

A green, efficient and one-pot synthesis of 4-(aryl)-3,4-dihydro-benzochromene-2,5,10-triones

Maryam Razavi-Heidari and Alireza Hassanabadi*

Department of Chemistry, Zahedan Branch, Islamic Azad University, Zahedan, Iran

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Abstract: We reported a green and efficient method for the synthesis of 4-(aryl)-3,4-dihydro-benzochromene-2,5,10-triones from the condensation of 2-hydroxy-1,4-naphthoquinone, Meldrum's acid and aryl aldehydes in the presence of catalytic amounts of piperidine under reflux. The structures of compounds were deduced from elemental analysis and their IR, ¹H NMR, ¹³C NMR spectra. This new protocol offers advantages such as simply available starting materials, short reaction time, easy and clean work-up, and use of an inexpensive and non-toxic catalyst, high yields of biological active products and does not involve any hazardous solvent. Therefore, this procedure could be classified as green chemistry.

Keywords: 2-Hydroxy-1,4-naphthoquinone, Meldrum's acid, Piperidine, Aryl aldehydes, 3,4-Dihydro-benzochromene-2,5,10-triones.

Introduction

Chromenes often appears as an important component in both biologically active and natural compounds. Benzopyran fragment is widely performed in natural alkaloids, flavonoids, tocopherols and anthocyanins [1,2]. Multicomponent reactions (MCRs), by virtue of their convergence, productivity, facile execution, and generally high yields, have attracted much attention in the area of combinatorial chemistry[3-5]. Many important heterocyclic syntheses are MCRs. A number of methods have been reported for the synthesis of chromenes which involve the condensation of phenolic compounds with dicarbonyl compounds such as β-ketoester[6-8], malonic acid[9], malonic ester[9] and malonyl chloride[9,10].

Also have been reported another many studies on the synthesis of the heterocyclic chromene ring structure[11,12]. It is well-known that the Meldrum's acid can react with aromatic and heteroaromatic aldehydes to produce corresponding arylidene derivatives[13]. arylidene Meldrum's acids are important intermediates in the synthesis of other heterocyclic compounds with new and extensive structures[14]. Here we wish to report that the three-component reaction between 2-hydroxy-1,4-naphthoquinone, Meldrum's acid and aryl aldehydes in the presence of piperidine as catalyst.

Result and Discussion

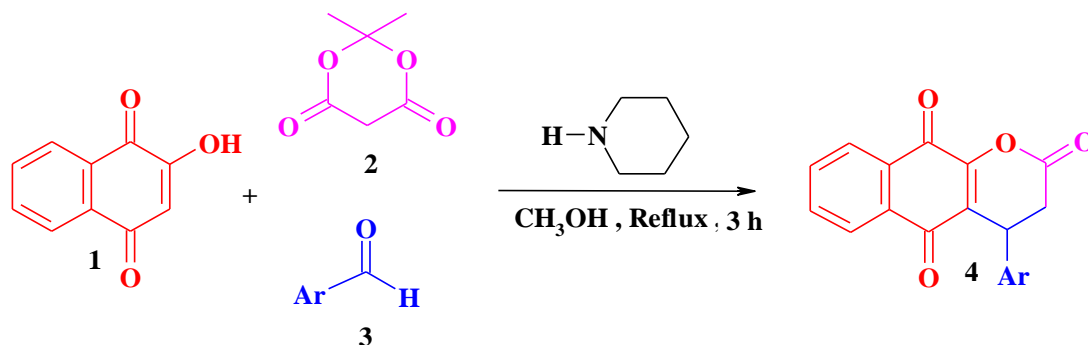
Reaction between 2-hydroxy-1,4-naphthoquinone **1**, Meldrum's acid **2** and aryl aldehydes **3** in the presence of piperidine affords 4-(aryl)-3,4-dihydro-

*Corresponding author: Tel: 0098-8633677201-9; Fax: 0098-8633677203, E-mail: ar_hasanabadi@yahoo.com

benzochromene-2,5,10-triones **4** in excellent yields. (Scheme 1 and Table 1).

To find out the optimum quantity of piperidine, the reaction of Meldrum's acid and 4-nitro benzaldehyde

with 2-hydroxy-1,4-naphthoquinone was carried out under reflux using different quantities of piperidine (Table 2). piperidine of 5% gave excellent yield in 1 h (Table 2, entry 5).



Scheme 1: Synthesis of 4-(aryl)-3,4-dihydro-benzochromene-2,5,10-triones

Table 1: Yields of a series of 4-(aryl)-3,4-dihydro-benzochromene-2,5,10-triones (**4**) (Scheme 1)

Entry	Ar	Product	Yield% ^a
1	4-ClC ₆ H ₄	4a	86
2	4-BrC ₆ H ₄	4b	84
3	4-NO ₂ C ₆ H ₄	4c	90
4	4-CH ₃ OC ₆ H ₄	4d	80

^a Yields refer to the pure isolated products.

