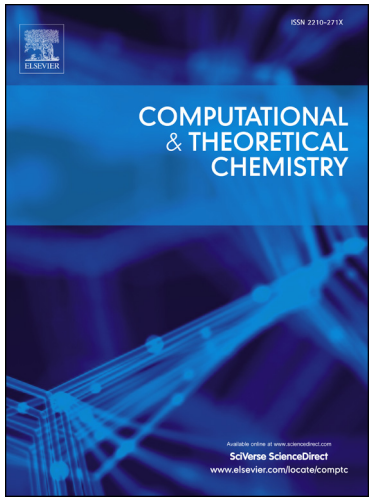

On the 6- and 7- substituted chromone system. A computational study

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On the 6- and 7- substituted chromone system. A computational study

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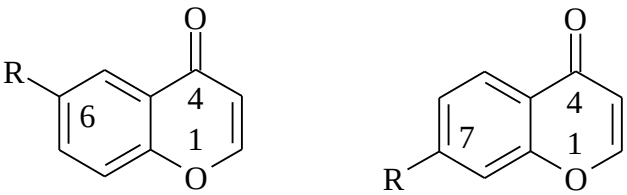
Abstract

We calculated multiple series of chromones 6- and 7-substituted in the benzene ring with substituents of different σ- and π-electron donor-acceptor properties at the B3LYP/aug-cc-pVTZ level. For two kinds of substitutions, we found and analyzed the correlations between the pEDA descriptor of the substituent effect on π- electron systems, the energy of the homodesmotic reaction of the chromone formation, the ν(C=O) and ν(C=C) stretching vibrations in the pyranone ring, the aromaticity of the chromone rings, and the NBO charge of the pyranone ring O atoms. It has been hypothesized that by modifying the substituent at the 6- and 7- positions of the benzene ring, one can probably modify the interactions of chromones with pharmacological targets.

Key words: chromone, chromen, substituent effect, tautomerism, sEDA, pEDA, HOMA

1. Introduction

The chromone (chromen-4-one, Scheme 1) system is ubiquitous in nature [1]. Although the chromone core does not contain a nitrogen atom, chromone natural products are classified as alkaloids because nitrogenous moieties are usually attached to them [2]. The chromone core is one of the top 100 most frequently used ring systems for small molecule drugs listed in the FDA Orange Book [3]. Chromone-based drugs exhibit anticancer, anti-HIV, antioxidant, anti-inflammatory, analgesic, antimicrobial, antimalarial, anti-diabetic, anticonvulsant, antiplatelet, gastroprotective, antihistaminic, antihypertensive, and insecticidal activity [4,5]. The chromen-4-one core has recently been identified as a potent and selective orphan G protein-coupled receptor (GPR35) agonist [6] in which, according to 3D-QSAR studies [7], steric, electrostatic, and hydrophobic substituents play a significant role.



Scheme 1. Structural formulas of the 6- and 7-substituted chromen-4-one molecules
R=BF_2, BH_2, Br, CHO, Cl, CN, COOH, F, H, Li, $N(CH_3)_2$, NH_2, NO_2, OCH_3,OH, SH, *t*Bu

The substitution of a chemical system by a group is the most important fundamental modification in the search for new molecular properties. The structural unit called a "substituent" should be considered as [8]: