7, 26.0; MS (FAB)  $m/z$  (%): 316 ([M+1]<sup>+</sup>, 100), 274 (20), 261 (10), 246 (17), 232 (10), 218 (25), 204 (50), 191 (36), 176 (15). Anal. Found: C, 68.43; H, 7.83; N, 13.41. C<sub>18</sub>H<sub>25</sub>N<sub>3</sub>S requires C, 68.56; H, 7.92; N, 13.33; S, 10.16%.

**(8Z)-5-(Heptadec-8-en-1-yl)-4-phenyl-1,2,4-triazole-3-thion, 3b:** White crystals; yield 85%; m.p. 88-90°C; IR (KBr, cm<sup>-1</sup>): 3181 (NH), 1540 (C=N), 1247 (C=S); <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  11.39 (1H, s, NH), 7.59-7.31 (5H, m, Ar-H), 5.53 (2H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 2.46 (2H, t,  $J = 7.5$  Hz, CH<sub>2</sub>-  $\alpha$  to ring), 2.04 (4H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 1.70 (2H, m, CH<sub>2</sub>-  $\beta$  to ring), 1.25 (20 H, br. s, (CH<sub>2</sub>)<sub>10</sub>), 0.87 (3H, dist. t, terminus CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  167.1, 153.5, 139.0 "one signal hidden", 131.5, 129.0, 126.8, 124.1, 37.1, 31.9, 29.7 "two signals are hidden", 29.6, 29.4 "three signals are hidden", 29.2, 29.1, 26.6, 22.6, 14.0; MS (FAB)  $m/z$  (%): 414 ([M+1]<sup>+</sup>, 100), 398 (15), 356 (10), 327 (15), 301 (15), 274 (20), 260 (24), 246 (15), 232 (15), 218 (20), 204 (45), 191 (55), 177 (10). Anal. Found: C, 72.49; H, 9.30; N, 10.27. C<sub>25</sub>H<sub>39</sub>N<sub>3</sub>S requires C, 72.63; H, 9.43; N, 10.16; S, 7.75%.

**(8Z)-5-(11-Hydroxy-heptadec-8-en-1-yl)-4-phenyl-1,2,4-triazole-3-thion, 3c:** Viscous solid; yield 67%; IR (KBr, cm<sup>-1</sup>): 3307 (OH), 3182 (NH), 1504 (C=N), 1248 (C=S); <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  11.39 (1H, s, NH), 7.55-7.29 (5H, m, Ar-H), 5.51 (2H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 3.59 (1H, m, CH-OH), 2.46 (2H, t,  $J = 7.5$  Hz, CH<sub>2</sub>-  $\alpha$  to ring), 2.17 (1H, br. s, CH-OH), 2.11 (4H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 1.72 (2H, m,

CH<sub>2</sub>-β to ring), 1.25 (18H, br. s, (CH<sub>2</sub>)<sub>9</sub>), 0.87 (3H, dist. t, terminus CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 163.2, 159.9, 139.8, 139.0, 131.2, 129.0, 126.8, 125.5, 70.5, 39.9, 39.7, 31.3, 29.4, 29.1, 29.0, 28.8, 28.5, 28.4, 28.3, 26.7, 25.8, 22.0, 13.6; MS (FAB) *m/z* (%): 430 ([M+1]<sup>+</sup>, 55), 412 (100), 397 (10), 354 (15), 327 (15), 332 (10), 314 (15), 274 (25), 260 (30), 232 (17), 218 (15), 213 (14), 204 (30), 190 (50), 175 (13). Anal. Found: C, 69.78; H, 8.96; N, 9.88. C<sub>25</sub>H<sub>39</sub>N<sub>3</sub>O<sub>2</sub>S requires C, 69.93; H, 9.08; N, 9.78; S, 7.46%.

