A Facile and Effective Four-Component Synthesis of Benzo[4,5]imidazo[1,2-α]-pyrimidine-3-carboxamides Based on Diketene

Manizheh Ghanbarian, Seyed Yahya Shirazi Beheshtiha, and Majid M. Heravi

ABSTRACT
A novel and efficient four component reaction involving diketene, primary amines, aromatic aldehydes and 2-aminobenzimidazole in the presence of I₂ in refluxing EtOAc for the synthesis of benzo[4,5]imidazo[1,2-α]-pyrimidine-3-carboxamides is reported. Good yields, mild reaction conditions and facile isolation of products in pure forms are advantageous of this methodology.

ARTICLE HISTORY
Received 25 May 2019
Accepted 17 November 2019

KEYWORDS
Aminobenzimidazole; benzo[4,5]imidazo[1,2-α]-pyrimidine-3-carboxamides; diketene; iodine-catalyzed reaction; MCR

Introduction
4-Methyleneoxetan-2-one or diketene (DK) is an organic compound with the formula (CH₂CO)₂. It is an inexpensive and relatively safe colorless liquid which commonly prepared by dimerization of easily accessible ketene at industrial level. DK has both electrophilic (E) and nucleophilic (Nu) sites, thus can be considered as a versatile reagent to react numerous substrates providing a wide variety of functionalized heterocycles. As a matter of fact DK is a β-lactone, thus, can be easily subjected to in situ ring opening by various nucleophiles such amines at ambient conditions. Thus, typically, DK is subjected into the addition reactions with simultaneous ring-opening of the β-lactone. Significantly, this classic reaction makes DK as a privileged synthon for the...
construction of various N-heterocycles. Nitrogen-containing fused heterocycles were found particularly invaluable as biological leads in drug design as well as drug discovery program. Different imidazopyrimidines have high prominence in drug design, drug discovery as well pharmaceutical industry due to their wide range of fascinating pharmacological activity. Several prescribed drugs such as Fasiplon, Taniplon, and Divaplon with anxiolytic properties contain imidazopyrimidine segments in their structures.

Furthermore, heterocycles bearing carboxamide groups are well recognized to have different biological potencies. For example, Carboxin, Furametpyr and Penthiopyrad are known market purchasable fungicides. Nevertheless, the synthesis of pyrazolopyrimidines containing carboxamide groups for being biologically screened has been largely overlooked, thus attempts for the synthesis of the aforementioned heterocyclic system is in much demand.

Synthesis of different and complex compounds from either market purchasable or easily available starting materials via multi-component reactions (MCRs) are an inspiring theme in contemporary organic synthesis. Selecting such one pot strategies for preparation of an anticipated object circumvents the separation and purification of various intermediates as well as tiresome protection, deprotection of certain functional moiety such as hydroxyl and amino groups, which commonly, needed in most multistep synthesis. In MCRs, the reaction steps are shortened, the atom efficiency is also achieved resulting in a higher degree of component-multiplicity thus provides, greener reaction conditions.

In 2012, Guchhait and coworkers achieved and reported the synthesis of imidazo-fused heterocycles via three component reaction involving 2-aminopyridines, alkynes and aldehydes in the presence of copper sulfate/glucose. The authors suggested that the reaction proceeds in exo-dig cyclization fashion. A facile and effective strategy for the synthesis of benzo[4,5]imidazo[1,2-a]pyrimido-[4,5-d]pyrimidin-4(1H)-ones was accomplished and reported by Lei and coworkers from uncatalyzed 3CR involving cyanoacetamide, 2-aminobenzimidazole, various aldehydes in water. In 2009, Shaabani and coworkers achieved the preparation of 1,4-dihydro-1,8-naphthyridine-3-carboxamides from diketene, aromatic or aliphatic amines, 2-aminopyridines and aromatic aldehydes at room temperature in the presence of p-toluenesulfonic acid as catalyst. In 2012, Cai and coworkers prepared a library of dihydrotetrazolopyrimidinyl carbamides via MCR involving amine, diketene, aldehyde and 5-aminotetrazole at ambient temperature to refluxing with iodine. In 2014, Shaabani et al. reported the synthesis of various dihydrobenzo[4,5]imidazo[1,2-a]-pyrimidine-3-carboxamide derivatives via a one-pot un-catalized sequential four component cyclocondensation of dimedone, aldehydes, amines and 2-aminobenzimidazole under solvent-free conditions as well in water, in good yields. In 2008, the preparation of [1,2,4]triazolo/benzimidazolo-quinazolinones and associated heterocyclic systems was achieved by cyclocondensation of 2-amino benzimidazole and an amine source such as 3-amino-1,2,4-triazole with dimedone and differently substituted benzaldehydes mediated by H₆P₂W₁₈O₆₂·18H₂O as a green and recyclable catalyst in CH₃CN under reflux condition.

