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# A GREEN APPROACH FOR THE SYNTHESIS OF THIAZOLYL HYDRAZONES

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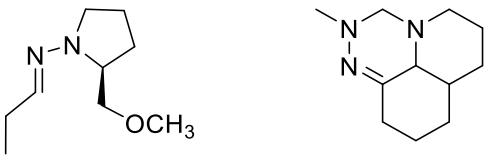
**ABSTRACT:**
A novel series of thiazolyl hydrazones (**5a-k)** was synthesized using a green chemistry approach. This was achieved by subjecting 2-(2-acetamido-thiazol-4-yl)acetohydrazide **3** to nucleophilic addition reactions with substituted aromatic/heterocyclic aldehydes (**4a-k**). The hydrazones (**5a-k**) were obtained in high yield without the need for further purification and could serve as important precursors for synthesizing bioactive natural products and drug molecules. The structures of the products were determined using analytical, spectral, and single-crystal X-ray diffraction analyses.

**Keywords:** Hydrazone, thiazole, green chemistry, natural product, drug molecules.

## INTRODUCTION:

Hydrazones have an azomethine -NHN=CH- proton and constitute the important class of alkaloids and various biologically active compounds, i.e., Pectinatone[i] and Cinachyramine[ii] (**Figure 1**).




Pectinatone Cinachyramine

Figure 1. Biologically active hydrazones.

Thus, the utility of hydrazides as key intermediates in the synthesis of several heterocyclic compounds and of their antimicrobial, antituberculosis and antitumour activities[iii-vi] has aroused interest in exploring them as versatile precursors for the synthesis of various substituted heterocycles. Likewise, the sulfur containing thiazole nucleus systems are found important heterocyclic moiety and present in natural products e.g., vitamin B1[vii], penicillin[viii] and also used in drug production to treat allergies[ix], hypertension[x], inflammation[xi], bacterial[xii], and HIV infections[xiii]. Thiazolyl hydrazones[xiv-xvi] have shown promising biological activity against microbial infections. Therefore, we aimed to synthesize a new series of thiazole-

containing molecules with bioactive heterocyclic/aromatic rings using hydrazone formation. We optimized a simple and efficient synthetic green method with excellent yields. **Scheme I** illustrate the synthetic pathway.

**EXPERIMENTAL**:

A digital melting point apparatus was used to record the melting points of the synthesized compounds. The proton NMR and carbon NMR spectra were obtained using a Bruker-DRX (300 MHz) and Bruker Advance (75 MHz), respectively, in solvent DMSO-$d_6$/$CDCl_3$ with TMS as the internal standard. The Mass spectra (TOF ES+) were recorded on an LCTKC455 (Micromass Autospec). The Perkin Elmer-2000 Spectrophotometer instrument was used to record the Infrared (FTIR) spectra. The X-ray diffraction parameters were collected using an Oxford X-Calibur Single Crystal Diffractometer instrument with a Sapphire CCD detector. The synthesis of 2-amino-4-(carboethoxymethyl)thiazole (**1**)[xvii], 2-acetamido-4-(carboethoxymethyl)thiazole (**2**)[xviii], and 2-(2-acetamidothiazol-4-yl)acetohydrazide (**3**)[xix] were carried out following the literature.

**GENERAL PROCEDURE:**

***General procedure for the preparation of thiazolyl hydrazones (5a-k).***

To synthesize compounds **5a-k**, a mixture of 2-(2-acetamido-thiazol-4-yl) acetohydrazide (**3**) (0.5 mmol) and aromatic/heterocyclic, aldehyde (0.5 mmol) (**4a-k**) was vigorously stirred in 20 mL of water at 80°C. The reaction progress was monitored using TLC. After one hour, the reaction content was allowed to cool and settle. The resulting white precipitate was filtered, and compounds **5a-k** were obtained after drying.

***(E)-N-(4-(2-(2-benzylidenehydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (5a).***

$R_f$: 0.43 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 197 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3290, 3159, 2985, 1719, 1667, 1499, 1359, 1237, 1138, 709. $^1$H NMR (δ): 11.80 (broad singlet, 1H, NH, $D_2O$ exchangeable proton), 11.13 (broad singlet, 1H, >NH, $D_2O$ exchangeable proton), 7.64 (multiplet, 2H), 7.49 (multiplet, 2H), 7.45 (singlet, 1H, =CH), 7.30 (multiplet, 1H), 6.70 (singlet, 1H), 3.84 (singlet, 2H, $CH_2$), 1.98 (singlet, 3H, $COCH_3$). $^{13}$C NMR (δ): 171.2 (C=O, amide), 168.9 (C=O, acetyl), 155.8 (C=N, hydrazone), 144.4, 142.8, 140.5, 133.2, 128.4, 127.8, 126.0, 106.7, 37.6, 23.2. Mass spectrum (MS), *m/z* (%): 303.201 ($M^+$+1).

