ISSN 1070-3632, Russian Journal of General Chemistry, 2017, Vol. 87, No. 2, pp. 316–321. © Pleiades Publishing, Ltd., 2017.

Synthesis and Antimicrobial Activity of Novel 5-[(1*H*-indol-3-yl)methylene]thiazolidine-2,4-dione–[1,2,3]triazole Hybrids[1]

L. Kamala[a], B. S. Veena[b], P. V. Anantha Lakshmi[a]*, P. Vasantha[a], and E. Sujatha[b]

[a] *Department of Chemistry, University College for Women, Osmania University, Hyderabad, Telangana, 500007 India*
**e-mail: pvanantha.ou@gmail.com*

[b] *Department of Botany, University College of Science, Osmania University, Hyderabad, Telangana, 500007 India*

Received September 9, 2016

Abstract—5-[(1*H*-Indol-3-yl)methylene]thiazolidine-2,4-dione–[1,2,3]triazole hybrid derivatives were synthesized by click chemistry reaction and screened for antimicrobial activity against Gram positive and Gram negative bacteria and fungal species. All synthesized compounds were characterized by ^{1}H and ^{13}C NMR, IR and MS spectra. Antibacterial study indicated that several products demonstrated high activity and some products were determined to be potentially antifungal active agents.

Keywords: Click reaction, 2,4-thiazolidinedione, indole, 1,2,3-triazole, antimicrobial
DOI: 10.1134/S107036321702027X

Compounds with the indole nucleus in their structures demonstrated a wide range of pharmacological activities [1–8]. Many compounds containing 2,4-thiazolidinedione scaffold were determined to be biologically active [9–12]. Triazole derivatives found a vast variety of applications in medicinal chemistry [13–22]. The current study targeted synthesis of 5-[(1*H*-indol-3-yl)methylene]thiazolidine-2,4-dione–[1,2,3]triazole hybrid derivatives and screening their antibacterial and antifungal activity.

