**Research Trip Summary Report**

**Task 2. Foreign mobility of WUST doctoral students**

## I. Data of the doctoral student

1.Full name: Joseph Daniel Gbubele

2.Year of studies: 4th year

3. Educational discipline: Chemical Sciences

## II. Foreign research trip (research visit)

1. Research institute in which the foreign research was implemented: Chemistry Department of Aarhus University

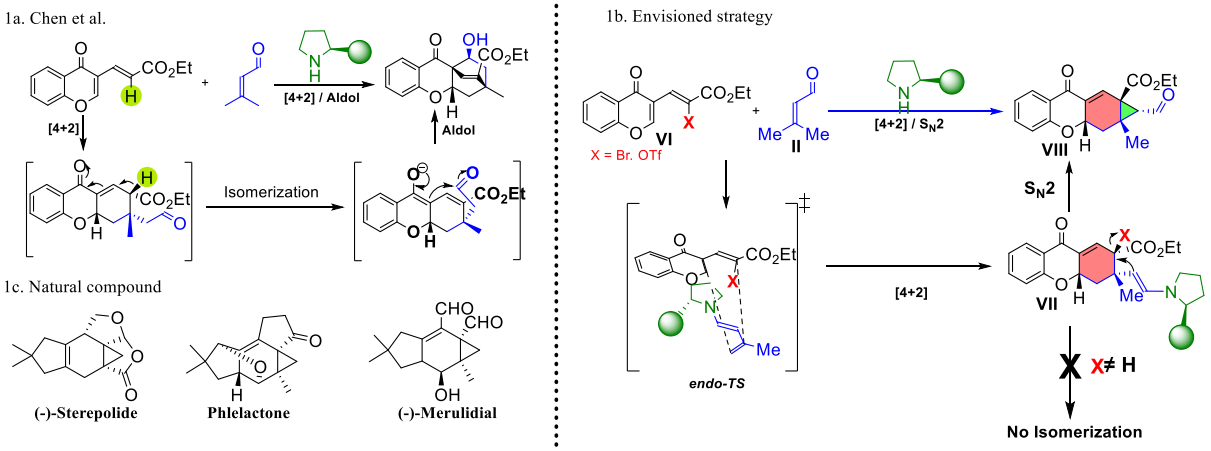
2. Name and surname of the host person (mentor): Professor Karl Anker Jørgensen.

3. Dates of the research trip: 1st April – 30th June 2022

4. Title and date of a seminar delivered during the research trip: Synthesis of organophosphorus compounds via hydrophosphonylation of chiral phosphorus nucleophile to carbon-heteroatom bond, 4th May 2022.

5. Description of work carried out and the main results during the research trip:

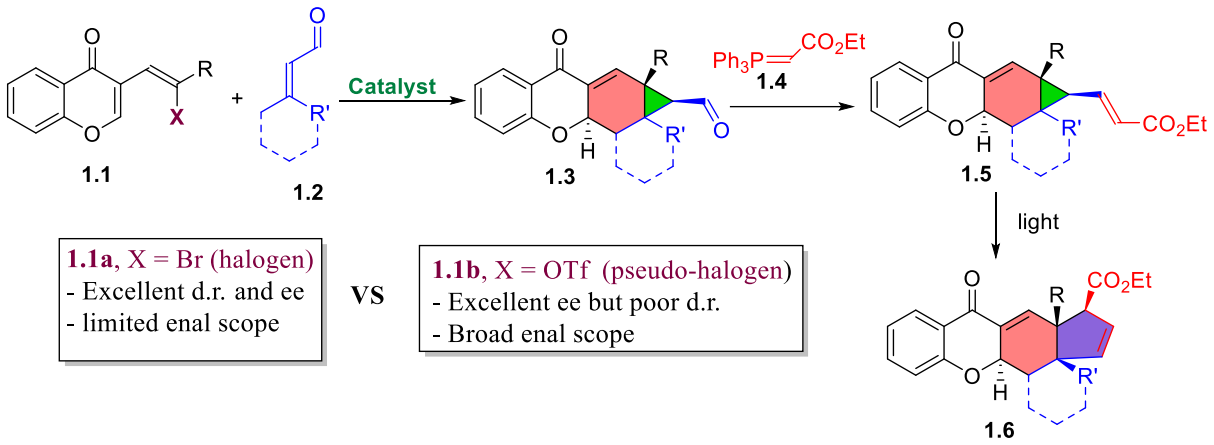
Chen's group have developed a synthetic protocol that involved the use of chromone-fused dienes to obtain complex bicyclic products via the inverse-electron-demand Diel-Alder and Aldo domino reaction (Scheme 1a)




