Chemistry in Germany - The Young Generation

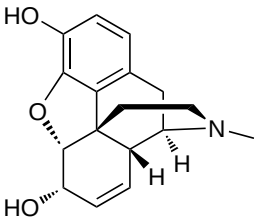
... a personal selection

Dirk Trauner
- born: April 17th 1967, Linz, Austria
- studies in biology and biochemistry, University of Vienna
- 1997 PhD with Johann Mulzer, Free University of Berlin
- 1998-2000 Postdoc with S. Danishefsky, New York
- 2000-2006 Assistant Professor, UC Berkeley
- 2006-2010 Associate Professor, UC Berkeley
- since 2008 Professor of Chemical Biology and Chemical Genetics, LMU Munich, Germany
- 113 publications (15 PhD and Postdoc)

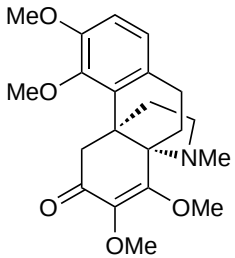
"I find it amazing that ... I am getting paid for sitting in my office and playing with toys and that my imagination occasionally corresponds to the material world."

"In a nutshell, my research involves ... natural products and neurons."
(Total synthesis of bioactive natural products, synthetic methodology, and chemical neurobiology)

Total Synthesis of Morphine and Hasubanan Alkaloids: The Hydrophenanthrenone Approach

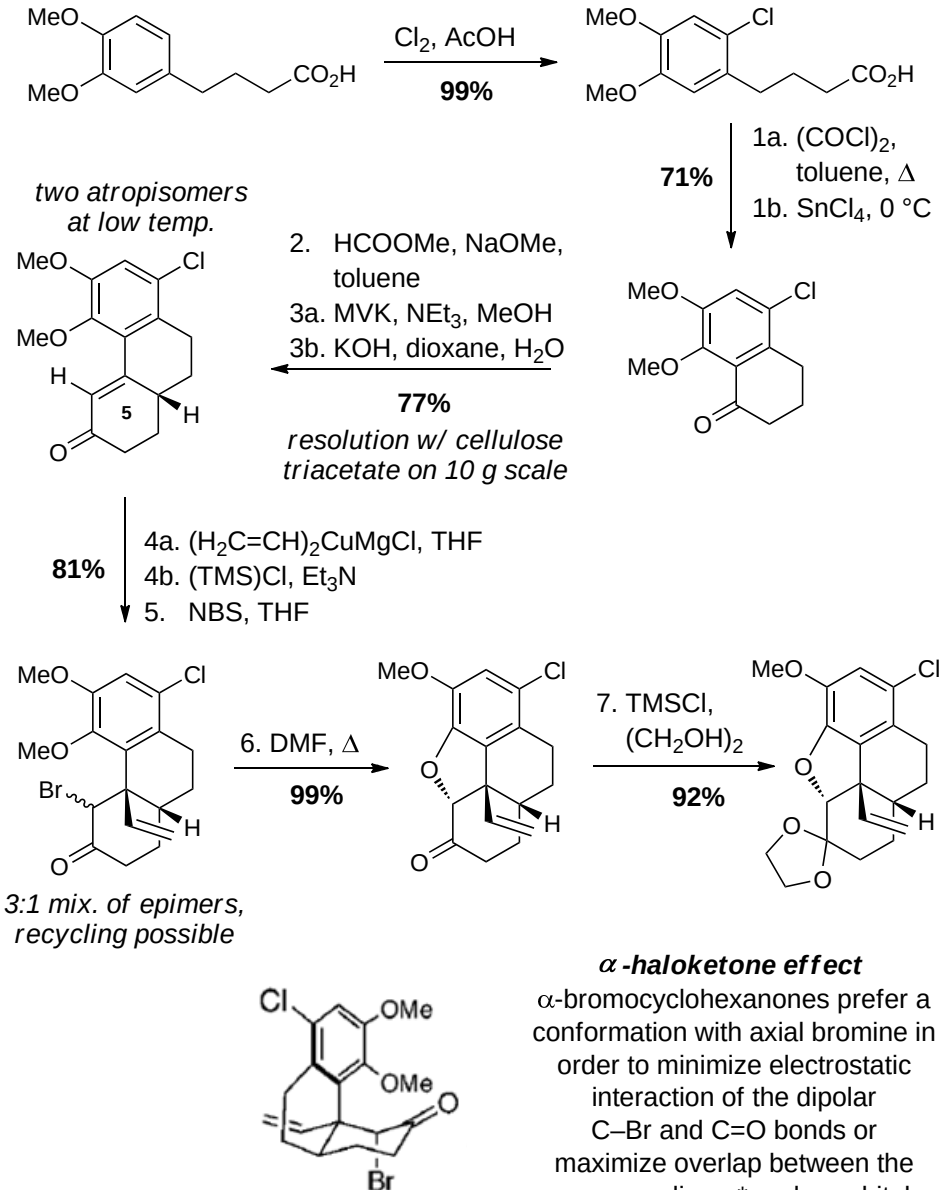


(-)-morphine



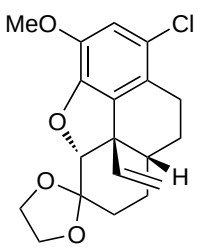
(-)-hasubanonine

Angew. Chem., Int. Ed. **1997**, *35*, 2830.
Synlett **1997**, *5*, 441.
Synthesis **1998**, 653.
J. Org. Chem. **1998**, *63*, 5908.
Chirality **1999,** *11*, 475.



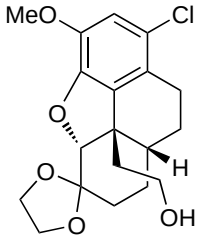
α-haloketone effect

α-bromocyclohexanones prefer a conformation with axial bromine in order to minimize electrostatic interaction of the dipolar C–Br and C=O bonds or maximize overlap between the corresponding σ* and p- orbitals



8a. BH_3*SMe_2, THF
8b. H_2O_2, OH^-

70%



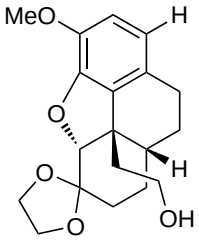
98%

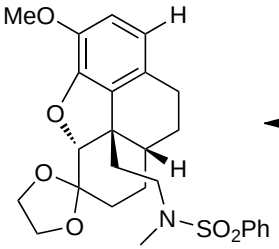
9. Raney-Ni, MeOH, KOH

Mitsunobu w/
N-methylbenzenesulfonamide,
1,1'-(azodicarbonyl)dipiperidine

10. $PhSO_2NHMe$, ADDP, Bu_3P

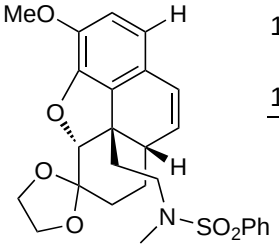
81%





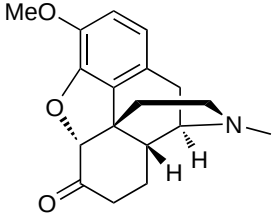
67%

11. NBS, $(PhCOO)_2$, CCl_4, Et_3N, reflux



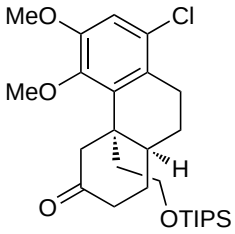
12. Li, NH_3, THF, *t*-BuOH
13. 3N HCl, 90 °C

75%



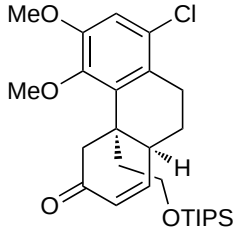
(-)-morphine

- only 13 isolated intermediates
- all of which are crystalline
- total yield: 11.5%
- inexpensive and readily available sm
- recycling of undesired isomers



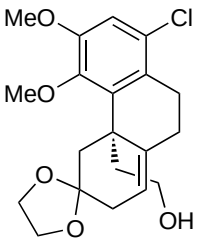
1a. KHDMS, TMSCl, THF
1b. $Pd(OAc)_2$, MeCN

70%



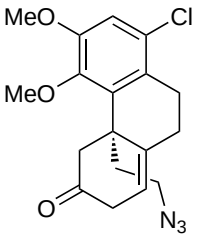
76%

2. $(CH_2OH)_2$, H^+
3. TBAF, THF



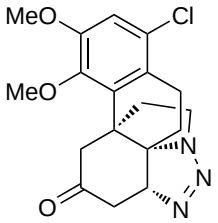
4a. NsCl, Et_3N, DCM
4b. SiO_2
4c. NaN_3, DMF

55%



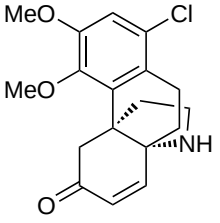
76%

5. benzene, reflux

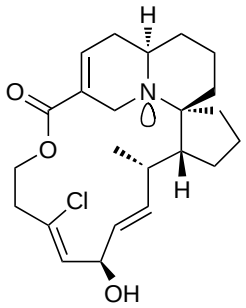


6. pyridine, reflux

73%



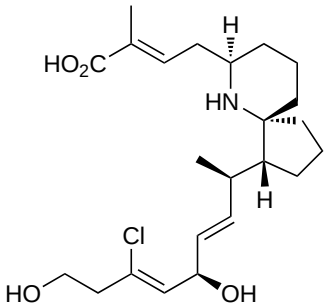
(-)-hasubanonine



halichlorin

Total Synthesis of Halichlorin

Angew. Chem., Int. Ed. **1999**, *38*, 3542.
Tetrahedron Lett. **1999**, *40*, 6513.



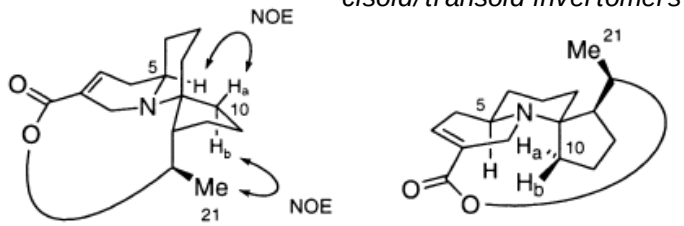
pinnaic acid

Helv. Chim. Acta **2000**, *83*, 2344.
Angew. Chem., Int. Ed. **2001**, *40*, 4450.
Angew. Chem. Int. Ed. **2001**, *40*, 4453.

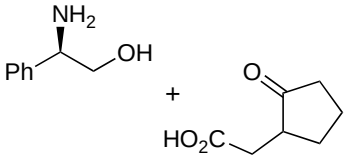
(structure elucidated by combination of spectroscopy, total synthesis, and degradation experiments)

- halichlorin exhibit considerable structural homology (e.g. quinolizidine subunit), but act upon different biological targets (VCAM-1 vs. $cPLA_2$)
- VCAM-1 has recently emerged as a potential target for drug discovery since it is supposed to be involved in regulating leukocyte trafficking
- derivatives for SAR studies

cisoid/transoid invertomers

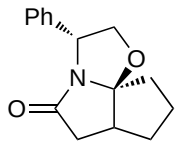


phenylglycinol

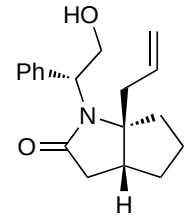


1. toluene, Δ
95%

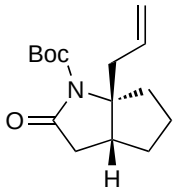
Meyer's lactam



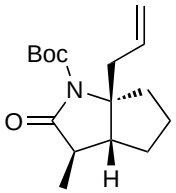
99%
2. $allylSiMe_3$, $TiCl_4$, DCM
Sakurai



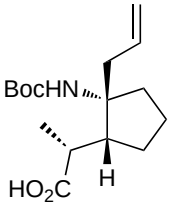
3. Na, NH_3, THF/EtOH
4. Boc_2O, DMAP
88%



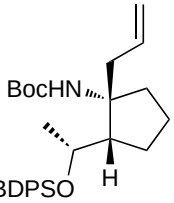
5. LiHMDS, THF, MeI
90%



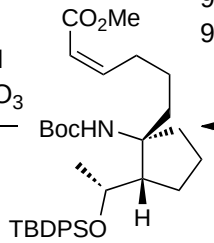
6. LiOH, THF/H_2O
89%



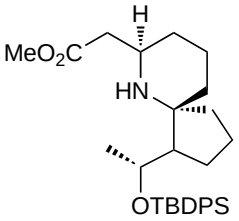
7a. ClCOOEt, Et_3N
7b. $NaBH_4$, MeOH
8. TBDPSCl, Et_3N
78%



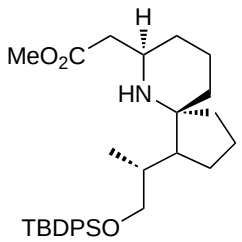
9a. 9-BBN, THF
9b. ICH=CH-COOMe, $Pd(dppf)Cl_2$, $AsPh_3$, Cs_2CO_3, DMF/H_2O



10a. TFA, DCM
10b. H_2O, K_2CO_3
72% over two steps

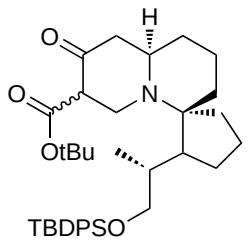


excellent review on β-alkyl Suzuki-Miyaura cross-coupling reactions:
Angew. Chem., Int. Ed. **2001**, *40*, 4544



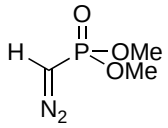
11. *t*BuOAc, LiHMDS, THF
12. H_2CO, EtOH

63%



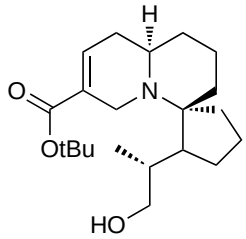
86%

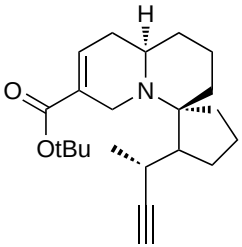
13a. LiHMDS, THF, 0°C
13b. $Cp_2Zr(H)Cl$, rt
14. HF*pyridine, THF



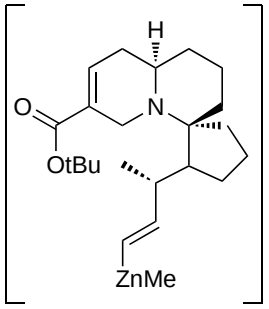
15. TPAP, NMO, MeCN
16. Seyferth-Gilbert, KOtBu, THF

57%



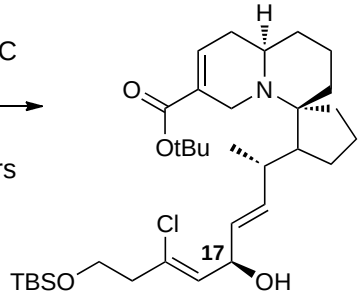


17a. $Cp_2Zr(H)Cl$, DCM
17b. Zn_2Me, heptane, -78 °C

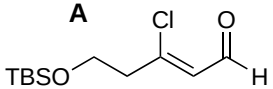


17c. **A**, -65 to -30 °C
17d. **B**, -30 to rt

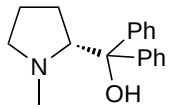
67%
4:1 mix. of epimers



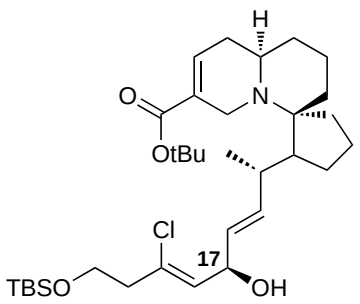
A



B

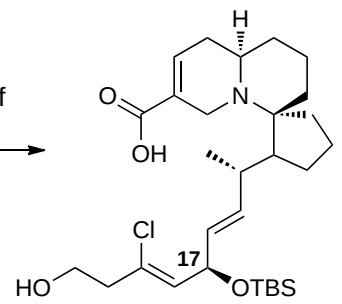


Soai's aminoalcohol



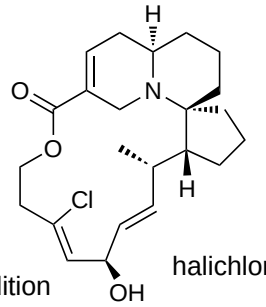
18. TBSOTf
19. TBAF

66%



51%

20. EDCI, DMAP, $CHCl_3$/THF
21. HF*pyridine

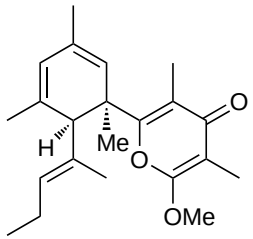


halichlorin

- 21 steps
- 1.3% overall yield

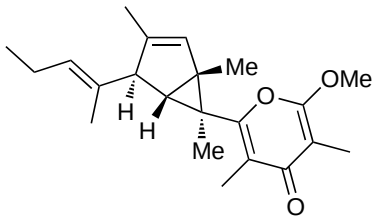
key steps:
- use of Meyer's lactam to install core structure
- β-alkyl-Suzuki coupling
- Claisen-Mannich sequence
- hydrozirconation-transmetalation-asymmetric addition

Biomimetic Syntheses applying Electrocyclization Cascades



9,10-deoxytridachione

hν
in vivo
or
in vitro

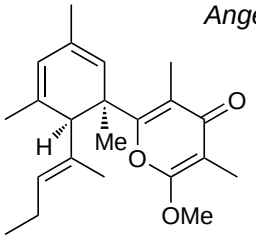


photodeoxytridachione

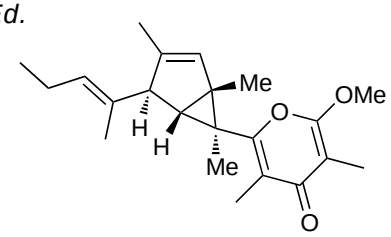
biosynthetic relationship

via triplett state, diradical mechanism: *Org. Lett.* **2005**, *7*, 4959.

Angew. Chem., Int. Ed. **2003**, *42*, 549.

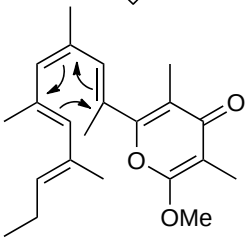


9,10-deoxytridachione



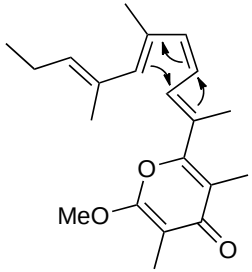
photodeoxytridachione

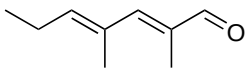
6π



common synthetic precursor?!

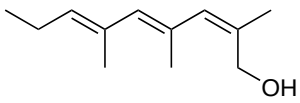
$\pi 4_a+\pi 2_s$





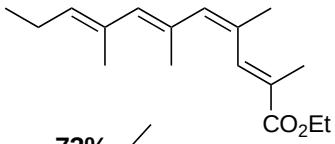
1. Still-Gennari
2. DiBAlH, DCM

73%



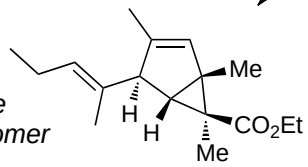
43%

3. TPAP/NMO
4. HWE



73%

5. Me_2AlCl cat., DCM

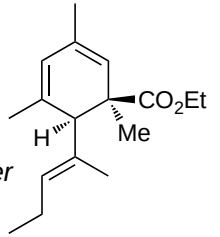


single diastereomer

mechanism?

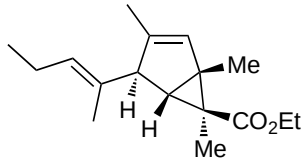
benzene, Δ

95%



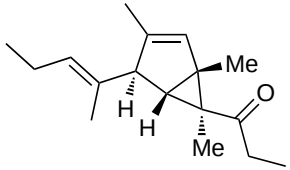
single diastereomer

divergent access to both frameworks



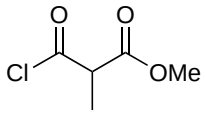
6. Weinreb
7. EtMgBr

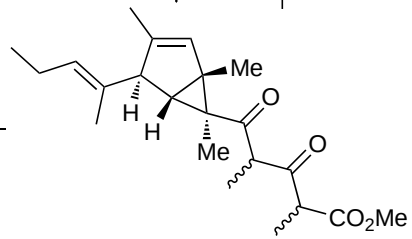
55%



59%
(95% brsm)

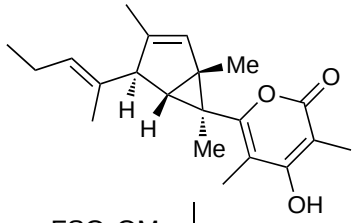
LiHMDS,





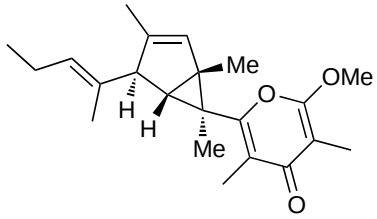
DBU, Δ, benzene

78%



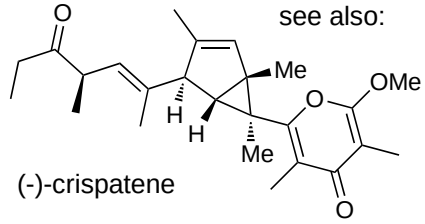
FSO_2OMe, DCM

77%



photodeoxytridachione

see also:

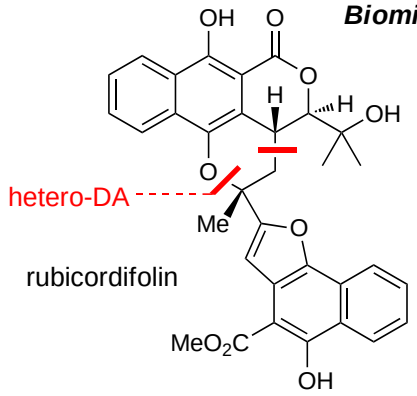


(-)-crispatene

PNAS **2004**, *101*, 12019.

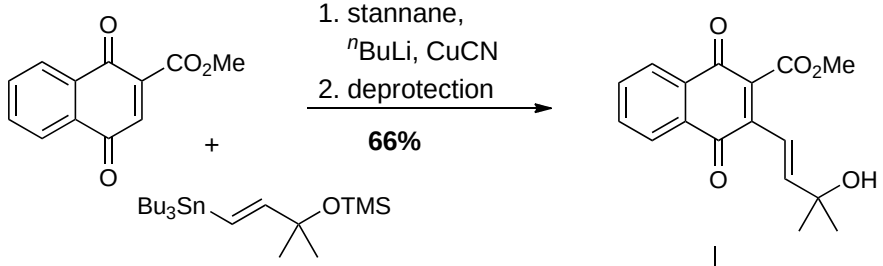
E. crispata, the ''lettuce slug''...

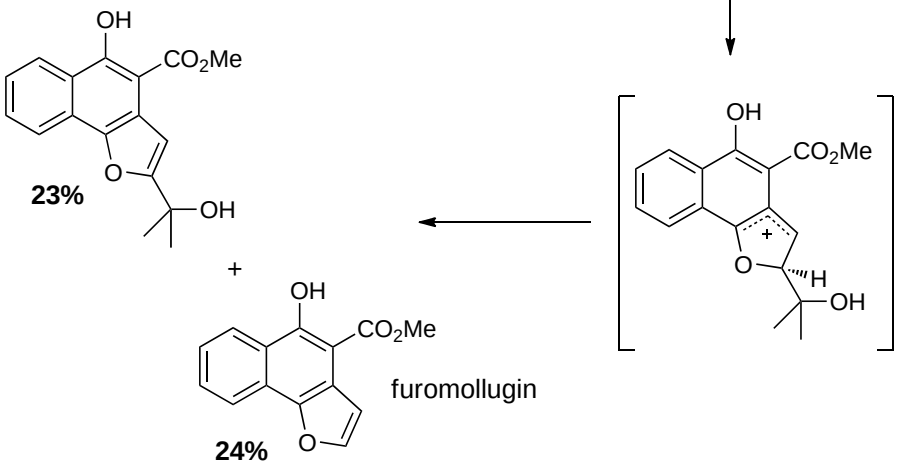
Biomimetic Synthesis of Rubicordifolin

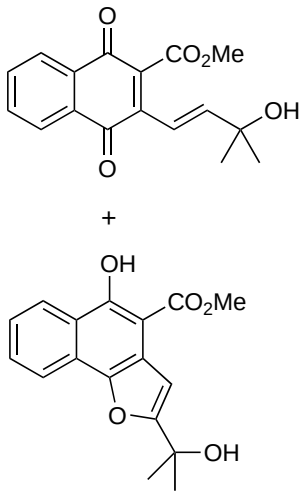


J. Am. Chem. Soc. **2005**, *127*, 2870.

Org. Lett. **2010**, *22*, 5162.
(theoretical investigations)





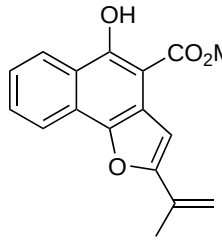


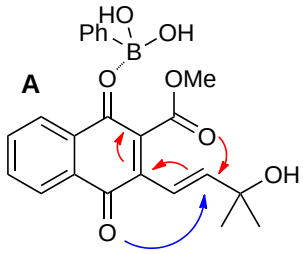
PhB(OH)$_2$,
toluene, Δ

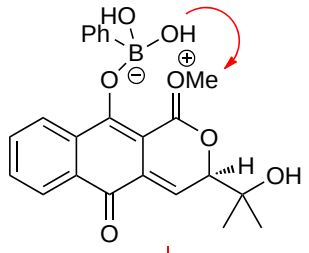
"several hundred milligram prepared"

rubicordifolin **10%**

+





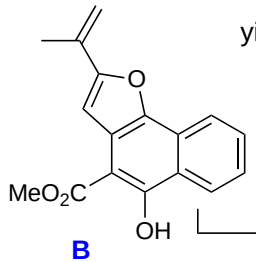


-H_2O

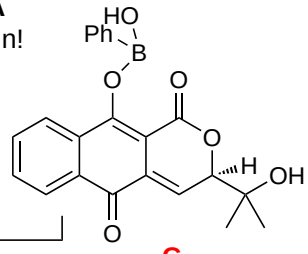
mechanism

direct conversion of **A**
yields 45% rubicordifolin!

-MeOH



B

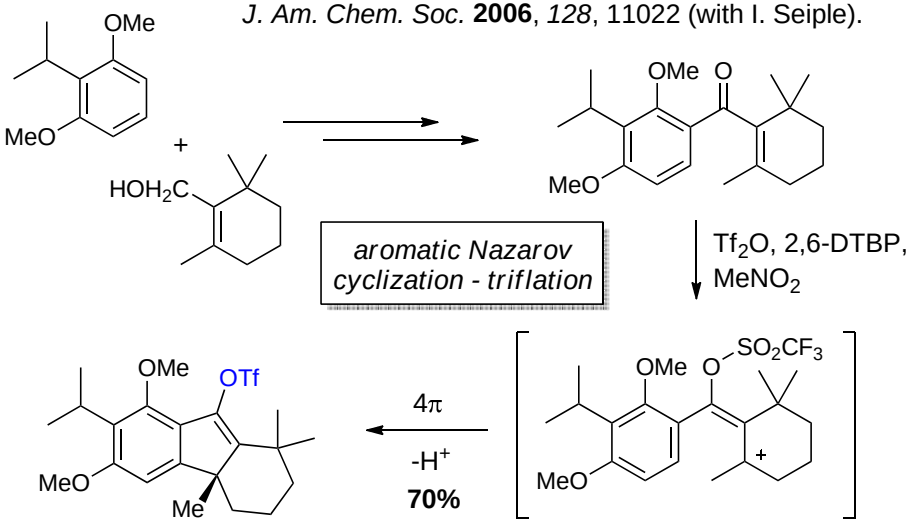


C

2+4

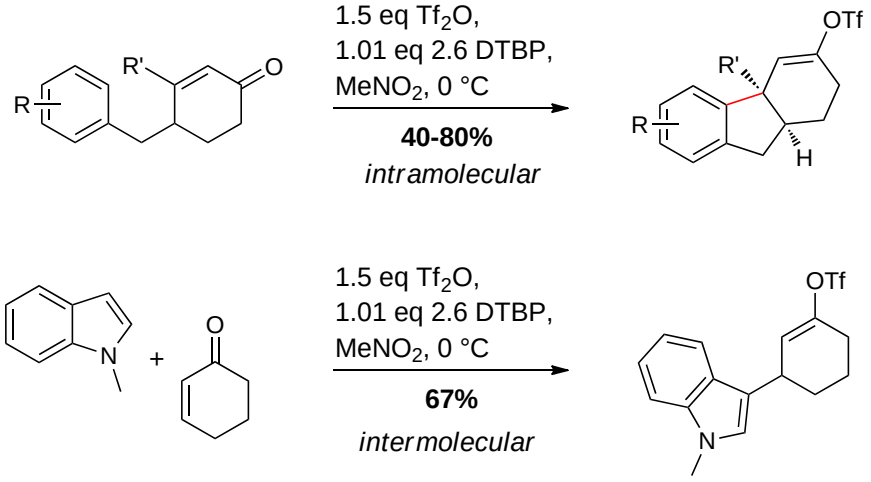
rubicordifolin

J. Am. Chem. Soc. **2006**, *128*, 11022 (with I. Seiple).

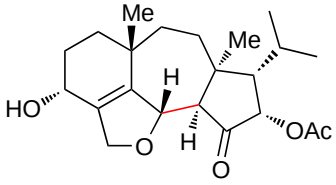


taiwaniaquinoids

also: Friedel-Crafts triflation



Org. Lett. **2006**, *8*, 5429.

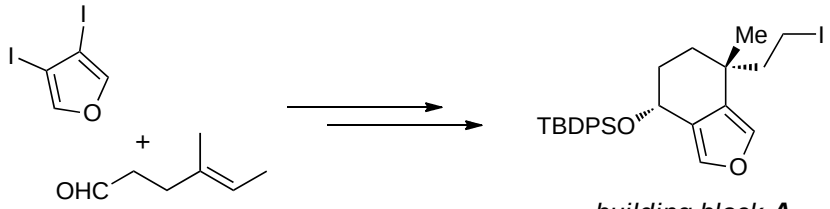


guanacastepene E

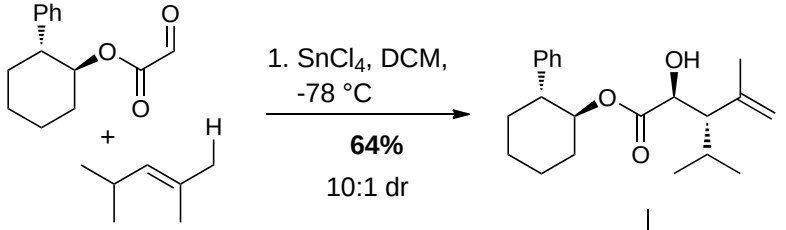
Total Synthesis of Guanacastepene E

key disconnection

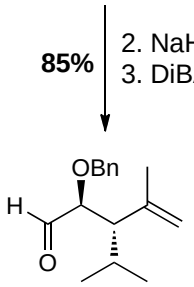
J. Am. Chem. Soc. **2006**, *128*, 17057.

