Recent Advances in Fluorine Chemistry

Véronique Gouverneur
University of Oxford - Chemistry Research Laboratory

Ischia Advanced School of Organic Chemistry
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Why Fluorine Chemistry?

Fluorine in Health →
- Pharmaceuticals
- Molecular Imaging [^{19}F MR and ^{18}F PET]
- Biomedical Materials

↓

^{19}F-Pharma-ceuticals →
- Metabolic Stability
- p*K*a, log P
- Conformation
- Affinity
- Bioavailability
- Racemisation
- Mechanism-based Inhibition

CF
CF_2
CF_3
SF_5

↓

^{18}F-Radio-Chemistry →
- Drug Discovery
- Diagnosis
- Response to Therapy

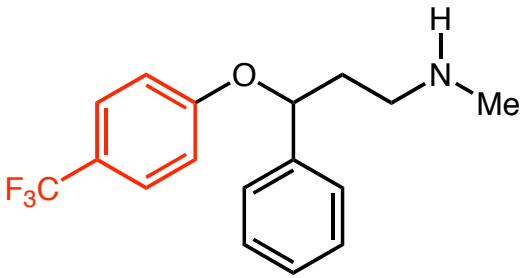
→ Synthesis: Fluorinated Building Blocks and Fluorination

"Fluorine in Health" Edited by Alain Tressaud and Günter Haufe Elsevier **2008**

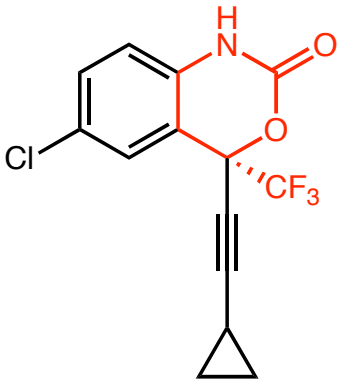
Fluorine and Medicinal Chemistry

Metabolic Stability, Affinity, Conformation, pKa, log P, Racemisation, Mechanism-based Inhibition

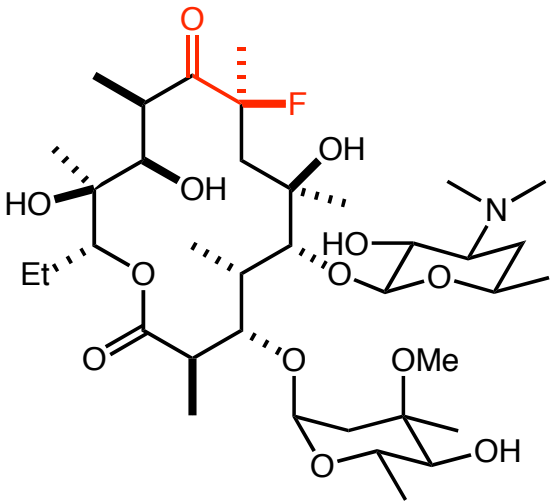
Prozac
Antidepressant



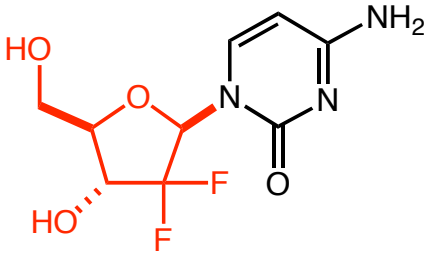
Efavirenz
Reverse transcriptase inhibitor



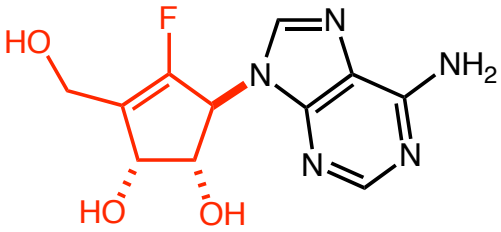
Flurithromycin
Macrolide antibiotic



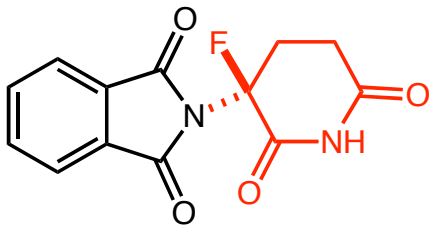
Gemcitabine
Antiherpetic



Fluoroneplanocin
broad spectrum antiviral drug

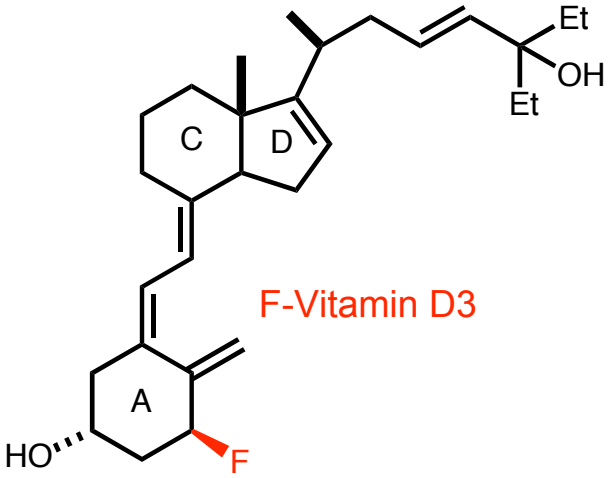


Fluorothalidomide

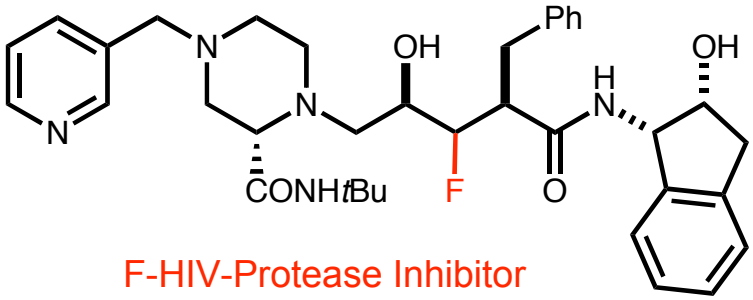


Fluorination of Less Activated Substrates

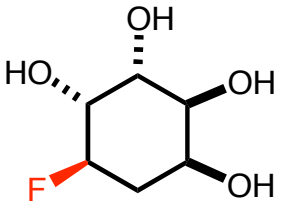
When possible, late fluorination for application in PET ….



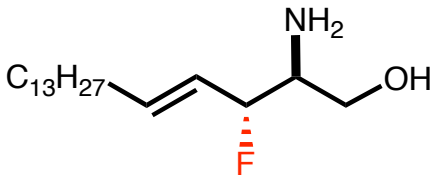
F-Vitamin D3



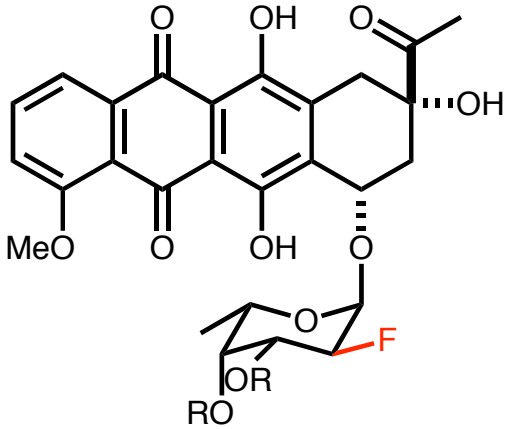
F-HIV-Protease Inhibitor



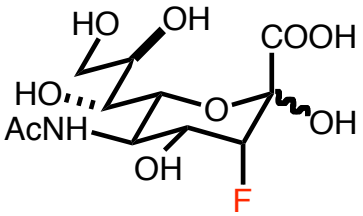
F-Cyclitols



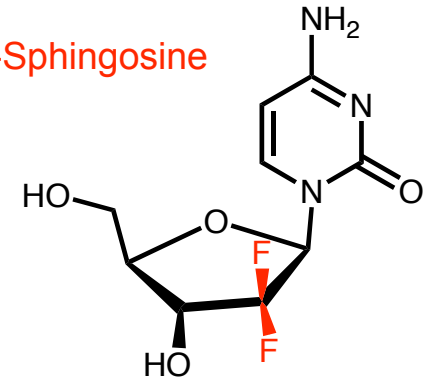
F-Sphingosine



F-Daunomycinone



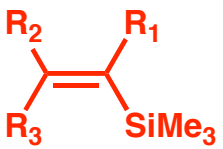
F-Sialic acid

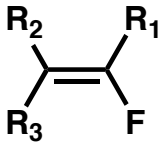


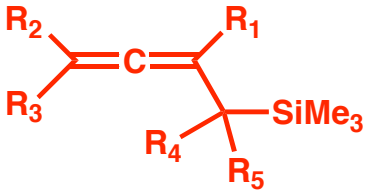
gemcitabine

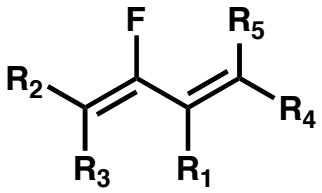
Electrophilic Fluorination of Organosilanes

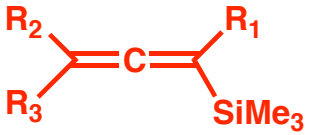
A Highly Versatile Reaction to Access F-Building Blocks