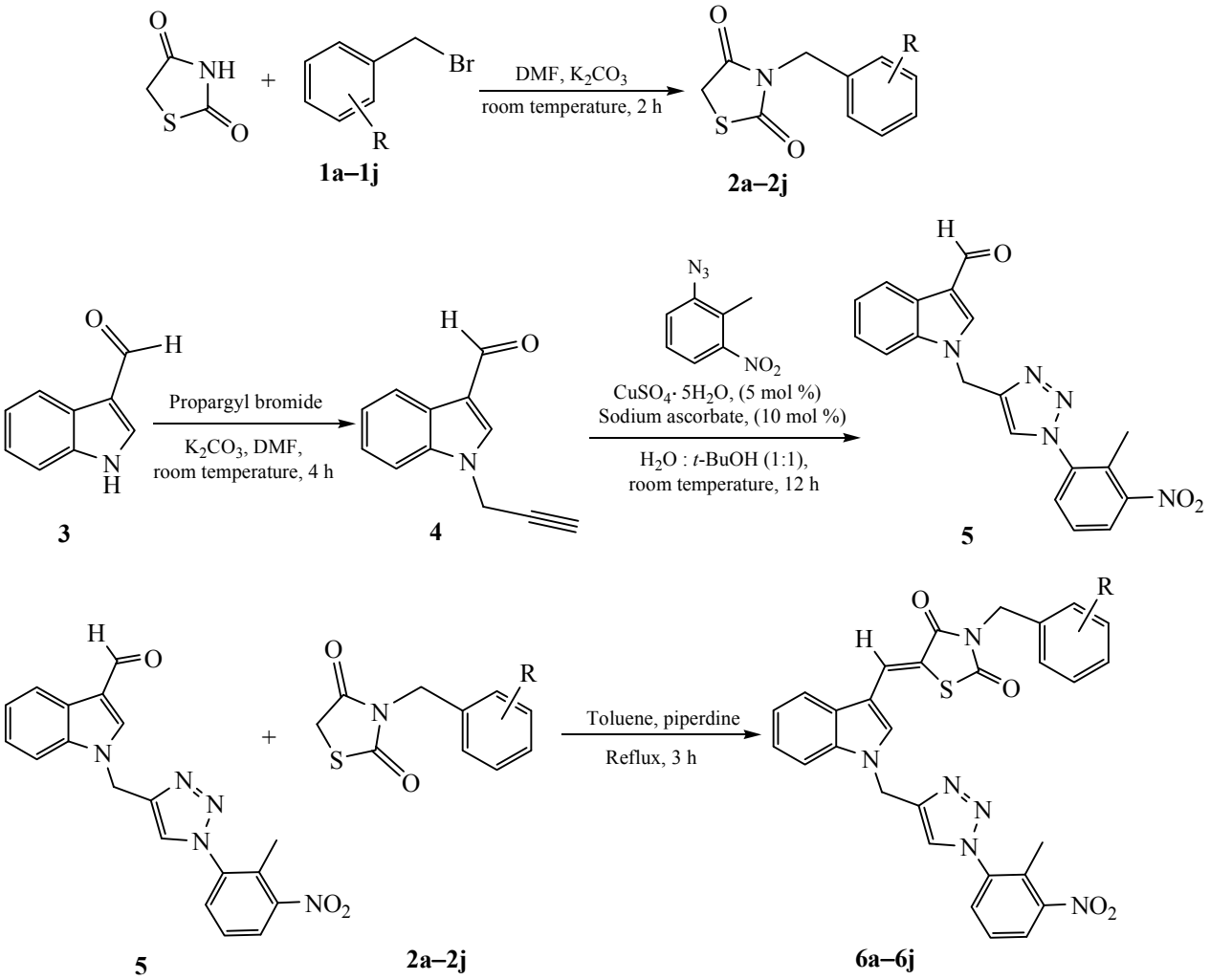
RESULTS AND DISCUSSION

A series of 3-phenyl-5-{(1-[(1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3-yl)methylene}thiazolidine-2,4-diones **6a–6j** were synthesized in four steps (Scheme 1). In the first step thiazolidine-2,4-dione reacted with substituted benzyl bromides **1a–1j** in the basic media to give respective 3-benzylthiazolidine-2,4-dione derivatives **2a–2j**. In the second step reaction of pro-pargylbromide with 1*H*-indole-3-carbaldehyde **3** in the presence of K_2CO_3 in dry DMF under reflux for 2 h led to intermediate 1-(prop-2-yn-1-yl)-1*H*-indole-3-carbaldehyde **4** which was subjected to cycloaddition with 1-azido-2-methyl-3-nitrobenzene under click chemistry reaction conditions in the presence of copper(I) as a catalyst in 1 : 1 water/*tert*-butanol mixture for 12 h to give 1-{[1-(2-methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]methyl}-1*H*-indole-3-carbaldehyde **5**. The latter was common to all derivatives synthesized. In the final step intermediate compound **5** was condensed with a compound **2a–2j** in the presence of catalytic quantity of piperidine in toluene under reflux to give respective 3-benzyl-5-{(1-[(1-(2-methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3-yl)methylene}thiazolidine-2,4-diones **6a–6j** in quantitative yields. All products were characterized by ^{1}H and ^{13}C NMR, IR, and ESI-MS spectra.

Antibacterial activity. All synthesized compounds **6a–6j** were screened *in vitro* for their antibacterial activity against gram-positive bacterial strains [*Staphylococcus aureus, Bacillus subtilis*] and gram-negative bacterial strains [*Escherichia coli, Klebsiella pneumonia*] at concentration of 100 μg/mL. The zones of inhibition (mm) were compared with standard drug ampicilline (see the table). Compounds **6a**, **6d**, **6e,** and **6h** demonstrated promising activity against bacterial strains and compounds **6b**, **6c**, **6f**, **6g**, **6i,** and **6j** exhibited moderate zones of inhibition, indicating the highest activity of compounds with electron-withd-

[1] The text was submitted by the authors in English.

Scheme 1. Synthesis of thiazolidinedione-1,2,3 triazole derivatives.



