Using Kiwi Juice as a Green Biocatalyst for the Synthesis of Pyrano[2,3-\textit{d}]pyrimidines in the Facile One-pot, Three-Component Reaction

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Abstract: In this research, kiwi juice was used as an effective biocatalyst in reacting aryl aldehydes, malononitrile, and 1,3-dimethylbarbituric acid to synthesize pyrano[2,3-\textit{d}]pyrimidines in high yields (85-98%). The distinct aspects of the current method are short reaction time, safe, clean, cheap, readily available, and green properties of the kiwi juice as an effective catalyst.

Keywords: kiwi juice; aryl aldehyde; biocatalyst; 1,3-dimethylbarbituric acid; malononitrile, pyrano[2,3-\textit{d}]pyrimidine.

1. Introduction

In recent years, fruits extraction has gained great attention as a green biocatalyst in its environmentally friendly properties [1-10]. One of the main aims of this concept is to demonstrate such routes for the synthesis of important biologically active compounds in medicinal and material sciences [11-13]. In organic chemistry, selecting catalysts with high efficiency to reach the expected products with excellent yields in chemical reactions is increasingly important [14-19]. The kiwi fruit (Actinidia deliciosa) is one of the delicious fruits rich in fiber, bioactive compounds, and minerals [20-22]. Furthermore, the kiwi fruit has Vitamin C and antioxidant capacity in high level that its ingredients can act as free radical scavengers [23]. Due to kiwi juice's high potential as a biological active compound [24-26], it has been used as a catalyst for synthesizing pyrano[2,3-\textit{d}]pyrimidines for the first time. Pyrano[2,3-\textit{d}]pyrimidines are the heterocyclic systems that exhibit antibronchitic, antifungal, antimalarial, antiviral, and antihypertensive properties [27-34]. The antimicrobial, antioxidant, and cytotoxic activities of some pyrano[2,3-\textit{d}]pyrimidines such as compounds 1 and 2 are well documented in the literature (Fig. 1) [35,36].

![Antioxidant and cytotoxic active compounds](image1.png)

![Anticancer and antibacterial active compounds](image2.png)

Figure 1. Pyrano[2,3-\textit{d}]pyrimidines with biological activities.
The synthesis of pyrano[2,3-d]pyrimidines has been described in many reports that in some routes, harsh conditions such as acidic, reflux, etc., have been used for the synthesis of them [37-42]. Following our previous investigations in synthesizing important pharmaceutical compounds and due to the safety of this catalyst in the synthesis procedures [43-52], it has been decided to synthesize pyrano[2,3-d]pyrimidines using kiwi juice as a green catalyst in a three-component reaction of aryl aldehydes, malononitrile, and 1,3-dimethylbarbituric acid.

2. Materials and Methods

Melting points for all obtained compounds were measured using a Barnstead Electrothermal 9200 apparatus, while the IR spectra of the compounds were recorded on a Thermo-Nicolet Nexus 670 FT-IR spectrometer. Further consideration on the structure of achieved molecules was conducted with $^1$H and $^{13}$C NMR spectroscopy, in which the spectra were obtained with a BRUKER DRX-300 and 400 AVANCE instruments using DMSO-$d_6$ as a solvent and TMS as an internal standard at 400 and 100.6 MHz, respectively. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. In addition, the mass spectra were recorded on an Agilent Technologies (HP) MS Model: 5975C VL MSD mass spectrometer operating at an ionization potential of 70 eV. The kiwi fruits have been supplied from Gorgan province in the north of Iran. All the chemicals used were purchased from Merck, Sigma-Aldrich, and Fluka companies, and no further purification was carried out before use. Thin-layer chromatography (TLC) was accomplished with 60 mesh sheets purchased from Merck Company.

