Synthetic study of oxidative metabolites in mushrooms starting from ergosterol

([1]*Faculty of Engineering, Osaka Institute of Technology*, [2]*Graduate School of Engineering, Osaka Institute of Technology*) ○Edric Wilbert[1], Saki Nagayasu[2], Tomoka Taguri[1], Shoji Kobayashi[1]

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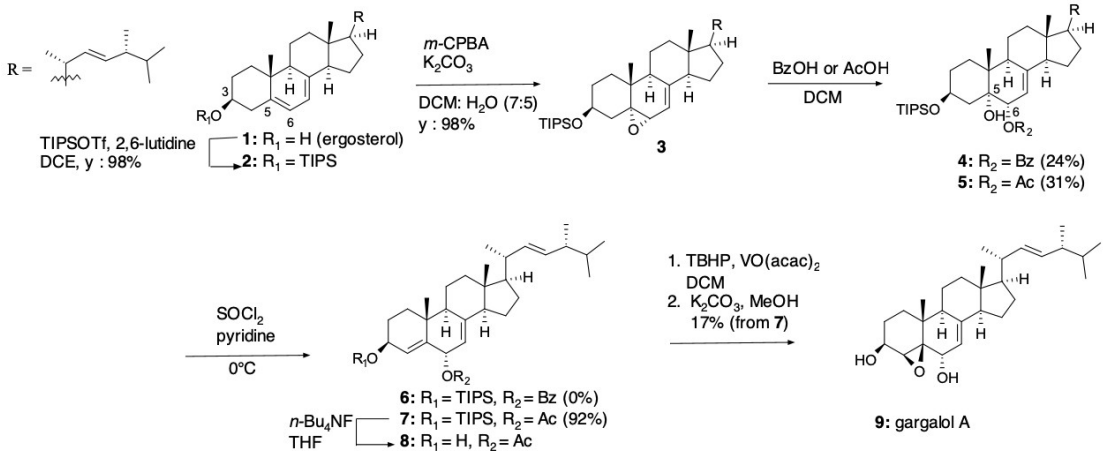
Mushrooms are widely consumed as health food and their health-promoting functions are thought to be partially attributed to the steroidal metabolites contained. This study focuses on straightforward syntheses of oxidized steroidal metabolites from ergosterol (**1**), a presumed biosynthetic precursor. The following scheme shows the synthetic route of gargalol A (**9**) isolated from the edible mushroom *Grifola gargal*.[1] The C3-hydroxyl group in **1** was first protected as its TIPS ether, and the C5-C6 olefin was epoxidized to give α-epoxide **3** in regio- and stereoselective manners. Nucleophilic epoxide opening by benzoic or acetic acids proceeded stereoselectively, giving rise to α-benzoate **4** and α-acetate **5** probably via S_N1 reaction pathways. Subsequent dehydration was achieved with thionyl chloride and pyridine. Interestingly, the benzoate **4** was inert under these conditions while the acetate **5** smoothly underwent dehydration to give **7** in 92% yields. It is likely that the sterically hindered benzoyl group inhibited chlorination of the C5-alcohol. Removal of the TIPS group in **7** turned out problematic because of the instability of the resulting allylic alcohol **8**. Eventually, careful isolation of the intermediate (**8**) followed by epoxidation using TBHP/$VO(acac)_2$ and deacetylation gave gargalol A (**9**) whose spectra matched the natural product.[1] Although an overall yield was moderate, such straightforward synthesis gives valuable insights into the biosynthetic routes of steroidal metabolites.



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