R = 4-NO_2 (**2a**), 4-Br (**2b**), 4-F (**2c**), 4-COOH (**2d**), 2-NO_2 (**2e**), 2-F (**2f**), 2-Cl (**2g**), 2-CN (**2h**), 3-Cl (**2i**), 2,4-Cl (**2j**), 4-NO_2 (**6a**), 4-Br (**6b**), 4-F (**6c**), 4-COOH (**6d**), 2-NO_2 (**6e**), 2-F (6**f**), 2-Cl (**6g**), 2-CN (**6h**), 3-Cl (**6i**), 2,4-Cl (**6j**),

rawing substitutions on the phenyl ring (–COOH, –NO_2 and –CN). In cases of R = F, Cl and Br the activity was moderate.

Antifungal activity. Antifungal activity of compounds **6a–6j** was tested against Aspergillus niger, *Aspergillus flavus* and *Candida albicans* at concentration of 100 μg/mL. The zones of inhibition (mm) were compared with the standard drug Clotrimazole (see the table). Fluorine containing compounds **6c** and **6f** and the compound **6h** containing the cyano substituent demonstrated the highest activity. The compound **6d** with the acid substituent was the most active against *Aspergillus flavus*. The other products exhibited moderate activity.

EXPERIMENTAL

Melting points were recorded on a Casia-Siamia (VMP-AM) apparatus. IR spectra were recorded on a Perkin–Elmer FT-IR spectrophotometer in KBr discs. NMR spectra were measured on a Bruker Avance 300 MHz spectrometer in $CDCl_3$ and DMSO-d_6 using TMS as the internal standard. Electron impact (EI) and chemical ionization mass spectra were measured on a VG Micro mass model 7070H instrument. All reactions were monitored by TLC (Merck silica gel) and visualized under UV light. Silica gel from Merck (100–200 mesh) was used for column chromatography.

Synthesis of 3-benzylthiazolidine-2,4-dione derivatives (2a–2j). To the mixture of thiazolidine-2,4-

Antimicrobial activity of compounds **6a–6j**[a]

Compound	Zone of inhibition, mm						
	gram positive bacteria		gram negative bacteria		fungi		
	S. aeureus	*B. subtilis*	*E. coli*	*K. pneumonia*	*A. niger*	*A. flavus*	*C. albicans*
6a	12	10	11	8	10	11	9
6b	11	9	9	6	9	10	7
6c	10	11	8	5	12	10	10
6d	12	14	11	10	12	14	9
6e	12	12	11	8	10	11	9
6f	9	11	8	8	13	12	10
6g	9	10	7	10	8	6	7
6h	11	13	8	9	13	13	10
6i	9	10	9	7	8	7	7
6j	10	11	10	8	9	10	7
Ampicillin	15	16	18	14	–	–	–
Clotrimazole	–	–	–	–	13	14	11

[a] Concentration 100 μg/mL.

dione (1.0 mol) and potassium carbonate (1.5 mol) in DMF a solution of substituted a benzyl bromide **1a–1j** (1.5 mol) in DMF was added. The reaction mixture was stirred for 2–3 h. Upon completion of the reaction (TLC), the mixture was extracted with chloroform (2×50 mL). The combined chloroform extracts were washed with water (50 mL) and brine solution (20 mL), dried over anhydrous Na_2SO_4, filtered off, and concentrated under reduced pressure. The residue was purified by column chromatography (ethyl acetate : *n*-hexane = 25 : 75) to give a corresponding pure compound.

Synthesis of 1-(prop-2-ynyl)-1*H*-indole-3-carbaldehyde (4). Indole-3-carboxaldehyde **3** (23.60 mmol) and potassium carbonate (22 mmol) were mixed with 10 mL of dry DMF. Propargyl bromide (23 mmol) was added slowly upon stirring followed by 2 h of stirring of the mixture. The reaction mixture was extracted by ethyl acetate. The crude residue was purified by column chromatography (ethyl acetate : hexane = 15 : 85) to give the pure product **4**.

Synthesis of 1-[(1-(2-methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indole-3-carbaldehyde (5). Compound **4** (3 mmol) and 1-azido-2-methyl-3-nitrobenzene (3 mmol) were suspended in 12 mL of a 1 : 1 water–*tert*-butanol mixture. Addition of aqueous solution of sodium ascorbate (0.3 mmol) was followed by addition of aqueous solution of $CuSO_4{\cdot}5H_2O$ (0.03 mmol). The heterogeneous mixture was stirred vigorously overnight, at which point it turned clear and TLC indicated complete consumption of the reactants. The resulting mixture was diluted with 50 mL of water and cooled in the ice. The precipitate was filtered off, washed with cold water (2×25 mL) and dried under vacuum to give the pure product in the form of powder.

