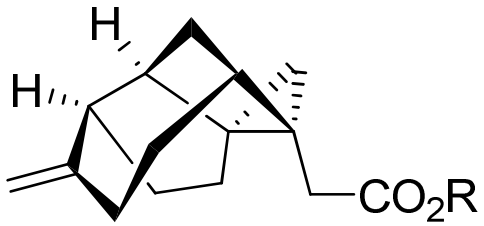
Formal asymmetric synthesis of Echinopine A and B

Chen *et al*, *Angew. Chem. Int. Ed,* **2011**, *50*, 1-5



R = H -> Echinopine A
R = Me -> Echinopine B

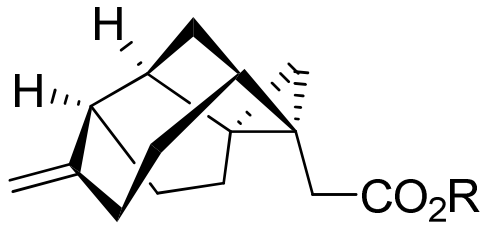
Introduction:

- Isolation of these two new sesquiterpenes from *Echinops spinosus* in 2008 by Kiyota *et al*[1]

- No real interesting biological activities but unprecedent architectures….

- Represent an enticing challenge for the synthetic community because of their unique carbocyclic framework caracterized by a [3,5,5,7] ring system

5 stereogenic centers
2 quaternary carbons



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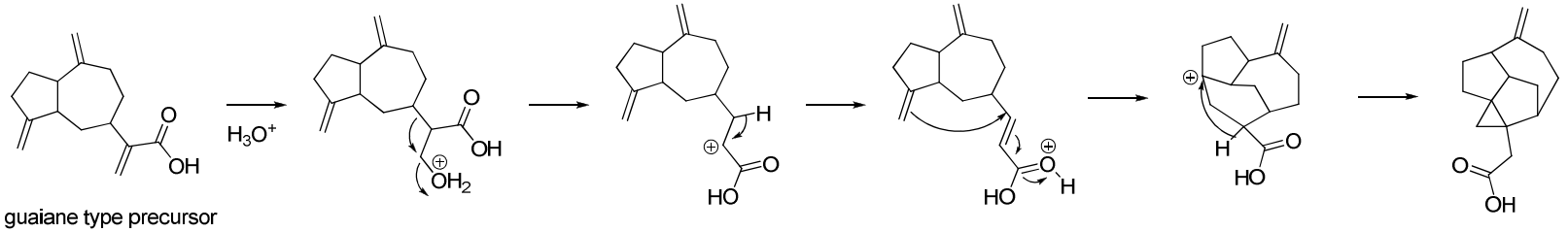
1 : Kiyota *et al*, *Org. Lett*, **2008**, *10*, 701

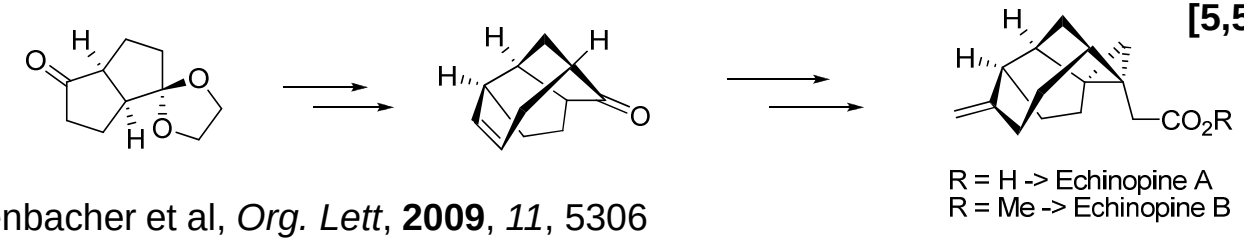
Precedent on the subject

➡ Proposed biosynthetic pathway:



➡ Already two total synthesis of these compounds:

