Research Article

Rational Design of Disubstituted 1, 3, 4-Thiadiazoles with Potential Utility as Anti-Cancer Drugs

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Abstract

A series of disubstituted 1, 3, 4-thiadiazoles were designed, synthesized and evaluated as multi-potent anti-cancer drug candidates. The synthesized compounds have been evaluated for in-vitro anti-cancer activity against human cervical cancer cell line (HeLa). The screening results showed that most of them exhibited a significant ability to inhibit human cervical cancer cell line (HeLa). All IC_{50} values of biological activity were at the micro molar range. Especially, compound TZ1 displayed greatest ability to inhibit with 74.85 percentage of cell inhibition against the human cervical cancer cell line (HeLa), which have dimethylamino group at C-2 position in the thiadiazole nucleus with an IC50 value of 45.70. Other compounds TZ5, TZ6 and TZ10 showed moderate cell line inhibition.

Keywords: 1, 3, 4-Thiadiazole; Anti-cancer; Human Cell Lines; Cell Inhibition; In-vitro

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Introduction

Cancer is an important public health on concern and in developed countries it represents the second leading cause of death, after cardiovascular disease. The resistance to chemotherapeutic anti-tumor agents by cancer cells could be minimized using a combination of drugs with different and complementary mechanism of action. Therefore, there is a need to discover and develop useful new lead compounds of simple structure, exhibiting optimal *in vitro* anti-tumor potency and new mechanism of action.

As a part of our ongoing new drug development program of ACD, disubstituted 1, 3, 4-thiadiazoles have been explored as possible anticancer agents. 1,3,4-thiadiazoles belong to an important class of heterocyclic compound containing sulphur and nitrogen atom and received much attention of medicinal chemists due to their potential biological activities [1-5]. 1, 3, 4-thiadiazoles are reported to possess significant hypoglycemic, anti-inflammatory, cholerectic, anti-HIV, diuretic, immunosuppressant, antipsychotic and anticonvulsant activities [6]. Among these, the pharmacological activities of 2, 5-disubstituted 1, 3, 4-thiadiazoles are interesting [7-9]. Prompted by these reports, we aimed at preparing a series of 2, 5- disubstituted 1, 3, 4-thiadiazoles for anticancer activity.

Experimental

Chemistry

Melting points (mp) were taken in open capillaries on Thomas Hoover melting point apparatus and are uncorrected. The IR spectra were recorded in film or in potassium bromide disks on a Perkin-Elmer 398 spectrometer. The 1H spectra were recorded on a DPX-500 MHz Bruker FT-NMR spectrometer. The chemical shifts were reported as parts per million (ppm) tetramethylsilane (TMS) as an internal standard. Mass spectra were obtained on a JEOL-SX-102 instrument using fast atom bombardment (FAB positive). Elemental analysis was performed on a Perkin-Elmer 2400 C, H, N analyzer and values were within the acceptable limits of the calculated values. The progress of the reaction was monitored on readymade silica gel plates (Merck) using chloroform-methanol (9:1) as a solvent system. Iodine was used as a developing agent. Spectral data (IR, NMR and mass spectra) confirmed the structures of the synthesized compounds and the purity of these compounds was ascertained by microanalysis. Elemental (C,H,N) analysis indicated that the calculated and observed values were within the acceptable limits (± 0.4%). All chemicals and

reagents were obtained from Aldrich (USA), Lancaster (UK) or Spectrochem Pvt.Ltd (India) and were used without further purification.

General Procedure for synthesis of substituted N-(5-aryl-1, 3, 4-thiadiazole-2-yl)-2-alkyl / aryl substituted acetamides (TZ 1-10)

A mixture of thiosemicarbazide (0.1mol) and aryl carboxylic acid (0.1mol) in conc.sulphuric acid (10 drops) was reflux for 1 hr & poured onto crushed ice. The solid separated out was filtered, washed with water (I&Ia). Further, 5-aryl -1, 3, 4-thiadiazol-2-amine (I&Ia) (0.3mol) were dissolved in glacial acetic acid (20ml) containing 20ml of saturated solution of sodium acetate. In case the substance did not dissolve completely, the mixture was warmed and the solution was cooled in ice bath with stirring. To this chloroacetyl chloride was added drop wise (0.06mol) with stirring. After half an hour white product separated and filtered. The product was washed with 50% aqueous acetic acid and finally with water. Finally, a mixture of N-(5 aryl-1, 3, 4-thiadiazole-2-yl)-2-chloroacetamides (II &IIa) (0.01mol) were taken in a 25ml of ethyl alcohol and alkyl and aryl substituted derivatives (0.01mol) were added and refluxed for 4hr. The resulting mixture was purified by recrystallization from alcohol.

