Regular Article

ORGANIC CHEMISTRY RESEARCH
Published by the
Iranian Chemical Society
www.orgchemres.org

Org. Chem. Res., *Vol. 4, No. 2, 182-193, September 2018.*

Silica Sodium Carbonate as an Effective and Reusable Catalyst for the Three-Component Synthesis of Pyrano Coumarins

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(Received 4 September 2017, Accepted 9 May 2018)

Silica sodium carbonate (SSC) has been prepared, characterized and then used as a valuable silica-supported catalyst for the preparation of a range of known and novel pyrano coumarins *via* the three-component reactions of aryl aldehydes, active methylene compound (malononitrile or ethyl cyanoacetate), and hydroxycoumarin (5,7-dihydroxy-4-substituted coumarins or 4-hydroxycoumarin). The heterogeneous catalyst showed much the same efficiency when employed in following reaction runs.

Keywords: Pyrano coumarins, 5,7-Dihydroxy-4-substituted coumarins, 4-Hydroxycoumarin

INTRODUCTION

Preparation of hybrid heterocycles including biologically active bones is an important topic in organic transformations [1,2]. The coumarin ring system is used regularly as a scaffold in medicinal and agricultural chemistry [3,4]. Pyrano coumarins, as fused dihydropyran with coumarin nucleus, received great attention because of their extensive range of applications in different fields of chemistry [5-7]. They have shown various pharmacological activities such as anti HIV, antitumor, anticancer, antibacterial, and anti-inflammatory properties [8-11]. Moreover, they can be utilized as cosmetics and pigments and exploited as potential biodegradable agrochemicals [12, 13]. The unique properties and broad applications of pyrano coumarins have promoted considerable studies for the production of these useful compounds.

With growing public concerns about environmental pollution, green reusable supported catalysts, as eco-friendly materials, have turned into the potential alternatives for conventionally chemical catalysts [14,15]. Many solid supports such as charcoal, alumina, silica and polymers have been used for the synthesis of immobilized recoverable catalysts which have shown many advantages. For instance, after completion of the reaction, separation of catalyst from products and solvents can be easily performed by filtration or centrifugation [16,17]. Also, immobilization of catalysts on a solid support makes them more reactive and more stable, which are all factors significant in industry [18]. So, use of recyclable supported heterogeneous catalysts has economical and environmental advantages. Silica sodium carbonate (SSC) is an inexpensive and recyclable alternative to sodium carbonate employed as superior base catalyst in some heterogeneous organic reactions [19,20].

One-pot multi-component reactions (MCRs) play an important role in combinatorial chemistry, so this field remained as one of the most interesting research areas in recent years. During multi-component reaction, target products are prepared with attachment of at least three functional groups by covalent bonds [21]. These reactions represent a very powerful tool for the synthesis of multipart molecules with potential biological properties due to their effective atom economy, convergent nature, time saving and straightforward experimental routs [22].

In the course of our research program into design of new methods for the synthesis of different biologically active

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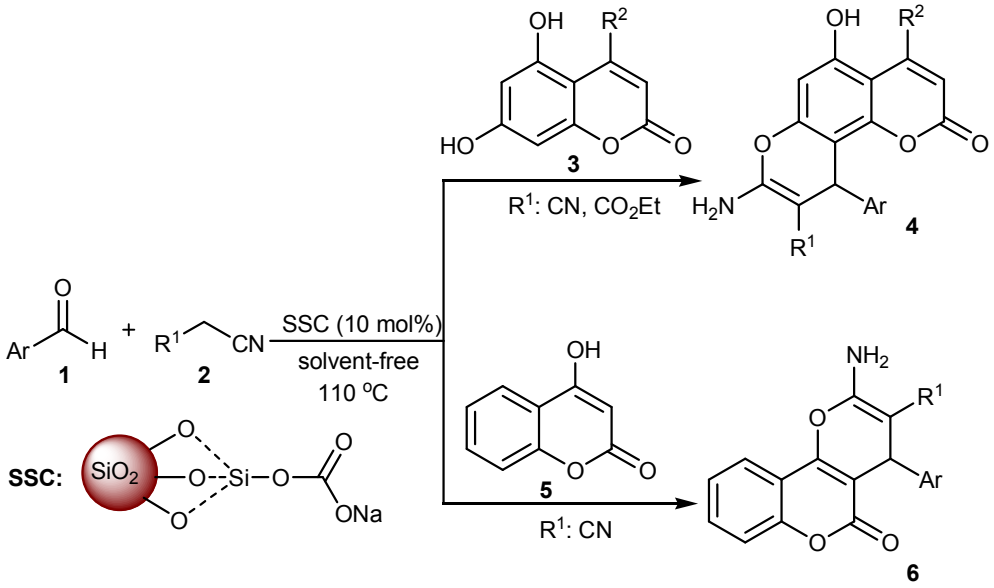


Scheme 1. Preparation of pyrano coumarins 4 and 6 in the presence of SSC

heterocyclic compounds in the presence of heterogeneous solid catalysts [23-26], herein, we describe the application of silica sodium carbonate in the synthesis of pyrano coumarins 4 and 6 as the hybrid heterocyclic scaffold carrying coumarin (Scheme 1).