Table 2: Optimisation amount of piperidine on the reaction

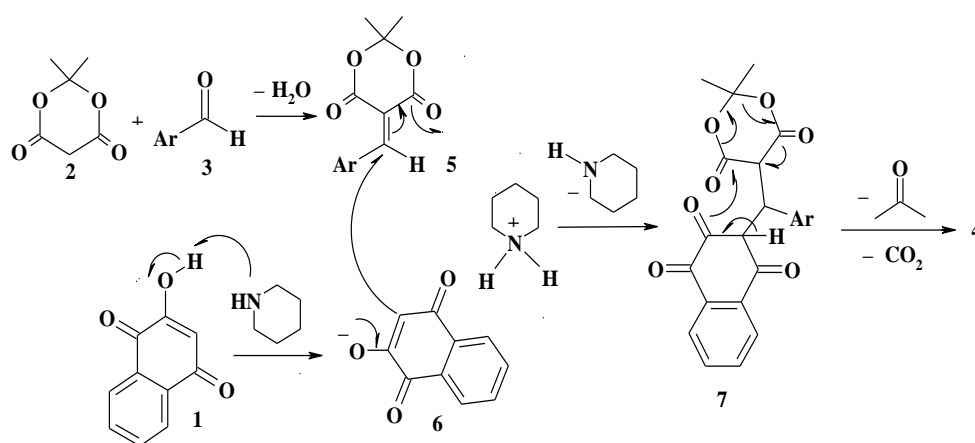
Entry	Catalyst/mol%	Time/h	Yield/% ^a
1	0	5	10
2	2	4	50
3	3	3	55
4	4	3	70
5	5	3	90
6	5	2	80
7	6	3	91
8	7	3	91

^aIsolated yield.

The structures of compounds **4a-d** were deduced from elemental analysis and their IR, ^1H NMR, ^{13}C NMR spectra. The mass spectra of compounds **4a-d** are fairly similar and display molecular ion peaks. For example, the mass spectrum of compound **4c** showing a molecular ion peak at m/z 349 confirmed that compound **4c** is a condensation product of 4-nitrobenzaldehyde and Meldrum's acid with 2-hydroxy-1,4-naphthoquinone. The ^1H NMR spectrum of compound **4c** displayed as multiples at $\delta = 7.20\text{--}8.29$ ppm for the aromatic protons. The ^{13}C NMR spectrum of compound **4c** shows 17 distinct signals consistent

with the proposed structure. The IR spectrum of compound **4c** also supported the suggested structure.

Although we didn't study the mechanism of the reaction, but a reasonable possibility is presented in Scheme 2. As can be seen from this Scheme, firstly, Knoevenagel condensation between Meldrum's acid and aldehyde will occur and arylidene Meldrum's acid **5** is formed. From Michael type nucleophilic attack of intermediate **6** (that was obtained from the reaction of 2-hydroxy-1,4-naphthoquinone with piperidine) to arylidene Meldrum's acid **5**, intermediate **7** was obtained.



Scheme 2: Suggested mechanism for formation of compound **4**.

Conclusions

In conclusion, here we reported a green and efficient method for the synthesis of 4-(aryl)-3,4-dihydrobenzochromene-2,5,10-trione from the condensation of 2-hydroxy-1,4-naphthoquinone, Meldrum's acid and aryl aldehydes in the presence of catalytic amounts of piperidine under reflux. This new protocol offers advantages such as simply available starting materials, short reaction time, easy and clean work-up, and use of an inexpensive and non-toxic catalyst, high yields of biological active products and does not involve any hazardous solvent. Therefore, this procedure could be classified as green chemistry.

Experimental

Elemental analysis was performed using a Heraeus CHN-O-Rapid analyser. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra of selected compounds were recorded on a Shimadzu IR-470 spectrometer in KBr discs. ^1H and ^{13}C NMR spectra were obtained on a Bruker DRX-300 Avance spectrometer in DMSO-d_6 using TMS as internal standard. The chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and were used without further purification.

General procedure for preparation of compounds 4a-d:

To a stirred solution of the Meldrum's acid (0.144 g, 1 mmol) and aryl aldehyde (1 mmol) in 10 mL methanol, in the presence of basic catalytic amount of piperidine (3 drops), the 2-hydroxy-1,4-naphthoquinone (1 mmol) under reflux condition was added. The progress of the reaction was monitored by TLC. After completion of the reaction (3h), the viscose oil brown was collected and washed with 20 ml of water to afford the pure title compounds.