**(11Z)-5-(8-Hydroxy-heptadec-11-en-1-yl)-4-phenyl-1,2,4-triazole-3-thion, 3d:** White powder; yield 77%; m.p. 198°C; IR (KBr, cm<sup>-1</sup>): 3297 (OH), 3182 (NH), 1504 (C=N), 1247 (C=S); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 10.96 (1H, s, NH), 7.43-7.30 (5H, m, Ar-H), 5.38 (2H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 3.57 (1H, m, CH-OH), 2.45 (2H, t, *J* = 7.5 Hz, CH<sub>2</sub>-α to ring), 2.15 (1H, br. s, CH-OH), 2.13 (4H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 1.68 (2H, m, CH<sub>2</sub>-β to ring), 1.24 (18H, br. s, (CH<sub>2</sub>)<sub>9</sub>), 0.88 (3H, dist. t, terminus CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 167.7, 159.9, 139.1 "one signal hidden", 130.0, 129.8, 127.9, 125.5, 70.4, 38.6, 34.1, 32.0, 29.7, 29.6, 29.5, 29.4 "one signal hidden", 29.3, 29.2, 28.8, 25.0, 22.6, 14.0; MS (FAB) *m/z* (%): 430 ([M+1]<sup>+</sup>, 40), 412 (100), 383 (10), 356 (15), 342 (15), 327 (13), 313 (10), 302 (35), 274 (23), 260 (25), 246 (18), 232 (18), 218 (15), 211 (10), 204 (35), 191 (25), 176 (15), 155 (18), 111 (16), 97 (20). Anal. Found: C, 69.82; H, 9.01; N, 9.83. C<sub>25</sub>H<sub>39</sub>N<sub>3</sub>O<sub>2</sub>S requires C, 69.93; H, 9.08; N, 9.78; S, 7.46%.

**General procedure for synthesis of *N*-[2-(phenylimino)-3-yl]-alkenamide-4-thiazolidinone, 4a-d**

A mixture of thiosemicarbazide **2a-d** (0.01 mole) and chloroacetylchloride (0.01 mole) were refluxed in chloroform (50 mL) for 6 hr. Excess solvent was removed by distillation under reduced pressure and the solid obtained was filtered and washed with ethanol and recrystallized in mixture of DMF-water to obtain thiazolidinone **4a-d**. These compounds were identified from their spectral data of IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, MS and elemental analysis.

***N*-[2-(phenylimino)-3-yl]undec-10-enamide-4-thiazolidinone, 4a:** White powder; yield 70%; m.p. 175-77°C; IR (KBr, cm<sup>-1</sup>): 3226 (NH), 1660 (C=O), 1496 (C=N), 666 (C-S-C); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 8.65 (1H, s, NH), 7.39-7.07 (5H, m, Ar-H), 5.77 (tdd, 1H, *J*<sub>H-<sup>9</sup>CH<sub>2</sub></sub> = 6.6 Hz, *J*<sub>H-H<sub>Z</sub></sub> = 10.2 Hz, *J*<sub>H-H<sub>E</sub></sub> = 17.1 Hz, CH<sub>2</sub>=CH-), 5.01 (1H, dd, *J*<sub>H<sub>Z</sub>-H</sub> = 10.2 Hz,

*J*<sub>H<sub>Z</sub>-H<sub>E</sub></sub> = 2.1 Hz, H<sub>Z</sub>C=CH), 4.92 (1H, dd, *J*<sub>H<sub>E</sub>-H</sub> = 17.1 Hz, *J*<sub>H<sub>E</sub>-H<sub>Z</sub></sub> = 2.1 Hz, H<sub>E</sub>C=CH-), 2.93 (2H, s, CH<sub>2</sub> ring), 2.33 (2H, t, *J* = 7.5 Hz, CH<sub>2</sub>-CO), 2.04 (2H, m, CH<sub>2</sub>=CH-CH<sub>2</sub>), 1.64 (2H, m, CH<sub>2</sub>CH<sub>2</sub>-CO), 1.26 (10H, br. s, (CH<sub>2</sub>)<sub>5</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 174.3, 164.1, 153.4, 139.0, 130.8, 129.0, 127.9, 125.6, 114.4, 37.1, 33.7, 28.9 "two signals signals hidden", 28.7 "two signals signals hidden", 25.8; MS (FAB) *m/z* (%): 374 ([M+1]<sup>+</sup>, 15), 281 (17), 241 (100), 183 (15), 167 (26), 139 (32), 111 (8), 97 (12), 91 (20). Anal. Found: C, 64.27; H, 7.18; N, 11.33. C<sub>20</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub>S requires C, 64.35; H, 7.23; N, 11.25; S, 8.58%.

