Synthetic Lignans Targeting Cardiovascular Diseases: Chemical Aspects

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This contribution highlights the modular synthesis of tetrahydrofuran-type lignans to be tested in various anti-inflammatory screenings. Leoligin 1, a natural product which had previously been isolated from Leontopodium alpinum,[1] inhibits the proliferation of smooth muscle cells (SMCs) [2] in addition to possessing other biological activities. For the preparation of a library of analog compounds we first used a 5-step procedure [3,4] to obtain intermediate 2. After silyl protection, this served as a starting material in a one-pot hydroboration / Suzuki coupling / deprotection sequence to give compounds of type 3, typically in 50 to 70% yield over 4 steps while covering a wide scope of electron-rich and -deficient (hetero)aryl moieties (see Scheme 1). Further modifications of the hydroxyl function finally led to lignans of structure 4.

We prepared approx. 150 leoligin-like compounds in this way, and we conclude that this expedient synthesis is a useful route to assemble a range of analogs of the original natural product for subsequent activity profiling.

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References: