One-pot Synthesis and Characterization of Highly Functionalized Thiazoles

Beyzaei, Hamid*[+]; Beygi, Adel; Aryan, Reza

Department of Chemistry, Faculty of Science, University of Zabol, Zabol, I.R. IRAN

ABSTRACT: *A facile and efficient one-pot three-step process for the synthesis of 5-acetyl-2-imino-4-methylthiazoles via the cyclocondensation of 3-thiocyanatoacetylacetone with various hydrazine or hydrazide derivatives in EtOH has been developed. 3-Thiocyanatoacetylacetone itself has been synthesized as the intermediate from substitution reaction of thiocyanate with 3-chloroacetylacetone. Better results were obtained by three-step procedures vs one-step reaction. The proposed method does not required techniques such as extraction and chromatography. Surprisingly, 3,5-dimethyl-4-thiocyanato-1H-pyrazoles were not produced in this reaction, it was proved based on the existence of the acetyl group in the products. The molecular structures of newly synthesized compounds were elucidated on the basis of elemental analysis and spectral data.*

KEYWORDS: *One-pot synthesis; Thiazole; Cyclocondensation; Hydrazine; Hydrazide.*

INTRODUCTION

Thiazole derivatives are appeared in many natural and synthetic products with a wide range of pharmacological activities. For example, thiazole ring is present in vitamin B_1 and its coenzyme, which play in the electron sink and the decarboxylation of α-keto acids, respectively [1]. They are also helpful in the normal function of the nervous system due to their role in the synthesis of acetylcholine (a neurotransmitter).

Thiazole ring system occurs in the antibiotics bacitracin, penicillin and in numerous synthetic drugs. Synthetic drugs belonging to the thiazole family include the antimicrobial agents sulfathiazole and acinitrazole [2], anti-HIV drug ritonavir [3], the antidepressant pramipexole [4], antineoplastic agents bleomycin and tiazofurin [5], the antiasthmatic drug cinalukast [6], antiulcer agent nizatidine [7]. Thiazole derivatives such as the non-steroidal anti-inflammatory drug meloxicam [8] and fanetizole [9] were also used in wide range. Thiazole derivatives containing 1,3,4-thiadiazole, 1,3,4-oxadiazole and 1,2,4-triazole substituents have showed the distinct antibacterial and antifungal activities [10]. Thiazole is known as a ligand of estrogen receptors [11] and the novel class of antagonists for adenosine receptors [12].

Commercial significant thiazoles are found in many fungicides and dyes. Thifluzamide, tricyclazole, and thiabendazole are marked for control of various agricultural pests [13, 14]. Red and yellow dyes of rhodanine and primuline are some examples of the thiazole derivatives [15, 16].

According to the emerging importance of thiazoles and their derivatives, several methods for their synthesis were developed by using the various catalysts [17-21], conditions [22-27] and strategies [28-34]. The development of novel methods for the improvement of time, yield,

* *To whom correspondence should be addressed.*
+ E-mail: hbeyzaei@yahoo.com
1021-9986/2016/4/31 7/$/5.70

and reaction conditions is still in demand. In this study, highly functionalized thiazoles were synthesized in moderate to good yields *via* an efficient method, without necessity of using the toxic and expensive solvents and catalysts. Besides, the products were purified in a simple and quick process.

Based on the above information and our interest in thiazole as a biologically active pharmacophore [35-39] and the widespread application of one-pot processes in the synthesis of heterocyclic compounds [40-44], we have developed a one-pot procedure for the synthesis of highly functionalized thiazoles, starting from 3-chloroacetylacetone and potassium thiocyanate (KSCN) without isolation of the intermediate 3-thiocyanatoacetylacetone. The synthesized compounds are characterized by NMR, IR spectral data, and elemental analysis.

EXPERIMENTAL SECTION

All chemicals and solvents were purchased from Merck and TCI chemical companies and were used without purification. All yields refer to isolated products. Melting points were recorded on a Kruss type KSP1N melting point meter and are uncorrected. The IR spectra of products were determined as KBr pellets on Bruker Tensor-27 FT-IR spectrometer. The ^{1}H and ^{13}C NMR spectra of DMSO-d_6 solutions were recorded on a Bruker FT-NMR Ultra Shield-400 spectrometer with residual protons of the solvent as internal standard (2.50 ppm for ^{1}H and 39.48 ppm for ^{13}C). Elemental analyses were performed for C, H, N and S on a Thermo Finnigan Flash EA microanalyzer. Monitoring of the progress of reactions and the purity of the products were effected by TLC on alufoil plates pre-coated with silica gel (60, Merck), eluent was $CHCl_3$-CH_3OH, 9:1, visualization with I_2 vapor.