5-p-tolyl-1, 3, 4-thiadiazol-2-amine (I)

Yield 91%, mp 156-158 °C; IR (KBr, cm^{-1}): 3375, 3291 (NH_2), 1620 (C=N Str), 675 (C-S-C). 1HNMR ($CDCl_3$) δ (ppm): 2.35 (s, 3H, CH_3), 5.93 (s, 2H, NH_2), 7.12 (d, *J = 8.0 Hz*, 2H, Ar-H), 7.36 (d, *J = 8.0Hz*, 2H, Ar-H). MS (m/z): 191 [M+]. Anal. Calcd. for $C_9H_9N_3S$: 56.50; H, 4.73; N, 21.95. Found: C, 56.52; H, 4.74; N, 21.97.

5-(4-bromophenyl)-1, 3, 4-thiadiazol-2-amine (Ia)

Yield 76%, mp 197-199 °C; IR (KBr, cm^{-1}): 3375, 3290 (NH_2), 1620 (C=N Str), 675 (C-S-C), 651 (C-Br). 1HNMR ($CDCl_3$) δ (ppm): 5.93 (s, 2H, NH_2), 7.37 (d, *J = 8.0 Hz*, 2H, Ar-H), 7.49 (d, *J = 8.0Hz*, 2H, Ar-H). MS (m/z): 256 [M+], 258(M+2). Anal. Calcd. for $C_9H_9N_3S$: C, 37.50; H, 2.35 ; N, 16.40.. Found: C, 37.52; H, 2.36; N, 16.41.

2-chloro-N-(5-methyl-1, 3, 4-thiadiazol-2-yl)acetamide (II)

Yield 79%, mp 142-145 °C; IR (KBr, cm^{-1}): 3426 (NH Str), 1710 (C=O), 1620 (C=N Str), 674 (C-S-C). 1HNMR ($CDCl_3$) δ (ppm): 2.37(s, 3H, CH_3), 4.27 (s, 2H, CH_2), 7.12 (d, *J = 8.0 Hz*, 2H, Ar-H), 7.36 (d, *J = 8.0Hz*, 2H, Ar-H), 8.02 (s, 1H, NH). MS (m/z): 191 [M+]. Anal. Calcd. for $C_5H_6ClN_3OS$: C, 31.32; H, 3.15 N, 21.90.Found: C, 31.32; H, 3.16 N, 21.92.

N-(5-bromo-1, 3, 4-thiadiazol-2-yl) - 2-chloroacetamide (IIa)

Yield 80%, mp 208-210 °C; IR (KBr, cm^{-1}): 3432 (NH Str), 1718 (C=O), 1626 (C=N Str), 683 (C-S-C), 631(C-Br).^{1}HNMR ($CDCl_3$) δ (ppm): 4.28 (s, 2H, CH_2), 7.35 (d, *J = 8.0 Hz*, 2H, Ar-H), 7.45 (d, *J = 8.0Hz*, 2H, Ar-H), 8.01 (s, 1H, NH). MS (m/z): 305[M+], 307(M+2). Anal. Calcd. for $C_4H_3BrClN_3OS$: C, 18.71; H, 1.17; N, 16.36..Found: C, 18.73; H, 1.18; N, 16.38.

2-(dimethylamino)-N-(5-p-tolyl-1, 3, 4-thiadiazol-2-yl)acetamide(TZ1)

Yield 70%, mp 150-152 °C; IR (KBr, cm^{-1}): 3457 (NH Str), 2929($N(CH_3)_2$, 1716 (C=O), 1622 (C=N Str), 651 (C-S-C).^{1}HNMR ($CDCl_3$) δ (ppm): 2.27 (d, 3H, CH_3), 2.35(s, 3H, CH_3), 3.25 (s, 2H,CH_2), 7.14(d, *J = 8.0 Hz*,2H, Ar-H), 7.34 (d, *J =8.0Hz*,2H, Ar-H),8.06(s,1H,NH).MS (m/z): 276[M+]. Anal. Calcd. for $C_{13}H_{16}N_4OS$: C, 56.48; H, 5.83; N, 20.25.Found: C, 56.50; H, 5.84; N, 20.27.