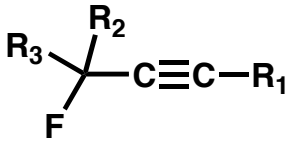


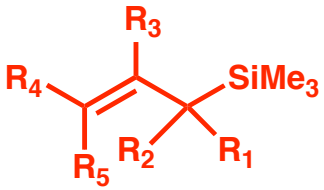


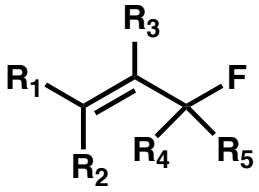


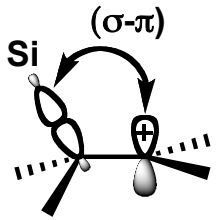




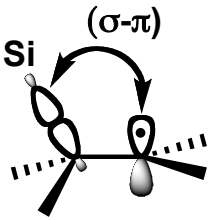






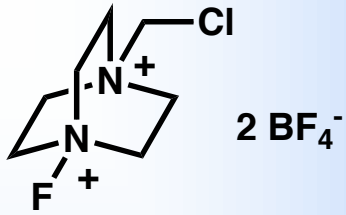


~30 kcal/mol

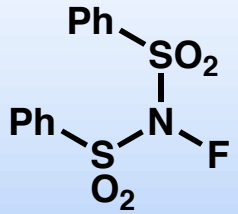


~ 3.5 kcal/mol

Selectfluor

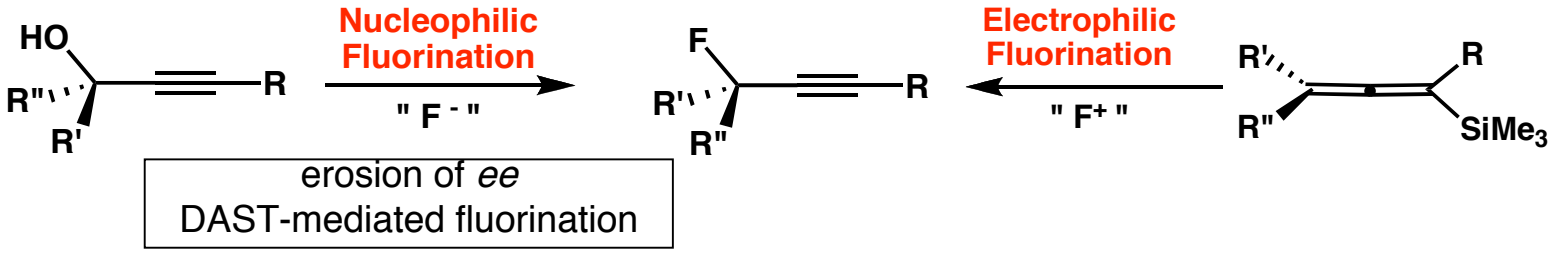


N-Fluorosulfonimide [NFSI]

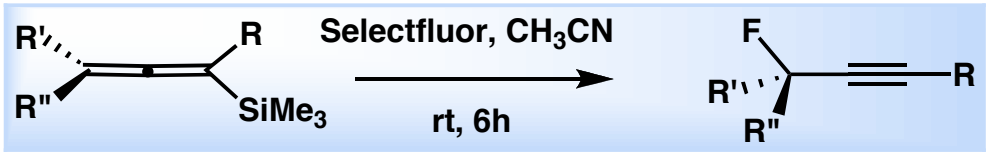


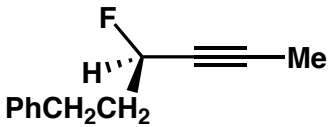
Electrophilic Fluorodesilylation of Allenylsilanes

Solving the Problem of Erosion of Enantiomeric Excess

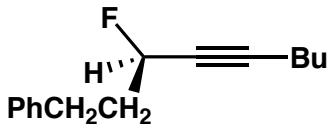


erosion of *ee*
DAST-mediated fluorination

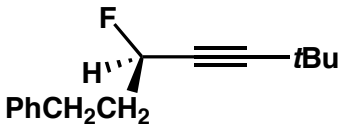




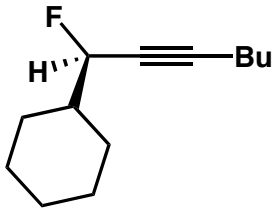
78%



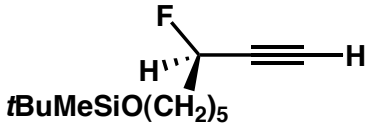
69%



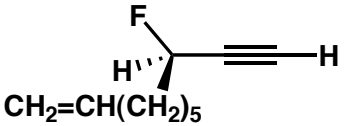
40%



59%



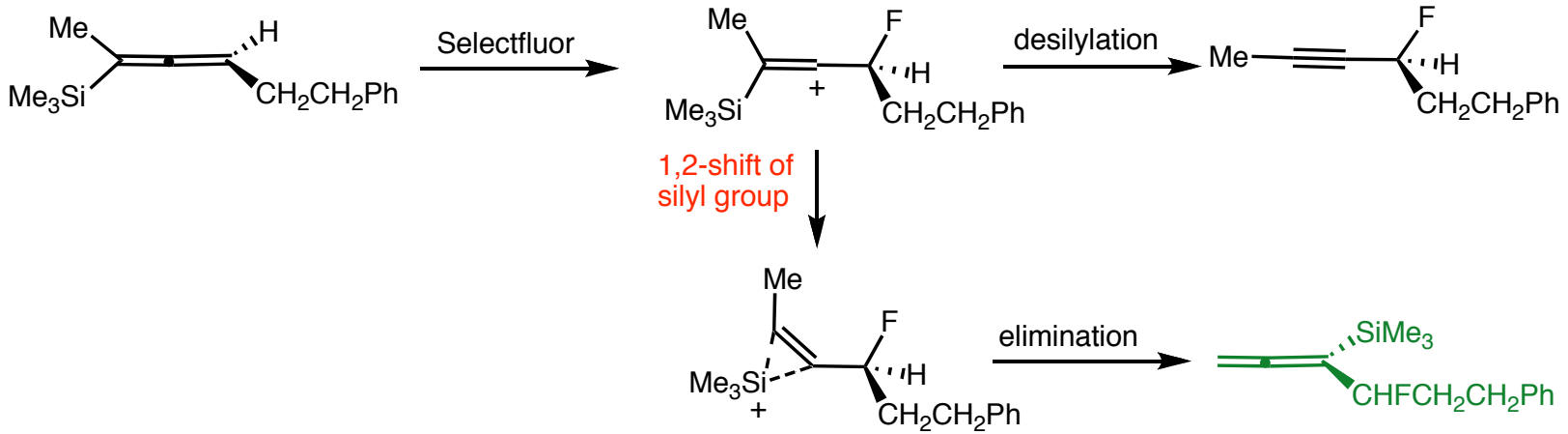
51%



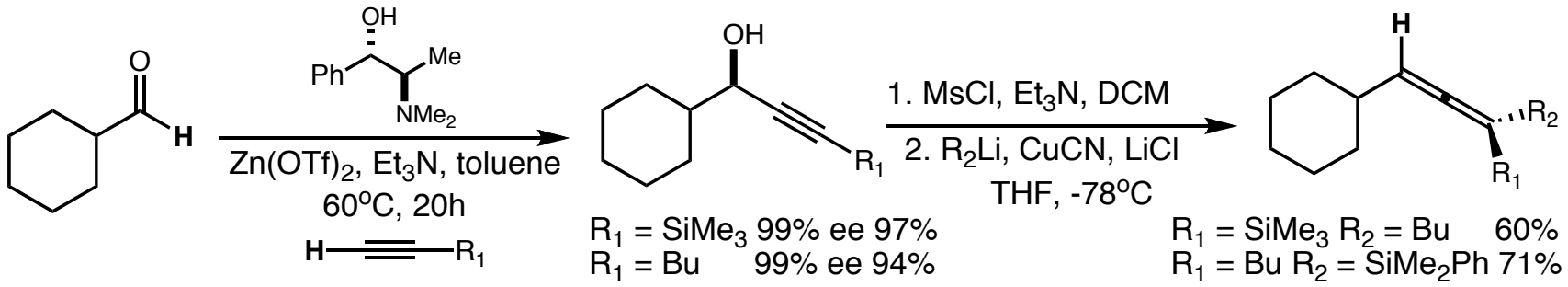
56%

Electrophilic Fluorodesilylation of Allenylsilanes

Solving the Problem of Erosion of Enantiomeric Excesses



Synthesis of enantioenriched allenylsilanes:

