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Authors: Nurcan BERBER

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# Synthesis and Characterization of Thiazole Compounds in the Presence of Various Reagents, Catalysts and Solvents

Nurcan BERBER *[1]


## Abstract

The reaction medium plays a key role in organic synthesis and pharmaceutical research. There are many opinions on choosing the best condition, including cost and environmental implications, but the main requirement is that they have the necessary interaction with solvents to cause dissolution, precipitation, stabilization, or instability. For this purpose, in this article synthesis of the thiazole ring was made under various reaction conditions. So new compounds 2-(isoquinolin-5-ylimino)-3-phenylthiazolidin-4-one (1), (4-amino-3-phenylthiazol-2(3H)-ylidene) isoquinolin-5-amine (2), (4-amino-3-phenylthiazol-2(3H)-ylidene) isoquinolin-5-amine (3) were synthesized from the reaction between thiourea derivative and monochloroacetic acid, diethyloxalate and chloro acetonitrile. For this synthesizes were created in various reaction conditions, using different bases (sodium acetate/sodyum etoksit/ triethylamine or pyridine) and solvents (1,4-dioxane, toluene, acetic acid, ethanol, tetrahydrofuran, dimethyl formamide). At the end of these reactions, the best efficiency was obtained with the one-pot reaction using THF/DMF, $Et_3N$. The structures of all novel compounds reported herein were established using FT-IR, $^1H$ NMR, and $^{13}C$ NMR spectra as well as elemental analysis technique.


**Keywords:** 5-aminoisoquinoline, thioureas, one-pot reaction, thiazole rings

## 1. INTRODUCTION

Hetero-cyclic compounds or ring structures have an important role in organic chemistry due to their wide range of pharmacological properties [1-3]. Heterocyclic compounds are widely distributed in nature. Many of them show drug active properties have increased the importance of such compounds and led organic synthesizers to make various reactions.

Six-membered hetero-cyclic compounds, pyridine and benzo derivatives, especially quinoline and isoquinoline derivatives are widely used in many chemical syntheses due to their biological activities [4-6]. They play are key structural components due to their various

* Corresponding author: nberber@comu.edu.tr
[1] Çanakkale Onsekiz Mart University
ORCID: https://orcid.org/0000-0002-1595-585X

biological activities such as antimalarial [7], antibacterial [8], antifungal [9], antidepressant [10, 11], anticonvulsant [12, 13], anti-inflammatory [14], antidiabetic [15], antiviral [16], antihistamine [17], anticarcinogen and antioxidant [18]. For example, quinine was isolated from the bark of Cinchona trees and has been used for the treatment of malaria [19]. Its structure determination and SAR studies resulted in the discovery of newer antimalarial drugs like chloroquine, primaquine, mefloquine [20]. Besides, nitrogen and sulfur-containing aromatic heterocyclic compounds such as thiazole are widely used in many types of treatments due to their interesting physicochemical properties and pronounced biological activities [21-26]. Some important heterocyclic compound derivatives are given (Figure 1). Also, thioureas and substituted thioureas play important roles in the formation of these heterocyclic systems [27-29].

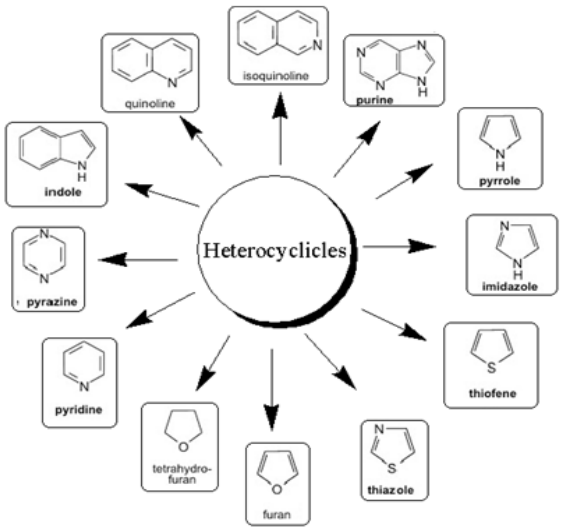



Figure 1 Some important heterocyclic compounds derivatives

The conventional synthesis in previous work several methods have been reported for the preparation of thiazole rings for example ethanol/ sodium ethoxide [30], ethanol/ anhydrous sodium acetate [31, 32], acetic acid/ anhydrous sodium acetate [33], dioxane/ anhydrous sodium acetate [34], solvent/scavenger-free conditions [35]. This article describes of synthesis of new heteroaryl isoquinoline derivatives [2-(isoquinolin-5-ylimino)-3-phenylthiazolidin-4-one (1), (4-amino-3-phenylthiazol-2(3H)-ylidene) isoquinolin-5-amine (2), (4-amino-3-phenylthiazol-2(3H)-ylidene) isoquinolin-5-amine (3)] under various conditions. For this purpose, the thiazole ring was formed from adding monochloroacetic acid, chloroacetonitrile, diethyl oxalate in the using three different bases (EtONa, AcONa, Pyridine) and solvents (1,4-dioksan, Toluene, AcOH).

