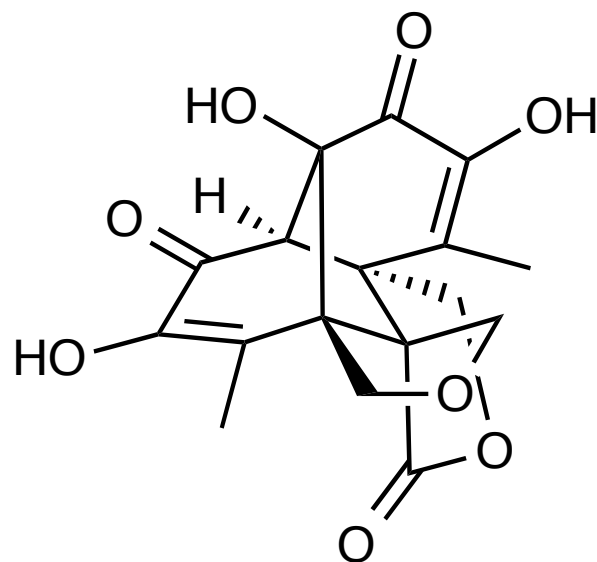


An Eight-Step Synthesis of Epicolactone Reveals its Biosynthetic Origin

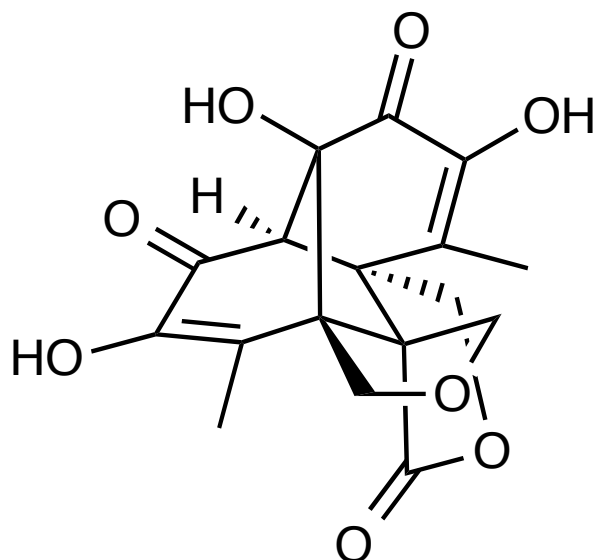
P. Ellerbrock, N. Armanino, M. K. Ilg, R. Webster, and D. Trauner
Ludwig Maximilians University



Evan Carder
Wipf Group Current Literature
November 21, 2015

[1] *Nat. Chem.* **2015**, *7*, 879.

Epicolactone



- Isolated from an endophytic fungi *Epicoccum* – a plant fungi found on sugar cane and cocoa tree.
- Displays antimicrobial and antifungal activity.
- Features a pentacyclic framework that contains four tetrasubstituted carbons and five contiguous stereocenters.

[1] Eur. J. Org. Chem. **2012**, 5225–5230.

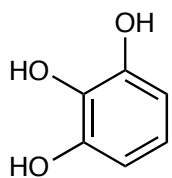
[2] Eur. J. Org. Chem. **2013**, 3174–3180.

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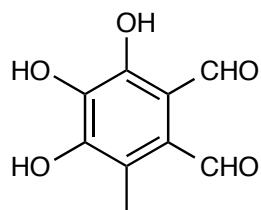
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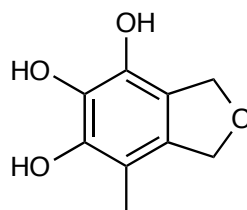
Fungal metabolites



