ICC
Iranian Chemical Communication
Original Research Article
Payame Noor University http://icc.journals.pnu.ac.ir

The green synthesis of pyrano[3,2-c]quinoline-2,5-dione derivatives catalyzed by acidic ionic liquid under ultrasound irradiation

Esmayeel Abbaspour-Gilandeh[a,*], Seyyedeh Cobra Azimi[b]

[a]*Young Researchers and Elites Club, Ardabil Branch, Islamic Azad University, Ardabil, Iran*

[b]*Young Researchers and Elites Club, Rasht Branch, Islamic Azad University, Rasht, Iran*

Received: 22 September 2014, Accepted: 26 November 2014, Published: 1 January 2015

Abstract

A novel and efficient method has been developed for the synthesis of pyrano[3,2-c]quinoline-2,5-dione derivatives by the convenient ultrasound-mediated condensation of 4-hydroxyquinolin-2-one with Meldrum's acid and aldehydes in the presence of a catalytic amount of [HMIm]HSO_4 as a green, efficient and reusable acidic ionic liquid medium. The stability of the ionic liquid during the reaction was high and was used for several times recycle the form. we had lower energy consumption and achieved to the desired product in the optimal time when Placing the reaction mixture under ultrasound condition. The method is simple, starts from readily accessible commercial starting materials, and provides biologically interesting products in good yields and short reaction times.

Keywords: Ultrasonic irradiation; meldrum's acid; pyrano[3,2-c]quinoline; ionic liquid.

Introduction

The introduction of functionality into the structure of ionic liquids not only changes this balance between non-coulombic interactions, including hydrogen bonding and van der Waals type interactions, but also introduces a significant opportunity for the ionic liquid to participate or even control chemistry within the liquid itself. So there is a great possibility to design and tune their properties for various applications just by a careful selection of the cation or anion or

*Corresponding author: Esmayeel Abbaspour-Gilandeh
Tel: +98 (45) 33332238, Fax: +98 (45) 33363199
E-mail: abbaspour1365@yahoo.com

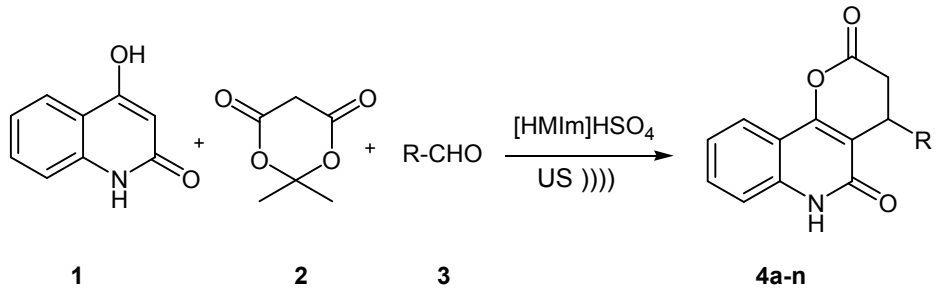
both [1], due to their attractive properties like, negligible volatility, good thermal and chemical stability, high ionic conductivity, and wide working temperature range [2]. They can replace organic solvents, reduce the chemical wastage and improve the safety of processes and products [3]. Many of the ILs are both air and moisture stable; however, this depends on the hydrophilic/hydrophobic character of the IL. The degree of the hydroscopic character of the IL and consequently the interaction between water and IL are strongly depended on anions of the IL [4]. Although ionic liquids were initially introduced as an alternative green reaction medium, today they march far beyond this border, showing their significant role in controlling the reactions as solvent or catalysts [5-10].

Pyranoquinolinones constitute the parent ring structure of pyranoquinoline alkaloids which occur in the plant family *Rutaceae*. These Pyranoquinolines have recently attracted attention of synthetic and medicinal chemists. They constitute the basic skeleton of a number of alkaloids, such as flindersine, oricine and verprisine [11-13]. Structures incorporating this moiety show marked psychotropic, antiallergenic, anti-inflammatory, antihistaminic, and estrogenic activities, and are thus of prime interest for biological applications [14-16]. In addition to this they are used as pharmaceuticals [17]. Furthermore, many of these alkaloids exhibit cancer cell growth inhibitory activity and are investigated as potential anticancer agents [18]. These structural motifs which are also useful intermediates in the manufacture of azo dyestuffs can be used for dyeing both naturally occurring and synthetic fibers [19].

In recent years, ultrasound has become a highly useful method for performing a wide range of chemical reactions and processes, including chemical synthesis, materials production and water treatment [20–22].

Ultrasonic irradiation offers an alternative energy source for organic reactions which are ordinarily accomplished by heating. The ultrasonic sonochemical phenomenon is the result of proper interactions between the acoustic waves and a potentially reacting chemical system. Ultrasound-assisted reactions can proceed with the formation, growth and collapse of acoustic bubbles in the reaction medium. Also, these factors result in in shortening the time span of reactions and increase the yield of products [23–30]. Furthermore, the implosion of the micro-bubbles the enclosed reactants may be fractured to form highly reactive intermediates which could carry on the reactions more efficiently through

shortened or selective pathways [31-34]. Since in this technique the reaction is carried out normally at lower temperature relative to the usually thermal methods, the possibility of occurrence of undesired reactions is reduced, and, as a result of a cleaner reaction, the workup is easier .In order to expand the application of ultrasound in the synthesis of heterocyclic compound, we introduce our findings achieved on development of an efficient method for synthesis of pyrano[3,2-*c*]quinoline-2,5-diones under ultrasound irradiation (Scheme 1).