The first



[5,5] -> [5,5,7] -> [3,5,5,7] strategy

Tiefenbacher et al, *Org. Lett*, **2009**, *11*, 5306

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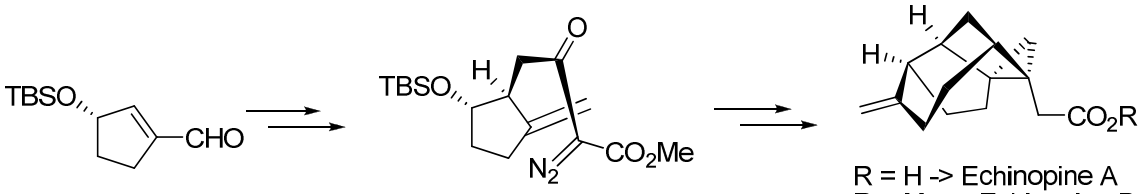
The second



[5] -> [3,5,5] -> [3,5,5,7] strategy

Chen *et al*, *J. Am. Chem. Soc,* **2010**, *132*, 3815

R = H -> Echinopine A
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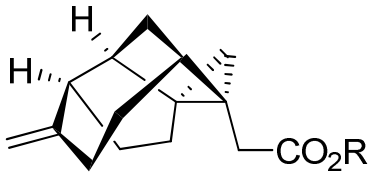
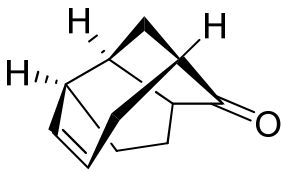
His strategy

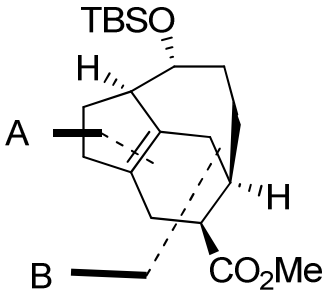
A one pot preparation of a [5,6,7] system and its conversion to the [5,5,7] framework system



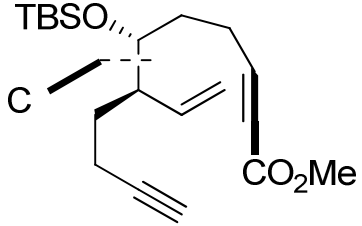
R = H -> Echinopine A
R = Me -> Echinopine B