EXPERIMENTAL

Chemicals were purchased from Aldrich and Merck chemical companies. 5,7-Dihydroxy-4-substituted coumarins and SSC were prepared according to the reported procedure in the literature [19,27]. X-ray diffraction (XRD) pattern was obtained by Philips X Pert Pro X diffractometer operated with a Ni filtered Cu Kα radiation source. X-ray fluorescence (XRF) spectroscopy was recorded by X-Ray Fluorescence Analyzer, Bruker, S_4 Pioneer, Germany. IR spectra were recorded on FT-IR JASCO-680 using KBr disks. The NMR spectra were recorded on a Brucker instrument 400 MHz ultra-shield model as dimethyl sulfoxide (DMSO) solutions. The varioEl CHNS Isfahan Industrial University was used for elemental analysis.

Preparation of Silica Sodium Carbonate (SSC)

To a 250 ml round bottom flask equipped with a reflux condenser, 10 g of silica gel 60 that was previously dried at 120 °C for 6 h was added. Then, 40 ml of thionyl chloride was added dropwise to this flask which was perched in an ice bath. After the addition of thionyl chloride, the reaction mixture was removed from the ice bath and stirred for 0.5 h in room temperature and 48 h under reflux conditions. Afterwards, the reaction mixture was filtrated to obtain silica chloride. In the next step, to a stirred 250 ml round bottom flask containing 10 g of sodium bicarbonate and 25 ml of *n*-hexane under reflux conditions, 10 g of silica chloride (after drying at 120 °C for 6 h) was added. After 24 h, the reaction mixture was filtrated to separate the catalyst and the solid product was washed with 50 ml of distilled water ten times, using 5 ml each time until filtrate became quite neutral, in order to remove the remaining sodium bicarbonate. Finally, after drying the catalyst at 100 °C for 12 h, 14 g of SSC was obtained [19].

General Procedure for the Synthesis of Pyrano Coumarins 4 and 6

SSC (0.1 mmol, 0.2 g) was added to a mixture of malononitrile/ethyl cyanoacetate, aryl aldehyde, and 5,7-dihydroxy-4-substituted coumarin/4-hydroxycoumarin at 110 °C under solvent-free conditions. The reaction progress was monitored by thin layer chromatography (TLC) (*n*-hexane/EtOAc, 3:2). After completion of the reaction,

boiling EtOAc (10 ml) was added, and the catalyst was separated by filtration. To further purification of the product, obtained powder was recrystallized from EtOH.

Spectral Characterization

8-Amino-10-(3-bromophenyl)-5-hydroxy-4-methyl-2-oxo-2H,10H-pyrano[2,3-f]chromene-9-carboxylic acid ethyl ester (4d). Yield 90% (0.423 g); m.p.: 271-273 ºC. FT-IR (KBr): υ_{max} 3459, 3307, 1733, 1683, 1633 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 11.10 (s, 1H), 7.63 (s, 1H), 7.31-7.37 (m, 3H), 7.12-7.22 (m, 2H), 6.53 (s, 1H), 6.12 (d, J = 1.2 Hz, 1H), 4.98 (s, 1H), 4.04 (q, J = 7.2 Hz, 2H), 2.68 (s, 3H), 1.17-1.20 (m, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 168.17, 160.71, 160.68, 159.89, 154.63, 153.75, 149.62, 148.08, 130.99, 130.77, 129.26, 127.05, 121.41, 111.98, 111.00, 102.44, 98.92, 77.11, 59.44, 34.55, 24.47, 14.74. Anal. Calcd. for $C_{22}H_{18}BrNO_6$: C, 55.95; H, 3.84; N, 2.97. Found: C, 55.93; H, 3.84; N, 2.95.

8-Amino-10-(2,4-dichlorophenyl)-5-hydroxy-4-methyl-2-oxo-2H,10H-pyrano[2,3-f]chromene-9-carboxylic acid ethyl ester (4f). Yield 89% (0.410 g); m.p.: 251-253 ºC. FT-IR (KBr): υ_{max} 3438, 3324, 1706, 1671, 1633 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 11.00 (s, 1H), 7.67 (s, 2H), 7.20-7.40 (m, 3H), 6.42 (s, 1H), 6.09 (s, 1H), 5.29 (s, 1H), 4.11-4.37 (m, 2H), 2.51-2.67 (m, 3H), 1.06 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 168.25, 159.83, 159.35, 157.96, 154.29, 153.36, 147.45, 142.90, 133.43, 132.74, 130.87, 128.33, 127.06, 111.35, 109.33, 101.56, 98.06, 75.45, 50.38, 32.01, 24.02, 18.52. Anal. Calcd. for $C_{22}H_{17}Cl_2NO_6$: C, 57.16; H, 3.71; N, 3.03. Found: C, 57.18; H, 3.69; N, 3.04.

8-Amino-10-(2-chloro-6-florophenyl)-5-hydroxy-4-methyl-2-oxo-2H,10H-pyrano[2,3-f]chromene-9-carboxylic acid ethyl ester (4g). Yield 87% (0.387 g); m.p.: 234-235 ºC. FT-IR (KBr): υ_{max} 3423, 3297, 1693, 1670 cm^{-1}, ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 11.02 (s, 1H), 7.67 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2 Hz, 2H), 7.20-7.29 (m, 2H), 6.44 (s, 1H), 6.10 (s, 1H), 5.30 (s, 1H), 4.05 (q, J = 7.2 Hz, 2H), 2.69 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 168.76, 160.35, 160.30, 159.88, 158.32, 154.81, 153.89, 147.96, 133.95, 133.27, 131.40, 128.86, 127.57, 111.88, 109.81, 102.09, 96.56, 75.97, 60.25, 32.55, 24.54, 14.56. Anal. Calcd. for $C_{22}H_{17}ClFNO_6$: C, 59.27; H, 3.84; N, 3.14. Found: C, 59.30; H, 3.85; N, 3.15.