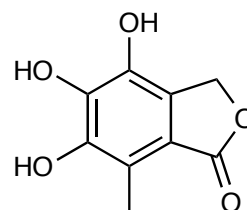
Pyrogallol



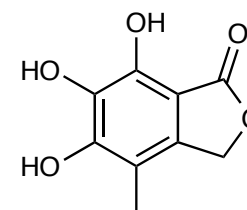
Flavipin



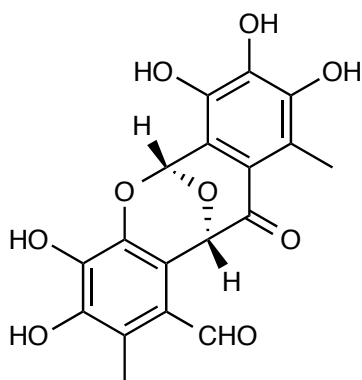
Epicoccine



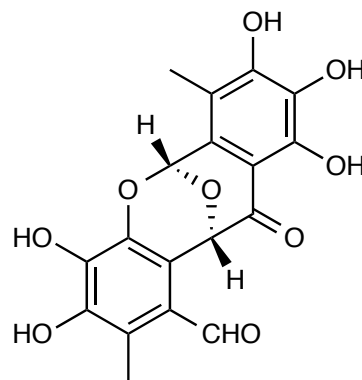
Epicoccone A



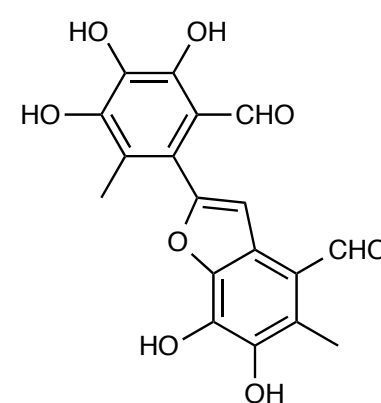
Epicoccone B



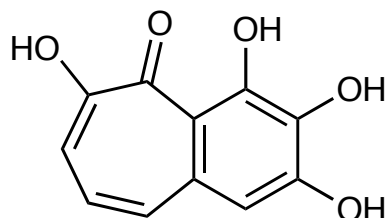
Epicoccolide A



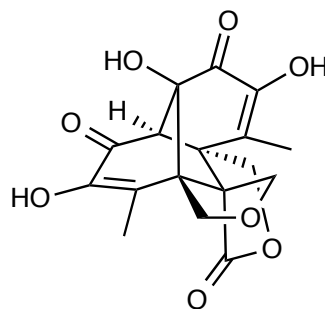
Epicocconigrone A



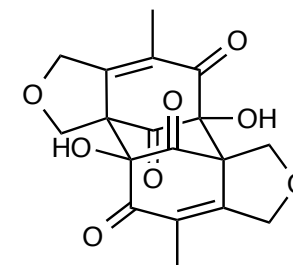
Epicoccolide B



Purpurogallin



Epicolactone



Dibefurin

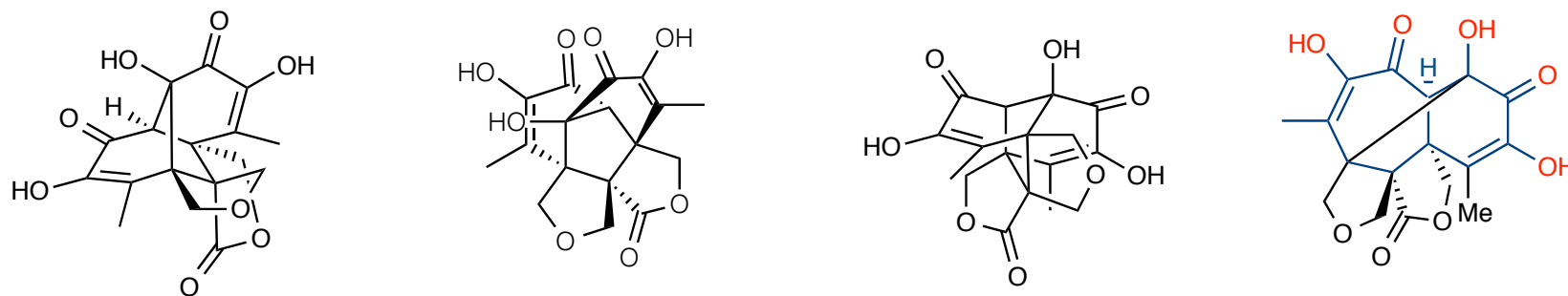
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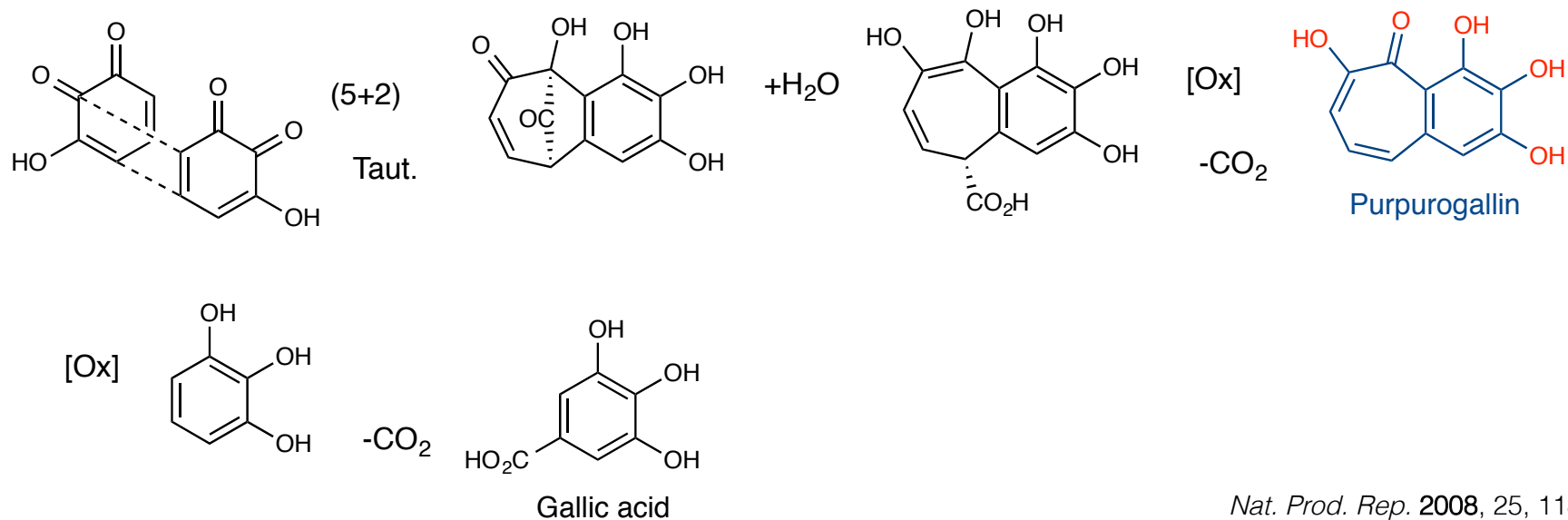
3

Pattern Recognition

Epicolactone from different perspectives:

