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Design, Synthesis, and Anticancer Activity of Novel 2-(4-Arylsubstituted-1*H*-1,2,3-triazol-1-yl)-*N*-{4-[2-(thiazol-2-yl)-benzo[*d*]thiazol-6-yl]phenyl}acetamide Derivatives

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Abstract—A number of novel benzothiazole derivatives bearing 1,2,3-triazole has been synthesized. Molecular structures of the products are confirmed by ^{1}H and ^{13}C NMR, and mass spectral data. Anticancer activity of the products has been tested against human cancer cell lines: MCF-7 (breast), A549 (lung), Colo-205 (colon), and A2780 (ovarian). The synthesized compounds have demonstrated high to moderate activity. Six of those have been characterized by higher activity than that of the standard drug.

Keywords: NSC-710305, tazobactum, benzothiazole, 1,2,3-triazoles, anticancer activity

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INTRODUCTION

Benzothiazole derivatives demonstrate a range of pronounced biological activities including anticancer [1], antiinflammatory [2], antitubercular [3], analgesic [4], antifungicidal [5], antiviral [6], antimalarial [7], and antimicrobial [8]. Benzothiazole is a building block of the anticancer compound NSC-710305 (**1**, Fig. 1), which has been processed to phase-1 clinical trials [9]. 1,2,3-Triazole derivatives are well known as biologically active, including anticancer, agents [10]. Molecular structures of antibiotic drug tazobactum (**2**) [11] incorporate the 1,2,3-triazole unit.

In view of the above, we have designed and synthesized novel 2-(4-aryl-1*H*-1,2,3-triazol-1-yl)-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}acetamide derivatives (**11a**–**11j**) and tested their anticancer activity towards four human cell lines.

EXPERIMENTAL

All chemicals involved were obtained from Aldrich (Sigma-Aldrich, St. Louis, MO, USA) and Lancaster (Alfa Aesar, Johnson Matthey Company, Ward Hill, MA, USA), and used without further purification. Reactions were monitored by TLC performed on silica gel glass plates containing 60 F-254, and visualized under UV light or by iodine indicator. ^{1}H and ^{13}C NMR spectra

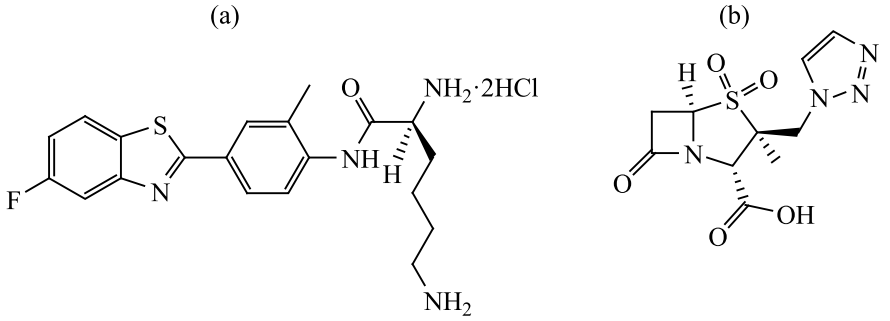


Fig. 1. Structures of (a) NSC710305 (**1**) and (b) tazobactum (**2**).

were measured on a Bruker UXNMR/XWIN-NMR (400 MHz) spectrometer using TMS as an internal standard. ESI spectra were recorded on a Micro mass, Quattro LC using ESI+ software with capillary voltage 3.98 kV and ESI mode positive ion trap detector. Melting points were determined on an electrothermal melting point apparatus, and are uncorrected.

