

**“Synthesis of Trimeric, Tetrameric, Pentameric, and Higher Oligomeric Epicatechin-Derived Procyanidins and Their Inhibition of Cancer Cell Growth Through Cell Cycle Arrest”**

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We report an improved synthesis of bis(5,7,3',4'-tetra-O-benzyl)epicatechin 4 $\beta$ ,8-dimer (**1**) from 5,7,3',4'-tetra-O-benzylepicatechin (**2**) and 5,7,3',4'-tetra-O-benzyl-4-(2-hydroxyethoxy)epicatechin (**3**) by utilizing the clay mineral Bentonite K-10, as opposed to the Lewis acid titanium tetrachloride. Also, under the same conditions, the benzyl-protected all-4 $\beta$ ,8-trimer, -tetramer, and -pentamer products were obtained in decreasing yields. Reaction of **2** with an organoaluminum thiolate gave 3-O-acetyl-4-[(2-benzothiazolyl)thio]-5,7,3',4'-tetra-O-benzylepicatechin (**4**). Medium-sized oligomers were obtained using **4** as an electrophile and silver tetrafluoroborate as an activator; they are isolated by reverse-phase HPLC. These were then deprotected by ester saponification, followed by hydrogenolysis. This yielded the free Procyanidins, characterized as their peracetates. Chain extension by two members was demonstrated using a dimeric electrophile obtained by self-condensation of **4**. Both the synthetic and natural pentamer inhibit the growth of several breast cancer cell lines.

**Bibliography**

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