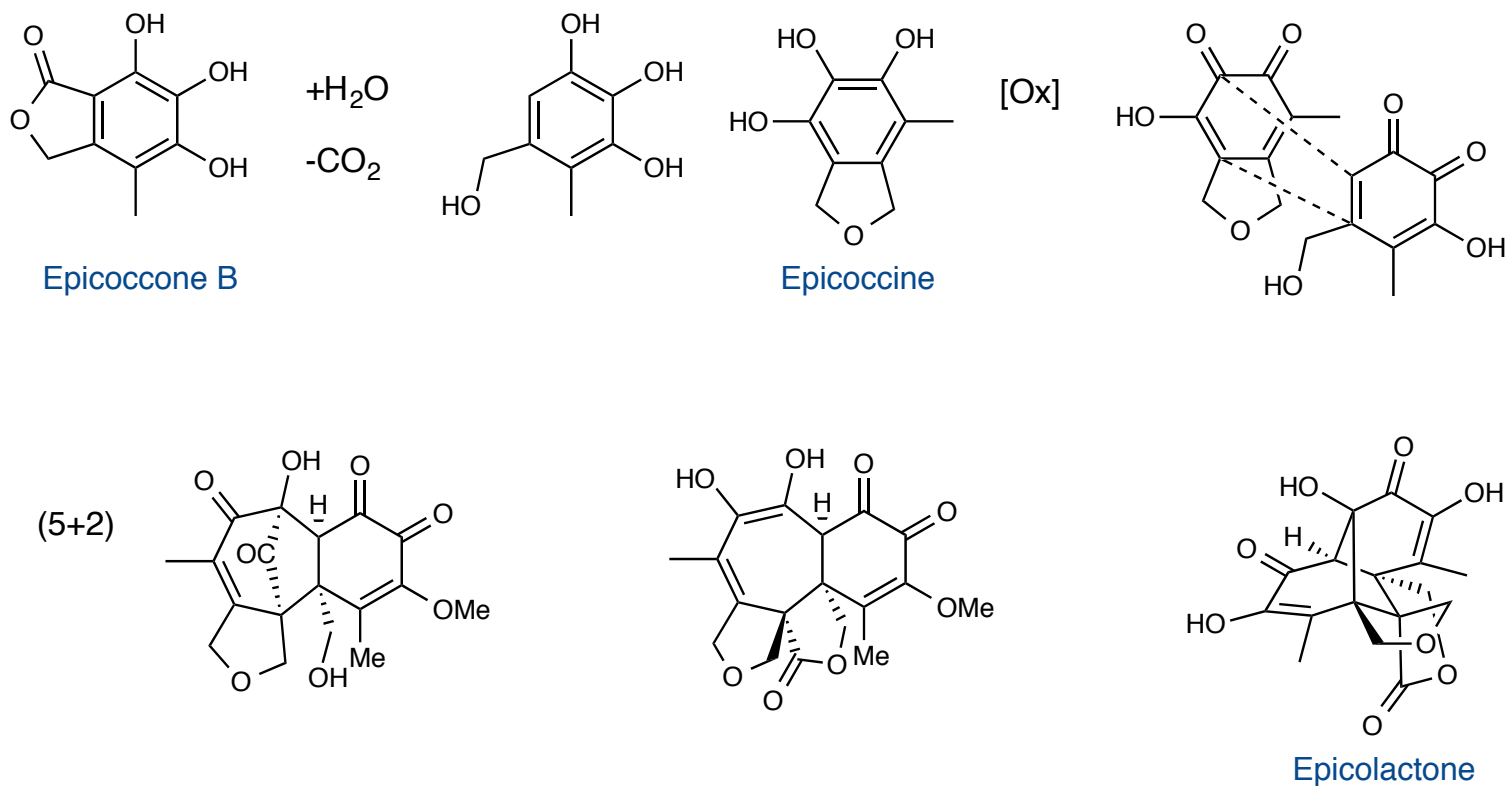


Established purpurogallin biosynthesis:

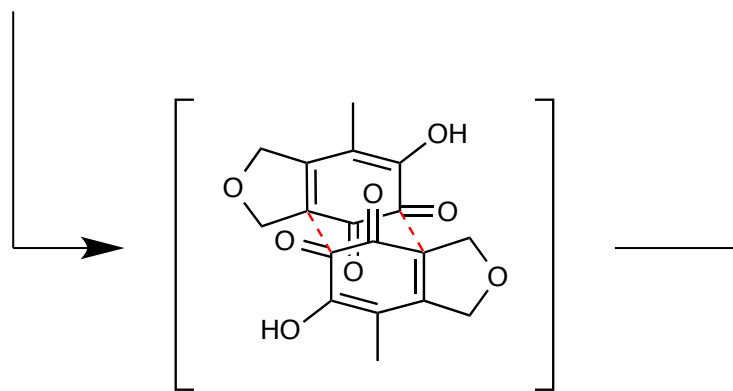
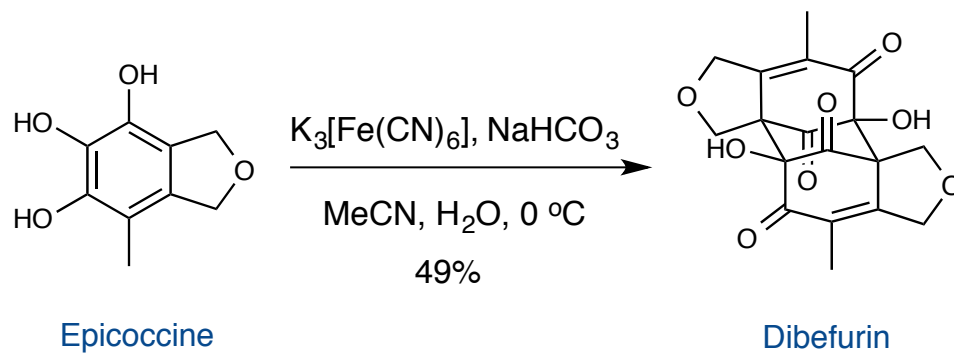


Nat. Prod. Rep. **2008**, 25, 118.

Proposed biosynthesis of Epicolactone



Previous work: Synthesis of Dibefurin



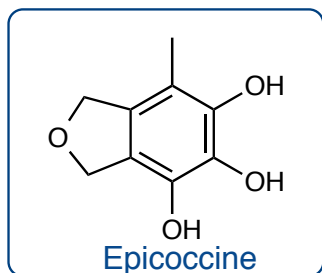
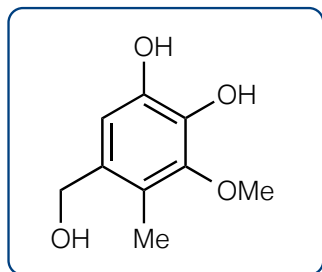
Angew. Chem. Int. Ed. **2014**, 53, 13414.