## 2. EXPERIMENTAL

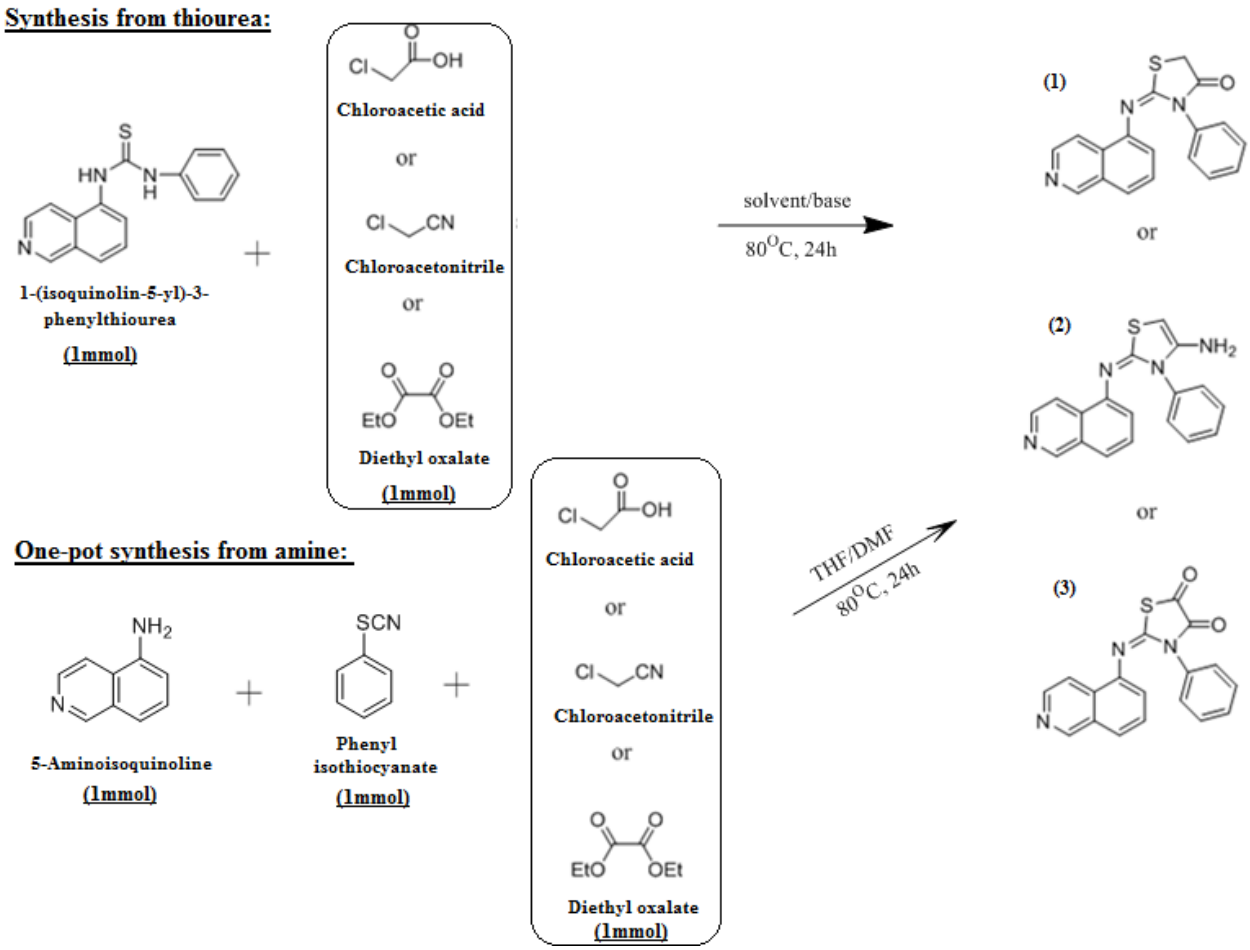
All starting materials and reagents were purchased from commercial suppliers. Reactions were monitored by TLC; the plates were visualized with short wave UV fluorescence (k = 254 nm). Melting points were taken on a Yanagimoto micromelting point apparatus. FT-IR spectra (ν, $cm^{-1}$) were measured on a SHIMADZU Prestige21 (200 VCE) spectrometer. $^{1}H$ NMR and $^{13}C$ NMR spectra were taken on JEOL NMR-400 MHz instrument in DMSO-d6 using TMS as the internal standard. All chemicals were purchased from Merck (Darmstadt, Germany) and Sigma-Aldrich (Taufkirchen, Germany). The ele-mental analysis was carried out with a Leco CHNS-932 (St. Joseph,Michigan)instrument.

### 2.1. General synthesis of the new heteroaryl isoquinoline derivatives (1-3)

**Synthesis from thiourea:** A solution of the appropriate 1-(isoquinolin-5-yl)-3-phenylthiourea (1mmol) in 1,4-dioxane/ toluene/ acetic acid/ ethanol/ tetrahydrofuran or dimethylformamide (10mL) was refluxed with the appropriate monochloroacetic acid (1mmol)/chloro acetonitrile(1mmol), or diethyl oxalate(1mmol) in the presence of base EtONa/AcONa/ Pyridine or $Et_3N$ (2mmol) for 24 h. The reaction mixture was then cooled poured into ice and the oily residue was recrystallized into ethanol/10% HCl mixture (Scheme 1).

**One-pot synthesis from amine:** To a solution of 5-aminoisoquinoline (1mmol) in THF/DMF (5/0,5mL) was added Phenyl isothiocyanate (1mmol), monochloroacetic acid (1mmol)/chloro acetonitrile (1mmol), or diethyl oxalate (1mmol) and triethylamine (3drop). The reaction mixture

was heated at 80 ˚C for 24 h. The reaction mixture was cooled and poured into ice. And then the oily residue was transferred to another vessel and precipitated in EtOH / 10% HCl mixture.




