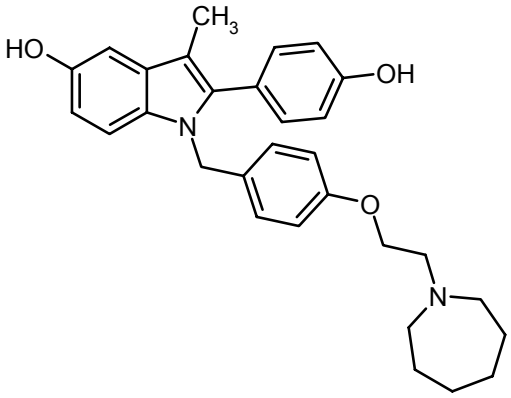
SYNTHESIS OF OF THE ANTICANCER AGENT BAZETOXIFENE

Dirk Röseling[a] , Ving J. Lee[b] , and Ulrich Jordis[a]

[a] Institute of Applied Synthetic Chemistry, Vienna University of Technology
Getreidemarkt 9, 1060 Vienna, Austria, ujordis@pop.tuwien.ac.at
[b] Iconix Pharmaceuticals, 325 East Middlefield Road, Mountain View, CA 94043 USA

Abstract. Within the large family of estrogens are tissue-selective estrogens that have been classified as selective estrogen receptor modulators (SERMs). These compds. are characterized by the fact that they exhibit both estrogen agonist and antagonist activity dependent upon the gene promoter and target tissue being examd. SERMs have been intensively studied over the past decade, esp. since one, raloxifene, has been approved for the prevention and treatment of postmenopausal osteoporosis. In order to develop an improved SERM, a stringent screening process was described to select compounds that did not stimulate the uterus or breast. Under these strict conditions, bazedoxifene (WAY-140424) was developed and is presently in phase I and II trials. [1,2].
We will report an optimized synthesis of bazedoxifene that we developed in the context of the collaboration with the DrugMatrix program [3], the world's largest chemogenomics reference database and informatics system.



Leading references: [1] Developing a SERM: Stringent preclinical selection criteria leading to an acceptable candidate (WAY-140424) for clinical evaluation. Komm, Barry S.; Lyttle, C. Richard. Women's Health Research Institute, Wyeth-Ayerst Research, Collegeville, PA, USA. Annals of the New York Academy of Sciences (2001), 949(Selective Estrogen Receptor Modulators (SERMs)), 317-326. CAN 136:256748
[2] Method of treating certain cancers using an estrogen agonist/antagonist. Rosati, Robert Louis. Eur. Pat. Appl. (2002), EP 1226823 CAN 137:119650.
[3] http://www.iconixpharm.com/products/products_main.html