Biomimetic Synthesis of Anthrapyrane Antibiotics

The 4*H*-anthra[1,2-*b*]pyranes are well known for their antibacterial and antitumor activity. Their chemistry, biochemistry and biological activities were extensively reviewed. In most cases, the angulary condensed benzo[*a*]anthraquinone skeleton was constructed by a Diels-Alder reaction. It is anticipated that a series of Claisen condensations give molecules with *β*-polyketone functionalities (polyketides), whose intramolecular condensation and enolization generate aromatic nuclei such as naphthalenes, anthracenes, benz[*a*]-anthracene and anthrapyranes. Therefore we used the methodology of Yamaguchi to construct anthraquinones with ester functions in the side chain.

Up to the present they were mentioned theoretically and conformed through findings of the isolated „end"-structure. Only the identification of open chain structure as intermediate provides crucially the contribution for the biosynthesis clarification. Indeed they were not isolated yet, so that such open chain precursors were formulated hypothetically so far. The natural behaviour of these open chain substances tend to intramolecular cyclisation. For countering these unavoidable aldolkondensation we have to use protecting groups. Preferentially silyl-protecting groups were used because of the easily deprotection under mild reaction conditions. For this project three most interesting substances were emerged from these inquisitions, namely the tricycle hemiacetals **66a/b**, the open chain ketoesters **65a/b** and the bis-silylprotected open chain structure **68**. In establishing our objectives for identification of biosynthesis precursors we have successively synthezied the bis-silylprotected open chain structure **68**.

With regard to the total synthesis of indomycinone-derivatives two synthetic pathways were haunted, namely the linear total synthesis and the convergent pathway. The linear pathway is based on the proved method for synthesizing *γ*-indomycinone through Baker-Venkataraman rearrangement. Using propionylchlorid the ethylanthrapyrane **62** as a key-step was formed. The missing side chain which leads to the indomycinone-derivatives were tied up at the ethyl side chain of ethylanthrapyrane **62**.

Parallel to the linear total synthesis two synthetic building blocks were formed for the convergent pathway. The silyl-protected isocoumarin was developed after five steps and construct the anthraquinone skeleton. The acetylacetone **90**, as the second synthetic building block, was synthesized in few steps which contains information about stereochemistry of the alkyl chain. The combination of these two synthetic building blocks gave tricyclic silylether **91**. The silylgroup was removed by the known method in literature e.g. HF to afford anthraquinone **98**. 1,3-Diketo substance **98** was cyclised by using triflouroactic acid to benzyl protected *γ*-indomycinone **99**.