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Facile and convenient synthesis of 2-amino-5,10-dioxo-4-aryl-5,10-dihydro-4*H*-benzo[g]chromene-3-carbonitrile derivatives by electrocatalytically chemical transformation

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Abstract

2-Amino-5,10-dioxo-4-aryl-5,10-dihydro-4*H*-benzo[g]chromene-3-carbonitrile derivatives are obtained in excellent yields with a simple and efficient procedure. This reaction can occur using electrocatalytic multicomponent chain transformation of aryl aldehydes, 2-hydroxynaphthalene-1,4-dione and malononitrile under neutral and mild conditions. Moreover, electrolysis is done in CH_3CN as solvent, Tetrabutylammonium fluoride (TBAF) as an effective supporting electrolyte and an iron electrode as the cathode and a graphite electrode as the anode in undivided cell. Also Excellent conversions of the starting materials were obtained under 10 mA/cm^2 current densities after 0.54 F/mol of electricity had been passed and I=50 mA at room temperature. The key advantages of this method are the high yields, simple work-up and the non-chromatographic purification of products.

Keywords: 2-Amino-4*H*-chromene; multicomponent; electrosynthesis; 2-hydroxynaphthalene-1,4-dione.

Introduction

Today, the multicomponent chemical reactions (MCRs) like domino reactions are valuable and interesting methods that have high importance in synthesis of various and relatively large organic structures. Obtained compounds have been synthesized through MCRs which have now been found as having various applications as functional chromophores [1], pharmaceutically active compounds [2-5] and marine alkaloids and derivatives [6].

The MCRs provide easy and rapid access to form a large library of various active macromolecules with different and multiple substitution patterns while a number of synthetic steps can reduce. These convenient properties make the MCRs as appropriates candidate in green chemistry reactions category [7-8].

However, in many of these transformations, the use of hazardous and polluting solvents and catalysts cause ignoring the mentioned benefits.

4*H*-Benzo[g]chromene-5,10-dione derivatives show a variety of biological activities, including anti-inflammatory [9], anticancer [10-11], pesticide activities [12], antimalarial [13-15] and

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antibacterial and anti-anaphylactic activities [16].

For synthesis of these important compounds, many methods with different conditions have been reported [17-19]. However, some of these protocols require long reaction times, multi-step reactions and complex synthetic pathways and afford products with only modest yields. So, it is necessary to introduce milder, faster and generally more green approaches accompanied with higher yields to the preparation of 4*H*-Benzo[g]chromene-5,10-dione derivatives.

The electro synthetically multicomponent reactions (EMCRs) can be defined as modified MCRs while previous disadvantages are not seen. In the EMCRs, the electron transfer between an electrode and the substrate molecules was occured and followed by the formation of highly reactive intermediates which are achieved under mild conditions.

Therefore and according to the above-mentioned notes, It seems that EMCRs can be regarded as an appropriate technique in the synthesis of these organic compounds.

According to our previous studies [20-22], we evaluated synthesis of 2-amino-5,10-dioxo-4-aryl-5,10-dihydro-4*H*benzo[g]chromene-3-carbonitrile derivatives with EMCR method without the addition of base or any additive catalyst *via* the direct addition of only simple and available substrates such as various aromatic aldehydes, malononitrile and 2-hydroxynaphthalene-1,4-dione.

The structural evaluation studies of compounds were performed with various experimental techniques such as ^{1}H and ^{13}C NMR spectroscopies. Notably, in examining their synthetic performance, it has been shown that this method is capable of promoting organic synthesis of 2-amino-5,10-dioxo-4-aryl-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile derivatives in an environmentally friendly condition.

Experimental

All reagents were obtained from Merck and Aldrich and used without additional purification. All melting points were measured with an Electrothermal 9100 apparatus. The NMR spectra were recorded on a Bruker Avance DPX 400 and 300 MHz instrument with DMSO as solvent. Chemical shifts were recorded as δ values in parts per million (ppm). TLC was performed on silica-gel Poly Gram SIL G/UV 254 plates. Electrolysis were performed using a coulometry BHP2050 potentiostat/galvanostat.