6-Bromo-2-(thiazol-2-yl)benzo[*d*]thiazole (5). A mixture of 2-amino-5-bromobenzenethiol (**3**) (10 g, 48.9 mmol) with thiazole-2-carbaldehyde (**4**) (4.3 mL, 48.9 mmol) and ZnO NPs (362 mg, 4.44 mmol) in absolute ethanol (40 mL) was stirred at room temperature for ca 8 min (TLC). The solvent was evaporated under vacuum, and the crude solid product was purified by column chromatography using ethyl acetate–hexane (1 : 1) as an eluent to obtain pure compound **5**, yield 93%. ^{1}H NMR spectrum, δ, ppm: 7.49 d (1H, J = 8.09 Hz), 7.68 d (1H, J = 8.10 Hz), 7.75 d (1H, J = 8.09 Hz), 7.84 d (1H, J = 8.10 Hz), 7.93 s (1H). MS (FAB): *m/z*: 298 $[M]^+$.

4-[2-(Thiazol-2-yl)benzo[*d*]thiazol-6-yl]benzenamine (7). To a mixture of compound **5** (13 g, 43.7 mmol) with 4-aminophenylboronic acid hydrochloride **6** (10.7 g, 61.8 mmol) dissolved in 1,4-dioxane (70 mL), $Pd(PPh_3)_4$ (504 mg, 0.437 mmol) catalyst was added. Then an aqueous solution of Cs_2CO_3 (10 mL, 28.4 g, 87.4 mmol) was added upon stirring and the mixture was refluxed for 4 h. Upon cooling the mixture down, the solvent was evaporated under vacuum, diethyl ether (100 mL) was added, and the mixture was washed with brine (3 × 30 mL), dried over Na_2SO_4, and evaporated to dryness. The crude product was recrystallized from ethyl acetate to obtained pure compound **7**, yield 84%. ^{1}H NMR spectrum, δ, ppm: 4.89 s (2H), 7.16 d (2H, J = 7.19 Hz), 7.50 d (1H, J = 8.10 Hz), 7.60 d (2H, J = 7.19 Hz), 7.66 d (1H, J = 8.11 Hz), 7.73 d (1H, J = 8.10 Hz), 7.75 d (1H, J = 8.11 Hz), 7.80 s (1H). MS (ESI): *m/z*: 311 $[M + H]^+$.

2-Azido-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]-phenyl}acetamide (9). To the solution of compound **7** (10 g, 32.2 mmol) in 25 mL of anhydrous dichloromethane, were added 2-azidoacetic acid (**8**) (2.4 mL, 32.2 mmol), EDCI (7.4 g, 48.3 mmol) and HOBt (400 mg, 0.0322 mmol). The reaction mixture was stirred at room temperature for 6 h, then washed with saturated solution of $NaHCO_3$, extracted with CH_2Cl_2, and dried over anhydrous Na_2SO_4. The crude product was subjected to column chromatography with ethyl acetate–hexane (6 : 4) to give pure compound **9**, yield 89%. ^{1}H NMR spectrum, δ, ppm: 5.37 s (2H), 7.52 d (1H, J = 8.12 Hz), 7.57 d (2H, J = 7.25 Hz), 7.67 d (1H, J = 8.13 Hz), 7.73–7.80 m (3H), 7.82 s (1H), 7.86 d (1H, J = 8.12 Hz), 9.86 s (1H). MS (ESI): *m/z*: 394 $[M + H]^+$.

Synthesis of 2-(4-arylsubstituted-1*H*-1,2,3-triazol-1-yl)-*N*-(4-(2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl)-phenyl) acetamide derivatives (11a–11j). Azide **9** (300 mg, 7.6 mmol) and the desired ethynylbenzene **10a** (7.6 mmol) were dissolved in a 1 : 1 mixture of water with *tert*-butyl alcohol (15 mL). Sodium ascorbate (225 mg, 15 mol%, 1.14 mmol) was added followed by copper(II) sulfate pentahydrate (95 mg, 5 mol%, 0.38 mmol). The mixture was stirred vigorously in darkness for 24 h. Upon completion of the reaction *tert*-butyl alcohol was evaporated in vacuo, and the aqueous phase was extracted with ethyl acetate (3×30 mL). The combined organic phases were washed with water and dried over Na_2SO_4. After removal of the solvent under vacuum the crude product was purified by column chromatography using ethyl acetate–hexane (1 : 1) to obtain the corresponding pure compound **11a–11j.**

