Synthesis of the Sporolide Ring Framework through a Cascade Sequence Involving an Intramolecular [4+2] Cycloaddition Reaction af an *o*-Quinone

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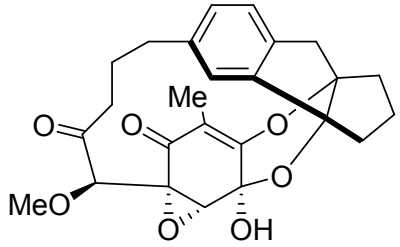
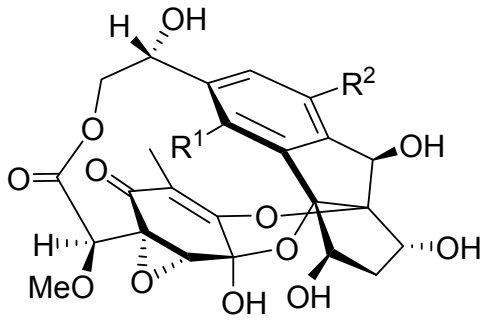
ACIE **2008**, *47*, 1432.



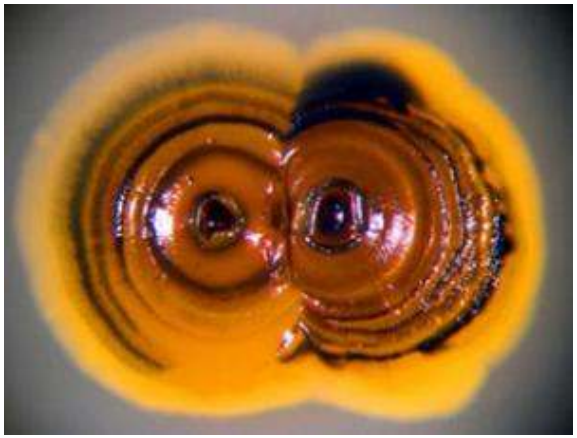
Marija Manojlovic

Wipf group current literature meeting
2/16/08

Sporolides



R^1 = Cl, R^2 = H **Sporolide A**
R^1 = H, R^2 = Cl **Sporolide B**



Salinospora tropica

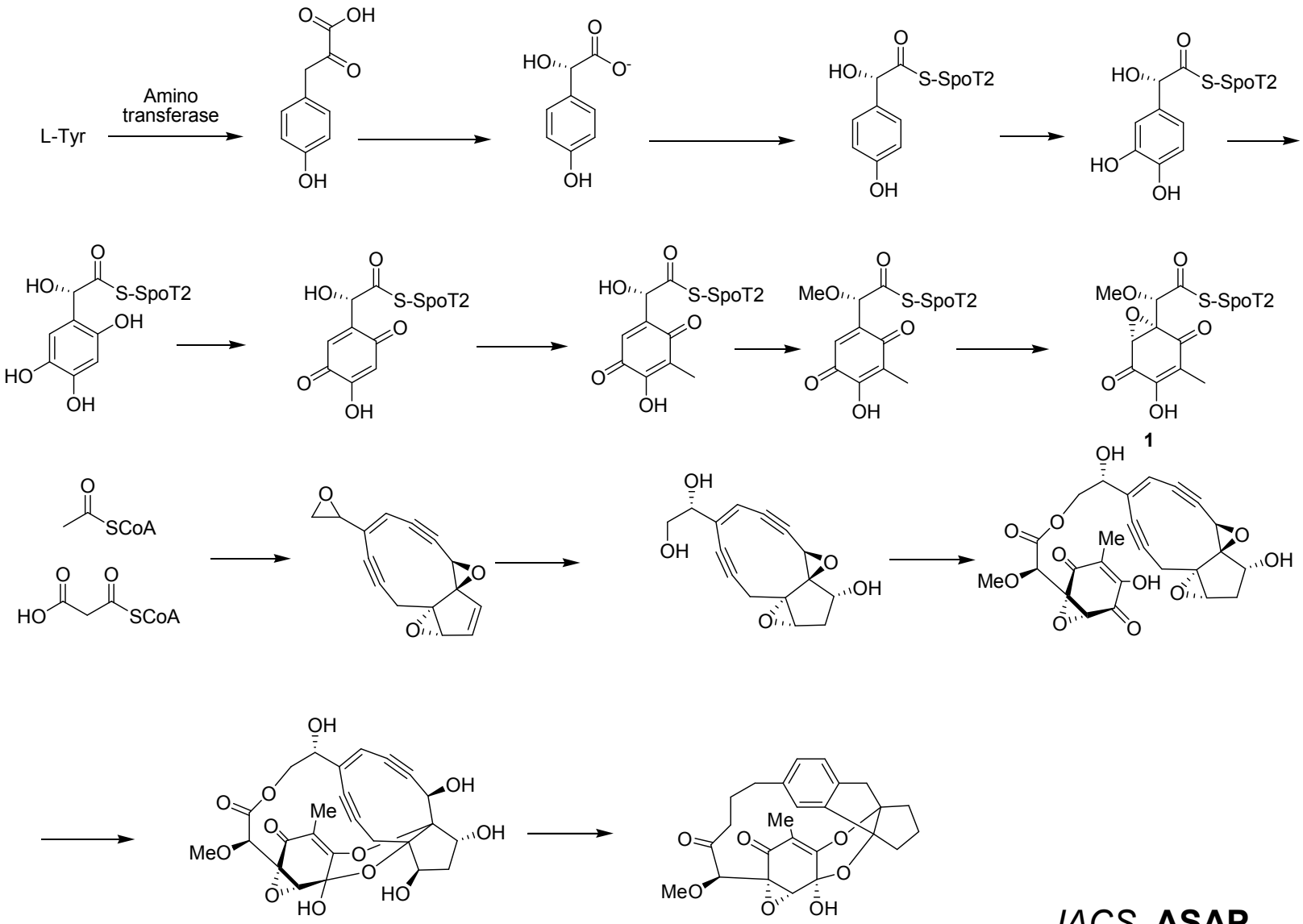
-Isolated in 2005 from a strain of the marine-derived actinomycete *Salinospora tropica*

- No reported biological activity so far

-Structurally very interesting with 24 carbons of which 22 are either oxygenated or sp^2 hybridized, 10 stereocenters and 7 rings.

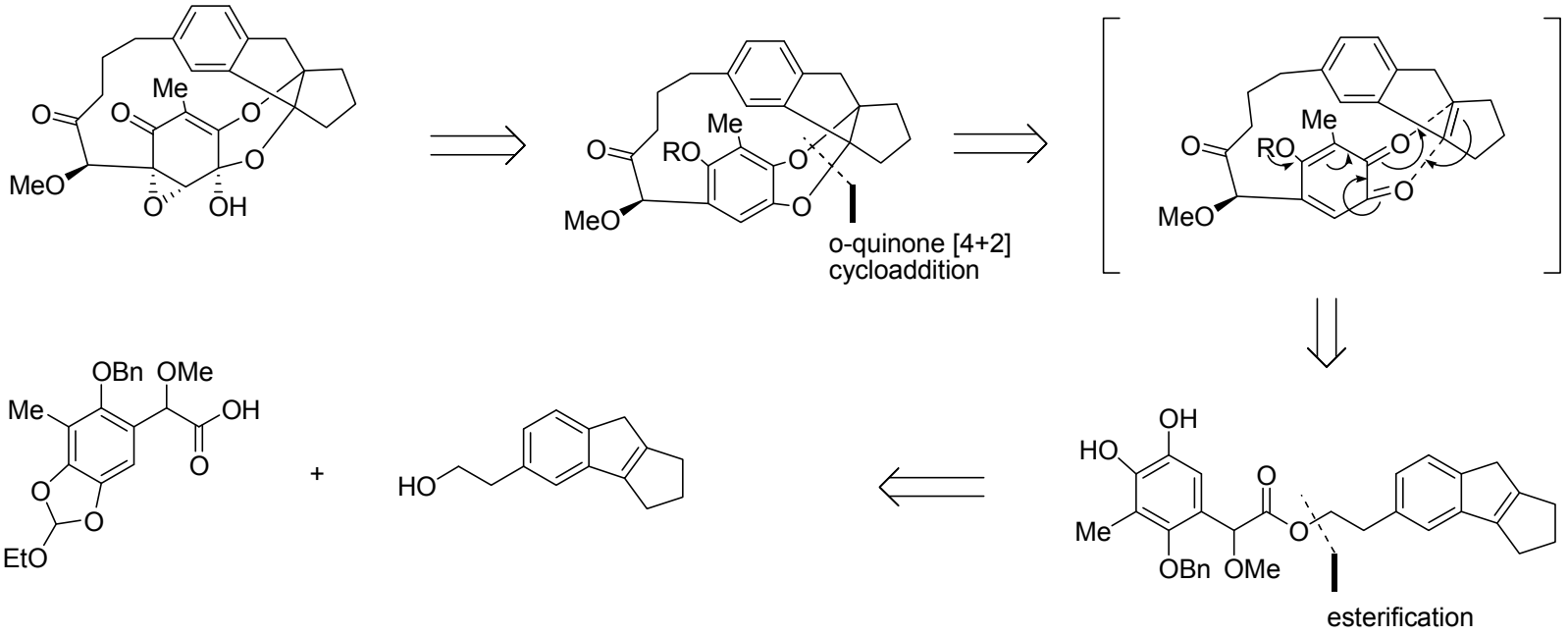
OL **2005**, *7*, 2713.