Typical experimental procedure for electrocatalytic synthesis of 2-amino-5,10-dioxo-4-aryl-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile

A mixture of aryl aldehyde (2 mmol), malononitrile (3 mmol), 2-hydroxynaphthalene-1,4-dione (2 mmol), and tetrabutylammonium bromide (TBAB) (0.161g, 0.5 mmol) in acetonitrile (20 mL) was electrolyzed in an undivided cell equipped with a magnetic stirrer, a graphite anode, and an iron cathode at 25 °C under a constant current density of 10 mA/cm^2 [electrodes square 5 cm^2] until the catalytic quantity of 0.54 F/mol of electricity was passed. After the electrolysis was finished, the precipitated products were separated by filtration which was then twice rinsed with an ice-cold ethanol/water solution (1:1, 5 mL), and dried under reduced pressure.

Analytical data for selected compounds (Table 2)

2-Amino-4-(2,4-dichlorophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (4e, Entry 5)

m.p: 292-294^{o}C, ^{1}H NMR (300 MHz, DMSO-d_6): δ = 4.6 (1H, s, CH), 7.30-7.33 (3H, m, 1H, ArH and 2H, NH_2), 7.82-7.84 (3H, m, ArH), 8.04-8.07 (1H, s, ArH) ppm.

2-Amino-4-(2-nitrophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (4o,Entry 15)

m.p: 234-236^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.40 (1H, s, CH), 7.46-7.60(3H, m, 1H, ArH and 2H, NH_2), 7.80-7.82 (3H, m, ArH), 7.83-7.95 (1H, m, ArH), 8.02-8.07 (1H, m, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 31.5, 56.1, 119.2, 121.6, 124.5, 126.3, 126.6, 128.9, 131.1, 131.2, 131.8, 134.3, 138.8, 135.0, 149.0, 149.5, 159.4, 177.2, 183.1 ppm.

2-Amino-4-(2,6-dichlorophenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (4q, Entry 17)

m.p: 276-278 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.65 (1H, s, CH), 7.29-7.39 (2H, m, ArH), 7.52 (2H, s, NH_2), 7.56 (1H, d, ArH), 7.84-7.89 (3H, m, ArH), 8.05-8.07 (1H, m, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 33.9, 53.2, 119.0, 120.5, 126.4, 126.6, 129.2, 130.6, 130.5, 130.7, 131.1, 134.8, 135.0, 135.3, 136.0, 136.1, 150.2, 159.6, 177.1, 182.8 ppm.

2-Amino-4-(2,4-dimethoxyphenyl)-5,10-dioxo-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile (4r, Entry 18)

m.p: 249-251 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.72 (3H, s, OMe), 3.77 (3H, s, OMe), 4.83 (1H, s, CH), 6.43 (1H, d, ArH), 6.55 (1H, s, ArH), 7.10 (1H, d, ArH), 7.17 (2H, s, NH_2), 7.82-7.88 (3H, m, ArH), 8.044-8.065 (1H, s, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 31.2, 55.6, 56.2, 57.1, 99.2, 105.5, 120.0, 122.4, 124.1, 126.2, 126.5, 130.3, 130.9, 131.5, 134.5, 135.0, 149.8, 158.2, 159.2, 160.1, 177.5, 183.0 ppm.

Results and discussion

Our investigations on the electrocatalytic multicomponent chain transformation of aryl aldehydes, 2-hydroxynaphthalene-1,4-dione and malononitrile into 2-amino-5,10-dioxo-4- aryl-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile derivatives under neutral and mild conditions by electrolysis in an undivided cell began with the optimization of the reaction conditions. The synthetic pathway is shown in scheme 1.

Table 1 lists the representative data obtained for the synthesis of 2-amino-5,10-dioxo-4-phenyl-5,10-dihydro-4*H*-benzo[g]chromene-3-carbonitrile **4a** from benzaldehyde, malononitrile and 2-hydroxynaphthalene-1,4-dione, and under various experimental conditions.