**Scheme 1**: a) IED Diels-Alder and Aldol domino reaction reported by Chen's group. b) Envisioned strategy in the formation of chiral norcarane structure. c) natural and biologically active compounds containing similar norcarane scaffold

Inspired by Chen et al. work, it was envisioned that replacing the acidic proton with (pseudo)-halogen on the chromone-fused diene could prevent isomerization and therefore enhance the reactivity of the cycloaddition via the (pseudo)-halogen effect. Through $S_N2$-like substitution reaction, complex norcarane products could be obtained with four stereocenters and two of which are all carbon quaternary stereocenters (Scheme 1b). This protocol would give access to chiral norcarane scaffolds which are found in natural compounds such as (-)-sterepolide phelactone, (-)-Merulidal, and possess great biological activity (Scheme 1c).

The reaction's feasibility was assessed by utilizing the optimal reaction conditions with brominated dienes **1.1a** and **1.2** to give the products **1.3a**, which subsequently undergo Wittig transformation to obtain **1.5a** in moderate to good yields and excellent selectivity (Scheme 2). The Wittig transformation is essential for the retention of the d.r. of the products **1.3**, which changes during flash column chromatography. We ran into a reactivity dilemma when utilizing **1.1a** in the aldehyde scope under the optimised reaction conditions. As a result, we used pseudo-halogenated diene **1.1b** which is more reactive than the brominated diene to solve this problem. The reactivity of **1.1b** with various enals **1.2** yielded **1.3b** compounds, which were then Wittig transformed to generate **1.5b** products with high yields and excellent enantioselectivity (up to 99% ee). We were pleased to discover that, in the presence of light, the generated products **1.5** may undergo vinylcyclopropane-cyclopentene rearrangement to provide quantifiable yields of 6-6-6-5 fused tetracycle products **1.6** while retaining stereoselectivity (Scheme 2).




**Scheme 2**: Synthesis of norcarane compounds via combination of (pseudo)-halogen effect and dienamine catalysis **1.1a**) brominated dienes. In the discussion '**a'** products obtained from reaction of brominated dienes with enal. While **'b'** products obtained from reaction with *O*-triflated diene and various enals.

In conclusion, this research pushes the boundaries of halogen and pseudo-halogen effects, as well as asymmetric aminocatalysis, to promote an inverse electron demand Diels-Alder reaction. The intermediate goes through an $S_N2$-like reaction by using a halogen or pseudo-halogen as a leaving group in the ring-closing to form complex norcarane products with four stereocenters, two of which are all carbon quaternary stereocenters.

6. Future collaborations (if applicable):

This visit is an excellent starting point for potential future collaboration, which might result in Prof. Jorgensen giving open lectures on asymmetric aminocatalysis to researchers and students at the Faculty of Chemistry of Wroclaw University of Science and Technology (WUST). Further scientific research collaborations between Prof. Jorgensen's research group and WUST researchers and students, which is in line with the goals of the NAWA STER program, could also be possible.

7. Title and date of a seminar presenting the results of the trip delivered at Wroclaw University of Science and Technology after returning from the research trip: Asymmetric Domino-reactions towards Norcarane Structures through the Combination of Dienamine Catalysis and the (Pseudo)-halogen effect, 24.11.2022 at 10.00 am

## III. Doctoral student's signature

…….. (Date)

……..... (doctoral student's signature)

## IV. Confirmation and information from the host

1. Confirmation of compliance of the information contained in the report: I CONFIRM / ~~DO NOT CONFIRM~~. (*In justified cases, the confirmation of the host may be sent by e-mail to the Dean's Office of the Doctoral School email: interdocschool@pwr.edu.pl*)

2. Additional information and comments

Joseph Daniel Gbubele did a good job during his stay. He was easily integrated in the research group and learned the techniques relatively fast. Joseph Daniel Gbubele contributed significantly to the research project he was involved in, and we are expecting that this will result in a publication in the near future.

…… (Date)

…..…… (signature of Host Surpevisor)