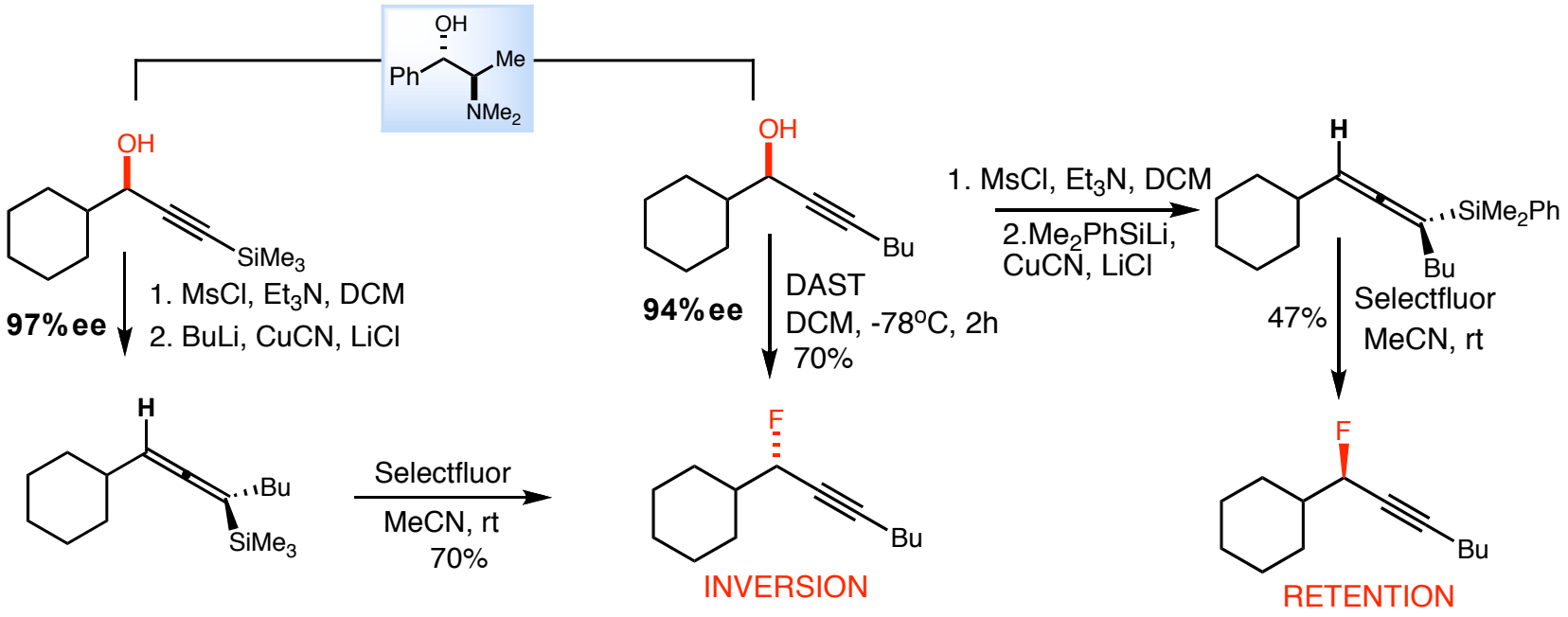


R_1 = $SiMe_3$ 99% ee 97%
R_1 = Bu 99% ee 94%

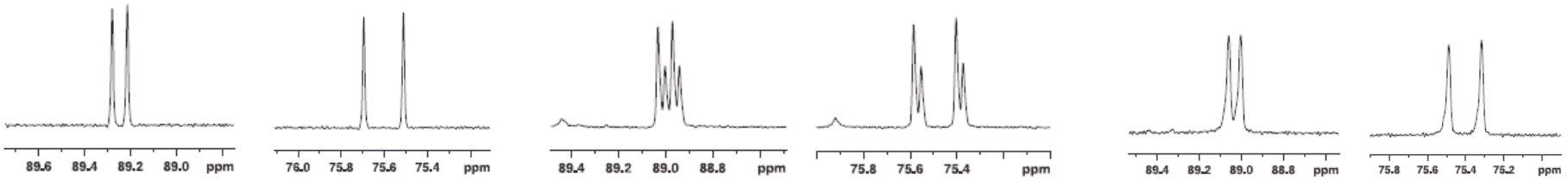
R_1 = $SiMe_3$ R_2 = Bu 60%
R_1 = Bu R_2 = $SiMe_2Ph$ 71%

Electrophilic Fluorodesilylation of Allenylsilanes

Solving the Problem of Erosion of Enantiomeric Excesses



95% ee **~ 30% ee** **95% ee**

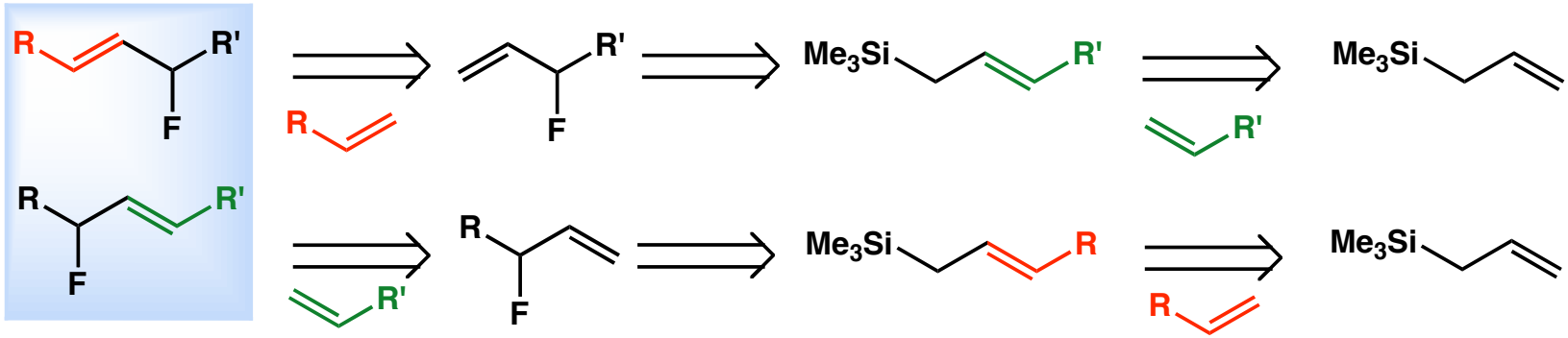


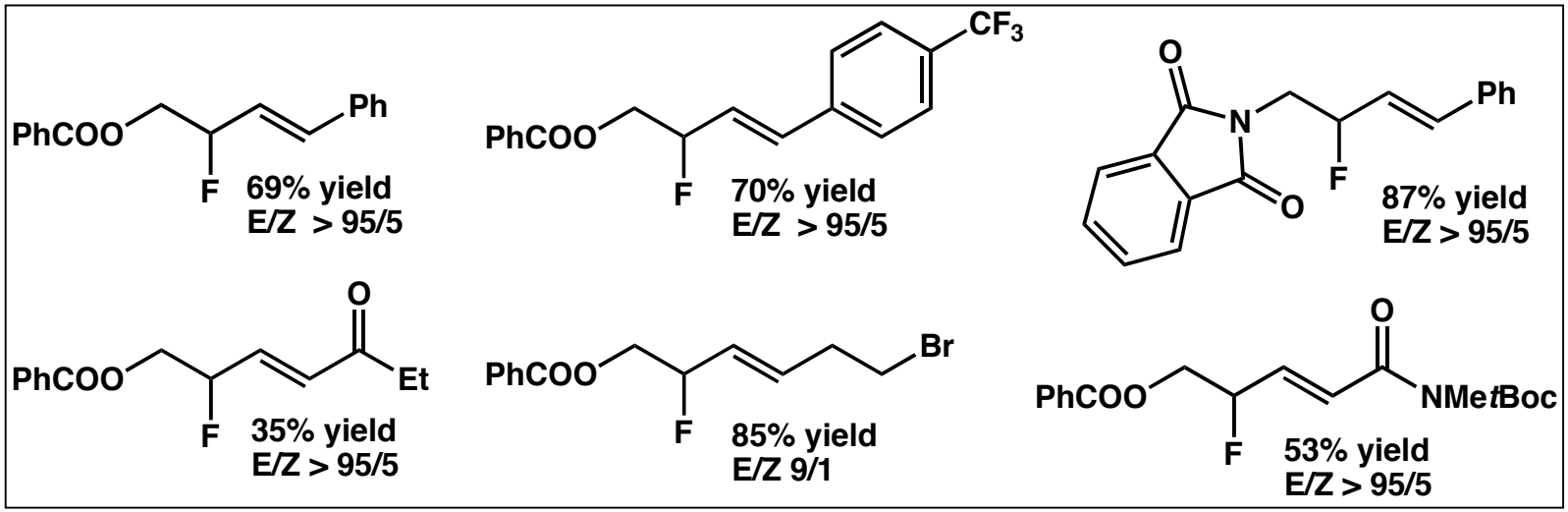
^{13}C NMR Chiral Liquid Crystal [poly(γ–benzyl-L-glutamate)] (PBLG)

with L. Carroll in *Chem. Commun* **2006** 4113 & in *OBC* **2008** 1731

Metathesis & Electrophilic Fluorodesilylation

Solving the Problem of Double Transposition for the Synthesis of Allylic Fluorides





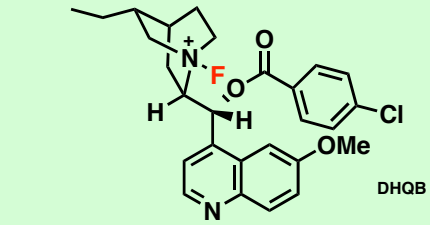
Fluorination: 1.2 eq. Selectfluor, 1.2 eq. $NaHCO_3$; *CM*: 5 mol % Grubbs II, DCM, sealed tube

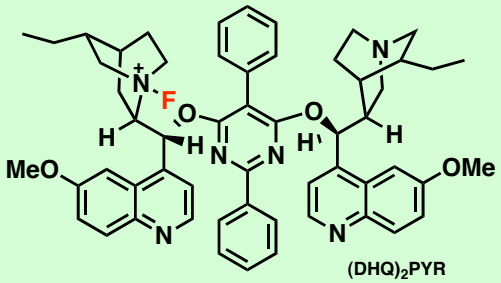
With S. Thibaudeau & M. Tredwell *Org. Lett.* **2003**, 4891-4893; *Org. & Biomol. Chem.* **2004** 1110.

Enantioselective Electrophilic Fluorodesilylation

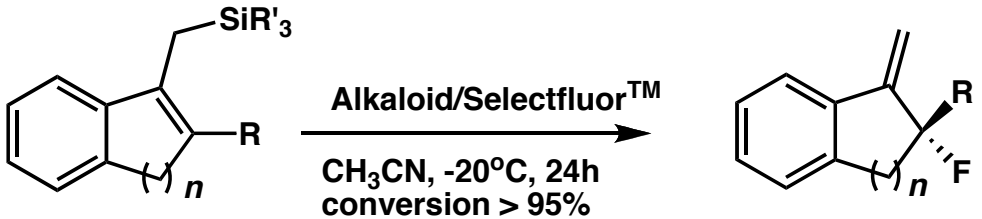
with in-situ generated chiral N-F Reagents