Initially, we evaluated the synthesis of compound **4a** as a model reaction in CH_3CN, in an undivided cell containing an iron electrode as the cathode and a geraphite electrode as the anode at various constant current in the presence of electrolyte of NaBr at room temperature (Table1, Entries 1-4). It could be seen that Excellent conversions of the starting materials were obtained under 10 mA/cm^2 current densities after 0.54 F/mol of electricity which had been passed and I=50 mA.

An increase in the current density up to 15 mA/cm^2 (I=75 mA) resulted in a slight decrease in the reaction yield,

and it may also be a result of the activation of the undesired direct electrochemical processes that lead to oligomerization of the starting material (Table 1, Entry 5).

On the other hand, the use of other solvents such as EtOH, MeOH, *n*-PrOH afforded lower yield of the desired product **4a** under similar conditions (Entries 6-8).

Then, we examined the effect of various electrolytes and found that when the electrolysis was supported by TBAF as the electrolyte; the yield of **4a** was satisfactory (Entry 9-11).

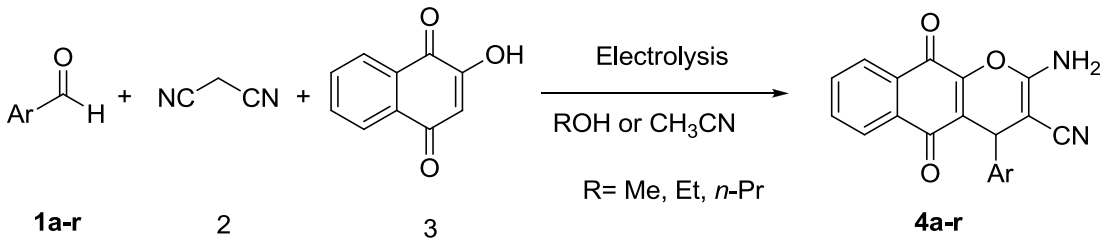
Finally, excellent conversions of the starting materials were obtained under 10 mA/cm^2 current densities after 0.54 F/mol of electricity which had been passed and I=50 mA, electrodes surface (5cm^2) was found to be optimal for the electrochemically induced chain process and allowed for the highest yield of **4a** in solvent of CH_3CN and electrolyte of tetrabutyl ammonium fluoride.

Using the optimized conditions, we also probed the scope and generality of the reaction of several aryl aldehydes with malononitrile and 2-hydroxynaphthalene-1,4-dione for synthesis of 2-amino-5,10-dioxo-4-aryl-5,10-dihydro-4*H*-benzo[g]chromene-3-carbonitrile derivatives (Table 2, **4a-r**).

As shown in Table 2, products were obtained in excellent yields.

The proposed mechanism for the preparation of related products is depicted in scheme 2. As the initiation step of the catalytic cycle, deprotonation of a CH_3CN molecule at the cathode leads to formation of cyanomethyl anion [23].

Benzylidenemalononitrile (4), is formed quantitatively by Knoevenagel addition of malononitrile to the benzaldehyde. Then, the 2-benzylidenemalononitrile has been attacked by the 2-hydroxynaphthalene-1,4-dione (3) in the presence of cyanomethyl anion, which leads to the intermediate (5). Tautomerization and cyclization (5) gave the intermediate (6). The subsequent tautomerization produced the desired product.

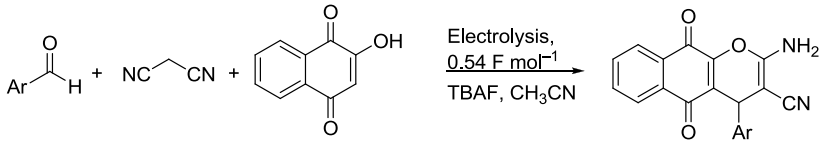


Scheme 1.

