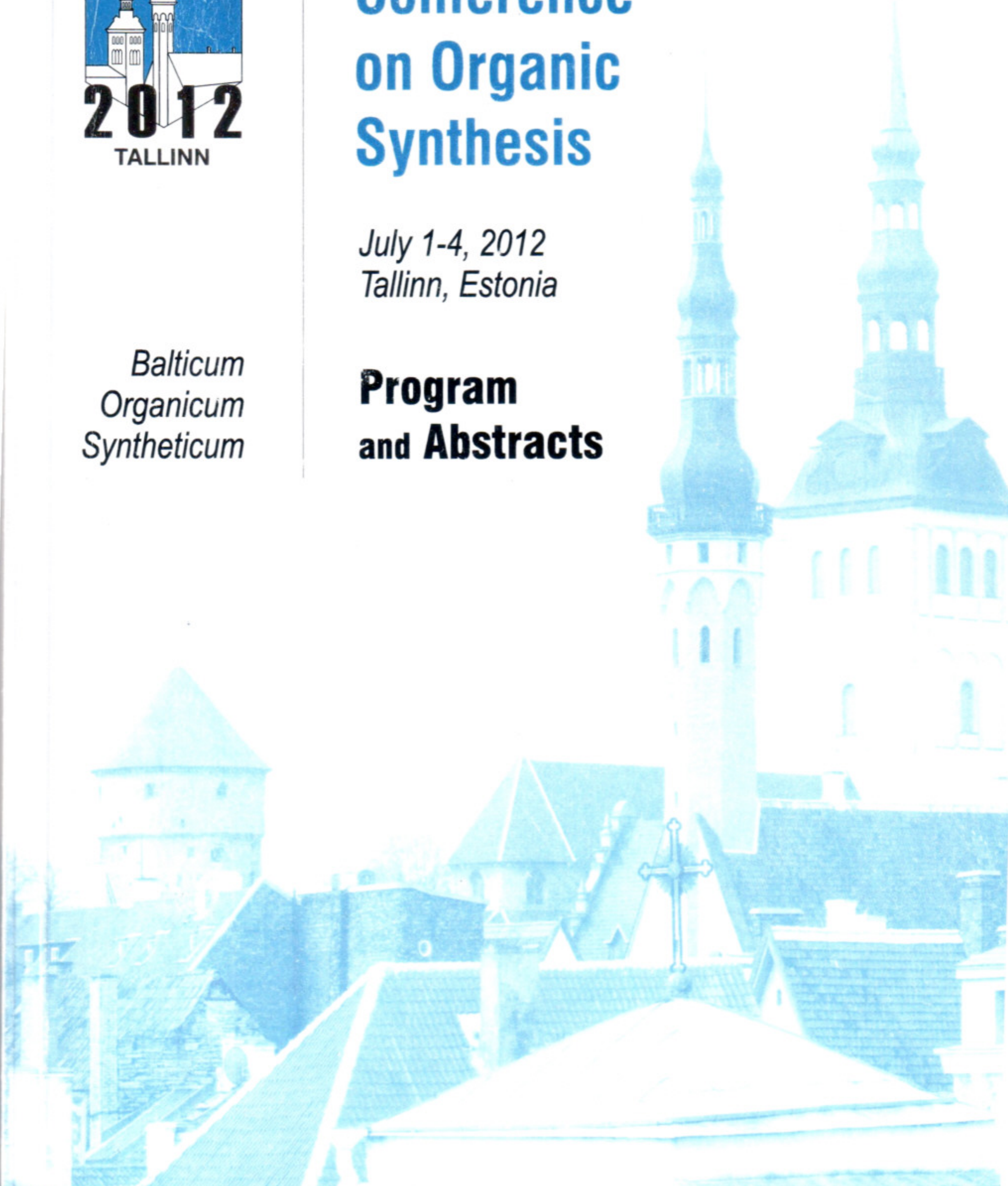
BOS 2012
TALLINN

International Conference on Organic Synthesis

July 1-4, 2012
Tallinn, Estonia

Balticum
Organicum
Syntheticum

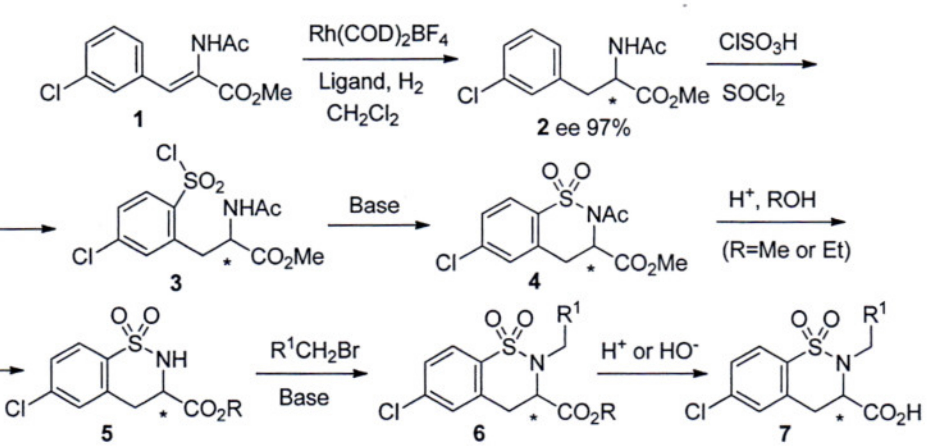
Program and Abstracts



ASYMMETRIC SYNTHESIS OF 3,4-DIHYDRO-2-SUBSTITUTED-2*H*-BENZOTHIAZINE-3-CARBOXYLIC ACID 1,1-DIOXIDE

Bluke, Z. and **Kauss, V.**
Aizkraukles 21, Riga, LV-1006, Latvian Institute of Organic Synthesis
Latvia
valerjan@osi.lv

For many years 2*H*-1,2-benzothiazine derivatives, particularly, a series of 4-hydroxy-2*H*-1,2-benzothiazine-3-carboxylic acid amides are known as useful medicines. Surprisingly, 2*H*-1,2-benzothiazine-3-carboxylic acid has again attracted pharmacological interest. Thus, 3,4-dihydro-2*H*-1,2-benzothiazine-3- carboxylic acid 1,1-dioxide was incorporated in the structure



of dipeptide mimetic inhibitors of calpain, a cysteine protease.[1] Bicyclic 1,2-benzothiazine structure served as specific conformational constraint of phenylalanine. To use the structure of 3,4-dihydro-2*H*-1,2-benzothiazine-3-carboxylic acid in the synthesis of ligands for ionotropic glutamate receptors it was necessary to check the possibility of enantioselective synthesis of acids **7**. Therefore we selected phenylalanine derivative **2** to find the conditions, most appropriate for preventing the racemization. High enantiomeric purity of **2** was reached by Rh-catalyzed asymmetric hydrogenation of compound **1**, using MonoPhos chiral ligands.[2] Results of step by step optimization, based on chiral HPLC analysis will be presented.

1. Wells, G. J.; Tao, M.; Josef, K. A.; Bichovsky, R. *J. Med. Chem.* **2001**, *44*, 3488-3503.

2. Van den Berg, M.; Minnaard, A. J.; Haak, R. M.; *et al. Adv. Synth. Catal.* **2003**, *345*, 308-323.