2-(pyrrolidino)-N-(5-p-tolyl-1, 3, 4 -thiadiazol-2-yl) acetamide(TZ 2)

Yield 67%, mp 184-186 °C; IR (KBr, cm^{-1}): 3478 (NH Str), 1704 (C=O), 1647 (C=N Str), 693 (C-S-C).^{1}HNMR ($CDCl_3$) δ (ppm): 1.59 (d, 2H, CH_2), 2.25 (d, 2H, CH_2), 2.32(s,3H,CH_3), 3.24(s,2H,CH2), 7.14(d, *J= 7.5 Hz*, 2H, Ar-

H),7.38(d, *J = 8.0 Hz*, 2H, Ar-H), 8.06(s,1H,NH). MS (m/z): 302[M+]. Anal. Calcd. for $C_{15}H_{18}N_4OS$: C, 59.56; H, 5.99; N, 18.53. Found: C, 59.58; H, 6.00; N, 18.51.

2-(piperidino)-N-(5-p-tolyl-1, 3, 4 -thiadiazol-2-yl) acetamide (TZ 3)

Yield 73%, mp 216-218 °C; IR (KBr, cm^{-1}): 3418 (NH Str), 2929(CH_3),1714 (C=O), 1629 (C=N Str),689(C-S-C).^{1}HNMR ($CDCl_3$) δ (ppm): 1.50 (s, 2H, CH_2), 2.24 (s, 2H, CH_2), 2.25 (s, 2H, CH_2) 2.35(s,3H,CH_3), 3.27(s,2H,CH_2), 7.10(m, *J= 7.5 Hz*, 4H, Ar-H),7.66(m, *J = 8.0 Hz*, 8H, Ar- H), 8.01(s,1H,NH).. MS (m/z): 316[M+]. Anal. Calcd. for $C_{16}H_{20}N_4OS$: C, 60.70; H, 6.36; N, 17.69. Found: C, 60.68; H, 6.35; N, 17.67.

2-(imidazolo)-N-(5-p-tolyl-1, 3, 4-thiadiazol-2-yl) acetamide (TZ 4)

Yield 76%, mp 190-192 °C; IR (KBr, cm-1): 3417 (NH Str), 2929(CH3),1710 (C=O), 1626 (C=N Str),689(C-S-C).1HNMR (CDCl3) δ (ppm): 2.32 (s,3H,CH3), 3.52(s,2H,CH2), 6.88 (s, 1H,CH), 7.0(s,1H,CH) 7.12(d, J= 7.5 Hz, 2H, Ar-H),7.35(d,J=8.0Hz, 4H, Ar- H), 7.45 (s, J=8.0Hz 4H,CH), 8.03(s,1H,NH). MS (m/z): 299[M+]. Anal. Calcd. for C14H13N5OS: C, 56.15; H, 4.37; N, 23.38. Found: C, 56.17; H, 4.38; N, 23.40.

2-(morpholino)-N-(5-p-tolyl-1, 3, 4-thiadiazol-2-yl) acetamide (TZ 5)

Yield 71%, mp 204-206 °C; IR (KBr, cm^{-1}): 3465 (NH Str), 2929(CH_3), 1702 (C=O), 1620 (C=N Str),689(C-S-C). ^{1}HNMR($CDCl_3$)δ(ppm): 2.34(s,3H,CH_3), 2.37(s,2H,CH_2),(s,2H,CH_2), 3.25(s,2H,CH_2), 3.67(d,2H,CH_2), 7.12(m,*J=7.5Hz*,4H,Ar-H), 7.34(m,*J=8.0Hz*,8H,Ar-H), 8.05(s,1H,NH). MS (m/z): 318[M+]. Anal. Calcd. for $C_{15}H_{18}N4O_2S$: C, 56.56; H, 5.69; N, 17.58.Found: C, 56.58; H, 5.70; N, 17.60.

