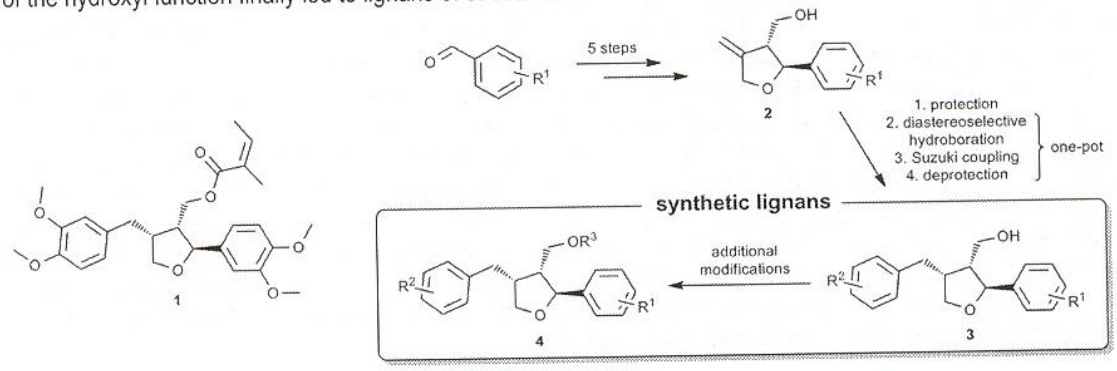
Poster P 21

Synthetic Lignans Targeting Cardiovascular Diseases: Chemical Aspects

Harhammer K[1], Linder T[1], Geyrhofer S[1], Stuppner H[2], Schnürch M[1], Mihovilovic MD[1]
[1] Institute of Applied Synthetic Chemistry, Vienna University of Technology, Getreidemarkt 9/163, 1060 Vienna, Austria;
[2] Institute of Pharmacy/Pharmacognosy, University of Innsbruck, Innrain 80/82, 6020 Innsbruck, Austria

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**.



Scheme 1

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.

Acknowledgements: Financial support by the Austrian Science Fund (Project # FWF S10701 and S10703) is gratefully acknowledged.

References:
1. Dobner, M. J., Ellmerer, E. P., Schwaiger, S., Batsugkh, O., Narantuya, S., Stuetz, M., Stuppner, H. (2003) Helv. Chim. Acta 86:284-285.
2. Reisinger, U., Schwaiger, S., Zeller, I., Messner, B., Stigler, R., Wiedemann, D., Mayr, T., Seger, C., Schachner, T., Dirsch, V. M., Vollmar, A. M., Bonatti, J. O., Stuppner, H., Laufer, G., Bernhard, D. (2009) Cardiovasc. Res. 82:542-549.
3. Mandal, P. K., Maiti, G., Roy, S. C. (1998) J. Org. Chem. 63:2829-2834.
4. Stambasky, J., Malkov, A. V., Kocovsky, P. J. (2008) Org. Chem. 73:9148-9150.