Biosynthesis Proposal



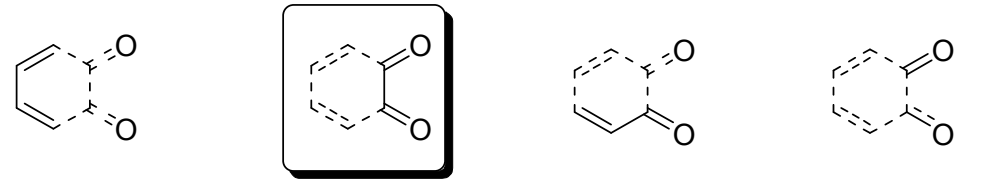
JACS **ASAP**.

Framework Synthetic Strategy

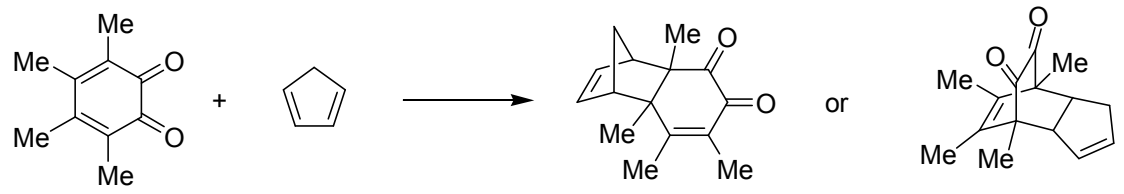


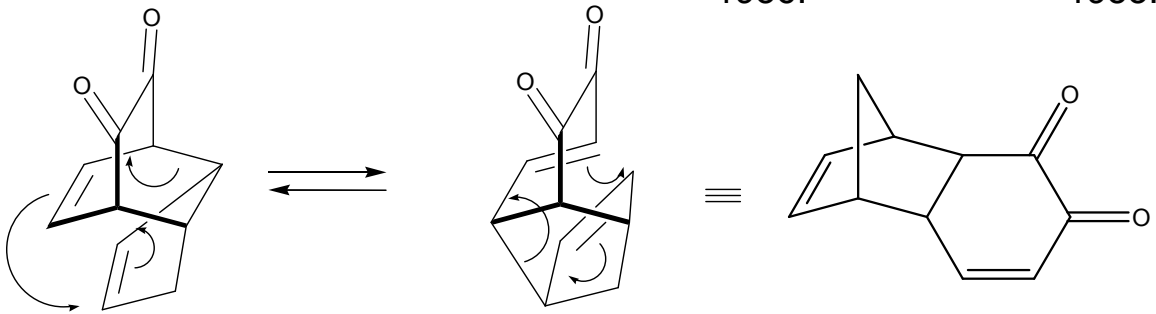
ACIE **2008**, *47*, 1432.