8-Amino-5-hydroxy-4-methyl-2-oxo-10-phenyl-2H,10H-pyrano[2,3-h]chromene-9-carbonitrile (4i). Yield 85% (0.294 g); m.p.: 250-251 ºC. FT-IR (KBr): ν_{max} 3460, 3390, 2191, 1652, 1617, 1399 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 7.27-7.23 (m, 2H), 7.18-7.13 (m, 3H), 6.88 (s, 2H), 6.10 (s, 1H), 5.80 (s, 1H), 4.61 (s, 1H), 2.55 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 163.69, 160.10, 160.05, 155.26, 153.51, 147.59, 145.81, 128.16, 127.01, 126.19, 120.53, 109.70, 107.89, 98.92, 98.57, 57.68, 36.31, 23.97.

8-Amino-5-hydroxy-4-methyl-2-oxo-10-(2-chlorophenyl)-2H,10H-pyrano[2,3-h] chromene-9-carbonitrile (4l). Yield 90% (0.342 g); m.p.: 325-326 ºC. FT-IR (KBr): ν_{max} 3397, 2201, 1733, 1664 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 10.94 (s, 1H), 7.39 (dd, J = 7.6 Hz, J = 1.2 Hz, 1H), 7.26-7.18 (m, 2H), 7.07 (dd, J = 7.2 Hz, J = 1.6 Hz, 1H), 7.00 (s, 2H), 6.45 (s, 1H), 6.08 (s, 1H), 5.18 (s, 1H), 2.64 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 159.89, 159.82, 158.09, 155.04, 153.86, 148.30, 143.03, 132.38, 130.55, 129.68, 128.59, 128.08, 120.05, 111.94, 107.89, 128.08, 98.89, 56.63, 33.78, 24.54.

8-Amino-5-hydroxy-4-methyl-10-(4-methylphenyl)-2-oxo-2H,10H-pyrano[2,3-h]chromene-9-carbonitrile (4n). Yield 70% (0.252 g); m.p.: 221-222 ºC. FT-IR (KBr):ν_{max} 3402, 1730, 1666 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 10.95 (s, 1 H), 7.09 (d, J = 8 Hz, 2H), 7.03 (d, J = 8 Hz, 2H), 6.99 (s, 2H), 6.51 (s, 1H), 4.59 (s, 1H), 2.62 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 160.06, 159.78, 157.95, 154.77, 153.83, 148.03, 142.71, 136.14, 129.41, 127.40, 120.59, 111.96, 109.24, 102.37, 99.02, 58.12, 36.37, 24.48, 21.06.

8-Amino-5-hydroxy-4-methyl-10-(2-methoxylphenyl)-2-oxo-2H,10H-pyrano[2,3-h]chromene-9-carbonitrile (4p). Yield 70% (0.263 g); m.p.: 300-301 ºC. FT-IR (KBr): ν_{max} 3414, 3322, 3202, 1691, 1661 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 10.80 (s, 1H), 7.17 (t, J = 7.6 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 6-88-6.81 (m, 4H), 6.48 (s, 1H), 6.10 (s, 1H), 4.96 (s, 1H), 3.74 (s, 3H), 2.64 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 160.53, 159.95, 157.95, 157.21, 154.68, 153.91, 148.87, 133.31, 128.91, 128.28, 120.90, 120.66, 112.05, 111.82, 108.43, 102.12, 98.79, 57.05, 56.09, 31.49, 24.53.

8-Amino-5-hydroxy-4-methyl-2-oxo-10-(3-bromoph

enyl)-2H,10H-pyrano[2,3-h] chromene-9-carbonitrile (4q). Yield 90% (0.381 g); m.p.: 296-298 ºC. FT-IR (KBr): ν_{max} 3423, 3346, 3205, 1690, 1647 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 11.06 (s, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.34 (s, 1H), 7.27 (t, J = 7.6 H, 1H), 7.17 (d, J = 8 Hz, 1H), 7.09 (s, 2H), 6.50 (s, 1H), 6.08 (s, 1H), 4.76 (s, 1H), 2.62 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 160.10, 159.79, 157.93, 155.01, 153.78, 148.37, 147.97, 131.22, 130.21, 130.03, 126.78, 122.05, 120.37, 112.05, 108.16, 102.44, 99.11, 57.27, 36.55, 24.51.

8-Amino-5-hydroxy-4-methyl-10-(3-nitrophenyl)-2-oxo-2H,10H-pyrano[2,3-h]chromene-9-carbonitrile (4s). Yield 87% (0.340 g); m.p.: 390-391 ºC. FT-IR (KBr): ν_{max} 3401, 1731, 1660 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 11.57 (s, 1H), 8.11-8.09 (m, 1H), 8.02 (s, 1H), 7.67-7.60 (m, 2H), 7.19 (s, 1H), 6.51 (s, 1H), 6.12 (s, 1H), 4.88 (s, 1H), 2.63 (s, 3H). ^{13}C NMR (DMSO-d_6 100 MHz) δ (ppm) 160.23, 159.75, 157.92, 155.14, 153.77, 148.23, 147.97, 147.79, 134.53, 130.66, 122.33, 122.03, 120.22, 112.17, 107.78, 102.50, 99.15, 56.74, 36.56, 24.49.