General procedure for the preparation of 5-acetyl-2-imino-4-methylthiazoles (3a-f)

A suspension of 3-chloroacetylacetone (**1**) (1.35 g, 10 mmol) and potassium thiocyanate (KSCN) (0.97 g, 10 mmol) in absolute ethanol (10 mL) was mixed at room temperature for 2h. Then, hydrazine or hydrazide derivatives **2a-f** were added dropwise to the reaction mixture. The mixture was stirred for a further 3h at the same temperature before it was heated under reflux for 6-8 h (8 h for **3a,b**; 6 h for **3c,d,f** and 7 h for **3e**). After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and poured gradually onto crashed ice. The slurry was filtered off, dried, and recrystallized from various ratios of ethanol-water mixtures to provide the pure products **3a-f**.

1-(3-Amino-2-imino-4-methyl-2,3-dihydrothiazol-5-yl) ethan-1-one (3a)

Bright orange powder, Yield 0.82 g, 48%, m.p 188–189 °C. IR (KBr): 3467, 3340, 1693, 1623, 1506, 1471, 1278, 1243, 1106, 774, 513 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): 2.14 (s, 3H, CH_3-C=C), 2.31 (s, 3H, CH_3CO), 8.00 (s, 2H, NH_2), 12.53 (b, 1H, C=NH). ^{13}C NMR (100 MHz, DMSO-d_6): 14.2 ($\underline{C}H_3$-C=C), 29.3 ($\underline{C}H_3CO$), 106.4 (CH_3-C=$\underline{C}$), 158.1 (C=NH), 170.0 (CH_3-$\underline{C}$=C), 186.1 (C=O). Anal. Calcd for $C_6H_9N_3OS$: C, 42.09; H, 5.30; N, 24.54; S, 18.72. Found: C, 42.02; H, 5.26; N, 24.61; S, 18.75.

1-(3-((2,4-Dinitrophenyl)amino)-2-imino-4-methyl-2,3-dihydrothiazol-5-yl)ethan-1-one (3b)

Dark orange powder, Yield 1.85 g, 55%, m.p 111–112 °C. IR (KBr): 3325, 2987, 1707, 1618, 1505, 1448, 1380, 1341, 1317, 1256, 1100, 922, 836, 759, 742 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): 2.12 (s, 3H, CH_3-C=C), 2.32 (s, 3H, CH_3CO), 8.07, 8.64 (d, 1H, J = 8.2 Hz, m, 2H, Ph), 8.91 (s, 1H, NNH), 12.49 (s, 1H, C=NH). ^{13}C NMR (100 MHz, DMSO-d_6): 12.2 ($\underline{C}H_3$-C=C), 29.3 ($\underline{C}H_3CO$), 107.8 (CH_3-C=$\underline{C}$), 121.2 (C-3), 128.6 (C-1), 130.1 (C-6), 133.0 (C-5), 146.4 (C-2), 154.1 (C-4), 156.0 (C=NH), 170.2 (CH_3-$\underline{C}$=C), 186.3 (C=O). Anal. Calcd for $C_{12}H_{11}N_5O_5S$: C, 42.67; H, 3.32; N, 20.82; S, 9.45. Found: C, 42.73; H, 3.29; N, 20.76; S, 9.50.

N-(5-Acetyl-2-imino-4-methylthiazol-3(2H)-yl)benzamide (3c)

Bright yellow powder, Yield 2.2 g, 80%; m.p 217–218 °C. IR (KBr): 3199, 3011, 1701, 1632, 1578, 1535, 1488, 1447, 1339, 1279, 989, 933, 784, 689 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): 2.12 (s, 3H, CH_3-C=C), 2.31 (s, 3H, CH_3CO), 7.51 (s, 1H, H-4), 7.54 (d, 2H, J = 7.6 Hz, H-3,5), 7.93 (d, 2H, J = 7.0 Hz, H-2,6), 10.52 (s, 1H, C=NH), 12.67 (b, 1H, NNH). ^{13}C NMR (100 MHz, DMSO-d_6): 13.3 ($\underline{C}H_3$-C=C), 29.2 ($\underline{C}H_3CO$), 117.1 (CH_3-C=$\underline{C}$), 127.4 (C-2,6), 128.4 (C-3,5), 130.7 (C-4), 131.8 (C-1), 154.4 (C=NH), 165.8 (NHCO), 170.3 (CH_3-$\underline{C}$=C),