Scheme 1. The synthesis of pyrano[3,2-*c*]quinoline-2,5-diones derivatives in presence $[HMIm]HSO_4$ under ultrasound irradiation

Experimental

Chemicals and Apparatus

All of the solvents and reagents were purchased from Fluka or Merck chemical companies. Melting points were measured with an Electrothermal 9100 apparatus. The FTIR spectra were recorded on a PerkinElmer 781 Spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER DRX-400 AVANCE spectrometer at 400.22 and 100.63 MHz, respectively. ^{1}H and ^{13}C NMR spectra were obtained on solutions in DMSO using TMS as internal standard. Elemental analyses for C, H and N were performed using a Foss Heraus CHN-O-rapid analyzer. BANDELIN Sonorex (with a frequency of 35 kHz and a nominal power 200 W) ultrasonic bath was used for ultrasonic irradiation. Built-in heating, 30–80 ^{o}C thermostatically adjustable. The reaction flask was located at the maximum energy area with the cleaner, and the surface of the reactants was placed slightly lower than the level of the water.

The procedure for the synthesis of the [HMIm]HSO$_4$:

In a 25 mL flask, 1-methylimidazole (1.59 mL, 20 mmol) and acetonitrile (5 mL) were stirred together in 0 ^{o}C for 1min. After that, concentrated sulfuric acid (97%, 1.03 mL)

was added drop wise to the reaction mixture in 0 ^{o}C and in the duration of 1 h. The contents of the flask were stirred at room temperature for 2 hours. After this step, the brønsted acidic ionic liquid was washed with diethylether (2×5 mL). Impurities were dissolved in the diethylether and the reaction mixture was divided into two phases. The ionic liquid was separated from the organic phase using the separatory funnel and the remaining solvent in the ionic liquid was evaporated at 80 ^{o}C. Finally, the yellow viscous ionic liquid was produced.

General procedure for preparation of 4-(4-methylphenyl)-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4a):

Conventional heating procedure

Ionic liquid ([HMIm]HSO_4, 0.5 mL) was added to a mixture of 4-hydroxyquinolin-2-one (0.161 g, 1 mmol), Meldrum's acid (0.144 g, 1 mmol) and 4-methylbenzaldehyde (0.119 g, 1 mmol). The mixture was stirred at 80 ^{o}C for 65 min. After completion of the reaction, as indicated by TLC, the ionic liquid was separated from the reaction mixture by extraction with 2 ×15 mL of water. The solid residue was recrystallized from EtOH (95.5%).

Ultrasound irradiation procedure

A mixture of 4-hydroxyquinolin-2-one (0.161 g, 1 mmol), Meldrum's acid (0.144 g, 1 mmol) and 4-methylbenzaldehyde (0.119 g, 1 mmol) was added to a vial containing a magnetic stirring bar and the ionic liquid ([HMIm]HSO_4, 0.5 mL). The mixture was sonicated in the water bath of an ultrasonic cleaner at 80 ^{o}C for 20 min. Then it was filtered to recover the catalyst and the residue was crystallized from EtOH (95.5%).

4-(4-Methylphenyl)-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4a):

White powder (0.260 g, 85%); mp 330-332 ^{o}C. IR (KBr): 3184, 3006, 2955, 2903, 1779, 1657 (C=O), 1382, 1311, 1119, 1106 cm^{-1}. ^{1}H NMR (400.22 MHz, DMSO): δ= 2.25 (s, 3H, CH_3), 2.91 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.47 (dd, 1H, *J*= 16.0 and *J*= 7.8 Hz, 3-H_A), 4.48 (d, 1H, *J*= 7.8 Hz, 4-H), 7.07 (d, 2H, *J*= 8.0 Hz, 4-Aryl), 7.12 (d, 2H, *J*= 8.0 Hz, 4-Aryl), 7.30 (t, 1H, *J*= 7.8 Hz, 9-H), 7.40 (d, 1H, *J*= 7.8 Hz, 7-H), 7.62 (t, 1H, *J*= 7.8 Hz, 8-H), 7.83 (d, 1H, *J*= 7.8 Hz, 10-H), 12.00 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 21.04 (CH_3), 34.62 (C-3), 36.84 (C-4), 112.27, 112.81, 115.93, 122.11, 122.70, 126.96, 129.92, 131.81, 136.86, 138.28, 138.68, 154.92, 161.36, 166.80. *Anal*. Calcd. for $C_{19}H_{15}NO_3$ (305.11): C, 74.74; H, 4.95; N, 4.59%. Found: C, 74.87; H, 4.83; N, 4.64%.

4-(4-Chlorophenyl)-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4b):

White powder (0.290 g, 89%); mp 333-335 ^{o}C. IR (KBr): 3195, 3005, 2912, 1789, 1659 (C=O), 1488, 1427, 1165, 1112 cm^{-1}. ^{1}H NMR (400.22 MHz, DMSO): δ= 2.96 (d, 1H, *J*= 16.0 Hz, 3-H$_B$), 3.51 (dd, 1H, *J*= 16.0 and *J*= 7.4 Hz, 3-H$_A$), 4.53 (d, 1H, *J*= 7.4 Hz, 4-H), 7.23 (d, 2H, *J*= 8.4 Hz, 4-Aryl), 7.31 (t, 1H, *J*= 7.8 Hz, 9-H), 7.39 (d, 1H, *J*= 8.4 Hz, 4-Aryl), 7.41 (d, 1H, *J*= 7.8 Hz, 7-H), 7.63 (t, 1H, *J*= 7.8 Hz, 8-H), 7.84 (d, 1H, *J*= 7.8 Hz, 10-H), 12.03 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 34.62 (C-3), 36.84 (C-4), 112.27, 112.81, 115.93, 122.11, 122.70, 126.96, 129.92, 131.81, 136.86, 138.28, 138.68, 154.92, 161.36, 166.80. *Anal*. Calcd. for $C_{18}H_{12}ClNO_3$ (325.05): C, 66.37; H, 3.71; N, 4.30%. Found: C, 66.42; H, 3.82; N, 4.23%.

