Regioselective synthesis of mehylated catechin and synthetic study of theaflavins

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Tea polyphenols show various bioactivities, especially methylated catechin is well known for its strong antiallergic and antioxidant activities. Theaflavins, a major color source of black tea, has attracted mach attention because of its antibacterial and anticancer activities. Although medical applications of these polyphenols are promising, there is a serious problem with its supply because of the scarcity within tea leaves. So the development of an efficient synthetic method for these polyphenols is needed.

Previously, we accomplished an efficient semi-synthesis of 4"-Me-EGCG from natural EGCG. In this study, we next tried to synthesize novel dimethylated catechin derivatives for the analysis of structure-activity relationships (SAR). We found that the direct methyltion of the synthesized 4"-Me-EGCG proceeded site-selectively to afford 4',4"-diMe-EGCG. This method could be applied to the synthesis of ^{11}C-labelled dimethylated catechin for PET analysis since the methylation was completed within 3 min.

On the other hand, we established the biomimetic synthetic pathway of neotheaflavin. Site-selective oxidation of the A-ring nitrobenzenesufonyl (Ns)-protected catechin, followed by coupling with A-ring Ns-protected epigallocatechin proceeded smoothly to construct benzotropolone-ring of neotheaflavin. In this reaction, it was turned out that the addition of Molecular Sieves® was important for the efficient oxidative coupling. We also found that odorless 2-aminothiophenol was also usable instead of thiophenol for the removal of the Ns groups. In addition, purification of the synthesized neotheaflavin became easier since the side-product derived from the protecting groups could be removed by simple extraction under acid condition. In conclusion, we improved our synthetic pathway of neotheaflavin and achieved the large scale synthesis of theaflavins. The study on SAR and various bioactivities of the synthesized neotheaflavin are under way.