2.1. Kiwi juice catalyst preparation.

First, all kiwi skins were peeled off, then chopped into small parts and separated and extracted their juice from the pulps with a filter paper. The pH of the kiwi juice (4.1) was measured by a Metrohm 710 pH meter (Herisau, Switzerland). The obtained juice (25 mL) was allowed to evaporate at room temperature for 10 days in a beaker, and the remaining material was converted to a grease mode with brown color. Then, the grease residue was used as a catalyst for synthesizing pyrano[2,3-d]pyrimidines.

2.2. General procedure for synthesizing pyrano[2,3-d]pyrimidines (Exemplified by 6a).

1,3-Dimethylbarbituric acid (1 mmol) in ethanol (0.5 mL) was added dropwise to a vigorously stirring solution of aryl aldehyde (1 mmol) in the presence of concentrated kiwi juice (24 mg) as a catalyst in ethanol (5 mL) over 5 min at room temperature. Afterward, the reaction mixture was heated up to 60 °C. The progress of the reaction was monitored by TLC in the solvent combination ethylacetate/n-hexane (6:4) as the mobile phase ($R_f$ value for compound 6a is 0.63). After completion of the reaction, the mixture was cooled to room temperature, and the resulting precipitate was filtered and washed with (3×2 mL) of ethanol. The crude product was recrystallized from ethanol (5 mL) to obtain the pure compound 6a.

2.2.1. 7-Amino-1,3-dimethyl-2,4-dioxo-5-phenyl-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (6a).

Light yellow solid: yield 98% (320 mg), mp 219-222 °C. IR $\nu_{\max}$: 3380, 3310 (NH$_2$), 2198 (CN), 1038 (C-O), 1701 (C=O) cm$^{-1}$. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ = 3.07 (s, 3H,
CH₃), 3.35 (s, 3H, CH₃), 4.31 (s, 1H, CH), 7.19 (s, 2H, exchanged by D₂O addition, NH₂), 7.21 (s, 1H, ArH), 7.25 (d, 2H, J = 6 Hz, ArH), 7.29 (d, 2H, J = 6.9 Hz, ArH).

2.2.2. 7-Amino-5-(4-chlorophenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyran[2,3-d]pyrimidine-6-carbonitrile (6b).

Light yellow solid: yield 93% (337 mg), mp 199-201 °C. IR νmax: 3372, 3308 (NH₂), 2194 (CN), 1689 (C=O), 1037 (C-O), 750 (C-Cl) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ = 3.04 (s, 3H, CH₃), 3.34 (s, 3H, CH₃) 4.34 (s, 1H, CH), 7.26 (s, 2H, exchanged by D₂O addition, NH₂), 7.30 (d, 2H, J = 6 Hz, ArH), 7.36 (d, 2H, J = 6 Hz, ArH). ¹³C NMR (100.6 MHz, DMSO-d₆): δ = 160.43, 157.58, 151.15, 149.95, 143.12, 129.28, 128.14, 118.85, 88.29, 58.12, 35.97, 29.08, 27.61.

2.2.3. 7-Amino-5-(4-methoxyphenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyran[2,3-d]pyrimidine-6-carbonitrile (6c).

Yellow solid, yield 85% (305 mg), mp 195-198 °C. IR νmax: 3321, 3374 (NH₂), 2195 (CN), 1020 (C-O), 1686 (C=O) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ = 3.10 (s, 3H, CH₃), 3.71 (s, 3H, CH₃), 3.88 (s, 3H, OCH₃), 4.26 (s, 1H, CH), 6.82 (s, 2H, exchanged by D₂O addition, NH₂), 7.14 (d, 2H, J = 6.3 Hz, ArH), 7.19 (d, 2H, J = 6.3 Hz, ArH). ¹³C NMR (100.6 MHz, DMSO-d₆): δ = 165.86, 164.34, 160.43, 157.53, 133.33, 128.37, 115.19, 113.89, 113.58, 89.07, 58.90, 55.90, 35.71, 29.04, 27.73 ppm.

2.2.4. 7-Amino-5-(2-nitrophenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyran[2,3-d]pyrimidine-6-carbonitrile (6d).

Light yellow solid: yield 86% (320 mg), mp 199-201 °C. IR νmax: 3383, 3310 (NH₂), 2197 (CN), 1690 (C=O), 1526, 1393 (NO₂), 1042 (C-O) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ = 2.84 (s, 3H, CH₃), 3.34 (s, 3H, CH₃), 4.44 (s, 1H, CH), 6.62 (s, 2H, exchanged by D₂O addition, NH₂), 7.42-7.52 (m, 3H, ArH), 7.63 (s, 1H, ArH).

2.2.5. 7-Amino-5-(3-nitrophenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyran[2,3-d]pyrimidine-6-carbonitrile (6e).

Yellow solid, yield 92% (343 mg), mp 195-198 °C. IR νmax: 3362, 3308 (NH₂), 2199 (CN), 1693 (C=O), 1531, 1349 (NO₂), 1028 (C-O) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ = 3.05 (s, 3H, CH₃), 3.34 (s, 3H, CH₃), 4.55 (s, 1H, CH), 7.46 (s, 2H, exchanged by D₂O addition, NH₂), 7.57-8.08 (m, 4H, ArH).

2.2.6. 7-Amino-5-(4-nitrophenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyran[2,3-d]pyrimidine-6-carbonitrile (6f).

Yellow solid, yield 92% (343 mg), mp 196-199 °C. IR νmax: 3388, 3305 (NH₂), 2204 (CN), 1693 (C=O), 1513, 1381 (NO₂), 1035 (C-O) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ = 3.06 (s, 3H, CH₃), 3.35 (s, 3H, CH₃), 4.52 (s, 1H, CH), 7.48 (s, 2H, exchanged by D₂O addition, NH₂), 7.56 (s, 2H, J = 6.6 Hz, ArH), 8.15 (d, 2H, J = 6.6 Hz, ArH).
7-Amino-5-(4-tolyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (6g).

Yellow solid, yield 87% (298 mg), mp 189-192 °C; IR \( \nu_{\text{max}} \): 3380, 3312 (NH\(_2\)), 2199 (CN), 1687 (C=O), 1036 (C-O) cm\(^{-1}\). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \( \delta = 2.07 \) (s, 3H, CH\(_3\)), 2.49 (s, 3H, CH\(_3\)), 3.09 (s, 3H, CH\(_3\)), 4.25 (s, 1H, s CH), 7.08 (s, 2H, exchanged by D\(_2\)O addition, NH\(_2\)), 7.43 (d, 2H, \( J = 6.3 \) Hz, ArH), 7.85 (d, 2H, \( J = 6.3 \) Hz, ArH).

7-Amino-5-(3-pyridyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (6h).

Light yellow solid: yield 88% (289 mg), mp 201-202 °C. IR \( \nu_{\text{max}} \): 3421, 3070 (NH\(_2\)), 2094 (CN), 1679 (C=O), 1065 (C-O) cm\(^{-1}\). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \( \delta = 3.06 \) (s, 3H, CH\(_3\)), 3.44 (s, 3H, CH\(_3\)), 4.44 (s, 1H, CH), 6.24 (s, 2H, exchanged by D\(_2\)O addition, NH\(_2\)), 7.91-7.95 (m, 2H, ArH), 8.62 (d, 2H, \( J = 6 \) Hz, ArH). \(^13\)C NMR (100.6 MHz, DMSO-d\(_6\)): \( \delta = 174.4, 170.0, 161.2, 155.0, 152.1, 142.1, 133.1, 123.1, 123.3, 113.9, 76.3, 56.1, 37.7, 26.2, 25.8 ppm; \( m/z \): 311.1 [M\(^+\)] (3), 233.1 (61), 269.2 (37), 234.1 (100), 199 (13). Found: C, 57.81; H, 4.27; N, 22.58%. C\(_{15}\)H\(_{13}\)N\(_3\)O\(_3\) (311.30); Calc: C, 57.87; H, 4.21; N, 22.50%.

7-Amino-5-(3,4,5-trimethylphenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (6i).

Light yellow solid: yield 87% (324 mg), mp 188-191 °C. IR \( \nu_{\text{max}} \): 3407, 3315 (NH\(_2\)), 2195 (CN), 1695 (C=O), 1119 (C-O) cm\(^{-1}\). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \( \delta = 2.02 \) (s, 3H, CH\(_3\)), 2.23 (s, 6H, 2×CH\(_3\)), 3.24 (s, 3H, CH\(_3\)), 3.62 (s, 3H, CH\(_3\)), 4.29 (s, 1H, CH), 6.49 (s, 2H, exchanged by D\(_2\)O addition, NH\(_2\)), 7.31 (d, 2H, \( J = 6 \) Hz, ArH). \(^13\)C NMR (100.6 MHz, DMSO-d\(_6\)): \( \delta = 161.6, 158.6, 153.5, 149.8, 138.5, 136.0, 132.3, 125.4, 117.4, 88.3, 57.2, 38.1, 29.1, 28.4, 21.3, 19.6 ppm; \( m/z \): 352.3 [M\(^+\)] (6), 325.1 (11), 234.0 (100), 210.0 (33), 190.1 (39). Found: C, 64.58; H, 5.69; N, 15.96%. C\(_{19}\)H\(_{20}\)N\(_4\)O\(_3\) (352.39); Calc: C, 64.76; H, 5.72; N, 15.90%.

7-Amino-5-(2-hydroxy-3-methoxyphenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (6j).

Light yellow solid: yield 90% (338 mg), mp 202-205 °C. IR \( \nu_{\text{max}} \): 3417 (OH), 3288, 3224 (NH\(_2\)), 2232 (CN), 1712 (C=O), 1104 (C-O) cm\(^{-1}\). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \( \delta = 2.83 \) (s, 3H, CH\(_3\)), 3.55 (s, 3H, CH\(_3\)), 3.92 (s, 3H, OCH\(_3\)), 4.36 (s, 1H, CH), 7.33 (s, 2H, exchanged by D\(_2\)O addition, NH\(_2\)), 8.94 (s, 1H, OH), 7.38-7.51 (m, 3H, ArH). \(^13\)C NMR (100.6 MHz, DMSO-d\(_6\)): \( \delta = 165.9, 164.3, 160.3, 156.5, 149.2, 139.0, 133.5, 129.6, 128.3, 113.4, 89.1, 58.9, 55.9, 38.8, 29.0, 27.7 ppm; \( m/z \): 356.1 [M\(^+\)] (11), 329.4 (5), 312.0 (100), 235.2 (73), 209.5 (13). Found: C, 57.19; H, 4.48; N, 15.77%. C\(_{17}\)H\(_{16}\)N\(_4\)O\(_3\) (356.34); Calc: C, 57.30; H, 4.53; N, 15.72%.

7-Amino-5-(3,4,5-trimethoxyphenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (6k).

Light yellow solid: yield 91% (383 mg), mp 193-196 °C. IR \( \nu_{\text{max}} \): 3290, 3221 (NH\(_2\)), 2238 (CN), 1714 (C=O), 1115 (C-O) cm\(^{-1}\). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): \( \delta = 3.08 \) (s, 3H, CH\(_3\)), 3.33 (s, 3H, CH\(_3\)), 3.66 (s, 3H, OCH\(_3\)), 3.67 (s, 3H, OCH\(_3\)), 3.70 (s, 3H, OCH\(_3\)), 4.29 (s,
1H, CH), 6.82 (s, 2H, exchanged by D2O addition, NH2), 6.48 (d, 2H, J = 6 Hz, ArH). 13C NMR (100.6 MHz, DMSO-d6): δ = 163.4, 161.7, 157.9, 153.5, 150.5, 149.3, 131.7, 124.6, 113.1, 90.2, 59.7, 57.5, 56.7, 38.4, 29.2, 28.3 ppm; m/z: 400.1 [M]+ (15), 370.3 (19), 356.3 (5), 345.1 (7), 235.2 (100). Found: C, 56.94; H, 5.08; N, 14.05%. C19H20N4O6 (400.39); Calc: C, 57.00; H, 5.04; N, 13.99%.

