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Rapid Ecofriendly Synthesis of Benzocoumarins by Microwave Irradiation and Their Antimicrobial Screening

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ABSTRACT

Benzo-annulated coumarin derivatives show wide application in organic light-emitting devices and are used as electron transporting emitters. In addition, coumarin family is an important building block for the synthesis of a variety of fascinating polycyclic unnatural products. 5-6Benzocoumarin derivatives show antimicrobial, antiinflammatory and anticancer activities. The utility of microwaves in heterocyclic synthesis is now receiving considerable attention. As a part of our study, aiming to explore potential utility of microwaves as an energy source for heterocyclic synthesis, it has been reported that synthesis of benzocoumarins of potential interest as pharmaceuticals and/or photochromic dyes and investigation of the possibility of conducting these reactions under microwave irradiation in addition to the standard thermal conditions has taken place. The compounds are synthesized by conventional and microwave method. Malonamic acid of 4-Chloro-2,5-dimethoxy aniline was treated with 2-hydroxy-1-naphthaldehyde. The synthesis by microwave provides better yield, more pure compounds and cleaner synthesis route. This study explains the synthesis and wide range of pharmaceutical properties of new substituted benzocoumarins.

Keywords: Benzocoumarins, schiff bases, microwave irradiation, antimicrobial activities.

1. INTRODUCTION

Coumarin and its derivatives occur as structural subunits in numerous natural products that exhibit a wide range of biological activities [1]. Sulpha drugs are well recognized for their various physiological activities,[2,3] likewise, many pyrimidine derivatives are used as therapeutic agents,[4,5]. 5-6Benzocoumarin derivatives show antimicrobial[6], antiinflammatory[7] and anticancer[8] activities.Buu-Hoi and Lavit[9] obtained an angular benzocoumarin by using dry HCl as condensing agent. Pardanani and Sethna[10] have reported that they obtained a linear benzocoumarin with 80 % H_2SO_4.The utility of microwaves in heterocyclic synthesis is now receiving considerable attention[11-14] and, although enaminones has been recently extensively utilized as precursors for the synthesis of heteroaromatics, the solvent less reaction of enaminones with nucleophilic reagents under microwave irradiation has not been previously investigated. As a part of our study, aiming to explore potential utility of microwaves as an energy source for heterocyclic synthesis, it has been reported that synthesis of 3-heteroarylsubstituted coumarins and benzocoumarins of potential interest as pharmaceuticals and/or photochromic dyes[15-17] and investigation of the possibility of conducting these reactions under microwave irradiation in addition to the standard thermal conditions has taken place.With the above views in mind we have synthesized new benzocoumarins as potential antimicrobial agents.

2. MATERIAL AND METHODS

Melting points were determined in open capillary tubes and are uncorrected. The purity of the compound was checked on silica-gel-coated Al plates (Merck). IR spectra were recorded in KBr on a Perkin Elmer Spectrum RX-1 FT-IR spectrophotometer. 1H-NMR spectra was done from CDRI Lucknow. Nitrogen was estimated by Dumas method. Microwave irradiations were carried out in Kenstar domestic microwave oven. All chemicals were of analytical grade.

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Conventional method

A mixture of N-(4-chloro-2,5-dimethoxy) phenyl malonamic acid and 2-hydroxy-1-naphthaldehyde (1:1 moles ratio) and a trace of pyridine was heated in an oil bath at 105-110°C maintained for 4 hrs. After the completion of reaction it was cooled and treated with a saturated solution of sodium bicarbonate (10 ml) and filtered. The residue was then boiled with ethanol (15 ml) and filtered hot. The brownish yellow solid left was purified by repeated washing with boiling methanol, ethanol and acetone. On analysis it was found to be 5:6-benzocoumarin-3-carboxy-4-chloro2,5dimethoxylamide. The filtrate was reduced to half and cooled . the dark brown product obtained was identified to be 2-hydroxy-1-naphthylidine-4-chloro 2,5dimethoxylamine.