Cahard, Plaquevent, Roques *Org. Lett.* 2000
Takeuchi, Shibata *JACS* 2000





Prepared *in situ* from alkaloid and Selectfluor

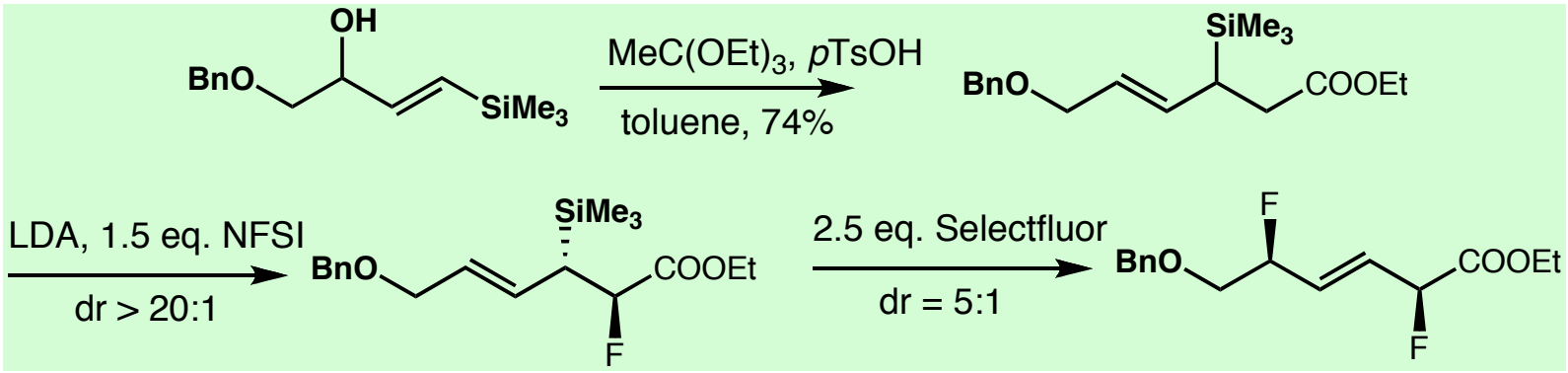


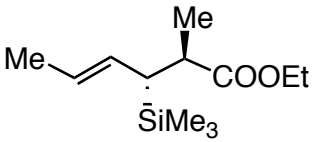
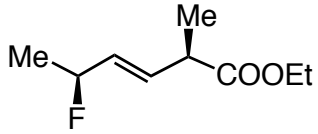
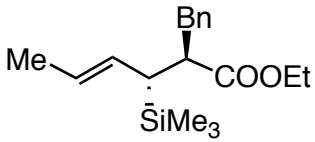
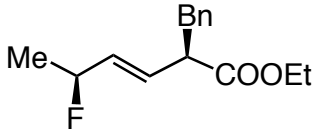
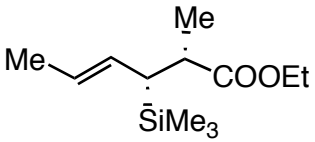
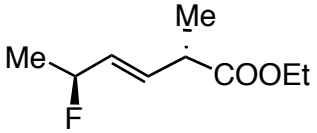
		Alkaloid	ee (%)
R' = Me	*n* = 1 R = H	$(DHQ)_2PYR$	60
R' = Me	*n* = 1 R = Bn	DHQB	85
R' = Me	*n* = 1 R = Bn	$(DHQ)_2PYR$	96
R' = Me	*n* = 1 R = Bn	DHQMQE	93
R' = Me	*n* = 2 R = H	$(DHQ)_2PYR$	22
R' = Me	*n* = 2 R = Me	$(DHQ)_2PYR$	45
R' = Me	*n* = 2 R = Bn	$(DHQ)_2PYR$	83
R' = Ph	*n* = 1 R = H	$(DHQ)_2PYR$	87

With B. Greedy in *Angew. Chem. Int. Ed.* **2003**, *42,* 3291; N. Shibata et al Alkaloid/NFSI K_2CO_3 in *Angew. Chem. Int. Ed.* **2008**, *ASAP*.

[3,3] Sigmatropic & Electrophilic Fluorodesilylation

Transfer of Chirality C-Si to C-F

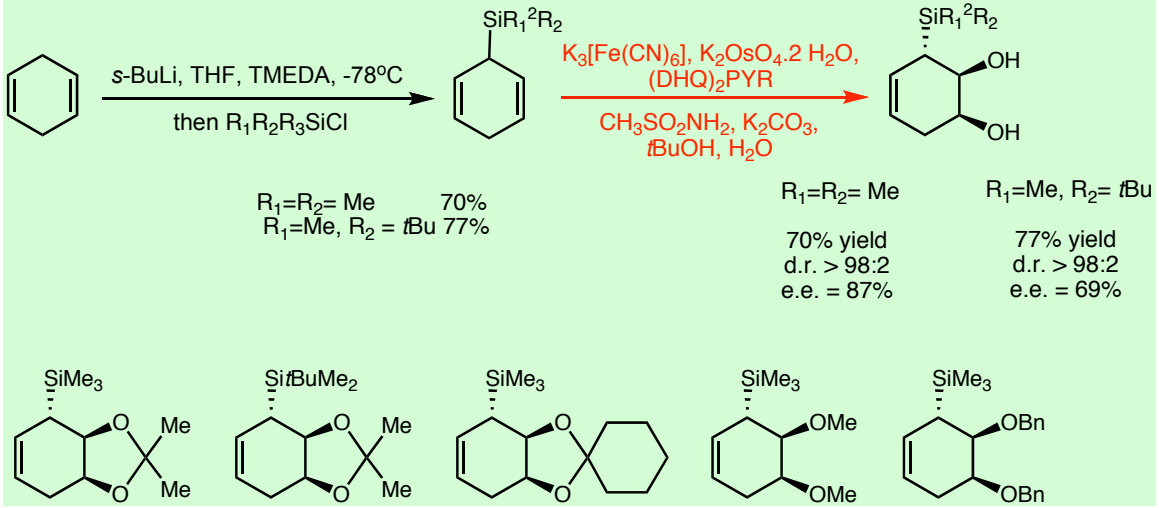


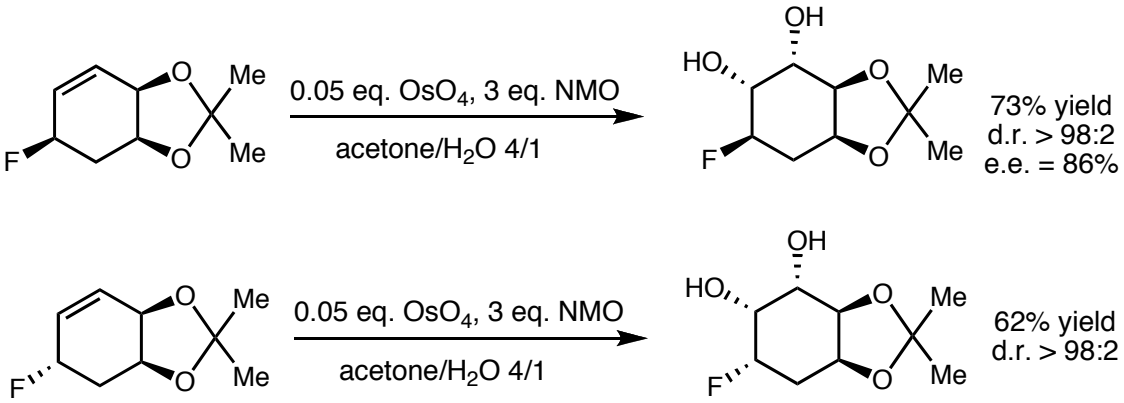
Starting Material	Product	d.r. [%]	Yield [%]
		>20:1	95
		>20:1	90
		>20:1	96

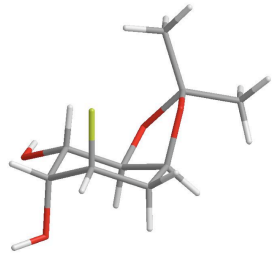
De Novo Synthesis of Enantioenriched F-Cyclitols

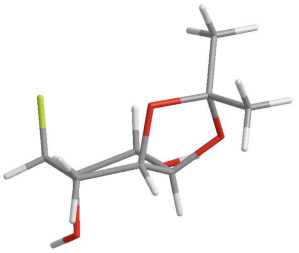
Catalytic Asymmetric Dihydroxylation-Fluorodesilylation

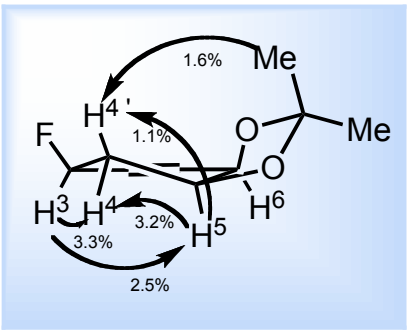
Y. Landais *Eur. J. Org. Chem.* 2004 3173