Scheme 1 General reaction condituons of thiazole ring

**2-(isoquinolin-5-ylimino)-3-phenylthiazolidin-4-one (1):** Yellow solid, **y**ield based on one-pot synthesis from amine reaction; %65, mp. 205-208°C. IR (KBr, $cm^{-1}$) ν = 3070-3040 (Ar CH), 1670 (CO); $^{1}H$ NMR (DMSO-d6) δ = 9.68-7.40 (11H, m, Ar H), 4.25 (2H, s, $CH_2$); $^{13}C$ NMR (DMSO-d6) δ = 170.24 (CO), 156.60 (-N=C-), 150.60-126.06 (Ar C), 34.20 ($CH_2$); Anal. Calcd. For. $C_{18}H_{13}N_3OS$ (319.38): C, 67.69; H, 4.10; N, 13.16; found. C, 67.83; H, 4.37; N, 13.31.

**(4-amino-3-phenylthiazol-2(3H)-ylidene) isoquinolin-5-amine (2):** Brown solid, yield based on one-pot synthesis from amine reaction %77, mp. 189-191°C. IR (KBr, $cm^{-1}$) ν = 3271 ($NH_2$), 3075-3012 (Ar CH); $^{1}H$ NMR (DMSO-d6) δ = 9.70-7.76 (11H, m, Ar H), 6.95 (1H, s, CH), 5.69, (2H, s, $NH_2$); $^{13}C$ NMR(DMSO-d6) δ = 169.62 (-N=C-), 150.60-126.06 (Ar C), 60.05 (-CH=); Anal. Calcd. For. $C_{18}H_{14}N_4S$ (318.40): C, 67.90; H, 4.43; N, 17.60; found. C, 68.05; H, 4.87; N, 17.81.

**(4-amino-3-phenylthiazol-2(3H)-ylidene) isoquinolin-5-amine (3):** Dark Brown solid, Yield based on one-pot synthesis from amine reaction; %83, mp. 181-183°C. IR (KBr, $cm^{-1}$) ν = 3113-3081 (Ar CH), 1683,1675 (CO); $^{1}H$ NMR (DMSO-d6) δ = 9.80-7.45 (11H, m, Ar H); $^{13}C$ NMR(DMSO-d6) δ = 183.40, 170.11 (CO), 160.30 (-N=C-), 150.60-126.06 (Ar-C); Anal. Calcd. For. $C_{18}H_{11}N_3O_2S$ (333.37): C, 64.85; H, 3.33; N, 12.61; found. C, 65.05; H, 3.51; N, 12.83.

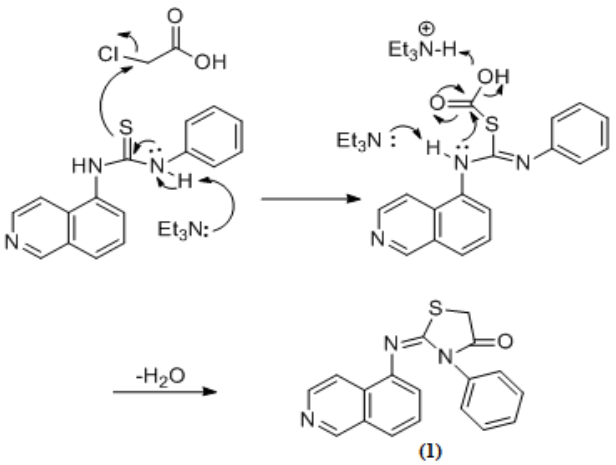
## 3. RESULTS AND DISCUSSION

This study was designed to synthesize and characterize the new heteroaryl isoquinoline derivatives (1-3) from both 1-(isoquinolin-5-yl)-3-phenylthiourea and 5-aminoisoquinoline (in one-pot). Firstly, the designed compound was synthesized by condensation of 1-(isoquinolin-5-yl)-3-phenylthiourea with monochloroacetic acid/chloro acetonitrile, or diethyl oxalate using polar/apolar solvents (1,4-dioxane/ toluene/ acetic acid/ ethanol/ tetrahydrofuran or dimethylformamide) and bases (EtONa/ AcONa/ Pyridine or $Et_3N$) for 24 h. In apolar solvents, toluene and 1,4-dioxane, product (a) was obtained in higher yields, whereas it was obtained in lower yields in polar solvents such as tetrahydrofuran, acetic acid. Also, the synthesis of heteroaryl isoquinoline derivatives (1-3) used different bases such as sodium ethoxide, triethylamine, pyridine, or sodium acetate. The best yield was obtained with sodium acetate in the apolar solvent. When the reaction was carried out at 80 ° C under base-free conditions, no reaction took place. The results obtained were given in Table 1.

Table 1 Effect of base on synthesis (E)-2-(isoquinolin-5-ylimino)-3-phenylthiazolidin-4-one (a)

| | **Base** | **Solvent** | **Base** | **Chloro acetic Acid** | **Yield (%)** |
|---|---|---|---|---|---|
| **1** | Pyridine | 1,4-Dioksane | 2 | 1 | 40 |
| **2** | NaOAc | 1,4-Dioksane | 2 | 1 | 55 |
| **3** | NaOEt | 1,4-Dioksane | 2 | 1 | 45 |
| **4** | Pyridine | Toluene | 2 | 1 | 36 |
| **5** | NaOAc | Toluene | 2 | 1 | 40 |
| **6** | NaOEt | Toluene | 2 | 1 | 25 |
| **7** | NaOAc | AcOH | 2 | 1 | 35 |
| **8** | - | 1,4-Dioksane | - | 1 | - |

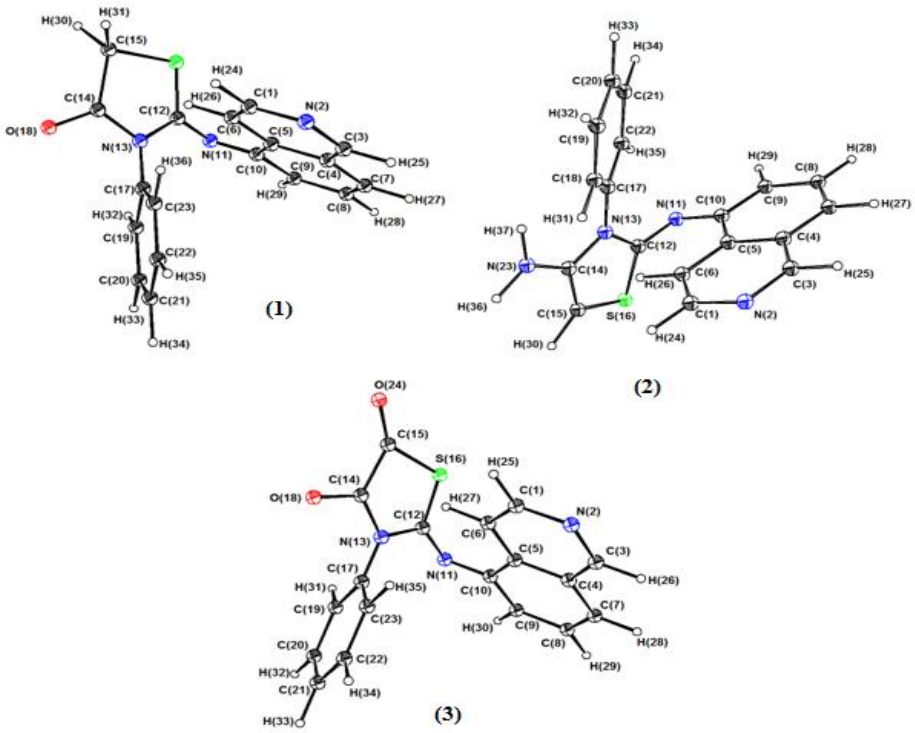
Secondly, the one-pot reaction has been achieved by condensation of 5-aminoisoquinoline, phenyl isothiocyanate with monochloroacetic acid/chloro acetonitrile or diethyl oxalate using THF/DMF(5/0,5mL) and $Et_3N$ (3 drops) for 24 h. Compounds (1-3) were achieved with the one-pot reaction at a higher yield of 70-75%. The oily residue obtained at the end of the reaction was recrystallized with Ethanol/10% HCl mixture. It is known that such one-pot reactions are used in many thiazole derivatives synthesis because of mild reaction conditions, shorter reaction times, high efficiencies, and facile isolation of the desired product. [35-37]. A plausible mechanism for these syntheses is shown in Scheme 2. Also, it is varies depending on the pKa of the amine attached to the thiourea moiety with acylation taking place toward the amine having a lower pKa [38-41]. The measured pKa of 5-aminoisoquinoline and aniline respectively are 5.48 and 4.58. For unsymmetrical 1-(isoquinolin-5-yl)-3-phenylthiourea, aniline nitrogen is more basic compared with isoquinoline nitrogen of the carbodiimide intermediate. Thus, the former is acylated from aniline nitrogen (in Scheme 2). Also, asymmetric attack of acetic acid to carbodiimide will lead to protonation towards the amine with higher pKa without affecting the imine group on the other side [38].




Scheme 2 A plausible mechanism for the formation of 2-(isoquinolin-5-ylimino)-3-phenylthiazolidin-4-one

The structural analysis of the obtained molecules was made using FT-IR, $^{1}$H NMR, $^{13}$C NMR, spectroscopy and elemental analysis techniques. In the infrared spectrum of compound (2) displayed a significant vibrational band at 3271 $cm^{-1}$ for the presence of amine [26,27]. In aromatic compounds, the C–H stretching vibrations appear to be between 3113 and 3012 $cm^{-1}$. In compound (1-3), in addition to aromatic compound bonds, there are isoquinoline and phenyl aromatic rings, C=C, C-C, and C-N bonds. These stretching vibrations have been observed between 1675-1450 $cm^{-1}$ [42]. Also, the absorption of C=O stretching vibrations was seen around 1670-1683 $cm^{-1}$ in compounds (1) and (3) [37]. Also, important IR absorptions of the synthesized molecules are given in Table 2.

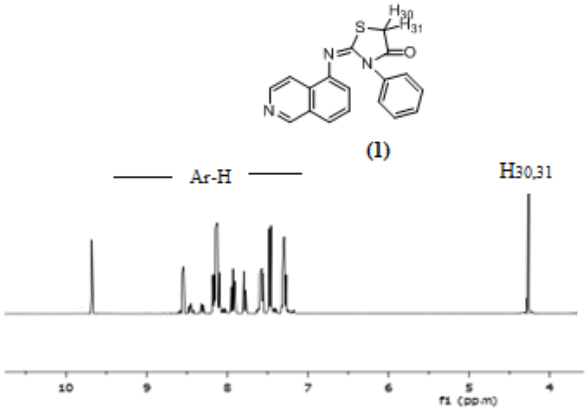
In $^{1}$H NMR spectrum of all the compounds showed the signals of the aromatic protons of isoquinoline and phenyl ring at 7,40- 9.80 ppm [43]. The $^{1}$H NMR spectrum of compounds (1) and (2) gave signals at 4.25 and 6.95 ppm attributed to thiazole ring $CH_2$ (H30-H31) and CH (H30), respectively [32]. Also, the signal belongs the $NH_2$ (H36-H37) on the thiazole ring in compound 2 was shown at 5.69 ppm. In their $^{13}$C NMR spectra, the signal due to the thiazole carbonyl carbon (C14-O18, C15-O24) appeared at 170.11–183.40 ppm. Also -C=N- (C12-N11) signals were seen around 160 ppm [26,27]. The isoquinoline and phenyl carbons resonated at the range 125.90−168.31and 118.95−160.87 ppm, respectively. All spectra and elemental analyses support the structure of the synthesized compounds.

