INTRODUCTION

Chromene and its derivatives belong to a major class of natural heterocyclic compounds, which occur widely in edible vegetables and fruits. They frequently expose a variety of biological and pharmacological activities. Based on the extensive researches, it has been observed that chromene derivatives include biological, such as antioxidant, spasmolytic, anti-HIV, anticancer, anti-anaphylactic, antibacterial activity antihypertensive, anti-tubulin, antiviral, activator of potassium channels and inhibition of phosphodiesterase IV or dihydrofolate reductase, etc. As a result, a number of methodologies have been developed to synthesize chromene compounds.

Several methods have been reported for the synthesis of 2-amino-4H-chromene derivatives using malononitrile, resorcinol and aldehyde. Various catalysts such as TFE, MgAl/HT, cetyltrimethylammonium bromide ([BDBDMIm]Br) and tungstic acid functionalized mesoporous SBA-15 have been used for these reactions. Most of these reported methods require a long reaction time, high temperature, and unsatisfactory yields.

The use of ionic liquids as reaction media and catalyst can offer a solution to solvent, emission and catalyst recycling problems. Ionic liquids are accompanied with some pluses or let us call them advantages; some of which are negligible vapor pressure, non-flammability, non-miscibility with non-polar solvents, reasonable thermal and chemical stability and recyclability. They dissolve many organic and inorganic substrates and are tunable to specific chemical tasks.

EXPERIMENTAL

Materials and measurements

Chemicals were purchased from Merck and Fluka. All solvents used were dried and distilled according to standard procedures. Thin Layer Chromatography (TLC) was done with TLC Silica gel 60; Aluminum sheet from Merck. Melting points were determined on an Electrothermal 9100 apparatus. IR spectra were determined on a Shimadzu FT-IR 8600 spectrophotometer. 1H and 13C NMR spectra were determined on a Bruker 400 DRX Avance instrument at 500 and 125 MHz. Elemental analyses were done on a Carlo-Erba EA1110CNNO-S analyzer and agreed with the calculated values.

General procedure for the synthesis of 2-amino-4H-chromene 1a-p

A mixture containing benzyl alcohol (2.0 mmol), 1-naphthol (2.0 mmol), malononitrile (2.0 mmol) and 4mol% of [BDBDMIm]Br and 0.05g of CAN was stirred at room temperature for the required reaction times. The progress of the reaction was monitored by TLC (EtOAc: petroleum ether 1:2). After completion of the reaction, we extracted the product with CHCl3 and 0.05g of CAN was stirred at room temperature for the required reaction times. The progress of the reaction was monitored by TLC (EtOAc: petroleum ether 1:2). After completion of the reaction, we extracted the product with CHCl3 and washed with 4 mol% of CAN. The aqueous phase was concentrated under reduced pressure to recover the ionic liquid for subsequent use.

Selected data:

2-Amino-3-cyano-4-(4-chlorophenyl)-4H-benzo[1]benzocromene (4b)

Yellow solid, mp 231-233°C; FT-IR (KBr): ν 3320, 3450, 2210, 1660, 1570 cm-1. 1H NMR (CDCl3, 400 MHz): δ = 4.79 (s, 2H, NH), 4.96 (s, 1H), 7.09 (d, 1H, J = 8.4 Hz), 7.27 (d, 2H, J = 8.4 Hz), 7.38 (d, 2H, J = 8.4 Hz), 7.57-7.66 (m, 3H), 7.89 (d, 1H, J = 8.0 Hz), 8.23 (d, 1H, J = 8.0 Hz) ppm. 13C NMR (CDCl3, 100 MHz): δ = 41.2, 61.2, 117.3, 119.7, 120.2, 126.6, 123.3, 125.2, 127.4, 128.4, 128.9, 129.2, 130.2, 132.8, 133.4, 134.1, 145.7, 146.5, 148.9, 160.2 ppm. Anal Calc. for C27H16C3N2O: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.49; H, 4.56; N, 8.76.