4-(4-Methoxyphenyl)-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4c):

White powder (0.267 g, 83%); mp 335-337 ^{o}C. IR (KBr): 3200, 3060, 2961, 1783, 1660 (C=O), 1435, 1256, 1114, 1028, 802 cm^{-1}. ^{1}H NMR (400.22 MHz, DMSO): δ= 2.92 (d, 1H, *J*= 16.0 Hz, 3-H$_B$), 3.46 (dd, 1H, *J*= 16.0 and *J*= 7.4 Hz, 3-H$_A$), 3.71 (s, 3H, OCH$_3$), 4.47 (d, 1H, *J*= 7.4 Hz, 4-H), 6.88 (d, 2H, *J*= 8.4 Hz, 3′ and 5′-H), 7.10 (d, 1H, *J*= 8.4 Hz, 2′ and 6′-H), 7.30 (t, 1H, *J*= 7.8 Hz, 9-H), 7.40 (d, 1H, *J*= 7.8 Hz, 7-H), 7.62 (t, 1H, *J*= 7.8 Hz, 8-H), 7.83 (d, 1H, *J*= 7.8 Hz, 10-H), 12.00 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 34.19 (C-3), 36.92 (C-4), 55.53 (O<u>C</u>H$_3$), 112.47, 112.82, 114.73, 115.93, 122.09, 122.69, 128.17, 131.79, 133.11, 138.66, 154.81, 158.83, 161.37, 166.87. *Anal*. Calcd. for $C_{19}H_{15}NO_4$ (321.10): C, 71.02; H, 4.36; N, 4.65%. Found: C, 70.98; H, 4.42; N, 4.69%.

4-(4-Fluorophenyl)-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4d):

White powder (0.257 g, 83%); mp 333-335 ^{o}C. IR (KBr): 3187, 3045, 2960, 1789, 1661 (C=O), 1503, 1429, 1263, 1113, 1026, 802 cm^{-1}. ^{1}H NMR (400.22 MHz, DMSO): δ= 2.97 (d, 1H, *J*= 16.0 Hz, 3-H$_B$), 3.49 (dd, 1H, *J*= 16.0 and *J*= 7.2 Hz, 3-H$_A$), 4.55 (d, 1H, *J*= 7.2 Hz, 4-H), 7.15 (t, 2H, *J*= 8.6 Hz, 3′ and 5′-H), 7.25 (dd, 2H, J_{HH}= 8.6 and J_{HF}= 5.6 Hz, 2′ and 6′-H), 7.30 (t, 1H, *J*= 7.7 Hz, 9-H), 7.41 (d, 1H, *J*= 7.7 Hz, 7-H), 7.62 (t, 1H, *J*= 7.7 Hz, 8-H), 7.84 (d, 1H, *J*= 7.7 Hz, 10-H), 12.01 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 34.31 (C-3), 36.69 (C-4), 111.97, 112.80, 115.97, 116.12 (d, J_{CF}= 22.1 Hz),122.14, 122.68, 129.10 (d, J_{CF}= 9.0 Hz), 131.86, 137.44 (d, J_{CF}= 3.0 Hz), 138.76, 155.05, 161.33, 161.75 (d, $J_{C\text{-}F}$= 243 Hz), 166.62. *Anal*. Calcd. for $C_{18}H_{12}FNO_3$ (309.08): C, 69.90; H, 3.91; N, 4.53%. Found: C, 70.01; H, 3.95; N, 4.47%.

4-(3-Bromophenyl)-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4e):

White powder (0.323 g, 87%); mp 305-307 °C. IR (KBr): 3190, 3035, 2963, 1783 (C=O), 1658, 1430, 1263, 1113, 1028, 804 cm^{-1}. ^1H NMR (400.22 MHz, DMSO): δ= 2.99 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.51 (dd, 1H, *J*= 16.0 and *J*= 7.2 Hz, 3-H_A), 4.55 (d, 1H, *J*= 7.2 Hz, 4-H), 7.16 (d, 1H, *J*= 7.8 Hz, 4′-H); 7.29 (t, 1H, *J*= 7.8 Hz, 5′-H), 7.31 (t, 1H, *J*= 7.6 Hz, 9-H), 7.41 (d, 1H, *J*= 7.6 Hz, 7-H),. 7.46 (s, 1H, 2′-H), 7.47 (d, 1H, *J*= 7.8 Hz, 6′-H), 7.63 (t, 1H, *J*= 7.6 Hz, 8-H), 7.84 (d, 1H, *J*= 7.6 Hz, 10-H), 12.03 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 34.69 (C-3), 36.35 (C-4), 111.38, 112.76, 116.02, 122.20, 122.62, 122.74, 125.90, 130.24, 130.68, 131.61, 131.97, 138.81, 144.15, 155.26, 161.29, 166.50. *Anal*. Calcd. for $C_{18}H_{12}BrNO_3$ (369.00): C, 58.40; H, 3.27; N, 3.78%. Found: C, 58.29; H, 3.22; N, 3.86%.