2-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}acetamide (11a). Yield 56%, mp 249–251°C. ^{1}H NMR spectrum, δ, ppm: 5.60 s (2H), 7.51 d (1H, J = 8.12 Hz), 7.56 d (2H, J = 7.24 Hz), 7.61 d (2H, J = 7.24 Hz), 7.64–7.68 m (3H), 7.72–7.79 m (4H), 7.81 s (1H), 7.84 d (1H, J = 8.12 Hz), 8.23 s (1H), 10.09 s (1H). ^{13}C NMR spectrum, δ, ppm: 55.3, 114.7, 116.3, 120.4, 124.5, 125.3, 126.4, 127.2, 128.3, 129.5, 131.5, 132.8, 134.6, 143.4, 143.7, 147.5, 148.5, 149.6, 152.8, 157.4, 162.8. MS (ESI): *m/z*: 496 $[M + H]^+$.

2-[4-(3,4,5-Trimethoxyphenyl)-1*H*-1,2,3-triazol-1-yl]-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thia zol-6-yl]phenyl}-acetamide (11b). Yield 49.7%, mp 256–258°C. ^{1}H NMR spectrum, δ, ppm: 3.86 s (3H), 3.90 s (6H), 5.61 s (2H), 7.32 s (2H), 7.52 d (1H, J = 8.09 Hz), 7.55 d (2H, J = 7.23 Hz), 7.63 d (2H, J = 7.23 Hz), 7.67 d (1H, J = 8.14 Hz), 7.72 d (1H, J = 8.14 Hz), 7.78 s (1H), 7.82 d (1H, J = 8.09 Hz), 8.24 s (1H), 10.10 s (1H). ^{13}C NMR spectrum, δ, ppm: 55.4, 57.4, 61.9, 110.8, 114.5, 116.4, 117.8, 120.5, 124.3, 125.6, 126.7, 127.3, 131.2, 134.7, 143.5, 144.4, 145.6, 147.6, 148.5, 149.4, 152.7, 155.7, 157.5, 162.7. MS (ESI): *m/z*: 586 $[M + H]^+$.

2-[4-(3,5-Dimethoxyphenyl)-1*H*-1,2,3-triazol-1-yl]-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}-acetamide (11c). Yield 59%, mp 253–255°C. ^{1}H NMR spectrum, δ, ppm: 3.91 s (6H), 5.60 s (2H), 7.10 s (1H), 7.34 s (2H), 7.51 d (1H, J = 8.08 Hz), 7.54 d (2H, J = 7.24 Hz), 7.63 d (2H, J = 7.24 Hz), 7.66 d (1H, J = 8.13 Hz), 7.72 d (1H, J = 8.12 Hz), 7.79 s (1H), 7.82 d

(1H, J = 8.08 Hz), 8.23 s (1H), 10.08 s (1H). ^{13}C NMR spectrum, δ, ppm: 55.3, 57.4, 99.5, 110.5, 114.7, 116.4, 117.5, 120.5, 124.6, 125.3, 126.7, 131.2, 132.7, 134.5, 143.4, 145.2, 147.5, 148.3, 149.4, 154.3, 157.3, 160.4, 162.9. MS (ESI): m/z: 556 $[M + H]^+$.