Table 1. Optimization of reaction conditions for synthesis of 2-amino-5,10-dioxo-4-phenyl-5,10-dihydro-4*H*-benzo[g]chromene-3-carbonitrile at room temperature

Entry	electrolyte	I (mA)	Current Density (mA/ cm^2)	Time (h)	Solvent	Electricity passed (F mol^{-1})	Yield (%)
1	NaBr	5	1	5	CH_3CN	0.92	20
2	NaBr	10	2	3	CH_3CN	0.85	35
3	NaBr	20	4	2	CH_3CN	0.85	45
4	NaBr	50	10	1	CH_3CN	0.54	90
5	NaBr	75	15	1	CH_3CN	0.92	70
6	NaBr	50	10	1	EtOH	0.74	40
7	NaBr	50	10	1	MeOH	0.74	41
8	NaBr	50	10	1	*n*-PrOH	0.82	20
9	KBr	50	10	1	CH_3CN	0.54	50
10	KI	50	10	1	CH_3CN	0.54	65
11	TBAF	50	10	1	CH_3CN	0.54	95
12	TBAF	50	10	1	EtOH	0.74	60

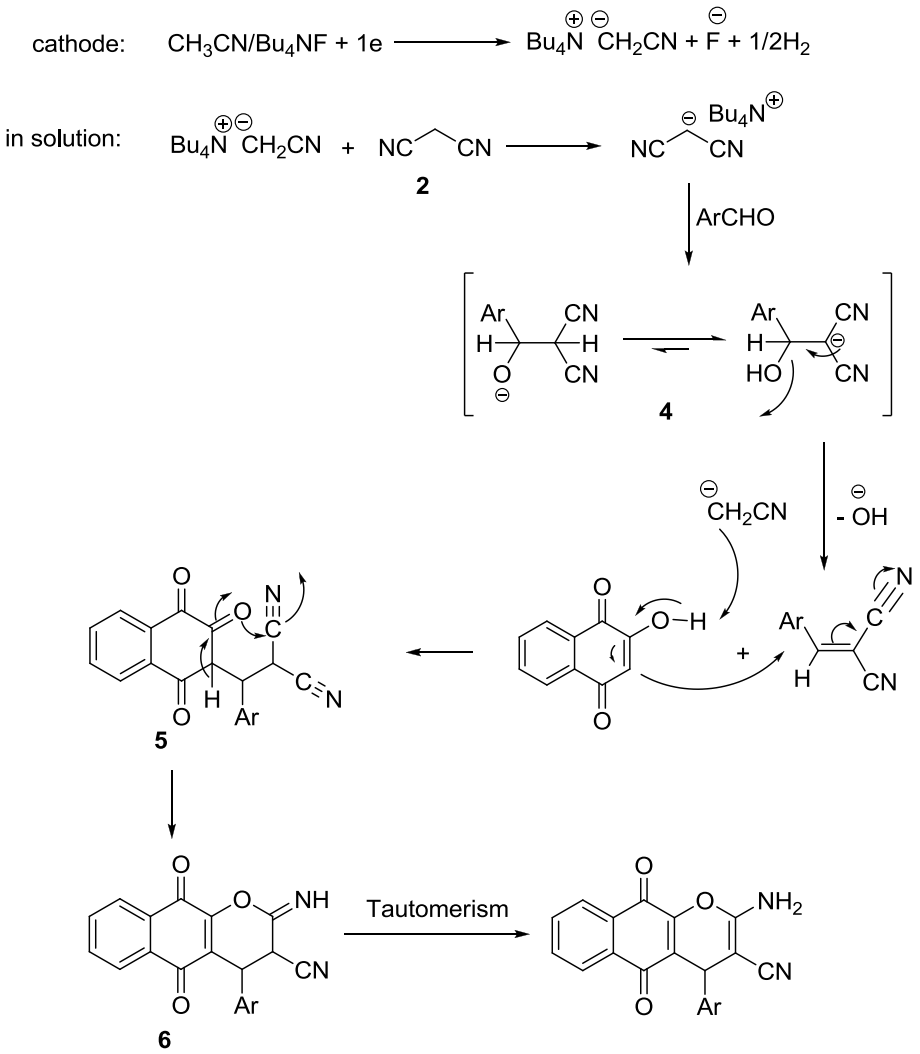
Table 2. Electrocatalytic multicomponent synthesis of 2-amino-5,10-dioxo-4-aryl-5,10-dihydro-4*H*-benzo[g]chromene-3-carbonitrile derivatives under optimized conditions