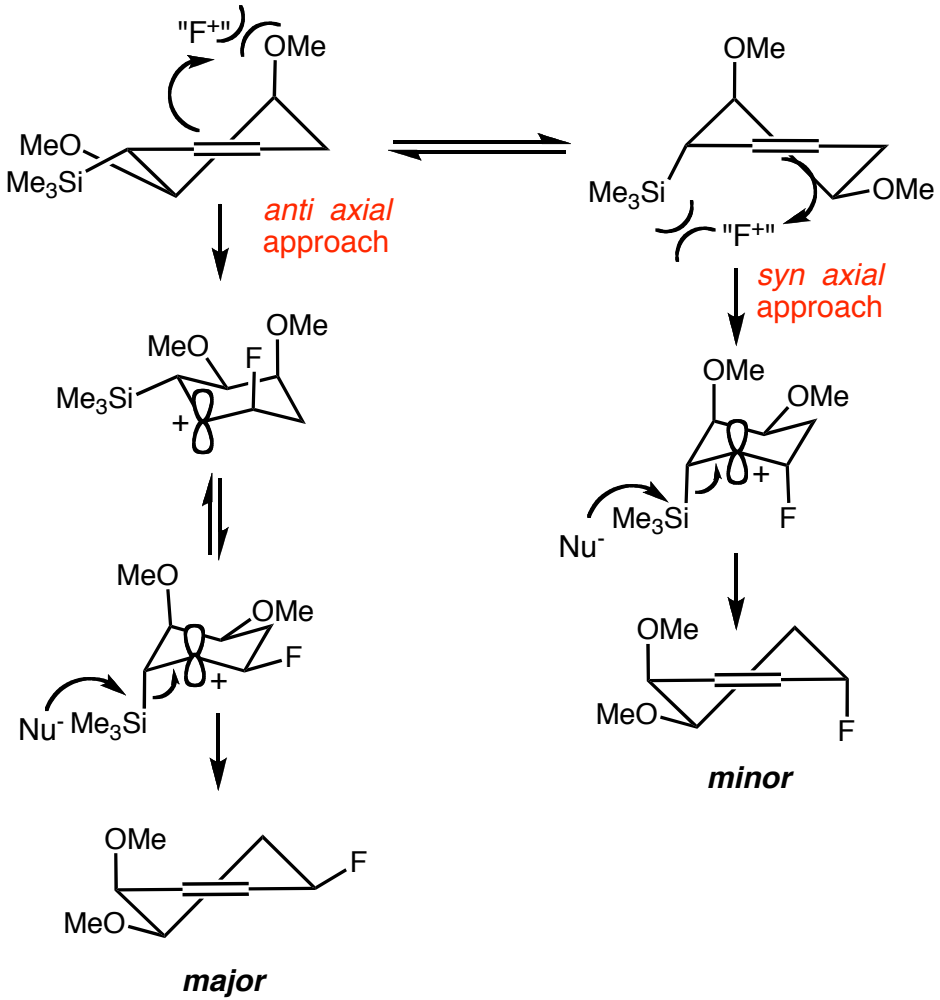


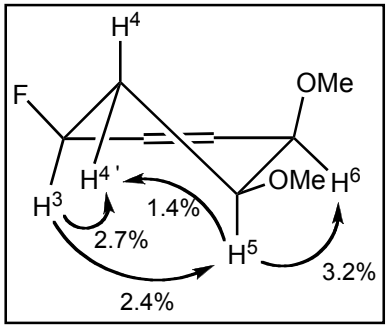


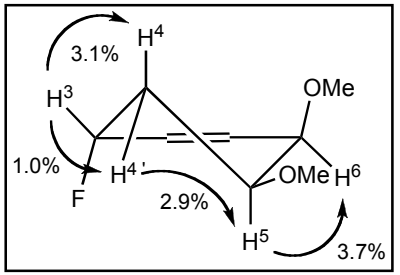
with S Purser in *Chemistry A European Journal* **2006** *12* 9179

De Novo Synthesis of Enantioenriched F-Cyclitols

Catalytic Asymmetric Dihydroxylation-Fluorodesilylation

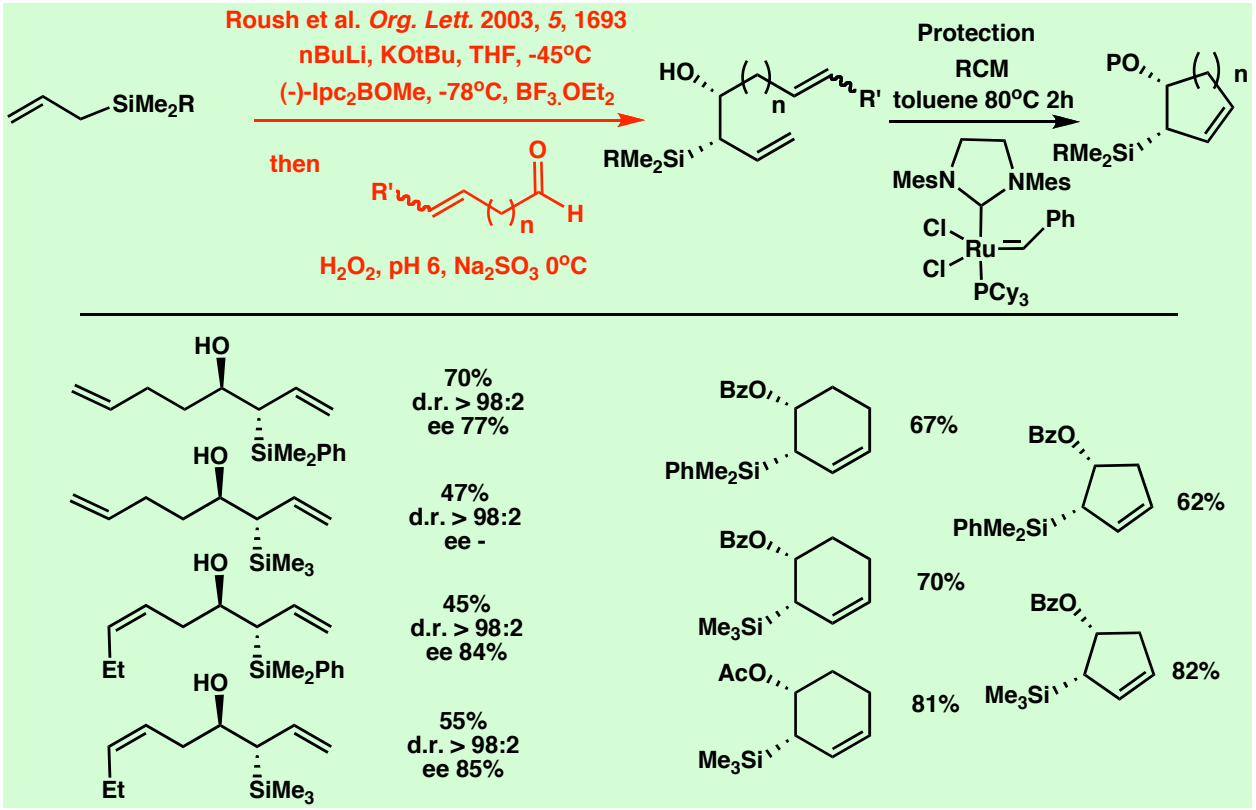






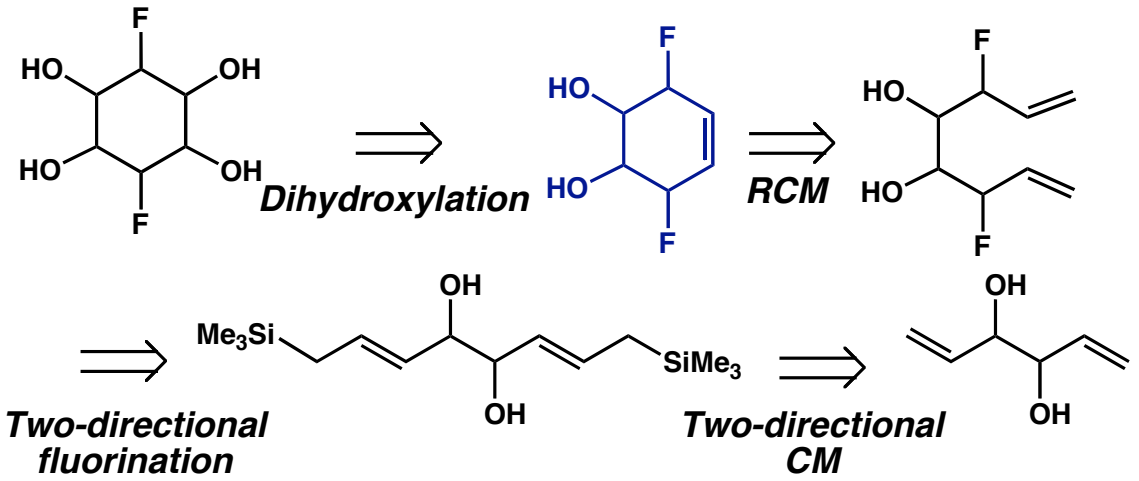
Synthesis of Enantioenriched F-Cyclitols

Asymmetric Allylation-RCM-Fluorination



Synthesis of Enantioenriched Difluorinated Cyclitols

The Two-directional Approach

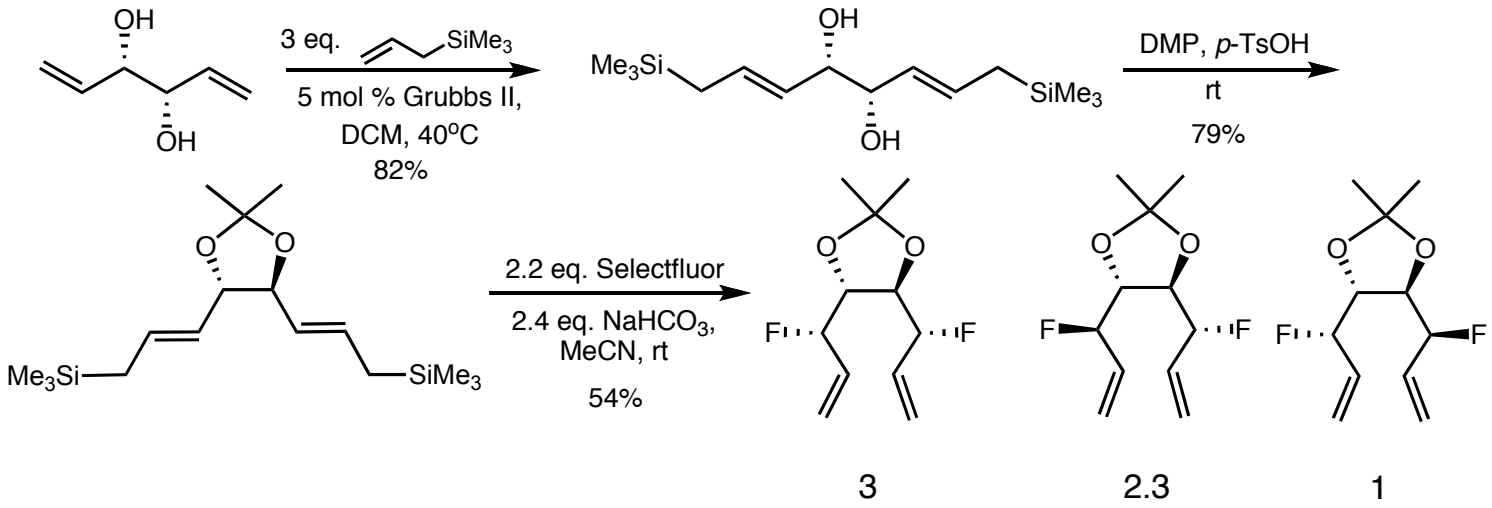


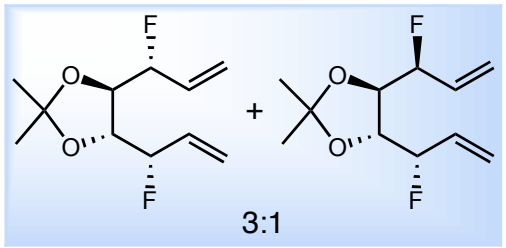
1. Novel deoxyfluoro-*myo*-inositols are highly valuable compounds to intervene with the phosphatidylinositol cycle
2. Cyclic *anti*- and *syn*- 1,4-difluorocycloalkenes are unknown
3. No information is available on their reactivity or physical properties.

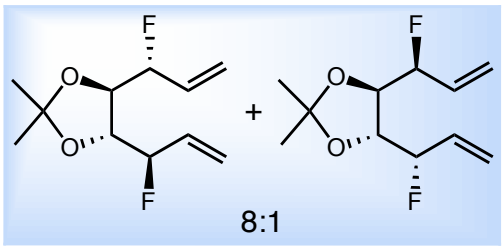
With S. Purser in *Org. Lett.* **2008** *ASAP* 15

Synthesis of Enantioenriched Difluorinated Cyclitols

The Two-Directional Approach



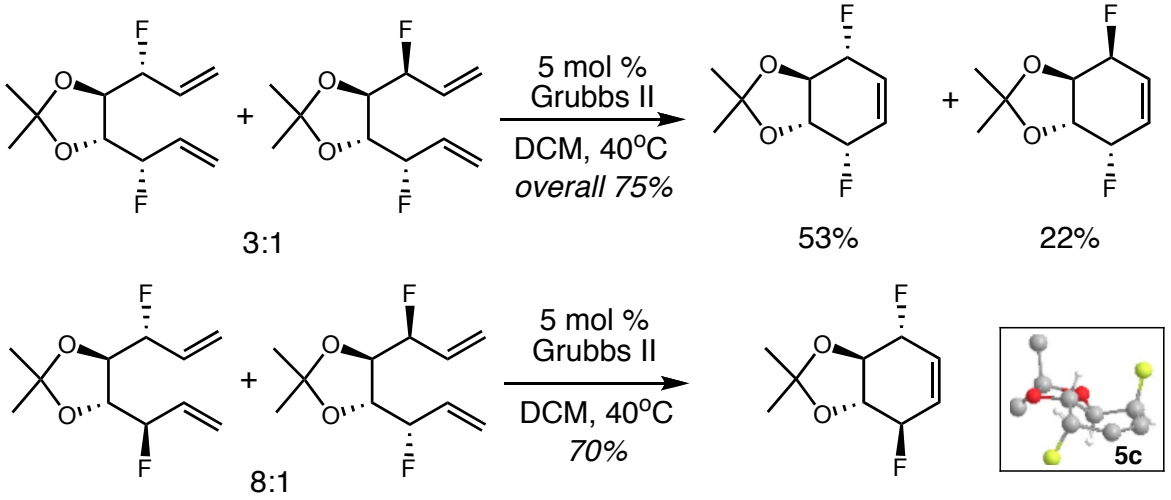


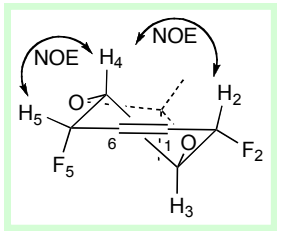


With S. Purser in *Org. Lett.* **2008** *ASAP* 16

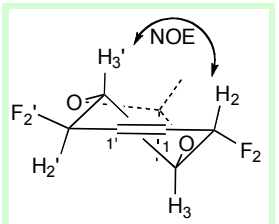
Synthesis of Enantioenriched Difluorinated Cyclitols

The Two-Directional Approach

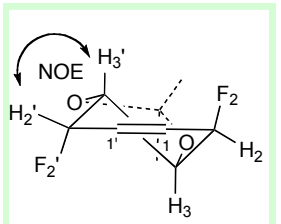




$^5J_{F2,5}$ = 8.5 Hz
δF= -181.7, -188.2 ppm



$^5J_{F2,2'}$ = 11.4 Hz
δF= -180.8 ppm

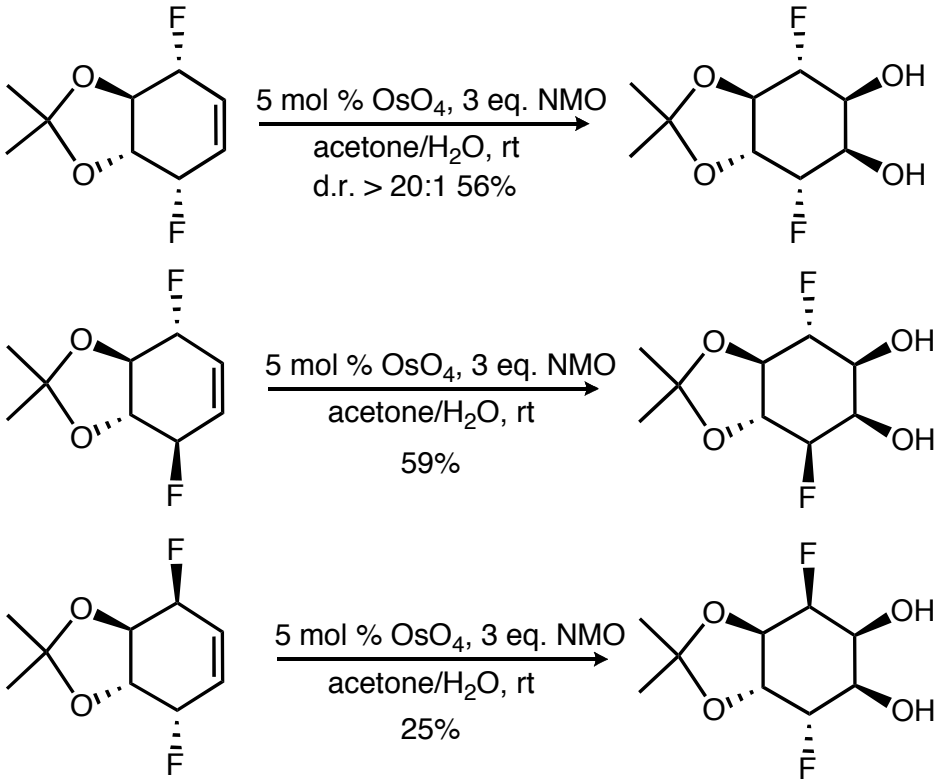


$^5J_{F2,2'}$ = 18.6 Hz
δF= -197.6 ppm

With S. Purser in *Org. Lett.* **2008** *ASAP* 17

Synthesis of Enantioenriched Difluorinated Cyclitols

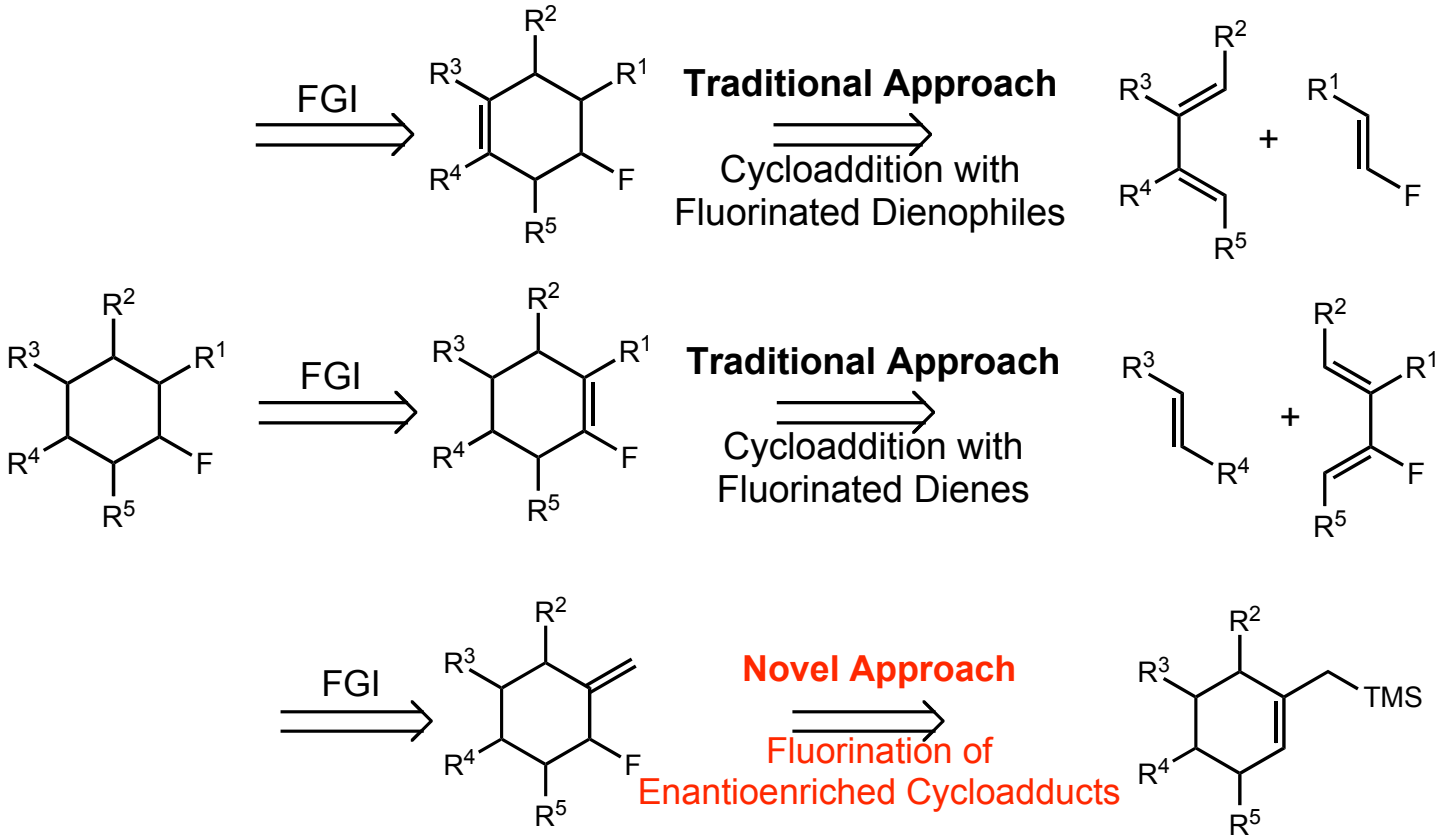
The Two-Directional Approach



With S. Purser in *Org. Lett.* **2008** *ASAP* 18

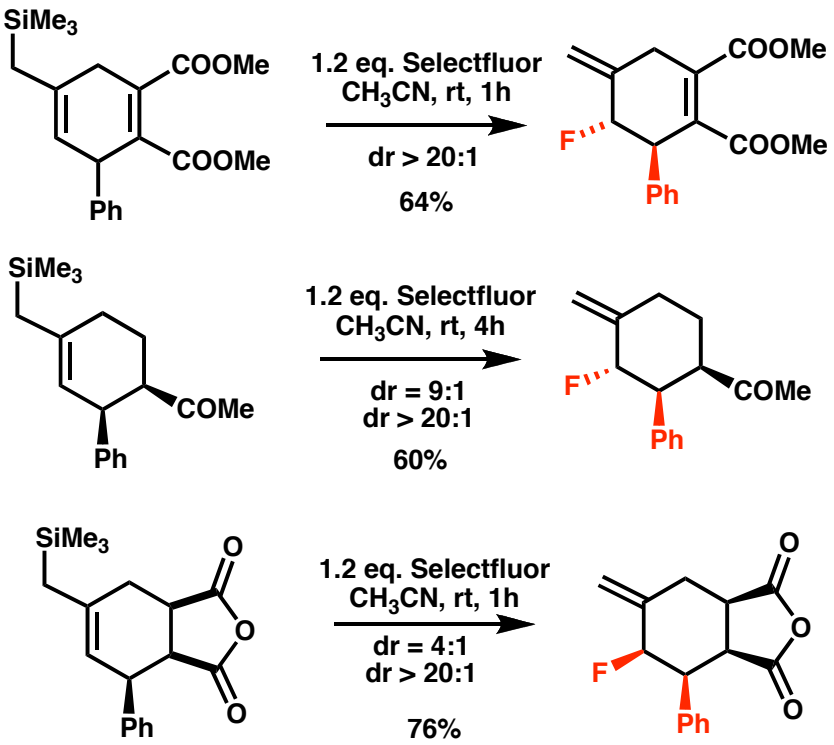
Diels-Alder & Electrophilic Fluorination

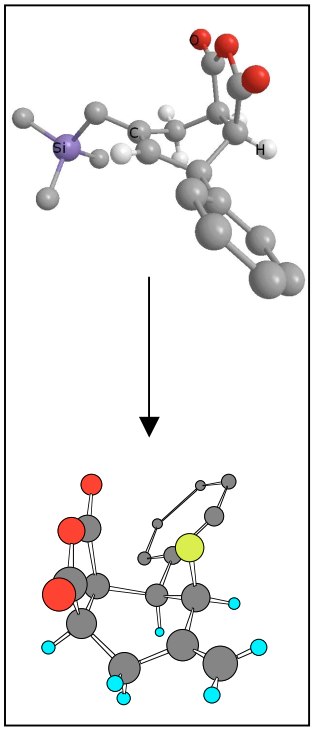
The REVERSE Approach



Diels-Alder & Electrophilic Fluorination

The REVERSE Approach

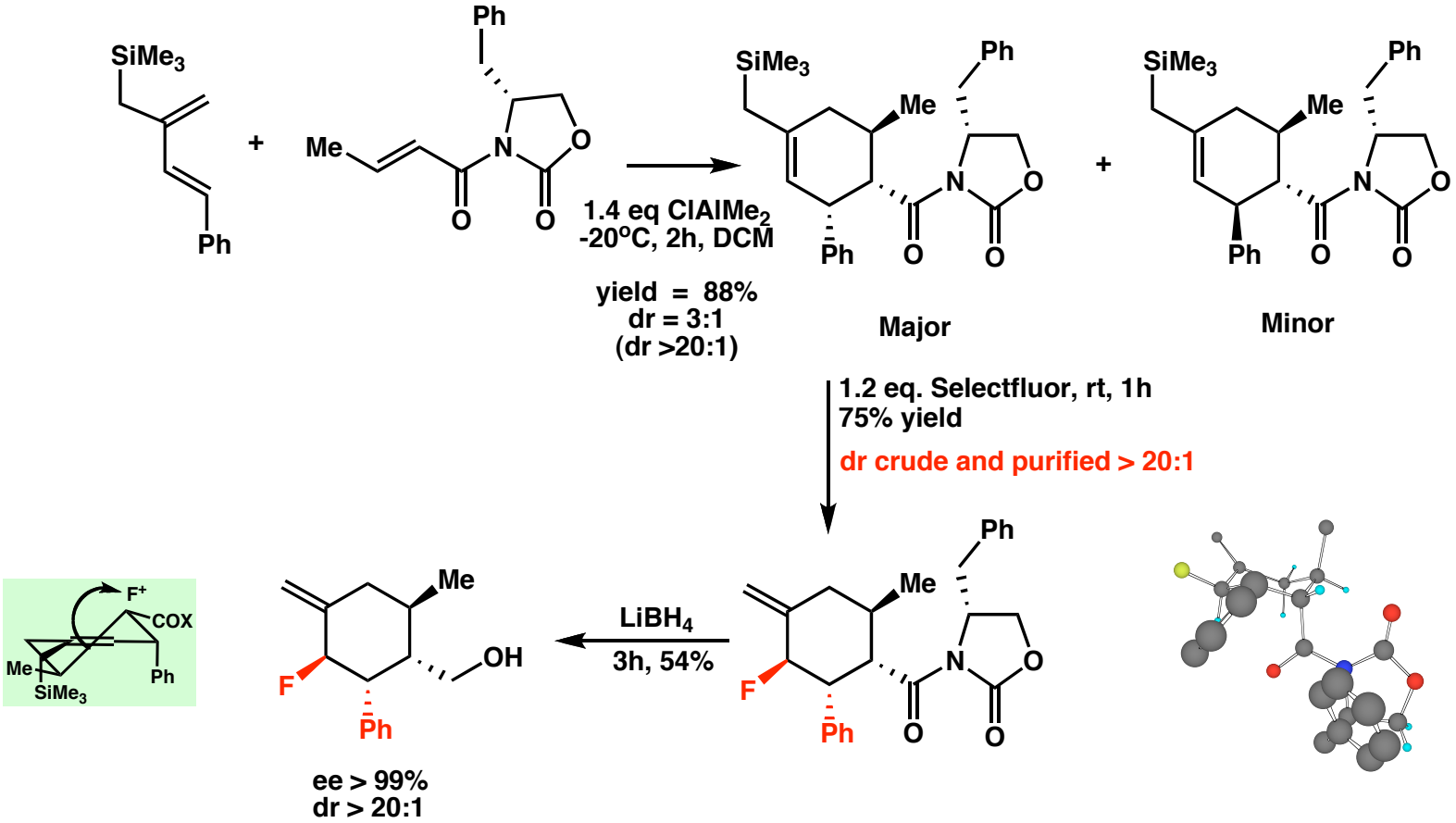




With C. Lam in *Angew. Chem. Int. Ed.* **2007**, *46*, 5106-5110.

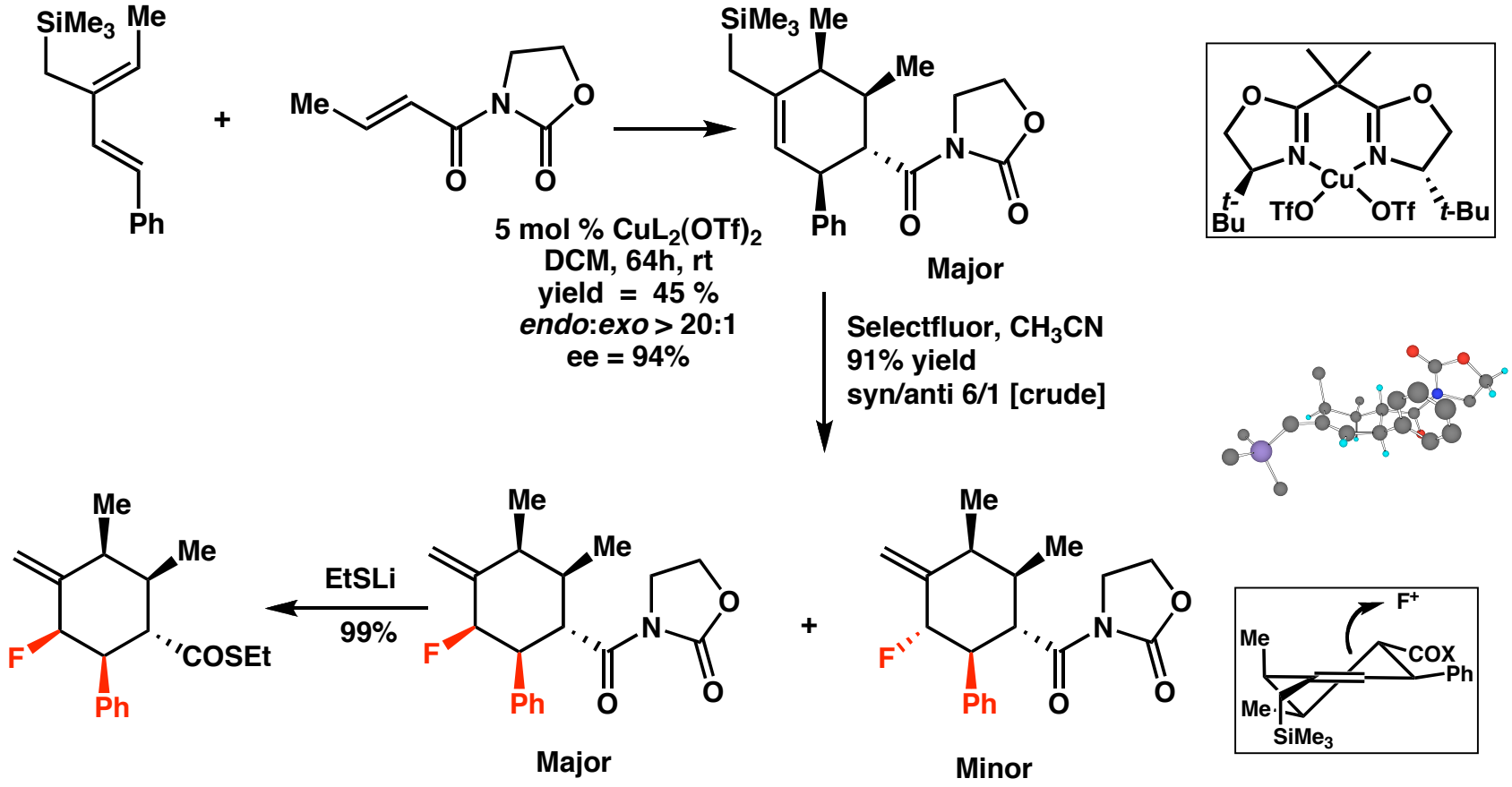
Diels-Alder & Electrophilic Fluorination

