Studies Towards the Synthesis of Oximidines I and II:

Oximidines I (**1**) and II (**2**) are closely related metabolites isolated from *Pseudomonas sp.* Q52002 which display significant antitumor activity (IC_{50} (**2**) = 9.0 ng/mL) against *v*-H-*ras* transformed HR-3Y1 cells, as well as cell cycle inhibition of *ras* and *src*-transformed 3Y1 cells at G1 phase. The compound shares the same biological target (H^+-V-ATPases) as the related natural products lobatamides and salicylihalamides. Relative and absolute stereochemistry assignments were based on extensive NMR studies, including modified Mosher ester analysis. Both **1** and **2** contain a highly unsaturated 12-membered macrolactone and (*Z*)-enamide side chain, differing only in epoxidation at C12-C13. Oximidine II possesses an (*E,Z,Z*) conjugated triene within the macrolactone which is very uncommon in natural products. We have accomplished the first total synthesis of (-)-oximidine II (**2**) using RCM of a well-defined bis-diene substrate **3** to construct the unusual macrocyclic triene core, and stereoselective copper-mediaed amidation of (*Z*)-vinyl iodide **4** to construct the enamide side chain. Bis-diene **3** was prepared from base-mediated transesterification of alcohol **5** (*cis*-diene) and *4H*-1,3-benzodioxin-4-one **6** (*trans*-diene). Further synthetic studies on the oximidines and their biological evaluation are on the way. ("Total Synthesis of the Salicylate Enamide Macrolide Oximidine II" *J. Am. Chem. Soc.* **2003**, ASAP)