**(9Z)-*N*-[2-(phenylimino)-3-yl]-octadec-9-enamide-4-thiazolidinone, 4b:** Dull white powder; yield 73%; m.p. 184-86°C; IR (KBr, cm<sup>-1</sup>): 3222 (NH), 1666 (C=O), 1491 (C=N), 668 (C-S-C); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 8.65 (1H, s, NH), 7.59-7.28 (5H, m, Ar-H), 5.32 (2H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 2.91 (2H, s, CH<sub>2</sub> ring), 2.32 (2H, t, *J* = 7.5 Hz, CH<sub>2</sub>-CO), 2.02 (4H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 1.64 (2H, m, CH<sub>2</sub>CH<sub>2</sub>-CO), 1.26 (20H, br. s, (CH<sub>2</sub>)<sub>10</sub>), 0.88 (3H, dist. t, terminus CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 174.4, 167.5, 164.0, 131.2, 131.1, 129.8, 126.1, 125.5, 124.3, 37.1, 33.7, 29.7, 29.6, 29.4, 29.2, 29.1, 28.9 "three signals hidden", 28.7 "one signal hidden", 26.0, 22.7, 14.1; MS (FAB) *m/z* (%): 472 ([M+1]<sup>+</sup>, 10), 394 (18), 380 (15), 318 (17), 304 (15), 281 (20), 265 (17), 237 (27), 223 (17), 209 (15), 195 (25), 181 (15), 167 (20), 153 (32), 139 (32), 113 (12), 97 (100). Anal. Found: C, 68.54; H, 8.61; N, 8.99. C<sub>27</sub>H<sub>41</sub>N<sub>3</sub>O<sub>2</sub>S requires C, 68.79; H, 8.69; N, 8.91; S, 6.80%.

**(9Z)-*N*-[2-(phenylimino)-3-yl]-12-hydroxy-octadec-9-enamide-4-thiazolidinone, 4c:** White powder; yield 68%; m.p. 155-57°C; IR (KBr, cm<sup>-1</sup>): 3308 (OH), 3226 (NH), 1666 (C=O), 1491 (C=N), 667 (C-S-C); <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 8.40 (1H, s, NH), 7.55-7.31 (5H, m, Ar-H), 5.55 (2H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 3.59 (1H, m, CH-OH), 2.96 (2H, s, CH<sub>2</sub> ring), 2.31 (2H, t, *J* = 7.5 Hz, CH<sub>2</sub>-CO), 2.21 (1H, br. s, CH-OH), 2.00 (4H, m, CH<sub>2</sub>-CH=CH-CH<sub>2</sub>), 1.67 (2H, m, CH<sub>2</sub>CH<sub>2</sub>-CO), 1.26 (18H, br. s, (CH<sub>2</sub>)<sub>9</sub>), 0.88 (3H, dist. t, terminus CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 174.9, 167.5, 164.0, 131.2, 131.1, 129.8, 126.1, 125.5, 124.3, 72.0, 37.1, 33.7, 29.7, 29.6, 29.4, 29.2, 29.1, 28.9 "three signals hidden", 28.7, 26.0, 22.4, 14.2; MS (FAB) *m/z* (%): 488 ([M+1]<sup>+</sup>, 11), 470 (13), 412 (14), 396 (10), 297 (100), 281 (20), 265 (35), 236 (8), 208 (12), 194 (15), 181 (15), 154 (12), 138 (12), 112 (28), 97 (40).