2.2.12. 7-Amino-5-(2,4-dimethoxyphenyl)-1,3-dimethyl-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (6i).

Light yellow solid: yield 88% (343 mg), mp 191-194 °C. IR νmax: 3279, 3228 (NH2), 2217 (CN), 1717 (C=O), 1105 (C-O) cm⁻¹. 1H NMR (400 MHz, DMSO-d6): δ = 3.08 (s, 3H, CH3), 3.34 (s, 3H, CH3), 3.54 (s, 3H, OCH3), 3.85 (s, 3H, OCH3), 4.13 (s, 1H, CH), 7.67 (s, 2H, exchanged by D2O addition, NH2), 6.62-8.30 (m, 3H, ArH), 8.30 (s, 1H, OH). 13C NMR (100.6 MHz, DMSO-d6): δ = 164.2, 162.5, 157.3, 154.5, 147.8, 143.7, 132.7, 130.8, 129.3, 127.3, 113.4, 90.6, 56.3, 59.2, 54.9, 38.1, 28.9, 28.3 ppm; m/z: 370 [M]+ (47), 355.1 (7), 233.1 (100), 209.1 (35), 165.4 (10). Found: C, 58.29; H, 5.11; N, 15.27%. C18H18N4O5 (370.37); Clac: C, 58.37; H, 4.90; N, 15.13%.

3. Results and Discussion

The reaction between aryl aldehydes 3a-l, malononitrile (4), and 1,3-dimethylbarbituric acid (5) using kiwi juice as a green and safe catalyst for the synthesis of pyrano[2,3-d]pyrimidines 6a-l in an efficient one-pot route was carried out (Scheme 1).

![Scheme 1. Synthesis of pyrano[2,3-d]pyrimidines.](image)

Synthesis of pyrano[2,3-d]pyrimidines was reported under different conditions ranging from mild to some harsh conditions. The reaction of benzaldehyde (3a) and malononitrile (4) in the presence of 1,3-dimethylbarbituric acid (5) was fulfilled as a model reaction to obtain the compound 6a.

In the first step, a reaction was performed with no catalyst. The reaction proceeding without kiwi juice was not acceptable at room temperature. The reaction was carried out in various solvents such as CHCl3, H2O, EtOH, EtOH:H2O, and MeOH to realize the most appropriate solvent for this reaction. EtOH was selected as the best solvent among the solvents above through its high efficiency. The results are shown in Table 1.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Catalyst/mg</th>
<th>Time/min</th>
<th>Isolated Yield/%</th>
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<tbody>
<tr>
<td>1</td>
<td>H2O</td>
<td>1</td>
<td>20</td>
<td>80</td>
</tr>
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<td>2</td>
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<td>75</td>
</tr>
<tr>
<td>3</td>
<td>EtOH</td>
<td>1</td>
<td>60</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>EtOH:H2O (1:1)</td>
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<td>70</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>CH3Cl</td>
<td>1</td>
<td>100</td>
<td>70</td>
</tr>
</tbody>
</table>

