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ORIGINAL ARTICLE

Diastereoselective synthesis of *trans*-2, 3-dihydrofuro[3,2-c]coumarins by MgO nanoparticles under ultrasonic irradiation

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Abstract MgO nanoparticles have been used as an efficient catalyst for the diastereoselective preparation of *trans*-2-benzoyl-3-(aryl)-2H-furo[3,2-c]chromen-4(3H)-ones by the multi-component reaction of 2,4′-dibromoacetophenone, pyridine, benzaldehydes and 4-hydroxycoumarin under ultrasonic irradiation. This interesting result revealed that the pyridinium ylide assisted tandem three-component coupling reaction is highly diastereoselective. Atom economy, wide range of products, high catalytic activity, excellent yields in short reaction times, diastereoselective synthesis and environmental benignity are some of the important features of this protocol.

1. Introduction

Furocoumarins exhibit important biological properties such as anti-cancer [1], antifungal [2], antibacterial [3], vasorelaxant [4], inhibition of human CYP 1B1 isoform [5], inhibiting nuclear factor kappa B (NF-κB) [6,7], antimicrobial [8], and photobiological [9] activities. A series of new biphenyl-furocoumarin skeleton serves as promising vasodilatory candidates as well as fluorescent indicators [10]. Furocoumarins undergo photolysis when subjected to UVA radiation in solution [11]. Therefore, the development of simple methods for the synthesis of furocoumarins is still desirable and in demand. The synthesis of furocoumarins has been reported in the presence $I_2/K_2S_2O_8$ [12], mixture of AcOH and $AcONH_4$ [13], [BMIm]OH [14], Et_3N [15], N-methylimidazolium [16], and $Pd(CF_3COO)_2$ [17], 4-dimethylaminopyridine (DMAP) [18], and sodium hydroxide [19]. Some of these methods have certain drawbacks, including long reaction times, use of toxic and non-reusable catalyst and use of specific conditions. Synthesis of bioactive compounds should be facile, flexible and useful in organic synthesis. Multi-component reactions (MCRs) present a wide range of possibilities for the synthesis of bioactive compounds. The possibility of accomplishing multicomponent reactions under ultrasonic irradiations using heterogeneous catalyst could improve their efficiency in

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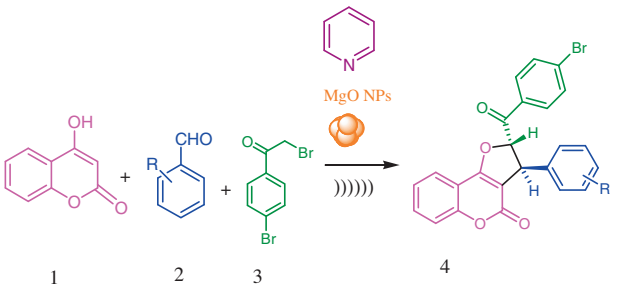

Scheme 1 One-pot syntheses of furo[3,2-c] coumarins in the presence of MgO nanoparticles under sonication conditions.

cost-effectiveness and environmental points of view. Ultrasound irradiations have been utilized to accelerate the chemical reactions proceed through the adiabatic collapse of transient cavitations bubbles. Ultrasonic cavitation has been highlighted in the fields of chemistry, materials and physics to develop reaction conditions [20,21]. Ultrasound irradiations have also been used for the synthesis of a wide variety of compounds such as (E)-Ethyl 2-cyano-3-phenylacrylate [22], arylethynyl linked triarylamines [23], tetrahydropyridines [24], pyrazolones [25]. In the present study, we combined the advantages of ultrasonic irradiations and nanotechnology for the synthesis of furo[3,2-c]coumarins. Among the various catalysts, MgO finds a widespread application as heterogeneous catalysts in various organic reactions. Recently, magnesium oxide have been used in different organic reactions such as the synthesis of tetrahydrobenzopyran and 3,4-dihydropyrano[c]chromene [26] pyranopyrazoles [27], 2-amino-4H-pyrans [28] and pyrano[3,2-c]chromene [29]. Meanwhile, magnesium oxide nanoparticles have been prepared using ultrasonic conditions of Mg-alkoxides by Stengl et al. [30], using non-hydrothermal sol–gel approach [31]. We wish to report herein a highly efficient procedure for the preparation of furo[3,2-c] coumarins using MgO nanoparticles as an efficient heterogeneous catalyst under ultrasonic irradiation (Scheme 1).

2. Experimental

2.1. Materials and apparatus

All organic materials were purchased commercially from Sigma–Aldrich and Merck and were used without further purification. Analytical thin-layer chromatography was performed with E. Merck silica gel 60F glass plates. Visualization of the developed chromatogram was performed by UV light (254 nm). A multiwave ultrasonic generator (Sonicator 3200; Bandelin, MS 73, Germany), equipped with a converter/transducer and titanium oscillator (horn), 12.5 mm in diameter, operating at 20 kHz with a maximum power output of 200 W, was used for the ultrasonic irradiation. The ultrasonic generator automatically adjusted the power level. All melting points are uncorrected and were determined in capillary tube on Boetius melting point microscope. FT-IR spectra were recorded with KBr pellets using a Magna-IR, spectrometer 550 Nicolet. NMR spectra were recorded on a Bruker 400 MHz spectrometer with $CDCl_3$ as solvent and TMS as internal standard. CHN compositions were measured by Carlo ERBA Model EA 1108 analyzer. Powder X-ray diffraction (XRD) was carried out on a Philips diffractometer of X'pert Company with monochromatized Cu Kα radiation (λ = 1.5406 Å). Microscopic morphology of catalyst was visualized by SEM (LEO 1455VP).