O-Quinones in Cycloadditions



-The first Diels-Alder reactivity of o-benzoquinones reported in 1936. by Smith and Hac

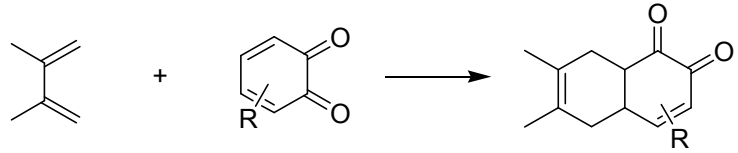




Synlett **1997**, 1143.

O-Quinones in Cycloadditions

-In Diels-Alder reactions with acyclic dienes o-benzoquinones always function as dienophiles, addition occurring preferentially to the more electron deficient double bond.

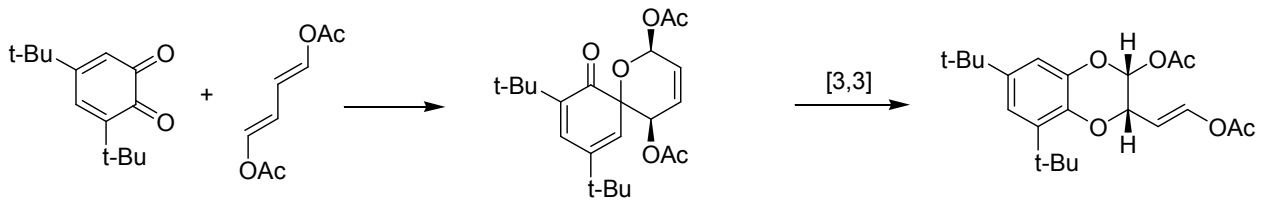


Entry	R	Yield (%)	Site of addition
1	H	51	3,4=5,6
2	3-Me	27	5,6
3	4-Me	39	5,6
4	3-MeO	75	5,6
5	4-MeO	80	5,6
6	3-Cl	90	5,6
7	4-Cl	60	5,6
8	4-NHAc	87	5,6
9	4-CO_2Me	75	3,4
10	4-CN	19	3,4
11	3-Me, 5-Me	44	3,4 and 5,6
12	4-Me, 5-CO_2Me	63	5,6
13	3-Me, 5-CN	13	5,6

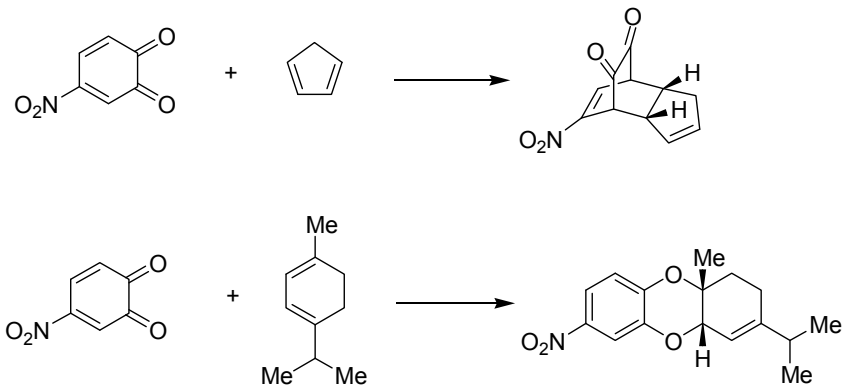
J. Chem. Soc. (C) **1971**, 1414.

O-Quinones in Cycloadditions

-Very electron rich acyclic dienes react with o-benzoquinones to give benzodioxin adducts. The reaction is proposed to be stepwise, involving Diels-Alder reaction followed by Cope rearrangement.