***(E)-N-(4-(2-(2-(4-fluorobenzylidene)hydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (5b).***

$R_f$: 0.45 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 208 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3345, 2893, 1722, 1636, 1459, 1220, 1148, 711. $^1$H NMR (δ): 11.78 (broad singlet, 1H, NH, $D_2O$ exchangeable proton), 11.16 (broad singlet, 1H, >NH, $D_2O$ exchangeable proton), 7.69 (doublet, 2H, $J_{coupling\ constant}$ = 8.4 Hz), 7.58 (singlet, 1H, =CH), 7.36 (doublet, 2H, $J_{coupling\ Constant}$ = 8.4 Hz), 6.73 (singlet, 1H), 4.07 (singlet, 2H, $CH_2$ ), 2.13 (singlet, 3H, $COCH_3$). $^{13}$C NMR (δ): 175.7 (C=O, amide), 167.2 (C=O, acetyl), 154.6 (C=N, hydrazone), 144.8, 143.2, 138.2, 129.4, 128.8, 126.4, 106.4, 37.2, 22.9. Mass spectrum (MS), m/z (%): 321.121 ($M^+$+1).

***(E)-N-(4-(2-(2-(4-chlorobenzylidene)hydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (5c).***

$R_f$: 0.46 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 212 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3355, 3201, 2924, 1751, 1676, 1427, 1297, 1181, 712. $^1$H NMR (δ): 11.89 (singlet, 1H, NH, $D_2O$ exchangeable proton), 11.43 (broad singlet, 1H, >NH, $D_2O$ exchangeable proton), 8.11 (singlet, 1H, =CH), 7.67 (doublet, 2H, $J_{coupling\ constant}$ = 8.4 Hz), 7.49 (duoblet, 2H,

$J_{coupling\ constant}$ = 8.4 Hz), 6.70 (singlet, 1H), 4.11 (singlet, 2H, $CH_2$ ), 2.42 (singlet, 3H, $COCH_3$). $^{13}$C NMR (δ): 173.5 (C=O, amide), 167.7 (C=O, acetyl), 155.6 (C=N, hydrazone), 144.9, 144.6, 137.1, 130.4, 127.7, 126.8, 105.4, 36.9, 22.4. Mass spectrum (MS), m/z (%): 337.001 ($M^+$+1).

***(E)-N-(4-(2-(2-(4-bromobenzylidene)hydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (5d).***

$R_f$: 0.48 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 235 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3352, 3298, 2928, 1754, 1670, 1510, 1303, 1110, 720.$^1$H NMR (δ): 11.79 (broad singlet, 1H, NH, $D_2O$ exchangeable), 11.31 (broad singlet, 1H, >NH, $D_2O$ exchangeable), 8.21 (singlet, 1H, =CH), 7.61 (doublet, 2H, $J_{coupling\ constant}$ = 8.0 Hz), 7.12 (doublet, 2H, $J_{coupling\ constant}$ = 8.0 Hz), 6.90 (singlet, 1H), 4.01 (singlet, 2H, $CH_2$), 2.19 (singlet, 3H, $COCH_3$). $^{13}$C NMR (δ): 171.9 (C=O, amide), 169.1 (C=O, acetyl), 155.7 (C=N, hydrazone), 144.4, 143.7, 137.8, 134.4, 126.4, 125.8, 107.4, 35.6, 22.7. Mass spectrum (MS), m/z (%): 381.007 ($M^+$+1).

***(E)-N-(4-(2-(2-(4-methylbenzylidene)hydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (5e).***

$R_f$: 0.40 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 232 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3430, 3170, 2966, 1752, 1654, 1549, 1396, 1307, 1276, 1235, 1019, 788. $^1$H NMR (δ): 11.86 (broad singlet, 1H, NH, $D_2O$ exchangeable), 11.27 (broad singlet, 1H, >NH, $D_2O$ exchangeable), 8.25 (singlet, 1H, =CH), 7.55 (doublet, 2H, $J_{coupling\ constant}$ = 8.2 Hz), 7.12 (doublet, 2H, $J_{coupling\ constant}$ = 8.2 Hz), 6.95 (singlet, 1H), 4.12 (singlet, 2H, $CH_2$), 2.30 (singlet, 3H, $CH_3$), 2.08 (singlet, 3H, $COCH_3$). $^{13}$C NMR (δ): 172.2 (C=O, amide), 169.2 (C=O, acetyl), 155.9 (C=N, hydrazone), 146.4, 144.5, 139.8, 131.4, 129.2, 124.5, 108.2, 35.16, 21.0. Mass spectrum (MS), m/z (%): 317.107 ($M^+$+1).

