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RESEARCH ARTICLE

Synthesis of new N-arylhydrazone derivatives of 7- N-benzylamino-2-Oxo-2H-chromene-3-carbohydrazide using CuO nanocatalyst

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Abstract

A series of N-Arylhydrazone derivatives of N-benzylamino-2-Oxo-2H-chromene-3- carbohydrazide were synthesized. The ethyl-7-aminocoumarin-3-carboxylate used as appropriate starting material for synthesis of ethyl-N-benzylamino-2-Oxo-2H-chromene-3- carboxylate as the key intermediate by N-benzylation of amino group via nucleophilic substitution reaction. Reaction of the key intermediate ethyl-N-benzylamino-2-Oxo-2H-chromene-3- carboxylate with hydrazine hydrate yield the corresponding hydrazide derivative.

The target compounds were synthesized by CuO nanoparticles catalyzed condensation of the hydrazide with the corresponding aromatic ketone/aldehydes and their structures were confirmed by IR and NMR techniques.

INTRODUCTION

Hydrazones consisting -NHN=CH- group, have been found as an important class of compounds for new drug developments. Therefore, a variety of these ompounds have been synthesized as target products that possess varied biological activities (Lau et al., 1999) Hydrazones have been developed to possess, antimycobacterial, anticonvulsant, analgesic and anti-inflammatory (Kalsi et al., 2006), antimalarial (Walcourt et al.,2004, Gemma et al., 2006), anticancer (Bernardino et al., 2006, Terzioglu et al., 2003) antiviral (Savini et al., 2004) and other biological activities(8. Silva et al., 2005). So in the present study catalytic amount of nano CuO was used for synthesis of some novel N- arylhydrazone based on 7- N-benzylamino coumarin. Copper oxide nanoparticles have been of considerable interest because of the role of CuO in catalysis of organic reactions and other applications such as gas sensors and semiconductors (Rahnama and Gharagozlou, 2012).The application of copper oxide nanoparticles for organic reactions has attracted huge attention in recent years [Sadjadi et al., 2010, Alonso et al., 2012 Albadi et al. 2012, Ahmadi et al., 2011). Because this class of catalysts appears as one of the most promising solutions toward efficient reactions under mild conditions in the context of green chemistry (Nezhad et al., 2011, Mehrabi et al., 2011

Experimental

All chemicals were purchased from Aldrich and Merck and other companies with highly pure synthetic grade and used without any purification.

All melting points were obtained by Electrothermal IA9000 apparatus and are uncorrected. 1H and 13C NMR spectra were recorded in DMSO-d6 on a Bruker 500 MHz spectrometer. Infrared spectra were recorded by Bruker FTIR.

Equinax-55 spectrophotometer in KBr with absorption in cm_1. All products were characterized by their spectra and physical data.

Synthesis of nano sized -CuO

Solution of NaOH (75 mL, 0.1 mol/L) was added to solution of Cu(CH3COO)2.2H2O (0.1 mol/L) in ethanol-water. The obtained mixtures were sonicated for 30 min with 50 W ultrasound power. To investigate the role of

surfactants on the size and morphology of nanoparticles, we used 1 g of polyvinyl alcohol (PVA) in the reaction. The morphology, structure and size of the samples were investigated by Scanning Electron Microscopy (SEM). Fig. 1 indicates that the original morphology of the particle was approximately spherical with the diameter varying between appropriate nanosized paticles.

Synthesis of ethyl-N-benzylamino-2-Oxo-2H-chromene-3- carboxylate (3)

4-N-benzylamino salicylaldehyde **(1)** (0.01 mol) and diethylmalonate **(2)** (0.01 mol) were dissolved in ethanol to give clear solution. Piperidine (2 mL) was added and the mixture was refluxed for 5 h. The solution was concentrated to small volume. The product (**3)** was poured onto crushed ice, filtered out and crystallized from ethanol to give white shiny crystals, M.p. 120-122OC; Yield: 90%; IR (KBr, cm-1) 1710 (CO, coumarin), 1670 (C=O), 1750 (C=O, ester), 1200 (C-O); 1HNMR (DMSO-d6, 300 MHz), ppm: 7.5 (4H, m, Ar-H), 8.1 (1H, s, Ar-H, H-4), 1.83 (3H, t).