2.2. Preparation of magnesium oxide nanoparticles

We prepared magnesium oxide nanoparticles (NPs) in this study using ultrasound technique [29]. A solution of 1 mol/L sodium hydroxide was added drop-wise to a solution prepared from dissolving 2 g of $Mg(NO_3)_2{\cdot}6H_2O$ and 0.5 g polyvinyl pyrolydon (PVP) as surfactant. Then the reaction mixture was sonicated for 30 min ultrasonic power 90 W. The prepared gel was centrifuged and washed several times with deionized water and ethanol, and finally calcined in a furnace at 600 °C for 2 h.

2.3. General procedure for the synthesis of furo[3,2-c]coumarins

A mixture of pyridine (1 mmol) and 2,4′-dibromoacetophenone (1 mmol) was stirred for 1 min to which, subsequently, aromatic aldehydes (1 mmol), 4-hydroxycoumarin (1 mmol) and nano-MgO (3 mol%) in 5 mL ethanol was added and sonicated at 20 kHz frequency and 80 W power, for about 10 min at room temperature. After completion of the reaction (TLC), $CHCl_3$ was added. The catalyst was insoluble in $CHCl_3$ and it could therefore be recycled by a simple filtration. The solvent was evaporated and the solid obtained recrystallized from ethanol to afford the pure furo[3,2-c]coumarins. The products were characterized by IR, ^{1}H NMR, ^{13}C NMR and elemental analyses.

2.4. Spectral data

2.4.1. trans-2-4′-Bromo-benzoyl-3-phenyl-2H-furo[3,2-c]chromen-4(3H)-one (**4a**)

White powder, m.p 243–244 °C, IR (KBr) cm^{-1}: 2931, 2853, 1718, 1644, 1452, 1404, 1025, 753, 576; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.82 (d, J = 5.2 Hz, CH, 1H), 6.11 (d, J = 5.2 Hz, CH, 1H), 6.88 (t, J = 8 Hz, CH, 2H), 7.03 (t, J = 7.2 Hz, CH, 1H), 7.08 (t, J = 8 Hz, CH, 1H), 7.12 (d, J = 7.2, CH, 2H), 7.20 (t, J = 7.2 Hz, CH, 2H), 7.34 (m, CH, 1H), 7.55 (d, J = 7.4 Hz, CH, 2H), 7.84 (d, J = 7.4 Hz, CH, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 48.32 (*C*H of benzylic), 92.19 (*C*H–O), 105.22 (C of alkene), 112.22 (C of aromatic), 117.32 (*C*H of aromatic), 121.25 (*C*H of aromatic), 122.38 (*C*H of aromatic), 123.98 (*C*H of aromatic), 127.24 (*C*–Br of aromatic), 128.62 (2*C*H of aromatic), 129.22 (*C*H of aromatic), 130.50 (2*C*H of aromatic), 131.96 (2*C*H of aromatic), 133.20 (2*C*H of aromatic), 134.42 (*C*–CO of aromatic), 138.50 (C of aromatic), 155.62 (*C*–OOC of aromatic), 159.41 (*C*OO), 166.34(*C*–O of alkene), 192.03 (C═O); Anal. Calcd for $C_{24}H_{15}BrO_4$: C, 64.45; H, 3.38; found: C, 64.33; H, 3.27.

2.4.2. trans-2-4′-Bromo-benzoyl-3-(3-methylphenyl)-2H-furo[3,2-c]chromen-4(3H)-one (**4b**)

White powder, m.p 222–224 °C, IR (KBr) cm^{-1}: 2927, 2854, 1720, 1648, 1455, 1405, 1026, 753, 576; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.50 (s, CH_3, 3H), 4.80 (d, J = 4.4 Hz, CH,

1H,), 6.09 (d, J = 4.4 Hz, CH, 1H), 7.04 (d, J = 7.2 Hz, CH, 1H), 7.07 (s, CH, 1H), 7.10 (d, J = 7.6 Hz, CH, 1H), 7.15 (t, J = 8 Hz, CH, 2H), 7.25 (t, J = 7.4 Hz, CH, 1H), 7.34 (m, CH, 1H), 7.60 (d, J = 8 Hz, CH, 1H), 7.65 (d, J = 7.4 Hz, 2H), 7.80 (d, J = 7.4 Hz, CH, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2 (CH_3), 48.78 (*C*H of benzylic), 92.11 (*C*H–O), 104.54 (C of alkene), 112.02 (C of aromatic), 117.22 *C*H of aromatic), 120.93 (*C*H of aromatic), 122.31 (*C*H of aromatic), 124.25 (*C*H of aromatic), 127.23 (*C*H of aromatic), 127.99 (C–Br of aromatic), 128.32 (*C*H of aromatic), 128.45 (*C*H of aromatic), 129.11 (*C*H of aromatic), 130.51 (2*C*H of aromatic), 132.46 (2*C*H of aromatic), 133.25 (*C*–CO of aromatic), 134.40 (*C*–CH_3 of aromatic), 139.12 (*C* of aromatic), 155.61 (*C*–OOC of aromatic), 159.42 (*C*OO), 166.36 (*C*–O of alkene), 192.02 (*C*═O); Anal. calcd for $C_{25}H_{17}BrO_4$: C, 65.09; H, 3.71; found: C, 65.16; H, 3.88.