2-[4-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-1-yl]-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}-acetamide (11d). Yield 59%, mp 240–242°C. ^{1}H NMR spectrum, δ, ppm: 3.88 s (3H), 5.61 s (2H), 7.13 d (2H, J = 7.20 Hz), 7.52 d (1H, J = 8.10 Hz), 7.55 d (2H, J = 7.22 Hz), 7.59–7.67 m (5H), 7.70 d (1H, J = 8.13 Hz), 7.79 s (1H), 7.83 d (1H, J = 8.10 Hz), 8.24 s (1H), 10.09 s (1H). ^{13}C NMR spectrum, δ, ppm: 55.6, 57.6, 114.7, 115.3, 116.4, 117.6, 120.6, 124.3, 125.6, 125.9, 126.3, 127.5, 131.8, 134.6, 143.2, 143.6, 147.6, 148.5, 149.3, 154.2, 156.8, 157.6, 162.8. MS (ESI): m/z: 526 $[M + H]^+$.

2-[4-(4-Nitrophenyl)-1*H*-1,2,3-triazol-1-yl]-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}acetamide (11e). Yield 65%, mp 259–261°C. ^{1}H NMR spectrum, δ, ppm: 5.67 s (2H), 7.51 d (1H, J = 8.10 Hz), 7.54 d (2H, J = 7.26 Hz), 7.59 d (2H, J = 7.26 Hz), 7.61 d (2H, J = 7.28 Hz), 7.65 d (1H, J = 8.13 Hz), 7.69 d (1H, J = 8.12 Hz), 7.80 s (1H), 7.83 d (1H, J = 8.10 Hz), 8.27 s (1H), 8.32 d (2H, J = 7.28 Hz), 10.14 s (1H). ^{13}C NMR spectrum, δ, ppm: 55.7, 114.5, 116.5, 117.6, 120.6, 124.5, 125.3, 126.4, 127.5, 130.6, 131.5, 134.5, 135.6, 143.5, 144.5, 147.4, 148.5, 149.7, 150.3, 154.3, 157.8, 162.9. MS (ESI): m/z: 541 $[M + H]^+$.

2-[4-(3,5-Dinitrophenyl)-1*H*-1,2,3-triazol-1-yl]-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}-acetamide (11f). Yield 63%, 264–266°C. ^{1}H NMR spectrum, δ, ppm: 5.69 s (2H), 7.51 d (1H, J = 8.11 Hz), 7.54 d (2H, J = 7.27 Hz), 7.60 d (2H, J = 7.27 Hz), 7.65 d (1H, J = 8.14 Hz), 7.68 d (1H, J = 8.12 Hz), 7.81 s (1H), 7.83 s (1H), 8.28 s (1H), 8.36 s (2H), 8.40 s (1H), 10.15 s (1H). ^{13}C NMR spectrum, δ, ppm: 55.7, 114.7, 116.5, 117.4, 118.5, 120.6, 124.5, 125.4, 126.5, 131.4, 133.5, 134.7, 135.5, 143.5, 147.4, 148.2, 149.5, 150.3, 151.7, 154.7, 157.8, 162.9. MS (ESI): m/z: 586 $[M + H]^+$.

2-[4-(4-Chlorophenyl)-1*H*-1,2,3-triazol-1-yl]-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}-acetamide (11g). Yield 61%, mp 260–262°C. ^{1}H NMR spectrum, δ, ppm: 5.62 s (2H), 7.50 d (1H, J = 8.11 Hz), 7.55 d (2H, J = 7.26 Hz), 7.58 d (2H, J = 7.28 Hz), 7.62 d (2H, J = 7.26 Hz), 7.67 d (1H, J = 8.14 Hz), 7.71 d (1H, J = 8.10 Hz), 7.77 d (2H, J = 7.28 Hz), 7.82 s (1H), 7.84 d (1H, J = 8.11 Hz), 8.25 s (1H), 10.11 s (1H). ^{13}C NMR spectrum, δ, ppm: 55.6, 114.5, 116.5, 117.3, 120.7, 124.5, 125.4, 126.5, 128.6, 130.6, 131.5, 132.5, 133.4, 134.7, 143.2, 144.7, 148.3, 149.3, 149.8, 154.6, 157.9, 162.9. MS (ESI): m/z: 530 $[M + H]^+$.

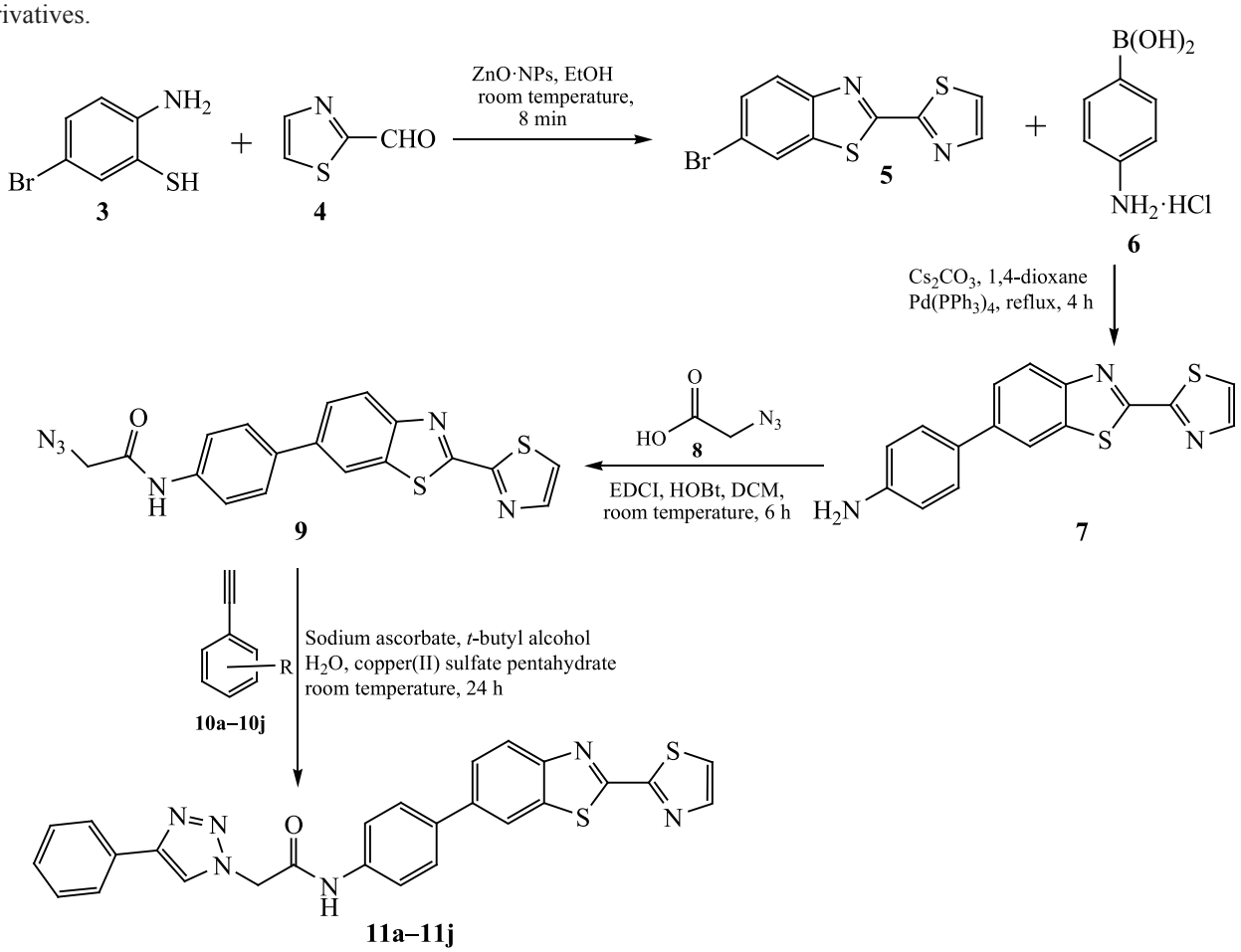
2-[4-(4-Bromophenyl)-1*H*-1,2,3-triazol-1-yl]-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}-acetamide (11h). Yield 66%, mp 266–268°C. ^{1}H NMR spectrum, δ, ppm: 5.64 s (2H), 7.48 d (2H, J = 7.29 Hz), 7.53 d (1H, J = 8.10 Hz), 7.56 d (2H, J = 7.25 Hz), 7.59 d (2H, J = 7.29 Hz), 7.63 d (2H, J = 7.25 Hz), 7.67 d (1H, J = 8.09 Hz), 7.72 d (1H, J = 8.07 Hz), 7.81 s (1H), 7.84 d (1H, J = 8.10 Hz), 8.27 s (1H), 10.10 s (1H). ^{13}C NMR spectrum, δ, ppm: 55.7, 114.5, 116.4, 117.3, 120.5, 122.4, 124.6, 125.3, 126.5 128.6, 130.5, 131.2, 132.6, 134.4, 143.5, 144.3, 147.6, 148.4, 149.5, 154.6, 157.9, 162.8. MS (ESI): m/z: 575 $[M + H]^+$.

2-(4-Mesityl-1*H*-1,2,3-triazol-1-yl)-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}acetamide (11i). Yield 52%, mp 247–249°C. ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H), 2.41 s (6H), 5.49 s (2H), 7.16 s (2H), 7.50 d (1H, J = 8.09 Hz), 7.55 d (2H, J = 7.25 Hz), 7.60 d (2H, J = 7.25 Hz), 7.66 d (1H, J = 8.13 Hz), 7.70 d (1H, J = 8.12 Hz), 7.79 s (1H), 7.83 d (1H, J = 8.09 Hz), 8.22 s (1H), 10.09 s (1H). ^{13}C NMR spectrum, δ, ppm: 23.5, 24.8, 55.6, 114.5, 116.4, 117.3, 120.5, 124.5, 125.6, 126.3, 129.6, 130.2, 131.3, 134.5, 136.4, 138.6, 143.2, 144.5, 147.6, 148.6, 149.7, 154.6, 157.8, 162.7. MS (ESI): m/z: 538 $[M + H]^+$.

2-[4-(3,5-Dimethylphenyl)-1*H*-1,2,3-triazol-1-yl]-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}-acetamide (11j). Yield 54%, mp 262–264°C. ^{1}H NMR spectrum, δ, ppm: 2.37 s (6H), 5.46 s (2H), 7.10 s (2H), 7.17 s (1H), 7.50 d (1H, J = 8.08 Hz), 7.53 d (2H, J = 7.23 Hz), 7.57 d (2H, J = 7.23 Hz), 7.63 d (1H, J = 8.11 Hz), 7.69 d (1H, J = 8.10 Hz), 7.78 s (1H), 7.83 d (1H, J = 8.08 Hz), 8.23 s (1H), 10.09 s (1H). ^{13}C NMR spectrum, δ, ppm: 23.7, 55.7, 114.7, 116.4, 117.5, 120.6, 124.5, 125.4, 126.5, 129.6, 131.3, 132.6, 134.5, 135.8, 140.5, 143.3, 146.8, 147.4, 148.4, 149.7, 154.6, 157.8, 162.6. MS (ESI): m/z: 524 $[M + H]^+$.

MTT assay. Individual wells of a 96-well tissue culture micro titre plate were inoculated with 100 μL of complete medium containing 1×10^4 cells. The plates were incubated at 37°C in a humidified 5% CO_2 incubator for 18 h prior to the experiment. After medium removal, 100 μL of fresh medium containing the test compounds and etoposide (Eto) at concentrations 0.5, 1 or 2 μM were added to each well and incubated at 37°C for 24 h. Then the medium was discarded and replaced with 10 μL of MTT dye. Plates were incubated at 37°C for 2 h. The resulting formazan crystals were solubilized in 100 μL

Scheme 1. Synthesis of 2-(4-arylsubstituted-1*H*-1,2,3-triazol-1-yl)-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}acetamide derivatives.



