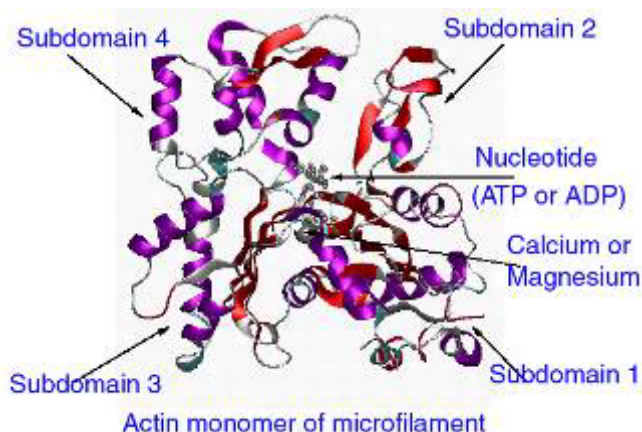


Enantioselective total synthesis of Microcarpalide and Sapinofuranone B

Total synthesis of bioactive natural products occupies keystone position in organic chemistry. The synthesis of complex biologically active compounds with multiple chiral centers is one of the most challenging tasks and therefore has always attracted the attention of chemists world-wide. Asymmetric synthesis of bioactive molecules is in the forefront of synthetic organic chemistry due to varied applications in drug and pharmaceutical industries. A large number of enantiomerically pure compounds have been obtained from nature, but quite a few of them are either not easily isolated or not available in useful amounts. However, an organic chemist can provide multi-gram biologically active compounds by synthesizing them in the laboratory. In view of this it is more elegant and economical to prepare just the wanted isomer by asymmetric synthesis and through inexpensive catalytic process which provides an especially practical entry into the chiral world due to their economical use of asymmetry inducing agents. A practical and efficient total synthesis of two very important molecules, microcarpalide and sapinofuranone using a common intermediate and asymmetric catalysis was developed by NCL team led by Dr. Pradeep Kumar.

Microcarpalide, an alkyl substituted ten membered lactone was isolated by Hemscheidt and co-workers in 2001 from fermentation broths of an unidentified endophytic fungus growing on the bark of *Ficus microcarpa* L. Since its discovery, it has aroused a great deal of interest among synthetic and medicinal chemists due to its ability to act as a strong microfilament disrupting agent at very low concentration. It displayed a weak cytotoxicity to mammalian cells, thus making it an attractive tool for studying cell motility and metastasis and a potential lead structure to develop new anti-cancer drug.

The salient structural features associated with microcarpalide are the presence of a *trans*- double bond at C7-C8 and four stereogenic centres. Most of the previous approaches described for this



molecule are based on the ring closing metathesis for the key macrolactonization to construct the olefin where the selectivities obtained were between 2:1 to 10:1 in favor of the desired *trans*-isomer. The stereogenic centres were mainly derived from the chiral pool materials. The synthetic strategy devised at NCL for microcarpalide is based on a convergent approach which utilises 1,4-butanediol as one of the common achiral starting materials to synthesize both the target compounds. The Sharpless asymmetric dihydroxylation has been executed to generate all the stereogenic centres in high enantioselectivity. The regioselective

opening of an epoxide with various nucleophiles to establish exclusively the *trans*-olefin geometry and Yamaguchi protocol to achieve the lactone moiety were employed as the key steps.

Sapinofuranone B, a novel metabolite isolated from fermentation extract of fungus *Acremonium strictum*, was synthesized for the first time from achiral substrate using asymmetric catalytic process. The earlier method uses dimethyl-L-tartrate, a chiral pool material to establish all the stereocentres. Thus, the synthetic strategy developed by NCL team is easily amenable for the preparation of other isomers. It has also considerable flexibility for the construction of related non-natural analogues for the study of structure-activity relationship.

Pradeep Kumar, S. Vasudeva Naidu and Priti Gupta, *J. Org. Chem.* 2005, 70, 2843. (This is one of the most accessed articles during January- June 2005, http://pubs.acs.org/journals/joceah/promo/most_accessed/index.html)

Pradeep Kumar and S. Vasudeva Naidu, *J. Org. Chem.* 2005, 70, 4207

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