2.4.3. trans-2-4′-Bromo-benzoyl-3-(2-methylphenyl)-2H-furo [3,2-c]chromen-4(3H)-one (**4c**)

White powder, m.p 171–173 °C, IR (KBr) cm^{-1}: 2923, 2851, 1721, 1645, 1453, 1407, 1029, 575; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43(s, CH_3, 3H), 5.20 (d, J = 5.6 Hz, CH, 1H), 6.02 (d, J = 5.6 Hz, CH, 1H), 6.89 (m, 1H), 7.27 (d, J = 7.2 Hz, CH, 1H), 7.30 (d, J = 7.4 Hz, CH, 1H), 7.45(m, 3H), 7.60 (t, J = 8.8 Hz, 1H), 7.67 (d, J = 7.4 Hz, CH, 1H), 7.75 (d, J = 8.8 Hz, CH, 2H); 7.83 (d, J = 8.8 Hz, CH, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 22.3 (CH_3), 48.79 (*C*H of benzylic), 92.14 (*C*H–O), 104.63 (C of alkene), 112.05 (C of aromatic), 117.25(*C*H of aromatic), 120.95 (*C*H of aromatic), 122.33 (*C*H of aromatic), 124.26 (*C*H of aromatic), 127.25 (*C*H of aromatic), 128.08 (C–Br of aromatic), 128.48 (*C*H of aromatic), 129.14 (*C*H of aromatic), 130.57 (*C*H of aromatic), 130.59 (*C*H of aromatic), 132.46 (*C*H of aromatic), 133.27 (*C*–CH_3 of aromatic), 134.44 (*C*–CO of aromatic), 139.15 (*C* of aromatic), 155.64 (*C*–OOC of aromatic), 159.44 (COO), 166.37 (*C*–O of alkene), 192.10 (*C*═O); Anal. calcd for $C_{25}H_{17}BrO_4$: C, 65.09; H, 3.71; found: C,65.12; H, 3.82.

2.4.4. trans-2-4′-Bromo-benzoyl-3-(4-chlorophenyl)-2H-furo [3,2-c]chromen-4(3H)-one (**4d**)

White powder, m.p 250–252 °C, IR (KBr) cm^{-1}: 2924, 2824, 1722, 1646, 1412, 1024, 752, 534; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 4.77 (d, J = 5.0 Hz, CH, 1H), 6.63 (d, J = 5.0 Hz, CH, 1H,), 7.22 (t, J = 8 Hz, CH, 2H), 7.26 (d, J = 8 Hz, CH, 2H), 7.29 (t, J = 8 Hz, CH, 1H), 7.32 (d, J = 8 Hz, CH, 2H), 7.50 (d, J = 8 Hz, CH, 1H), 7.70 (d, J = 8.4 Hz, CH, 2H), 8.03 (d, J = 8 Hz, CH, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 49.66 (*C*H of benzylic), 93.51 (*C*H–O), 105.22 (C of alkene), 112.20 (*C* of aromatic), 117.35(*C*H of aromatic), 121.28 (*C*H of aromatic), 122.45 (*C*H of aromatic), 126.32 (C–Br of aromatic), 127.25 (*C*H of aromatic), 128.63 (2*C*H of aromatic), 129.19 (2*C*H of aromatic), 130.59 (2*C*H of aromatic), 133.04 (*C*–Cl of aromatic), 133.21 (2*C*H of aromatic), 135.14 (*C*–CO of aromatic), 139.15 (*C* of aromatic), 155.60 (*C*–OOC of aromatic), 159.42 (COO), 166.42 (*C* of alkene), 192.24 (*C*═O); Anal. calcd for $C_{24}H_{14}BrClO_4$: C, 59.84; H, 2.93; found: C, 59.75; H, 2.82.

2.4.5. trans-2-4′-Bromo-benzoyl-3-(2-chlorophenyl)-2H-furo [3,2-c]chromen-4(3H)-one (**4e**)

White powder, m.p 219–221 °C, IR (KBr) cm^{-1}: 2922, 2853, 1718, 1644, 1453, 1402, 1024, 755, 574; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.58 (d, J = 5.2 Hz, CH, 1H), 6.08 (d, J = 5.2 Hz, CH, 1H), 7.17–7.31 (m, 3H), 7.37 (d, J = 7.4 Hz, CH, 1H), 7.40 (d, J = 7.4 Hz, CH, 1H), 7.43 (t, J = 8.2 Hz, CH, 1H), 7.55 (d, J = 7.2 Hz, CH, 1H), 7.65 (d, J = 8.2 Hz, CH, 1H), 7.70 (d, J = 8.0 Hz, CH, 2H), 7.96 (d, J = 8.0 Hz, CH, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 48.82 (CH of benzylic), 92.19 (*C*H–O), 105.12 (C of alkene), 112.14 (C of aromatic), 117.28 (CH of aromatic), 121.08 (*C*H of aromatic), 122.36 (*C*H of aromatic), 124.28 (*C*H of aromatic), 127.28 (*C*H of aromatic), 128.17 (C–Br of aromatic), 128.57 (*C*H of aromatic), 129.24 (*C*H of aromatic), 130.58 (*C*H of aromatic), 130.69 (2*C*H of aromatic), 132.54 (2*C*H of aromatic), 133.27 (*C*–Cl of aromatic), 134.41 (*C*–CO of aromatic), 139.14 (*C* of aromatic), 155.62 (*C*–OOC of aromatic), 159.42 (COO), 166.38 (*C*–O of alkene), 192.18 (*C*═O); Anal. calcd for $C_{24}H_{14}BrClO_4$: C, 59.84; H, 2.93; found: C, 59.72; H, 2.79.