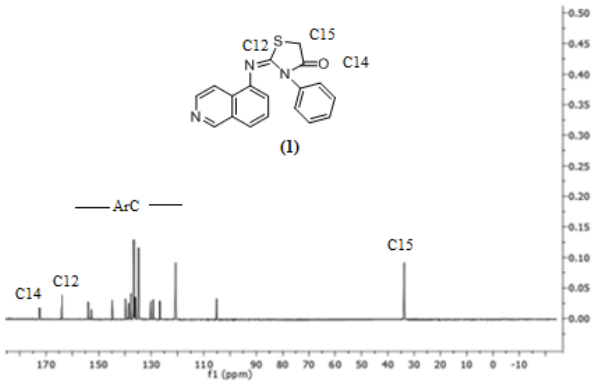


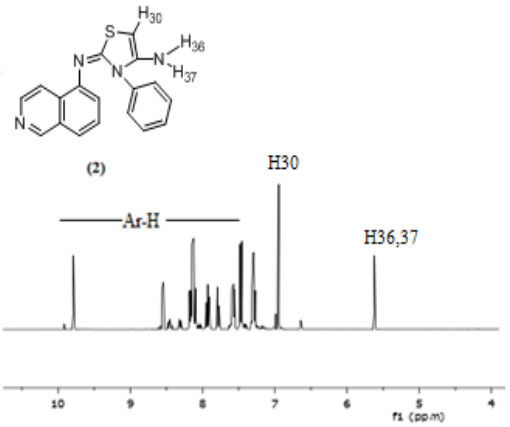

Scheme 3 ORTEP plot of the molecular structure of compound (1-3)

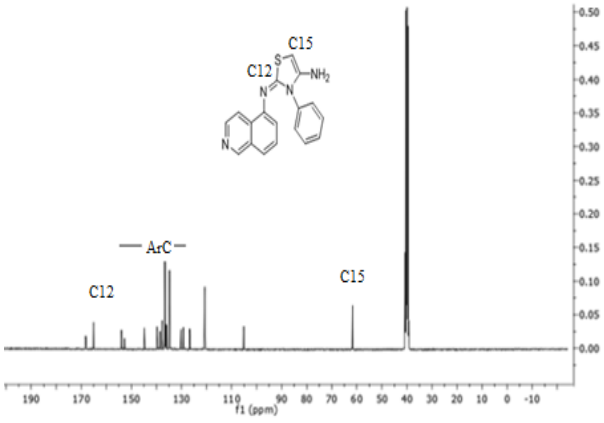
Table 2 $^{1}H$ and $^{13}C$ NMR (ppm) spectral data of compounds (1-3)

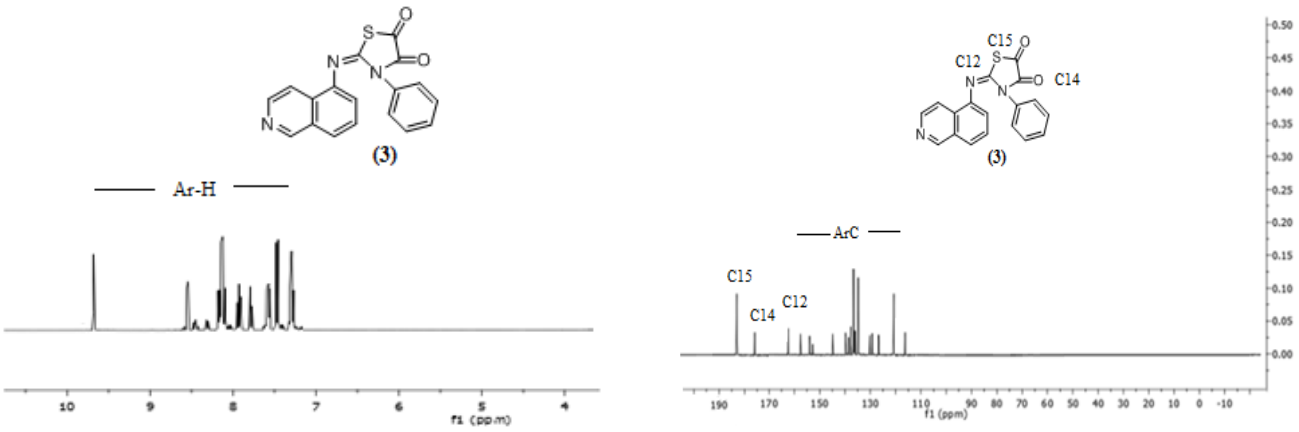
| Compd. | IR ($cm^{-1}$) | | | $^{1}H$ NMR (PPM) | | | $^{13}C$ (PPM) | |
|---|---|---|---|---|---|---|---|---|
| | $NH_2$ | Ar CH | CO | Ar H (m) | thiazole $CH_2$ or CH | $NH_2$ | -C=O | -N=C- |
| **(1)** | - | 3070-3040 | 1670 | 9.68-7.40 | 4.25 | - | 170.24 | 156.60 |
| **(2)** | 3271 | 3075-3012 | - | 9.70-7.76 | 6.95 | 5.69 | - | 169.62 |
| **(3)** | - | 3113-3081 | 1683,1675 | 9.80-7.45 | - | - | 170.11, 183.40 | 160.30 |