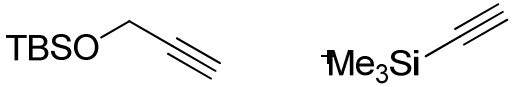
Ring contraction

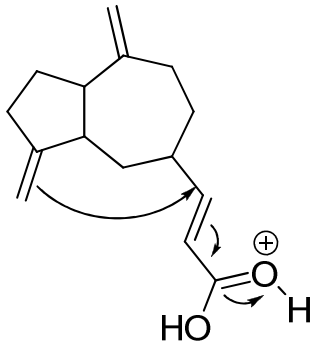


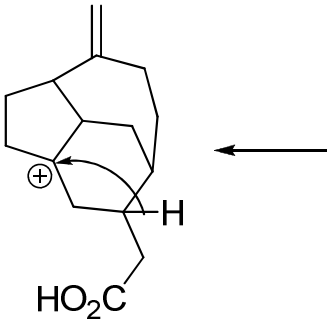
Cascade process



Hosomi- Sakurai reaction

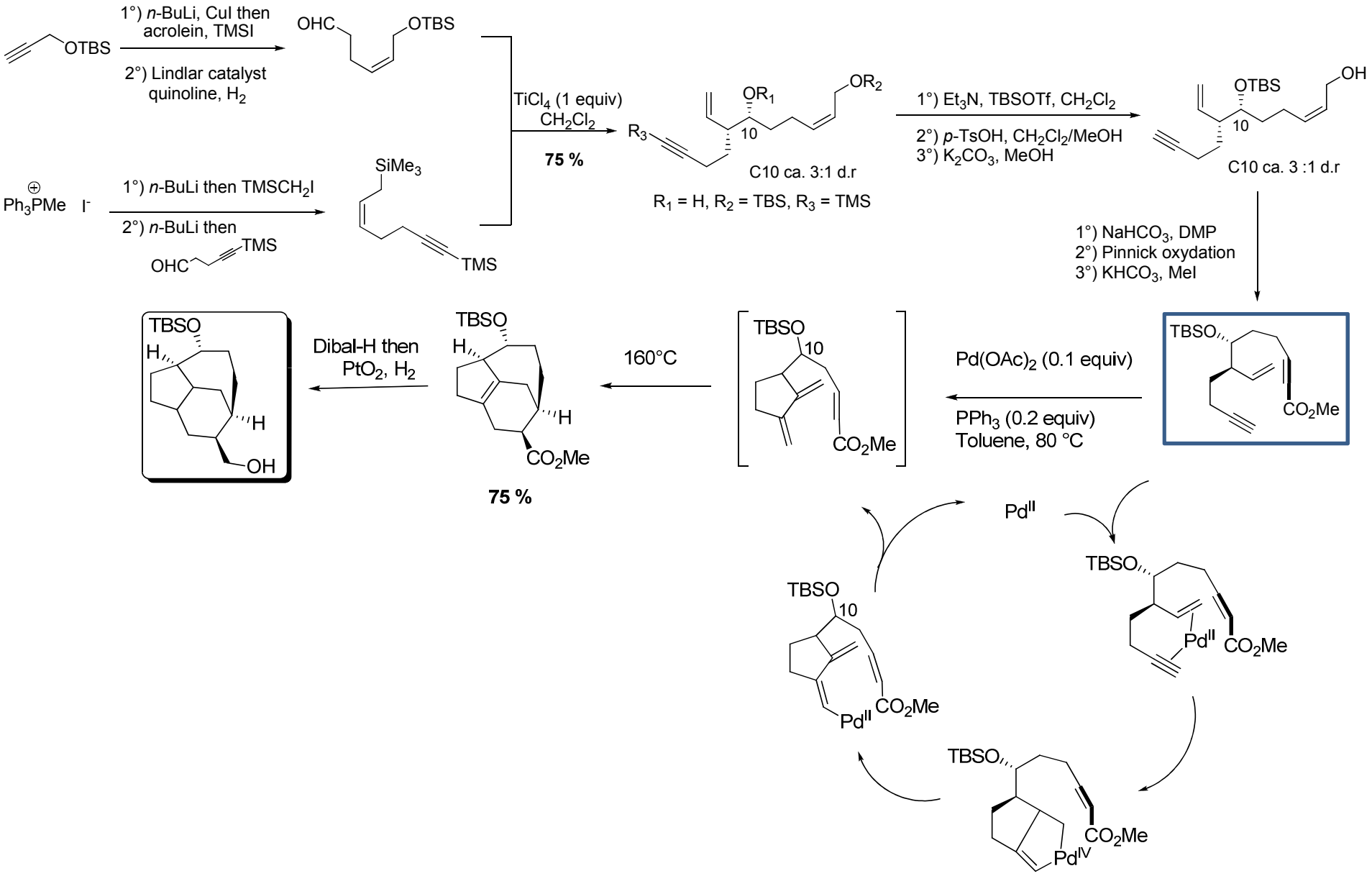




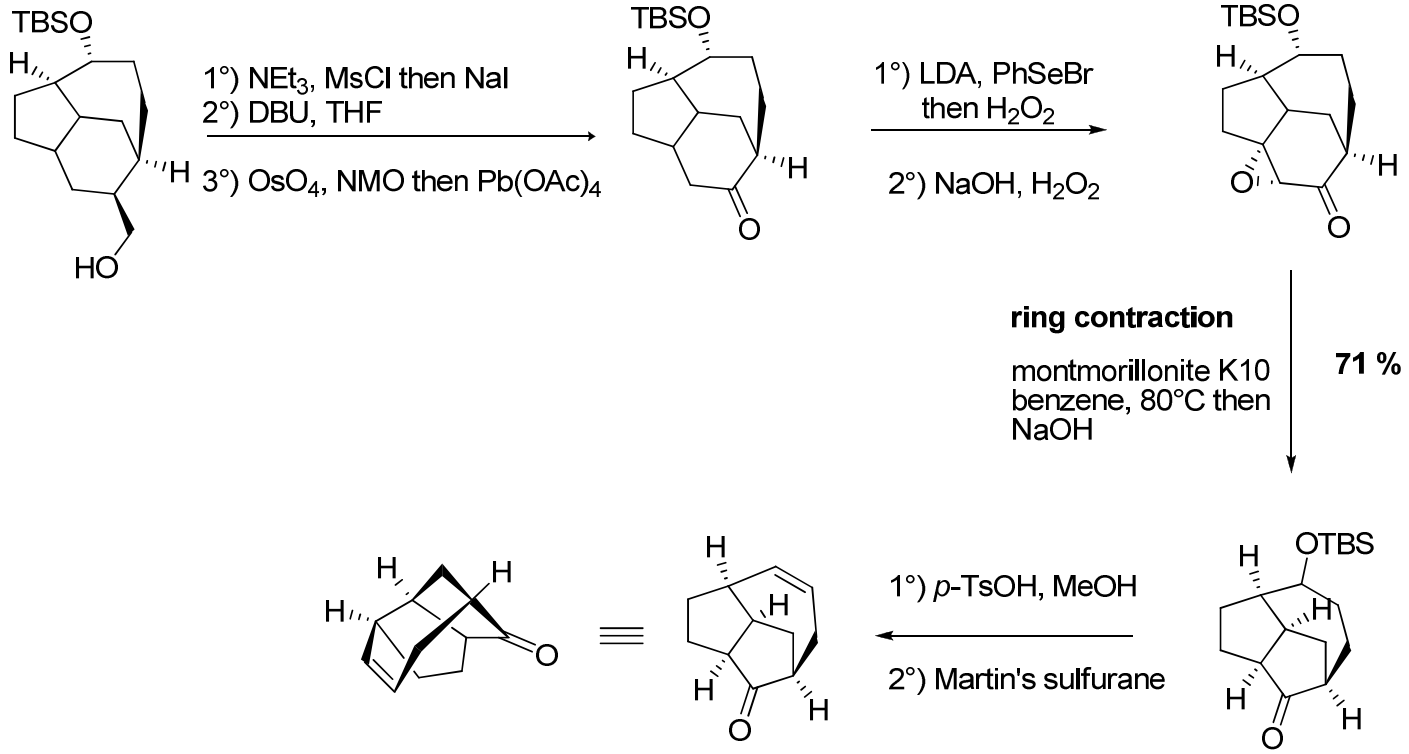


biosynthetic pathway

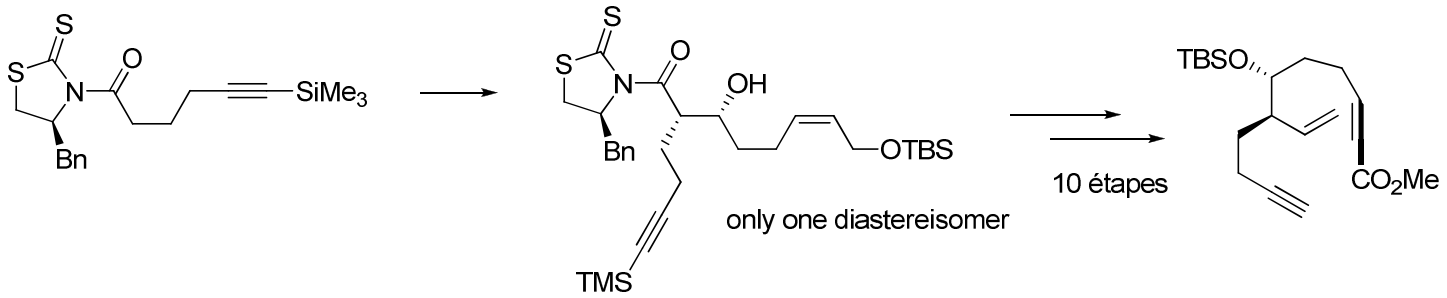
Synthetic pathway:



Final steps…



Enantioselective synthesis



Conclusion

- Elegant formal synthesis of Echinopine A and B thanks to **3 key steps**
- 18 steps to synthezise key compound in 12 % overall yield
- Conceptually contrasting sequence involving a one pot preparation of a [5,6,7] system and its conversion to the [5,5,7] ring framework