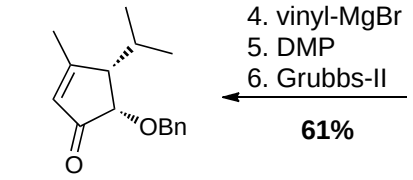


building block ***A***

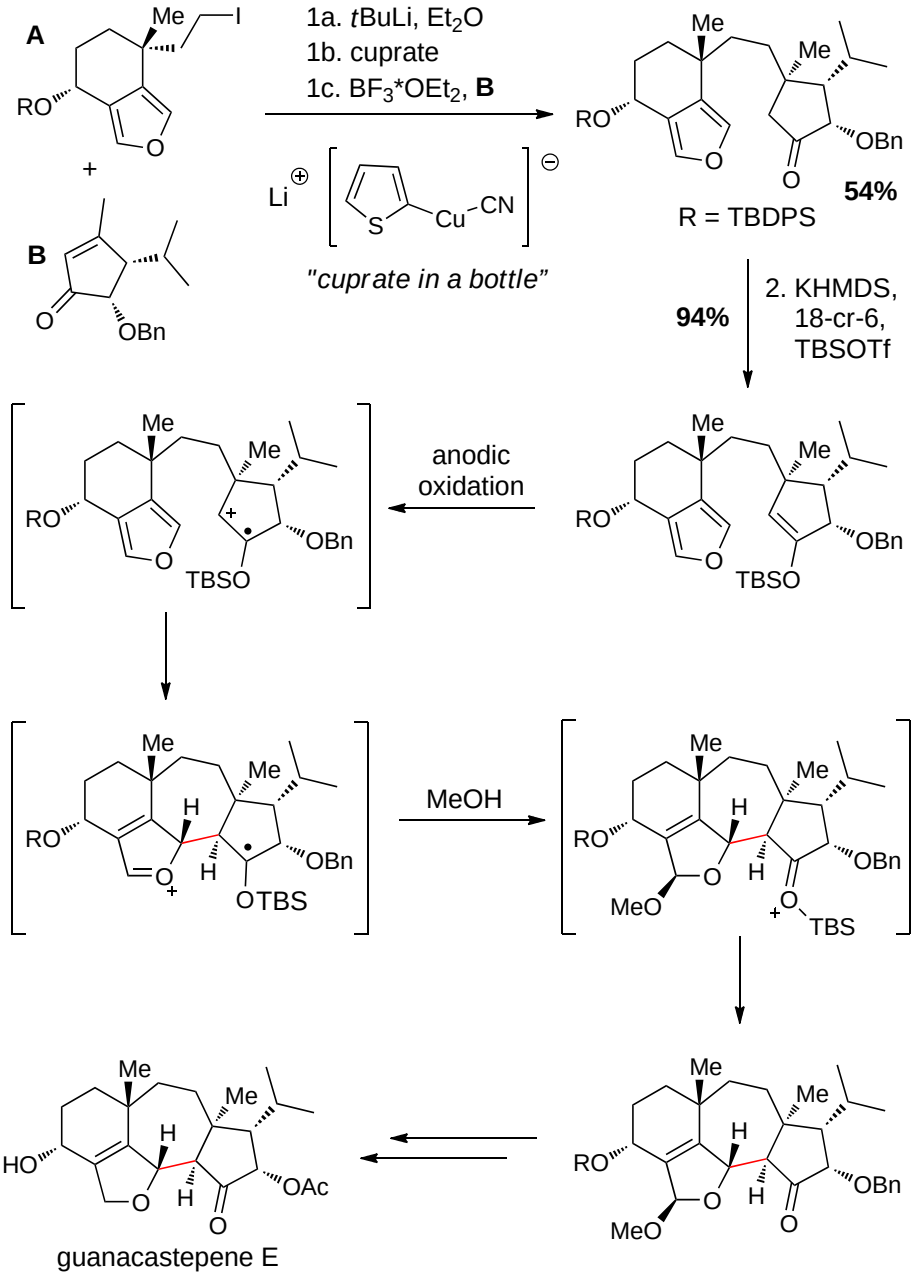


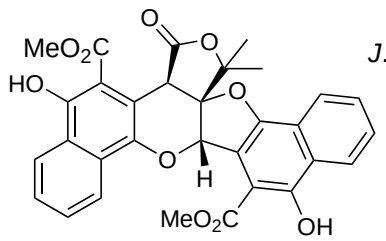
asymmetric carbonyl ene-reaction





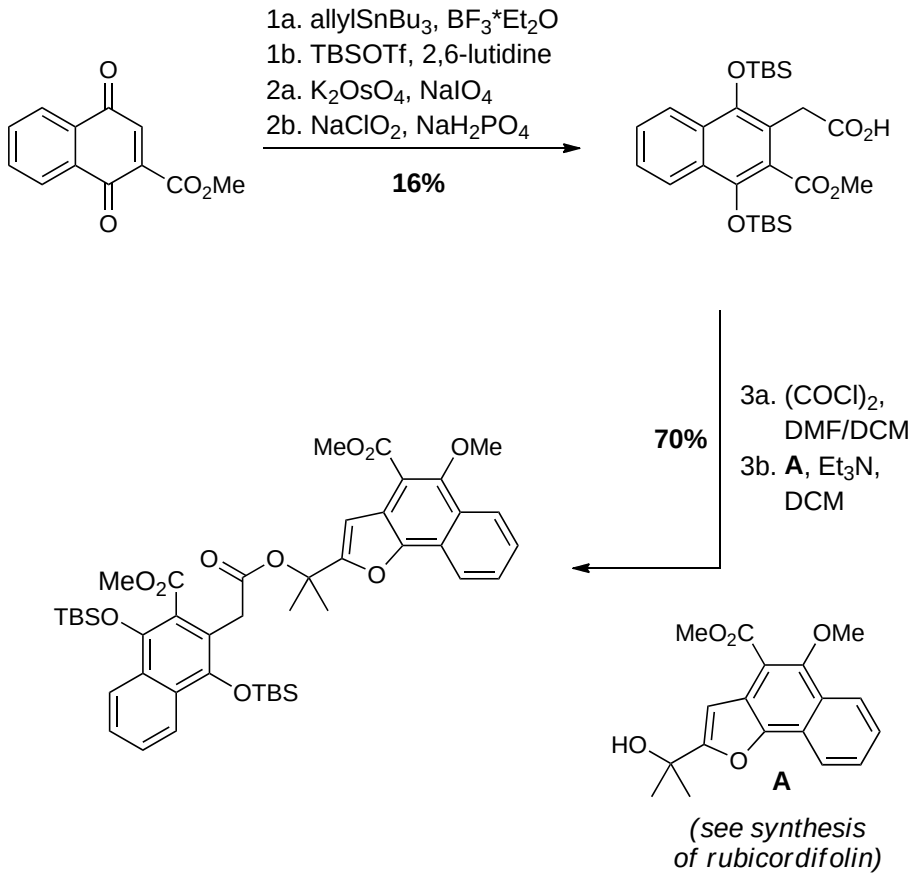
building block ***B***

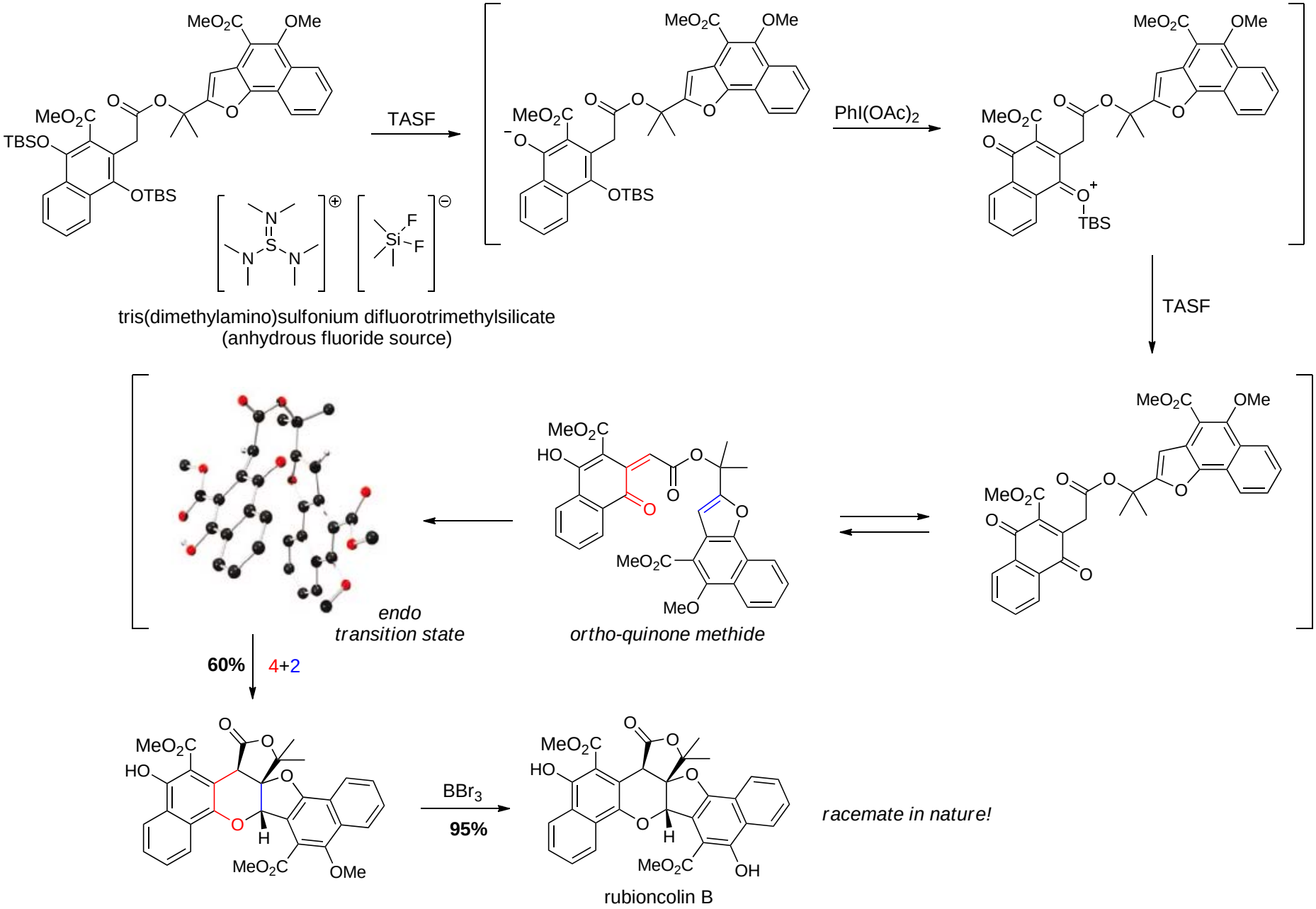


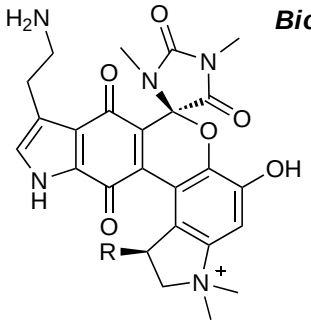

rubioncolin B

J. Am. Chem. Soc. **2008**, *130*, 9230-9231.

Biomimetic Total Synthesis of Rubioncolin B



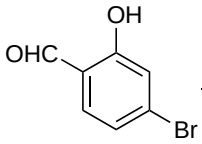

MeO2C
OMe
TBSO
OTBS
TASF
PhI(OAc)2
TBS
tris(dimethylamino)sulfonium difluorotrimethylsilicate
(anhydrous fluoride source)
endo
transition state
ortho-quinone methide
60%
4+2
BBr3
95%
rubioncolin B
racemate in nature!



Biomimetic Synthesis of Exiguamines

Nature Chem. Bio. **2008**, *4*, 535-537.

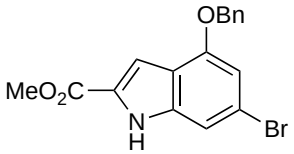
R = H: exiguamine A
R = OH: exiguamine B



1. $BnCl$, K_2CO_3
2a. $N_3CH_2CO_2Me$, NaOMe, MeOH
2b. *o*-xylene, 160 °C

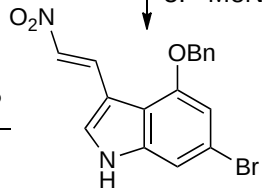
39%

mechamism?
name reaction?



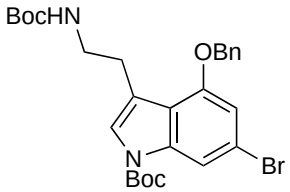
3a. NaOH
3b. decarbox.
4. $POCl_3$, DMF
5. $MeNO_2$

29%



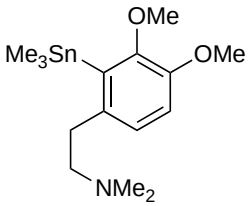
6. $LiAlH_4$
7. Boc_2O, DMAP

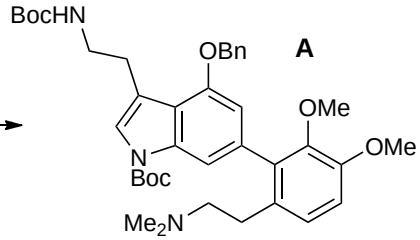
80%



8. $Pd(PPh_3)_4$, CuCl, LiCl, DMSO, 60 °C

71%



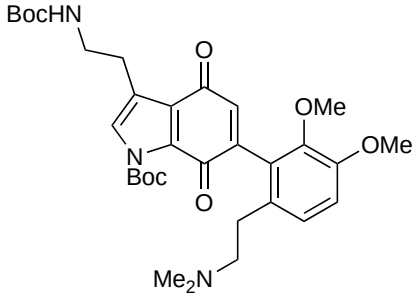


A

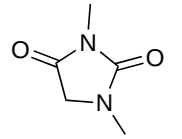
9. Pd black, HCO_2NH_4
10a. salcomine, O_2, MeCN
10b. 1% aqu. formic acid

A

72%

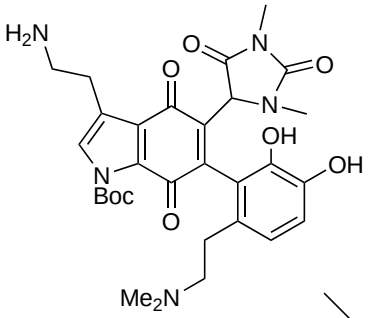


+ *ortho*-isomer (1:2.5)



11. LiHMDS, THF

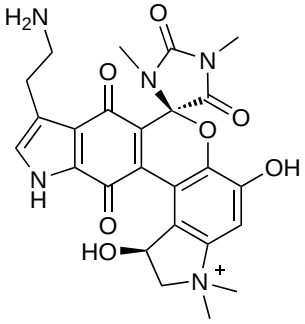
12a. BBr_3
12b. MeOH, 2% formic acid



AgO (**20 eq.**), MeOH/2% formic acid

47%

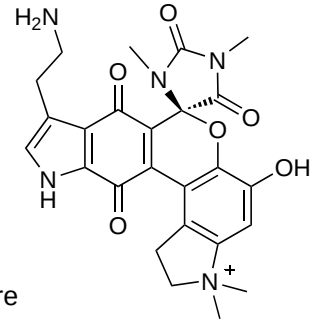
exiguamine B



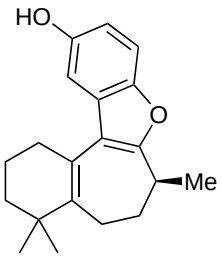
46%

AgO (**10 eq.**), MeOH/2% formic acid

exiguamine A



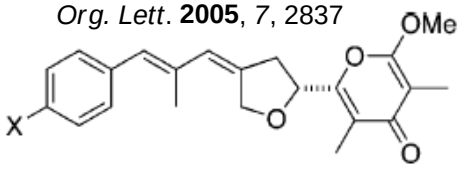
- two oxidations
- amine ring closure
- tautomerization
- oxa-6π-electrocyclization



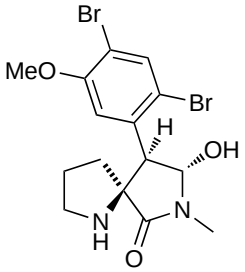
S-(+)-frondosin B

Angew. Chem., Int. Ed. **2002**, *41*, 1569.

Org. Lett. **2005**, *7*, 2837



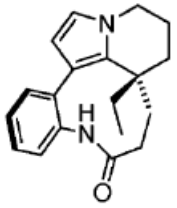
X = NO_2: aureothin
X = NHAc: *N*-acetylaureothamine
X = CN: aureonitrile



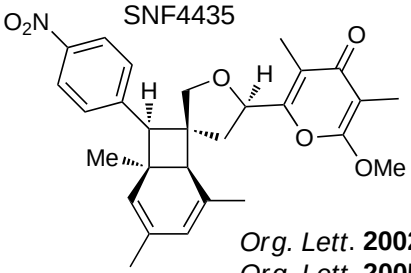
amathaspiramide F

Angew. Chem., Int. Ed. **2002**, *41*, 4556

J. Org. Chem. **2009**, *74*, 1581.
Org. Lett. **2005**, 7, 5207.

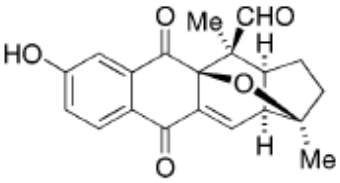


rhazinilam



SNF4435

Org. Lett. **2002**, *4*, 2221.
Org. Lett. **2005**, **7**, 4475.

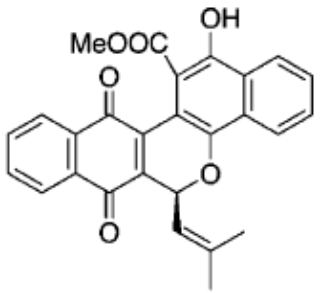


pinnatal (**1**)

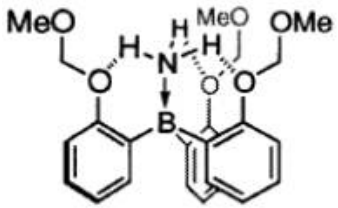
J. Am. Chem. Soc. **2005**, *127*, 6276.

REVIEW: "Biosynthetic and Biomimetic Electrocyclizations." *Chem. Rev*. **2005**, *105*, 4757.

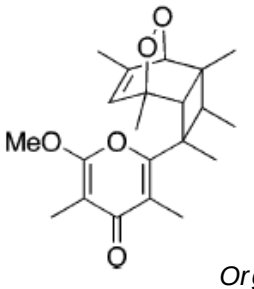
Org. Lett. **2005**, *7*, 5865.

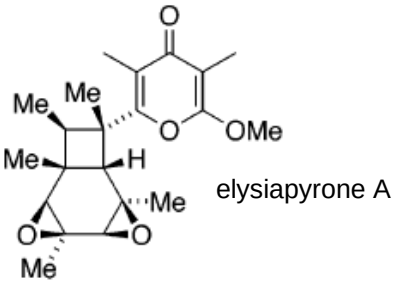


microphyllaquinone



Org. Lett. **2002**, 4, 4109.

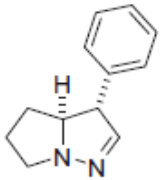




elysiapyrone A

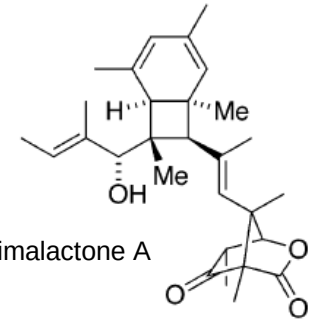
Org. Lett. **2005**, 7, 2901.
Angew. Chem., Int. Ed. **2005**, *44*, 4602.

Studies Toward the Haouamines: *Org. Lett*. **2006**, *8*, 23.
Studies Toward Maoecrystal V: *Org. Lett*. **2010**, *12*, 5656-5659.



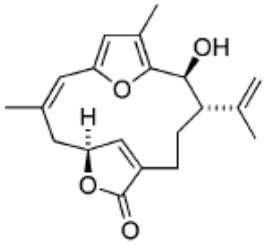
newbouldine

Tetrahedron **2010**, *66*, 6626-6631.

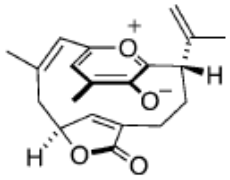


shimalactone A

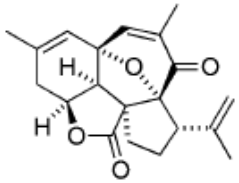
Org. Lett. **2008**, *10*, 149.



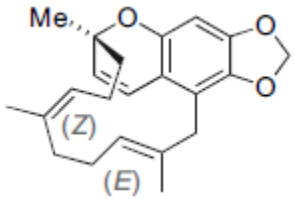
bipinnatin J



Org. Lett. **2006**, *8*, 345.
Org. Lett. **2006**, *8*, 5901.

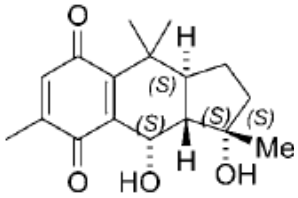


intricarene



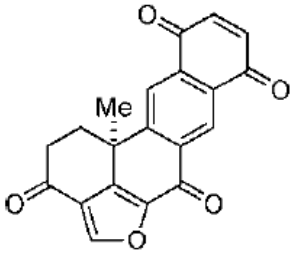
smenochromene B

Tetrahedron **2007**, *63*, 6529.



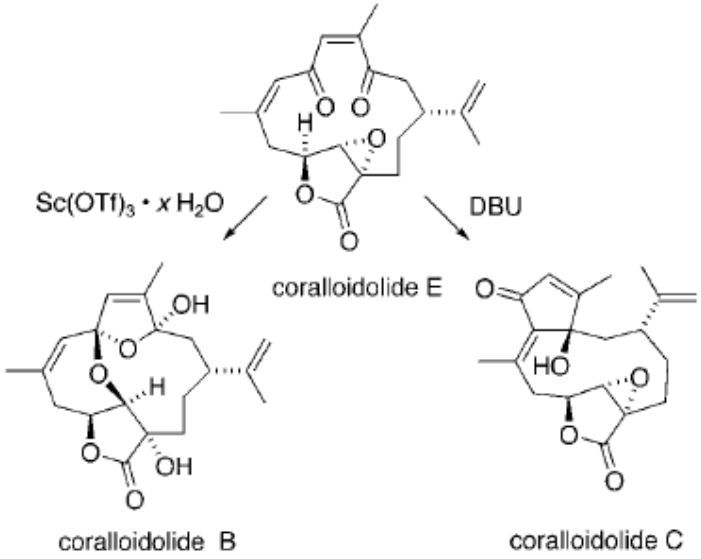
pycnanthuquinone C

Angew. Chem. Int. Ed. **2010**, *49*, 6199–6202.

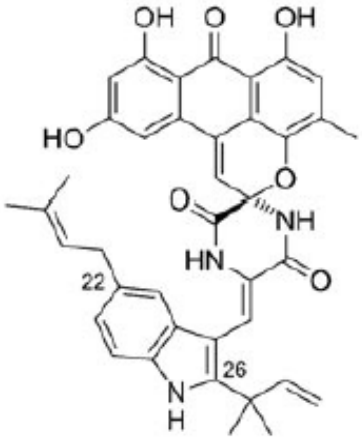


halenaquinone

J. Am. Chem. Soc. **2008**, *130*, 8604-8605.
(Vinyl Quinones as Diels-Alder Dienes)

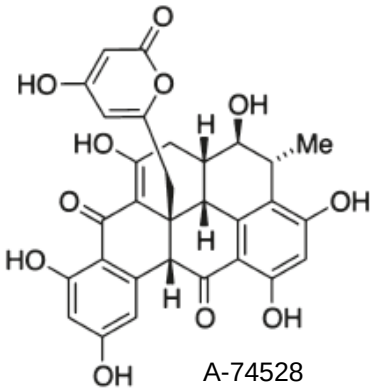


Angew. Chem. Int. Ed. **2010**, *49*, 2619-2621.



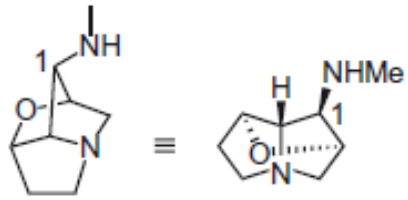
variecolortide A

Angew. Chem. Int. Ed. **2011**, *50*, 1402-1405.



A-74528

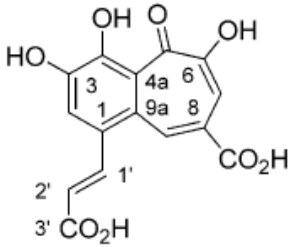
Org. Lett. **2011**, *13*, 1386-1389.



loline

Nat. Chem. **2011**, *3*, 543-545.

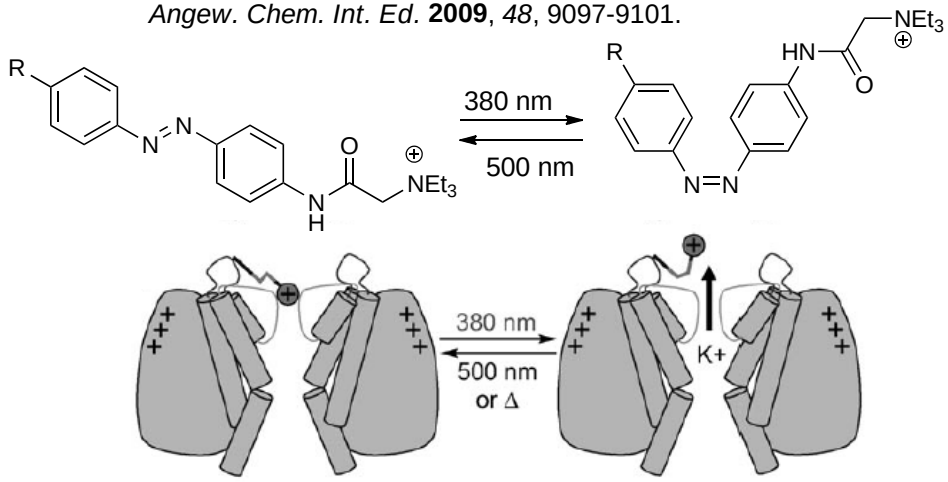
not covered: "***Chemical Neurobiology***"
excellent review: *Introduction: Chemical Approaches to Neurobiology*, *Chem. Rev*. **2008**, *105*, 1499.



crocipodin

Tetrahedron **2011**, *67*, 1536-1539.

Angew. Chem. Int. Ed. **2009**, *48*, 9097-9101.



... don't miss the zebra-fish experiment!
(*Nature* **2009**, *461*, 407-410.)

Thorsten Bach:

- born: 1965, Ludwigshafen, Germany
- studies in chemistry, University of Heidelberg / USC LA
- 1991 PhD with Manfred Reetz, University of Marburg

("Enantioselective C-C Coupling Using Chiral Catalysts")

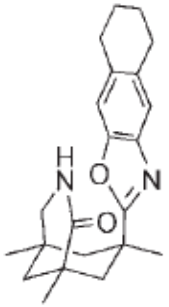
- 1991-1992 Postdoc with D. Evans, Harvard University

("Histidine Analogs by Pd-mediated C,C Bond Formation")

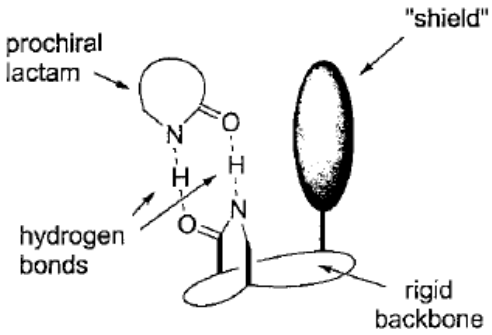
- 1992-1996 Habilitation, University of Münster
- 1997-2000 Full Professor, University of Marburg
- since 2000 Chair of Organic Chemistry I, TU Munich
- 188 publications

main research interests:

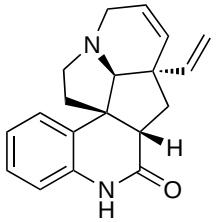
- photochemistry
- catalysis
- chemistry of heterocycles
- total synthesis



chiral host **A**



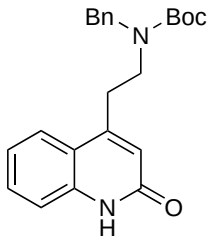
Angew. Chem. Int. Ed. **2000**, *39*, 2302-2304.
J. Org. Chem. **2006**, *71*, 5662-5673.
Synlett **2004**, 2588-2509.
Synthesis **2001**, 1395-1405 (preparation of host).

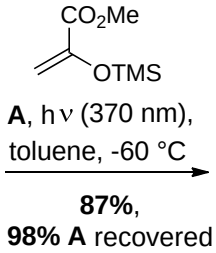


(+)-meloscine

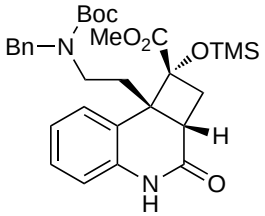
Total Synthesis of Meloscine

Angew. Chem. Int. Ed. **2008**, *47*, 5082-5084.
Chem. Eur. J. **2009**, *15*, 3509-3525.

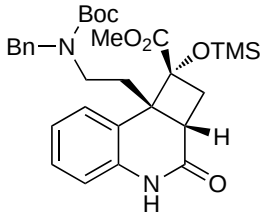


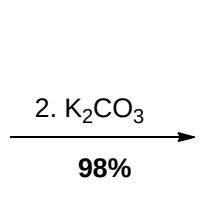


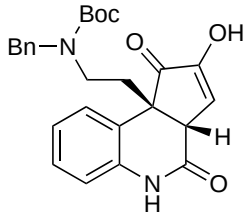
enantioselective [2+2] photocycloaddition

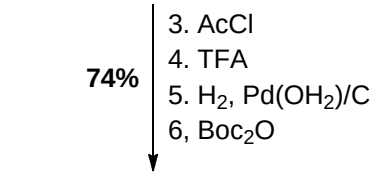


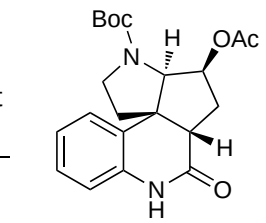
79% ee
>99% ee (after HPLC)

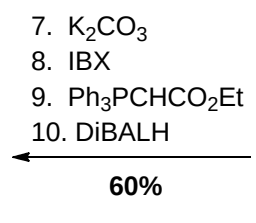


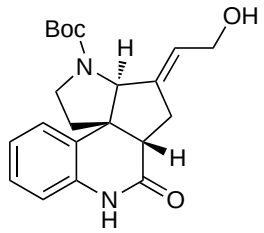


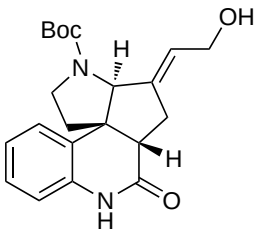


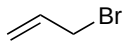






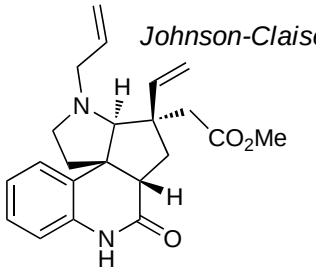




11. $MeC(OMe)_3$, Δ
12. TFA
13. K_2CO_3, 

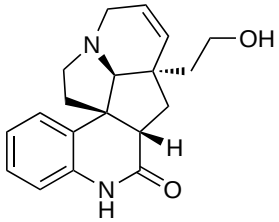
55%

Johnson-Claisen

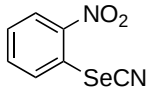


14. Grubbs-II
15. DiBALH
16. $NaBH_4$

67%

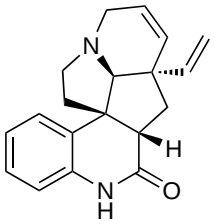


17. $TsCl$, NEt_3
18. $NaBH_4$,



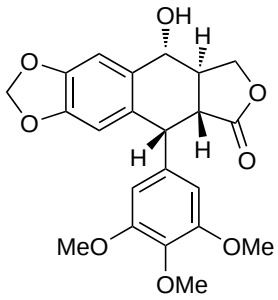
19. TFA, *m*CPBA

61%



(+)-meloscine

Overman intermediate



(-)-podophyllotoxin

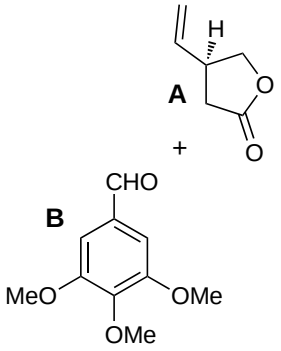
Total Synthesis of Podophyllotoxin

Angew. Chem. Int. Ed. **2008**, *47*, 7557-7559.

J. Org. Chem. **2009**, *74*, 312-318.
(chiral carbocations, theoretical investigations)

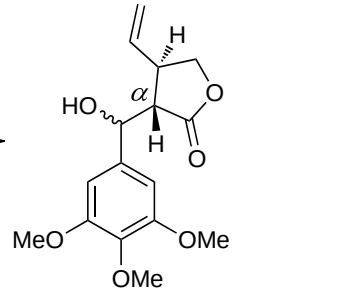
Synlett **2011**, 1235-1238.
(enantioselective FC with chiral Broensted acids)

- lignane class of natural products
- antiviral properties
- several total syntheses (e.g. 1st synthesis by Meyers, 24 steps)



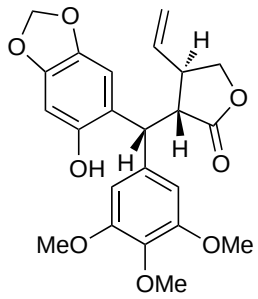
1. LDA, THF, -78°C; then **B**

94%
(*dr* 52:48)



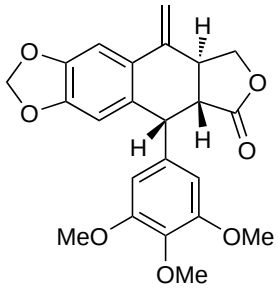
99%
(*dr* 94:6)

2. sesamol, rt, $FeCl_3$, DCM *or* $Bi(OTf)_3$, $MeNO_2$



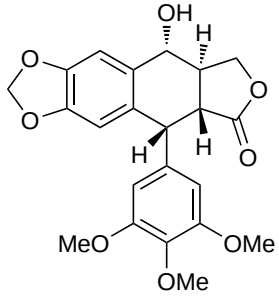
3. Tf_2O, NEt_3, DCM
4. $Pd(OAc)_2$, PPh_3, K_2CO_3, MeCN

52%



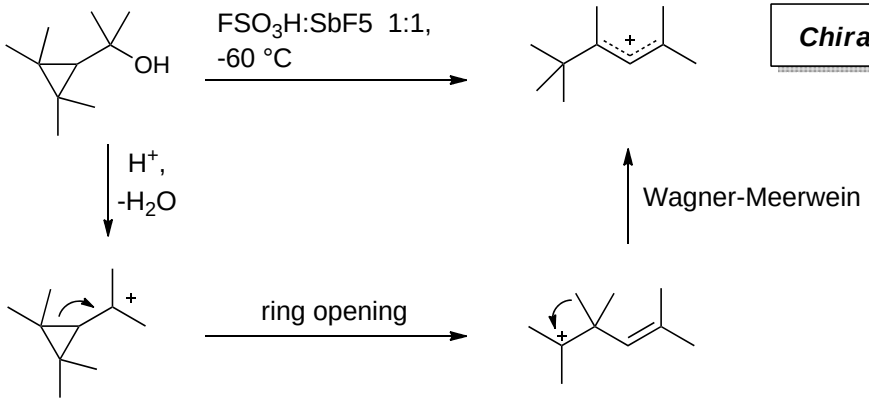
79%
(*dr* 98:2)