Synthesis of 3-phenyl-5-{(1-[(1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3-yl)methylene}thiazolidine-2,4-diones (6a–6j). The intermediate **5** (1.0 mmol) and catalytic amount of piperdine were dissolved in toluene (10 mL). A compound **2a–2j** (1.0 mmol) was added upon stirring. The reaction mixture was refluxed for 3 h. The solvent was removed under reduced pressure and the residue was diluted with distilled water and extracted thrice with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated, and a crude compound was purified by column chromatography (ethyl acetate : hexane) to give a yellow solid product .

(*Z*)-5-{(1-[(1-(2-Methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3yl)methylene}-3-(4-nitrobenzyl)thiazolidin-2,4-dione (6a). Yield 86%, mp 250–252°C. IR spectrum, ν, cm^{-1}: 3136, 3105, 2866,

1714, 1665, 1594, 1385. ^{1}H NMR spectrum, δ, ppm: 2.27 s (3H), 4.93 s (2H), 5.65 s (2H), 7.30–7.39 m (2H), 7.44–7.58 m (3H), 7.58 d (*J* = 6.76 Hz, 2H), 7.61 d (*J* = 9.03 Hz, 2H), 7.86 d (*J* = 9.26 Hz, 1H), 8.05 d (*J* = 10.03 Hz, 1H), 8.19 s (1H), 8.20 s (1H), 8.26 s (1H). ^{13}C NMR spectrum, δ, ppm: 3.8, 41.4, 43.9, 110.1, 111.3, 113.9, 118.8, 121.7, 123.5, 123.8, 125.7, 126.1, 127.5, 127.9, 128.3, 128.7, 131.0, 131.9, 136.0, 137.4, 142.8, 143.2, 146.9, 150.6, 165.2, 167.0. ESI-MS: *m/z* 595 [*M* + 2]. $C_{29}H_{21}N_7O_6S$.

(*Z*)-3-(4-Bromobenzyl)-5-{(1-[(1-(2-methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3-yl)methylene}thiazolidine-2,4-dione (6b) Yield 85%, mp 242–244°C. IR spectrum, ν, cm^{-1}: 3103, 1719, 1668, 1598, 1385. ^{1}H NMR spectrum, δ, ppm: 2.10 s (3H), 4.82 s (2H), 5.80 s (2H), 7.23–7.35 m (4H), 7.56 d.d (*J* = 2.00 Hz, *J* = 2.00 Hz, 2H), 7.65 (t, *J* = 1.25 Hz, 1H), 7.76 d (*J* = 8.28 Hz, 1H), 7.81 d.d (*J* = 1.50 Hz, *J* = 1.25 Hz, 1H), 7.96 d (*J* = 8.03 Hz, 1H), 8.08 s (1H), 8.15 d.d (*J* = 1.50 Hz, J=1.25 Hz, 1H), 8.20 s (1H), 8.67 s (1H). ^{13}C NMR spectrum, δ, ppm: 13.8, 41.3, 43.8, 110.1, 111.3, 113.9, 118.7, 120.9, 121.7, 123.4, 125.5, 125.6, 126.1, 127.4, 128.3, 129.8, 131.0, 131.5, 131.7, 135.1, 135.9, 137.4, 142.9, 150.5, 165.3,166.9. ESI-MS: *m/z* 629 [*M* + 1]. $C_{29}H_{21}N_7O_4S$.