***(E)-N-(4-(2-(2-(4-methoxybenzylidene)hydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (5f).***

$R_f$: 0.46 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 222 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3318, 3192, 2964, 1760, 1665, 1563, 1374, 1248, 1239, 962, 827, 758. $^1$H NMR (δ): 12.03 (broad singlet, 1H, NH, $D_2O$ exchangeable), 11.42 (broad singlet, 1H, >NH, $D_2O$ exchangeable), 8.34 (singlet, 1H, =CH), 7.59 (doublet, 2H, $J_{coupling\ constant}$ = 8.1 Hz), 7.01 (doublet, 2H, $J_{coupling\ constant}$ = 8.2 Hz), 6.87 (singlet, 1H), 3.98 (singlet, 2H, $CH_2$), 3.87 (singlet, 3H, $OCH_3$), 2.22 (singlet, 3H, $COCH_3$). $^{13}$C NMR (δ): 173.4 (C=O, amide), 169.4 (C=O, acetyl), 155.2 (C=N, hydrazone), 147.1, 144.8, 139.2, 131.7, 130.2, 124.9, 108.9, 55.2, 36.26, 24.0. Mass spectrum (MS), m/z (%): 333.10 ($M^+$+1).

***(E)-N-(4-(2-(2-(3,4-dimethoxybenzylidene)hydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (5g).***

$R_f$: 0.42 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 229 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3319, 3190, 2929, 1742, 1670, 1549, 1270, 1241, 1026, 746. $^1$H NMR (δ): 12.11 (broad singlet, 1H, NH, $D_2O$ exchangeable), 11.43 (broad singlet, 1H, >NH, $D_2O$ exchangeable), 8.21(singlet, 1H, =CH), 7.23 (singlet, 1H), 7.21 (doublet, 1H, $J_{coupling\ constant}$ = 8.1 Hz), 7.18 (doublet, 1H, $J_{coupling\ constant}$ = 8.1 Hz), 6.97 (singlet, 1H), 4.03 (singlet, 2H, $CH_2$), 3.78 (singlet, 6H, 2x $OCH_3$), 1.87 (singlet, 3H, $COCH_3$). $^{13}$C NMR (δ): 173.4 (C=O, amide), 170.1 (C=O, acetyl), 157.4 (C=N, hydrazone), 150.5, 144.9, 142.6, 126.8, 121.5, 111.3, 109.5, 108.1, 55.4, 38.5, 22.3. Mass spectrum (MS), m/z (%): 363.301 ($M^+$+1).

***(E)-N-(4-(2-oxo-2-(2-(3,4,5-trimethoxybenzylidene)hydrazinyl)ethyl)thiazol-2-yl)acetamide (5h).***

$R_f$: 0.40 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 236 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3352, 3218, 2970, 1734, 1670, 1582, 1324, 1278, 1127, 741. $^1$H NMR (δ): (broad singlet, 1H, NH, $D_2O$ exchangeable), 11.52 (broad singlet, 1H, >NH, $D_2O$ exchangeable), 7.49 (singlet, 1H, =CH), 6.99 (singlet, 2H), 6.90 (singlet, 1H), 4.01 (singlet, 2H, $CH_2$), 3.84 (singlet,

6H, 2x $OCH_3$), 3.69 (singlet, 3H, $OCH_3$), 2.16 (singlet, 3H, $COCH_3$). $^{13}C$ NMR (δ): 170.0 (C=O, amide), 168.3 (C=O, acetyl), 158.1 (C=N, hydrazone), 165.3, 157.6, 153.1, 146.4, 145.0, 142.5, 139.1, 129.7, 109.6, 103.8, 60.5 (2x $OCH_3$), 55.4 ($OCH_3$), 38.8 ($CH_2$), 22.3 ($COCH_3$). Mass spectrum (MS), m/z (%): 393.101 ($M^+$+1).