R = H (**10a**, **11a**), 3,4,5-trimethoxy (**10b**, **11b**), 3,5-dimethoxy (**10c**, **11c**), 4-methoxy (**10d**, **11d**), 4-nitro (**10e**, **11e**), 3,5-dinitro (**10f**, **11f**), 4-chloro (**10g**, **11g**), 4-bromo (**10h**, **11h**), 2,4,6-trimethyl (**10i**, **11i**), 3,5-dimethyl (**10j**, **11j**).

of extraction buffer. Optical density (O.D) was read at 570 nm with a micro plate reader (Multi-mode Varioskan Instrument-Themo Scientific). Percentage of DMSO in the medium never exceeded 0.25%.

RESULTS AND DISCUSSION

The synthetic route to the target compounds **11a**–**11j** is presented in Scheme 1. 2-Amino-5-bromobenzenethiol (**3**) was reacted with thiazole-2-carbaldehyde (**4**) in presence of zinc oxide nanoparticles used as the catalyst in absolute ethanol to afford pure compound 6-bromo-2-(thiazol-2-yl)benzo[*d*]thiazole (**5**). The intermediate **5** was subjected to the Suzuki-coupling reaction with 4-aminophenylboronic acid hydrochloride (**6**) in presence of Cs_2CO_3 base and $Pd(PPh_3)_4$ catalyst to afford pure intermediate **7**, which was coupled with 2-azidoacetic acid (**8**) in presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDCI) and hydroxybenzotriazole (HOBt) in anhydrous dichloromethane to afford pure compound **9**. Its following cycloaddition reaction with substituted arylalkynes **10a**–**10j** in presence of sodium ascorbate and copper(II) sulfate pentahydrate used as a catalyst in *tert*-butyl alcohol–H_2O (1 : 1) led to the corresponding products **11a**–**11j.**

Biological activity. *In vitro cytotoxicity.* The products **11a**–**11j** were tested for their anticancer activity towards four different human cancer cell lines: MCF-7 (breast), A549 (lung), Colo-205 (colon), and A2780 (ovarian) using the MTT assay and etoposide as a standard drug (Table 1). All derivatives demonstrated activity in the range of IC_{50} values 0.10±0.039 to 20.5±6.23 μM and the standard drug was characterized by IC_{50} 0.13±0.017 to 3.08 ± 0.135 μM. Their structure-activity relationship (SAR) indicated that compound **11b** with 3,4,5-trimethoxy substituents on the phenyl ring of triazole

Table 1. In vitro cytotoxicity activity of the products **11a**–**11j**

Compounds	IC_{50}, μM[a]			
	MCF-7	A549	Colo-205	A2780
11a	4.78±2.33	6.12±3.01	12.2±4.34	–
11b	0.10±0.039	0.15±0.037	0.18±0.034	1.22±0.62
11c	1.37±0.66	1.42±0.69	0.98±0.073	1.65±0.80
11d	2.89±1.55	1.99±0.82	1.73±0.76	2.08±1.92
11e	0.12±0.036	0.19±0.04	1.83±0.74	0.54±0.044
11f	1.29±0.77	2.00±1.48	2.10±1.58	Not active
11g	1.63±0.11	1.88±0.78	Not active	1.60±0.45
11h	13.2±5.78	9.15±4.55	8.12±4.51	3.44±1.23
11i	14.02±5.11	5.87±2.34	Not active	18.3±6.11
11j	20.5±6.23	Not active	3.99±2.09	Not active
Etoposide	2.11±0.024	3.08 ± 0.135	0.13±0.017	1.31±0.27

[a] Each data represents as mean ±S.D values.