Synthesis of* N-benzylamino-2-Oxo-2H-chromene-3- carbohydrazide *(4):

A solution of **(3)** (2 mmole) in ethanol and 80% hydrazine hydrate (10mmole) refluxed for 10 hrs and poured into crushed ice –water mixture. The precipitate was filtered and recrystallized with diethyl ether.

Synthesis of N-arylhydrazone derivatives of* N-benzylamino-2-Oxo-2H-chromene-3- carbohydrazide *(5a-g):

A mixture of 1.9 mmol of hydrazide (4) and 1.9 mmol of the corresponding aldehyde/ ketone derivative in 20 ml of absolute ethanol and 0.05 mmol CuO nanocatalyst was stirred under reflux for 4 to10 hours. The progress of the reaction was observed by TLC, and the hydrazones **5a-g** were isolated by concentration of the reaction mixture under reduced pressure. The resulting precipitate was filtered, washed with 10 ml water and crystallized from a suitable solvent.

Results and discussion:

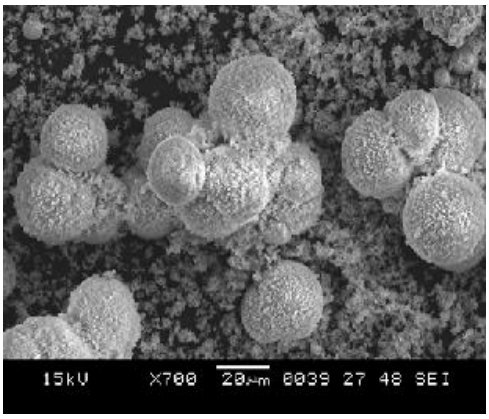
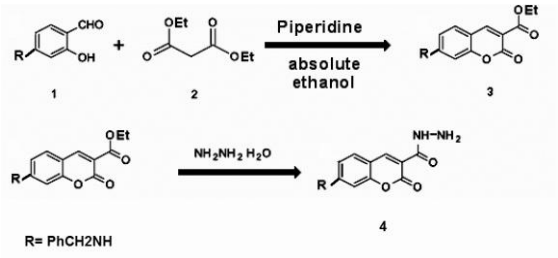
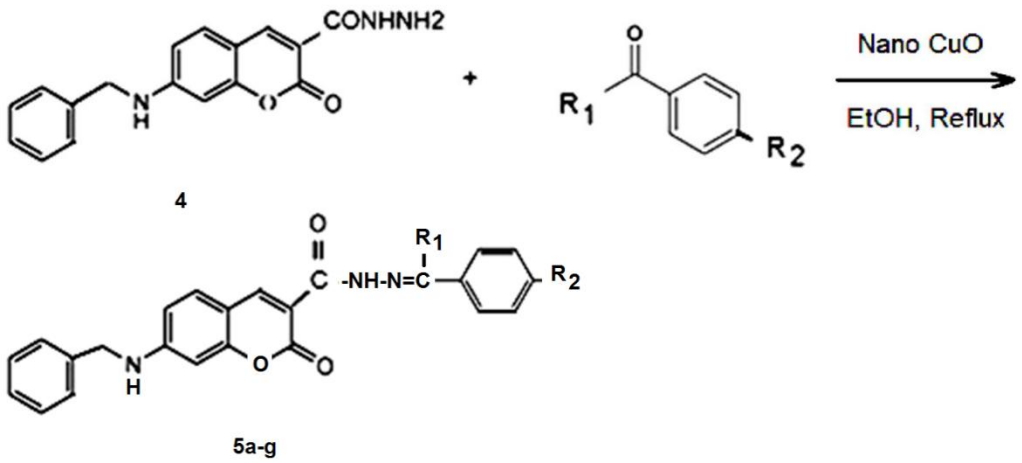


Fig. 1: SEM image of synthesized CuO nanoparticles

The synthesized compounds were recognized by IR and 1H NMR spectral analysis. The compound(4), N-benzylamino-2-Oxo-2H-chromene-3- carbohydrazide
were obtained by the compound (3), on further treatment with hydrazine hydrate in ethanol (scheme1) and finally hydrazide (4) reacted with different aromatic aldehyde/ketones in the presence of catalytic amount of CuO nanocatalyst yields different N-arylhydrazone derivatives of N-benzylamino-2-Oxo-2H-chromene-3-carbohydrazide (Scheme 2). The yield was found to be in the range of 60-70%.



Scheme 1- preparation of starting materials



Scheme 2- preparation of final hydrazone products

Table 1- melting points and yield percent of the 5a-5g products

Compound	R1	R2	M.P. (°C)	Yield(%)
5a	H	H	161	73
5b	H	CH3	172	76
5c	H	NO2	166	61
5d	CH3	H	184	68
5e	CH3	CH3	178	78
5f	CH3	NO2	245	64
5g	CH3	Cl	202	72

Table 2-Spectral data of the 5a-5g products

Compound	IR & H1-NMR
5a	IR (cm-1): 1654, 1699 (C=O), 3421, 3315 (NH), 1517 (C=N), 3020, 3067 (Ar-CH), 2960 (methylene C-H) 1HNMR (δ ppm): 6.77-7.74 (m, 14 H, Ar), 9.37 (b 1H, NH), 10.15 (s, 1H, NH), 5.61 (s, 1H, CH), 3.4 (s, 2H, CH2)
5b	IR (Cm-1): 1653, 1690 (C=O), 3423, 3319 (NH), 1519 (C=N), 3020, 3059 (Ar-CH), 2962, 2985 (Methyl and methylene C-H) 1HNMR (δ ppm):6.75-7.46 (m, 13 H), 9.36 (b, 1H, NH), 10.15 (s, 1H, NH), 5.8 (s, 1H, CH), 3.4 (s, 2H, CH2), 2.35(s, 3H, methyl protons)
5c	IR (cm-1): 1656, 1709 (C=O), 3514, 3356 (NO2), 3425, 3317 (NH), 1522 (C=N), 3020, 3067, 3035 (Ar-CH), 2966 (methylene C-H) 1HNMR (δ ppm): 6.77-8.44 (m, 13 H, Ar), 9.41 (b 1H, NH), 10.25 (s, 1H, NH), 1.71 (s, 1H, CH), 3.45(s, 2H, CH2)
5d	IR (cm-1): 1657, 1695 (C=O), 3422, 3314 (NH), 1520 (C=N), 3023, 3068 (Ar-CH), 2960, 2983 (methyl and methylene C-H) 1HNMR (δ ppm): 6.67-7.44 (m, 14 H, Ar), 9.41 (b 1H, NH), 10.25 (s, 1H, NH), 3.45(s, 2H, CH2), 2.53(s, 3H, methyl protons)
5e	IR (cm-1): 1654, 1699 (C=O), 3421, 3315 (NH), 1517 (C=N), 3020, 3067 (Ar-CH), 2960 (methylene C-H), 2963, 2980 (methyl and methylene C-H) 1HNMR (δ ppm): 6.61-7.48 (m, 13 H, Ar), 9.47 (b 1H, NH), 10.30 (s, 1H, NH), 3.41(s, 2H, CH2), 2.31(3H, tolyl CH3 group), 2.4(3H methyl on imine carbon)

5f	IR (cm-1): 1666, 1712 (C=O), 3510, 3366 (NO2), 3428, 3327 (NH), 575 (C=N), 3026, 3057, 3030 (Ar-CH), 2961 (methylene C-H) 1HNMR (δ ppm): 6.67-8.40 (m, 13 H, Ar), 9.31 (b 1H, NH), 10.20 (s, 1H, NH), 3.45(s, 2H, CH2), 2.39(3H methyl on imine carbon)
5g	IR (cm-1): 1656, 1716 (C=O), 3418, 3320 (NH), 1525 (C=N), 3016, 3059, 3030 (Ar-CH), 2961 (methylene C-H) 1HNMR (δ ppm): 6.60-7.40 (m, 13 H, Ar), 9.52 (b 1H, NH), 10.26 (s, 1H, NH), 3.40(s, 2H, CH2), 2.40(3H methyl on imine carbon)

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