We have been engaged in the synthesis of different heterocycles, especially those prepared via MCRs. We have also accomplished and reported couple of five-component reactions, which are rarely found in the chemical literature. In recent years, we have disclosed the vital role of ketenes and diketenes as the advanced synthons in the synthetic heterocyclic chemistry, which have been published as five back to back chapters in Advances in Heterocyclic Chemistry. Armed with these experiences, we recently reported a couple of MCR based on diketenes. We recently also developed a new five-component protocol, comprising inexpensive commercially available diketene, malononitrile, differently substituted aromatic aldehydes and various primary amines for the synthesis of poly-functionalized 1, 4-dihydropyridines in satisfactory yields. We also reported on the diastereoselective synthesis of cyclohexane-1, 3-dicarboxamide derivatives through a pseudo-five-component reaction based on diketenes. An effective synthesis of N-fused, pyrido [1,2-a] pyrimidines was successfully
accomplished through a sequential, five-component reaction, in one-pot fashion. The MCR including diketene (DK), various primary amines, differently substituted aromatic aldehydes, nitro ketene dithioacetal and propanediamine gave \( N \)-fused, pyrido [1,2-\( a \)] pyrimidines.\(^{29} \) An effective and convenient synthetic protocol was developed for the synthesis of spiro [indoline-3,4'-pyrano-pyrazole] carbonitrile derivatives \( \text{via} \) a four-component reaction including hydrazine hydrate, diketene, substituted isatins and malononitrile in one pot manner.\(^{30} \)

In continuation of these interest and experiences on the chemistry of diketenes, in this communication, we wish to report a convenient and effective MCR based on DK for the preparation of a series of dihydrobenzo[4,5]imidazo[1,2-\( a \)]pyrimidine-3-carboxamides through four-component cyclocondensation reaction of DK, 2-aminobenzimidazole, primary amines and aromatic aldehydes in the presence of catalytic amount of I\(_2\) in refluxing EtOAc.

**Experimental**

**General**

Melting points were measured on an Electrothermal 9200 apparatus and are uncorrected. IR spectra were recorded on a Shimadzu IR-470 spectrometer. \(^1\)H-NMR spectra were recorded on a Bruker DRX-300 Avance spectrometer at 300.13 MHz; \(^13\)C-NMR spectra were recorded on a Bruker DRX-300 Avance spectrometer at 75 MHz, Bruker DRX-500 Avance spectrometer at 100 MHz, respectively. The elemental analyses were performed with an Elementar Analysensysteme GmbH VarioEL. All products were characterized by FT-IR, \(^1\)H-NMR and \(^13\)C-NMR spectra.

**Synthesis of pyrimidine-3-carboxamides (5a-o). general procedure**

A mixture of diketene 1 (1/2 mmol), amines 2 (1/2 mmol), aldehydes (1/2 mmol), 2-aminobenzimidazole (1/2 mmol) and iodine (20 mol%) was reflux in EtOAc for 4–8 h. The progress of the reaction was monitored by TLC (EtOAc: \( n \)-hexane, 3:2). Upon completion of the reaction sodium thiosulphate (Na\(_2\)S\(_2\)O\(_3\)) was added for the separation of iodine. The mixture was set aside for a while, then the solid was filtered off, washed with ethylacetate and dried at room temperature to afford the title compounds.

**5a**: \( N \)-benzyl-2-methyl-4-(4-chlorophenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-\( a \)]pyrimidine-3-carboxamide. White powder (80%, 171 mg): mp 293–294 °C (dec). IR (KBr) cm\(^{-1}\): 3308, 3029, 2924, 1670, 1629, 1539, 1514, 1093, 1013, 732. \(^1\)H-NMR (500.13 MHz, DMSO-d\(_6\)) \( \delta \): 2.19 (3H, s, \( \text{CH}_3 \)), 4.13–4.17 (\( \text{Ha} \), dd, \( J_{\text{H-H}} = 4.5 \text{ Hz} \)), 4.38–4.42 (\( \text{Hb} \), dd, \( J_{\text{H-H}} = 4.5 \text{ Hz} \)), 6.55 (1H, s, \( \text{CH} \)), 6.90–7.37 (13H, m, \( \text{H-Ar} \)), 8.28–8.30 (1H, t, \( J = 3 \text{ Hz} \), NHCO), 10.10 (1H, s, NH). \(^13\)C-NMR (76 MHz, DMSO-d\(_6\)) \( \delta \): 17.99, 42.53, 56.81, 104.07, 109.90, 116.84, 120.10, 122.09, 126.93, 127.00, 127.32, 128.47, 129.05, 129.53, 132.09, 133.02, 135.41, 139.87, 140.16, 142.92, 146.90, 146.51.

**5b**: \( N \)-benzyl-2-methyl-4-(4-nitrophenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-\( a \)]pyrimidine-3-carboxamide. Yellow powder (84%, 184 mg): mp 261 °C. IR (KBr) cm\(^{-1}\): 3267, 3026, 2920, 2850, 1671, 1624, 1518, 1459, 1416, 1278, 1009, 738. \(^1\)H-NMR (300.13 MHz, DMSO-d\(_6\)) \( \delta \): 2.23 (3H, s, \( \text{CH}_3 \)), 4.14–4.21 (\( \text{H}_a \), dd, \( J_{\text{H-H}} = 7.5 \text{ Hz} \)), 4.34–4.41 (\( \text{H}_b \), dd, \( J_{\text{H-H}} = 7.5 \text{ Hz} \)), 6.79 (1H, s, \( \text{CH} \)), 6.90–7.37 (13H, m, \( \text{H-Ar} \)), 8.28–8.30 (1H, t, \( J = 3 \text{ Hz} \), NHCO), 10.10 (1H, s, NH). \(^13\)C-NMR (76 MHz, DMSO-d\(_6\)) \( \delta \): 17.99, 42.53, 56.81, 104.07, 109.90, 116.84, 120.10, 122.09, 126.93, 127.00, 127.32, 128.47, 129.05, 129.53, 132.09, 133.02, 135.41, 139.87, 140.16, 142.92, 146.90, 146.51.

**5c**: 2-methyl-4-(4-nitrophenyl)-\( N \)-propyl-1,4-dihydrobenzo[4,5]imidazo[1,2-\( a \)]pyrimidine-3-carboxamide. Yellow powder (66%, 129 mg): mp 278–280 °C. IR (KBr) cm\(^{-1}\): 3329, 2962, 2925, 2854.59,
5d:  2-methyl-4-(3-nitrophenyl)-N-propyl-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. Yellow powder (68%, 133 mg): mp 261°C. IR (KBr) cm⁻¹: 3261, 3062, 2964, 2931, 2872, 1672, 1628, 1599, 1580, 1532, 1460, 1385, 728. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 0.70–0.75 (3H, t, J = 7.5 Hz, CH₃), 1.31–1.39 (2H, m, CH₂), 2.18 (1H, s, CH), 2.98–3.05 (2H, m, CH₂), 6.69 (1H, s, CH), 6.88–8.18 (8H, m, H-Ar), 7.81–7.85 (1H, t, J = 6 Hz, NHCO), 10.20 (1H, s, NH). ¹³C-NMR (76 MHz, DMSO-d₆) δ: 11.79, 17.92, 22.71, 56.67, 63.56, 103.69, 109.74, 116.96, 120.26, 122.26, 124.33, 128.53, 131.91, 135.59, 142.93, 146.98, 147.49, 148.40, 166.15.

5e:  N-butyl-2-methyl-4-phenyl-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. White powder (57%, 103 mg): mp 289°C. IR (KBr) cm⁻¹: 3335, 2956, 2926, 2856, 1675.82, 1631, 1538, 1516, 1460, 1384, 732. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 0.79–0.84 (3H, t, J = 7.5 Hz, CH₃), 1.06–1.18 (2H, m, CH₂), 1.26–1.35 (2H, m, CH₂), 2.17 (1H, s, CH₃), 3.01–3.07 (2H, m, CH₂), 6.51 (1H, s, CH), 7.00–7.33 (9H, m, H-Ar), 7.72–7.76 (1H, t, J = 6 Hz, NHCO), 10.02 (1H, s, NH). ¹³C-NMR (75 MHz, DMSO-d₆) δ: 14.14, 17.79, 19.90, 31.16, 31.62, 57.34, 104.77, 109.84, 116.72, 119.93, 121.94, 127.24, 128.28, 128.93, 132.17, 134.78, 141.25, 142.97, 147.27, 166.37.

5f:  N-butyl-2-methyl-4-(4-chlorophenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. White powder (57%, 107 mg): mp 292–294°C. IR (KBr) cm⁻¹: 3319, 2959, 2926, 2856, 1729, 1673, 1673, 1529, 1540, 1514, 1461, 1269, 729. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 0.79–0.84 (3H, t, J = 7.5 Hz, CH₃), 1.05–1.13 (2H, m, CH₂), 1.25–1.32 (2H, m, CH₂), 2.16 (3H, s, CH₃), 3.01–3.07 (2H, m, CH₂), 6.52 (1H, s, CH), 6.90–7.38 (8H, m, H-Ar), 7.72–7.76 (1H, t, J = 6 Hz, NHCO), 10.06 (1H, s, NH). ¹³C-NMR (75 MHz, DMSO-d₆) δ: 14.12, 17.81, 19.89, 31.16, 31.60, 56.78, 109.84, 116.72, 119.93, 121.94, 127.24, 128.93, 132.04, 132.91, 134.79, 140.14, 142.88, 147.04, 166.24.

5g:  4-(4-chlorophenyl)-N-(3,4-dimethoxyphenethyl)-2-methyl-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. White powder (75%, 188 mg). mp 267–268°C. IR (KBr) cm⁻¹: 3304, 2928, 2839, 1670, 1617, 1516, 1457, 1263, 1142, 1019, 739. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 2.11 (3H, s, CH₃), 2.59–2.65 (2H, m, CH₂), 3.19–3.31 (2H, m, CH₂), 3.73–3.75 (6H, s, OCH₃), 6.52 (1H, s, CH), 6.61–7.35 (11H, m, H-Ar), 7.86 (1H, br s, NHCO), 10.12 (1H, s, NH). ¹³C-NMR (75 MHz, DMSO-d₆) δ: 17.78, 34.94, 55.83, 55.97, 56.57, 104.21, 109.75, 112.27, 112.90, 115.90, 116.89, 120.11, 120.91, 122.10, 129.01, 131.96, 132.04, 132.34, 132.84, 135.45, 140.27, 142.94, 147.13, 147.66, 149.07, 166.40.

5h:  4-(4-chlorophenyl)-N-cyclopropyl-2-methyl-1,4 dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. White powder (77%, 146 mg). mp 295–296°C. IR (KBr) cm⁻¹: 3326, 3026, 2847, 1673.10, 1612, 1512, 1459, 733. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 0.26–0.42 (2H, m, CH₂), 0.58–0.60 (2H, m, CH₂), 2.15 (3H, s, CH₃), 2.59–2.61 (1H, m, CH), 6.52 (1H, s, CH), 6.88–7.39 (8H, m, H-Ar), 7.86 (1H, br s, NHCO), 10.14 (1H, s, NH). ¹³C-NMR (75 MHz, DMSO-d₆) δ: 5.98, 6.53, 17.76, 22.91, 56.56, 103.82, 109.79, 116.86, 120.11, 122.11, 129.01, 132.01, 132.88, 135.69, 140.27, 142.91, 147.02, 167.62 (CO).

