

Towards the Total Synthesis of Disorazole Analogues

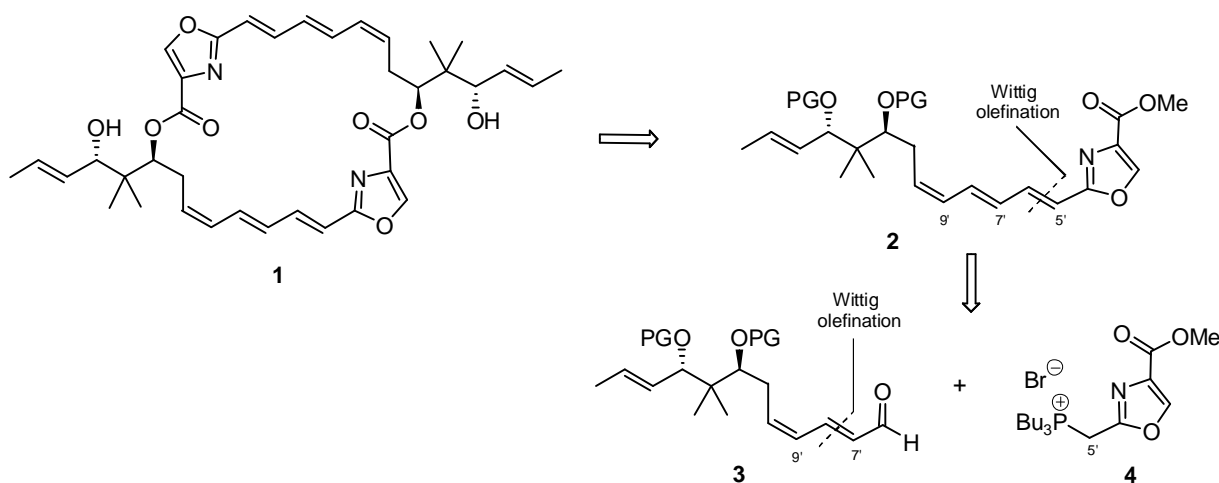
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The Disorazoles are a structurally interesting family of 29 closely related macrocyclic dilactones. They were isolated in 1994 at the HZI in Braunschweig by Höfle and co-workers from the fermentation broth of the myxobacterium *Sorangium Cellulosum* (Strain So ce12).^[1] Their structures are modified in the carbon chain by variation of the position and configuration of double bonds and oxygen substituents like epoxide, hydroxyl, or methyl ether groups.

In 2004 another derivative (**1**) of the Disorazoles was isolated at the HZI. Like the whole Disorazole family, **1** also possesses significant cytotoxic activities.



Because of the homodimeric structure of **1** cyclodimerisation of the trienoxy ester **2** forms the shortest synthetic approach to **1**. Via an *E*-selective Wittig reaction the two fragments **3** and **4** are coupled to install the C₅=C₆' double bond of the triene unit.

On one hand the achiral oxazole fragment **4** is built up over four steps and on the other hand the aldehyde **3** is obtained after nine steps. This convergent synthesis allows to build up a broad variety of Disorazole analogues.

[1] Jansen R., Irschik, H., Reichenbach, H., Wray, V., Höfle, G. *Liebigs Ann. Chem.* **1994**, 759-773.