4-Phenyl-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4f):

White powder (0.254 g, 87%); mp 320-322 °C. IR (KBr): 3160, 3003, 2980, 2964, 1785 (C=O), 1658, 1502, 1438, 1386, 1223, 1118, 751 cm^{-1}. ^1H NMR (400.22 MHz, DMSO): δ= 2.95 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.50 (dd, 1H, *J*= 16.0 and *J*= 7.4 Hz, 3-H_A), 4.53 (d, 1H, *J*= 7.4 Hz, 4-H), 7.20 (d, 2H, *J*= 7.0 Hz, 4-Ph); 7.24–7.35 (m, 4H, 4-Ph), 7.41 (d, 1H, *J*= 8.0 Hz, 7-H), 7.62 (t, 1H, *J*= 8.0 Hz, 8-H), 7.84 (d, 1H, *J*= 8.0 Hz, 10-H), 12.0 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 35.01 (C-3), 36.75 (C-4), 112.08, 112.81, 115.96, 122.12, 122.69, 127.08, 127.68, 129.39, 131.83, 138.73, 141.33, 155.03, 161.37, 166.71. *Anal*. Calcd. for $C_{18}H_{13}NO_3$ (291.09): C, 74.22; H, 4.50; N, 4.81%. Found: C, 74.13; H, 4.58% N, 4.76%.

4-(2,4-Dichlorophenyl)-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4g):

White powder (0.324 g, 90%); mp 335-337 °C. IR (KBr): 3158, 3016, 2960, 2904, 1784 (C=O), 1659, 1576, 1429, 1388, 1260, 1122 cm^{-1}. ^1H NMR (400.22 MHz, DMSO): δ= 2.84 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.60 (dd, 1H, *J*= 16.0 and *J*= 7.4 Hz, 3-H_A), 4.81 (d, 1H, *J*= 7.4 Hz, 4-H), 6.96 (d, 1H, *J*= 8.4 Hz, 6′-H), 7.31 (dd, 1H, *J*= 8.4 Hz and *J*= 2.0 Hz, 5′-H), 7.34 (t, 1H, *J* = 8.0 Hz, 9-H), 7.43 (d, 1H, *J*= 8.0 Hz, 7-H), 7.66 (t, 1H, *J*= 8.0 Hz, 8-H), 7.74 (d, 1H, *J*= 2.0 Hz, 3′-H), 7.87 (d, 1H, *J*= 8.0 Hz, 10-H), 12.06 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 32.60 (C-3), 34.96 (C-4), 110.10, 112.69, 116.06, 122.26, 122.79, 128.51, 129.22, 130.13, 132.15, 133.38, 134.07, 137.13, 138.99, 156.17, 161.00, 165.83. *Anal*. Calcd. for $C_{18}H_{11}Cl_2NO_3$ (359.01): C, 60.02; H, 3.08; N, 3.89%. Found: C, 60.06; H, 3.12; N, 3.83%.

4-(4-Nitrophenyl)-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4h):

White powder (0.302 g, 90%); mp 329-331°C. IR (KBr): 3416, 2987, 2350, 1789, 1718 (C=O), 1646, 1427, 1167, 1113cm^{-1}. ^{1}H NMR (400.22 MHz, DMSO): δ= 2.91 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.47 (dd, 1H, *J*= 16.0 and *J* 7.6 Hz, 3-H_A),4.48 (d, 1H, *J*= 7.2 Hz, 4-H), 7.06 (d, 2H, *J*= 8.0 Hz, 3′ and 5′-H), 7.13 (t, 1H, *J*= 8.0 Hz, 9-H), 7.30 (d, 1H, *J*= 7.2 Hz, 7-H), 7.32 (d, 1H, *J*= 7.6 Hz, 2′ and 6′-H), 7.62 (t, 1H, *J*= 8.0 Hz, 8-H), 7.83 (d, 1H, *J*= 8.0 Hz, 10-H),11.99 (s, 1H, NH),^{13}C NMR (100.63 MHz, DMSO): δ=34.69 (C-3), 36.99 (C-4), 111.37, 112.76, 116.06, 122.20, 122.58, 122.74, 125.22, 130.24, 131.38, 138.13, 144.15, 155.17, 161.00, 166.83. *Anal*. Calcd. for $C_{18}H_{12}N_2O_5$ (336.07): C, 66.37; H, 3.71; N, 8.33%. Found: C, 66.42; H, 3.82; N, 8.26%.

4-(4-Hydroxyphenyl)-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4i):

White powder (0.276 g, 92%); mp 320-322°C. IR (KBr): 3405, 2978, 2345, 1788, 1690 (C=O), 1612, 1420, 1163, 1110cm^{-1}. ^{1}H NMR (400.22 MHz, DMSO): δ= 2.98 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.50 (dd, 1H, *J*= 16.0 and *J* 6.8 Hz, 3-H_A),4.48 (d, 1H, *J*= 8.4 Hz, 4-H), 7.13 (d, 2H, *J*= 7.6 Hz, 2′ and 6′-H), 7.24 (t, 1H, *J*= 7.6 Hz, 9-H), 7.34 (d, 1H, *J*= 8.0 Hz, 7-H), 7.46 (d, 1H, *J*=7.6 Hz, 3′ and 5′-H), 7.56 (t, 1H, *J*=7.2 Hz, 8-H),7.79 (d, 1H, *J*= 7.6 Hz, 10-H),9.43 (s, 1H, OH)11.90 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ=36.28 (C-3), 36.51 (C-4), 111.76, 112.06, 113.20, 114.13, 114.81, 121.30, 121.80, 123.22, 131.08, 138.38, 140.15, 153.95, 161.58, 167.41. *Anal*. Calcd. for $C_{18}H_{13}NO_4$ (307.08): C, 69.37; H, 3.95; N, 4.23%. Found: C, 69.40; H, 3.75; N, 4.18%.

4-Ethyl-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4j):

White powder (0.195 g, 80%); mp 282-284 °C. IR (KBr): 3415, 2962, 1776, 1661 (C=O), 1402, 1261, 1098, 1026, 804 cm^{-1}. ^{1}H NMR (400.22 MHz, DMSO): δ= 0.88 (t, 3H, *J*= 7.2 Hz, CH_3), 1.41–1.48 (m, 1H, 1′-H_B), 1.55-1.60 (m, 1H, 1′-H_A), 2.82 (d, 1H, *J*= 14.8 Hz, 3-H_B), 3.10-3.17 (m, 2H, 3-H_A and 4-H), 7.26 (t, 1H, *J*= 8.0 Hz, 9-H), 7.37 (d, 1H, *J*= 8.0 Hz, 7-H), 7.58 (t, 1H, *J*= 8.0 Hz, 8-H), 7.75 (d, 1H, *J*= 8.0 Hz, 10-H), 11.93 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 11.01 (CH_3), 26.49 (C-1′), 30.85 (C-3, C-4), 32.86, 112.88, 113.29, 115.82, 121.85, 122.56, 131.49, 138.39, 154.04, 161.62, 167.50. *Anal*. Calcd. for $C_{14}H_{13}NO_3$ (243.09): C, 69.12; H, 5.39; N, 5.76%. Found: C, 69.07; H, 5.43; N, 5.84%.

4-Propyl-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4k):

White powder (0.207 g, 80%); mp 250-252 °C. IR (KBr): 3413, 3068, 2951, 2858, 1775 (C=O), 1661, 1439, 1399, 1149 cm^{-1}. ^1H NMR (400.22 MHz, DMSO): δ= 0.87 (t, 3H, *J*= 7.2 Hz, CH_3), 1.22–1.54 (m, 4H, 1′-H, 2′-H), 2.80 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.11 (dd, 1H, *J*= 16.0 Hz and 6.9 Hz, 3-H_A), 3.22 (dt, 1H, *J*= 6.9 and 6.0 Hz, 4-H), 7.25 (t, 1H, *J*= 8.0 Hz, 9-H), 7.36 (d, 1H, *J*= 8.0 Hz, 7-H), 7.57 (t, 1H, *J*= 8.0 Hz, 8-H), 7.74 (d, 1H, *J*= 8.0 Hz, 10-H), 11.91 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 14.36 (CH_3), 19.54 (C-2′), 29.30 (C-1′), 33.27 (C-3), 35.77, 112.89, 113.72, 115.80, 121.80, 122.52, 131.43, 138.36, 153.95, 161.58, 167.47. *Anal*. Calcd. for $C_{15}H_{15}NO_3$ (257.11): C, 70.02; H, 5.88; N, 5.44%. Found: C, 69.95; H, 5.96; N, 5.49%.

4-Hexyl-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4l):

White powder (0.227 g, 76%); mp 200-202 °C. IR (KBr): 3425, 3035, 2962, 2920, 1790 (C=O), 1657, 1428, 1263, 1096, 1027, 803 cm^{-1}. ^1H NMR (400.22 MHz, DMSO): δ= 0.84 (t, 3H, *J*= 6.4 Hz, CH_3), 1.23–1.55 (m, 10H, 5CH_2), 2.80 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.10 (dd, 1H, *J*= 16.0 Hz and 7.0 Hz, 3-H_A), 3.21 (dt, 1H, *J*= 7.0 and 6.4 Hz, 4-H), 7.26 (t, 1H, *J*= 8.0 Hz, 9-H), 7.37 (d, 1H, *J*= 8.0 Hz, 7-H), 7.57 (t, 1H, *J*= 8.0 Hz, 8-H), 7.75 (d, 1H, *J*= 8.0 Hz, 10-H), 11.89 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 14.38, 22.48, 26.15, 29.11, 29.49, 31.57, 33.29, 33.53, 112.90, 113.73, 115.81, 121.81, 122.50, 131.42, 138.38, 153.94, 161.57, 167.42. *Anal*. Calcd. for $C_{18}H_{21}NO_3$ (299.15): C, 72.22; H, 7.07; N, 4.68%. Found: C, 72.16; H, 7.15; N, 4.60%.

4-Octyl-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4m):

White powder (0.242 g, 74%); mp 260-262 °C. IR (KBr): 3423, 3026, 2921, 1791 (C=O), 1662, 1391, 1139, 1042, 754 cm^{-1}. ^1H NMR (400.22 MHz, DMSO): δ= 0.84 (t, 3H, *J*= 6.8 Hz, CH_3), 1.22–1.50 (m, 14H, 7CH_2), 2.80 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.11 (dd, 1H, *J*= 16.0 Hz and 7.0 Hz, 3-H_A), 3.21 (dt, 1H, *J*= 7.0 and 6.4 Hz, 4-H), 7.26 (t, 1H, *J*= 8.0 Hz, 9-H), 7.37 (d, 1H, *J*= 8.0 Hz, 7-H), 7.58 (t, 1H, *J*= 8.0 Hz, 8-H), 7.75 (d, 1H, *J*= 8.0 Hz, 10-H), 11.90 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 14.41, 22.53, 26.13, 29.05, 29.24, 29.41, 29.47, 31.70, 33.28, 33.49, 112.90, 113.73, 115.81, 121.82, 122.55, 131.46, 138.36, 153.95, 161.58, 167.41. *Anal*. Calcd. for $C_{20}H_{25}NO_3$ (327.18): C, 73.37; H, 7.70; N, 4.28%. Found: C, 73.29; H, 7.76; N, 4.33%.