(*Z*)-3-(4-Fluorobenzyl)-5-{(1-[(1-(2-methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3-yl)methylene}thiazolidine-2,4-dione (6c). Yield 90%, mp 245–247°C. IR spectrum, ν, cm^{-1}: 3143, 2955, 1720, 1668, 1597, 1365. ^{1}H NMR spectrum, δ, ppm: 2.22 s (3H), 4.86 s (2H), 5.64 s (2H), 6.91–7.04 m (2H), 7.30 d.d (*J* = 1.25 Hz, *J* = 1.00 Hz, 1H), 7.34–7.37 m (2H), 7.43–7.46 m (1H), 7.47 d (*J* = 4.51 Hz, 1H), 7.49 d (*J* = 4.01 Hz, 1H), 7.45 d (*J* = 2.008 Hz, 1H), 7.54 s (1H), 7.84 d.d (*J* = 2.00 Hz, *J* = 1.50Hz, 1H), 8.01 d.d (*J* = 2.25 Hz, *J* = 2.00 Hz, 1H), 8.23 s (1H). ^{13}C NMR spectrum, δ, ppm: 13.2, 41.2, 43.8, 110.1, 111.0, 113.8, 118.4, 120.9, 121.7, 123.2, 125.4, 25.5, 126.1, 127.4, 127.2, 128.0, 129.7, 131.0, 131.4, 131.9, 135.5, 135.2, 137.5, 142.8, 150.8, 166.2170.1. ESI-MS: *m/z* 568 [*M* + 1]. $C_{29}H_{21}FN_6O_4S$.

(*Z*)-4-{(5-[(1-{[1-(2-Methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]methyl}-1*H*-indol-3-yl)methylene]-2,4-dioxothiazolidin-3-yl)methyl}benzoic acid (6d). Yield 92%, mp 166–167°C. IR spectrum, ν, cm^{-1}: 2924, 2853, 1714, 1675, 1527, 1349, 1115, 1012. ^{1}H NMR spectrum, δ, ppm: 2.10 s (3H), 4.28 s (1H), 4.30 s (1H), 4.76 s (1H), 4.93 d (*J* = 8.533 Hz, 1H), 5.43–5.46 m (2H), 7.24–7.35 m (1H), 5.80 s (1H), 7.41–7.45 m (1H), 7.54–7.58 m (1H), 7.60–7.67 m (1H), 7.75–7.82 m (1H), 7.91–8.00 m (2H), 8.03–8.06 d.d (*J* = 2.25 Hz, *J* = 2.00 Hz, 1H), 8.09 s (1H), 8.14–8.16 d (*J* = 8.28 Hz, 1H), 8.22 s (1H), 8.69 s (1H). ^{13}C NMR spectrum, δ, ppm: 13.9, 41. 8, 44.1, 110.4, 111.0, 113.8, 118.4, 120.9, 121.7, 123.2, 125.4, 25.5, 126.1, 127.4, 127.2, 128.0, 129.7, 131.0, 131.4, 131.9, 135.5, 135.2, 137.5, 144.5, 151.4, 165.3, 169.2. ESI-MS: *m/z* 594 [*M* + 1]. $C_{30}H_{22}N_6O_6S$.

(*Z*)-5-{(1-[(1-(2-Methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3-yl)methylene}-3-(2-nitrobenzyl)thiazolidine-2,4-dione (6e). Yield 85%, mp 232–234°C. IR spectrum, ν, cm^{-1}: 3016, 2970, 2223, 1737, 1685, 1523, 1348. ^{1}H NMR spectrum, δ, ppm: 2.23 s (3H), 5.15 s (2H), 5.66 s (2H), 7.30–7.32 m (1H), 7.33–7.35 m (1H), 7.37–7.39 m (2H), 7.40–7.42 d.d (*J* = 1.00 Hz, *J* = 1.00 Hz, 1H), 7.46–7.50 m (2H), 7.52–7.54 d.d (*J* = 1.75 Hz, *J* =1.25 Hz, 1H), 7.56 s (1H), 7.58 s (1H), 7.68–7.70 d.d (, *J* = 1.50 Hz, *J* = 1.25 Hz, 1H), 7.84–7.86 d (*J* = 8.28 Hz, 1H), 8.00–8.03 d.d (*J* = 2.00 Hz, *J* = 1.50 Hz, 1H), 8.280 s (1H). ESI-MS: *m/z* 595 [*M* + 2]. $C_{29}H_{21}N_7O_6S$.