186.2 ($CH_3\underline{C}$=O). Anal. Calcd for $C_{13}H_{13}N_3O_2S$: C, 56.75; H, 4.82; N, 15.28; S, 11.57. Found: C, 56.71; H, 4.76; N, 15.26; S, 11.64.

N-(5-Acetyl-2-imino-4- methylthiazol-3(2H)-yl)-4-hydroxybenzamide (3d)

Dark yellow powder, Yield 1.89 g, 65%, m.p 182–183 °C. IR (KBr): 3409, 3258, 2360, 1717, 1616, 1541, 1508, 1457, 1324, 1291, 922, 781, 669 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): 2.14 (s, 3H, CH_3-C=C), 2.31 (s, 3H, CH_3CO), 6.90 (d, 2H, J = 8.5 Hz, H-3,5), 7.89 (d, 2H, J = 8.5 Hz, H-2,6), 8.06 (s, 1H, OH), 10.14 (s, 1H, C=NH), 12.50 (s, 1H, NNH). ^{13}C NMR (100 MHz, DMSO-d_6): 13.0 ($\underline{C}H_3$-C=C), 29.2 ($\underline{C}H_3CO$), 110.6 (CH_3-C=$\underline{C}$), 114.8 (C-3,5), 129.4 (C-1), 134.1 (C-2,6), 153.6 (C=NH), 162.0 (C-4), 166.5 (NHCO), 170.2 (CH_3-$\underline{C}$=C), 186.3 ($CH_3\underline{C}$=O). Anal. Calcd for $C_{13}H_{13}N_3O_3S$: C, 53.64; H, 4.55; N, 14.37; S, 10.93. Found: C, 53.60; H, 4.50; N, 14.42; S, 11.00.

N-(5-Acetyl -2-imino-4- methylthiazol-3 (2H) -yl) acetamide (3e)

Dark yellow powder, Yield 1.09 g, 51%, m.p 198–199 °C. IR (KBr): 3287, 3179, 2372, 1745, 1611, 1506, 1418, 1372, 1336, 1273, 984, 961, 670 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): 2.10 (s, 3H, NHCOC$\underline{H}_3$), 2.13 (s, 3H, CH_3-C=C), 2.30 (s, 3H, CH_3CO), 10.24 (s, 1H, C=NH), 12.60 (b, 1H, NNH). ^{13}C NMR (100 MHz, DMSO-d_6): 14.2 ($\underline{C}H_3$-C=C), 17.2 ($\underline{C}H_3$CONH), 29.3 ($\underline{C}H_3CO$), 109.2 (CH_3-C=$\underline{C}$), 160.1 (C=NH), 168.6 (NHCO), 170.1 (CH_3-$\underline{C}$=C), 186.0 ($CH_3\underline{C}$=O). Anal. Calcd for $C_8H_{11}N_3O_2S$: C, 45.01; H, 5.15; N, 19.78; S, 14.99. Found: C, 45.06; H, 5.20; N, 19.70; S, 15.03.

N-(5-Acetyl-2-imino-4-methylthiazol -3(2H)-yl)furan-2-carboxamide (3f)

White powder, Yield 1.91 g, 72%, m.p 278–279 °C (dec). IR (KBr): 3433, 3297, 2367, 1687, 1607, 1558, 1500, 1462, 1348, 1290, 1030, 954, 878, 784, 600 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): 2.13 (s, 3H, CH_3-C=C), 2.31 (s, 3H, CH_3CO), 7.95 (d, 1H, J = 3.6 Hz, H-5), 8.18 (m, 1H, H-3), 8.83 (m, 1H, H-4), 10.37 (s, 1H, C=NH), 12.43 (s, 1H, NNH). ^{13}C NMR (100 MHz, DMSO-d_6): 13.3 ($\underline{C}H_3$-C=C, 29.2 ($\underline{C}H_3CO$), 107.1 (CH_3-C=$\underline{C}$), 112.8 (C-3), 124.6 (C-4), 144.5 (C-5), 149.2 (C-2), 155.5 (NHCO), 159.9 (C=NH), 170.3 (CH_3-$\underline{C}$=C), 186.3 ($CH_3\underline{C}$=O). Anal. Calcd for $C_{11}H_{11}N_3O_3S$: C, 49.73; H, 4.23; N, 15.88; S, 12.04. Found: C, 49.80; H, 4.18; N, 15.84; S, 12.09.

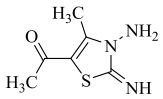
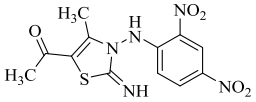
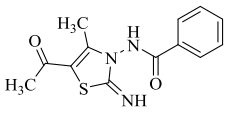
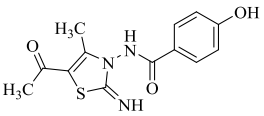
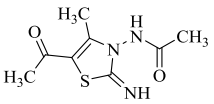
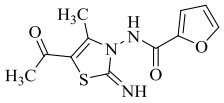
RESULTS AND DISCUSSION

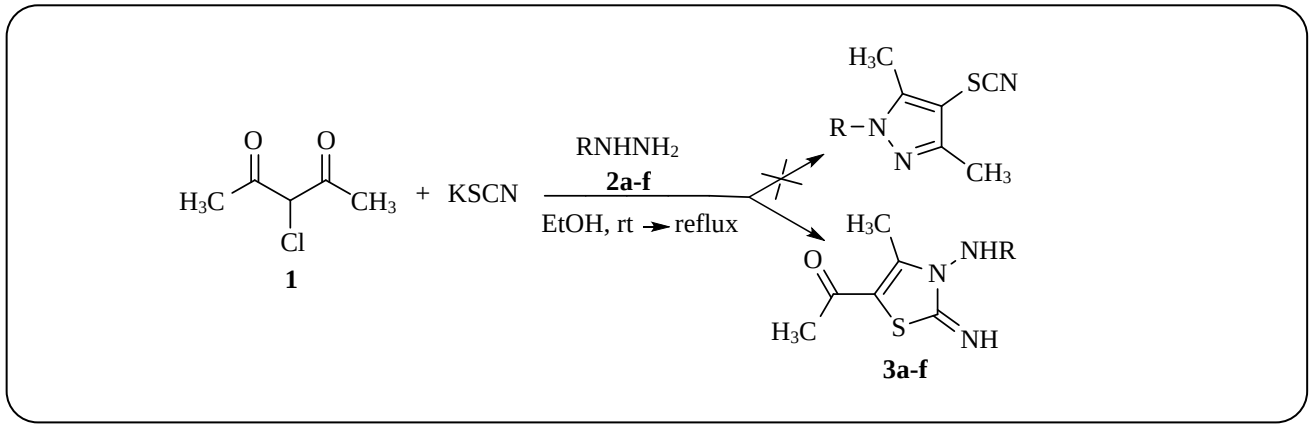
Highly functionalized thiazoles **3a-f** were prepared in a simple and facile one-pot three-step procedure. Initially, 3-chloroacetylacetone (**1**) was reacted with potassium thiocyanate (KSCN) in ethanol at room temperature for 2 h to give 3-thiocyanatoacetylacetone as intermediate. Then, this compound was reacted with various hydrazine or hydrazide derivatives **2a-f** under the same conditions for another 3 h to complete the ketone-amine condensation reaction. Finally, the reaction mixture was refluxed for 6-8 h before being poured into crashed ice to precipitate out new thiazoles **3a-f** as white or colored solids in 48–80% yields after recrystallization from ethanol-water (Scheme 1). The structure of all products are presented in Table 1.

The one-step reaction between reagents led to various unidentified by-products which resulted in the lower yield of the desired products. Therefore, a three-step process was preferably used. During this process, 3,5-dimethyl-4-thiocyanato-1*H*-pyrazoles were not produced, it can be easily proved by the presence of acetyl group in products. A plausible mechanism is depicted for the formation of thiazoles (**3a-f**) (Scheme 2). As shown, the nucleophilic substitution of chloride by thiocyanate led to formation of intermediate **1'** as an unstable solid [45], although its analogues have been successfully prepared [46]. Then, compound **2** was condensed with hydrazine and hydrazide derivatives **3a**–**f** to generate intermediates **2′a**–**f**. Finally, intramolecular nucleophilic addition of the NH group to the carbon atom of the C≡N bond were afforded thiazoles **3a-f**.

