International Journal for Pharmaceutical Research Scholars (IJPRS)

V-3, I-3, 2014 ISSN No: 2277 - 7873

RESEARCH ARTICLE

Synthesis and Characterization of Some Novel Benzothiazole Fused Thiazolidine Derivatives

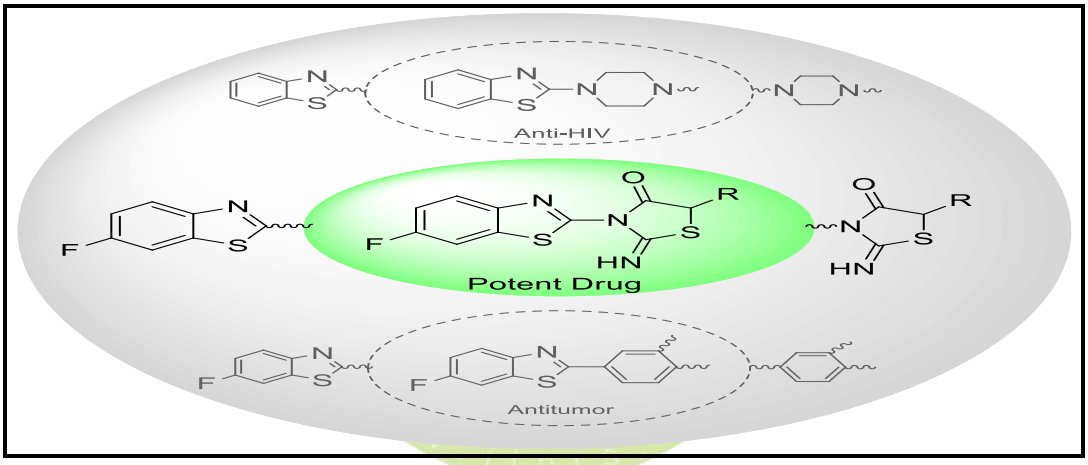
Gondaliya MB*, Manawar RB, Jadeja JJ, Baluja SH, Shah MK

Chemistry Department, Saurashtra University, Rajkot, Gujarat-360005, India.

Manuscript No: IJPRS/V3/I3/00333, Received On: 10/07/2014, Accepted On: 20/07/2014

ABSTRACT

A series of novel benzothiazole fused with thiazolidine derivatives were synthesized and analyzed. Substituted aniline was reacted with bromine, potassium thiocynate in the presence of glacial acetic acid to give substituted benzothiazole. Substituted benzothiazole was further reacted with chloroacetyle chloride and cyclized with potassium thiocynate to give benzothiazole fused thiazolidine system. This fused ring were derivatised by different aldehydes which were characterized by MASS, IR and ^{1}H and $^{13}CNMR$.



KEYWORDS

Synthesis, Benzothiazole, Thiazolidines

INTRODUCTION

Fused systems are becoming the dwindling interest in numerous academia and industrial research laboratories. Due to its applicability as newer drug discovery potential. Various benzothiazole fused thiadiazole rings had shown anticonvulsant activity[1] and some of them are very interestingly protects against seizures spread. While benzothiazole fused barbituric acid derivatives have also shown anticonvulsant activity[2]. While benzthiazole fused piperazine derivatives had shown anti-cancer activity[4]. Benzothiazole fused peperazine fused 1,8-naphthyridone derivatives are reported as anti-HIV agents[5]. with the aim of therapeutic usage and their preparation, we undertook experimentally synthesis of some benzothiazole fused with thiazolidine system.

***Address for Correspondence:**
Mitesh B. Gondaliya
Chemistry Department, Saurashtra University,
Rajkot, Gujarat-360005, India.
E-Mail Id:miteshgondaliya@scientist.com

EXPERIMENTAL

For the synthesis 100ml RBF fitted with a condenser was used in oil bath and used magnetic stirrer with Hot. All the solvents were used were of either Spectrochem® or Finar®. Melting point is uncorrected and taken in the open capillaries. All Mass, IR and NMR spectral proofs were given in Electronic supplementary Information. Typical Preparation of 6-fluoro-1,3-benzothiazol-2-amine (1) was adapted from else[6].