N-(5-(4-bromophenyl)-1, 3, 4-thiadiazol-2-yl)-2-(dimethylamino) acetamide (TZ 6)

Yield 80%, mp 157-159 °C; IR (KBr, cm^{-1}): 3420 (NH Str), 2816(CH_3), 1713 (C=O), 1626 (C=N Str), 689(C-S-C), 654 (C-Br)..^{1}HNMR ($CDCl_3$) δ (ppm): 2.27 (d, 6H, CH_3), 3.24 (s, 2H, CH_2), 7.37 (d, *J = 8.0Hz*, 2H, Ar-H), 7.69 (d, 2H, Ar-H), 8.02 (s, 1H, NH). MS (m/z): 341(M+), 343 (M+2). Anal. Calcd. for $C_{12}H_{13}BrN_4OS$: C, 42.22; H, 3.84; N, 16.40. Found: C, 42.24; H, 3.84; N, 16.42.

N-2-(Pyrolidino) (5-(4-bromophenyl)-1, 3, 4-thiadiazol-2-yl) acetamide (TZ 7)

Yield 84%, mp 217-219 °C; IR (KBr, cm^{-1}): 3442 (NH Str), 2946 (CH_3), 1704 (C=O), 1647 (C=N Str), 672(C-S-C), 654 (C-Br).^{1}HNMR ($CDCl_3$) δ (ppm): 1.59 (d, 2H, CH_2), 2.25 (d,1H, OH),3.23 (s, 2H, CH_2),7.36(d,*J=8.0Hz*,2H, Ar-H),7.48(d, *J=8.0Hz*, 2H, Ar-H), 8.01(s,1H,NH).MS (m/z): 367(M+), 369(M+2). Anal. Calcd. for $C_{14}H_{15}BrN_4OS$: C, 45.76; H, 4.11; N, 15.25. Found: C, 45.78; H, 4.12; N, 15.26.

N-2-(Piperidino)(5-(4-bromophenyl)-1, 3, 4-thiadiazol-2-yl) acetamide (TZ 8)

Yield 79%, mp 222-224 °C; IR (KBr, cm^{-1}): 3443 (NH Str), 2989 (CH_3), 1714 (C=O), 1629 (C=N Str), 689(C-S-C), 659 (C-Br).^{1}HNMR ($CDCl_3$) δ (ppm): 1.52(d, 2H,CH_2), 2.24 (s, 2H, CH_2), 6.21 (d,8H, CH_2), 7.37 (d, *J = 8.0 Hz*, 2H, Ar-H), 7.45 (d, *J = 8.0 Hz*, 2H, Ar-H), 8.02(s,1H,NH).MS (m/z): 305(M+), 307(M+2). Anal. Calcd. for $C_9H_{13}BrN_4OS$: C, 35.40; H, 4.28; N, 18.34.. Found: C, 35.42; H, 4.29; N, 18.36.

N-2-(Piperidino)(5-(4-bromophenyl)-1, 3, 4-thiadiazol-2-yl) acetamide (TZ 9)

Yield 76%, mp 245-247 °C; IR (KBr, cm^{-1}): 3478 (NH Str), 2929 (CH_3), 1710 (C=O), 1626 (C=N Str), 689(C-S-C), 653 (C-Br).^{1}HNMR ($CDCl_3$) δ (ppm): 3.44 (s, 2H, CH_2), 6.21 (d, 2H, CH_2), 7.01 (s, 2H, CH), 7.36(d, *J = 8.0 Hz*,2H, Ar- H),7.47 (d, *J =7.0Hz*, 2H, Ar-H), 8.0(s,1H,NH).MS (m/z): 288(M+), 290(M+2). Anal. Calcd. for $C_7H_6BrN_5OS$: C, 29.15; H, 2.10; N, 24.29. Found: C, 29.18; H, 2.10; N, 24.31.

N-2-(Morpholino) (5-(4-bromophenyl)-1, 3, 4-thiadiazol-2-yl) acetamide (TZ 10)

Yield 81%, mp 226-228 °C; IR (KBr, cm^{-1}): 3474 (NH Str), 2876 (CH_3), 1712 (C=O), 1620 (C=N Str), 689(C-S-C),

655 (C-Br).^{1}HNMR ($CDCl_3$) δ (ppm): 2.90 (d, 4H, CH_2), 3.42 (s, 2H, CH_2), 3.65 (s, 4H, CH_2), 7.37-(d, *J = 8.0 Hz*,2H, Ar-H),7.49 (d, *J =7.0Hz*, 2H, Ar-H), 8.02(s,1H,NH)..MS (m/z): 307(M+), 309(M+2). Anal. Calcd. for $C_8H_{11}BrN_4O_2S$: C, 31.26; H, 3.61; N, 18.22.. Found: C, 31.28 H, 3.61; N, 18.24.