1a-r 2 3 4a-r

Entry	Aldehyde	Product	Yield (%)	M.p (ºC)	Ref
1	Ph	4a	90	259-260	260-262[24]
2	4-$NO_2C_6H_4$	4b	91	233-236	234-235[25]
3	3-$NO_2C_6H_4$	4c	93	244-245	248-250[26]
4	4-ClC_6H_4	4d	90	270-272	278-280[24]
5	2,4-$Cl_2C_6H_3$	4e	91	292-294	293-295[23]
6	3-BrC_6H_4	4f	93	256-258	258-259[25]
7	2 -ClC_6H_4	4g	90	239-241	236-239[25]
8	4-OHC_6H_4	4h	90	254-256	254-256[25]
9	4-FC_6H_4	4i	91	284-286	286-288[25]
10	4-$OCH_3C_6H_4$	4j	90	245-247	248 [26]
11	2,3,4-$(OCH_3)_3C_6H_2$	4k	93	287-289	291-292[26]
12	3,4-$(OCH_3)_2C_6H_3$	4l	91	270-271	272-273[26]
13	3-$OCH_3C_6H_4$	4m	90	243-245	242-244[26]
14	4-BrC_6H_4	4n		251-253	252-253[26]
15	2-$NO_2C_6H_4$	4o	90	234-236	232-234[25]
16	4-$CH_3C_6H_4$	4p	90	242-244	241-243[25]
17	2,6-$Cl_2C_6H_3$	4q	91	276-278	278-280[25]
18	2,4-$(OCH_3)_2C_6H_3$	4r	90	249-251	248-250[25]

[a]General procedure: Aldehyde (2 mmol), malononitrile (3 mmol), 2-hydroxynaphthalene-1,4-dione (2 mmol), and tetrabutylammonium fluoride (0.5 mmol), Acetonitrile (20 mL), iron cathode (5 cm^2), and graphite anode (5 cm^2)
[b]Isolated Yield



Scheme 2. Proposed mechanism for preparation 2-amino-5,10-dioxo-4-aryl-5,10-dihydro-4*H*-benzo[g]chromene-3-carbonitrile derivatives

Conclusion

In conclusion, we have described the synthesis of 2-amino-5,10-dioxo-4-aryl-5,10-dihydro-4H-benzo[g]chromene-3-carbonitrile derivatives in excellent yields by a simple and efficient procedure under neutral and mild conditions in the presence of tetrabutylammonium fluoride as an electrolyte. The key advantages of this method are the high yields, simple work up the non-chromatographic purification of products.

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References

[1] A.M. Asiri, S.A. Khan, SH. Al-Thaqafya, *J. Fluoresc.*, **2015**, *25*, 1203-1213.
[2] S. Bhagat, A.K. Chakraborti., *J. Org. Chem.*, **2007**, *72*, 1263-1270.
[3] M. Baumann, I. R. Baxendale, *Beilstein J. Org. Chem.*, **2016**, *11*, 1194–1219.
[4] A. Domling,W. Wang, K. Wang, *Chem. Rev.*, **2012**, *112*, 3083–3135.
[5] M.N. Elinson, V.M. Merkulova, A.I. Ilovaiskya, F. Barba, B. Batanero, *Electrochem. Acta.*, **2011**, *56*, 8219–8223.