2.4.6. trans-2-4′-Bromo-benzoyl-3-(2-nitrophenyl)-2H-furo [3,2-c]chromen-4(3H)-one (**4f**)

White powder, m.p 232–234 °C, IR (KBr) cm^{-1}: 2926, 2843, 1725, 1647, 1518, 1406, 1028, 745, 576; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.14 (d, J = 4.8 Hz, CH, 1H,), 6.05 (d, J = 4.8 Hz CH, 1H), 7.35 (m, 2H), 7.39 (t, J = 8.2 Hz, 1H), 7.42 (d, J = 8 Hz, CH, 1H,), 7.45 (m, 1H), 7.55 (d, J = 7.4 Hz, CH, 1H), 7.64 (d, J = 8 Hz, CH, 2H), 7.80 (t, J = 7.4 Hz, CH, 1H), 7.95 (d, J = 8 Hz, 2H) 8.17 (d, J = 7.6 Hz, CH, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 48.95 (CH of benzylic), 93.12 (*C*H–O), 105.29 (C of alkene), 112.26 (*C* of aromatic), 117.35 (*C*H of aromatic), 121.28 (*C*H of aromatic), 122.39 (*C*H of aromatic), 124.29 (*C*H of aromatic), 127.28 (*C*H of aromatic), 128.2 (C–Br of aromatic), 128.69 (*C*H of aromatic), 129.28 (*C*H of aromatic), 130.04 (2*C*H of aromatic), 130.69 (2*C*H of aromatic), 132.55 (*C*H of aromatic), 133.29 (*C* of aromatic), 134.45 (*C*–CO of aromatic), 139.16 (*C*–NO_2 of aromatic), 155.65 (*C*–OOC of aromatic), 159.45 (*C*OO), 166.48 (C–O alkene), 193.03 (*C*═O); Anal. calcd for $C_{24}H_{14}BrNO_6$: C, 58.56; H, 2.87; N, 2.85; found: C, 58.43; H, 2.77; N, 2.79.

2.4.7. trans-2-4′-Bromo-benzoyl-3-(4-methylthiophenyl)-2H-furo[3,2-c]chromen-4(3H)-one (**4g**)

White powder, m.p 206–208 °C, IR (KBr) cm^{-1}: 2925, 2829, 1724, 1647, 1406, 1027, 754, 538; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.66 (s, CH_3, 3H), 4.77 (d, J = 4.8 Hz, CH, 1H), 6.07 (d, J = 4.8 Hz, CH, 1H), 7.16 (m, 4H), 7.25 (t, J = 8.2 Hz, CH, 1H), 7.30 (d, J = 7.4 Hz, CH, 2H), 7.35 (d, J = 8 Hz, CH, 1H), 7.41 (d, J = 8.2 Hz, CH, 2H), 7.87 (d, J = 8.2 Hz, CH, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 15.68 (CH_3S), 48.80 (CH of benzylic), 92.04(CH–O), 104.52 (*C* of alkene), 112.03 (*C* of aromatic), 117.21 (*C*H of aromatic), 120.94 (*C*H of aromatic), 122.31 (*C*H of aromatic), 124.24 (2*C*H of aromatic), 127.22 (C–Br of aromatic), 127.99 (2*C*H of aromatic), 128.32 (*C*H of aromatic), 130.53 (2*C*H of aromatic), 132.46 (2*C*H of aromatic), 133.25 (*C*–SCH_3 of aromatic), 134.40 (*C*–CO of aromatic), 139.17 (*C* of aromatic),

155.61 (*C*–OOC of aromatic), 159.42 (COO), 166.38 (*C*–O of alkene), 192.03 (C═O). Anal. calcd for $C_{25}H_{17}BrO_4S$: C, 60.86; H, 3.47; found: C, 60.74; H, 3.54.

*2.4.8. trans-2-4′-Bromo-benzoyl-3-(4-bromophenyl)-2H-furo[3,2-c]chromen-4(3H)-one (**4h**)*

White powder, m.p 256–258 °C, IR (KBr) cm^{-1}: 2919, 2821, 1718, 1644, 1402, 1024, 751, 535; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.86 (J = 5.2 Hz, CH, 1H), 6.05 (J = 5.2 Hz, CH, 1H), 7.18 (d, J = 7.4 Hz, CH, 2H), 7.20 (d, J = 8.2 Hz, CH, 2H), 7.23 (m, 1H), 7.30 (d, J = 8 Hz, CH, 1H), 7.34 (d, J = 7.4 Hz, CH, 2H), 7.50 (d, J = 8 Hz, CH, 2H), 7.93 (d, J = 8 Hz, CH, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 48.51 (CH of benzylic), 92.28 (*C*H–O), 105.24 (*C* of alkene), 112.24 (*C* of aromatic), 117.31 (C–Br of aromatic), 121.25 (*C*H of aromatic), 122.38 (*C*H of aromatic), 124.21 (*C*H of aromatic), 127.22 (C–Br of aromatic), 128.51 (*C*H of aromatic), 129.17 (2*C*H of aromatic), 130.57 (2*C*H of aromatic), 132.53 (2*C*H of aromatic), 133.21 (2*C*H of aromatic), 134.42 (*C*–CO of aromatic), 139.14 (*C* of aromatic), 155.62 (*C*–OOC of aromatic), 159.43 (*C*OO), 166.44 (C–O of alkene), 192.16 (C═O); Anal. calcd for $C_{24}H_{14}Br_2O_4$: C, 54.78; H, 2.68; found: C, 54.61; H, 2.55.

*2.4.9. trans-2-4′-Bromo-benzoyl-3-(4-nitrophenyl)-2H-furo[3,2-c]chromen-4(3H)-one (**4i**)*

White powder, m.p 250–252 °C, IR (KBr) cm^{-1}: 2934, 2853, 1727, 1647, 1522, 1410, 747, 575; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.17 (d, J = 4.8 Hz, CH, 1H), 6.07 (d, J = 4.8 Hz, CH, 1H), 7.34 (m, 2H), 7.39 (t, J = 8 Hz, CH, 1H), 7.42 (d, J = 8 Hz, CH, 1H), 7.47 (d, J = 8.4 Hz, CH, 2H), 7.50 (d, J = 7.6 Hz, CH, 2H), 7.92 (d, J = 7.6 Hz, CH, 2H), 8.12 (d, J = 8.4 Hz, CH, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 49.04 (CH of benzylic), 93.50(*C*H–O), 105.24 (*C* of alkene), 112.28 (*C* of aromatic), 117.38 (2*C*H of aromatic), 121.29 (*C*H of aromatic), 122.43 (*C*H of aromatic), 124.33 (*C*H of aromatic), 126.54 (C–Br of aromatic), 127.37 (*C*H of aromatic), 128.33 (2*C*H of aromatic), 128.39 (2*C*H of aromatic), 129.44 (*C*H of aromatic), 131.73 (*C*–CO of aromatic), 132.54 (*C*–NO_2 of aromatic), 139.16 (*C* of aromatic), 155.71 (*C*–OOC of aromatic), 159.48 (*C*OO), 166.52 (*C*–O of alkene), 193.10 (C═O); Anal. calcd for $C_{24}H_{14}BrNO_6$: C, 58.56; H, 2.87; N, 2.85; found: C, 58.47; H, 2.79; N, 2.80.

*2.4.10. trans-2-4′-Bromo-benzoyl-3-(4-methylphenyl)-2H-furo[3,2-c]chromen-4(3H)-one (**4j**)*

White powder, m.p 204–206 °C, IR (KBr) cm^{-1}: 2932, 2862, 1721, 1646, 1458, 1403, 1025, 756, ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.45 (s, CH_3, 3H), 5.58 (d, J = 5.4 Hz, CH, 1H), 6.08 (d, J = 5.4 Hz, CH, 1H), 7.02(d, J = 7.4 Hz, CH, 2H), 7.05 (d, J = 7.4 Hz, CH, 2H), 7.12 (m, CH, 2H), 7.16 (t, J = 8 Hz, CH, 1H), 7.20 (d, J = 8 Hz, CH, 1H), 7.55(d, J = 7.6 Hz, CH, 2H), 7.95 (d, J = 7.6 Hz, CH, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.5 (CH_3), 48.65 (CH of benzylic), 92.05 (*C*H–O), 104.52 (*C* of alkene), 111.95 (*C* of aromatic), 117.18 (*C*H of aromatic), 120.82 (*C*H of aromatic), 124.22 (*C*H of aromatic), 127.83 (C–Br of aromatic), 128.45 (2*C*H of aromatic), 128.65 (*C*H of aromatic), 129.14 (2*C*H of aromatic), 130.32 (2*C*H of aromatic), 132.42 (2*C*H of aromatic), 133.18 (*C*–CH_3 of aromatic), 134.32 (*C*–CO of aromatic), 139.02 (*C* of aromatic), 155.55 (C–OOC of aromatic), 159.44 (*C*OO), 166.30 (*C*–O of alkene), 192.14 (C═O); Anal. calcd for $C_{25}H_{17}BrO_4$: C, 65.09; H, 3.71; found: C, 65.21; H, 3.85.

3. Results and discussion

3.1. Structural analysis of MgO nanoparticles

In order to study the morphology and particle size of MgO nanoparticles, scanning electron microscopy (SEM) image of MgO NPs is presented in Fig. 1. The crystalline nature of the synthesized MgO NPs sample was further verified by X-ray diffraction pattern (XRD). The crystallite size diameter (D) of the MgO NPs has been calculated by the Debye–Scherrer equation ($D = K\lambda/\beta\cos\theta$). The results show that MgO NPs, were gained with an average diameter of 18 nm (Fig 2).