5. OsO_4, NMO, DCM; then $NaIO_4$
6. $LiAlH(OtBu)_3$, Et_2O

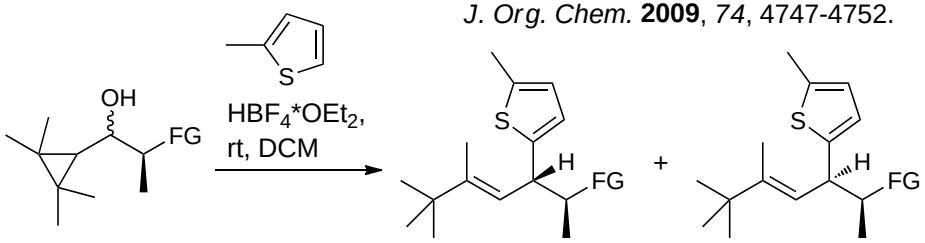


- 6 steps
- 35% overall yield
- enantiomerically pure material
- clever use of carbenium ion with adjacent stereogenic center

Chiral Carbenium Ions

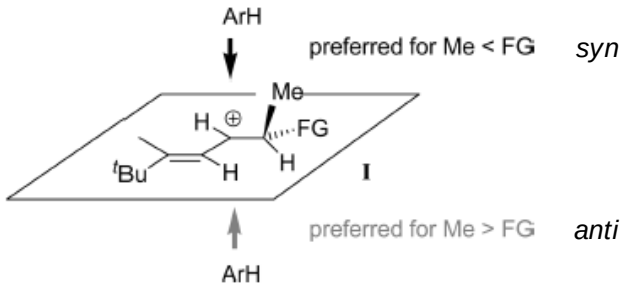


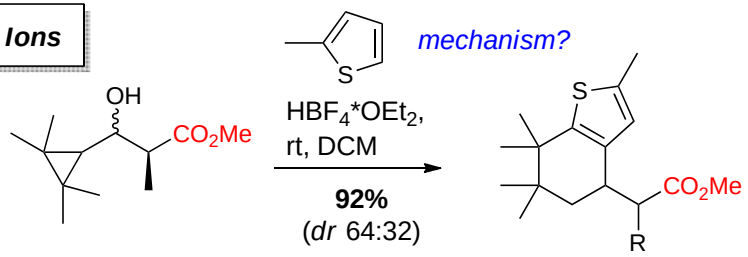
J. Org. Chem. **2009**, *74*, 4747-4752.

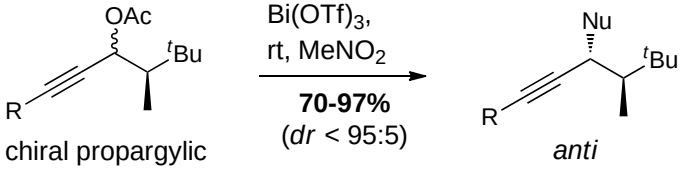


entry[a]	alcohol	FG	product	yield [%]	d.r.[b] (*anti:syn*)
1	**3a**	^{t}Bu	**17a**	84	3:97
2	**4a**	Ph	**18a**	97	77:23
3	**5a**	CN	**19a**	86	76:24
4	**6a**	$PO(OEt)_2$	**20a**	87	74:26

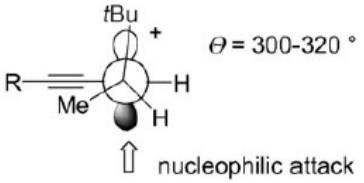
simple model for predicting the outcome





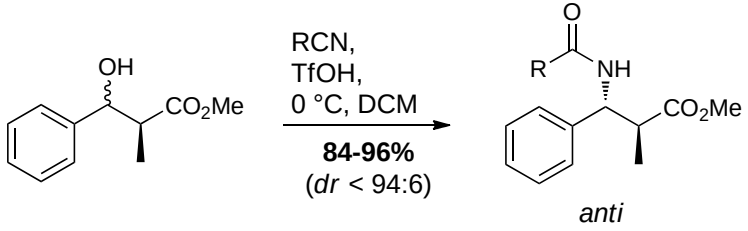


simple model for predicting the outcome



Angew. Chem. Int. Ed. **2008**, *47*, 10106-10109.

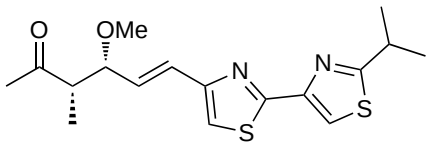
diastereoselective Ritter reactions:



Chem. Commun. **2009**, 2130-2132.

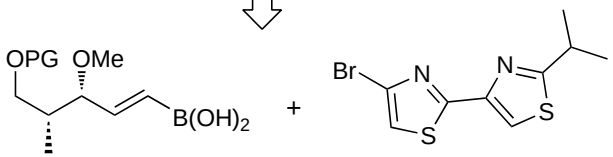
Total Synthesis of Cystothiazole E

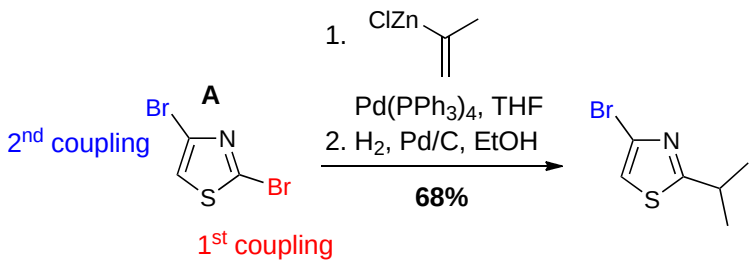
Angew. Chem. Int. Ed. **2001**, *40*, 3184-3185



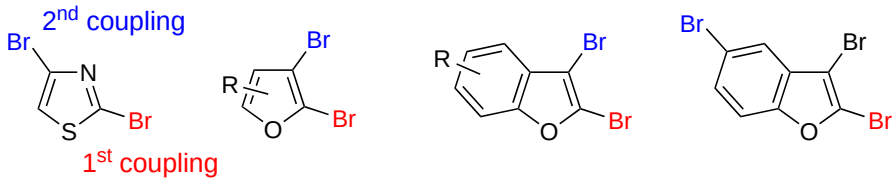
cystothiazole E

regioselective cross-coupling on polyhalogenated heterocycles



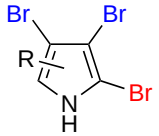


- 10 steps
- 21% overall yield
- three sequential couplings as key sequence
- usually bithiazole core established by classical Hantzsch thiazole methodology (e.g. Boger's bleomycin synthesis; *Angew. Chem. Int. Ed.* **1999**, 38, 448-476.)

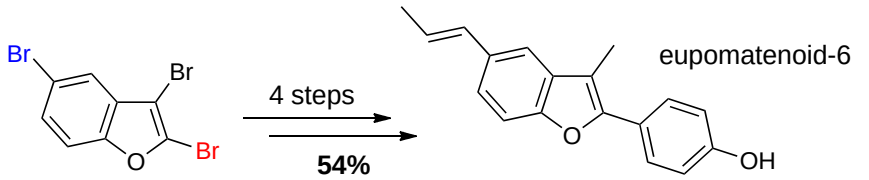


Thiazoles: *Tetrahedron Lett.* **2000**, *41*, 1707-1710.
J. Org. Chem. **2002**, *67*, 5789-5795.
Synthesis **2011**, 199-206.

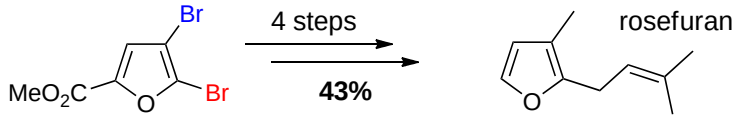
Pyrroles: *Synlett* **2005**, 1957-1959.
Heterocycles **2007**, *74*, 569-594.



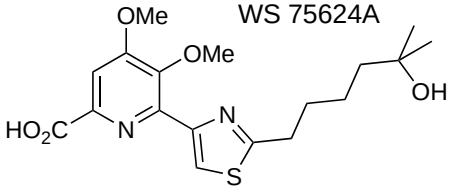
review: *Tetrahedron* **2005**, *61*, 2245-2267.



Tetrahedron Lett. **2002**, *43*, 9125-9127.
Synlett **2001**, 1284-1286.
Synthesis **2003**, 925-939.

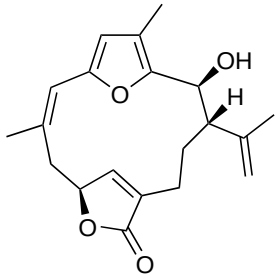


Eur. J. Org. Chem. **1999**, 2045-2057.



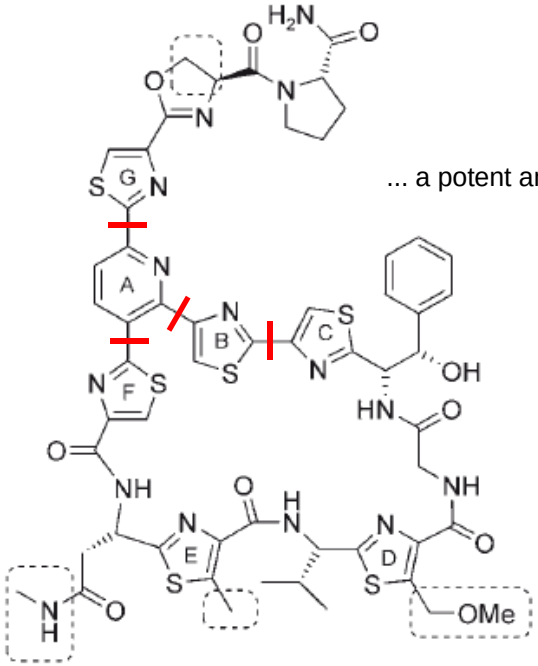
Synlett **2002**, 2089-2091.

Regioselective C,C Coupling Reactions on Polyhalogenated Heterocycles



furanocembranes

Synlett **2005**, 511-513.
J. Org. Chem. **2001**, *66*, 3427-3434.

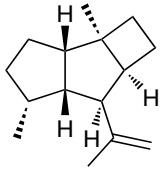


GE2270 A

... a potent antibiotic thiazolylpeptide

structure variation in other GE2270 antibiotics

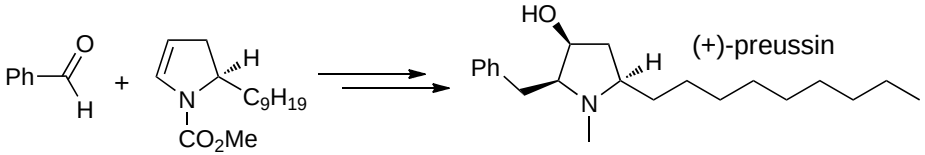
Chem. Eur. J. **2008**, *14*, 2322-2339.
Angew. Chem. Int. Ed. **2007**, *46*, 4771-4774.



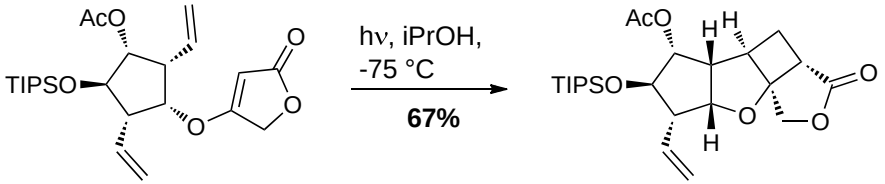
kelsoene

Synlett **2002**, 1305-1307.
Top. Curr. Chem. **2005**, *243*, 1-42.

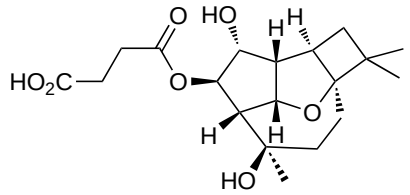
Stereoselective [2+2] Photocycloadditions (e.g. Paterno-Büchi Reactions)



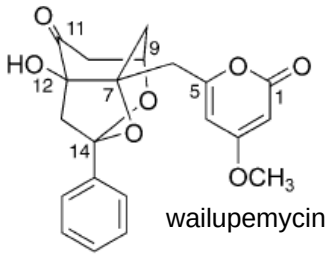
Angew. Chem. Int. Ed. **1998**, *37*, 3400-3402.



Angew. Chem. Int. Ed. **2008**, *47*, 6189-6191.
Chem. Eur. J. **2010**, *16*, 6015-6032.