2-Amino-3-cyano-4-(3-methylphenyl)-4H-benzo[1]benzocromene (4c)

Yellow solid, mp 206-208°C; FT-IR (KBr): ν 3370, 3420, 3320, 2200, 1580, 1650 cm-1. 1H NMR (CDCl3, 400 MHz): δ = 4.77 (s, 1H), 6.62-6.67 (m, 2H), 6.76 (d, 1H, J = 7.6 Hz), 7.03-7.18 (m, 2H), 7.17 (s, 2H, NH2), 7.58-7.68 (m, 3H), 7.84 (d, 1H, J = 8.0 Hz), 8.25 (d, 1H, J = 8.4 Hz), 9.39 (s, 1H, OH) ppm. 13C NMR (CDCl3, 100 MHz): δ = 48.6, 61.7, 116.9, 119.2, 121.8, 123.3, 123.5, 123.7, 125.1, 123.5, 127.1, 129.8, 129.5, 133.4, 141.5, 145.7, 146.5, 148.9, 160.2 ppm. Anal Calc. for C27H16C3N2O: C, 73.62; H, 4.49; N, 8.91. Found: C, 76.49; H, 4.56; N, 8.76.

2-Amino-3-cyano-4-(3-nitrophenyl)-4H-benzo[1]benzocromene (4d)

Yellow solid, mp 201-213°C; FT-IR (KBr): ν 3320, 3450, 3320, 2210, 1657 cm-1. 1H NMR (CDCl3, 400 MHz): δ = 2.23 (s, 3H, CH3), 4.73 (s, 2H, NH2), 4.84 (s, 1H), 7.05 (d, 1H, J = 8.2 Hz), 7.13-7.45 (m, 4H), 7.47-7.66 (m, 3H), 7.74 (d, 1H, J = 8.2 Hz), 8.23 (d, 1H, J = 8.4 Hz) ppm. 13C NMR (100 MHz, CDCl3): δ = 22.9 (CH3), 42.6, 61.8, 116.6, 119.0, 120.8, 129.2, 124.4, 126.6, 126.8, 127.2, 128.8, 128.5, 128.9, 130.4, 133.7, 147.2, 159.6 ppm. Anal Calc. for C27H16C3N2O: C, 69.96; H, 3.82; N, 12.24. Found: C, 70.09; H, 3.92; N, 12.37.

2-Amino-3-cyano-4-(4-nitrophenyl)-4H-benzo[1]benzocromene (4e)

Dark yellow solid, mp 234-236°C; FT-IR (KBr): ν 3346, 2202, 1666, 1525 cm-1. 1H NMR (CDCl3, 400 MHz): δ = 1.55 (s, 2H, NH2), 4.87 (s, 1H), 7.13 (d, 1H, J = 8.4 Hz), 7.33-7.87 (m, 7H), 7.85 (d, 1H, J = 8.4 Hz), 8.19 (d, 1H, J = 8.4 Hz) ppm. 13C NMR (CDCl3, 100 MHz): δ = 46.8, 61.6, 117.8, 119.2, 121.1, 123.4, 123.7, 123.8, 125.3, 125.6, 127.7, 127.8, 129.2, 130.4, 133.3, 134.8, 145.7, 147.0, 149.2, 159.9 ppm. Anal Calc. for C27H16C2N3O: C, 69.96; H, 3.82; N, 12.24. Found: C, 69.85; H, 3.94; N, 12.18.

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ABSTRACT

A clean and environmentally benign route to 2-amino-4H-chromenes has been developed via three-component condensation reaction of various benzylic alcohols, malononitrile and 1-naphthol, using a catalytical amount of CAN and a reusable ionic liquid ([BDBDMIm]Br) as a catalyst at room temperature. The present methodology offers several advantages such as solvent-free conditions, excellent yields, simple procedure, mild conditions and reduced environmental consequences. The ionic liquid was recovered and reused. All of synthesized compounds were characterized by IR, NMR and elemental analyses.