possessed the most potent anticancer activity against all cell lines (MCF-7 = 0.10±0.039, A549 = 0.15±0.037, Colo-205 = 0.18±0.034, and A2780 = 1.22±0.62 μM). The compound **11c** containing 3,5-dimethoxy groups demonstrated lower activity (MCF-7 = 1.37±0.66, A549 = 1.42±0.69, Colo-205 = 0.98±0.073, and A2780 = 1.65±0.80 μM) than **11b**. Compound **11d** with the mono electron-donating (4-methoxy) substituent exhibited even lower activity (MCF-7 = 2.89±1.55, A549 = 1.99±0.82, Colo-205 = 1.73±0.76, and A2780 = 2.08±1.92 μM) than **11b** and **11c.** Replacement of 4-methoxy group with electron-withdrawing (4-nitro) group in compound **11e** resulted in its increased anticancer activity (MCF-7 = 0.12±0.036, A549 = 1.99±0.82, Colo-205 = 1.73±0.76, and A2780 = 2.08±1.92 μM) higher than **11d**. Two electron-withdrawing groups, 3,5-dinitro, of **11f** on the phenyl ring led to a remarkable decline in activity (MCF-7 = 1.29±0.77, A549 = 2.00±1.48, and Colo-205 = 2.10±1.58 μM).

CONCLUSIONS

We have designed and synthesized ten novel derivatives of 2-(4-arylsubstituted-1*H*-1,2,3-triazol-1-yl)-*N*-{4-[2-(thiazol-2-yl)benzo[*d*]thiazol-6-yl]phenyl}-acetamide (**11a**–**11j**), and their structures have been confirmed by ^{1}H and ^{13}C NMR, and mass spectral data.

The products have been studied for their anticancer activity towards human cancer cell lines MCF-7 (breast), A549 (lung), Colo-205 (colon), and A2780 (ovarian). Among the synthesized compounds, six products demonstrate activity higher than the standard drug.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

1. Huang, S.T., Hsei, I.J., and Chen, C., *Bioorg. Med. Chem.,* 2006, vol. 14, p. 6106. https://doi.org/10.1016/j.bmc.2006.05.007
2. Gurupadayya, B.M., Gopal, M., Padmashali, B., and Vaidya, V.P., *Ind. J. Heterocy. Chem.,* 2005, vol. 15, p. 169.
3. Palmer, F.J., Trigg, R.B., and Warrington, J.V., *J. Med. Chem.,* 1971, vol. 14, p. 248. https://doi.org/10.1021/jm00285a022
4. Siddiqui, N., Alam, M., and Siddiqui, A.A., *Asian J. Chem.,* 2004, vol. 16, p. 1005.
5. Singh, S.P. and Segal, S., *Ind. J. Chem. B,* 1988, vol. 27, p. 941.
6. Akhtar, T., Hameed, S., Al-Masoudi, N., Loddo, R., and Colla, P., *Acta Pharm.,* 2008, vol. 58, p. 135. https://doi.org/10.2478/v10007-008-0007-2
7. Burger, A. and Sawhey, S.N., *J. Med. Chem.,* 1968, vol. 11, p. 270. https://doi.org/10.1021/jm00308a018
8. Singh, M., Singh, S.K., Gangwar, M., Nath, G., and Singh, S.K., *RSC Adv.,* 2014, vol. 4, p. 19013. https://doi.org/10.1039/C4RA02649G
9. Hutchinson, I., Bradshaw, T.D., Matthews, C.S., Stevens, M.F., and Westwell, A.D., *Bioorg. Med. Chem. Lett,,* 2003, vol. 13, p. 471. https://doi.org/10.1016/S0960-894X(02)00930-7
10. Cho, S., Oh, S., Um, Y., Jung, J.H., Ham, J., Shin, W.S., and Lee, S., *Bioorg. Med. Chem. Lett.,* 2009, vol. 19, p. 382. https://doi.org/10.1016/j.bmcl.2008.11.067
11. Yang, Y., Rasmussen, B.A., and Shlaes, D.M., *Pharmacol. Ther.,* 1999, vol. 83, p. 141. https://doi.org/10.1016/s0163-7258(99)00027-3