Scheme 4 $^{1}H$ and $^{13}C$ NMR spectrum of Compound (1-3)

## 4. CONCLUSIONS

In conclusion, a one-pot reaction protocol for the new heteroaryl isoquinoline derivatives (1-3) has been reported. The optimum conditions were found to be with 1 equivalent of phenyl isothiocyanate with monochloroacetic acid/chloro acetonitrile or diethyl oxalate using THF/DMF(5/0,5mL) and $Et_3N$ (3 drops) affording a good yield of the new heteroaryl isoquinoline derivatives (1-3). Mild reaction conditions, shorter reaction times, high efficiencies, and facile isolation of the desired product make the present methodology a most suitable alternative. Unlike the one-pot reaction, the reaction stage increases in reactions carried out over thiourea, because firstly you must synthesis thiourea structure. Also, compounds are taken with a lower yield. Within the scope of literature studies, it has been observed for unsymmetrical thioureas in which amine attached to the thiourea having lower pKa is a part of the imino component and the amine having higher pKa is the contributor to the other heterocyclic nitrogen.

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### *The Declaration of Conflict of Interest/ Common Interest*

No conflict of interest or common interest has been declared by the authors.

### *Authors' Contribution*

The author solemly performed the computations and wrote the manuscript.

### *The Declaration of Ethics Committee Approval*

The author declare that this study does not require an ethics committee approval or any special permission.

### *The Declaration of Research and Publication Ethics*

The authors of the paper declare that they comply with the scientific, ethical and quotation rules of SAUJS in all processes of the paper and that they do not make any falsification on the data collected. In addition, they declare that Sakarya

University Journal of Science and its editorial board have no responsibility for any ethical violations that may be encountered, and that this study has not been evaluated in any academic publication environment other than Sakarya University Journal of Science.

## REFERENCES

[1] T. Akiyama, J. Iwai, "Scandium trifluoro-methanesulfonate-catalyzed chemoselective allylation reactions of carbonyl compounds with tetraallylgermane in aqueous media," Tetrahedron, vol. 55, no. 24, pp. 7499-7508, 1999.

[2] M. S. Saini, A. Kumar, J. Dwivedi, R. Singh, "A review: biological significances of heterocyclic compounds," International Journal of Pharma Sciences and Research, vol. 4, no. 3, pp. 66-77, 2013.

[3] Y. Cheng, Z. T. Huang, M. X. Wang, "Heterocyclic enamines: The versatile intermediates in the synthesis of heterocyclic compounds and natural products," Current Organic Chemistry, vol. 8, no. 4, pp. 325-51, 2004.

[4] N. Kaur "Review on the synthesis of six-membered N, N-heterocycles by microwave irradiation," Synthetic Communications, vol. 45, no. 10, pp. 1145-82, 2015.

[5] N. Kaur "Photochemical reactions: synthesis of six-membered N-heterocycles," Current Organic Synthesis, vol. 14, no. 7, pp. 972-98, 2017.

[6] M. Haji "Multicomponent reactions: A simple and efficient route to heterocyclic phosphonates," Beilstein Journal of Organic Chemistry, vol. 12, no. 1, pp. 1269-1301, 2016.

[7] S. Sarkar, A. A. Siddiqui, S. J. Saha, De. Rudranil, S. Mazumder, C. Banerjee, M. S. Iqbal, S. Nag, S. Adhikari, U. Bandyopadhyay, "Antimalarial Activity of small-molecule benzothiazole hydrazones," Antimicrob Agents Chemother, vol. 60, no. 7, pp. 4217-28, 2016.

[8] G. Negri, C. Kascheres, A. J. Kascheres, "Recent development in preparation reactivity and biological activity of enamino ketones and enamino thiones and their utilization to prepare heterocyclic compounds," Journal of Heterocyclic Chemistry, vol. 41, no. 4, pp. 461-491, 2004.

[9] A. Hazra, S. Mondala, A. Maitya, S. Naskara, P. Sahaa, R. Pairaa, K. B. Sahua, P. Pairaa, S. Ghoshb, C. Sinhab, A. Samanta, S. Banerjeea, N. B. Mondal, "Amberlite–IRA-402 (OH) ion exchange resin mediated synthesis of indolizines, pyrrolo [1, 2-a] quinolines and isoquinolines: Antibacterial and antifungal evaluation of the products," European Journal of Medicinal Chemistry, vol. 46, no. 6, pp. 2132-40, 2011.

[10] S. Saeed, N. Rashid, P. G. Jones, M. Ali, R. Hussain, "Synthesis, characterization and biological evaluation of some thiourea derivatives bearing benzothiazole moiety as potential antimicrobial and anticancer agents," European Journal of Medicinal Chemistry, vol. 45, no. 4, pp. 1323-31, 2010.

[11] P. Zajdel, A. Partyka, K. Marciniec, A. J. Bojarski, M. Pawlowski, A. Wesolowska, "Quinoline-and isoquinoline-sulfonamide analogs of aripiprazole: novel antipsychotic agents?," Future Medicinal Chemistry, vol. 6, no. 1, pp. 57-75, 2014.

[12] D. C. Liu, H. J. Zhang, C. M. Jin, Z. S. Quan, "Synthesis and biological evaluation of novel benzothiazole derivatives as potential anticonvulsant agents," Molecules, vol. 21, no. 3, pp. 164, 2016.

[13] E. G. Paronikyan, A. S. Noravyan, S. F. Akopyan, I. A. Dzhagatspanyan, I. M. Nazaryan, R. G. Paronikyan, "Synthesis and anticonvulsant activity of pyrano [4′, 3′: 4,

5] pyrido [2, 3-b] thieno [3, 2-d] pyrimidine derivatives and pyrimido [5′, 4′: 2, 3]-thieno [2,3-c] isoquinoline derivatives," Pharmaceutical Chemistry Journal, vol. 41, no. 9, pp. 466-9, 2007.

[14] S. Shafia, M. Mahboob, A. Naveen, M. Chaitanya, M. G. Vanajad, A. M. Kalled, R. Pallud, M.S.Alama, "Synthesis of novel 2-mercapto benzothiazole and 1,2,3-triazole based bis-heterocycles: their anti-inflammatory and anti-nociceptive activities," European Journal of Medicinal Chemistry, vol. 49, no. 2012, pp. 324-33, 2012.

[15] V. S. Patilac, K. P. Nandreb, S. Ghoshd, V. J., Rao, B. A. Chopadede, B. Sridharf, S. V. Bhosaleg, S. V. Bhosaleab, "Synthesis, crystal structure and antidiabetic activity of substituted (E)-3-(Benzo[d]thiazol-2-ylamino)phenylprop-2-en-1-one," European Journal of Medicinal Chemistry, vol. 59, no. 2013, pp. 304-9. 2013.

[16] E. Pitta, A. Geronikaki, S. Surmava, P. Eleftheriou, V. P. Mehta, E. V. Van der Eycken, "Synthesis and HIV-1 RT inhibitory action of novel (4/6-substituted benzo[d]thiazol-2-yl) thiazolidin-4-ones Divergence from the non-competitive inhibition mechanism," Journal of Enzyme Inhibition and Medicinal Chemistry, vol. 28, no. 1, pp. 113-22, 2013.

[17] W. Krzysztof, R. Guryn, O. P. Zuiderveld, H. Timmerman, "Non-imidazole histamine H3 ligands, Part 2: new 2-substituted benzothiazoles as histamine H3 antagonists," Archiv der Pharmazie, vol. 332, no. 11, pp. 389-98, 1999.

[18] K. J. Wilson, C. R. Illig, N. Subasinghe, J. B. Hoffman, M. J. Rudolph, R. Soll, C. J. Molloy, R. Bone, D. Green, T. Randall, M. Zhang, F. A. Lewandowski, Z. Zhou, C. Sharp, D. Maguire, B. Grasberger, R. L. DesJarlais, J. Spurlino, "Synthesis of thiophene-2-carboxamidines containing 2-aminothiazoles and their biological evaluation as urokinase inhibitors," Bioorganic and Medicinal Chemistry Letters, vol. 11, no. 7, pp. 915-18, 2001.

[19] N. El-Ket, E. Kendjo, M. Thellier, L. Assoumou, V. Potard, A. Taieb, I. Tantaoui, E. Caumes, R. Piarroux, C. Roussel, P. Buffet, D. Costagliola, S. Jauréguiberry, "Propensity score analysis of artesunate versus quinine for severe imported Plasmodium falciparum malaria in France," Clinical Infectious Diseases, vol. 70, no. 2, pp. 280-87, 2020.

[20] S. D'Alessandro, D. Scaccabarozzi, L. Signorini, F. Perego, D. P. Ilboudo, P., Ferrante, S. Delbue, "The use of antimalarial drugs against viral infection," Microorganisms, vol. 8, no. 1, pp. 85, 2020.

[21] H. N. Karade, B. N. Acharya, M. Sathe, M. P. Kaushik, "Design, synthesis, and antimalarial evaluation of thiazole-derived amino acids," Medicinal Chemistry Research, vol. 17, no. 1, pp. 19–29, 2008.

[22] P. Ghosh, M. J. Deka, A. K. Saikia, "Lewis acid mediated intramolecular C–O bond formation of alkanol-epoxide leading to substituted morpholine and 1, 4-oxazepane derivatives: total synthesis of (±) – viloxazinec," Tetrahedron, vol. 72, no. 5, pp. 690-698, 2016.

[23] R. M. Abdel-Rahman "Role of uncondensed 1,2,4-triazine compounds and related heterobicyclic systems as therapeutic agents: a review," Pharmazie, vol. 56, no. 1, pp. 18-22, 2001.

[24] A. R. Surray "4-Thiazolidones.IV. The preparation of some 3-alkylaminoalkyl-2-aryl derivatives," Journal of the American Chemical Society, vol. 71, no. 10, pp. 3354–56, 1949.

[25] N. G. Voznesenskaia, O. I. Shmatova, M. M. Ilyin, M. M. Ilyin Jr, V. G. Nenajdenko, "Enantioselective synthesis of thiazole-derived α-perfluoroalkylated 5–7-membered amines," European Journal of

Organic Chemistry, vol. 2019, no. 9, pp. 1893-903, 2019.

[26] N. Berber, M. Arslan, F. Vural, A. Ergun, N. Gençer, O. Arslan, "Synthesis of new series of thiazol-(2(3H)-ylideneamino) benzene- sulfonamide derivatives as carbonic anhydrase inhibitors," Journal of Biochemical and Molecular Toxicology, vol. 34, no. 12, pp. e22596, 2020.