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Advanced intermediates

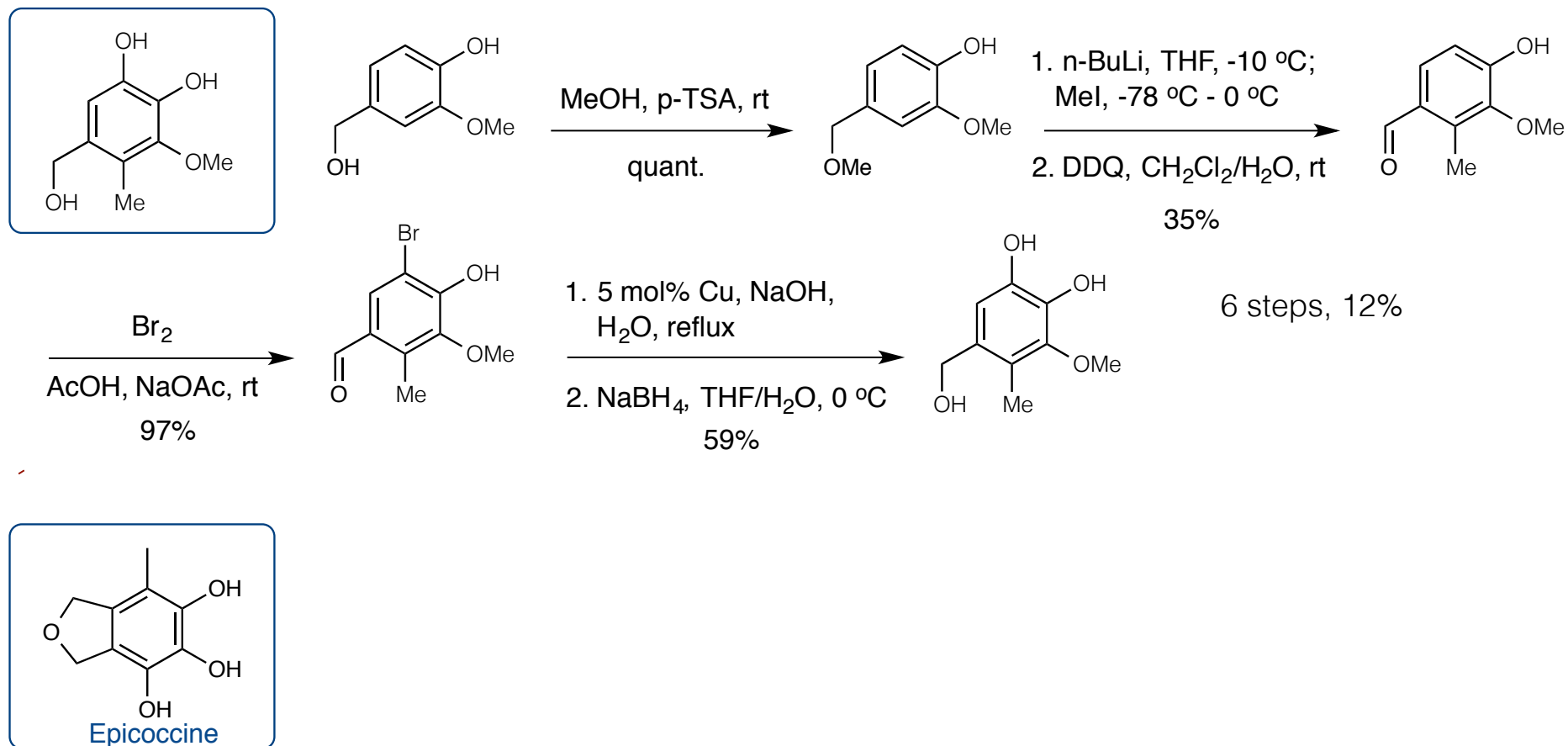


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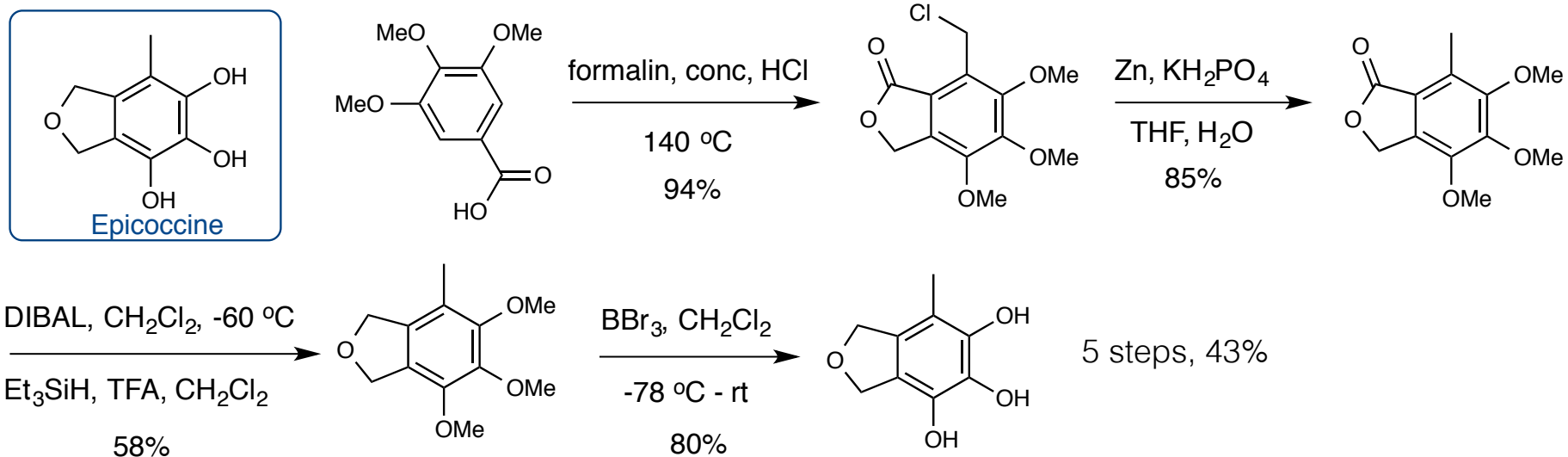
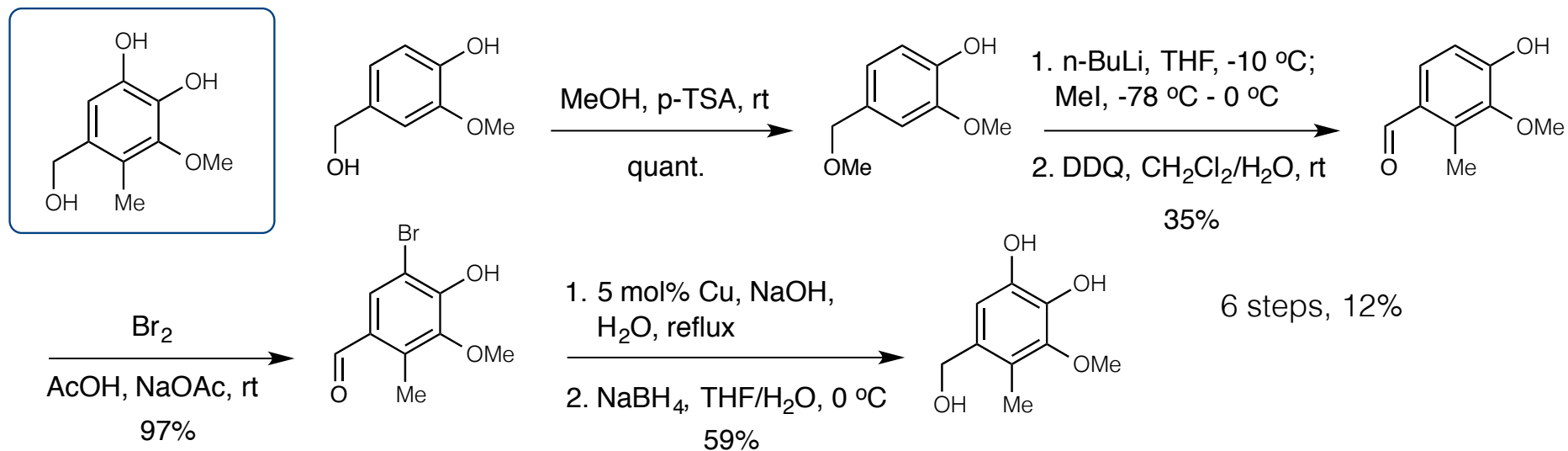
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Advanced intermediates