3.2. Synthesis of furo[3,2-c]coumarins under ultrasonic irradiation

The choice of an appropriate reaction medium is of vital importance for successful synthesis. Initially, we had explored and optimized different reaction parameters for the synthesis of furo[3,2-c]coumarins by the multi-component reaction of 2,4′-dibromoacetophenone, pyridine, benzaldehyde, and 4-hydroxycoumarin as a model reaction. The model reactions were carried out in the presence of various catalysts, such as *p*-TSA, $SnCl_2$, NEt_3, DBU, CuI, ZnO, CuO, CaO, MgO and nano-MgO. When the reaction was carried out using CaO, MgO and nano-MgO as the catalyst, the product could be obtained in a moderate to good yield. Several reactions were scrutinized using various solvents such as EtOH, CH_3CN, water, and DMF. The best results were obtained under ultrasonic irradiation in ethanol and found that the reaction gave satisfying results in the presence of MgO nanoparticles at 3 mol% which gave excellent yields of products. (Table 1). When 1, 3 and 5 mol% of nano-MgO nanoparticles were used; the yields were 82%, 91% and 91%, respectively. Consequently, 3 mol% of nano-MgO were expedient and excessive amount of nano-MgO did not change the yields, significantly. Nanoparticles exhibit a good catalytic activity owing to their

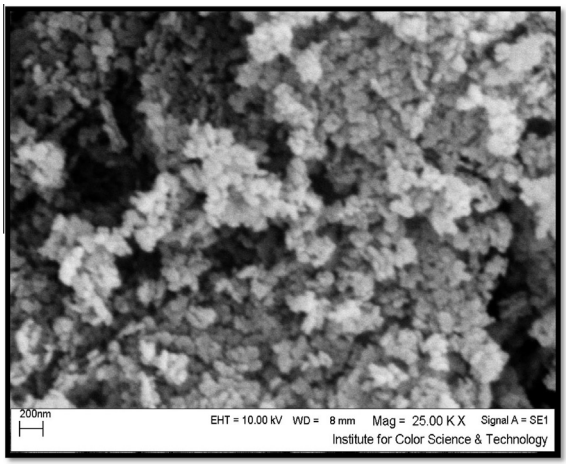

Figure 1 SEM image of the nano-MgO.

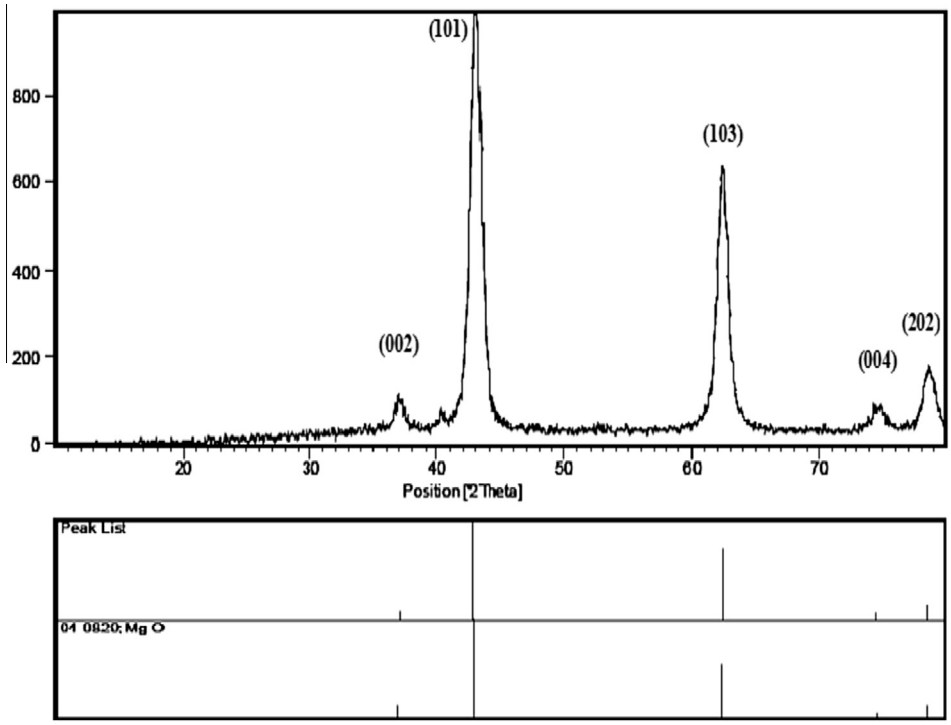

Figure 2 XRD pattern of nano-MgO.

Table 1 Optimization of the model reaction using various catalysts.[a]

Entry	Catalyst	Solvent[c]	mol%	Time (min) (thermal)	Yield %[b] (thermal)	Time (min) (ultrasonic)	Yield %[b] (ultrasonic)
1	*p*-TSA	EtOH	2	420	5	30	18
2	$SnCl_2$	EtOH	4	420	10	30	23
3	$SnCl_2$	CH_3CN	4	400	14	30	29
4	Et_3N	EtOH	10	250	33	25	53
5	Et_3N	H_2O	10	200	38	25	60
6	DBU	EtOH	7	300	23	25	42
7	DBU	H_2O	5	300	30	25	48
8	Nano-CuI	EtOH	5	300	18	25	35
9	Nano-CuI	H_2O	6	300	12	25	28
10	Bulk MgO	EtOH	5	110	40	20	64
11	Nano-MgO	EtOH	1	90	58	15	82
12	**Nano-MgO**	**EtOH**	**3**	**90**	**62**	**10**	**91**
13	Nano-MgO	EtOH	5	90	62	10	91
14	Nano-MgO	CH_3CN	3	90	53	10	79
15	Nano-MgO	H_2O	3	90	38	10	52
16	Nano-MgO	DMF	3	90	48	10	67
17	Nano-ZnO	EtOH	4	180	33	28	50
18	Nano-CuO	EtOH	5	160	36	25	53
19	Nano-CaO	EtOH	5	140	42	20	60
20	Nano-CaO	CH_3CN	5	140	34	20	48