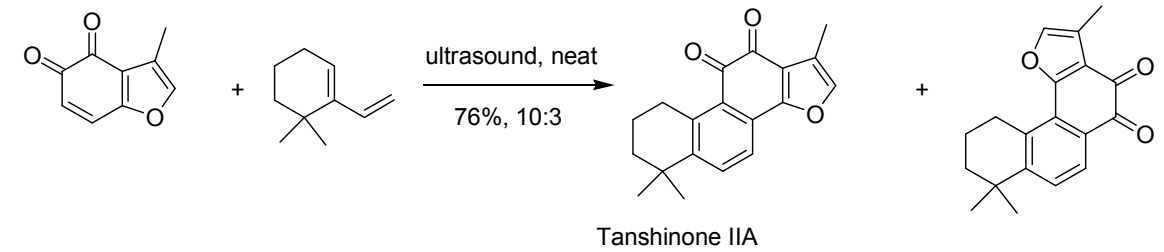
-Electron poor o-quinones can react in different ways with different cyclic electron rich dienes



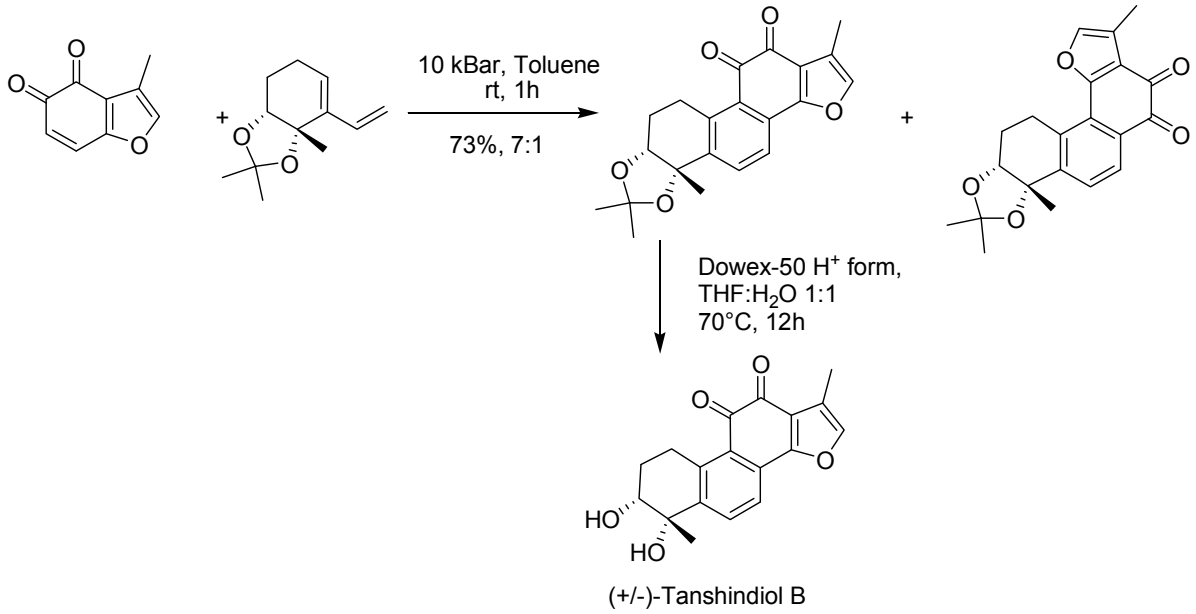
Synlett **1997**, 1143.

O-Quinones in Cycloadditions

-There are examples of applications of o-quinone reacting as carbodienophile in total synthesis of natural products. However, there are no examples of application of heterodiene reactivity of o-quinones.