8-Amino-5-hydroxy-4-(chloromethyl)-10-(2-chlorophenyl)-2-oxo-2H,10Hpyrano[2,3-h]chromene-9-carbonitrile (4u). Yield 91% (0.376 g); m.p.: 305-306 ºC. FT-IR (KBr): ν_{max} 3400, 1723, 1657 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 11.09 (s, 1H), 7.44-77.38 (m, 1H), 7.24-7.21 (m, 2H), 7.13 (s, 2H), 7.09-7.07 (m, 1H), 6.49 (s, 1H), 5.87 (s. 1H), 5.25-5.19 (m, 2H), 5.15 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 159.85, 158.48, 155.11, 152.68, 151.02, 147.61, 142.81, 132.39, 130.58, 129.75, 128.71, 119.98, 111.91, 108.14, 106.93, 99.89, 98.10, 56.41, 46.22, 33.74.

2-Amino-4-(4-cyanophenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile (6c). Yield 83% (0.283 g); m.p.: 252-254 ºC. FT-IR (KBr): ν_{max} 3380, 3311, 3189, 1714, 1675 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 7.92 (d, J = 8 Hz, 1H), 7.82 (s, 1H), 7.80 (d, J = 1.6 Hz, 1H), 7.76 (d, J = 1.6 Hz, 1H), 7.74 (s, 1H), 7.72 (d, J = 1.6 Hz, 1H), 7.54 (s, 1H), 7.52 (s, 1H), 7.49 (t, J = 3.6 Hz, 2H), 7.47 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 160.0, 158.5, 154.4, 152.7, 149.2, 133.5, 132.9, 129.3, 125.1, 123.0, 119.4, 119.2, 117.0, 113.4, 110.4, 103.3, 57.3, 37.5. Anal. Calcd. for $C_{20}H_{11}N_3O_3$: C, 70.38; H, 3.25; N, 12.31. Found: C, 70.40; H, 3.23; N, 12.29.

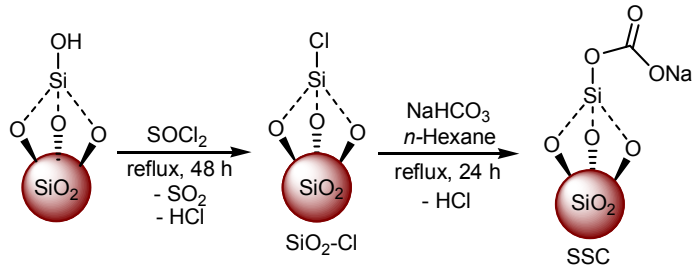
2-Amino-4-(4-benzyloxy)-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile (6e). Yield 78% (0.329 g); m.p.: 268-269 ºC. FT-IR (KBr): ν_{max} 3391, 3180, 1712, 1674, 1608 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 7.90 (dd, J = 8.0 Hz, 1H), 7.73-7.69 (m, 1H), 7.44-7.38 (m, 7H), 7.18 (d, J = 8.8 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 5.06 (s, 2H), 4.40 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 159.51, 157.87, 157.45, 153.09, 152.06, 137.05, 135.60, 132.83, 128.76, 128.40, 127.79, 127.64, 124.63, 122.41, 119.30, 116.53, 114.61, 112.97, 104.19, 69.17, 58.09, 36.13.

2-Amino-4-(2-chloro-4-fluorophenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile (6g). Yield 80% (0.294 g); m.p.: 293-295 ºC. FT-IR (KBr): ν_{max} 3408, 3280, 3175, 1705, 1674, 1602 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 7.90 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.76-7.72 (m, 1H), 7.55-7.48 (m, 4H), 7.55-7.19 (m, 3H), 5.19 (d, J = 1.6 Hz, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 159.38, 158.77, 152.11, 133.18, 133.09, 129.93, 129.83, 124.84, 124.70, 124.66, 122.29, 118.73, 116.68, 115.25, 112.56, 38.83.

2-Amino-4-(3-ethoxy-4-hydroxyphenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile (6i). Yield 75% (0.282 g); m.p.: 244-245 ºC. FT-IR (KBr): ν_{max} 3461, 3295, 3162, 1716, 1673, 1631 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 8.86 (s, 1H), 7.90 (d, J = 8 Hz, 1H), 7.74 (t, J = 8 Hz, 2H), 7.46-7.52 (m, 2H), 7.34 (s, 1H), 6.81 (d, J = 2 Hz, 1H), 6.72 (d, J = 2.1 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H), 4.35 (s, 1H), 3.94-4.01 (m, 2H), 1.32 (t, J = 6.8 Hz, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 160.0, 158.3, 153.4, 152.5, 146.5, 134.7, 133.2, 15.0, 122.9, 120.3, 119.8, 117.0, 116.0, 114.0, 113.5, 104.8, 64.4, 58.8, 36.9, 15.1. Anal. Calcd. for $C_{21}H_{16}N_2O_5$: C, 67.02; H, 4.28; N, 7.44. Found: C, 67.04; H, 4.26; N, 7.46.

RESULTS AND DISCUSSION

Silica sodium carbonate (SSC) was synthesized using the previously reports [19]. Initially, from the treatment of silica gel and thionyl chloride, silica chloride is prepared. Accordingly, sodium bicarbonate can react with silica chloride to give silica sodium carbonate (Scheme 2). SSC as a recyclable heterogeneous alternative to sodium carbonate could be easily recovered from the reaction mixtures. These properties make these reactions cleaner, faster and more efficient.



Scheme 2. Preparation of silica sodium carbonate (SSC)

SSC was then characterized by FT-IR, XRD, XRF, and titration with HCl (0.01 N) [19]. XRF data of SSC is presented in Table 1. As can be seen, XRF data of SSC show the composition of the catalyst as 68.96 (%W/W) Si (Entry 1) and 12.20 (%W/W) Na (Entry 2).

Figure 1 shows the XRD patterns of SSC which exhibits the presence of sodium carbonate phase supported on amorphous silica as a broad peak around 40° (2θ) (θ is the Bragg's angle). Also, the broad peaks around 10°, 34°, 36° and 43° (2θ) from the smaller inset could be attributed to linking of Si to OCO_2Na. The observed peak with the equivalent Bragg's angle at 2θ = 21.1° is correlated to amorphous silica. Other typical and sharp peaks at 2θ = 26.0, 30.0, 30.6, 35.5, 40.3 and 47.7 corresponding to $NaHCO_3$ reflection (crystal face indices: 210, 111, 111, 121, 320 and 301) could be clearly detected. Furthermore, the peak at 2θ = 34.3 is in a good agreement with the strongest diffraction (110) of metal Na. Therefore, the appearance of these peaks affirm the connection of -OCO_2Na in the SSC.

The mixing FT-IR spectra for the anhydrous sodium bicarbonate, silica chloride, and SSC are shown in Fig. 2. This comparable spectrum shows the characteristic bonds of anhydrous sodium bicarbonate and silica chloride. Also, the appearance of two distinguished adsorption bonds at 1640 and 1455 cm^{-1} in the catalyst spectrum reveals incorporation of sodium bicarbonate to the silica chloride.

We also evaluated the amounts of sodium bicarbonate supported on SiO_2 using two methods, including (a) titration with 0.01 N HCl and (b) calculating the weight difference between primary solid acid unattached chloride and new SSC. After these experiments, we found that 1 g catalyst includes 0.14 g -OCO_2Na. Regarding to the molecular weight of CO_3Na (83 g), therefore, 0.02 g of catalyst is equivalent to 0.01 mmol CO_3Na.

Table 1. XRF Data of SSC

Compound	Concentration (%W/W)
Si	68.96
Na	12.20
Ca	7.08
Zn	5.61
Cl	2.51
S	1.58
F	1.12
Al	0.510
Mn	0.457
Sr	0.139
Fe	0.124
Mg	0.090
Cu	0.062
Ti	0.057
Total	100.50

After characterization of the catalyst, we decided to use SSC for the synthesis of pyrano coumarins 4. Firstly, several 5,7-dihydroxy-4-substituted coumarins 3 were synthesized in high yields based on the literature methods [27]. Subsequently, for achievement the most suitable reaction conditions and to evaluate the catalytic potent of SSC, a three-component reaction of ethyl cyanoacetate, benzaldehyde, and 4-methyl-5,7-dihydroxycoumarin was selected as a model reaction at many different conditions. On

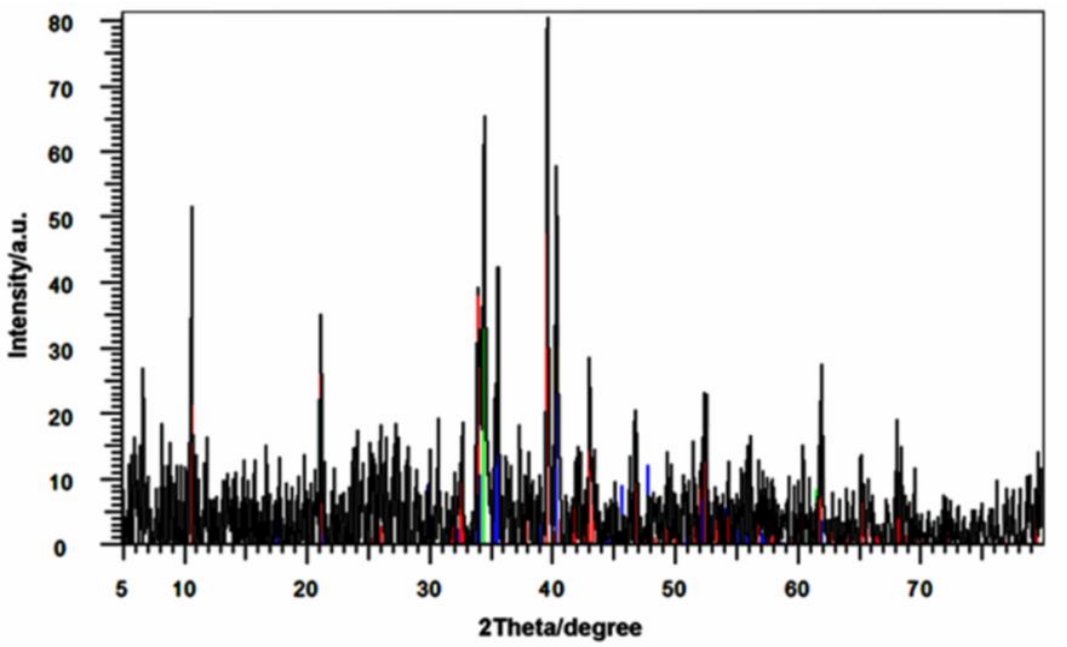


Fig. 1. Powder X-ray diffraction (XRD) pattern of SSC.