5i:  N-cyclohexyl-2-methyl-4-(4-nitrophenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. Yellow powder (89%, 191 mg). mp 298°C. IR (KBr) cm⁻¹: 3332, 3060, 2932, 2854, 1670, 1631, 1606, 1522, 1459, 1384, 1345, 778. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 1.02–1.25 (6H, m, CH₂), 1.58–1.66 (4H, m, CH₂), 2.16 (3H, s, CH₃), 3.51–3.60 (1H, m, CH), 6.70 (1H, s, CH), 6.88–8.19 (8H, m, H-Ar), 7.67–7.70 (1H, d, J = 9 Hz NHCO), 10.19 (1H, s, NH). ¹³C-NMR (75 MHz, DMSO-d₆) δ: 17.81, 25.19, 25.67, 32.86, 48.20, 56.72.
103.59, 109.72, 116.95, 120.23, 122.26, 124.30, 128.44, 131.92, 135.46, 142.93, 147.04, 147.46, 148.32, 165.18.

5j: N-cyclohexyl-2-methyl-4-(p-tolyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. White powder (98%, 196 mg). mp 296–297°C. IR (KBr) cm⁻¹: 3336, 3025, 2929, 2852, 1672, 1633, 1609, 1515, 1460, 1385, 1252, 733. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 1.05–1.29 (6H, m, CH₂), 1.54–1.64 (4H, m, CH₂), 2.15 (3H, s, CH₃), 2.22 (3H, s, CH₃), 3.50–3.59 (1H, m, CH), 6.51 (1H, s, CH), 6.86–7.61 (8H, m, H-Ar), 7.30–7.31 (1H, d, J = 6 Hz, NHCO), 10.01 (1H, s, NH). ¹³C-NMR (75 MHz, DMSO-d₆) δ: 17.70, 21.11, 25.21, 25.71, 32.75, 48.11, 57.05, 104.75, 109.87, 116.67, 119.87, 121.88, 127.07, 129.44, 134.70, 137.46, 138.36, 142.96, 147.35, 165.43.

5k: 4-(4-chlorophenyl)-N-cyclohexyl-2-methyl-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. White powder (62%, 109 mg). mp 276°C. IR (KBr) cm⁻¹: 3328, 3053, 2930, 2853, 1671, 1631, 1608, 1459, 1340, 1250. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 1.03–1.29 (6H, m, CH₂), 1.54–1.75 (4H, m, CH₂), 2.14 (3H, s, CH₃), 3.45–3.59 (1H, m, CH), 6.55 (1H, s, CH), 6.88–7.37 (8H, m, H-Ar), 7.57–7.68 (1H, br s, NHCO), 10.07 (1H, s, NH). ¹³C-NMR (75 MHz, DMSO-d₆) δ: 17.73, 25.18, 25.69, 32.71, 48.18, 56.72, 104.30, 109.81, 116.80, 120.03, 122.07, 128.94, 129.06, 132.04, 132.80, 134.86, 140.17, 142.94, 147.15, 165.32.

5n: 2-methyl-4-(4-nitrophenyl)-N-(p-tolyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. Yellow powder (196 mg, 90%): mp 248°C (dec). IR (KBr) cm⁻¹: 3257, 2923, 2853, 1676, 1630, 1580, 1348. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 2.24–2.25 (6H, s, CH₃), 6.82 (1H, s, CH), 6.91–8.19 (12H, m, H-Ar), 9.72 (1H, br s, NHCO), 10.40 (1H, br s, NH). ¹³C-NMR (100.65 MHz, DMSO-d₆) δ: 18.09, 20.91, 56.77, 103.79, 109.86, 117.11, 120.22, 120.43, 122.37, 124.44, 128.47, 129.47, 131.93, 132.86, 136.88, 137.25, 142.93, 146.86, 147.58, 148.44, 165.03.

5o: N-(4-bromophenyl)-4-(4-methoxyphenyl)-2-methyl-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carboxamide. White powder (196 mg, 80%): mp 245–246.5°C. IR (KBr) cm⁻¹: 3287, 2925, 2853, 1676, 1630, 1582, 1323. ¹H-NMR (300.13 MHz, DMSO-d₆) δ: 2.24 (3H, s, CH₃), 3.36 (3H, s, OCH₃), 6.63 (1H, s, CH), 6.81–7.93 (12H, m, H-Ar), 9.84 (1H, br s, NHCO), 10.28 (1H, br s, NH). ¹³C-NMR (100.65 MHz, DMSO-d₆) δ: 18.02, 55.47, 56.84, 104.68, 110.16, 114.44, 115.25, 116.90, 120.12, 121.94, 122.03, 128.49, 131.89, 132.17, 133.34, 137.04, 139.01, 142.93, 146.93, 159.31, 165.60.

**Results and discussion**

The reaction of 2-aminobenzimidazole, 4-Cl-benzaldehyde, benzylamine and diketene was chosen as a model reaction. Initially, we studied the progress of the reaction in various solvents and catalytic amounts of I₂ by calculating the isolated yield of the product, utilizing the same quantity of reactants in the presence of 10, 20 and 30 mol% of I₂. The progress of the reaction was monitored by TLC (EtOAc:n-hexane, 3:2). The results are summarized in Table 1. As shown in Table 1, the model reaction was performed in various solvents such as THF, ethyl acetate, DMF, H₂O, ethanol, solvent free and CH₂Cl₂ and refluxing EtOAc was found the solvent of choice in terms of reaction yields and times (Table 1, entries 8). The comparative results were shown in Table 1, entries 2, 9 and 10, in which the best amount of I₂ was 20 mol% (Table 1, entry 2).

To study the substituent scope of the reaction, we protracted our investigation using differently substituted benzaldehydes and various primary amines, diversely under already secured optimal reaction conditions. The results of synthesis **5a**–**o** are depicted in Table 2. As it can be realized this strategy tolerates differently substituted benzaldehydes bearing both electron-releasing and electron-withdrawing substituents at meta- or para-positions and a wide range of amines including benzyl, cyclo, aliphatic and differently substituted amines. When cyclo-amine and p-methyl-
Table 1. Reaction of diketene, benzylamine, 4-chlorobenzaldehyde and 2-aminobenzimidazole in the presence of I2 under various conditions and solvents.

| Entry | Solvent | Temp. (°C) | Time (h) | I2 (%mol) | Yield (%) |
|-------|---------|------------|----------|-----------|-----------|
| 1     | THF     | Reflux     | 8        | 20        | 30        |
| 2     | EtOAc   | Reflux     | 8        | 20        | 80        |
| 3     | EtOH    | Reflux     | 8        | 20        | 60        |
| 4     | DMF     | Reflux     | 8        | 20        | 20        |
| 5     | H2O     | Reflux     | 8        | 20        | 15        |
| 6     | Solvent-free | 80 | 8 | 20 | 60 |
| 7     | CH2Cl2  | 25         | 8        | 20        | 10        |
| 8     | EtOAc   | 25         | 8        | 20        | 40        |
| 9     | EtOAc   | Reflux     | 8        | 10        | 75        |
| 10    | EtOAc   | Reflux     | 8        | 30        | 70        |

Table 2. Synthesis of dihydrobenzo[4,5]imidazo[1,2-a]-pyrimidine-3-carboxamides.