4-(4-Chlorophenyl)-3,4-dihydro-benzo[g]chromene-2,5,10-trione (4a):

Brown oil; TLC (hexane/EtOAc, 3:1, R_f =0.60); IR (KBr) (ν_{\max} cm^{-1}): 1713 and 1645 (C=O); ^1H NMR (300 MHz, DMSO): δ 2.96 (1H, d, J 16 Hz, CH), 3.36 (1H, dd, $^2J_{\text{HH}}$ 16.0 Hz, $^3J_{\text{HH}}$ 7.2 Hz, CH), 4.94 (1H, d, $^3J_{\text{HH}}$ 6.0 Hz, CH), 7.15-7.91 (8H, m, aromatic) ppm.; ^{13}C NMR (75 MHz, DMSO): δ 25.68 (CH), 44.13 (CH₂), 111.64, 121.25, 125.04, 125.65, 127.24, 127.51, 129.60, 130.98, 131.64, 133.95, 145.93, 169.25, 170.59, 180.00 and 187.25 ppm.; EIMS: 338 (M^+ , 10); Analyses: Calcd. for C₁₉H₁₁ClO₄: C, 67.37; H, 3.27%. Found: C, 67.51; H, 3.35.

4-(4-Bromophenyl)-3,4-dihydro-benzo[g]chromene-2,5,10-trione (4b):

Brown oil; TLC (hexane/EtOAc, 3:1, R_f =0.54); IR (KBr) (ν_{\max} cm^{-1}): 1719, 1646 (C=O); ^1H NMR (300 MHz, DMSO): δ 2.97 (1H, d, J 16 Hz, CH), 3.42 (1H, dd, $^2J_{\text{HH}}$ 16.0 Hz, $^3J_{\text{HH}}$ 7.2 Hz, CH), 4.92 (1H, d, $^3J_{\text{HH}}$ 6.0 Hz, CH), 7.14-7.98 (8H, m, aromatic) ppm.; ^{13}C NMR (75 MHz, DMSO): δ 26.51 (CH), 44.23 (CH₂), 107.10, 121.18, 125.04, 125.76, 130.10, 130.41, 130.69, 131.63, 132.01, 135.74, 146.37, 169.58, 170.56, 180.07 and 185.44 ppm.; EIMS: 383 (M^+ , 4); Analyses: Calcd. for C₁₉H₁₁BrO₄: C, 59.55; H, 2.89%. Found: C, 59.64; H, 3.00.

4-(4-nitrophenyl)-3,4-dihydro-benzo[g]chromene-2,5,10-trione (4c):

Brown oil; TLC (hexane/EtOAc, 3:1, R_f =0.58); IR (KBr) (ν_{\max} cm^{-1}): 1729 and 1644 (C=O); ^1H NMR (300 MHz, DMSO): δ 2.84 (1H, d, J 16 Hz, CH), 3.31 (1H, dd, $^2J_{\text{HH}}$ 16.0 Hz, $^3J_{\text{HH}}$ 7.2 Hz, CH), 4.72 (1H, d, $^3J_{\text{HH}}$ 6.0 Hz, CH), 7.20-8.29 (8H, m, aromatic) ppm.; ^{13}C NMR (75 MHz, DMSO): δ 25.77 (CH), 44.01 (CH₂), 100.03, 123.00, 124.20, 125.50, 128.38, 128.80, 129.27, 130.67, 131.53, 148.02, 161.07, 167.37, 173.44, 180.41 and 187.03 ppm.; EIMS: 349 (M^+ , 8); Analyses: Calcd. for C₁₉H₁₁NO₆: C, 65.33; H, 3.17; N, 4.01%. Found: C, 65.45; H, 3.26; N, 4.15.

4-(4-Methoxyphenyl)-3,4-dihydro-benzo[g]chromene-2,5,10-trione (4d):

Brown oil; TLC (hexane/EtOAc, 3:1, R_f =0.59); IR (KBr) (ν_{\max} cm^{-1}): 1723 and 1634 (C=O); ^1H NMR (300 MHz, DMSO): δ 2.96 (1H, d, J 16 Hz, CH), 3.40 (1H, dd, $^2J_{\text{HH}}$ 16.0 Hz, $^3J_{\text{HH}}$ 7.2 Hz, CH), 3.78 (3H, s, OCH₃), 5.33 (1H, d, $^3J_{\text{HH}}$ 6.0 Hz, CH), 7.07-7.96 (8H, m, aromatic) ppm.; ^{13}C NMR (75 MHz, DMSO): δ 26.52 (CH), 44.15 (CH₂), 55.32 (OCH₃), 113.09, 121.73, 124.92, 125.59, 128.57, 128.86, 129.36, 130.59, 131.66, 135.90, 139.03, 169.54, 170.95, 179.87 and 187.39 ppm.; EIMS: 334 (M^+ , 5); Analyses: Calcd. for C₂₀H₁₄O₅: C, 71.85; H, 4.22%. Found: C, 71.96; H, 4.31.

Acknowledgements

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