

The Research Group

General Chemistry

has the honor to invite you to the public defense of the PhD thesis of

Xavier Deraet

to obtain the degree of Doctor of Sciences

Title of the PhD thesis:
Reactivity of carbonyl groups in homogeneous and heterogeneous media: a Density Functional Theory study

Promotor:

Prof. dr. Frank De Proft (VUB)

Prof. dr. Mercedes Alonso (VUB)

Prof. dr. Frederik Tielens (VUB)

Co-promotor :

Dr. Jan Turek (VUB)

The defense will take place on

Friday, February 18, 2022 at 15:00 in auditorium D.0.08

Due to COVID-19 measures, the capacity to physically assist the event at the Campus of Humanities, Sciences and Engineering of the Vrije Universiteit Brussel, Pleinlaan 2, 1050 Elsene, will be limited. The defense can also be followed through a live stream. Please contact Xavier.Deraet@vub.be for more information.

Members of the jury

Prof. dr. Yue Gao (VUB, chair)

Prof. dr. Ulrich Hennecke (VUB, secretary)

Prof. dr. ir. Annick Hubin (VUB)

Prof. dr. Shubin Liu (University of North Carolina)

Dr. Julia Contreras-Garcia (Sorbonne Université)

Prof. dr. Mark Saeys (Universiteit Gent)

Curriculum vitae

Xavier Deraet obtained his degree of Master of Science in Chemistry in 2017 at the Vrije Universiteit Brussel. Subsequently, he started his PhD within the General Chemistry research group (ALGC) of Prof. Dr. Frank De Proft and Prof. Dr. Frederik Tielens, which was funded with the financial support of a Strategic Research Program grant.

He is co-author of seven scientific papers published in peer-reviewed international journals, among which three times as a first author. Xavier Deraet presented his work at different (inter)national conferences and obtained the "ChemCYS best poster presentation in the session of Physical and Theoretical Chemistry" prize in 2018. Besides teaching activities, he also guided and supervised two master thesis students and one internship student.

Abstract of the PhD research

The research in this thesis aims to describe the reactivity of the carbonyl functionality in homogeneous and heterogeneous media using density functional theory (DFT). The carbonyl group is a prominent functional group in organic chemistry and susceptible to many chemical modifications. A well-known example of such a transformation is the reduction of a substituted cyclic ketone to an alcohol product by the addition of a hydride-based reducing reagent. Since the hydride can spatially approach the carbonyl moiety in several ways, this reaction often results in a mixture of stereoisomers, which can exhibit very different chemical and biochemical properties. Nevertheless, by prior understanding of the preferential attack side of the hydride and the factors that influence it, reaction conditions can be optimised in such a way that the desired isomer is obtained as a major product. In contrast to non-cyclic ketones, where all the driving forces are already well established, this remains a matter of discussion for cyclic ketones.

Starting from a benchmark study, the most appropriate computational procedure to describe the kinetics of the reduction of substituted cyclic ketones was determined with respect to the quantum chemical golden standard CCSD(T) method. A two-step procedure, in which geometry optimisations and single-point energy calculations are performed with different functionals, emerged as the most accurate, providing product ratios in excellent agreement with the experimental data. This protocol was then applied to investigate the factors influencing the stereoselectivity of substituted cyclohexanone reductions with a small reducing reagent. This allowed us to demonstrate that the diastereomeric ratio strongly depends on the substituent. Hence, we concluded that the stereoselectivity of the reduction of cyclohexanones with alkyl substituents is driven solely by the torsional strain in the transition states. As soon as heteroatoms are considered, the selectivity is reversed due to a subtle interplay between attractive and repulsive non-covalent interactions. Next, we investigated the reduction of substituted cyclobutanones, which constitute a valuable source of information for the pharmaceutical industry given their prevalence in natural products. The reduction of these compounds is nevertheless much less studied than cyclohexanone reductions. Our research showed that regardless of the reaction conditions, the hydride always approaches the carbonyl functionality from the same side. Based on geometrical analysis and the non-covalent interaction index, we determined that the driving forces behind the selectivity are rather diverse. The preferential attack of a small reducing agent on a single 3-alkyl or 3-arylsubstituted cyclobutanone is influenced exclusively by a reduction in torsional strain, whereas for alkoxy substituents a repulsive electrostatic interaction plays a major role. Furthermore, these findings allowed us to provide theoretical insights into a recently developed synthetic process of novel spirocarbocycles.

Besides the use of the hydride reagent, the carbonyl functionality can also be catalytically reduced in the presence of molecular hydrogen. While for many years only classical heterogeneous catalysts were used, the focus has recently shifted to new, more atom-efficient and thus more environmentally friendly catalytic systems. The concept of single-atom catalysts, in which individual metal atoms are dispersed over a supporting surface and are assumed to be almost entirely responsible for the catalytic activity, fits within this strategy and forms the subject of the second part of this thesis. Herein, the adsorption of the widely used Group 8 to 10 transition metals on two chemically different oxide supports, being a silica and an anatase surface, was carefully investigated. Moreover, the suitability of three conceptual DFT schemes for the description of the reactivity of such periodic models was tested and, importantly, a complete picture of the reactivity of these catalytic systems was presented for the first time. The main advantage of this approach lies in the fact that it does not require to explicitly model the interactions with external reagents, which makes it a valuable tool for a more concept-oriented and rational development of these catalytic systems.