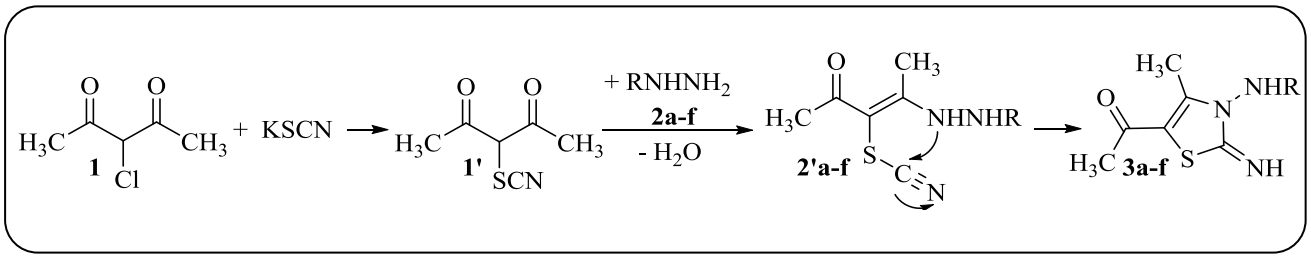
The structural assignments of compounds **3a-f** were based on their analytical and spectral data. The ^1H NMR spectra of compounds **3a-f** showed singlet signals due to methyl protons of acetyl group within δ = 2.30–2.32 ppm, signals of methyl and -NH- groups of the thiazole ring within δ = 2.12–2.14 ppm and δ = 10.14–12.53 ppm respectively, and singlet or broad signals appeared within δ = 8.91-12.67 ppm belonging to -NNH- groups. The ^{13}C NMR spectra of the products exhibited signals within δ = 29.2–29.3 ppm and δ = 186.0–186.3 ppm attributed to methyl and carbonyl carbons included in acetyl group,

Table 1: One-pot synthesis of highly functionalized thiazoles 3a-f.

Entry	R	Product
3a	H	
3b	2,4-$[NO_2]_2$-C_6H_3	
3c	C_6H_5CO	
3d	4-OH-C_6H_4CO	
3e	CH_3CO	
3f	2-C_4H_3O-CO	



Scheme 1: Synthesis of thiazole derivatives 3a-f.



Scheme 2: Proposed mechanism.

signals within δ = 12.2–14.2 ppm, δ = 106.4–117.2 ppm, δ = 170.0–170.3 ppm and δ = 153.6–160.1 ppm attributed to the $\underline{C}H_3$-C=C-, -S-$\underline{C}$=C-, -S-C=$\underline{C}$- and -C=NH carbons respectively, signals appeared within δ = 155.5-168.6 relating to carbonyl carbons adjacent to the -NH- groups of compounds **3c-f**. The FT-IR spectra of **3a-f** in KBr disk showed the absorption bands within ν = 3179–3467 cm^{-1} corresponding to –NH– groups, within ν = 1687–1715 cm^{-1} belonging to carbonyl groups, within ν = 1607–1632 cm^{-1} belonging to imine groups and within ν = 1505–1578 cm^{-1} attributed to the endocyclic –C=C–. Also absence of absorption band of nitrile group around 2200 cm^{-1} plus microanalytical data strongly support the formation of all products.

CONCLUSIONS

In summary, an efficient protocol for the one-pot synthesis of highly functionalized thiazoles have been described from the cyclocondensation of 3-thiocyanatoacetylacetone as intermediate with various hydrazines or hydrazides, which constitute potential precursors for the synthesis of various biological and pharmaceutical compounds.

Acknowledgement

The authors appreciate the University of Zabol for their support and assistance of this project.

Received: Aug. 28, 2015; Accepted: Aug. 23, 2016

REFERENCES

[1] Breslow R., On the Mechanism of Thiamine Action. IV.[1] Evidence from Studies on Model Systems, *J. Am. Chem. Soc*., **80**(14): 3719-3726 (1958).

[2] Borisenko V.E., Koll A., Kolmakov E.E., Rjasnyi A.G., Hydrogen Bonds of 2-Aminothiazoles in Intermolecular Complexes (1:1 and 1:2) with Proton Acceptors in Solutions, *J. Mol. Struct*., **783**(1-3): 101-115 (2006**)**.