***(E)-N-(4-(2-(2-(4-hydroxy-3-methoxybenzylidene)hydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (5i).***

$R_f$: 0.46 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 230 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3479, 3211, 2925, 1731, 1706, 1670, 1595, 1517, 1130, 1077, 720. $^1H$ NMR (δ): 11.95 (broad singlet, 1H, NH, $D_2O$ exchangeable), 11.13 (broad singlet, 1H, >NH, $D_2O$ exchangeable), 8.77 (singlet, 1H, OH, $D_2O$ exchangeable), 7.80 (singlet, 1H, =CH), 6.88 (singlet, 1H), 6.69 (doublet, 1H, $J_{coupling\ constant}$ =8.1 Hz), 6.78 (doublet, 1H, $J_{coupling\ constant}$ =8.1 Hz), 6.64 (singlet, 1H), 4.04 (singlet, 2H, $CH_2$), 3.86 (singlet, 3H, $OCH_3$), 2.26 (singlet, 3H, $COCH_3$). $^{13}C$ NMR (δ): 170.9 (C=O, amide), 168.3 (C=O, acetyl), 165.0, 158.4(C=N, hydrazone), 165.1, 148.8, 145.3, 143.8, 125.2, 121.9, 115.4, 109.4, 55.2, 38.4, 22.9. Mass spectrum (MS), m/z (%): 349.106 ($M^+$+1).

***(E)-N-(4-(2-(2-(furan-2-ylmethylene)hydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (5j).***

$R_f$: 0.45 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 204 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3487, 3199, 2924, 1733, 1679, 1601, 1543, 1465, 1270, 997, 745. $^1H$ NMR (δ): 11.79 (broad singlet, 1H, NH, $D_2O$ exchangeable), 11.13 (broad singlet, 1H, >NH, $D_2O$ exchangeable), 8.10 (singlet, 1H, =CH), 7.55 (doublet, 1H, $J_{coupling\ constant}$ =7.9 Hz ), 6.67 (doublet, 1H, $J_{coupling\ constant}$ =7.9 Hz), 6.52 (multiplet, 1H), 6.43 (singlet, 1H), 4.05 (singlet, 2H, $CH_2$ ), 2.19 (singlet, 3H, $COCH_3$). $^{13}C$ NMR (δ): 170.1 (C=O, amide), 168.7 (C=O, acetyl), 165.5, 158.2 (C=N, hydrazone), 149.3, 145.1, 136.3, 133.0, 113.4, 112.1, 109.8, 37.3, 22.4. Mass spectrum (MS), m/z (%): 293.213 ($M^+$+1).

***(E)-N-(4-(2-oxo-2-(2-(thiophen-2-ylmethylene)hydrazinyl)ethyl)thiazol-2-yl)acetamide (5k).***

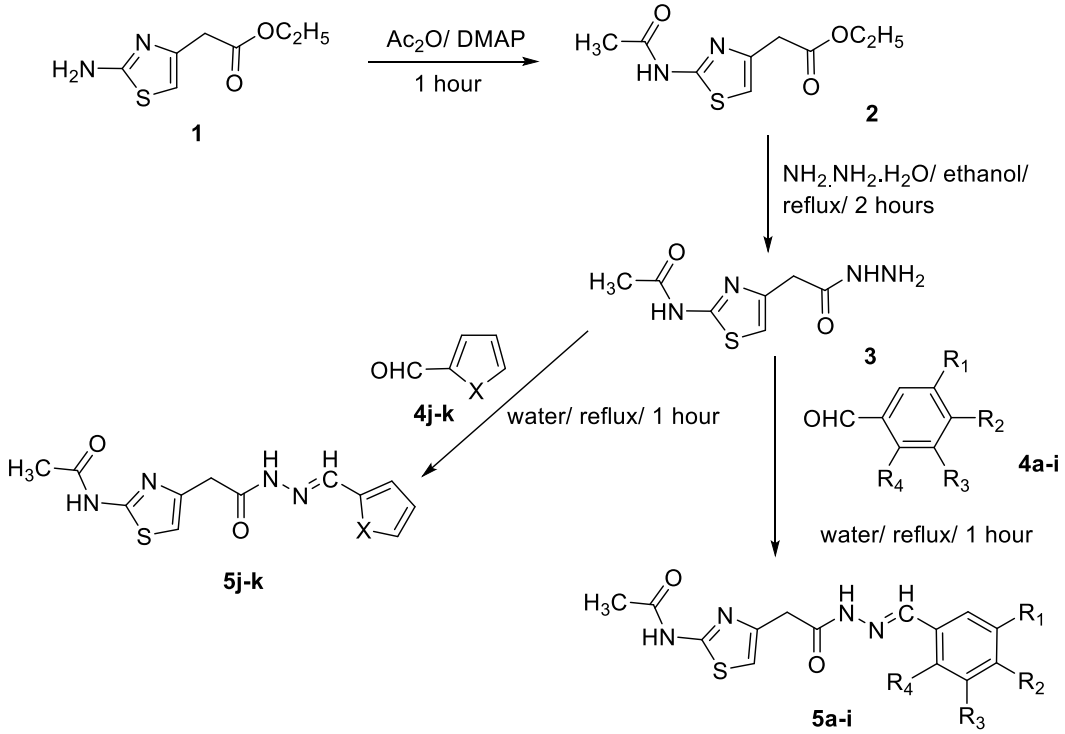
$R_f$: 0.44 (98:2 $CHCl_3$: $CH_3OH$, v/v); melting point (m.p.) 211 °C; Infrared (IR) Spectroscopy $\nu$ ($cm^{-1}$): 3199, 3044, 2925, 2857, 1736, 1663, 1597, 1551, 1374, 1085, 982, 855, 716. $^1H$ NMR (δ, DMSO-$d_6$, 400 MHz): 11.78 (broad singlet, 1H, NH, $D_2O$ exchangeable), 11.35 (broad singlet, 1H, >NH, $D_2O$ exchangeable), 7.78 (singlet, 1H, =CH), 7.49 (doublet, 1H, $J_{coupling\ constant}$ = 7.7 Hz), 7.44 (doublet, 1H, $J_{coupling\ constant}$ = 7.7 Hz), 7.22 (multiplet, 1H), 6.64 (singlet, 1H), 4.11 (singlet, 2H, $CH_2$ ), 2.20 (singlet, 3H, $COCH_3$). $^{13}C$ NMR (δ): 170.8 (C=O, amide), 169.3 (C=O, acetyl), 165.7, 158.9 (C=N, hydrazone), 157.4, 144.7, 141.6, 139.1, 130.4, 128.8, 109.0, 38.4, 22.2. Mass spectrum (MS), m/z (%): 309.014 ($M^+$+1).

