Synthetic study of (－)-epigallocatechin gallate (EGCG): Toward the development of probe molecles

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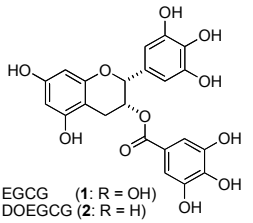
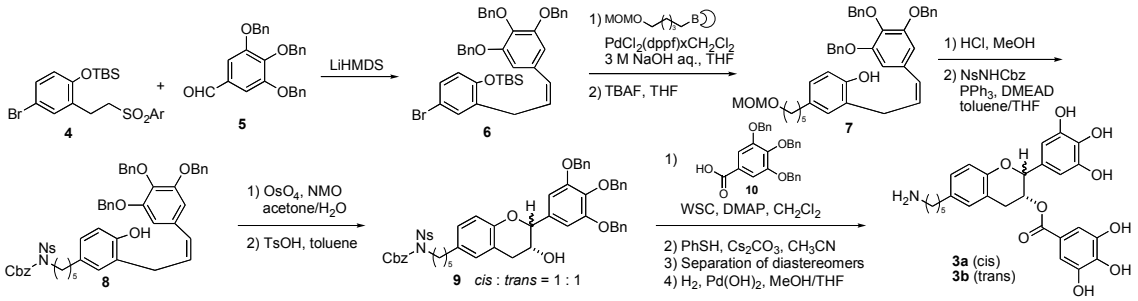
(－)-Epigallalocatechin gallate (EGCG) (**1**), which is a major constituent of green tea extract, has received special attention for its antitumoral, antiviral and other important bioactivities. Since these promising bioactivities of **1** was expected as a lead for drug development, an elucidation of target protein and dynamics of **1** has been strongly required. Although utilizing the probe molecule derived from **1** would be a significant approach, direct incorporation of probe unit into **1** has been difficult. During the course of our synthetic investigation of **1**, we found the synthetic derivative **2** possessed more potent anti-influenza activities than **1**. Inspired this finding, we have launched an investigation into the synthesis of EGCG probe molecule.



Based on the structure and activity relationship, the linker containing **3** was



emerged as a key intermediate for the probe. The synthesis was started from *cis* olefin **6**, which was readily obtained by coupling of PT-sulfone **4** and aldehyde **5**. After incorporation of linker unit by Suzuki-Miyaura reaction, conversion to amino group was accomplished by our Ns amide. After dihydroxylation, upon treatment with TsOH, the desired cyclization reaction proceeded smoothly to provide **9**. After the incorporation of gallic acid **10** and deprotection of Ns groups was accomplished by treatment with thiol. Finaly, the deprotection of benzyl groups and Cbz group under hydrogenolysis conditions afforded **3**.