[3] de Souza M.V.N., de Almeida M.V., Drugs Anti-HIV: Past, Present and Future Perspectives, *Quim. Nova*., **26**(3): 366-372 (2003) [in Portuguese].

[4] Maj J., Rogóż Z., Skuza G., Kolodziejezyk K., Antidepressant Effects of Pramipexole, a Novel Dopamine Receptor Agonist, *J. Neural. Transm*., **104**(4-5): 525-533 (1997).

[5] Milne G.W.A., Ed., "Ashgate Handbook of Antineoplastic Agents", Gower, London (2000).

[6] Poff C.D., Balazy M., Drugs that Target Lipoxygenases and Leukotrienes as Emerging Therapies for Asthma and Cancer, *Curr. Drug. Tar*., **3**(1): 19-33 (2004).

[7] Knadler M.P., Bergstrom R.F., Callaghan, J.T., Rubin A., Nizatidine, an H_2-Blocker. Its Metabolism and Disposition in Man, *Drug Metab. Dispos*., **14**(2): 175-182 (1986).

[8] Zia ur Rehman M., Choudary J.A., Ahmad S., An Efficient Synthesis of 2-Alkyl-4-hydroxy-2*H*-1,2-benzothiazine -3-carboxamide -1,1-dioxides, *Bull. Korean Chem. Soc*., **26**(11): 1771-1775 (2005).

[9] Lednicer D., Mitscher L.A., "Organic Chemistry of Drug Synthesis", Vol. 4, p 95, Wiley-InterScience, New York (1991).

[10] Shafiee A., Jalilian A.R., Tabatabaiee Yazdi M., Syntheses, Antibacterial and Antifungal Activities of Substituted-Thiazolo-1,3,4-Thiadiazoles, 1,3,4-Oxadiazoles and 1,2,4-Thiazoles, *Iran. J. Chem. Chem. Eng. (IJCCE)*, **17**(1): 14-20 (1998).

[11] Fink B.E., Mortensen D.S., Stauffer S.R., Aron Z.D., Katzenellenbogen J.A., Novel Structural Templates for Estrogen-Receptor Ligands and Prospects for Combinatorial Synthesis of Estrogens, *Chem. Biol.*, **6**(4): 205-219 (1999).

[12] van Muijlwijk-Koezen J.E., Timmerman H., Vollinga R.C., von Drabbe Künzel J.F., de Groote M., Visser S., IJzerman A.P., Thiazole and Thiadiazole Analogues as a Novel Class of Adenosine Receptor Antagonists, *J. Med. Chem.*, **44**(5): 749-762 (2001).

[13] Füßlein M., Bretschneider T., Fischer R., Jeschke P., Köhler A., Kluth J., Mühlthau F.A., Voerste A., Sato Y., Thiazole Derivatives as Pesticides, *US Patent*, 20110319428 A1 (2011).

[14] Wang Q., Li H., Li Y., Huang R., Synthesis and Herbicidal Activity of 2-Cyano-3-(2-chlorothiazol-5-yl)methylaminoacrylates, *J. Agric. Food Chem.*, **52**(7): 1918-1922 (2004).

[15] Tintcheva I., Maximova V., Deligeorgiev T., Zaneva D., Ivanov I., New Asymmetric Monomethine Cyanine Dyes for Nucleic-Acid Labelling: Absorption and Fluorescence Spectral Characteristics, *J. Photochem. and Photobiol. A: Chem.*, **130**(1): 7-11 (2000).

[16] Rucker V.C., Foister S., Melander C., Dervan P.B., Sequence Specific Fluorescence Detection of Double Strand DNA, *J. Am. Chem. Soc.*, **125**(5): 1195-1202 (2003).

[17] Hantzsch A., Weber J.H., Ueber Verbindungen des Thiazols (Pyridins der Thiophenreihe), *Ber. Dtsch. Chem. Ges.*, **20**(2): 3118-3132 (1887) [in German].

[18] Yadav J.S., Subba Reddy B.V., Gopala Rao Y., Narsaiah A.V., First Example of the Coupling of α-Diazoketones with Thiourea: a Novel Route for the Synthesis of 2-Aminothiazoles, *Tetrahedron Lett.*, **49**(15): 2381-2383 (2008).