**The monoclinic system X-ray data for 5a ($C_{14}H_{14}N_4O_2S_1$):** space group P21/c, V= 1455.3(2) $Å^3$, a = 11.2863(10) Å, b = 15.2072(8) Å, c = 9.0656(10) Å, α = 90°, β= 110.722(11)°, γ = 90°, crystal dimensions of 0.22 x 0.18 x 0.14 $mm^3$, the absorption coefficient of 0.22 $mm^{-1}$, and a unit cell volume of 1455.3(2) $Å^3$. The crystal structure was solved using SHELXS software and refined using SHELXL of the X-Step[xx] suite of programs. Anisotropic refinement of non-hydrogen atoms was done using full-matrix least-squares on F2 values, resulting in final R1=0.0548 and wR2=0.1614 for reflections (observed) and R1=0.0658 and wR2=0.1877 for all reflections and 195 parameters. Hydrogen atoms were placed according to the expected geometry and were not refined. Crystallographic data for **5a** (**CCDC 829123**) have been submitted to the Cambridge Crystallographic Data Centre.

## RESULTS AND DISCUSSION:

The synthetic approach adopted for the preparation of the target molecules is depicted in **Scheme-I**.

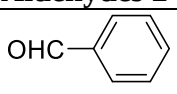
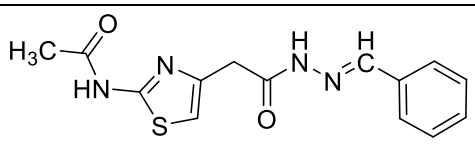
Compound 2-amino-4-(carboethoxymethyl)thiazole (**1**) was subjected to a series of reactions to synthesize hydrazone (**5a**). First, acetic anhydride was used to treat compound **1** for 1 hour to yield compound **2**. Subsequently, compound **2** was reacted with hydrazine hydrate for 2 hours to produce its hydrazide **3**. Compound **3** was then reacted with aromatic aldehydes (**4a**) in an equimolar ratio for vigorous stirring for 1 hour to obtain hydrazone (**5a**), which exhibited a molecular ion peak ($M^+$+1) at m/z 303.201 in TOF ES+. This indicated that two molecules had reacted with the loss of one molecule of water, and the molecular formula of the product was $C_{14}H_{14}N_4O_2S$. The formation of the respective hydrazone was confirmed by an absorption band at 1667 $cm^{-1}$ for >C=N stretching in the Infra-Red spectrum of compound **5a**. Moreover, the presence of NH stretching was depicted by a broad band at 3290-3159 $cm^{-1}$, and two $D_2O$ exchangeable protons in the $^1H$ NMR spectrum were observed as characteristic singlets at δ 11.80 and δ11.13. Additionally, six aromatic protons of both the condensed nucleus appeared at δ7.64 (multiplet, 2H), δ7.49 (multiplet, 2H), δ7.30 (multiplet, 1H), and δ6.70 (singlet, 1H), while the $^{13}C$ NMR spectrum displayed all the expected peaks for acetyl carbonyl, hydrazone formation, and aromatic carbons. **Scheme-I** outlines the entire process.