[27] N. Berber, M. Arslan, Ç. Bilen, Z. Sackes, N. Gencer, O. Arslan, "Synthesis and evaluation of new phthalazine substituted β-lactam derivatives as carbonic anhydrase inhibitors," Russian Journal of Bioorganic Chemistry, vol. 41, no. 4 pp. 414-20, 2015.

[28] N. Berber "Synthesis of certain new morpholine derivatives bearing a thiazole moiety," Sakarya University Journal of Science and Technology, vol. 23, no. 4, pp. 554-58, 2019.

[29] S. Kılıcaslan, M. Arslan, Z. Ruya, Ç. Bilen, A. Ergün, N. Gençer, O. Arslan, "Synthesis and evaluation of sulfonamide-bearing thiazole as carbonic anhydrase isoforms hCA I and hCA II," Journal of Enzyme Inhibition and Medicinal Chemistry, vol. 31, no. 6, pp. 1300-1305, 2016.

[30] H. Saad "The synthesis of some new sulfur-bearing various heterocyclic systems derived from asymmetrical n,n′-disubstituted thiourea derivatives," Phosphorus, Sulfur, and Silicon, vol. 181, no. 7, pp. 1557-1567, 2006.

[31] H. A. Abdel-Azız, H. S. El-Zahabi, K. M. Dawood, "Microwave-assisted synthesis and in-vitro anti-tumor activity of 1,3,4-triaryl-5-N-arylpyrazole carboxamides," European Journal of Medicinal Chemistry, vol. 45, no. 6, pp. 2427-2432, 2010.

[32] H. M. Abumelha "Synthesis and antioxidant assay of new nicotinonitrile analogues clubbed thiazole, pyrazole and/or pyridine ring systems," Journal of Heterocyclic Chemistry, vol. 57, no. 3, pp. 1011-1022, 2020.

[33] Y. Feng, X. Ding, T. Chen, L. Chen, F. Liu, X. Jia, X. Luo, X. Shen, K. Chen, H. Jiang, H. Wang, H. Liu, D. Liu, "Design, synthesis, and interaction study of quinazoline-2 (1 H)-thione derivatives as novel potential Bcl-xL inhibitors," Journal of Medicinal Chemistry, vol. 53, no. 9, pp. 3465-3479, 2010.

[34] H. A. Morsy, A. H. Moustafa "A facile approach for synthesis of thiazines-, thiazoles-and triazoles-annulated 6-styryl-2-thiouracil derivative," Journal of the Iranian Chemical Society, vol. 17, no. 1, pp. 119-125, 2020.

[35] M. Sathishkumar, S. Nagarajan, P. Shanmugavelan, M. Dinesh, A. Ponnuswamy, "A facile, rapid, one-pot regio/stereoselective synthesis of 2-iminothiazolidin-4-ones under solvent/ scavenger-free conditions," Beilstein Journal of Organic Chemistry, vol. 9, no. 1, pp. 689-697, 2013.

[36] A. R. Sayed, S. M. Gomha, E. A. Taher, Z. A. Muhammad, H. R. El-Seedi, H. M. Gaber, M. M. Ahmed, "One-pot synthesis of novel thiazoles as potential anti-cancer agents," Drug Design, Development and Therapy, vol. 14, no. 2020, pp. 1363, 2020.

[37] M. El-Naggar, W. M. Eldehna, H. Almahli, A. Elgez, M. Fares, M. M. Elaasser, H. A. Abdel-Aziz, "Novel thiazolidinone/ thiazolo [3,2-a] benzimidazolone-isatin conjugates as apoptotic anti-proliferative agents towards breast cancer: one-pot synthesis and in vitro biological evaluation," Molecules, vol. 23, no. 6, pp. 1420, 2018.

[38] C. B. Singh, H. Ghosh, S. Murru, B. K. Patel, "Hypervalent iodine (III)-mediated regioselective N-acylation of 1, 3-disubstituted thioureas," The Journal of Organic Chemistry, vol. 73, no. 7, pp. 2924-2927, 2008.

[39] T. Wirth, M. Ochiai, V. V. Zhdankin, G. F. Koser, H. Tohma, Y. Kita, "Topics in Current Chemistry: Hypervalent iodine chemistry-modern developments in organic synthesis," Wirth, T, vol. 2002, pp. 1-248. 2002.

[40] R. Yella, H. Ghosh, B. K. Patel, "It is "2-imino-4-thiazolidinones" and not thiohydantoins as the reaction product of 1,3-disubstituted thioureas and chloroacetylchloride," Green Chemistry, vol. 10, no. 12, pp. 1307-1312, 2008.

[41] H. Ghosh, S. Sarkar, A. R. Ali, B. K. Patel, "Oxidative desulfurization of disubstituted thioureas using Pb (II) salts and investigation of p K a-dependent regioselective N-acylation," Journal of Sulfur Chemistry, vol. 31, no. 1, pp. 1-11, 2010.

[42] V. Krishnakumar, N. Surumbarkuzhalı, S. Muthunatesan "Scaled quantum chemical studies on the vibrational spectra of 4-bromo benzonitrile," Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, vol. 71, no. 5, pp. 1810-1813, 2009.

[43] N. Subramanian, N. Sundaraganesan, J. Jayabharathi "Molecular structure, spectroscopic (FT-IR, FT-Raman, NMR, UV) studies and first-order molecular hyperpolarizabilities of 1, 2-bis (3-methoxy-4-hydroxybenzylidene) hydrazine by density functional method," Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, vol. 76, no. 2, pp. 259-269, 2010.