Pharmacological activity

Acute Toxicity Studies

Acute toxicity study was performed for all the synthesized compounds to ascertain safe dose by acute oral toxic class method of Organization of Economic Co-operation and Development, as per 423 guidelines (OECD). All the compounds tested for acute toxicity studies were also observed for gross behavioral changes in mice, continuously for 5 h at 1 h interval after administration of the compounds. There after the observations were recorded intermittently for 24 h and compared with that of control group. In the behavioral profile, the animals have been observed for changes in their awareness and mood.

Assay for Proliferation Studies - MTT Assay

MTT [(3-(4, 5-dimethyl thiazol-2yl)-2,5diphenyl tetrazolium bromide] measures the metabolic activity of the viable cells [10-13]. The assay can be performed entirely in a microtiterplate (MTP). It is suitable for measuring cell proliferation, Cell viability or Cytotoxicity. The reaction between MTT and mitochondrial dehydrogenase produces water-insoluble formazan salt. This method involves culturing the cells in a 96 well microtiterplate and then incubating with MTT solution for approximately 2 hours. During incubation period, viable cells convert MTT to a water insoluble formazan dye. The formazan dye in the MTP is solubilized and quantified with an ELISA plate reader. The absorbance directly correlates with the cell number. This is applicable for adherent cells cultured in MTP.

The human cervical cancer cell line (HeLa) was obtained from National Centre for Cell Science (NCCS), Pune. The cells were grown in Eagles Minimum Essential Medium containing 10% fetal bovine serum (FBS).

For screening experiment, the cells were seeded into 96-well plates in 100µl of medium containing 5 % FBS, at plating density of 10,000 cells/well and incubated at 37 ^{0}C, 5 % CO_2, 95 % air and 100 % relative humidity for 24 hours prior to addition of samples. The samples were solubilized in Dimethyl sulfoxide and diluted in serum free medium. After 24 hours, 100 µl of the medium containing the samples at various concentration (eg; 0.063, 0.125, 0.25, 0.5, 1.0 mM etc) was added and incubated at 37^{0}C, 5% CO_2, 95% air and 100% relative humidity for 48 hours. Triplicate was maintained and the medium containing without samples were served as control[41].After 48 hours, 15µl of MTT (5mg/ml) in phosphate buffered saline (PBS) was added to each well and incubated at 37 ^{0}C for 4 hours. The medium with MTT was then flicked off and the formed formazan crystals were solubilized in 100µl of DMSO and then measured the absorbance at 570 nm using micro plate reader. The % cell inhibition was determined using the following formula.

$$\% \text{ cell Inhibition} = 100 - \{(\text{sample}) / \text{Abs (control)}\} \times 100$$

Nonlinear regression graph was plotted between % Cell inhibition and Log10 concentration and IC50 was determined using GraphPad Prism software.