(*Z*)-3-(2-Fluorobenzyl)-5-{(1-[(1-(2-methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3-yl)methylene}thiazolidine-2,4-dione (6f). Yield 89%, mp 233–234°C. IR spectrum, ν, cm^{-1}: 3144, 2970, 1739, 1721, 1666, 1598, 1350, 825. ^{1}H NMR spectrum, δ, ppm: 2.23 s (3H), 5.00 s (2H), 5.65 s (2H), 7.03–7.08 m (2H), 7.10–7.12 m (1H), 7.32 d.d (*J* = 1.00 Hz, *J* = 1.25 Hz, 1H), 7.34–7.38 m (2H), 7.46–7.50 m (2H), 7.51 (t, *J* = 1.25, 1H), 7.54 s (1H), 7.56 s (1H), 7.83–7.58 d.d (*J* =1.00 Hz, *J* = 1.25 Hz, 1H), 8.00–7.02 d.d (*J* = 2.00 Hz, *J* = 1.75 Hz, 1H), 8.25 s (1H). ESI-MS: *m/z* 568 (M+ 1). $C_{29}H_{21}FN_6O_4S$.

(*Z*)-3-(2-Chlorobenzyl)-5-{(1-[(1-(2-methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3-yl)methylene}thiazolidine-2,4-dione (6g). Yield 82%, mp 242–243°C. IR spectrum, ν, cm^{-1}: 3111, 2970, 1735, 1677, 1597, 1346, 1034. ^{1}H NMR spectrum, δ, ppm: 2.23 s (3H), 5.06 s (2H), 5.66 s (2H), 7.15–7.19 m (2H), 7.21–7.24 m (1H), 7.32–7.35 m (1H), 7.37–7.40 m (1H), 7.46–7.52 m (2H), 7.55 s (1H), 7.60 s (1H), 7.60–7.63 m (1H), 7.86 d (*J* = 8.28 Hz, 1H), 8.01 d (*J* = 8.78 Hz, 1H), 8.24 d (*J* = 8.78 Hz, 1H), 8.26 s (1H). ^{13}C NMR spectrum, δ, ppm: 13.8, 41.3, 43.8, 110.1, 111.3, 113.9, 118.7, 120.9, 121.1, 121.8, 123.9, 125.5, 25.6, 126.1, 127.4, 127.9, 128.3, 129.8, 131.0, 131.5, 131.7, 135.1, 135.9, 137.4, 142.9, 150.5, 164.2, 166.6. ESI-MS: *m/z* 585 [*M* + 1]. $C_{29}H_{21}ClN_6O_4S$.

(*Z*)-2-{[5-({1-[(1-(2-Methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methyl]-1*H*-indol-3-yl}methylene)-2,4-dioxothiazolidin-3-yl]methyl}benzonitrile (6h). Yield 85%, mp 232–234°C. IR spectrum, ν, cm^{-1}: 3016, 2970, 2223, 1737, 1685, 1523, 1348. ^1H NMR spectrum, δ, ppm: 2.232 s (3H), 5.157 s (2H), 5.66 s (2H), 7.30–7.32 m (1H), 7.33–7.35 m (1H), 7.37–7.39 m (2H), 7.40–7.42 d.d (*J* = 1.00 Hz, *J* = 1.00 Hz, 1H), 7.46–7.50 m (2H), 7.52–7.54 d.d (*J* = 1.75 Hz, *J* =1.25 Hz, 1H), 7.56 s (1H), 7.58 s (1H), 7.68–7.70 d.d (*J* = 1.50 Hz, *J* = 1.25 Hz, 1H), 7.84–7.86 d (*J* = 8.28 Hz, 1H), 8.00–8.03 d.d (*J* = 2.00 Hz, *J* = 1.50 Hz, 1H), 8.28 s (1H), ESI-MS: *m/z* 585 [*M* + 1]. $C_{29}H_{21}ClN_6O_4S$.