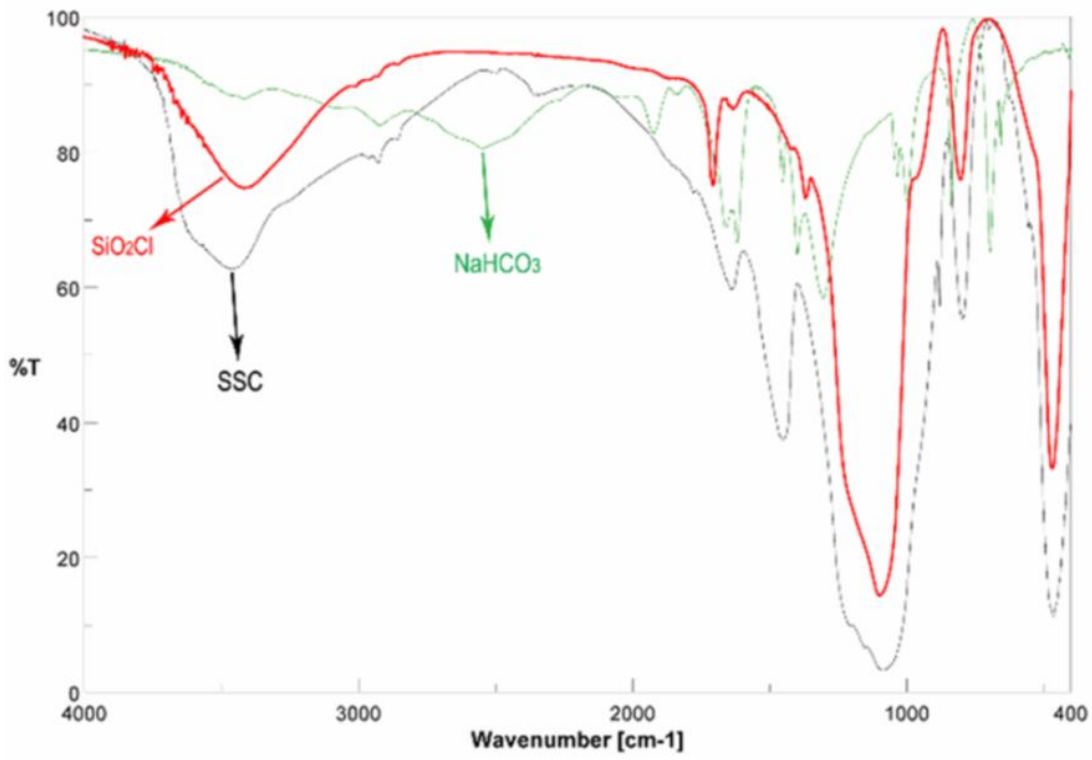


Fig. 2. FT-IR spectra of SiO_2Cl, $NaHCO_3$, and SSC.

Table 2. Screening Conditions for the Model Reaction

Entry	Solvent	Catalyst loading (mol%)	Temp. (°C)	Time (min)	Yield (%)[a]
1	None	SSC (5)	50-70	120	42
2	None	SSC (5)	70-80	120	50
3	None	SSC (5)	100	120	60
4	None	SSC (5)	110	120	65
5	None	SSC (5)	120	120	70
6	None	SSC (7)	110	100	75
7	None	SSC (10)	110	100	90
8	None	SSC (15)	110	100	80
9	None	SSC (2)	110	100	80
10	None	SSC (1)	110	100	77
11	MeOH	SSC (10)	70	120	65
12	EtOH	SSC (10)	70-80	120	80
13	EtOH/H_2O	SSC (10)	70-80	120	80
14	H_2O	SSC (10)	90-100	120	50
15	CH_3CN	SSC (10)	80	120	62
16	Toluene	SSC (10)	110	120	53

[a]Isolated yield.

the basis of the obtained results, we found that this reaction is performed well by using 10 mol% of SSC at 110 °C under solvent-free conditions (Table 2, entry 7).

After establishing the optimal condition, we then studied the application of the reaction for the construction of various substrates including malononitrile, various aromatic aldehydes and 5,7-dihydroxy-4-substituted coumarin derivatives, the results are shown in Table 3. In general, the reaction proceeded smoothly to afford the desired products 4 in good to excellent yields.

Next, we developed the catalytic activity of SSC in condensation reactions of aromatic aldehydes, malononitrile and 4-hydroxycoumarin to afford pyrano coumarins 6 (Scheme 1). A series of product 6 with different substituents was prepared using various aromatic aldehydes containing electron-withdrawing and electron-donating groups (Table 4).

The structures of the obtained products 4 and 6 were confirmed by their elemental analyses, IR, ^{1}H and ^{13}C NMR spectroscopy and compared with the reported samples [28-30]. Although both electron-rich and electron-poor aldehydes gave the desired products 4 and 6, aldehydes with electron-withdrawing groups performed this reactions in better yields compared to those containing electron-donating groups. This may be explained by more positive charge located on carbonyl group of aldehydes in electron-poor cases, making them more reactive electrophile center.