Preparation of 2-chloro-N-(6-fluoro-1,3-benzothiazol-2-yl) acetamide (2)

Equimolar amounts of 6-fluoro-1,3-benzothiazol-2-amine (0.1 mole) and chloro acetyl chloride (0.1 mole) were added to 30 ml of chloroform and the mixture was refluxed in the presence of K_2CO_3 (0.1 mole) for about 12 hours. Excess of solvent was removed in vacuum and the residue was stirred with water (50 ml). The residue was washed with 5% $NaHCO_3$ (30 ml) and subsequently with water (30 ml). The crude product was dried and crystallized from methanol. The % yield is about 80%. Melting point is 180 °c. Crystallized in Methanol. Mass M^+=244; IR (KBr) ν(cm^{-1}), 3138 (-NH), 1716 (C=O), 1602 (CONH), ; ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 7.3-8.1 (m, 3H, ArH benzothiazole), 4.25 (s, 2H, CH_2), 9.7 (s, 1H, NH) ; ^{13}C NMR (δ ppm) 171.55, 154.66, 153.43, 148.78, 134.23, 120.15, 113.67, 108.45, 41.99. Anal. calcd. (In %): C 44.18, H 2.47, N 11.45 and S 13.11. Found (in %): C 44.20, H 2.45, N 11.46 and S 13.10.

Preparation of 3-(6-fluoro-1,3-benzothiazol-2-yl)-2-imino-1,3-thiazolidin-4-one (3)

A mixture of 2-chloro-N-(6-fluoro-1,3-benzothiazol-2-yl) acetamide (0.01 mole), KSCN (0.02 mole) and dry acetone (50 mL) was refluxed for about 3 hours. Excess of solvent was removed in vacuum and the residue was stirred with water (50 ml). The solid product was filtered, washed with water and dried. The crude product was crystallized from methanol to furnish light brown solid. The % yield is about 75%. Melting point is 164 °c. Crystallized in Methanol. Mass M^+=267; IR (KBr) ν(cm^{-1}), 2989 (-NH), 1730 (C=O), 1566 (C=NH), ; ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 7.2-8.0 (m, 3H, ArH), 3.8 (s, 2H, CH_2), 4.7 (s, 1H, NH); ^{13}C NMR (δ ppm) 176.14, 160.44, 154.72, 149.16, 146.08, 134.65, 120.85, 114.97, 110.11, 31.79. Anal. calcd. (In %): C 44.93, H 2.26, N 15.72 and S 23.99. Found (in %): C 44.90, H 2.29, N 15.77 and S 23.94.

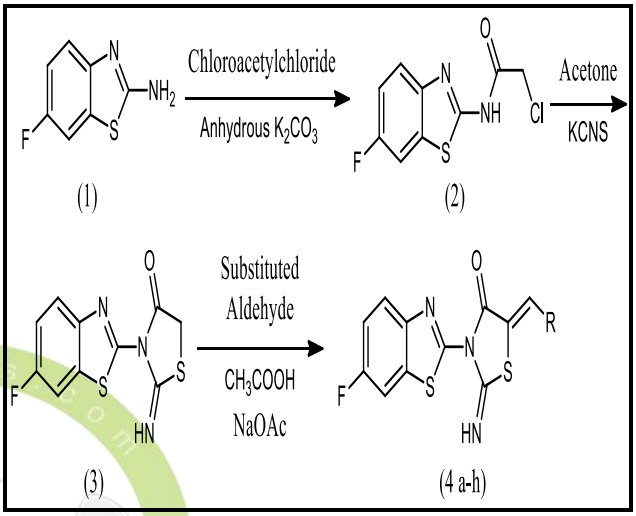


Figure 1: Synthetic Reaction Scheme

Preparation of 5-arylidene-3-(6-fluorobenzo[d]thiazol-2-yl)-2-iminothiazolidin-4-one (4a-h)

3-(6-fluorobenzo[d]thiazol-2-yl) -2-iminothiazolidin-4-one (0.01 mole) and aromatic Aldehyde (0.02 mole) were added to a solution of anhydrous Sodium acetate NaOAc (0.02 mole) in Acetic acid AcOH (30 ml). The mixture was refluxed for 5 hours at 120^{0}C and cooled to room temperature. The solid product was filtered from the mixture, washed with water and dried.

5-benzylidene-3-(6-fluorobenzo[*d*]thiazol-2-yl)-2-iminothiazolidin-4-one (4a): Mass M^+=355; IR (KBr) ν(cm^{-1}), 2960 (-NH), 1724 (C=O), 1589 (C=NH); ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 7.2-8.2 (m, 8H, ArH), 4.8 (s, 1H, NH); ^{13}C NMR (δ ppm) 175.75, 161.54, 154.72, 149.68, 149.16, 134.65, 132.83, 132.10, 130.07, 129.38, 129.38, 128.84, 128.84, 120.85, 120.18, 114.97, 110.11. Anal. calcd. (In %): C 57.45, H 2.84, N 11.82 and S 18.04. Found (in %): C 57.44, H 2.86, N 11.84 and S 18.06.

Table 1: Physical constants

Code	Substitutions -R	Molecular formula	M.Wt.	M.P. (°C)	% yield
1	-	$C_7H_5FN_2S$	168	180	70
2	-	$C_9H_6ClFN_2OS$	244	232	80
3	-	$C_{10}H_6FN_3OS_2$	267	164	75
4a	--C_6H_5	$C_{17}H_{10}FN_3OS_2$	355	182	75
4b	-C_6H_4-p-Cl	$C_{17}H_9ClFN_3OS_2$	389	188	72
4c	-C_6H_4-p-OH	$C_{17}H_{10}FN_3O2S_2$	371	202	80
4d	-C_6H_4-p-N(CH_3)$_2$	$C_{19}H_{15}FN_4OS_2$	398	178	65
4e	-CH=CH-C_6H_5	$C_{19}H_{12}FN_3OS_2$	381	216	78
4f	-C_6H_4-p-F	$C_{17}H_9F2N_3OS_2$	373	232	80
4g	-C_6H_4-o-Cl	$C_{17}H_9ClFN_3OS_2$	389	152	85
4h	-C_6H_4-m-CH_3	$C_{18}H_{12}FN_3OS_2$	369	198	74

5-(4-chlorobenzylidene)-3-(6-fluorobenzo[d]thiazol-2-yl)-2-iminothiazolidin-4-one (4b): Mass M^+=389; IR (KBr) ν(cm^{-1}), 2950 (-NH), 1728 (C=O), 1565 (C=NH); ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 7.1-8.1 (m, 7H, ArH), 4.7 (s, 1H, NH); ^{13}C NMR (δ ppm) 175.75, 161.54, 154.72, 149.68, 149.16, 135.58, 134.65, 132.48, 132.10, 130.33, 130.33, 129.35, 129.35, 120.85, 120.18, 114.97, 110.11. Anal. calcd. (In %): C 52.37, H 2.33, N 10.78 and S 16.45. Found (in %): C 52.35, H 2.39, N 10.77 and S 16.43.

3-(6-fluorobenzo[d]thiazol-2-yl)-5-(4-hydroxybenzylidene)-2-iminothiazolidin-4-one (4c): Mass M^+=371; IR (KBr) ν(cm^{-1}), 2950 (-NH), 1724 (C=O), 1570 (C=NH), 3580 (ArOH); ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 7.1-8.2 (m, 7H, ArH), 4.8 (s, 1H, NH), 5.3 (s, 1H, ArOH); ^{13}C NMR (δ ppm) 175.75, 161.54, 159.84, 154.72, 149.68, 149.16, 134.65, 132.10, 131.17, 131.17, 124.69, 120.85, 120.18, 115.77, 115.77, 114.97, 110.11. Anal. calcd. (In %): C 54.98, H 2.71, N 11.31 and S 17.27. Found (in %): C 54.96, H 2.70, N 11.30 and S 17.26.

5-(4-(dimethylamino)benzylidene)-3-(6-fluorobenzo[d]thiazol-2-yl)-2-iminothiazolidin-4-one (4d): Mass M^+=398; IR (KBr) ν(cm^{-1}), 2960 (-NH), 1718 (C=O), 1568 (C=NH), 2860 (CH_3) ; ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 7.0-8.2 (m, 7H, ArH), 4.7 (s, 1H, NH), 2.8 (s, 6H, N(CH_3)$_2$); ^{13}C NMR (δ ppm) 175.75, 161.54, 154.72, 150.78, 149.68, 149.16, 134.65, 132.10, 131.02, 131.02, 121.02, 120.85, 120.18, 114.97, 112.77, 112.77, 110.11, 41.91, 41.91. Anal. calcd. (In %): C 57.27, H 3.79, N 14.06 and S 16.09. Found (in %): C 57.25, H 3.77, N 14.05 and S 16.10.

3-(6-fluorobenzo[*d*]thiazol-2-yl)-2-imino-5-(3-phenylallylidene)thiazolidin-4-one (4e): Mass M^+=381; IR (KBr) ν(cm^{-1}), 2964 (-NH), 1716 (C=O), 1566 (C=NH); ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 6.7-8.1 (m, 11H, ArH), 4.8 (s, 1H, NH); ^{13}C NMR (δ ppm) 172.32, 161.54, 154.72, 149.68, 149.16, 139.28, 138.57, 136.75, 134.65, 129.12, 129.12, 128.76, 128.45, 127.56, 127.56, 122.09, 120.85, 114.97, 110.11. Anal. calcd. (In %): C 59.83, H 3.17, N 11.02 and S

16.81. Found (in %): C 59.80, H 3.19, N 11.06 and S 16.80.

3-(6-fluorobenzo[*d*]thiazol-2-yl)-5-(4-fluorobenzylidene)-2-iminothiazolidin-4-one (4f)

Mass M^+=373; IR (KBr) ν(cm^{-1}), 2950 (-NH), 1718 (C=O), 1564 (C=NH); ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 6.9-8.0 (m, 7H, ArH), 4.6 (s, 1H, NH); ^{13}C NMR (δ ppm) 175.75, 164.48, 161.54, 154.72, 149.68, 149.16, 134.65, 132.10, 131.57, 131.57, 130.75, 120.85, 120.18, 115.02, 115.02, 114.97, 110.11. Anal. calcd. (In %): C 54.68, H 2.43, N 11.25 and S 17.17. Found (in %): C 54.69, H 2.44, N 11.26 and S 17.15.

5-(2-chlorobenzylidene)-3-(6-fluorobenzo[d]thiazol-2-yl)-2-iminothiazolidin-4-one (4g)

Mass M^+=389; IR (KBr) ν(cm^{-1}), 2954 (-NH), 1715 (C=O), 1560 (C=NH); ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 7.1-7.3 (m, 4H, Cl-Benzene ArH), δ 7.2-7.9 (m, 3H, ArH), 4.7 (s, 1H, NH); ^{13}C NMR (δ ppm) 13C NMR (δ ppm) 175.75, 161.54, 154.72, 149.68, 149.16, 134.65, 133.17, 131.12, 130.73, 130.00, 129.20, 126.99, 123.18, 121.31, 120.85, 114.97, 110.11. Anal. calcd. (In %): C 52.37, H 2.33, N 10.78 and S 16.45. Found (in %): C 52.38, H 2.33, N 10.78 and S 16.44.

3-(6-fluorobenzo[d]thiazol-2-yl)-2-imino-5-(3-methylbenzylidene)thiazolidin-4-one (4h)

Mass M^+=369; IR (KBr) ν(cm^{-1}), 2958 (-NH), 1715 (C=O), 1568 (C=NH), 2895 (CH_3); ^{1}H NMR (δ ppm) (400 MHz, DMSO) δ 7.0-8.1 (m, 7H, ArH), 4.7 (s, 1H, NH); ^{13}C NMR (δ ppm) 13C NMR (δ ppm) 175.75, 161.54, 154.72, 149.68, 149.16, 138.32, 134.92, 134.65, 132.07, 131.19, 130.17, 128.12, 127.59, 120.85, 120.16, 114.97, 110.11, 21.21. Anal. calcd. (In %): C 58.52, H 3.27, N 11.37 and S 17.36. Found (in %): C 58.51, H 3.26, N 11.35 and S 17.38.

ACKNOWLEDGMENTS

The authors are thankful to SAIF, Chandigarh for NMR of the compounds. The authors are also grateful to the U.G.C. for the financial assistance.

REFERENCES

1. Siddiqui, N., Rana, A., Khan, S., Haque, S., Arshad, M., Ahmed, S., & Ahsan, W. (2009). Synthesis and preliminary screening of benzothiazol-2-yl thiadiazole derivatives for anticonvulsant activity. *Acta Pharmaceutica*, *59*(4), 441-451.
2. Siddiqui, N., & Ahsan, W. (2009). Benzothiazole incorporated barbituric acid derivatives: synthesis and anticonvulsant screening. *Archiv der Pharmazie*, *342*(8), 462-468.
3. Hazra, K., Nargund, L. V. G., Rashmi, P., Narendra, S. C. J. N., Nandha, B., Harish, M. S. (2012). Synthesis and Comparative Study of Anti-Mycobacterium Activity of a Novel Series of Fluoro nitro benzothiazolo pyrazoline Regioisomers. *Arch. Pharm. (Weinheim)*, *345*, 137–146.
4. Murty, M. S. R., Rao, B. R., Katiki, M. R., Nath, L. R., & Anto, R. J. (2013). Synthesis of piperazinyl benzothiazole/benzoxazole derivatives coupled with 1, 3, 4-oxadiazole-2-thiol: novel hybrid heterocycles as anticancer agents. *Medicinal Chemistry Research*, *22*(10), 4980-4991.
5. Massari, S., Daelemans, D., Barreca, M. L., Knezevich, A., Sabatini, S., Cecchetti, V., & Tabarrini, O. (2009). A 1, 8-naphthyridone derivative targets the HIV-1 Tat-mediated transcription and potently inhibits the HIV-1 replication. *Journal of Medicinal Chemistry*, *53*(2), 641-648.
6. Rana, A., Siddiqui, N., Khan, S. A., Ehtaishamul Haque, S., & Bhat, M. A. (2008). N-{[(6-Substituted-1, 3-benzothiazole-2-yl) amino] carbonothioyl}-2/4-substituted benzamides: Synthesis and pharmacological evaluation. *European Journal of Medicinal Chemistry*, *43*(5), 1114-1122.