(*Z*)-3-(3-Chlorobenzyl)-5-{[1-({1-(2-methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl}methyl)-1*H*-indol-3-yl]-methylene}thiazolidine-2,4-dione (6i). Yield 93%, mp 206–207°C. IR spectrum, ν, cm^{-1}: 3132, 2971, 1728, 1679, 1597, 1364, 1045. ^1H NMR spectrum, δ, ppm: 2.11 s (3H), 4.85 s (2H), 5.77 s (2H), 7.23–7.35 m (3H), 7.40 d.d (*J* = 2.51 Hz, *J* = 8.28 Hz, 3H), 7.64 t (*J* = 2.51Hz, 1H), 7.75–7.82 m (2H), 7.96 d (*J* = 8.282 Hz, 1H), 8.07 s (1H), 8.15 d (*J* = 8.53 Hz, 1H), 8.21 s (1H), 8.68 s (1H). ESI-MS: *m/z* 585 [*M* + 1]. $C_{29}H_{21}ClN_6O_4S$.

(*Z*)-3-(2,4-Dichlorobenzyl)-5-{[1-{[1-(2-methyl-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]methyl}-1*H*-indol-3-yl]methylene}thiazolidine-2,4-dione (6j). Yield 70%, mp 199–200°C. IR spectrum, ν, cm^{-1}: 3111, 2919, 1729, 1669, 1603, 1527, 1385. ^1H NMR spectrum, δ, ppm: 2.23 s (3H), 5.01 s (2H), 5.66 s (2H), 7.12–7.14 m (1H), 7.20 d.d (*J* = 2.25, *J* = 2.25 Hz, 1H), 7.30 d.d (*J* = 1.25 Hz, *J* = 1.00 Hz, 1H), 7.34 d.d (*J* = 1.50 Hz, *J* = 1.50 Hz, 1H), 7.37 d.d (*J* = 1.50 Hz, *J* = 1.25 Hz, 1H), 7.39–7.41 m (1H), 7.50 d.d (*J* = 1.50 Hz, *J* = 1.25 Hz, 1H), 7.56 s (1H), 7.58 s (1H), 7.84–7.86 d (*J* = 7.27 Hz, 1H), 8.03 m (1H), 8.26 s (1H). ESI-MS: *m/z* 585 [*M* + 1]. $C_{29}H_{21}ClN_6O_4S$.

ACKNOWLEDGMENTS

The authors are grateful to the Head, Department of Chemistry, University College for Women, Osmania University, Hyderabad for providing Laboratory facilities and the Director, CFRD, Osmania University, Hyderabad for providing spectral analysis. One of the authors, L. Kamala, is grateful to DST-FIST Program of India (SR/FST/CSI-213/2010) for financial support.