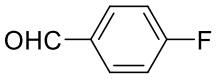
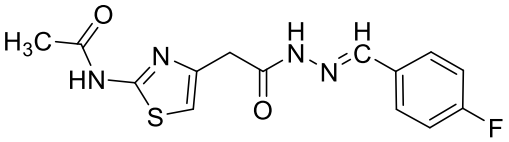
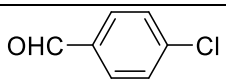
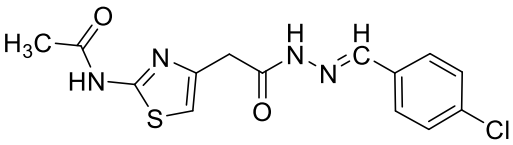
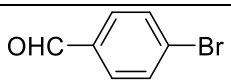
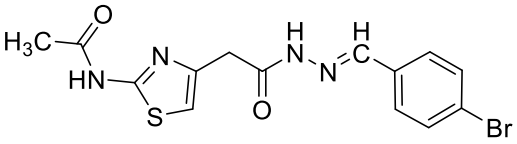
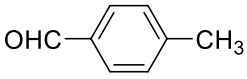
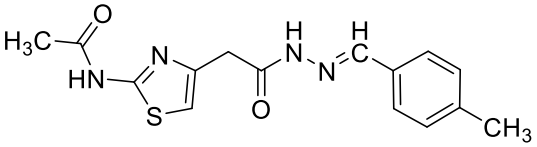
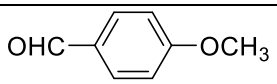
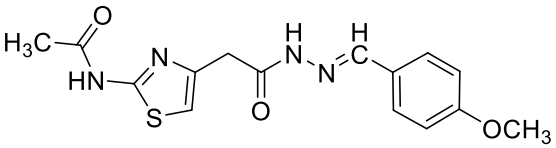
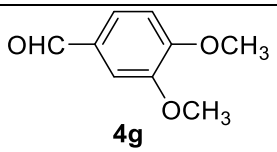
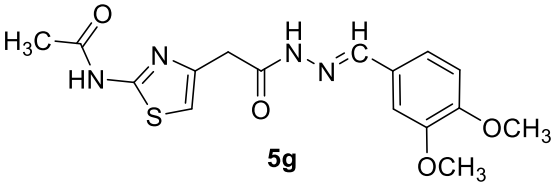
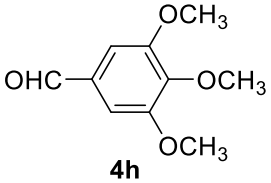
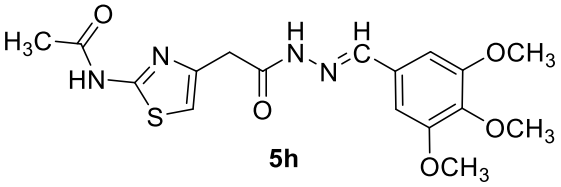
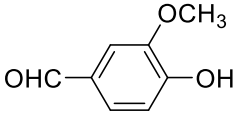
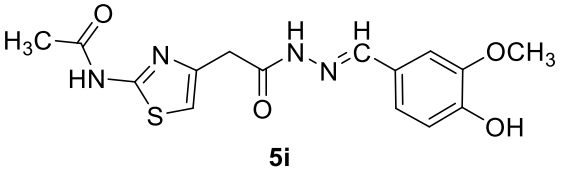
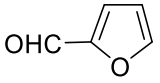
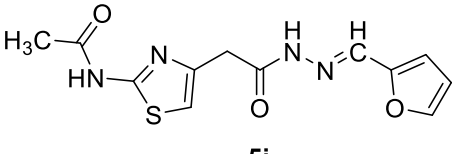


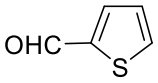
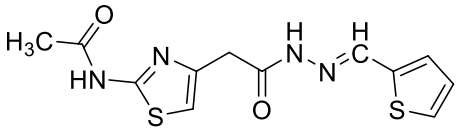

Scheme 1. Synthesis of (E)-N-(4-(2-(2-benzylidenehydrazinyl)-2-oxoethyl)thiazol-2-yl)acetamide (**5a**) using aldehyde and thiazolyl hydrazide.