Anal. Found: C, 66.41; H, 8.29; N, 8.71.  $C_{27}H_{41}N_3O_3S$  requires C, 66.54; H, 8.41; N, 8.62; S, 6.57%.

**(12Z)-N-[2-(phenylimino)-3-yl]-9-hydroxy-octadec-12-enamide-4-thiazolidinone 4d:** White powder; yield 73%; m.p. 156-58°C; IR (KBr,  $cm^{-1}$ ): 3287 (OH), 3228 (NH), 1666 (C=O), 1491 (C=N), 667 (C-S-C);  $^1H$  NMR; ( $CDCl_3$ )  $\delta$  8.8 (1H, s, NH), 7.46-7.30 (5H, m, Ar-H), 5.37 (2H, m,  $CH_2-CH=CH-CH_2$ ), 3.54 (1H, m,  $CH-OH$ ), 2.96 (2H, s,  $CH_2$  ring), 2.30 (2H, t,  $J = 7.5$  Hz,  $CH_2-CO$ ), 2.12 (1H, br. s,  $CH-OH$ ), 2.02 (4H, m,  $CH_2-CH=CH-CH_2$ ), 1.58 (2H, m,  $CH_2CH_2-CO$ ), 1.26 (18H, br. s,  $(CH_2)_9$ ), 0.88 (3H, dist. t, terminus  $CH_3$ );  $^{13}C$  NMR ( $CDCl_3$ ):  $\delta$  174.6, 167.3, 164.7, 139.4, 134.1, 129.8, 126.1, 125.5, 124.3, 72.0, 34.1, 31.7, 29.4, 29.2, 29.1, 28.9, 28.7, 28.4 "three signals hidden", 28.3, 25.6, 22.0, 14.0; MS (FAB)  $m/z$  (%): 488 ( $[M+1]^+$ , 14), 470(11), 396 (10), 297 (100), 281 (25), 263 (28), 222 (8), 207 (10), 152 (12), 138 (20), 111 (16), 97 (32), 82 (35). Anal. Found: C, 66.44; H, 8.32; N, 8.68.  $C_{27}H_{41}N_3O_3S$  requires C, 66.54; H, 8.41; N, 8.62; S, 6.57%.

#### Antibacterial activity

The *in vitro* antibacterial activity was carried out against *E. coli*, *E. aerogenes*, *S. aureus* and *S. typhi*. These strains were streaked on nutrient agar plates separately and grown overnight. Single well isolated colonies of each type of bacteria were incubated in separate nutrient medium for 16 hr at 37°C for the experiment. To determine the zone of inhibition cup-plate method was employed<sup>24</sup>. In this technique bacteria liquid culture of each type grown in log phase was added aseptically to the autoclaved LB agar medium maintained at 45°C, mixed well and poured immediately into sterile Petri dishes separately. After solidification wells of about 6 mm were cut into agar plates aseptically.

Solution of 100  $\mu g/mL$  of each compound was prepared in DMF. Standard antibiotic chloromycetin was screened under similar conditions, 100  $\mu L$  of these solutions were added to each well and incubated at 37°C. One of the wells was used as control by adding 100  $\mu g/mL$  of DMF. Zone of inhibition was measured in mm after 24 hr and compared with standard drug. Results of antibacterial screening are reported in **Table I**.

#### Acknowledgement

Authors are thankful to the Chairman, Department of Chemistry, Aligarh Muslim University, Aligarh for providing facilities, to carry out research work. Authors are also thankful to Director, CDRI Lucknow for spectral analysis. One of the authors (M. R. Banday) is also thankful to U.G.C, New Delhi, for the award of Research Fellowship.

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