REFERENCES

1. (a) DeSimone, R.W., Currie, K.S., Mitchell, S.A., Darrow, J.W., and Pippin, D.A., *Comb. Chem. High. Throughput Screen*., 2004 vol. 7, p. 473. doi org/10.2174/138620704332854; (b) Welsch, M.E., Snyder, S.A., and Stockwell, B.R., *Curr. Opin. Chem. Biol*., 2010, vol. 14, p. 347. doi org/10.1016/j.cbpa.2010.02.018
2. Narayana, B., Ashalatha, B.V., Vijayaraj, K.K., Fernandes, J., and Sarojini, B.K., *Bioorg. Med. Chem.,* 2005, vol. 13, p. 4638. doi org/10.1016/j.bmc.2005.04.068
3. Mascal, M., Modes, K.V., and Durmus, A., *Angew. Chem. Int. Ed. Engl*., 2011, vol. 50, p. 4445. doi 10.1002/anie.201006423
4. Al-Quawasmeh, R.A., Huesca, M., Nedunuri, V., Peralta, R., Wright, J., Lee, Y., and Young, A., *Bioorg. Med. Chem. Lett*., 2010, vol. 20, p. 3518. doi org/10.1016/j.bmcl.2010.04.137
5. Ty, N., Dupeyre, G., Chabot, G.G., Seguin, J., Tillequin, F., Scherman, D., Michel, S., and Cachet, X., *Bioorg. Med. Chem.*, 2008, vol. 16, p. 7494. doi org/10.1016/j.bmc.2008.06.002
6. Mandour, A.H., El-Sawy, E.R., Shaker, K.H., and Mustafa, M.A., *Acta Pharm.,* 2010, vol. 60, p. 73. doi org/10.2478/v10007-010-0009-8
7. Sechi, M., Derudas, M., Dallocchio, R., Dessi, A., Bacchi, A., Sannia, L., Carta, F., Palomba, M., Ragab, O., Chan, C., Shoemaker, R., Sei, S., Dayam, R., and Neamati, N., *J. Med. Chem.*, 2004, vol. 47, p. 5298. doi 10.1021/jm049944f
8. Zandt, M.C.V., Jones, M.L., Gunn, D.E., Geraci, L.S., Jones, J.H., Sawicki, D.R., Sredy, J., Jacot, J.L., Dicioccio, A.T., Petrova, T., Mitscchler, A., and Podjarny, A.D., *J. Med. Chem.,* 2005, vol. 48, p. 3141. doi 10.1021/jm0492094
9. Liu, X.F., Zheng, C.J., Sun, L.P., Liu, X.K., and Piao, H.R., *Eur. J. Med. Chem*., 2011, vol. 46, p. 3469. doi org/10.1016/j.ejmech.2011.05.012
10. Galli, A., Ceni, E., Mello, T., Polvani, S., Tarocchi, M., Buccoliero, F., Lisi, F., Cioni, L., Ottanelli, B., Foresta, V., Mastrobuoni, G., Moneti, G., Pieraccini, G., Surrenti, C., and Milani, S., *Hepatology*., 2010, vol. 52, p. 493. doi 10.1002/hep.23669
11. Jain, V.S., Vora, D.K., and Ramaa, C.S., *Bioorg. Med. Chem*., 2013, vol. 21, p. 1599. doi org/10.1016/j.bmc.2013.01.029
12. Garg, A., Chawla, P., Panjvani, D., and Saraf, S.A., *Int. J. Pharm. Sci. Nanotechnol*., 2011, vol. 4, p. 1373.
13. Whiting, M.J., Tripp, C., Lin, Y.C., Lindstrom, W., Olson, A.J., Elder, J.H., Sharpless, K.B., and Fokin, V.V., *J. Med. Chem.*, 2006, vol. 49, p. 7697. doi . 10.1021/jm060754+
14. Mossman, T., *J. Immunol. Methods.* 1983, vol. 65, p. 55. doi org/10.1016/0022-1759(83)90303-4
15. Shafi, S., Mahboob Alam, M., Mulakayala, N.,

Mulakayala, C., Vanaja, G., Kalle, A.M., Pallu, R., and Alam, M.S., *Eur. J. Med. Chem.*, 2012, vol. 49, p. 324. doi org/10.1016/j.ejmech.2012.01.032

16. Dorota, G.P., Jan, B., and Iwona, E.G., *Eur. J. Med. Chem.*, 2012, vol. 47, p. 501. doi org/10.1016/j.ejmech.2011.11.021
17. Boddy, I.K., Briggs, G.G., Harrison, R.P., Jones, T.H., O'Mahony, M.J., Marlow, I.D., Roberts, B.G., Willis, R.J., Bardsley, R., and Reid, J. *Pest Manage. Sci*., 1996, vol. 48, p. 189. doi 10.1002/(SICI)1096-9063(199610)48:2<189::AID-PS461>3.0.CO;2-#
18. Agalave, S.G., Maujan, S.R., and Pore, V.S., *Chem. Asian J.*, 2011, vol. 6, p. 2696. doi 10.1002/asia.201100432
19. Giffin, M.J., Heaslet, H., Brik, A., Lin, Y.C., Cauvi, G., Wong, C.H., McRee, D.E., Elder, J.H., Stout, C.D., and Torbett, B.E., *J. Med. Chem.*, 2008, vol. 51, p. 6263. doi 10.1021/jm800149m
20. Bektas, H., Karaali, N., Sahin, D., Demirbas, A., Karaoglu, S.A., and Demirbas, N., *Molecules*, 2010, vol. 15, p. 2427. doi 10.3390/molecules15042427
21. Ross, S.A., Gulve, E.A., and Wang, M., *Chem. Rev.*, 2004, vol. 104, p. 1255. doi 10.1021/cr0204653
22. Aher, N.G., Pore, V.S., Mishra, N.N., Kumar, A., Shukla, P.K., Sharma, A., and Bhat, M.K., *Bioorg. Med. Chem. Lett.*, 2009, vol. 19, p. 759. doi 10.1016/j.bmcl.2008.12.026