Table 1. Optimization of solvent in the synthesis of 6a at 60 °C.
After optimizing solvent type, the reaction time was measured in different conditions in terms of catalyst loading. Results exhibited the highest yield for the product obtained in 24 mg of kiwi juice extract as a catalyst, and any variation in the amount of catalyst had no positive effects on the reaction yield of 6a in EtOH at 60°C (Table 2).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Catalyst/mg</th>
<th>Temperature/°C</th>
<th>Time/min</th>
<th>Isolated Yield/%</th>
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<tbody>
<tr>
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<td>EtOH</td>
<td>51</td>
<td>60</td>
<td>75</td>
<td>74</td>
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To optimize and investigate the role of temperature in the synthesis of pyrano[2,3-d]pyrimidines, some temperatures have been examined, and 60°C was selected as the best temperature for the product generation. The results are shown in Table 3.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Catalyst/mg</th>
<th>Temperature/°C</th>
<th>Time/min</th>
<th>Isolated Yield/%</th>
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<tr>
<td>1</td>
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<td>EtOH</td>
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<td>75</td>
<td>70</td>
<td>77</td>
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</table>

After optimization of reaction conditions, several derivatives of pyrano[2,3-d]pyrimidine were synthesized with various aryl aldehydes bearing different substituents to evaluate the catalyst performance (Table 4) [40, 53–57].

The results indicate that due to the conditions and efficiency, the current procedure has advantages such as high efficiency, low reaction time, less pollution, non-toxic and hazardous catalyst usage.

Some methodologies for synthesizing pyrano[2,3-d]pyrimidines have been shown in Table 5. As shown in Table 5, current work has many advantages compared to reported procedures such as non-toxic, low cost, and easy workup.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Time/min</th>
<th>Isolated Yield/%</th>
<th>M.p/°C</th>
<th>Reported</th>
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<tbody>
<tr>
<td>6a</td>
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<td>98</td>
<td>219-222</td>
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<tr>
<td>6b</td>
<td>4-ClC₆H₄</td>
<td>45</td>
<td>93</td>
<td>199-201</td>
<td>200 [53]</td>
</tr>
<tr>
<td>6c</td>
<td>4-MeOC₆H₄</td>
<td>40</td>
<td>85</td>
<td>195-198</td>
<td>225-227 [54]</td>
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<tr>
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<td>2-O₂N₆C₆H₄</td>
<td>45</td>
<td>86</td>
<td>193-196</td>
<td>208-209 [55]</td>
</tr>
<tr>
<td>6e</td>
<td>3-O₂N₆C₆H₄</td>
<td>40</td>
<td>92</td>
<td>195-198</td>
<td>205-207 [56]</td>
</tr>
<tr>
<td>6f</td>
<td>4-O₂N₆C₆H₄</td>
<td>50</td>
<td>92</td>
<td>196-199</td>
<td>196-198 [57]</td>
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<tr>
<td>6g</td>
<td>4- Tolyl</td>
<td>65</td>
<td>87</td>
<td>189-192</td>
<td>202-203 [40]</td>
</tr>
<tr>
<td>6h</td>
<td>3-Pyridyl</td>
<td>55</td>
<td>88</td>
<td>201-202</td>
<td>---------</td>
</tr>
<tr>
<td>6i</td>
<td>3,4,5-(Me)₃C₆H₂</td>
<td>55</td>
<td>87</td>
<td>188-191</td>
<td>---------</td>
</tr>
<tr>
<td>6j</td>
<td>2-OH-3-MeOC₆H₃</td>
<td>75</td>
<td>90</td>
<td>202-205</td>
<td>---------</td>
</tr>
<tr>
<td>6k</td>
<td>3,4,5-(MeO)₂C₆H₂</td>
<td>45</td>
<td>91</td>
<td>193-196</td>
<td>---------</td>
</tr>
<tr>
<td>6l</td>
<td>2,4-(MeO)₂C₆H₃</td>
<td>40</td>
<td>88</td>
<td>191-194</td>
<td>---------</td>
</tr>
</tbody>
</table>
Table 5. The comparison of kiwi juice as a catalyst with other systems for the preparation pyrano[2,3-d]pyrimidines.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conditions</th>
<th>Time/min</th>
<th>Yield/%</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SBA-Pr-SO$_3$H</td>
<td>Solventless, 140 °C</td>
<td>5-45</td>
<td>30-90</td>
<td>[38]</td>
</tr>
<tr>
<td>2</td>
<td>Ionic Liquids</td>
<td>Solvent-free, 90 °C</td>
<td>3-5</td>
<td>82-95</td>
<td>[55]</td>
</tr>
<tr>
<td>3</td>
<td>PEG-Ni nps</td>
<td>Et$_2$O, r.t.</td>
<td>5-15</td>
<td>87-94</td>
<td>[53]</td>
</tr>
<tr>
<td>4</td>
<td>L-Proline</td>
<td>H$_2$O:EtOH, r.t.</td>
<td>30-90</td>
<td>68-86</td>
<td>[58]</td>
</tr>
<tr>
<td>5</td>
<td>Nano-ZnFe$_2$O$_4$</td>
<td>Solvent-free, 90 °C</td>
<td>7-30</td>
<td>86-96</td>
<td>[59]</td>
</tr>
<tr>
<td>6</td>
<td>Urea</td>
<td>EtOH:EtOH (1:1 v/v), r.t.</td>
<td>12-14</td>
<td>83-91</td>
<td>[60]</td>
</tr>
<tr>
<td>7</td>
<td>Fe$_3$O$_4$@SiO$_2$-Propyl-Pip-SO$_3$H-HSO$_4$</td>
<td>H$_2$O, 60 °C</td>
<td>10-35</td>
<td>92-98</td>
<td>[61]</td>
</tr>
<tr>
<td>8</td>
<td>Et$_3$N</td>
<td>Sonication, EtOH 50 °C</td>
<td>25-40</td>
<td>82-89</td>
<td>[62]</td>
</tr>
<tr>
<td>9</td>
<td>Kiwi juice</td>
<td>EtOH, 60 °C</td>
<td>30-75</td>
<td>85-98</td>
<td>Current work</td>
</tr>
</tbody>
</table>