4-Nonyl-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-dione (4n):

White powder (0.251 g, 74%); mp 235-237 °C. IR (KBr): 3423, 3045, 2961, 2919, 2853,

1789 (C=O), 1660, 1401, 1262, 1096, 1027, 804 cm^{-1}. ^1H NMR (400.22 MHz, DMSO): δ= 0.84 (t, 3H, *J*= 6.8 Hz, CH_3), 1.22–1.51 (m, 16H, $8CH_2$), 2.80 (d, 1H, *J*= 16.0 Hz, 3-H_B), 3.10 (dd, 1H, *J*= 16.0 Hz and 6.8 Hz, 3-H_A), 3.21 (dt, 1H, *J*= 6.8 and 6.4 Hz, 4-H), 7.26 (t, 1H, *J*= 8.0 Hz, 9-H), 7.37 (d, 1H, *J*= 8.0 Hz, 7-H), 7.57 (t, 1H, *J*= 8.0 Hz, 8-H), 7.75 (d, 1H, *J*= 8.0 Hz, 10-H), 11.89 (s, 1H, NH), ^{13}C NMR (100.63 MHz, DMSO): δ= 14.42, 22.55, 26.13, 29.13, 29.29, 29.36, 29.41, 29.48, 31.73, 33.29, 33.49, 112.90, 113.72, 115.81, 121.81, 122.52, 131.43, 138.37, 153.95, 161.58, 167.44. *Anal*. Calcd. for $C_{21}H_{27}NO_3$ (341.20): C, 73.87; H, 7.97; N, 4.10%. Found: C, 73.93; H, 8.05; N, 3.94%.

Results and discussion

Recently [35], we have prepared pyrano[3,2-c]quinoline-2,5-diones via a novel approach. This was done by the reaction of 4-hydroxyquinolin-2-one, Meldrum's acid and aldehydes in the presence of $[bmim]HSO_4$ at room temperature within 80 min. In order to optimize the reaction conditions, the reaction of 4-hydroxyquinolin-2-one **1**, Meldrum's acid **2** and 4-methylbenzaldehyde **3a** in the presence of $[HMIm]HSO_4$ was investigated as a model reaction. Before taking up the reaction using ultrasonic irradiation, it was tried out using different solvents such as DMF, CH_2Cl_2, CH_3CN, 1,4-dioxane, n-hexane and different amount of $[HMIm]HSO_4$ at different temperature ranging 25 ^oC to 80 ^oC for different periods of time by conventional heating (Table 1). First, the trial reaction which was performed in the absence of catalyst and solvent led to trace product even after 3h (Table 1, Entry 1). Among the solvents, the best result was obtained with 1ml of $[HMIm]HSO_4$ as the catalyst in ethanol at 80 ºC (Table 1, Entry 7). It can be seen that the best result was obtained using 1 mL of $[HMIm]HSO_4$ at 80 ˚C (Table 1, Entry 12). An increase in the reaction temperature led to increase in the rate of the condensation reaction, but it also gave same yield of the desired product (Table 1, entry 10-13). The results also revealed that when the amount of catalyst was reduced from 1 mLto 0.5 mL, the yield decreased from 85 to 65 % (entry 8). Similarly, when the amount of catalyst was increased from 1 mL to 1.5 mL, the yield decreased from 85 to 75 % (Entry 13). The catalytic efficiency of $[HMIm]HSO_4$ was obtained to be better than of the other reaction conditions because the high brønsted acidity of hydrogen sulphate counteranion.

Table 1. Effect of temperature, solvent, amount of catalyst on the synthesis of pyrano[3,2-c]quinoline-2,5-dione

Entry	Amount ofcatalyst (ml)	Temperature(^{o}C)	Solvent	Time(min)	Yield(%)[a]
1	---	80	Neat	180	trace
2	1	Reflux	DMF	180	30
3	1	Reflux	CH_2Cl_2	120	60
4	1	Reflux	CH_3CN	30	35
5	1	Reflux	1,4-dioxane	50	40
6	1	Reflux	n-hexane	55	45
7	1	Reflux	C_2H_5OH	80	78
8	0.5	80	Neat	70	65
9	1	25	Neat	80	85
10	1	40	Neat	80	85
11	1	60	Neat	70	85
12	1	80	Neat	65	85
13	1.5	80	Neat	60	75

[a]Yields refer to isolated pure products.

To study the effect of ultrasonic irradiation on this synthesis, we performed several experiments at 30, 60 and 80 ^{o}C (Table 2). For this purpose, the reaction of 4-hydroxyquinolin-2-one, Meldrum's acid and 4-methylbenzaldehyde was considered as a model reaction. The results show that in the absence of a catalyst, the yield of the reaction is reduced (Table 2, Entry 1), but this yield has a significantly increased in comparison with the stirring at 80 ^{o}C. In the absence of a catalyst, there is no solid phase, so this ultrasonic large acceleration is not related to additional effects of the liquid-solid systems. It can be explained that gravitational collapse in a liquid produces intense local heating, high pressures, and enormous heating and cooling rates. Therefore, acoustic cavitation provides a unique interaction of energy and matter, and ultrasonic irradiation of liquids causes high energy chemical reactions to occur. In the presence of the catalyst when we increase the temperature of the ultrasonic irradiation ranging from 30 to 80 ^{o}C, the reaction time decreased considerably and the yields of the product increased (Table 2, Entries 2-4). Thus, ultrasonic irradiation was found to have a beneficial effect on the synthesis of pyrano[3,2-c]quinoline-2,5-dione derivative.

