

Efficient Green Method For The Synthesis Of 3,4-Disubstituted Coumarin Derivatives

A. Koleva¹, N. Petkova¹, R. D. Nikolova^{1,*}

(1) Faculty of Chemistry and Pharmacy, Sofia University “St. Kliment Ohridski”, 1 James Bourchier Blvd., Sofia, Bulgaria; *rnikolova@chem.uni-sofia.bg

Extended Abstract

Coumarins are natural compounds with wide application in the organic synthesis as acceptors in different organic reactions with nucleophilic reagents and dienophiles in Diels-Alder reactions as well in reactions of [2+2] or [2+3] cycloaddition and as intermediates in the synthesis of products of practical interest.

On the other hand, this class of compounds has an important role as antimicrobial, antiviral, anticancer, enzyme inhibition, anti-HIV, and antioxidant agents, they even possess the ability to influence the central nervous system. A third large area of application of the coumarin derivatives is in the modern technologies. They can be applied as excellent luminophores and laser dyes. Coumarin derivatives may be used as ligands for metal complexes and for modification of organic and inorganic supports.

Here in we present our study on the chemical behaviour of 3-ethoxycarbonyl and 3-phosphonocoumarin with series of preformed organomagnesium compounds. Grignard, Reformatsky and Ivanov's reagents were used as nucleophiles too. Our investigations represented them as good acceptor in the 1,4-addition reactions.

The group noticed that when ultrasound is used the desired products are isolated with better yields for shorter reaction time and this method has better reproducibility than the typical condition for the Michael reaction. *Syn*-addition to the C3-C4 bond of the 2-oxopyran ring is observed which leads to *anti*-disposal of the incorporated group and the substituent in third position.

The compared coupling constants of spin-spin interaction of H3-H4 protons confirmed the formation of the *trans* isomer in all reaction conditions when nucleophilic addition to 3-substituted coumarins took place.

Importantly, the method is useful for the preparation of 3,4-disubstituted chromanes with an exact configuration of the C3-C4 bond. The stereochemistry of the products **2-7** was determined by NMR spectroscopy and single crystal X-ray spectra of product **4**. All products were isolated as *trans* isomers with pseudoaxial antiperiplanar disposition of the substituents at positions **3** and **4**.

Acknowledgements: The authors acknowledge the support by the EXTREME project, funded by the Bulgarian Ministry of Education and Science, D01-76/30.03.2021 through the programme “European Scientific Networks”.