The proposed mechanism for synthesizing pyrano[2,3-d]pyrimidines is shown in Scheme 2. The initial step in the mechanism is the activation of aryl aldehyde toward the synthesis of dicyanoalkene A as a conjugated electron-deficient system which can be attacked by nucleophilic systems such as 1,3-dimethylbarboturic acid (5) to obtain compound B. Then, the intramolecular attack of an oxygen atom to an active nitrile group leads to pyran ring synthesis can be converted to final compound 6 by a 1,3-proton shift.

Scheme 2. Proposed mechanism for the synthesis of pyrano[2,3-d]pyrimidines.

The reaction showed that the kiwi juice has high performance as a catalyst in synthesizing pyrano[2,3-d]pyrimidines. The reaction progress has been monitored by TLC, which reaction times were very acceptable. The structure of synthesized compounds was investigated with IR, $^1$H, and $^{13}$C NMR and melting points. The melting points of synthesized compounds were in good agreement with the reported values. No attempt was made to isolate the catalyst at the end of the reaction. Hence, the catalyst was used only once for each reaction.
In our experimental procedure, the used kiwi fruit was supplied from the Gorgan province in the north of Iran because another kind of kiwi fruit is unavailable for use in this season. Therefore, the catalytic effect of other kinds of kiwi fruit from other countries was not tested.

4. Conclusions

In conclusion, an efficient and safe one-pot procedure for synthesizing pyrano[2,3-d]pyrimidines was proposed using kiwi juice extract as a catalyst in EtOH at 60°C. We hope to expand its application to synthesize other important organic compounds with various relevant applications in the future.

Funding

This research received no external funding.

Acknowledgments

The authors gratefully acknowledge the financial support received from the research council of Urmia University.

Conflicts of Interest

The authors declare no conflict of interest.

References