[6] L.V. Frolova, I.V. Magedov, A.E. Romero, M. Karki, I. Otero, K. Hayden, N.M. Evdokimov, L.M.Y. Banuls, Sh.K. Rastogi, W.R. Smith, Sh.–L. Lu, R. Kiss, Ch. B. Shuster, E. Hamel, T. Betancourt, S. Rogelj, A. Kornienko, *Journal of medicinal chemistry.*,**2013**, *56*, 6886-6900.
[7] M.N. Elinson, A.S. Dorofeev, S.K. Feducovich, R.F. Nasybullin, S.V. Gorbunov, G.I. Nikishin, *Electrochem. Commun*., **2006**, *8*, **1567**-1571.
[8] M.N. Elinson, A. S. Dorofeev, R.F. Nasybullin, G. I. Nikishin, Synthesis, **2008**; 1933-1937
[9] D.O. Moon, Y.H. Choi, N.D. Kim, Y.M. Park, G.Y. Kim., *International Immunopharmacology.*, **2007**, *7*, 506-514.
[10] M. Ough, A. Lewis, E.A. Bey, J. Gao, J.M. Ritchie,W. Bornmann, D.A. Boothman, L.W. Oberley, J.J. Cullen, Cancer Biology and Therapy., **2005**, *4*, 102- 109.
[11] J. Tiwari, M. Saquib, S. Singh, F. Tufail, M. Singh, J. Singh, J. Singh, *Green Chemistry.*, **2016**, *18*, 3221–3231.
[12] A.M. Shestopalov, Y.M. Emelianova, V.N. Nesterov, Russian Chemical Bulletin., **2003**, *52*, 1164-1171.
[13] V.F. De Andrade-Neto, M.O.F. Goulart, J.F. Da Silva Filho, M.J. Da Silva, M.D.C.F.R. Pinto, A.V. Pinto, M.G. Zalis, L.H. Carvalho, A.U. Krettli, *Bioorganic and Medicinal Chemistry Letters.*, **2004**, *14*, 1145-1149.
[14] P.S. Elisa, E.B. Ana, A.G. Ravelo, D.J. Yapu, A.G. Turba, *Chemistry and Biodiversity.*, **2005**, *2*, 264-274.
[15] P. Sagar Vijay Kumar, L. Suresh, T. Vinodkumar, B. M. Reddy, G.V.P. Chandramouli, *ACS Sustainable Chem. Eng*., **2016**, 4, 2376-2386.
[16] S. D. Dindulkar, D. Jeong, E. Cho, D. Kimb, S. Jung, *Green Chemistry*., DOI: 10.1039/c6gc00137h.
[17] A. Shaabani, R. Ghadari, S. Ghasemi, M. Pedarpour, A.H. Rezayan, A. Sarvary, S.W. Ng, *Journal of Combinatorial Chemistry*., **2009**, *11*, 956–959.
[18] X.-H. Wang, X.-H. Zhang, S.-J. Tu, F. Shi, X. Zou, S. Yan, Z.-G. Han, W.-J. Hao, X.-D. Cao, S.-S. Wua, *Journal of Heterocyclic Chemistry*., **2009,** *46*, 832–836.
[19] Y. Yu, H. Guo, X. Li, *Journal of Heterocyclic Chemistry.*, **2011**, *48*, 1264–1268.
[20] Z. Vafajoo, H. Veisi, M. T. Maghsoodlou, H. Ahmadian; *Journal of Comptes Rendus Chimie.*, **2014**, *17*, 301-304.
[21] H. Veisi, Z. Vafajoo, B. Maleki, M. Taher Maghsoodlou, *Sulfur, and Silicon and the Related Elements.*, **2013**, *188*, 672-677.
[22] Z. Vafajoo, , N. Hazeri , M. T. Maghsoodlou, H. Veisi, *Journal of Chinese Chemical Letters*., **2015**, *26*, 973–976.
[23] R. Kazemi-Rad, J. Azizian, H. Kefayati, *Tetrahedron Letters.*, **2014**, *55* 6887–6890.
[24] Changsheng, Y. Chenxia, LI. Tuanjie, T. Shujiang, *Chinese Journal of Chemistry*., **2009**, *27*, 1989–1994.
[25] H.R. Shaterian, M. Kangani, *Scientia Iranica.*, **2013**, *20*, 571–579.
[26] H.R. Shaterian, M. Mohammadnia, *Journal of Molecular Liquids*, 2013, *177*, 353–360.