Advanced intermediates

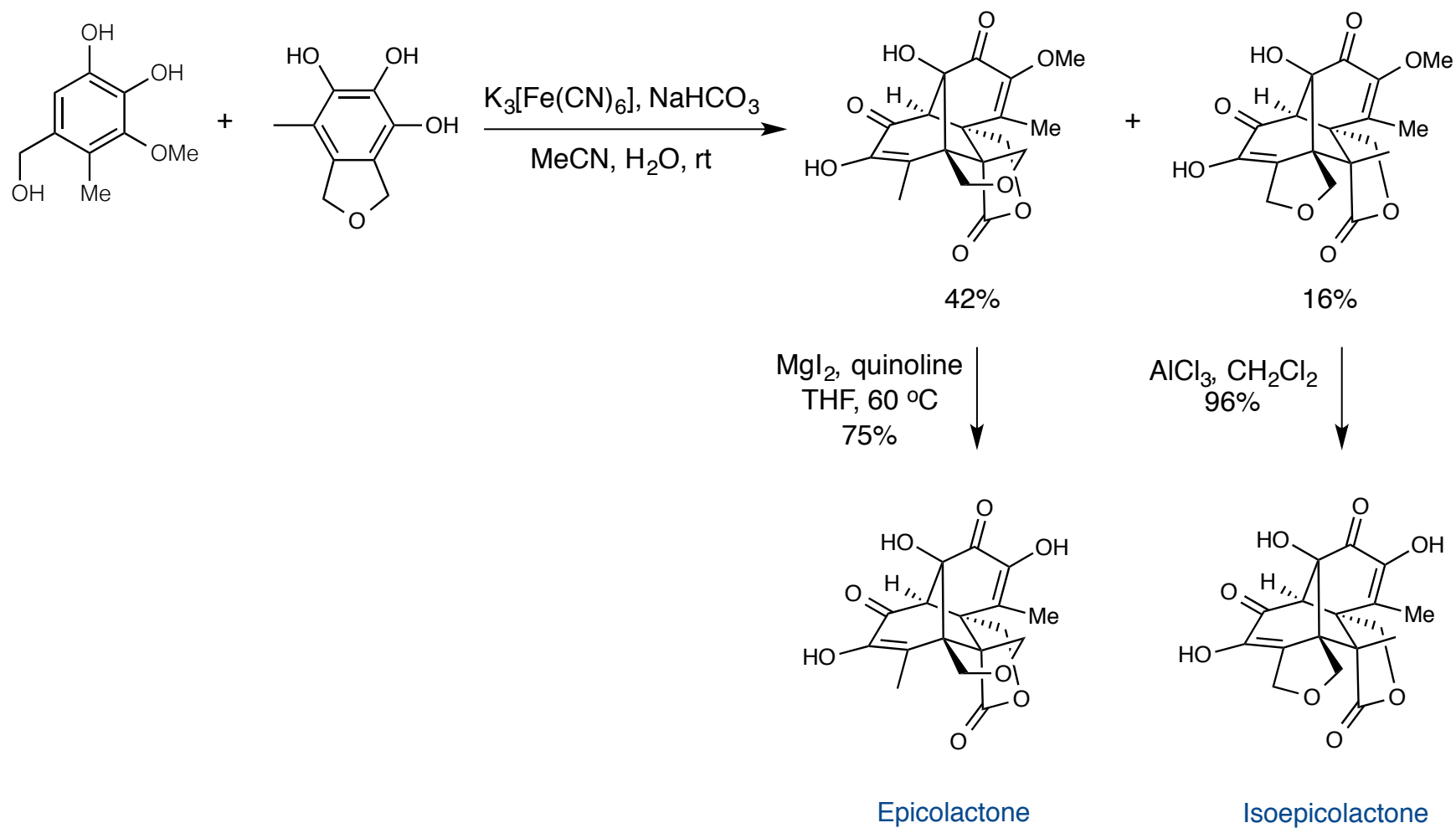


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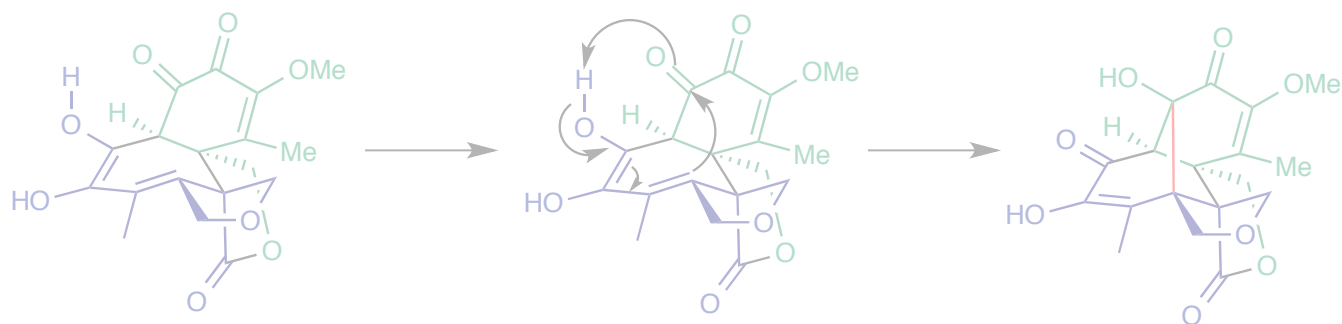
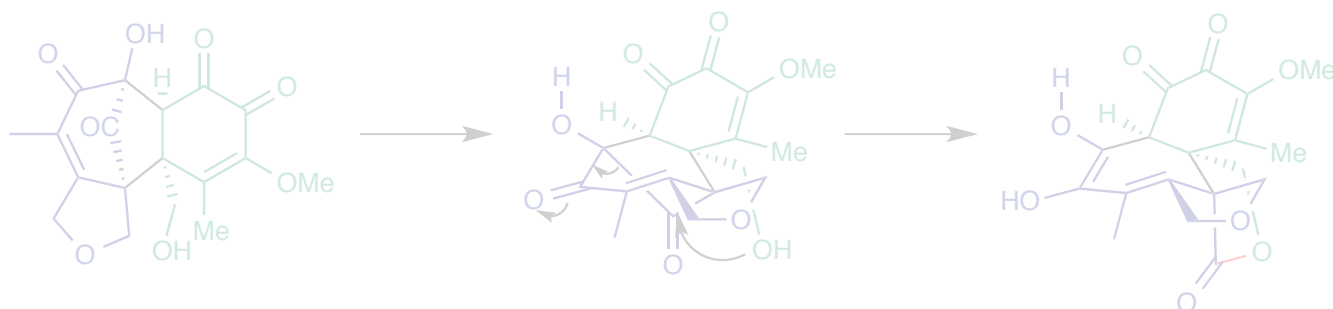
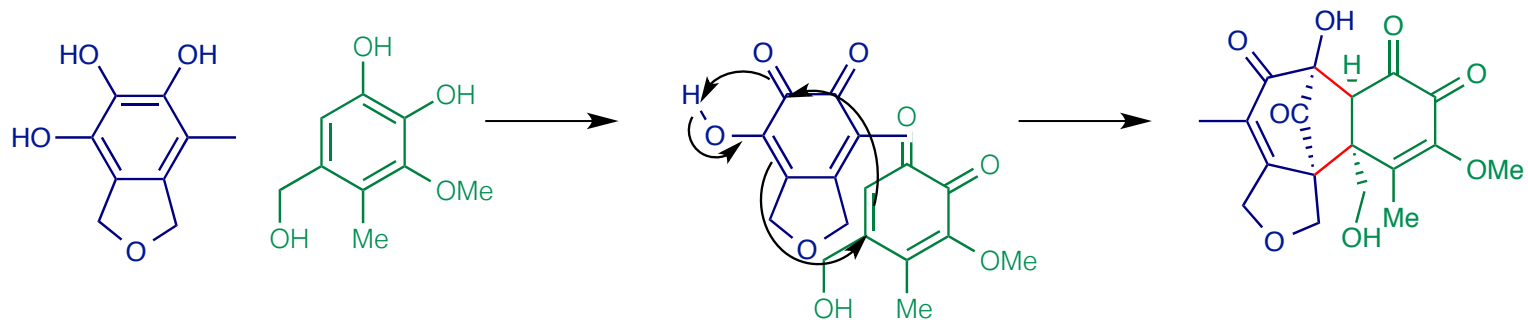
9

Synthesis of Epicolactone



Key transformation

(5+2) cycloaddition

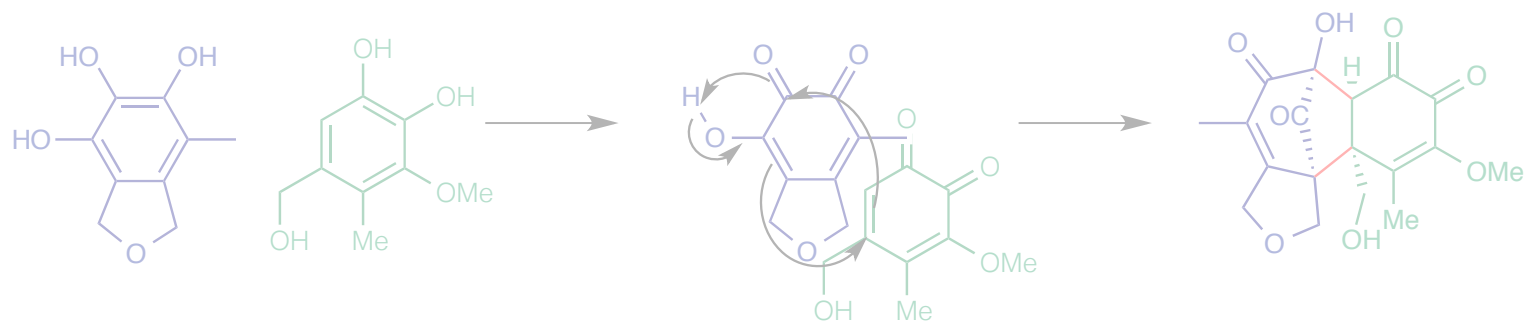


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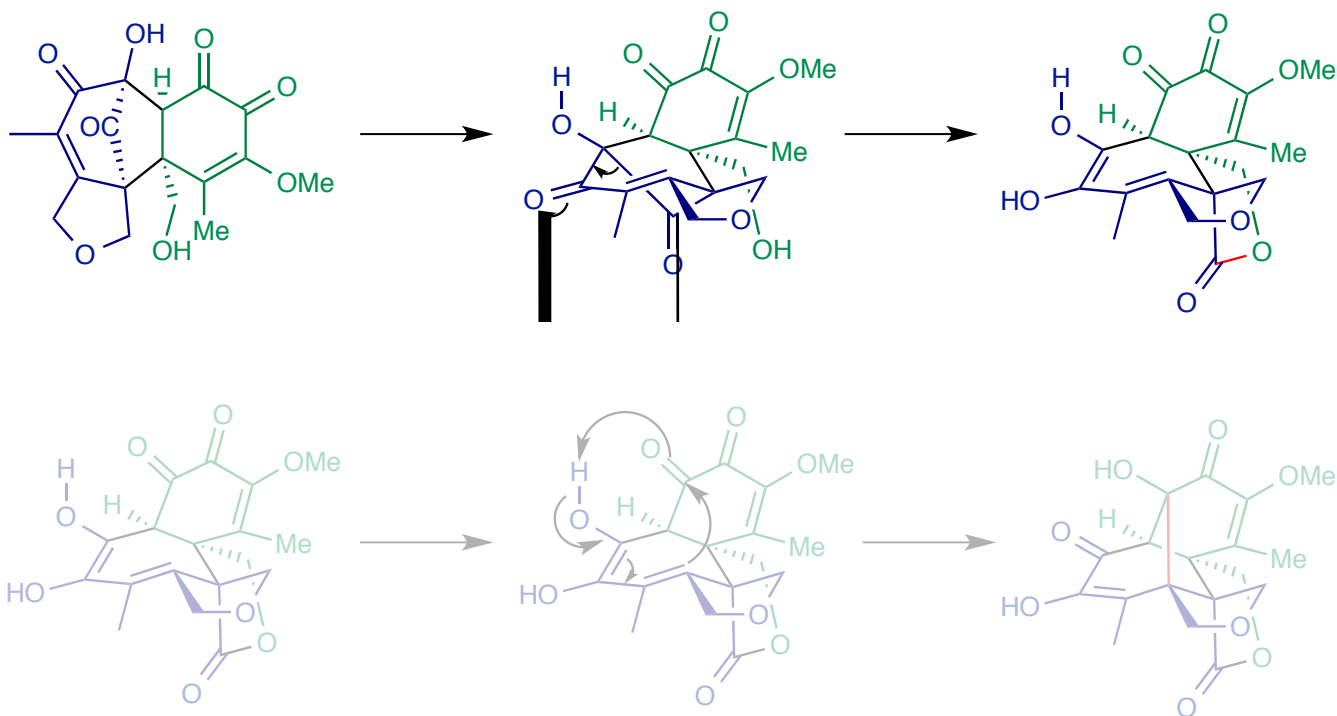
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Key transformation



