COMPUTATIONAL STUDY OF THE MOLECULES OF SELECTED ACYLATED PHLOROGLUCINOLS *IN VACUO* AND IN SOLUTION

BY

MWOMBEKI MWADHAM KABANDA

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Department of Chemistry
School of Mathematical and Natural Sciences
University of Venda, Thohoyandou, Limpopo Province

Supervisor: Prof. Liliana Mammino
Department of Chemistry, University of Venda, Thohoyandou, South Africa

Co-supervisor: Dr. Caterina Ghio
Institute for Physico-Chemical Processes
Molecular Modelling Lab, Pisa, Italy

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Abstract

This thesis is concerned with the computational study of acylphloroglucinols – a class of derivatives of phloroglucinol characterised by the presence of a COR group – using electronic structure methods. The compounds of this class are known to be biologically active and this is the reason for the interest in their study.

A preliminary investigation was conducted on the parent molecule (phloroglucinol), calculating it in vacuo and in solution and comparing it with the other hydroxybenzenes. The aim was to identify relevant characteristics, so as to be able to verify whether and to what extent these characteristics are carried on to acylphloroglucinols and maintain stabilizing influences for the whole class of compounds. The mutual orientation of the phenolic OH groups is one of these characteristics.

A systematic conformational study was performed on over 140 different acylphloroglucinol structures (both model and actual), *in vacuo* and in three solvents differing by polarity and hydrogen bonding abilities: chloroform, acetonitrile and water. The study in water solution was complemented by the study of adducts with explicit water molecules. The results show that the most stabilising factor in all the media and for all the structures is the intramolecular hydrogen bond engaging the sp^2 O of the COR group and one of the phenolic OH ortho to it; hence, particular attention was devoted to the study of the characteristics (parameters and energy) of this hydrogen bond. The results in solution show the influence of the solvent on the molecular structures (including the characteristics of the intramolecular hydrogen bond) and the energy aspects of the solution process. The results of the study of adducts with explicit water molecules show possible preferred arrangements of water molecules around the studied acylphloroglucinol molecule, up to approximating the first solvation layer, and facilitate the interpretation of the results in water solution.

Different computational methods (HF, MP2 and DFT were utilised, also depending on affordability considerations for structures of different sizes), so as to be able to compare their results and to obtain an assessment of the performance of less expensive methods (like HF), in view of their utilisation for larger acylphloroglucinol structures for which more sophisticated methods (like MP2) remain unaffordable. Comparisons show interesting similarity in the identification of trends for the most important aspects.