Green and Efficient Synthesis and Characterization of Amino Chromene Derivatives with Add Alkyl Tail

Madasamy Kumar, Veerappan Jeyachandran, Arumugam Sathamraja, Pandian Paulraj

Abstract: The reaction between substituted 4-hydroxybenzaldehyde, active methylene compounds and/or resorcinol yield aminochromene derivatives. Structures of these compounds were established upon the basis of 1H, 1HNMR, 13CNMR, and MASS data.

Keywords: chromenes, imines, amines, antioxidants

I. INTRODUCTION

Multicomponent reactions (MCRs) are reactions where numerous reactants involved in single synthetic operation and give new compounds.1 This type of reactions avoids purification process and often wide variety of complex molecule in a single step, in turn it is very useful for saving solvent and reagents. Among many heterocyclic compounds, chromenes are very important due to its biological activity such as antioxidants,2 anticancer,3 anti-microbial,4 anti-inflammatory,4 anti-HIV,5 and anti-tumor,6 alzheimer disease,7 antihypotensive8 and antileishmanial.9 There are many reports shown that synthesis of different chromene derivatives and its applications (Figure 1).1, 10, 11 A Knoevenagel condensation is the reaction between salicylaldehyde with active methylene compounds followed by intramolecular cyclisation to give imino derivatives 11. As per reports, different products are obtained by control of a solvent,12 ratio of reagents and temperature13 etc., Due to reports, different products are obtained by control of a solvent,12 ratio of reagents and temperature13 etc., Due to importance of these chromene derivatives, numerous green approaches14 have been developed under distinct conditions like thermal heating,15 microwave,16 ultrasonic,17 electrochemical, infrared, and solvent free conditions. We could not find many reports on variation of an alkyl side chain to see the effect on antioxidant properties of chromene derivatives. So we are motivated to synthesis aminochromenes by taking alkylated aldehyde and malonitrile. Currently, many investigations are going on.18, 19, 20

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II. EXPERIMENTAL METHOD AND TECHNIQUES

All NMR spectra were recorded using Bruker (300MHz) spectrometer, JASCO-FTIR spectrometer (4000-400 cm−1) used for recording Infrared spectra. Electro spray ionization mass spectrometry (ESI-MS) analysis was performed in the negative ion mode on a liquid chromatography-ion trap mass spectrometer (LCQ Fleet, Thermo Fisher Instruments Limited,US). The DPPH radical scavenging action of the compounds was dignified rendering to the method of Biosis.20 The assay of nitric oxide (NO), H2O2, (O2−) scavenging activity was determined using the method available in literature.22, 27, 28 A series of 2-amino-4-hydroxy-4-(4-(alkyloxy) phenyl)-4H-chromene-3-carbonitrile have been synthesized using calcium hydroxide as efficient and green catalyst. The structures were confirmed by 1H-NMR, 13C-NMR, FT-IR and massspectroscopic techniques.

III. RESULTS & DISCUSSION

A. General procedure for the synthesis of 4-alkoxybenzaldehyde: 2a-h

A mixture of 4-hydroxybenzaldehyde (10mmol,1eq) 1-bromoalkane(15mmol,1.5eq), anhydrousK2CO3(15mmol,1.5eq) and butanone 20ml, the catalytic amount of KI was added to the mixture was refluxed for 4 hours. Reaction mixture was concentrated, poured into water and extracted with dichloromethane(DCM)(20mlx2). The combined organic layer was washed with brine and over anhydrous Na2SO4. Evaporation of solvent furnished a brown colored mass which was purified by column chromatography on 60-120 mesh silica gel. Elution with a mixture of
ethylacetate–petether (1:9) furnished the pure light yellow oily liquid.  

**B. General procedure for the preparation of 4-alkoxybenzoic acid: 3a-h**

The 4-alkoxybenzaldehyde (1g) was dissolved in butanone (20mL) and Jones reagent (1.7g CrO₃, 2ml H₂SO₄ and 2ml H₂O) was slowly added to this mixture and stirred for 1 hour. After 1 hour, the mixture was filtered. The precipitate was filtered; it was washed with water and recrystallized by ethanolethanol gave pure product.  

**C. General procedure for the preparation of 4-formyl-3-hydroxyphenyl-4-(alkoxy)benzoate: 4a-h**

A stirred solution of 4-alkoxybenzoic acid (1eq), 2,4-dihydroxybenzaldehyde (1 eq), N,N-Dicyclohexylcarbodiimide (DCC) (3eq) and catalytic amount of DMAP (dimethylaminopyridine) (DCM) dichloromethane solution was added at the room temperature, mixture was vacuum created and stirred for overnight under N₂ atmosphere. The precipitate N,N-dicyclohexylurea was filtered off. The filtrate was diluted with (20ml) DCM and washed with water and dried over anhydrous Na₂SO₄. Evaporate solvent by vacuum pump and purified by column chromatography 60-120 meshsilicagel. Elution with a mixture of (1:9) ethylacetate–pet ether furnished the pure product. The product was recrystallized from CH₃Cl₂-acetonitrile too obtain a white solid.  

**D. 2-amino-7-hydroxy-4-(4-(alkoxy)phenyl)-4H-chromene-3-carbonitrile: 5a-h**

A mixture of resorcinol (1.0mmol), 2-(4-methoxybenzylidene), malonalonitrile (1.5mmol), and Ca(OH)₂ (1.0mmol) in 5mL of methanol was stirred at room temperature for 5 min. After completion of the reaction monitored by TLC, the crude was washed with ethylacetate, dissolved with THF and filter to separate the catalyst. Solvent was removed from filtrate gave the pure product.

**IV. CONCLUSIONS**

Spinel ZnAl₂O₄ sample was synthesized successfully by a facile microwave heating route using *H. rosa-sinensis* extract. XRD, EDX and FT-IR results specified that the prepared spinel ZnAl₂O₄ sample have spinel structure with well crystalline product and also free from other phase impurities. The HR-SEM result revealed that spinel ZnAl₂O₄ sample contain nanoparticle-like morphology. The specific M₄ values were obtained to be 0.023 emu/g for spinel ZnAl₂O₄ sample.

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