retro-Claisen condensation

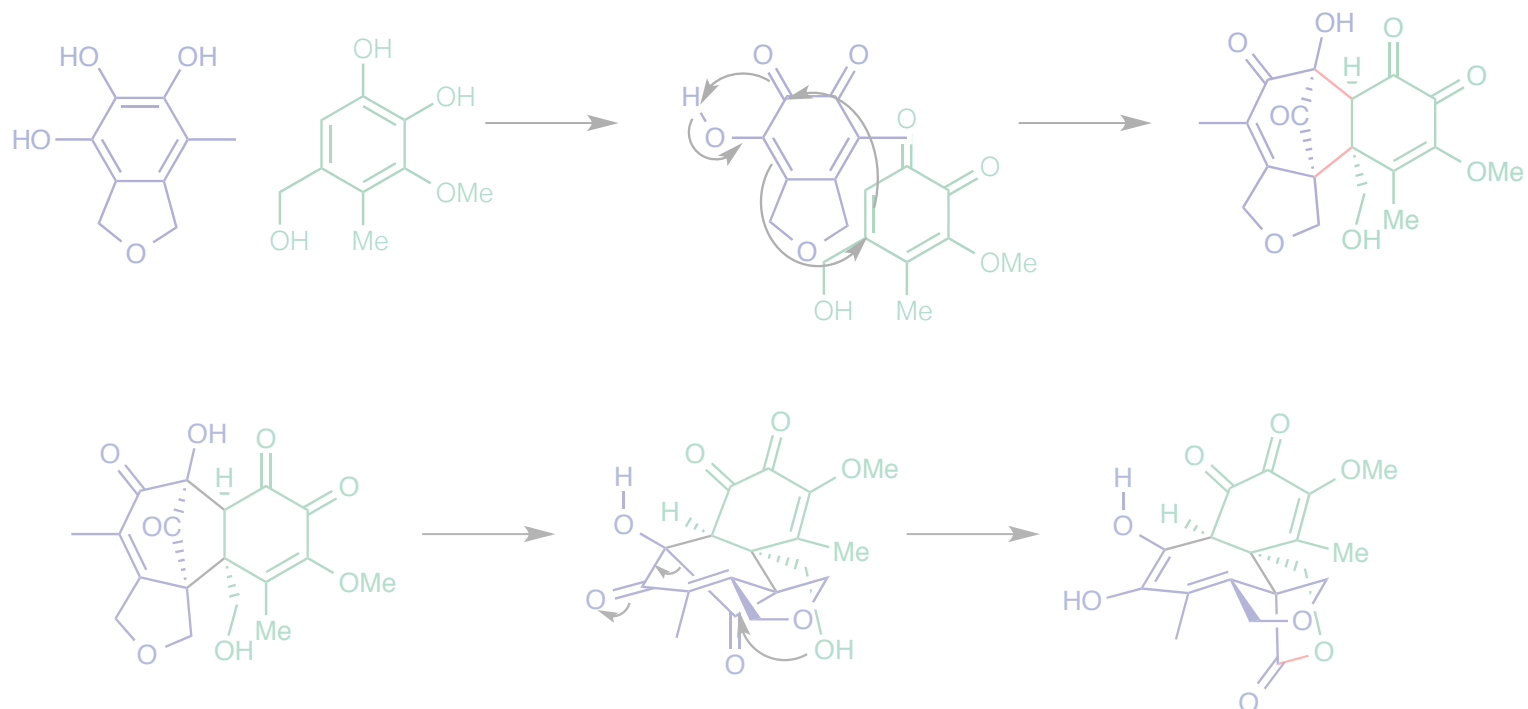


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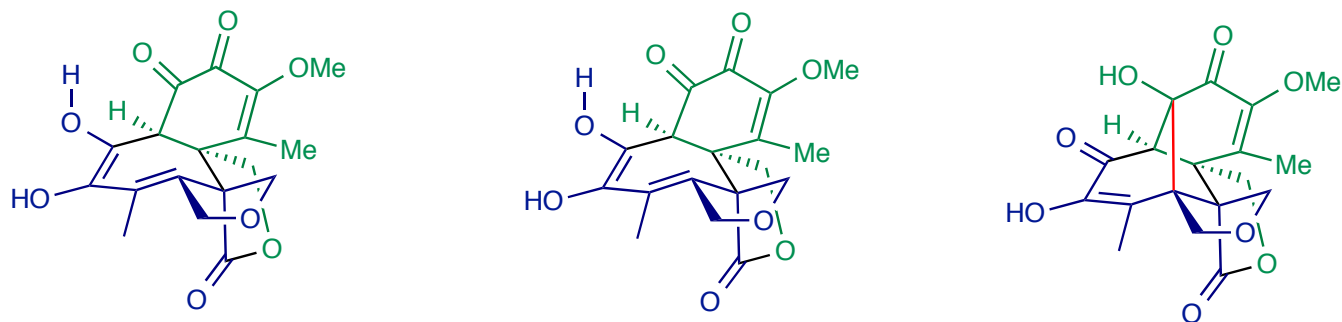
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Key transformation



