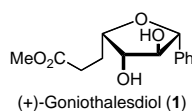


TOTAL SYNTHESIS OF (-)-GONIOTHALESIDIOL

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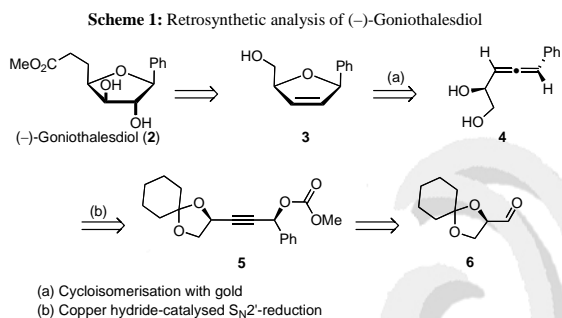
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Introduction



S. W. Goh *et al.* isolated (+)-Goniothalesdiol **1** from the bark of the Malaysian tree *Goniothalamus borneensis*.^[1] The structure and the relative configuration were determined by IR, MS and NMR whereas the absolute configuration was identified by a semisynthesis. In biological screenings, (+)-Goniothalesdiol has shown a high cytotoxic activity against P388 leukaemia cells in mice and a high insecticide activity.

Retrosynthesis

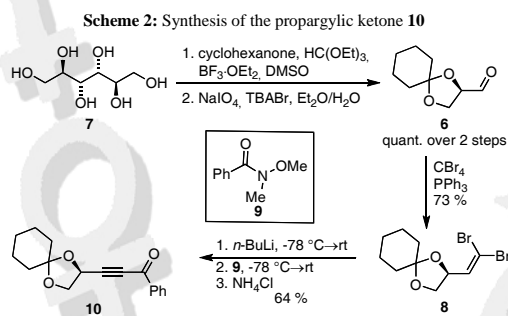


(+)-Goniothalesdiol can be considered as a C-glycosidic derivative of L-xylose. Its anomeric center is substituted by a phenyl group and the hydroxyl group at C-5 by α -methyl acetate equivalent. Recently, it has been shown by our group that C-glycosidic furanose derivatives can be efficiently synthesised from α,β -dihydroxyallenes by gold-catalysed cycloisomerisation and subsequent dihydroxylation of the double bond.^[2]

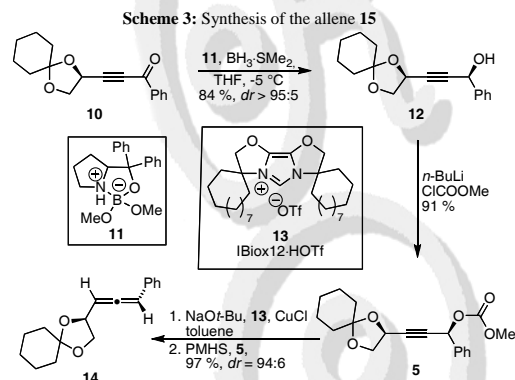
In this project, the enantiomer (-)-Goniothalesdiol (**2**) is synthesised according to this method. The dihydroxyallene **4** is formed from propargylic carbonate **5** by a copper hydride-catalysed S_N2' -reduction developed in our group.^[3] This compound is synthesised from protected (*R*)-glyceraldehyde (**6**), which can be easily prepared from D-mannitol.^[4]

Results

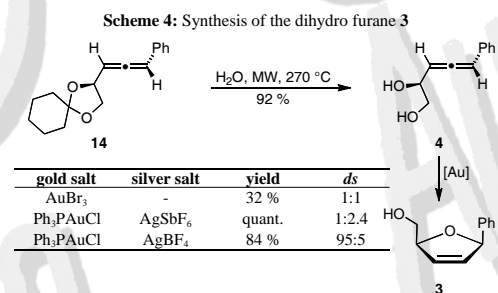
Starting from D-mannitol (**7**) the glyceric aldehyde derivative **6** was synthesised in two steps.^[4] The resulting lithium acetylide of the Corey-Fuchs-sequence was trapped by the Weinreb amide **9** to form the acetylenic ketone **10** (Scheme 2).



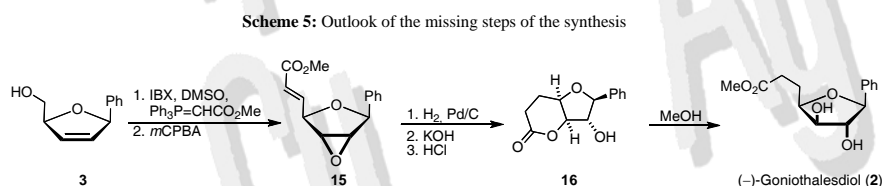
The acetylenic ketone **10** was stereoselectively reduced by borane-DMS complex using the CBS-type catalyst **11** according to *Ortiz-Marciales et al.* (Scheme 3).^[5] The subsequent carbonate formation by using *n*-BuLi as a base and methyl chloroformate gave substrate **5** for the S_N2' -reduction by using catalytic copper hydride.^[3] The IBiox12 carbene was found to efficiently stabilise the copper hydride during the reaction. As a stoichiometric hydride source polymethylhydrosiloxane (PMHS) was used. The resulting allene **14** was obtained in excellent yield and diastereoselectivity.



The allene was deprotected by using a microwave assisted reaction in pure water with a yield of 92% to form the α,β -dihydroxyallene **4**.^[6] The yield and the diastereoselectivity of the following gold-catalysed cycloisomerisation is dramatically influenced by the gold precatalyst (Scheme 4).^[7]



Outlook



The one-pot reaction with IBX and the Wittig reagent with subsequent epoxidation with *m*CPBA should give substrate **15**. The following steps were realised in the synthesis of the 5-methyl analogon and should be applicable to **15**.^[8]

Literature

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