Statistical Analysis

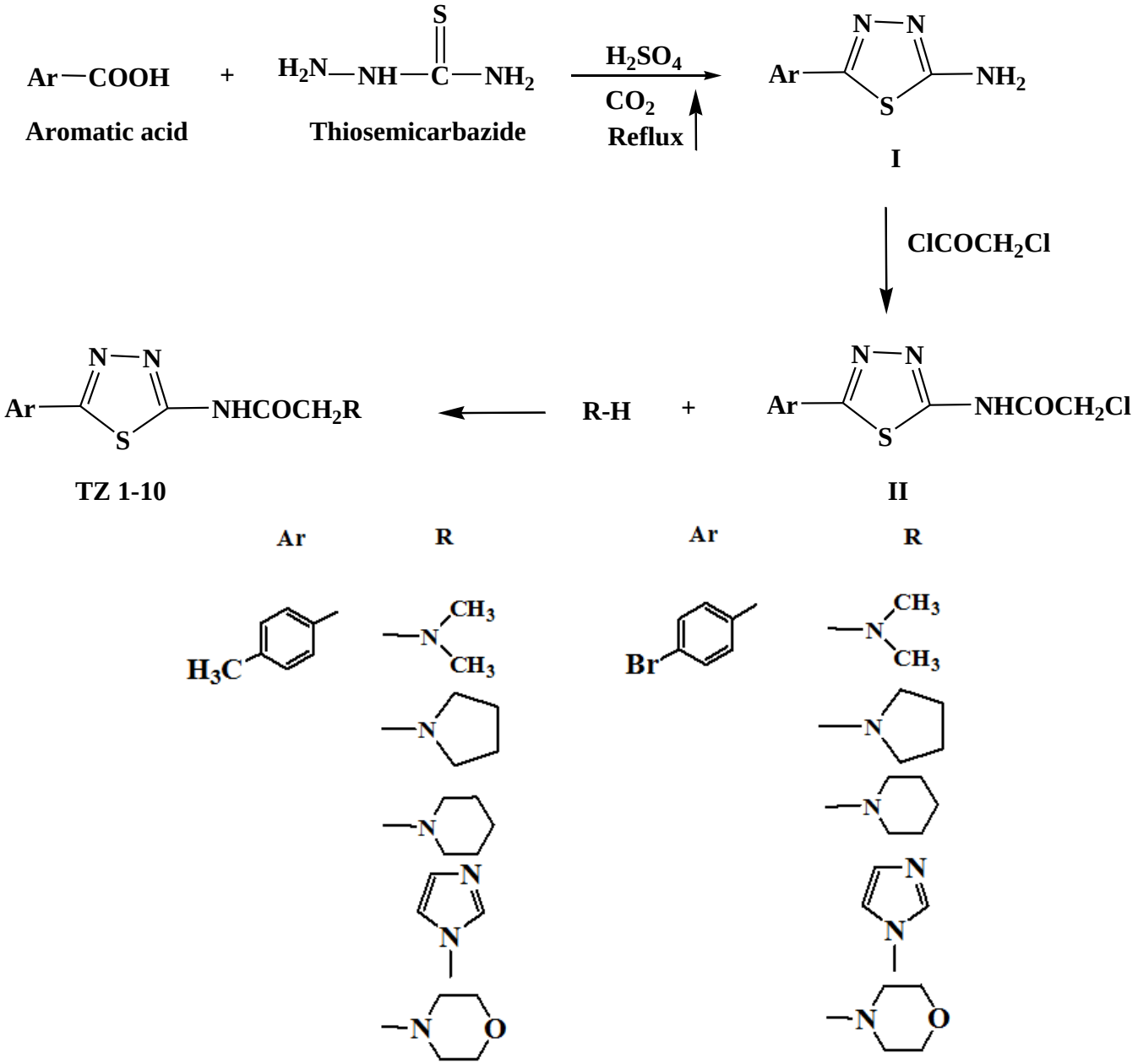
Data were analyzed by using Graph Pad PRISM software. A *p*-value < 0.05 was considered significantly different.

Results and Discussion

Chemistry

Synthetic route depicted in scheme outline the chemistry part of the present work. The N-(5-aryl-1, 3, 4-thiadiazole-2-yl)-2-alkyl / aryl substituted acetamides (TZ1-10) were obtained by the condensation of N-(5 aryl-1, 3, 4-thiadiazole-2-yl)-2-chloroacetamide with alkyl and aryl substituted derivatives in presence of ethanol. The formation of the 1,3,4-thiadiazole was confirmed by the presence of characteristic peaks in the IR spectra. It showed characteristic peaks at around 3400 cm^{-1} for NH_2 stretching and peak around 2900 cm^{-1} due to the presence of N=CH stretching. The NMR

spectrum of the compounds TZ1-10 showed the characteristic peak around δ 2.70 ppm for CH_3 group, δ 3.00 ppm for CH_2 and δ 5.70 ppm for NCH and also shows multiplet in the range of δ 6.80-7.80 ppm owing to aromatic protons. The appearance of peak due to chlorine, bromine and fluorine in IR spectra is around 700 -800 cm^{-1} and formation M+2 peak in the mass spectra. Further elemental analysis and molecular ion recorded in the mass spectra confirmed the assigned structures and confirmed their purity.



Scheme 1 Synthesis of 2, 5-disubstituted-1, 3, 4-thiadiazoles (TZ1-TZ10)

Pharmacology

All the synthesized compounds (TZ1-10) were evaluated for their in-vitro anticancer activity against human cervical cancer cell line (HeLa) by MTT assay method. In this assay the effective ranges of anticancer activity for compounds TZ1-10 were in the concentration of 0.1, 1.0, 10, 100 µM respectively in the human cervical cancer cell line (HeLa). Triplicate was maintained and the medium containing without samples were served as control. The data regarding the in-vitro anti-cancer screening of all the compounds are reported in **Table 1**.