[19] Banothu J., Vaarla K., Bavantula R., Crooks P.A., Sodium Fluoride as an Efficient Catalyst for the Synthesis of 2,4-Disubstituted-1,3-thiazoles and Selenazoles at Ambient Temperature, *Chinese Chem. Lett.*, **25**(1): 172-175 (2014).

[20] Hajinasiri R., Hossaini Z., Sheikholeslami-Farahani F., ZnO-Nanorods as the Catalyst for the Synthesis of 1,3-Thiazole Derivatives via Multicomponent Reactions, *Comb. Chem. High Throughput Screen.*, **18**(1): 42-47 (2015).

[21] Zheng H., Mei Y.J., Du K., Cao X.T., Zhang P.F., One-Pot Chemoenzymatic Multicomponent Synthesis of Thiazole Derivatives, *Molecules*, **18**(11): 13425-13433 (2013).

[22] Potewar T.M., Ingale S.A., Srinivasan K.V., Efficient Synthesis of 2,4-Disubstituted Thiazoles Using Ionic Liquid under Ambient Conditions: A Practical Approach towards the Synthesis of Fanetizole, *Tetrahedron*, **63**(45): 11066-11069 (2007).

[23] Prakash R., Kumar A., Aggarwal R., Prakash O., Singh S.P., α,α-Dibromoketones: A Superior Alternative to α-Bromoketones in Hantzsch Thiazole Synthesis, *Synth. Commun.*, **37**(15): 2501-2505 (2007).

[24] Narender M., Somi Reddy M., Sridhar R., Nageswar Y.V.D., Rama Rao K., Aqueous Phase Synthesis of Thiazoles and Aminothiazoles in the Presence of β-Cyclodextrin, *Tetrahedron Lett.*, **46**(35): 5953-5955 (2005).

[25] Kabalka G.W., Mereddy A.R., Microwave Promoted Synthesis of Functionalized 2-Aminothiazoles, *Tetrahedron Lett.*, **47**(29): 5171-5172 (2006).

[26] Carrol King L., Miller F.M., The Reaction of Diazoketones with Thioamide Derivatives, *J. Am. Chem. Soc.*, **71**(1): 367-368 (1949).

[27] Sheldrake P.W., Matteucci M., McDonald E., Facile Generation of a Library of 5-Aryl-2-arylsulfonyl-1,3-thiazoles, *Synlett*, **2006**(3): 460-462 (2006).

[28] Sasmal P.K., Sridhar S., Iqbal J., Facile Synthesis of Thiazoles via an Intramolecular Thia-Micheal Strategy, *Tetrahedron Lett.*, **47**(49): 8661-8665 (2006).

[29] Moreno I., Tellitu I., SanMartín R., Badía D., Carrillo L., Domínguez E., An Efficient Synthesis of Phenanthro-Fused Thiazoles by a non-Phenolic Oxidative Coupling Procedure of 4,5-diarylthaizoles, *Tetrahedron Lett.*, **40**(27): 5067-5070 (1999).

[30] Williams D.R., Brooks D.A., Moore J.L., Stewart A.O., The Preparation and Wittig Condensations of C-4 Thiazole Phosphonium Methylides, *Tetrahedron Lett.*, **37**(7): 983-986 (1996).

[31] Pavan Kumar V., Narender M., Sridhar R., Nageswar Y.V.D., Rama Rao K., Synthesis of Thiazoles and Aminothiazoles from β-Keto Tosylates under Supramolecular Catalysis in the Presence of β-Cyclodextrin in Water, *Synth. Commun.*, **37**(24): 4331-4336 (2007).

[32] Miyamoto K., Nishi Y., Ochiai M., Thiazole Synthesis by Cyclocondensation of 1-Alkynyl(phenyl)-λ^3-iodanes with Thioureas and Thioamides. *Angew. Chem.*, **117**(42): 7056-7059 (2005).

[33] Potewar T.M., Ingale S.A., Srinivasan K.V., Catalyst-Free Efficient Synthesis of 2-Aminothiazoles in Water at Ambient Temperature, *Tetrahedron*, **64**(22): 5019-5022 (2008).

[34] Zhu D., Chen J., Xiao H., Liu M., Ding J., Wu H., Efficient and Expeditious Synthesis of Di- and Trisubstituted Thiazoles in PEG Under Catalyst-Free Conditions, *Synth. Commun.*, **39**(16): 2895-2906 (2009).