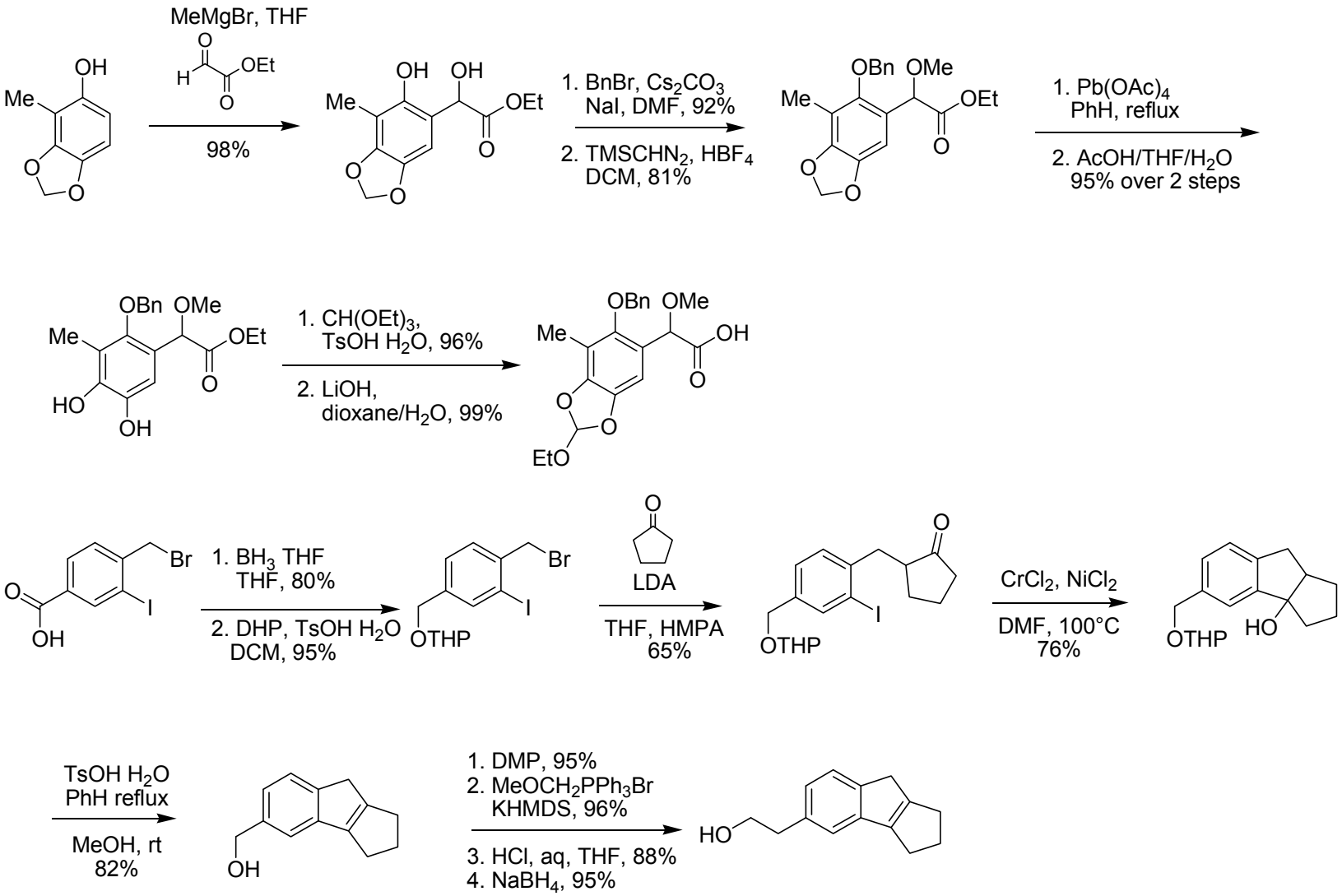
Tanshinone IIA



(+/-)-Tanshindiol B

JACS **1989**, *111*, 1522.

Synthesis of Sporolide Framework



ACIE **2008**, *47*, 1432.