vinylogous aldol reaction



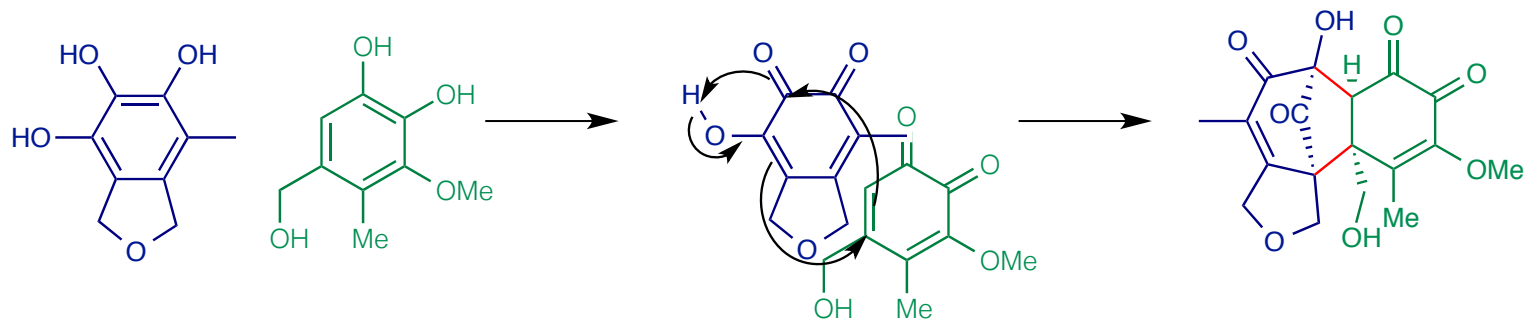
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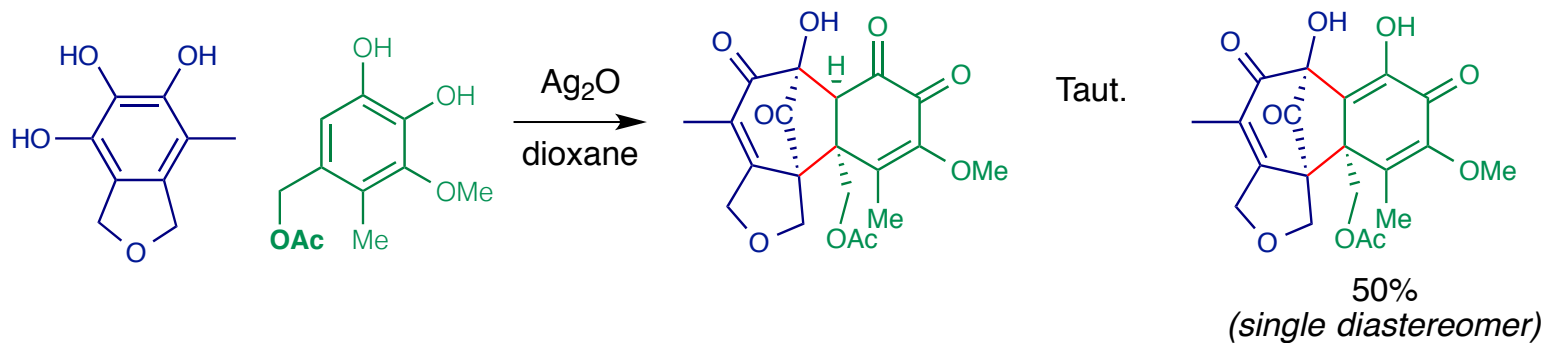
13

Diastereoselectivity

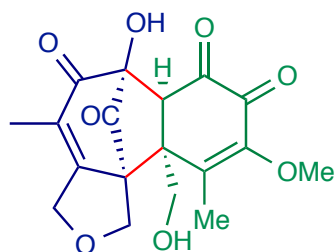
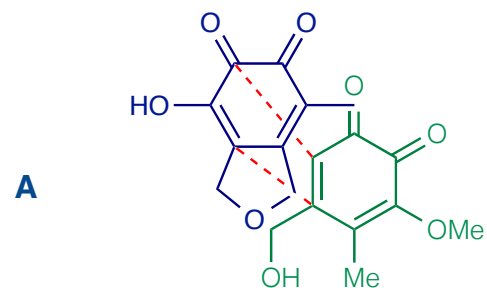
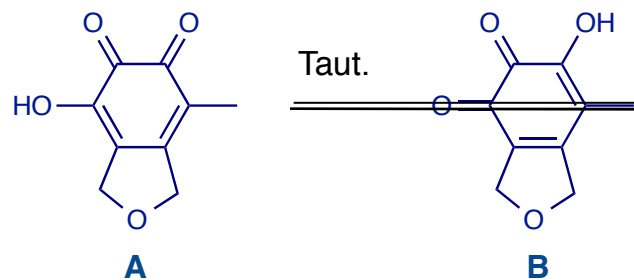
(5+2) cycloaddition



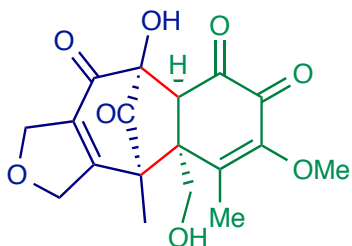
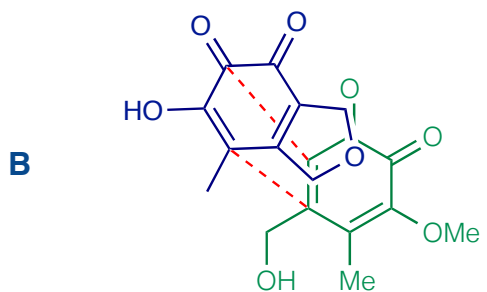
Isolation of the carbonyl-bridged intermediate



Regioisomers

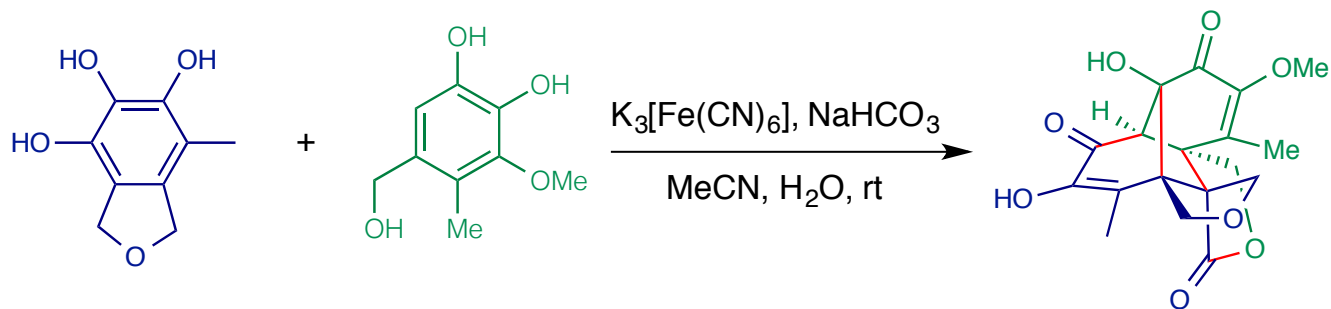


Epicolactone



Isoepicolactone

Conclusions



Major accomplishments:

- Concise synthesis of Epicolactone in 8 steps, LLS.
- The synthesis highlights a one-pot reaction cascade sequentially featuring a (5+2) cycloaddition, retro-Claisen condensation, and vinylogous aldol reaction to afford the rather complex framework of Epicolactone.
- Provided insight into the potential biosynthesis of Epicolactone