[35] Moraski G.C., Seeger N., Miller P.A., Oliver A.G., Boshoff H.I., Cho S., Mulugeta S., Anderson J.R., Franzblau S.G., Miller M.J., Arrival of Imidazo[2,1-*b*]thiazole-5-carboxamides: Potent Anti-tuberculosis Agents That Target QcrB, *ACS Infect. Dis.*, **2**(6): 393-398 (2016).

[36] Helal M.H., Salem M.A., El-Gaby M.S., Aljahdali M., Synthesis and Biological Evaluation of Some Novel Thiazole Compounds as Potential Anti-inflammatory Agents, *Eur. J. Med. Chem.*, **65**: 517-526 (2013).

[37] Rostom S.A.F., Faidallah H.M., Radwan M.F., Badr M.H., Bifunctional Ethyl 2-Amino-4-methylthiazole-5-carboxylate Derivatives: Synthesis and *in vitro* Biological Evaluation as Antimicrobial and Anticancer Agents, *Eur. J. Med. Chem.*, **76**: 170-181 (2014).

[38] Álvareza G., Varelaa J., Crucesa E., Fernándezb M., Gabaya M., Lealc S.M., Escobarc P., Sanabriad L., Sernad E., Torresd S., Figueredo Thiele S.J., Yaluffd G., Vera de Bilbaod N.I., Cerecettoa H., González M., Identification of New Amide Containing Thiazole as Drug Candidate for Treatment of Chagas' Disease, *Antimicrob. Agents Chemother.*, **59**(3): 1398-1404 (2015).

[39] Trisciuoglio D., Ragazzoni Y., Pelosi A., Desideri M., Carradori S., Gabellini C., Maresca G., Nescatelli R., Secci D., Bolasco A., Bizzarri B., Cavaliere C., D'Agnano I., Filetici P., Ricci-Vitiani L., Rizzo M.G., Del Bufalo D., CPTH6, a Thiazole Derivative, Induces Histone Hypoacetylation and Apoptosis in Human Leukemia, *Clin. Cancer Res.*, **18**(2): 475-486 (2012).

[40] Sheikhhosseini E., Sattaei Mokhtari T., Faryabi M., Rafiepour A., Soltaninejad S., Iron Ore Pellet, A Natural and Reusable Catalyst for Synthesis of Pyrano[2,3-d]pyrimidine and Dihydropyrano[c]chromene Derivatives in Aqueous Media, *Iran. J. Chem. Chem. Eng. (IJCCE)*, **35**(1): 43-50 (2016).

[41] Mohammadi Ziarani G., Mousavi S., Lashgari N., Badiei A., Shakiba M., Application of Sulfonic Acid Functionalized Nanoporous Silica (SBA-Pr-SO_3H) in the Green One-pot Synthesis of Polyhydroacridine Libraries, *Iran. Chem. Chem. Eng. (IJCCE)*, **32**(4): 9-16 (2013).

[42] Zhang J., Hu X., Zhou Z., Efficient and Eco-Friendly Procedure for the Synthesis of 2-Amino-4H-Chromenes Catalyzed by Diammonium Hydrogen Phosphate, *Iran. J. Chem. Chem. Eng. (IJCCE)*, **34**(4): 47-51 (2015).

[43] Souzangarzadeh S., 1,3-Dipolar Cycloaddition Reaction of Nitrile Oxides to Isatin Imines, *Iran. J. Chem. Chem. Eng. (IJCCE)*, **35**(1): 31-35 (2016).

[44] Shaabani A., Ghadari R., Rezayan A.H., Synthesis of Functionalized Coumarins, *Iran. J. Chem. Chem. Eng. (IJCCE)*, 30(4): 19-22 (2011).

[45] Atkins E.F., Dabbs S., Guy R.G., Mahomed A.A., Mountford P., Pseudohalogen Chemistry. XI. Some Aspects of the Chemistry of α-Thiocyanato-β-Dicarbonyl Compounds, *Tetrahedron*, **50**(24): 7253-7264 (1994).

[46] Guy R.G., "The Chemistry of the Cyanates and Their Thio Derivatives", Vol. 2, pp 819-886, Patai S., Ed., Wiley-Interscience, New York, (1977).