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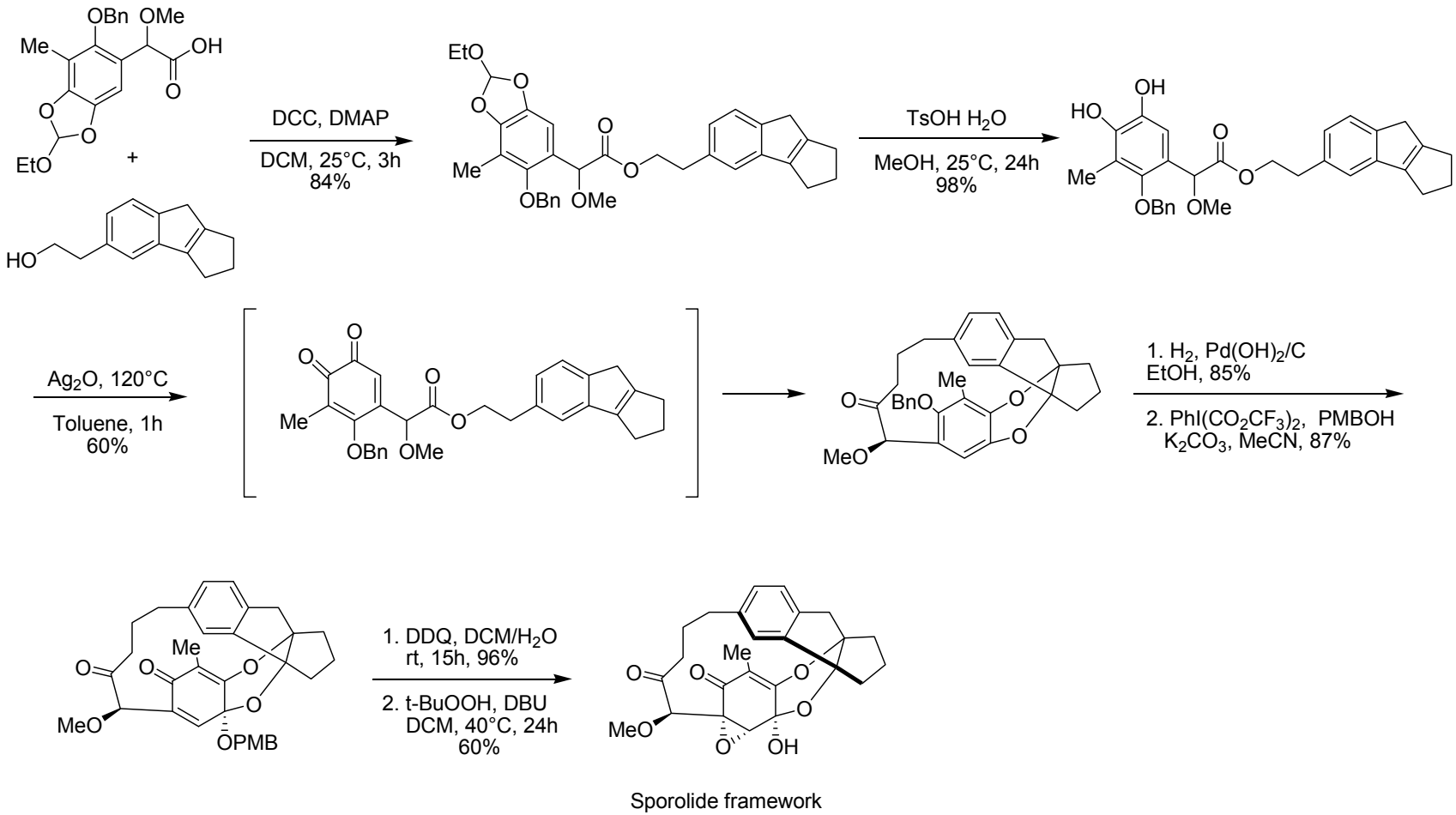