Keywords: Chromenes, Benzyl alcohols, Ionic Liquid, Multicomponent reaction, 1-Naphthol, Malononitrile.
RESULTS AND DISCUSSION

Furthering the ongoing studies to synthesize heterocyclic and pharmaceutical compounds by mild and practical protocols \(21-26\), the researchers would like to report the experimental results on the synthesis of 2-amino-4H-chromenes, using various benzyl alcohols, 1-naphthol and malononitrile in the presence of bis ionic liquid \(3,3\)-(Butane-1,4-diyl)bis(1,2-dimethyl-1H-imidazole-3-ium) bromide ([BDBDMIm]Br) and CAN at room temperature (Scheme 1).

To check the effect of catalyst, the model reaction between 4-nitro benzyl alcohol, 1-naphthol and malononitrile in the presence of different acidic catalysts was carried out. All the reactions were carried out with catalytic amounts of catalysts. As shown in Table 1 the results gained with 0.04 mmol of [BDBDMIm]Br were to a great extent satisfactory.

Table 1 showed other interesting points that the ability and efficiency of catalyst [BMIm]Br, [BMIm]OH and [BMIm]HSO\(_4\) are somehow similar, while liquid iodide [BDBDMIm]IBr was more efficient for the synthesis of 2-amino-4H-chromenes. The ionic liquid [BDBDMIm]Br, rather than ionic liquids [BMIm]Br, [BMIm]OH, and [BMIm]HSO\(_4\), can accelerate the reaction time.

Furthering the ongoing studies to synthesize heterocyclic and pharmaceutical compounds by mild and practical protocols \(21-26\), the researchers would like to report the experimental results on the synthesis of 2-amino-4H-chromenes, using various benzyl alcohols, 1-naphthol and malononitrile in the presence of bis ionic liquid \(3,3\)-(Butane-1,4-diyl)bis(1,2-dimethyl-1H-imidazole-3-ium) bromide ([BDBDMIm]Br) and CAN at room temperature (Scheme 1).

To check the effect of catalyst, the model reaction between 4-nitro benzyl alcohol, 1-naphthol and malononitrile in the presence of different acidic catalysts was carried out. All the reactions were carried out with catalytic amounts of catalysts. As shown in Table 1 the results gained with 0.04 mmol of [BDBDMIm]Br (Table 1; Entry 11) were to a great extent satisfactory.

![Scheme 1. Synthesis of 2-amino-4H-chromenes using [BDBDMIm]Br-CAN](image.png)
Scheme 2. A possible mechanism for the synthesis of 2-amino-4H-chromenes.

Table 2. Synthesis of 2-amino-4H-chromenes and comparison of efficiency [BDBDMIm]Br.

<table>
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<td>97</td>
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<tr>
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</table>

*All products were characterized by their physical constant, IR, NMR and Elemental analyses. *Yields based upon starting aldehyde.

Benzaldehyde and other aromatic aldehydes containing electron withdrawing groups (such as nitro, halide) or electron releasing groups (such as hydroxyl, alkoxyl group) were employed and reacted well to give the corresponding 2-amino-4H-chromenes in the yields ranging from 82 to 95% (Table 1).

5. ACKNOWLEDGEMENT

Financial support by Rasht Branch, Islamic Azad University is gratefully acknowledged.

6. CONCLUSIONS

Finally, we developed an efficient, green, fast and convenient procedure for the multicomponent synthesis of 2-amino-4H-chromenes through a tandem reaction; First, benzyl alcohols converted to benzaldehydes using a novel oxidant system [BDBDMIm]Br-CAN then, a cyclocondensation reaction of 1-naphthol, aldehydes and malononitrile was carried out. The remarkable advantages offered by this method are that catalyst is inexpensive, non-toxic, easy to handle and reusable. Other most noticeable pluses can be simple work-up procedure, short reaction time, high yields of product with better purity and green aspect by avoiding toxic catalyst and hazardous solvent. To the best of our knowledge, this is the first report on synthesis of 2-amino-4H-chromene derivatives using 3,3-(butane-1,4-diyl)bis (1,2-dimethyl-1H-imidazole-3-ium) bromide-CAN.

REFERENCES