| Entry | Aldehydes | Amines | Product | Time (h) | Mp (°C) | Yield (%) |
|-------|-----------|--------|---------|----------|---------|-----------|
| 1     | p-Chlorobenzaldehyde | Benzyl | 5a       | 8        | 293–294 | 80        |
| 2     | p-Nitrobenzaldehyde  | Benzyl | 5b       | 5        | 261     | 84        |
| 3     | p-Nitrobenzaldehyde  | n-propyl | 5c     | 5        | 278–280 | 66        |
| 4     | m-Nitrobenzaldehyde  | n-propyl | 5d     | 5        | 298 (dec) | 68    |
| 5     | Benzaldehyde        | n-Butyl | 5e       | 4        | 289     | 57        |
| 6     | p-Chlorobenzaldehyde | n-Butyl | 5f       | 4        | 292–294 | 57        |
| 7     | p-Chlorobenzaldehyde | 2-(3,4-dimethoxyphenyl)ethan | 5g | 6 | 267–268 | 75 |
| 8     | p-Chlorobenzaldehyde | Cyclo-propyl | 5h | 8 | 295–296 | 77 |
| 9     | p-Nitrobenzaldehyde  | Cyclo-hexyl | 5i    | 8        | 298     | 89        |
| 10    | p-Methylbenzaldehyde | Cyclo-hexyl | 5j    | 8        | 296–297 | 98        |
| 11    | p-Chlorobenzaldehyde | Cyclo-hexyl | 5k    | 8        | 276     | 62        |
| 12    | p-Methylbenzaldehyde | Benzyl | 5l       | 5        | 279–282 (292–294) | 70    |
| 13    | p-Methoxybenzaldehyde | Benzyl | 5m      | 4        | 284–288 (290–292) | 80    |
| 14    | p-Nitrobenzaldehyde | p-Methylphenyl | 5n | 4 | 248 (dec) | 90 |
| 15    | p-Methoxybenzaldehyde | p-Bromophenyl | 5o | 8 | 245–246.5 | 80 |

*Isolated yield.*
benzaldehyde, were used together the best results were obtained in the term of yield of the product (Table 2, entry 10).

A reasonable reaction mechanism for the synthesis of dihydrobenzo[4,5]imidazo[1,2-a]-pyrimidine-3-carboxamide derivatives 5 is suggested as illustrated in the Scheme 1. It is assumed that initially, diketene is attacked by amine as nucleophile to generate the intermediate 6 via ring-opening and proton transfer. The latter is reacted with activated aldehyde 3 by I\textsubscript{2} to afford compound 7 via the condensation reaction. Then, aminobenzimidazole 4 is reacted with compound 7 via the Michael addition to generate the intermediate 8, which upon isomerization, followed by intramolecular cyclization and simultaneous dehydration provides the desired target product 5 (Scheme 1).

It is worthy to mention that this strategy was compared with the previously published method for the synthesis of dihydrobenzo[4,5]imidazo[1,2-a]-pyrimidine-3-carboxamide derivatives to obtain the identical compounds to 5\textsubscript{a}, 5\textsubscript{l} and 5\textsubscript{m}.\textsuperscript{17}

As shown in Table 3, Shabani and coworkers in 2014 reported the formation of 5\textsubscript{a}, 5\textsubscript{l} and 5\textsubscript{m} from 2,2,6-trimethyl-4\textsubscript{H}-1,3-dioxin-4-one, aldehydes, amines and 2-aminobenzimidazole. In this method, we used DK instead of 2,2,6-trimethyl-4\textsubscript{H}-1,3-dioxin-4-one to make the desired products 5. Noticeably, only three derivatives are similar to the aforementioned strategy.\textsuperscript{17} It worthwhile to mention mentione that the synthesize dihydrobenzo[4,5]imidazo[1,2-a]-pyrimidine-3-carboxamide derivative 5d using 3-nitrobenzaldehyde and the propylamine were successful.
In conclusion, we have reported the synthesis of dihydrobenzo[4,5]imidazo[1,2-a]-pyrimidine-3-carboxamide derivatives via one pot sequential four-component condensation reaction of diketene, amines, 2-aminobenzimidazole, and aldehydes catalyzed by I$_2$. This method offers some advantages such as good yields, mild reaction conditions and simple work-up procedure.

**Acknowledgements**

The authors are thankful to the Alzahra Research Council for their support MMH is also thankful to Iran National Scientific Foundation (INSF) for the granted research chair. We are also grateful to Vahideh Zadsirjan for their kind assistance.

**ORCID**

Manizheh Ghanbarian [http://orcid.org/0000-0002-0172-2297](http://orcid.org/0000-0002-0172-2297)

Majid M. Heravi [http://orcid.org/0000-0003-2978-1157](http://orcid.org/0000-0003-2978-1157)

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