Sporolide framework

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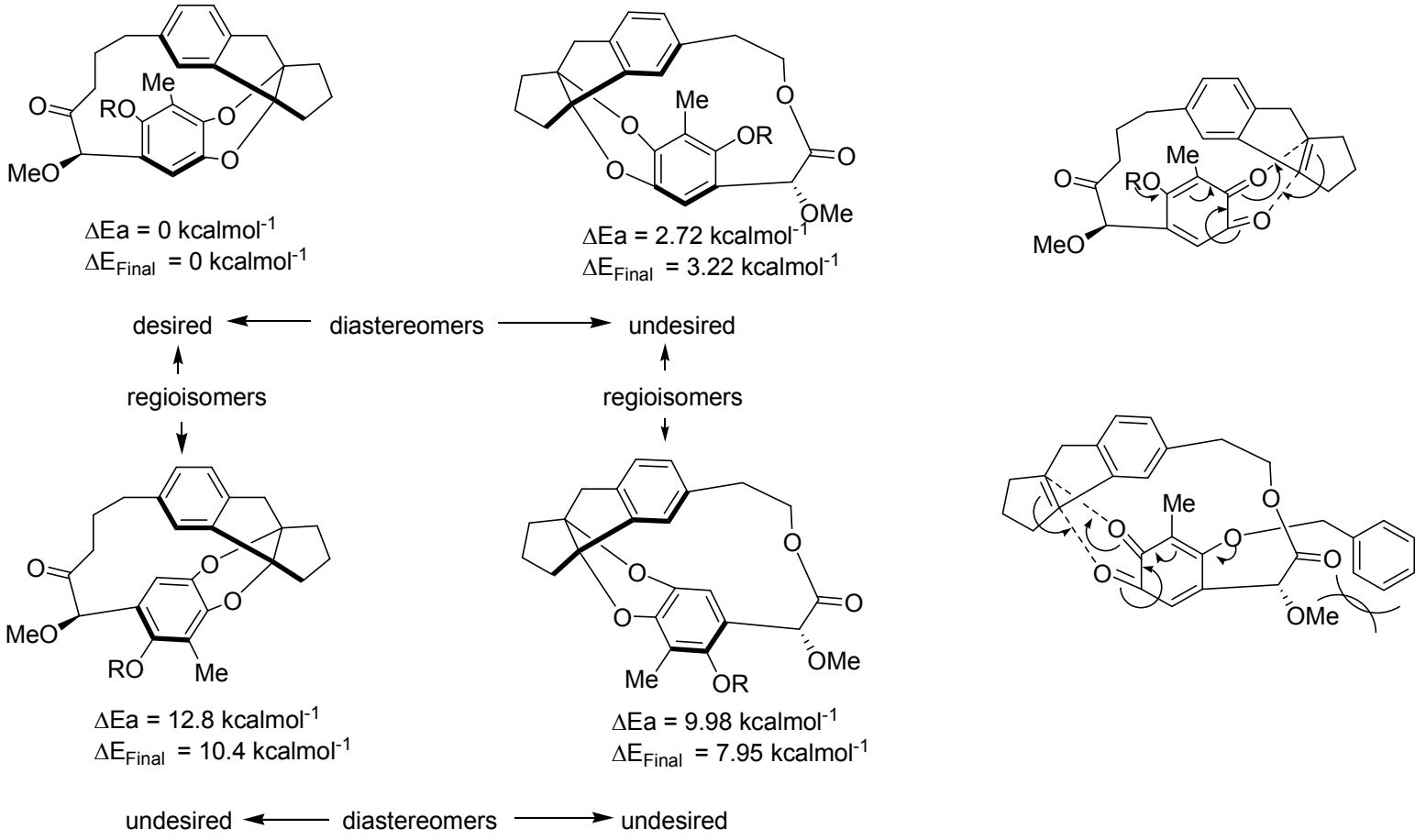
Stereoselectivity of Cycloaddition



ACIE **2008**, *47*, 1432.

Conclusions

- The feasibility of a cascade sequence involving a novel [4+2] cycloaddition reaction to construct the makrocyclic framework of sporolides A and B was demonstrated.
- The reaction occurs in regioselective and stereoselective manner.
- This reaction raises the possibility for this type of cycloadditions being involved in biosynthesis of these molecules.
- The work on the total synthesis of sporolides is ongoing.