Table 1 *In vitro* cytotoxicity studies on Human cervical cancer cell line (HeLa)

PERCENTAGE OF CELL INHIBITION					
Compounds	**Concentration**	**% cell Inhibition**	**Compounds**	**Concentration**	**% cell Inhibition**
TZ1	0.1 µM	1.3342	**TZ6**	0.1 µM	1.2342
	1 µM	12.6079		1 µM	12.3079
	10 µM	33.8761		10 µM	32.9861
	100 µM	**74.8578**		100 µM	**73.8578**
TZ2	0.1 µM	1.0424	**TZ7**	0.1µM	3.1895
	1 µM	10.4447		1 µM	14.2646
	10 µM	22.9848		10 µM	23.6772
	100 µM	52.8995		100 µM	**55.0587**
TZ3	0.1 µM	3.4112	**TZ8**	0.1µM	1.4315
	1 µM	13.7176		1 µM	19.6317
	10 µM	33.8976		10 µM	35.4864
	100 µM	**51.3006**		100 µM	**60.8275**
	0.1 µM	1.5342	**TZ9**	0.1 µM	1.4846
TZ4	1 µM	12.9079		1 µM	11.3278
	10 µM	30.9861		10 µM	30.3398
	100 µM	**62.8578**		100 µM	**60.0175**
TZ5	0.1 µM	1.4424	**TZ10**	0.1 µM	1.4579
	1 µM	11.4447		1 µM	11.0145
	10 µM	28.9848		10 µM	28.2358
	100 µM	**70.8995**		100 µM	**70.1268**

In-vitro anticancer Activity

All the synthesized compounds were evaluated for in-vitro anticancer activity and have shown promising anticancer activity. All the tested compounds showed ability to inhibit the cancerous human cell lines. From the biological activity data reported in Table 1, it may be inferred that the anti-cancer activity is strongly dependent on the nature of the substituent at C-2 and C-5 of the 1, 3, 4-thiadiazole ring. Compounds TZ1, TZ5, TZ6 and TZ10 showed a high significant anticancer activity against the human cervical cancer cell line (HeLa). In particular, a high activity level was observed for compound TZ1 possessing a dimethyl amino group at C-2 and a 4-methylphenyl ring at C-5. When dimethylamino group at C-2 and 4-methyl group at C-5 was replaced by pyrrolidine, piperidine group (TZ2 and TZ3) and 4-bromo group (TZ7 and TZ8) of the 1,3,4-thiadiazole ring, the anticancer activity was altered and has exhibited less significant effect and produced less IC50 value in case of the human cervical cancer cell line (HeLa). In the present study, the anti-cancer activity was enhanced by introducing aliphatic dimethyl amino and morpholine group at C-2 (1 and 5) and 4-methylphenyl group at C-5 of the 1,3,4-thiadiazole ring. Compounds (TZ1-TZ5) having 4-methyl phenyl substituent at C-5 of the 1, 3, 4-thiadiazole ring system have shown better activity and produced IC50 value of 45.70 µM in case of the human cervical cancer cell line (HeLa) which is relatively less IC50 value indicates the sample has more anticancer activity in comparison to 4-bromo phenyl subsistent (TZ6-TZ10). Among the test compounds, compound 2-(dimethylamino)-N-(5-p-tolyl-1, 3, 4-thiadiazol-2-yl)acetamide (TZ1) emerged as most active compound and shown a 74.85 percentage of cell inhibition against the human cervical cancer cell line (HeLa) in the highest concentration.

Conclusion

In summary, synthesis of new series of 2, 5-disubstituted 1, 3, 4-thiadiazoles (TZ1-TZ10) has been described. In this study, the title compounds 2, 5-disubstituted 1, 3, 4-thiadiazole was obtained by cyclization of substituted aromatic acid and thiosemicarbazide in good yield with improved yield. The title compounds have exhibited promising anti-cancer activity. Among the test compounds, compound 2-(dimethylamino)-N-(5-p-tolyl-1, 3, 4-thiadiazol-2-yl)acetamide (TZ1) emerged as most active compound and shown a 74.85 percentage of cell inhibition against the human cervical cancer cell line (HeLa) in the highest concentration.

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