Table 2. Reaction of 4-hydroxyquinolin-2-one, Meldrum's acid and 4-methylbenzaldehyde in the presence of $[HMIm]HSO_4$ under ultrasound conditions[a]

Entry	Amount of catalyst (ml)	Temperature (^{o}C)	Time (min)	Yield (%) [a]
1	---	80	100	49
2	1	30	80	87
3	1	60	45	89
4	1	80	20	91

[a]Isolated yields

The one-pot, three-component condensation reaction of 4-hydroxyquinolin-2-one **1**, Meldrum's acid **2** and various aldehydes **3a–n** in the presence of [HMIm] HSO_4 (1 mL) proceeded rapidly at 80 ^oC under ultrasonic irradiation and were complete after 20 min to afford pyrano [3,2-c] quinoline-2,5-diones **4a–n**, in good yields (Table 3). To the best of our knowledge, this new procedure provides the first example of an efficient and ultrasound-promoted approach for the synthesis of pyrano[3,2-c]quinoline-2,5-diones. This method is the most simple and convenient and would be applicable for the synthesis of different pyran moiety heterocyclic compounds. Compounds **4a–n** are stable solids whose structures were established by FTIR, ^1H- and ^{13}C NMR spectroscopy and elemental analysis.

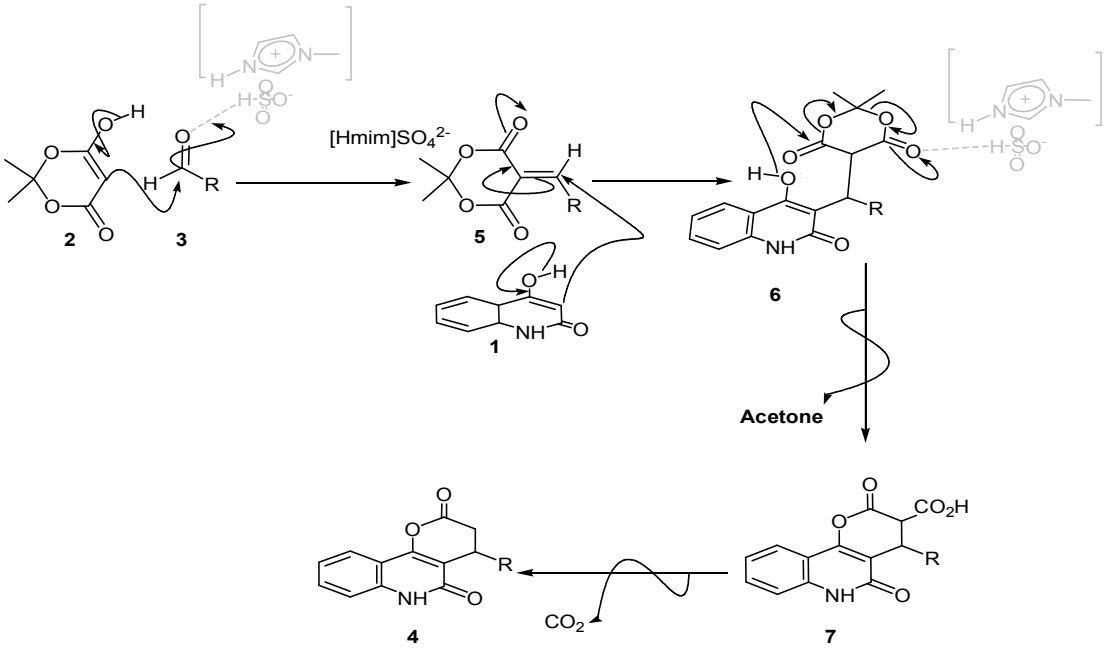
Table 3. Reaction of 4-hydroxyquinolin-2-one **1** with Meldrum's acid **2** and various aldehydes **3**

Entry	R	product[a]	Ultrasound Time (60 min)/Yield (%)	Classical[b] Time (80 min)/ Yield (%)
1	4-Me.C_6H_4	**4a**	87	85[c]
2	4-Cl.C_6H_4	**4b**	91	87[c]
3	4-MeO.C_6H_4	**4c**	86	81[c]
4	4-F.C_6H_4	**4d**	85	80[c]
5	3-Br.C_6H_4	**4e**	89	84[c]
6	C_6H_4	**4f**	90	85[c]
7	2,4-Cl.C_6H_4	**4g**	93	83[c]
8	4-NO_2.C_6H_4	**4h**	92	82
9	4-HO.C_6H_4	**4i**	91	85
10	Ethyl	**4j**	83	74[c]
11	n-Propyl	**4k**	82	74[c]
12	n-Hexyl	**4l**	80	73[c]
13	n-Octyl	**4m**	79	70[c]
14	n-Nonyl	**4n**	79	70[c]

[a]Isolated yields, [b]Room temperature. [c]Ref. 35.

We have not established the exact mechanism for the formation of pyrano[3,2-c]quinoline-2,5-diones **4**, however, a reasonable suggestion is offered in Scheme **2**. The process represents a typical cascade reaction in which the Meldrum's acid **2**

primarily condenced with aldehyde 3 affords intermediate **5**. This step was regarded as a fast Knoevenagel condensation. Subsequently This intermediate undergoes a Michael type addition with 4-hydroxyquinolin-2-one **1** to deliver the adduct **6** which may lose a molecule of acetone (intermediate **7**) and a molecule of CO_2 in subsequent steps to give the final product **4** (Scheme 2).



Scheme 2. Proposed mechanism for the formation of pyrano[3,2-*c*]quinoline-2,5-diones 4

Conclusion

In conclusion, synthesis of pyrano[3,2-*c*]quinoline-2,5-diones is efficiently catalyzed in the presence of [HMIm]HSO_4 under ultrasound condition. To the best of our knowledge, it is the first example of a multicomponent reaction to the synthesis of these compounds. The operational simplicity of the procedure, short reaction times, convenient work-up, and reusability of the ionic liquid make this method attractive.

