FIRST QUANTITATIVE OXIDATIVE SYNTHESIS OF FREE PHENOLIC 3,4-*CIS* PROCYANIDIN B3 OLIGOMER – A PROLIFERATIVE ANTI-OXIDANT

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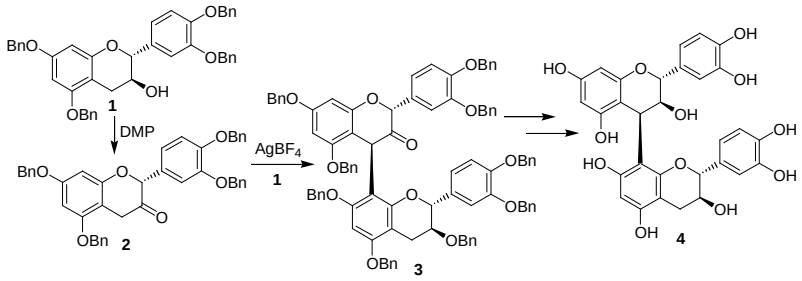
ABSTRACT

Proanthocyanidin which is a proliferative poly-phenolic compound prevalent in plants and a vital constituent of human and animal diet affords important biological properties and *in vitro* antioxidant, anti-atherosclerotic, anti-inflammatory, antitumor, anti-osteoporotic and antiviral activities. Classical synthetic methodologies for this compound consist of substituting a leaving group on a C-4-substituted flavan-3-ol monomer with an aromatic nucleophilic moiety of catechin **1** resulting in multiple by-products, coupled with uncontrolled self-condensation and thus the degree of polymerization. The self-condensation issue was addressed by our method of introducing an aromatic moiety into the unfunctionalized C-4 position of 3-oxo-catechin **2** *via* $AgBF_4$-promoted interflavanyl coupling. The C-3 carbonyl group activated the C-4 position towards carbocation formation and accordingly deactivates the C-8 position towards self-condensation. A method for the synthesis of free phenolic procyanidin B-3 analogues is described. Treatment of a solution of tetra-*O*-benzyl-3-oxocatechin **2** (1 equiv.) and penta-*O*-benzylcatechin **1** (3 equiv.) with silver tetrafluoroborate readily affords the per-*O*-benzyl ethers of 3-oxo-catechin-(4→8)-catechin **3** exclusively at 74% yield. Subsequent sodium borohydride reduction followed by catalytic hydrogenation provides access to the free phenolic procyanidin possessing 3,4-*cis* diastereoisomer **4**. The dimer **3** can allow stepwise formation of hetero-oligomers.



Key words: Procyanidin, antioxidant, free phenolic, silver tetrafluoroborate