Benzocoumarin 5:6-benzocoumarin-3-carboxy-4-chloro2,5dimethoxylamide

Molecular Formula:$C_{22}H_{16}O_5NCl$, Colour:Yellowish Brown, m.p.: 298°C

Yield: Conventional Method: 0.31g (75.70%), Microwave Irradiated Method : 0.39g (95.23%)

Nitrogen Estimation : Found : N-3.52%, Cal: N-3.41%

Schiff base 2-hydroxy-1-naphthylidine-4-chloro2,5dimethoxylamine

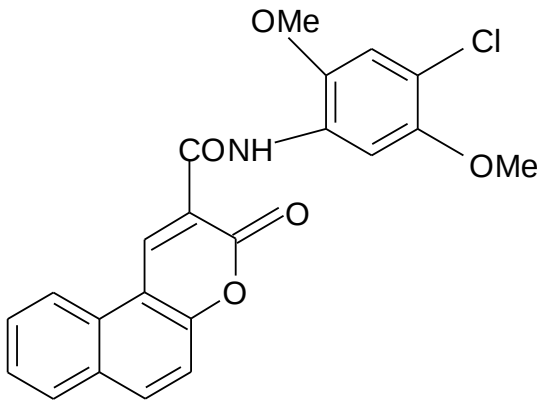
Molecular Formula:$C_{17}H_{16}O_4NCl$, Colour:Chocolate Brown, m.p.: 108°C

Yield : Conventional Method: 0.12g (35.98%),

Nitrogen Estimation : Found : N-4.22%, Cal: N-4.19%

Microwave irradiation method

A mixture of N-(4-chloro-2,5-dimethoxy) phenyl malonamic acid and 2-hydroxy-1-naphthaldehyde in (1:1 moles ratio) and a trace of pyridine was heated in a borosil beaker at a power of 80 W for 4 mins. The mixture first melted with some effervescence and later when kept at room temp it solidified to a dark brown mass. On analysis it was found to be 5:6-benzocoumarin-3-carboxy-4-chloro2,5dimethoxylamide. Schiff base was not obtained.



BENZOCOUMARIN

3. RESULT AND DISCUSSION

The microwave irradiation was successfully applied to the synthesis of benzo coumarins, the scope of the method is much broader.

All the reactions were carried out under both microwave irradiation and normal reflux conditions.

Comparisons of the two steps by conventional and microwave methods are depicted. Formation of the desired compounds were accelerated by microwave irradiation being obtained in 4 minutes - with higher yields as compared with the conventional method. Compared with the conventional method, this procedure uses more friendly reaction conditions, shorter reaction times and generally gives higher yields. The new compounds exhibit good biological activities.

The IR & NMR study reveals the following peaks thus confirming its structure of 5:6-benzocoumarin-3-carboxy-4-chloro2,5dimethoxylamide.

IR (KBr) cm^{-1} : 3460 (–NH stretching),1698 (> C=O), 1580 (C=C stretching), 1658 (amide),1603 (aromatic ring).

1H-NMR ($CDCL_3$, 300MHz) in δppm : 8.80(s, 1H, C_4H lactone ring), 7.20-8.22 (m, Ar-H), 0.55 (s, 1H, amide).

The synthesized compounds were screened for the presence of antimicrobial constituents against microorganisms: Staphylococcus aureus, Escherichia coli, Pseudomonas aeroginosa, Klebsiella, Streptococci and Basillus substilis using Disc diffusion method. The benzocoumarin showed moderate activity against E. Coli. at a conc of 100ug/ml. Further investigation is going on.

4. CONCLUSION

The environment needs to be protected from increasing chemical pollution associated with contemporary lifestyles and industrial production. Today the challenge for the researchers and scientists is to come together and pursue development in the field of greener chemistry by reducing or eliminating the use and generation of hazardous chemicals. In this view development of new synthetic routes in heterocycles has been fascinating, challenging and exciting area in Synthetic Organic Chemistry. Under the framework of "Green Chemistry" microwave assisted organic synthesis is a new and fast developing area in organic synthesis of heterocyclic compounds of pharmacological values. It gives the benefits of more pure compounds, increased yield and shorter reaction time.

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