Acknowledgment

We gratefully acknowledge financial support from the Research Council of Islamic Azad University of Ardabil and Islamic Azad University of Rasht Branch.

References

[1] J.S. Torrecilla, J. Palomar, J.N. Garcí, F. Rodríguez, K. J. *Chem. Eng. Data,* **2009**, *54*, b1297.

[2] Roshan,N., Ghader, S., **2012**. Developing models for correlating ionic liquids density: Part 1 – Density at 0.1 MPa., Fluid Phase Equilibria 331, p.33.

[3] Thermodynamics of room temperature ionic liquids: Thesis report for 2011, University of Aberdeen, Barcelo, P., May **2011**.

[4] R. Fortunato,C.A.M.A. Fonso, M.A.M. Reis, J.G. Crespo, *J. Memb. Sci.,* **2004**, *242*, 197-209.

[5] M.M. Khodaei, A.R. Khosropour, S. Ghaderi, J. *Iran. Chem. Soc.*, **2006**, *3*, 69-72.

[6] H.Y. Guo, Y.Yu, *Chin. Chem. Lett.*, **2010**, *21*, 1435-1438.

[7] X. Mi, S. Luo, J.P. Cheng, *J. Org. Chem*., **2005**, *70*, 2338-2341.

[8] D.C. Chen, H.Q. Ye, H. Wu, *Chin. Chem. Lett*., **2007**, *18*, 27-29.

[9] A. Davoodnia, S. Allameh, A.R. Fakhari, *Chin. Chem. Lett.*, **2010**, *21*, 550-553.

[10] A. Clark, *Pharm Res.,* **1996**, *13*, 1133-1141.

[11] M. Anniyappan, D. Muralidhran, P.T. Perumal, *Tetrahedron Lett*., **2003**, *44*, 3653-3657.

[12] N. Ravindranath, C. Ramesh, M.R. Reddy, B. Das, *Chem. Lett.*, **2003**, *32*, 222-223.

[13] I.C. Badhwar, K. Venkataraman, *J. Chem. Soc*., **1932**, 2420-2423.

[14] T.S. Chen, S. J. Wu, I. L. Tsai, T. S., Wu, J.M. Pezzuto, M.C. Lu, H. Chai, N. Suh, C.M. Teng, *J. Nat. Prod.*, **1994**, *57*, 1206-1211.

[15] T. Davion, B. Joseph, Y. Merour, *Syn. Let.,* **1998**, 1051-1052.

[16] Y. Fujita, H. Oguri, H. Oikawa. *J. Antibiot*., **2005**, *58*, 425-427.

[17] E.A. Mohamed, *Chem. Pap.*, **1994**, *48*, 261-267.

[18] F. Hanawa, N. Fokialakis, A. L. Skaltsounis, *Planta Med.,* **2004**, *70*, 531-535.

[19] M. Rufchahi M, A.G. Gilani, *Dyes. Pigm.*, **2012**, *95*, 632-636.

[20] M.R. Shaaban, T.S. Saleh, F.H. Osman, A.M. Farag, *J. Heterocycl. Chem*., 2007, *44,* 177-181.

[21] N.M. Abd El-Rahman, A.A. El-kateb, M.F. Mady, *Synth. Commun*., **2007**, *37,* 3961-3970.

[22] A.A. El-Kateb, N.M. Abd El-Rahman, *Phos. Sulf. Silicon*., **2006**, *181,* 249-259.

[23] J.Y. Winum, M. Kamal, A. Leydet, *Tetrahedron Lett.,* **1996**, *37,* 1781-1785.

[24] J.T. Li, W.Z. Yang, S.X. Wang, S.H. Li, T.S. Li, *Ultrason. Sonochem*., **2002**, *9*, 237-239.

[25] S.X. Wang, J.T. Li, W.Z. Yang, T.S. Li, *Ultrason. Sonochem*., **2002**, *9*, 159-161.

[26] J.T. Li, T.S. Li, L.J. Li, X. Cheng, *Ultrason. Sonochem.*, **1999**, *6,* 199-201.

[27] J.T. Li, L.J. Li, T.S. Li, H.Z. Li, I.K. Li, *Ultrason. Sonochem.,* **1996**, *3,* 141-148.

[28] S.J. Ji, Z.L. Shen, D.G. Gu, X.Y. Huang, *Ultrason. Sonochem*., **2005**, *12,* 161-163.

[29] J.T. Li, M.X. Sun, Y. Yin, *Ultrason. Sonochem*., **2010**, *17,* 359-362.

[30] C.L. Ni, X.H. Song, H. Yan, X.Q. Song, R.G. Zhong, *Ultrason. Sonochem*., **2010**, *17,* 367-369.

[31] M. A. Margulis, *Ultrasonics*, **1992**, *30,* 152-155.

[32] R. M. Martin-Aranda, E. Ortega-Cantero, M. L. Rojas-Cervantes, M. A. Vicente-Rodrigues, M. A. Ban-Ares-Mun-Oz, *Catal. Lett.,* **2002**, *84*, 201-204.

[33] V. Calvine-Casilda, A. J. Lopez. Peinado, R. M. Martin-Aranda, S. Ferrera-Escudero, C. *J. Duran-Valle. Carbon*, **2004**, *42,* 1363-1366.

[34] V. Tiwari, A. Parvez, J. Meshram, *Ultrason. Sonochem*., **2011**, *18,* 911-916.

[35] K. Rad-Moghadam, S.C. Azimi, E. Abbaspour-Gilandeh, *Tetrahedron Lett.*, **2013**, *54,* 4633-4636.