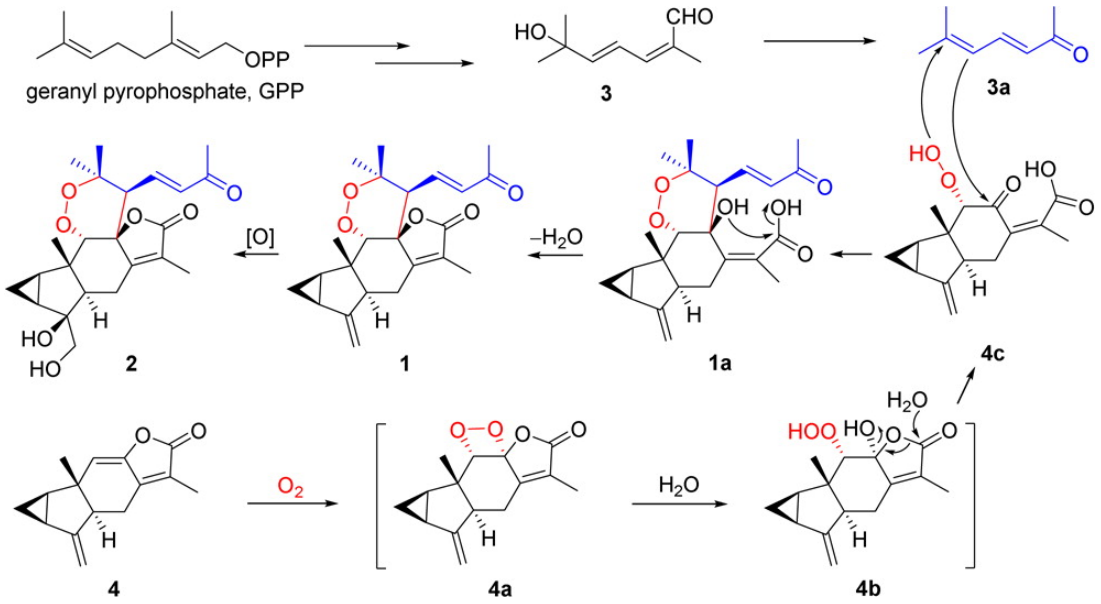
Organic Cumulative Exam (February 4, 2016)
Daesung Lee

1. (40 Points) Recently, Luo and coworkers reported the elucidation of structures of Sarglaperoxides A and B (DOI: 10.1021/acs.orglett.6b00112), and proposed putative biosynthetic pathways for these compounds as shown below.



(a) (10 Points) The proposed mechanism for the formation of **1** starting from **3a** and **4c** seems to be quite unusual. From typical reactivity considerations of the functional groups involved in these bond forming and breaking processes, this mechanism is most likely incorrect. What are potential problems of this proposed mechanism?

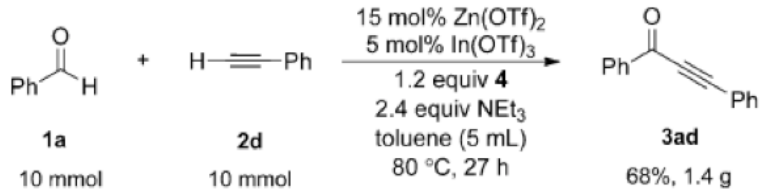
(b) (10 Points) Once you have recognized the problems of the originally proposed mechanism by the authors, you can think about a better or a different mechanism. On the basis of the structural characteristics of **3a** and **4a** and their expected reactivity, propose an alternative mechanism that bypasses the formation of intermediates **1a**, **4b**, and **4c**.

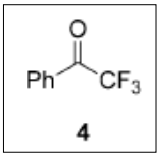
(c) **(5 Points)** Propose a plausible electron-pushing mechanism by using appropriate arrows for the formation of **4a** from **4** and triplet oxygen.

(d) **(5 Points)** If the oxygen in this reaction is in a singlet state, how would you propose a mechanism for the formation of **4a** from **4**? Draw an electron-pushing mechanism by using appropriate arrows.