In view of ecofriendly procedure, the reusability of

Table 3. SSC-Catalyzed Synthesis of Pyrano Coumarins 4

Entry	Ar	R^1	R^2	Yield (%)[a]	M.p. [Lit.] (°C)
4a	C_6H_5	CO_2Et	CH_3	90	260-262
4b	4-$CH_3C_6H_4$	CO_2Et	CH_3	75	280-282
4c	4-BrC_6H_4	CO_2Et	CH_3	86	215-217
4d	3-BrC_6H_4	CO_2Et	CH_3	90	271-273
4e	2-ClC_6H_4	CO_2Et	CH_3	93	274-276
4f	2,4-$Cl_2C_6H_3$	CO_2Et	CH_3	89	251-253
4g	2-Cl 6-FC_6H_3	CO_2Et	CH_3	87	234-235
4h	1-Naphthyl	CO_2Et	CH_3	75	208-210
4i	C_6H_5	CN	CH_3	85	250-251 [255-256][28]
4j	4-ClC_6H_4	CN	CH_3	93	245-247 [242-244][28]
4k	3-ClC_6H_4	CN	CH_3	96	202-204 [208-210][28]
4l	2-ClC_6H_4	CN	CH_3	90	325-326 [320-322][28]
4m	2,4-$Cl_2C_6H_3$	CN	CH_3	85	320-321 [322-324][28]
4n	4-$CH_3C_6H_4$	CN	CH_3	70	221-222 [225-226][28]
4o	4-$OCH_3C_6H_4$	CN	CH_3	65	260-262 [265-266][28]
4p	2-$OCH_3C_6H_4$	CN	CH_3	70	300-301 [303-305][28]
4q	3-BrC_6H_4	CN	CH_3	90	296-298 [295-296][28]
4r	4-$NO_2C_6H_4$	CN	CH_3	85	341-342 [345-347][28]
4s	3-$NO_2C_6H_4$	CN	CH_3	87	390-391 [393-395][28]
4t	2-ClC_6H_4	CN	Ph	85	241-242 [243-245][28]
4u	2-ClC_6H_4	CN	CH_2Cl	91	305-306 [308-310][28]

[a]Isolated yield.

catalyst is quite desirable. The recovered SSC in the synthesis of 4a was washed with chloroform and dried at 120 °C for 1 h. Using the reused catalyst for four successive times in the model reaction provided the product with a gradual decreasing of reaction yield (Fig. 3).

A reasonable mechanism for the formation of pyrano coumarins is outlined in Scheme 3. Firstly, intermediate 7 is formed *via* the Knoevenagel condensation of the aldehyde and active methylene compound. For the formation of pyrano coumarin 4, adduct 8 is produced from a Michael type addition of C-8 of dihydroxycoumarin to compound 7 using SSC as a base catalyst. Subsequently, cyclization of intermediate 8 gives pyrano coumarin 4. 4-Hydroxycoumarin can also attack to intermediate 7 to

Table 4. Synthesis of Pyrano Coumarins 6 Using SSC

Entry	Ar	Yield (%)[a]	M.p. [Lit.] (°C)
6a	C_6H_5	85	261-263 [256-258][29]
6b	4-$CH_3C_6H_4$	90	255-257 [265-267][29]
6c	4-CNC_6H_4	83	252-254
6d	4-*iso*-propylC_6H_4	87	240-242
6e	4-BenzyloxyC_6H_4	78	268-269 [270-272][30]
6f	3-BrC_6H_4	95	276-277 [276-278][30]
6g	2-Cl 6-FC_6H_3	80	293-295 [290-292][30]
6h	1-Naphthyl	86	260-261 [262-264][30]
6i	3-OEt 4-OHC_6H_3	75	244-245
6j	Thiophene-2-yl	80	265-266 [260-262][30]
6k	4-$OCH_3C_6H_4$	85	246-248 [242-244][29]
6l	4-$NO_2C_6H_4$	90	260-262 [257-260][29]
6m	4-ClC_6H_4	87	262-264 [266-267][29]
6n	3-$NO_2C_6H_4$	80	263-265 [260-263][29]
6o	2-ClC_6H_4	83	269-271 [270-272][30]
6p	2,4-$Cl_2C_6H_3$	80	259-260 [257-259][29]

[a]Isolated yield.

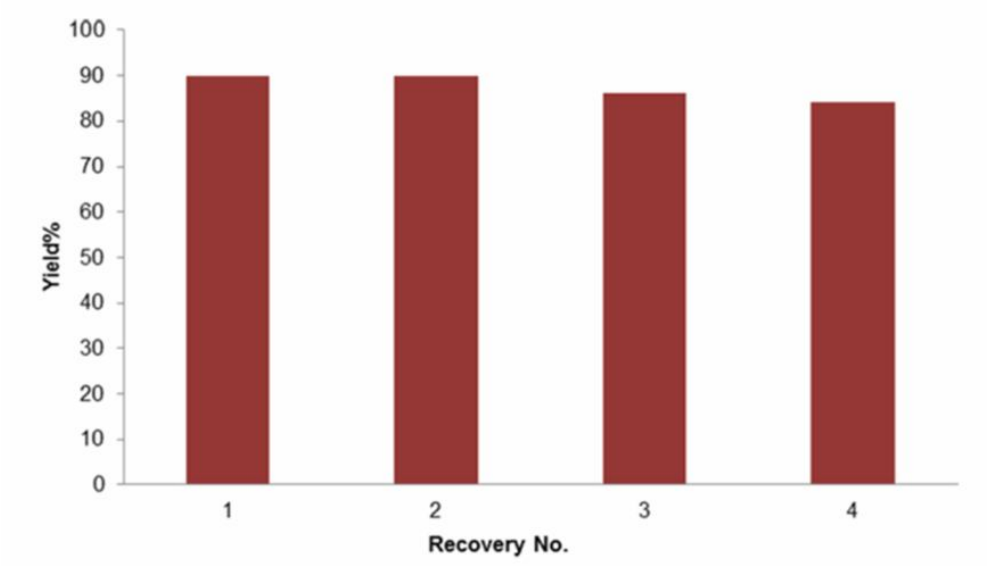
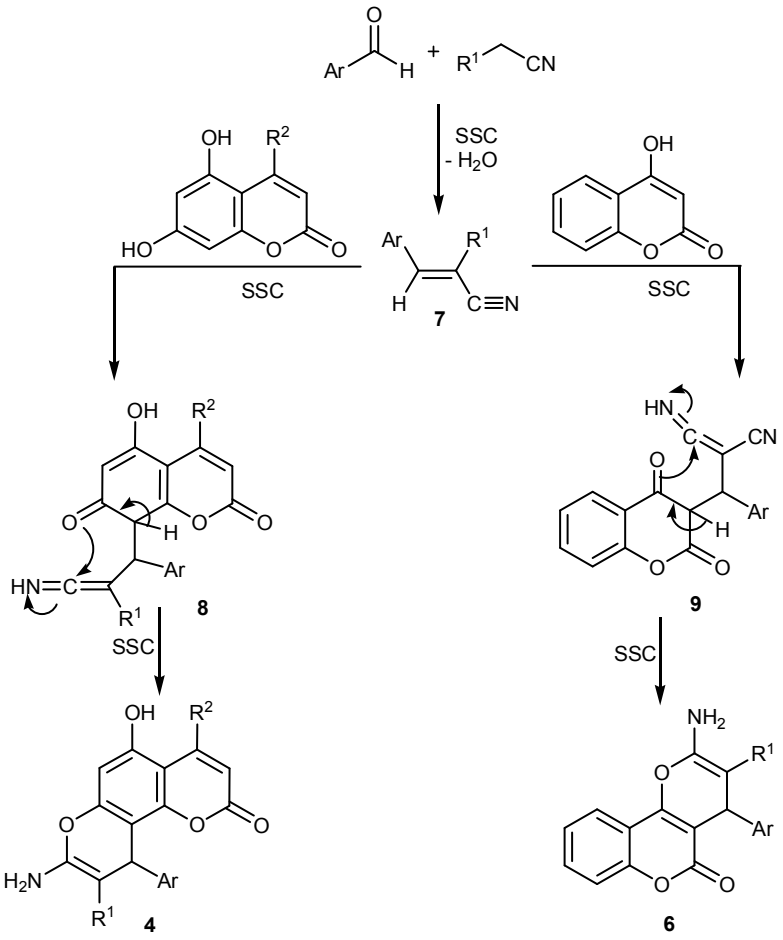


Fig. 3. Recyclability study of SSC in the synthesis of 4a at 110 °C under solvent-free conditions.



Scheme 3. Proposed mechanism for SSC-catalyzed synthesis of pyrano coumarins

produce 9 which is then converted to pyrano coumarin 6 after an intramolecular cyclization.

The major advantages of the presented protocol over existing methods can be realized by comparing our results with those of some reported procedures, as shown in Table 5. For example, use of SDS and TBBDA required high amounts of catalyst and long reaction times. In the case of piperidine and DABCO, these catalysts are not reusable. In other variations, such as DAHP, KF-Al_2O_3 and TEBA, the methods need too long reaction times.

CONCLUSIONS

Overall, novel group of hybrid heterocycles having the coumarin moiety was prepared by a mild silica sodium carbonate-catalyzed one-pot reaction of aryl aldehydes, malononitrile/ethyl cyanoacetate, and 5,7-dihydroxy-4-substituted coumarins/4-hydroxycoumarin. This work presents a simple reaction performed in the absence of dangerous organic solvents. The effective simplicity and high product yields, combined with step and atom-economic aspects, make this heterocycles synthetic strategy highly attractive. It should be mentioned that the existing of transformable functionalities in the products makes them potentially appreciated for further synthetic manipulations.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge partial support of this work by the Yasouj University, Yasouj, Iran.

Table 5. Comparison of the Present Work with other Reported Methods[a]

Entry	Conditions	Time (min)	Yield (%)
1	Piperidine (0.5 ml), EtOH, reflux	30	70 [31]
2	SDS (20 mol%), H_2O, 60 °C	120	85 [32]
3	DABCO (5 mol), 100 ºC	30	94 [33]
4	TBBDA (18 mol%), EtOH:H_2O (1:1), reflux	150	88 [34]
5	DAHP (10 mol%), H_2O:EtOH (1:1), room temperature	180	81 [35]
6	KF-Al_2O_3 (0.125 g), EtOH, reflux	240	90 [36]
7	TEBA (0.07 g), H_2O, 90 °C	420	96 [37]
8	SSC (10 mol%), solvent-free, 110 ºC	30	85[b]

[a]Synthesis of 6a. [b]Present work.

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