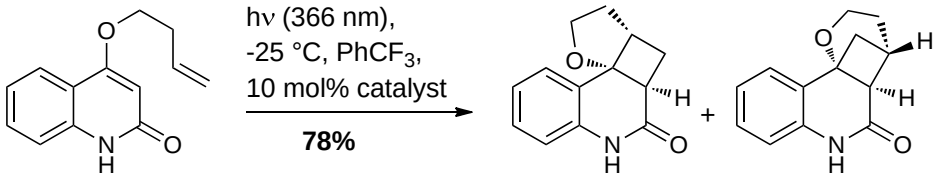
punctaporonin C

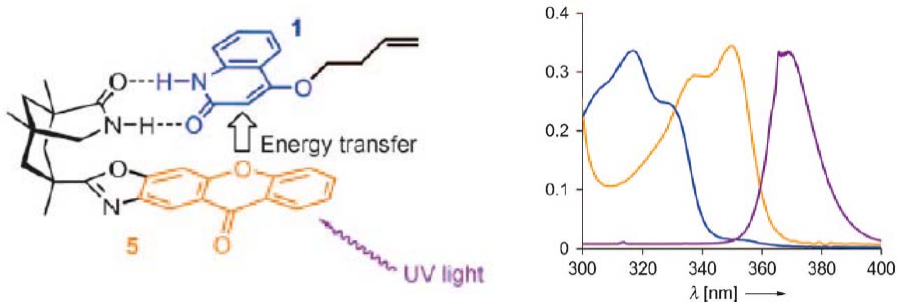


wailupemycin

Angew. Chem. Int. Ed. **2003**, *42*, 4685-4687.
Chem. Eur. J. **2005**, *11*, 7007-7023.

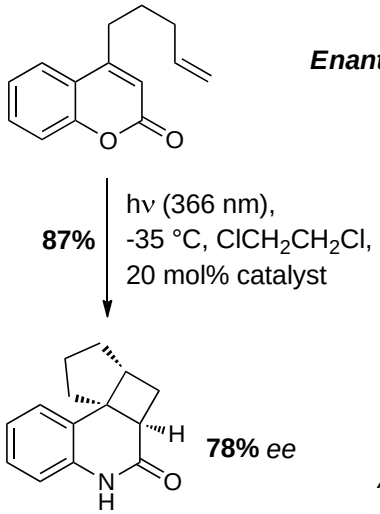
Light-Driven Organocatalysis

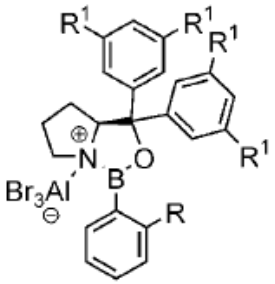




Angew. Chem. Int. Ed. **2009**, *48*, 6640-6642.

Chiral Lewis Acids in Enantioselective Photochemistry





Angew. Chem. Int. Ed. **2010**, *49*, 7782-7785.

Stefan Bräse:

- born: November 30th 1967, Kiel, Germany
- studies in chemistry, University of Göttingen
- 1995 PhD with Armin de Meijere
- 1995-1996 Postdoc with J. Bäckvall, University of Uppsala
- 1996-1997 Postdoc with K.C. Nicolaou, TSRI, La Jolla
  (Total synthesis of vancomycin)
- 1997-2001 Habilitation, RWTH Aachen (mentor: D. Enders)
- 2001-2003 Full Professor, University of Bonn, Germany
- since 2003 KIT, Karlsruhe, Germany
- around 110 publications

main research interests:

- ***combinatorial chemistry***
- ***solid-phase chemistry***
- ***nanostructures***
- ***total synthesis***

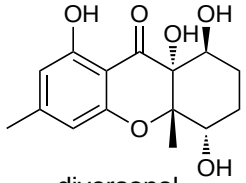
"If I were a car... I would be an Audi RS6."

My motto is... "I know!".

Hobbies: Chemistry...

Total Synthesis of Diversonol

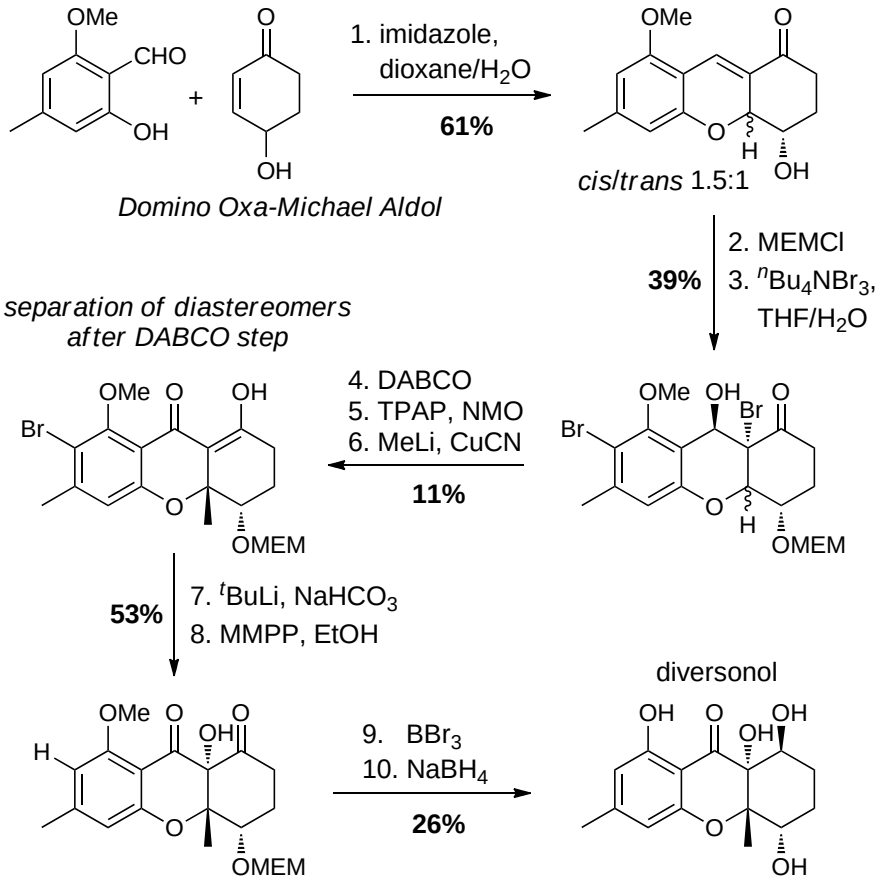
Angew. Chem. Int. Ed. **2006**, *45*, 307-309.



- isolated from *Penicillium diversum*
- absolute configuration unknown

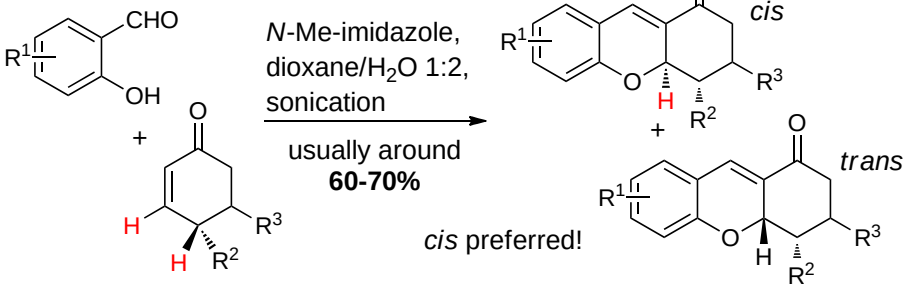
Chemistry in Germany - The Young Generation

Daniel Goetz

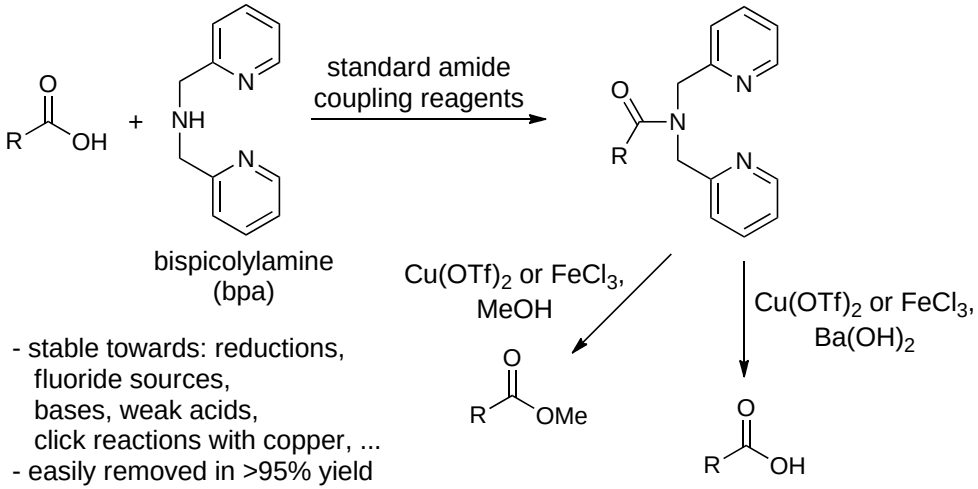


Domino Oxa-Michael Aldol Reaction

(*Eur. J. Org. Chem.* **2006**, 1535-1546.)



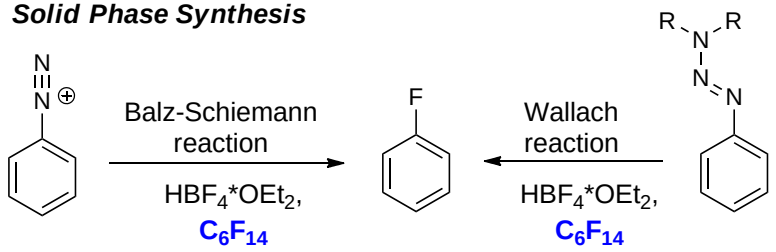
A Novel Protecting Group for RCOOH



- stable towards: reductions, fluoride sources, bases, weak acids, click reactions with copper, ...
- easily removed in >95% yield

Angew. Chem. Int. Ed. **2011**, *50*, 6175-6177.

Solid Phase Synthesis



perfluorohexanes C_6F_{14} as magic solvent:
- suppression of side product formation
- mild reactions conditions (80 °C)
- applicable to solid phase and in solution

Angew. Chem. Int. Ed. **2010**, *49*, 5986-5988.

... also worth reading:

Angew. Chem. Int. Ed. **1999**, *38*, 1071 (*C*,*C* couplings w/ immobilized subtrates).
Angew. Chem. Int. Ed. **2008**, *47*, 8120-8122 (solid phase synthesis of simple NP).
Eur. J. Org. Chem. **2009**, 4494-4502 (*fluorinating cleavage from solid support*).

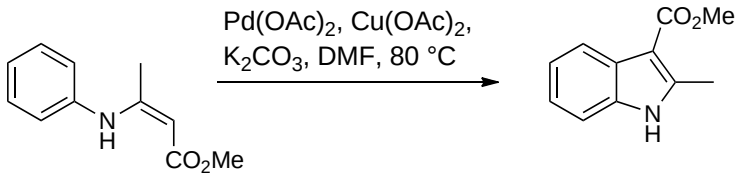
Frank Glorius:
- born: XX. XX. 1972, XX, Germany.
- studies in chemistry, University of Hannover
- 1995-1996 Research with Paul A. Wender, Stanford
- 2000 PhD with Andreas Pfaltz, MPI/University of Basel
- 2000-2001 Postdoc with D. A. Evans, Harvard University
- 2001-2004 Habilitation, MPI Mühlheim (mentor: A. Fürstner)
- 2004 Associate Professor, University of Marburg, Germany
- since 2007 Full Professor, University of Münster, Germany
- 91 publications

main research topics:
- **sterically demanding NHCs**
- **functional MOFs**
- **challenging cross-couplings**
- **CH activation**
- **asymmetric organocatalysis**
- **heterocyclic chemistry**

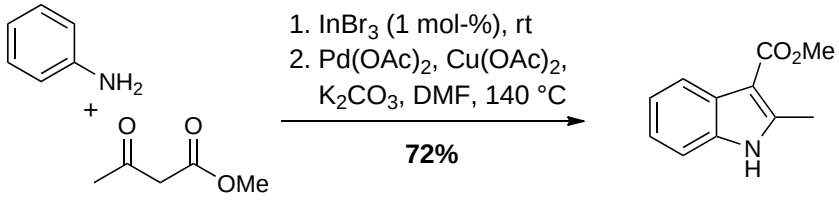
"When I wake up I... can't believe it's that time already."

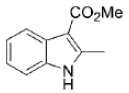
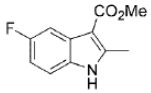
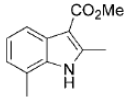
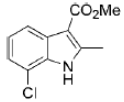
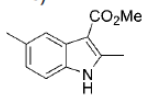
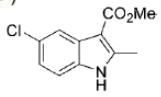
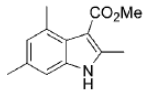
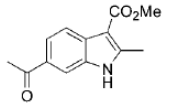
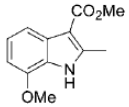
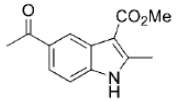
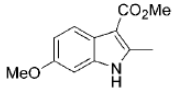
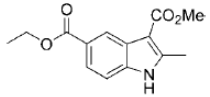
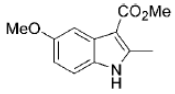
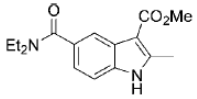
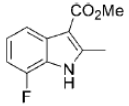
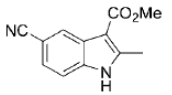
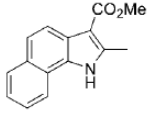
Indoles from Enamines by CH Activation

Angew. Chem. Int. Ed. **2008**, *47*, 7230-7233.

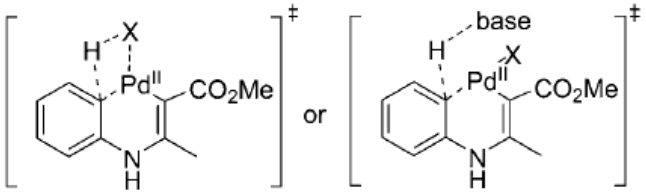


- very wide substrate scope
- steric demand determines outcome, not electronic influence; rarely regioisomers
- good yields, scalable
- one-pot reaction possible (see below)



Entry	Product	Yield[b] [%]	Entry	Product	Yield[b] [%]
1[c]	 **2a**	72	11[d]	 **2k**	74
2[d]	 **2b**	82	12[c]	 **2l**	53
3[d] (6-Me/4-Me)	**2c**	68 (92:8[e])	13[c] (6-Cl/4-Cl)	**2m**	76 (88:12[e])
4[c]	 **2d**	72	14[c]	 **2n**	64
5[d]	 **2e**	62	15[f]	 **2o**	54 (>99:1[e])
6[f]	 **2f**	64	16[f]	 **2p**	52
7[f]	 **2g**	68 (>99:1[e])	17[f]	 **2q**	64
8[f]	 **2h**	64	18[f]	 **2r**	70
9[d]	 **2i**	78	19[f]	 **2s**	65
10[d] (6-F/4-F)	**2j**	74 (53:47[e])	20[c]	 **2t**	85 (>99:1[e])

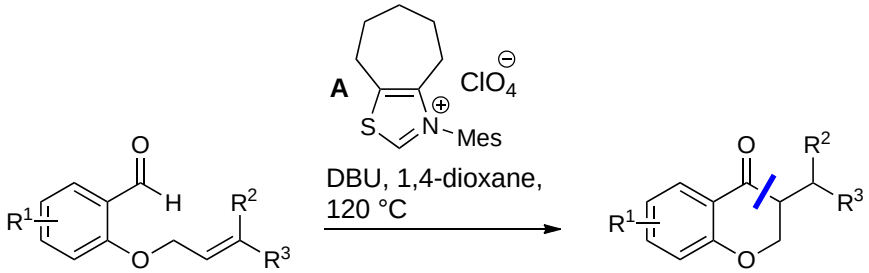
proposed mechanism:



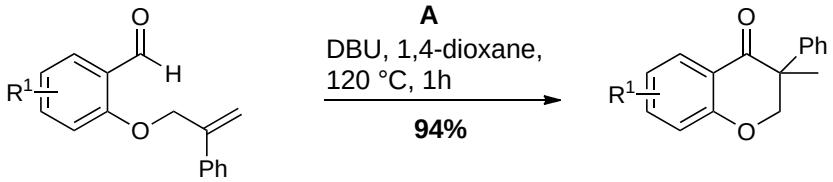
Initial mechanistic investigations unambiguously support a σ-bond metathesis or deprotonation pathway and not an electrophilic aromatic palladation of the aniline ring.

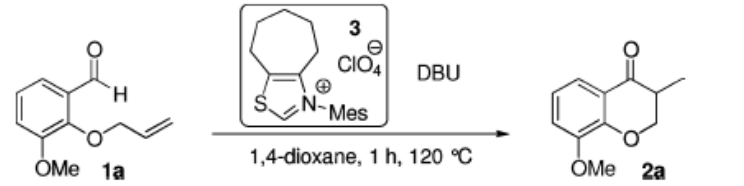
NHC-Catalyzed Hydroacylation of Unactivated Double Bonds (cp. Stetter reaction)

J. Am. Chem. Soc. **2009**, *131*, 14190-14191.
Org. Lett. **2008**, *10*, 4243-4246 (synthesis of NHC **A**).



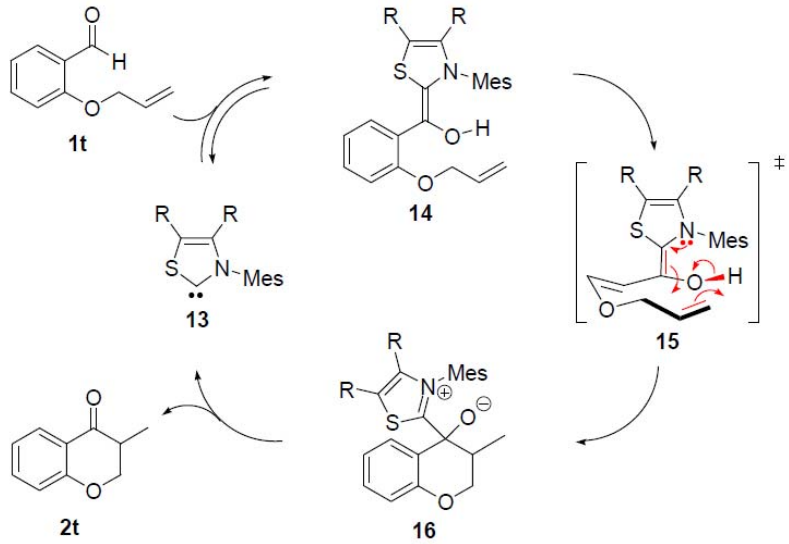
- very wide substrate scope
- good yields (70-96%)
- scalable
- formation of quartenary centers possible
- useful disconnection





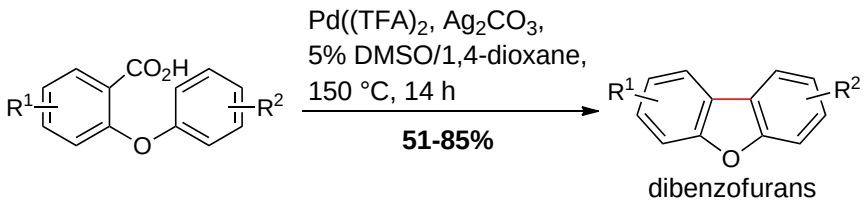
entry	variation of the standard conditions[a]	yield of **2a** (%)[b]
1	none	69
2	**4** instead of **3**	2
3	**5** instead of **3**	21
4	**6** instead of **3**	2
5	**7** instead of **3**	11
6	DBU: 20 mol % instead of 40 mol %	34
7	TEA instead of DBU	3
8	K_2CO_3 instead of DBU	32
9	KO*t*-Bu instead of DBU	69
~~10~~	~~10 mol % of **3**, 20 mol % DBU~~	~~65~~
11	**reaction time: 2 h instead of 1 h**	**81 (85)**[c]

proposed mechanism:



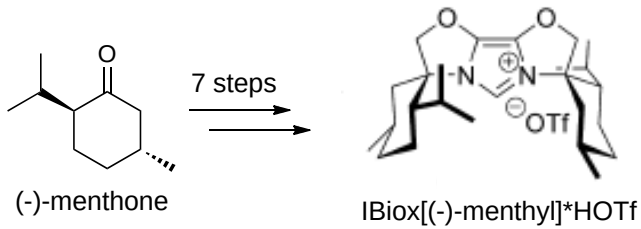
Intramolecular Direct Arylation of Benzoic Acids by Tandem Decarboxylation/C-H Activation

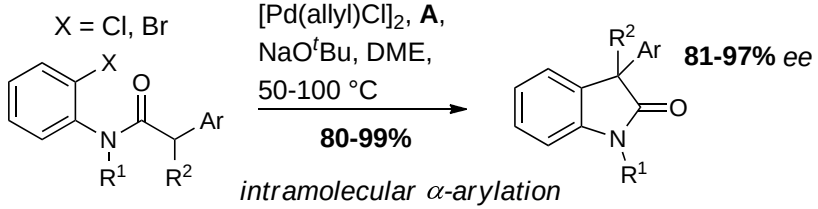
J. Am. Chem. Soc. **2009**, *131,* 4194-4195.



A Sterically Demanding Chiral NHC Ligand

J. Am. Chem. Soc. **2009**, *131*, 8344-8345.





- rigid geometry of NHC leads to excellent *ee*'s
- high yields
- aryl chlorides (X = Cl) can be used for the first time
- *N*-benzyl give higher *ee*'s than *N*-methyl
- highest *ee*'s for *ortho*-substituted aryls (Ar)

Mathias Christmann:

- born: XX. XX. 1972, Peine, Germany.
- studies in chemistry, University of Braunschweig
- 2000 PhD with M. Kalesse, University of Hannover (*Total Synthesis of (+)-Ratjadone*)
- 2001-2002 Postdoc with C. J. Forsyth, Univ. of Minnesota
- 2003-2007 Habilitation, RWTH Aachen (mentor: D. Enders)
- since 2008 Associate Professor, TU Dortmund, Germany
- 36 independent publications

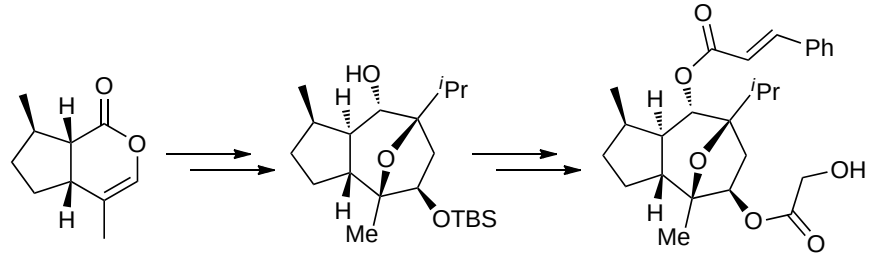
main research topics:

- **total synthesis**
- **method development**
- **organocatalysis**
- **catalytic transformations of renewable ressources**

We have recently initiated a program that is aimed at making larger substructures within natural products available from terpene feedstock. Using simple bulk terpenes such as geranyl and neryl acetate or nepetalactone we are aiming to find efficient ways to modify the carbon skeleton using oxidations, organocatalytic and metal-catalyzed reactions such as hydroformylations.

The Concept - e.g. (-)-Englerin A from (-)-Nepetalactone:

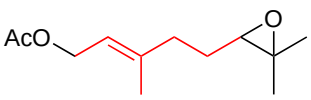
Angew. Chem. Int. Ed. **2009**, *48*, 9105 (1st generation synthesis).
Angew. Chem. Int. Ed. **2011**, *50*, 3998 (2nd generation synthesis).

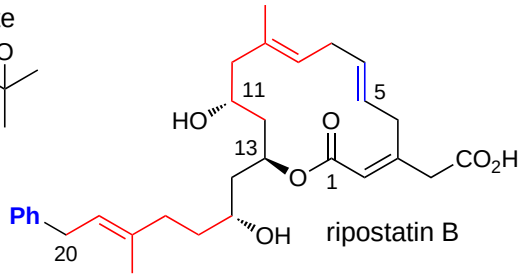


- multigram quantities of key intermediate available
- route allows for various late stage modifications for SAR studies
- derivatives with improved activity against renal cancer cell lines

The Concept - continued... *Chem. Commun.* **2011**, *47*, 394-396.

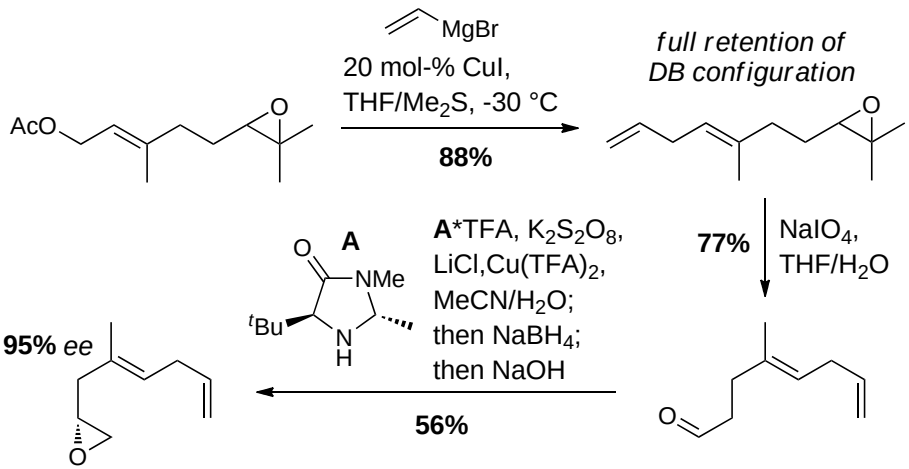
epoxygeranyl acetate



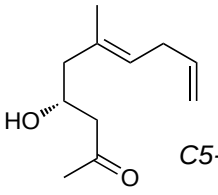


ripostatin B

selected examples of prepared building blocks:

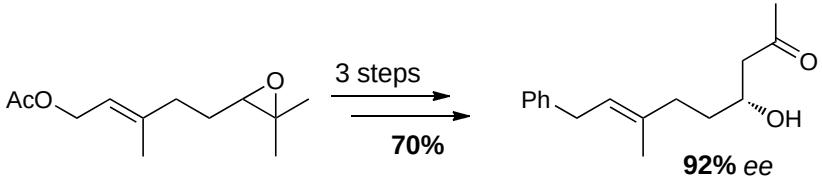


62% 1. 2-methyl-1,3-dithiane, ^{n}BuLi, THF
2. PhI(TFA)$_2$, $CaCO_3$, MeOH/MeCN



- valuable building blocks on multigram scale

C5-C14 fragment (see above)



92% *ee*

C12-C20 fragment (see above)

... the end!

not covered:

- Magnus Rüping, RWTH Aachen
- Dirk Menche, University of Heidelberg
- Armino Studer, University of Münster
- Benjamin List, MPI Mühlheim
- Christian Hertweck, HKI Jena
- Lutz Ackermann, University of Heidelberg
- ...

... part II to come ...