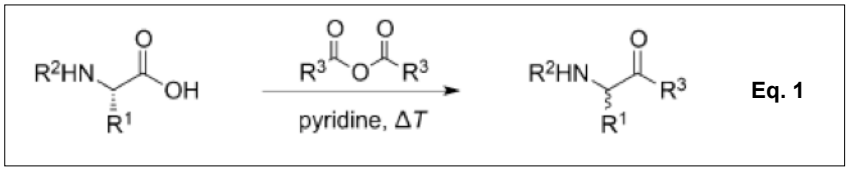
(e) **(10 Points)** Assuming that the oxygen involved in this reaction is triplet oxygen, the formation of **4a** can be precluded from the reaction pathway due to its supposed instability. Propose a reasonable mechanism for the formation of **1** starting from **4** and **3a** in the presence of triplet oxygen via a reaction pathway that does not involve dioxetane intermediate **4a**.

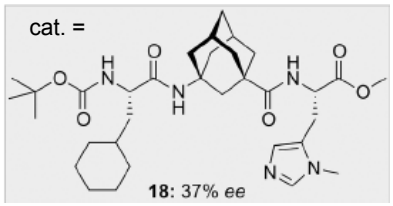
2. (15 Points) In general, reactions between aldehydes and organometallic species lead to alcohol products. By including a suitable additive such as highly electron-deficient ketone in the reaction, the initially formed alcohol product can further undergo a subsequent reaction to provide the corresponding ketone as the final product (*Angew. Chem. Int. Ed.* **2015**, 54, 15850). Provide a reasonable mechanism of the transformation shown below.

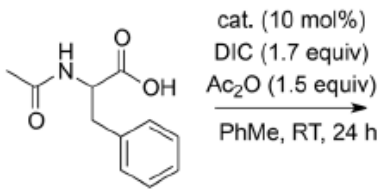




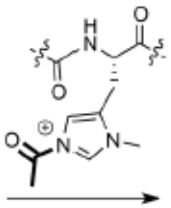
4. (15 points) The following classical transformation (Eq. 1) is called the Dakin-West reaction, which was recently accommodated in the asymmetric synthesis of α-amino ketones (*Angew. Chem. Int. Ed.* **2016**, DOI: 10.1002/anie.201509863). On the basis of the reagents provided, identify the structure of **A–C** in the reaction scheme below.



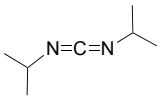




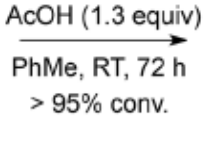
A



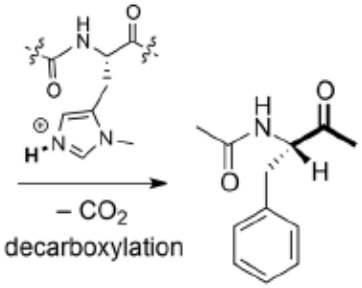
DIC = *N,N′*-diisopropylcarbodiimide



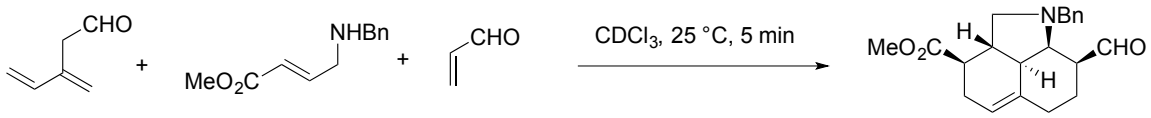
B



C



5. (15 points) The diene-transmissive Diels-Alder reaction is a powerful cycloaddition that can produce a complex molecular framework from one simple operational step (*Angew. Chem. Int. Ed.* **2016**, DOI: 10.1002/anie.201510925). Provide a reasonable reaction mechanism for the following transformation.



6. (15 points) Development of new transformations for functional group interconversion is highly important to increase the overall synthetic efficiency. The following transformation is considered to be a formal conversion of a ketone functional group to the corresponding alkyl chloride. (*Angew. Chem. Int. Ed.* **2016**, DOI: 10.1002/anie.201510909). Draw the structure of intermediate **A**, and provide a reasonable electron-pushing mechanism for the conversion of the starting hydrazone to intermediate **A** and its conversion to the final product.