[a] 2,4′-Dibromoacetophenone (1 mmol), benzaldehyde (1 mmol), 4-hydroxycoumarin (1 mmol).
[b] Isolated yield.
[c] Under reflux condition.

large number of active sites which are mainly responsible for their catalytic activity. Nanoparticle of magnesium oxide catalyst has a multidimensional structure in three dimensions with a high level of edge and corner that is caused by the inherent high reactivity [31].

With these hopeful results in hand, we turned to investigate the scope of the reaction by various aromatic aldehydes as substrates under the optimized reaction conditions (Table 2).

We also investigated recycling of the MgO NPs as catalyst under ultrasonic irradiation in ethanol (Fig. 3). After the

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Table 2 Synthesis of furo[3,2-c]coumarins using nano-MgO under ultrasonic conditions.

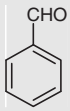
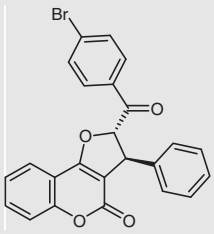
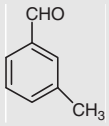
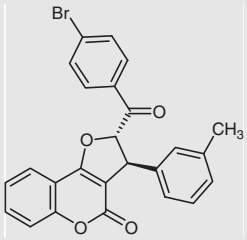
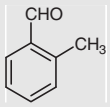
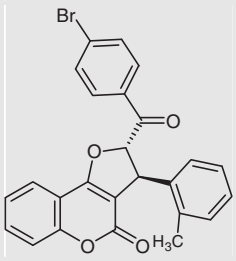
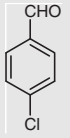
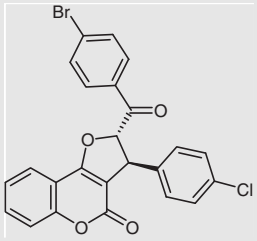
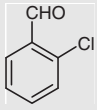
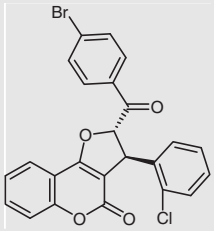
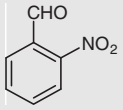
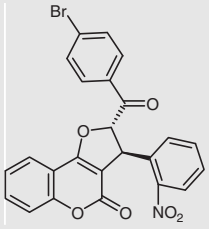
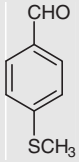
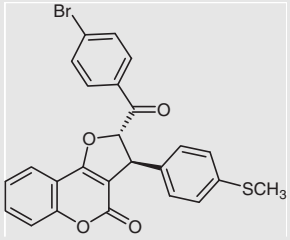
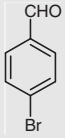
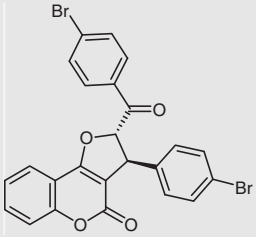
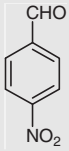
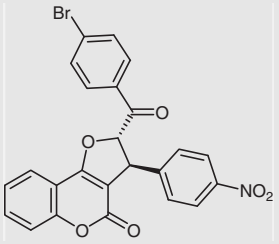
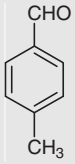
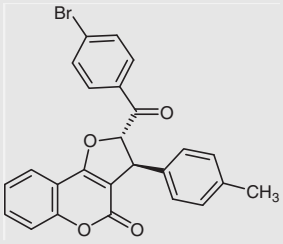
Entry	Aldehyde	Product	Product	Time (min)	Yield %[a]	m.p °C
1		4a		10	91	243–244
2		4b		15	86	22–224
3		4c		15	85	171–173
4		4d		10	92	250–252
5		4e		10	91	219–221
6		4f		10	92	232–234
7		4 g		15	85	206–208

Table 2 (*continued*)

Entry	Aldehyde	Product	Product	Time (min)	Yield %[a]	m.p °C
8		4 h		10	92	256–258
9		4i		10	91	250–252
10		4j		15	85	204–206

[a] Isolated yield.

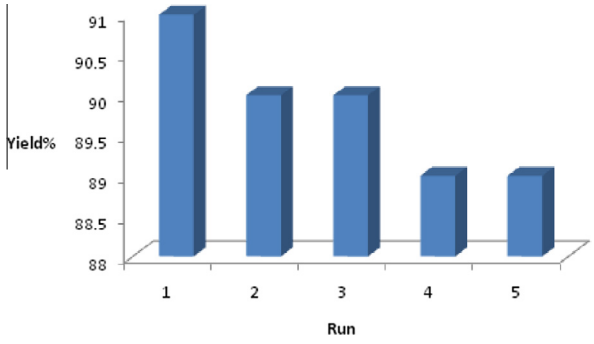


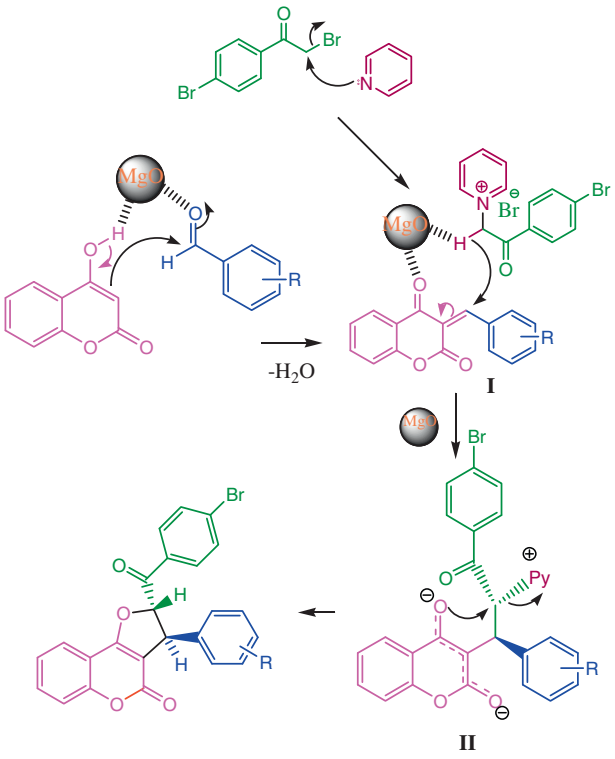
Figure 3 Recycling of the MgO NPs.

completion of the reaction (TLC), $CHCl_3$ was added. The catalyst was insoluble in $CHCl_3$ and it could therefore be recycled by a simple filtration. The nanoparticles were then washed three to four times with methanol and dried at 80 °C for 7 h. The catalyst could be reused for five times with a minimal loss of activity (yields 91 to 89). Perhaps, activity of MgO NPs is decreased by the number of regenerations.

The number of active cavitations bubbles and also the size of the individual bubbles increase the collapse temperature and reaction could be accelerated. The presence of dispersed nanoparticles in solution in sonication supplies additional nucleation sites for cavity creation over its surface, enhancing the number of micro-bubbles in the solution. In addition, this fact has been proven to be influenced by the roughness of the nanoparticles. Dispersed nanoparticles can act as a wall for the bubbles transmission, forming an asymmetric collapse of the cavitation bubbles and leading to the creation of a large number of tiny bubbles in the liquid solution. The increasing microcavities which were produced by above mentioned effects can improve the efficiency of the sonication technique [32,33].

A plausible mechanism for the preparation of furo[3,2-c] coumarins using nano-MgO is shown in Scheme 2. Firstly, we assumed that the reaction occurs *via* the Knoevenagel condensation between benzaldehyde and 4-hydroxycoumarin to form the intermediate **I** on the active sites of nano-MgO which are mainly responsible for their catalytic activity. Then, the Michael addition of pyridiniumylide with enones affords the zwitterionic intermediate and followed by cyclization affords the titled product. The final step is a classic intramolecular S_N2 substitution reaction. The stereochemistry of the S_N2 reaction necessitated nucleophilic enolate attack from the back side of the electrophilic carbon atom bearing the leaving pyridinium group, which afterward assumes 2-benzoyl and 3-aryl groups in a stereo-chemical opposite position for the sake of steric hindrance in transition states. Thus, only *trans* isomeric 2,3-dihydrofuran is obtained as the only product [16].

The observed stereoselective formation of *trans*-2-benzoyl-3-(aryl)-2H-furo[3,2-c]chromen-4(3H)-ones is in agreement with the lower heat of formation of trans-isomer, which is more stable than its cis isomer, as estimated using PM3 calculations [14]. The structures of the prepared *trans*-2-ben zoyl-3-(aryl)-2H-furo[3,2-c]chromen-4(3H)-ones were fully characterized by ^1H and ^{13}C NMR and IR spectra and elemental analysis. For example, in the ^1H NMR spectra of **4f,** the two protons at 2,3-position of dihydrofuran ring display two doublets at 5.14 and 6.05 ppm with the vicinal coupling constant $J = 4.8$ Hz. The similar peak pattern and coupling



Scheme 2 Possible mechanism for the synthesis of furo[3,2-c]coumarins in the presence of nano-MgO.

constant less than 6.0 Hz were also seen in the other ^{1}H NMR spectra of prepared furo[3,2-c]chromen derivatives. It has been established that in *cis*-2,3-dihydrofuran the vicinal coupling constant of the two methine protons J = 7–10 Hz, while in *trans*-2,3-dihydrofuran vicinal coupling constant J = 4–7 Hz [15].

4. Conclusions

In conclusion, we have developed the sonochemical synthesis of *trans*-2-benzoyl-3-(aryl)-2H-furo[3,2-c]chromen-4(3H)-ones catalyzed by MgO nanoparticles as the catalyst. These heterocycles will provide promising candidates for chemical biology and drug discovery. The present method tolerates most of the substrates, and the catalyst can be recycled at least five times without considerable loss of activity. The advantages of this method are the use of an efficient catalyst, reusability of the catalyst, little catalyst loading, low reaction times and easy separation of products.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jscs.2016.01.003.

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