ORGANO- AND BIOCATALYSIS FOR LIGNAN NATURAL PRODUCT SYNTHESIS

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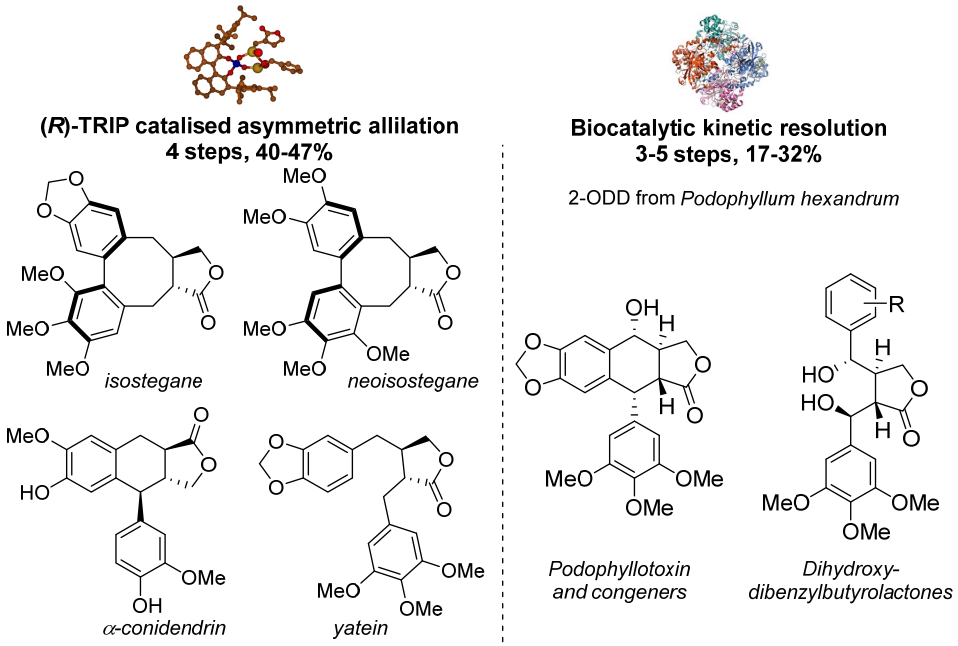

Lignan natural products are a large class of polyphenols produced by plants that exhibit important antiviral, anti-cancer and antimicrobial bioactivities.

Chiral phosphoric acids like 3,3′-Bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate (TRIP) can provide catalytic stereoinduction on the allylation of benzaldehydes. This methodology was applied for the synthesis of (-)-hydroxymatairesinol [1]. We have extended the short total synthetic procedure to other four lignans, namely (+)-yatein, (-)-α-conidendrin, (+)-iso- and (+)-neoisostegane with high overall yields and enantiomeric purity via only four steps.

In addition, a chemoenzymatic approach has been used to target podophyllotoxin. The asymmetric information has been given by a 2-oxoglutarate dependent dioxygenase from *Podophyllum hexandrum* that performs a biocatalytic kinetic resolution of the *rac*-4-hydroxyyatein substrate thus achieving the aryltetralin scaffold. Enantiopure deoxy-, isodeoxy-, *epi*- and podophyllotoxin have been obtained. With the same approach new potential APIs, namely dihydroxy-dibenzylbutyrolactones have been produced.

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[1] Fuchs, M.; Schober, M.; Orthaber, A.; Faber, K., *Adv. Synth. Catal.* **2013,** *355*, 2499-2505.