The scope of the above scheme was also investigated using 2-(2-acetamido-thiazol-4-yl)acetohydrazide (**3**) and various aromatic/ heterocyclic aldehydes **4a-k** which are provided in **Table 1**

Table 1. Synthesis of various hydrazones and their yields

| Entry | Aldehydes 2 | Product 3 | Yield (%)[a] |
|---|---|---|---|
| 1 |  **4a** |  **5a** | 96 |

| | | | |
|---|---|---|---|
| 2 |  **4b** |  **5b** | 95 |
| 3 |  **4c** |  **5c** | 93 |
| 4 |  **4d** |  **5d** | 96 |
| 5 |  **4e** |  **5e** | 95 |
| 6 |  **4f** |  **5f** | 94 |
| 7 |  **4g** |  **5g** | 96 |
| 8 |  **4h** |  **5h** | 96 |
| 9 |  **4i** |  **5i** | 96 |
| 10 |  **4j** |  **5j** | 89 |

| | | | |
|---|---|---|---|
| 11 |  **4k** |  **5k** | 92 |

Notes: [a]Yields refer to isolated products.

The substitution of the aromatic or heterocyclic ring with either electron-donating (alkyl) or electron-withdrawing (F, Cl, Br) groups was not found to significantly affect the final product yields. This observation was supported not only by analyzing the spectral data of all the compounds **5a-5k** but also by performing single crystal X-ray studies of **5a** (**Figure 2**).

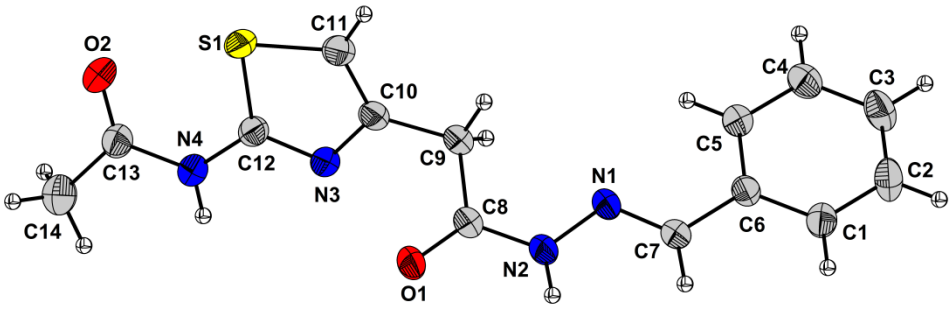



Figure 2. X-ray crystal structure of **5a** (**CCDC 829123**).

## CONCLUSION:

A novel set of thiazolyl hydrazones (**5a-k**) were synthesized using an eco-friendly method with significantly high yields. The hydrazone derivatives were prepared by introducing aldehydes to thiazolyl hydrazide in water, resulting in a straightforward reaction scheme completed in a short time with high product purity without the need for column chromatography. These hydrazones hold potential as building blocks for the synthesis of bioactive natural products and other drug molecules. The reaction can also be performed in a protic solvent, and the product yields of the synthesized compounds are unaffected by the presence of either a base or an acid.

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## REFERENCES:

i. Tadiparthi, K., Anand, P., Sakirolla, R., Gupta, T. P., Jadhav, K. A., Kishore Das, S., & Singh Yadav, J. (2022). Desymmetrisation of meso-2, 4-dimethyl-8-oxabicyclo [3.2.1]-oct-6-ene-3-ol and its Application in Natural Product Syntheses. *The Chemical Record*, **22**(3), e202100286.

ii. Barykina-Tassa, O. V., & Snider, B. B. (2015). Studies toward the synthesis of cinachyramine. An efficient route to 1, 5-diazabicyclo [4.4.0] dec-5-enes. *Tetrahedron letters*, **56**(23), 3151-3154.

iii. Mali, S. N., & Pandey, A. (2022). Synthesis of new hydrazones using a biodegradable catalyst, their biological evaluations and molecular modeling studies (Part-II). *Journal of Computational Biophysics and Chemistry*, **21**(7), 857-882.

iv. Tapera, M., Kekeçmuhammed, H., Tüzün, B., Sarıpınar, E., Koçyiğit, Ü. M., Yıldırım, E., & Zorlu, Y. (2022). Synthesis, carbonic anhydrase inhibitory activity, anticancer activity and molecular docking studies of new imidazolyl hydrazone derivatives. *Journal of molecular structure*, **1269**, 133816.

v. Devi, J., Kumar, S., Kumar, D., Jindal, D. K., & Poornachandra, Y. (2022). Synthesis, characterization, in vitro antimicrobial and cytotoxic evaluation of Co (II), Ni (II), Cu (II) and Zn (II) complexes derived from bidentate hydrazones. *Research on Chemical Intermediates*, **48**(1), 423-455.

vi. Aslan, E. K., Krishna, V. S., Armaković, S. J., Armaković, S., Şahin, O., Tønjum, T., & Gündüz, M. G. (2022). Linking azoles to isoniazid via hydrazone bridge: Synthesis, crystal structure determination, antitubercular evaluation and computational studies. *Journal of Molecular Liquids*, **354**, 118873.

vii. Zeng, L., Wu, X., Liu, L., Xu, L., Kuang, H., & Xu, C. (2020). Production of a monoclonal antibody for the detection of vitamin B 1 and its use in an indirect enzyme-linked immunosorbent assay and immunochromatographic strip. *Journal of Materials Chemistry B*, **8**(9), 1935-1943.

viii. Barker, C. I., Germovsek, E., & Sharland, M. (2017). What do I need to know about penicillin antibiotics?. *Archives of Disease in Childhood-Education and Practice*, **102**(1), 44-50.

ix. Hansen, A., Brans, R., & Sonsmann, F. (2021). Allergic contact dermatitis to rubber accelerators in protective gloves: Problems, challenges, and solutions for occupational skin protection. *Allergologie Select*, **5**, 335.

x. Fouad, S. A., El-Gendey, M. S., Ahmed, E. M., Hessein, S. A., Ammar, Y. A., & Zaki, Y. H. (2022). Convenient synthesis of some new thiophene, pyrazole, and thiazole derivatives bearing biologically active sulfonyl guanidine moiety. *Polycyclic Aromatic Compounds*, **42**(9), 6628-6646.

xi. Kamat, V., Santosh, R., Poojary, B., Nayak, S. P., Kumar, B. K., Sankaranarayanan, M., & Vootla, S. K. (2020). Pyridine-and thiazole-based hydrazides with promising anti-inflammatory and antimicrobial activities along with their in silico studies. *ACS omega*, **5**(39), 25228-25239.

xii. Hu, Y. Y., Wang, J., Li, T. J., Yadav Bheemanaboina, R. R., Ansari, M. F., Cheng, Y., & Zhou, C. H. (2020). An unexpected discovery toward novel membrane active sulfonyl thiazoles as potential MRSA DNA intercalators. *Future Medicinal Chemistry*, **12**(19), 1709-1727.

xiii. Farghaly, T. A., Alsaedi, A. M., Alenazi, N. A., & Harras, M. F. (2022). Anti-viral activity of thiazole derivatives: an updated patent review. *Expert Opinion on Therapeutic Patents*, 1-25.

xiv. Silva, I. R., Braga, A. V., de Abreu Gloria, M. B., de Resende Machado, R., César, I. C., & Oliveira, R. B. (2020). Preclinical pharmacokinetic study of a new thiazolyl hydrazone derivative with antifungal activity in mice plasma by LC-MS/MS. *Journal of Chromatography B*, **1149**, 122180.

xv. Muluk, M. B., Ubale, A. S., Dhumal, S. T., Rehman, N. N., Dixit, P. P., Kharat, K. K., & Haval, K. P. (2020). Synthesis, anticancer and antimicrobial evaluation of new pyridyl and thiazolyl clubbed hydrazone scaffolds. *Synthetic Communications*, **50**(2), 243-255.

xvi. Evren, A. E., Nuha, D., Dawbaa, S., Sağlık, B. N., & Yurttaş, L. (2022). Synthesis of novel thiazolyl hydrazone derivatives as potent dual monoamine oxidase-aromatase inhibitors. *European Journal of Medicinal Chemistry*, **229**, 114097.

xvii. Sinha, S., Doble, M., & Manju, S. L. (2018). Design, synthesis and identification of novel substituted 2-amino thiazole analogues as potential anti-inflammatory agents targeting 5-lipoxygenase. *European journal of medicinal chemistry*, **158**, 34-50.

xviii. Khake, S. M., & Chatani, N. (2022). Rhodium (III)-catalyzed oxidative C–H alkylation of aniline derivatives with allylic alcohols to produce β-aryl ketones. *ACS Catalysis*, **12**(8), 4394-4401.

xix. M Omar, A. M., Ihmaid, S., Habib, E. S. E., Althagfan, S. S., Ahmed, S., Abulkhair, H. S., & Ahmed, H. E. (2020). The rational design, synthesis, and antimicrobial investigation of 2-amino-4-methylthiazole analogues inhibitors of GlcN-6-P synthase. Bioorganic chemistry, **99**, 103781.

xx. Schlüter, A. D., Weber, T., & Hofer, G. (2020). How to use X-ray diffraction to elucidate 2D polymerization propagation in single crystals. Chemical Society Reviews, **49**(15), 5140-5158.

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