The REVERSE Approach



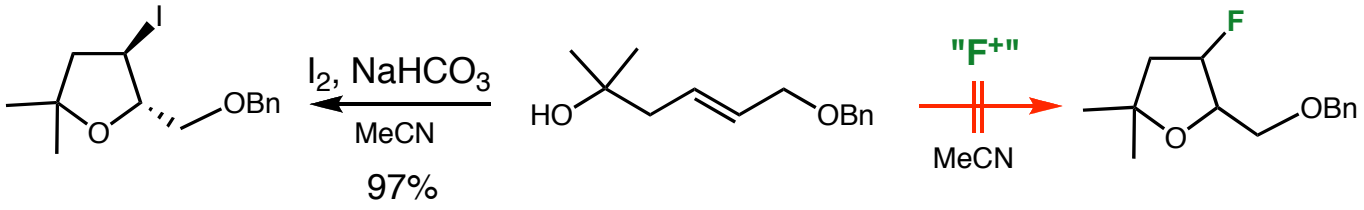
Diels-Alder & Electrophilic Fluorination

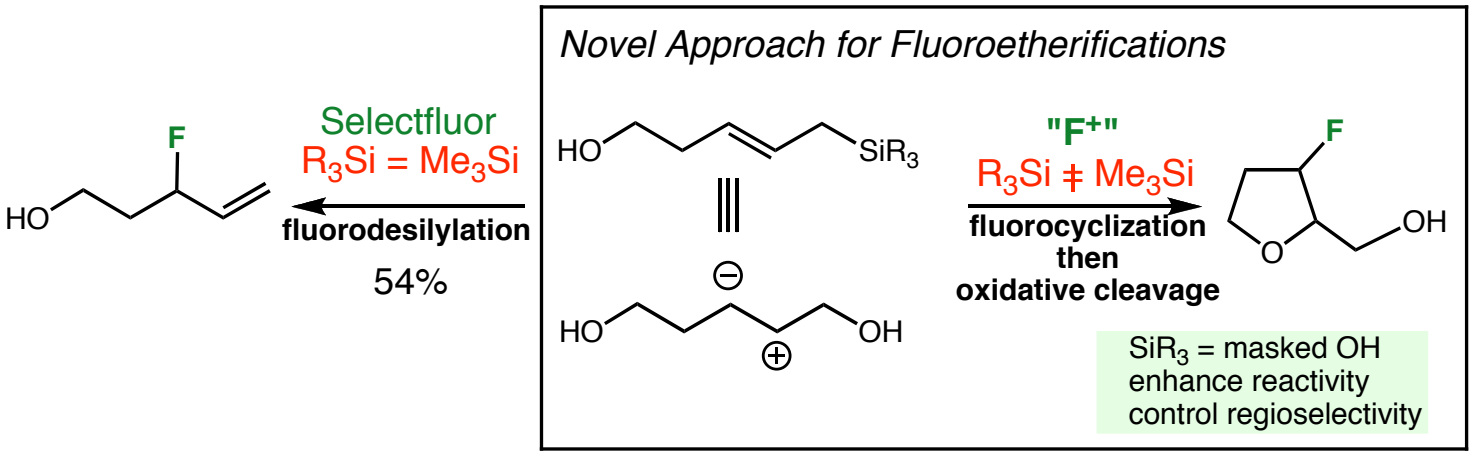
The REVERSE Approach



Fluorocyclisation: Fluoroetherification and Fluoroamination

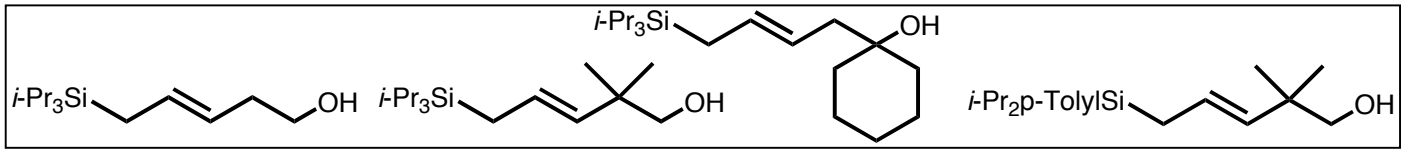
Access to both SYN and ANTI Fluorinated Heterocycles

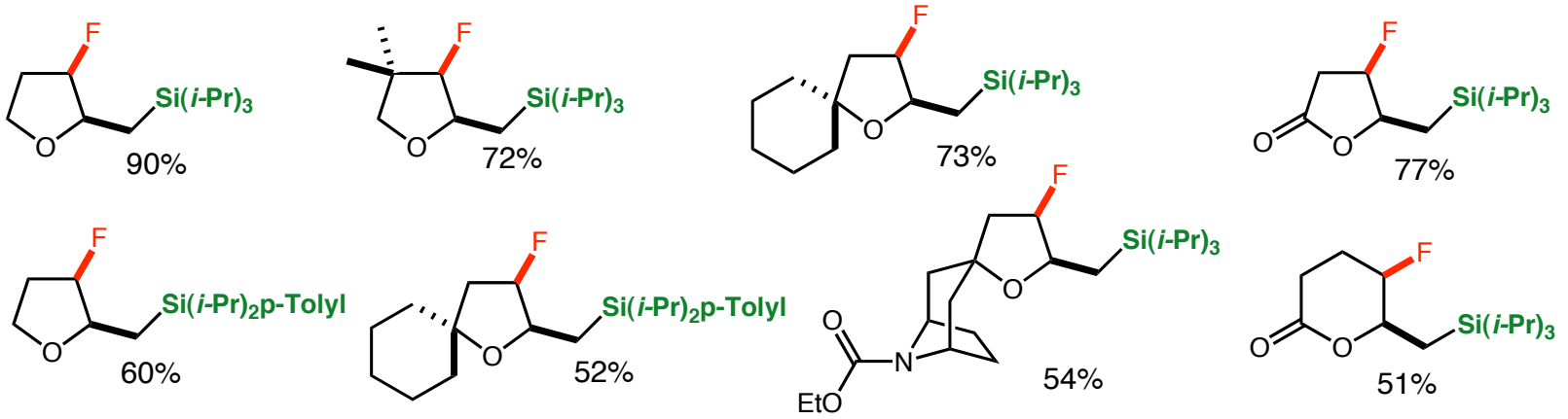




Endo Fluoroetherification and Fluoroamination

Access to both SYN and ANTI Fluorinated Heterocycles





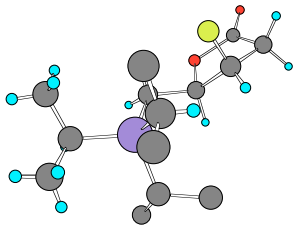
- SM accessible via CM
- Fluoroetherification with Si(*i*-Pr)$_3$

>>> Selectfluor in MeCN

- Fluoroetherification with Si(*i*-Pr)$_2$*p*-Tolyl

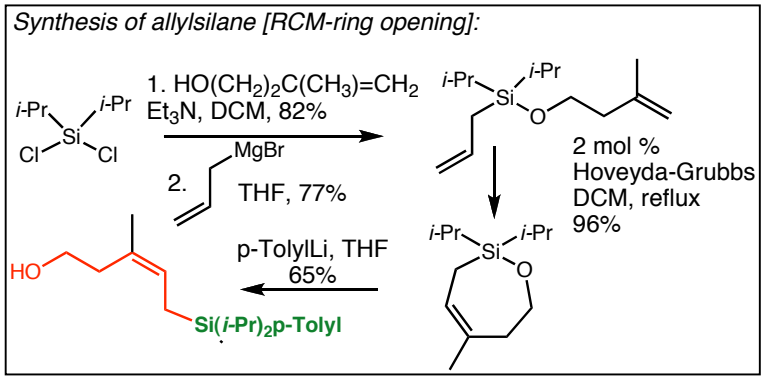
>>> NFSI in MeCN

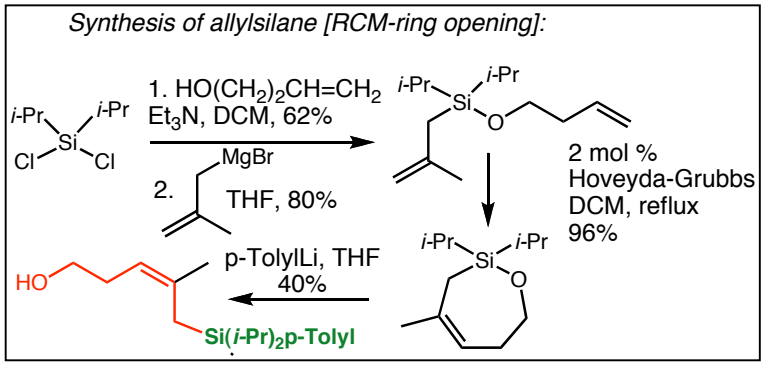
- *Syn* suprafacial
- *E*-allylsilanes ⟶ *Syn* selectivity

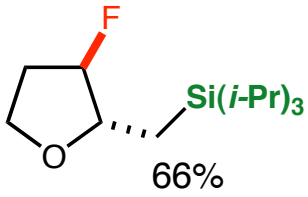


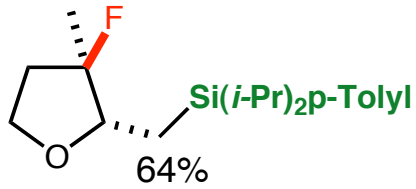
Endo Fluoroetherification and Fluoroamination

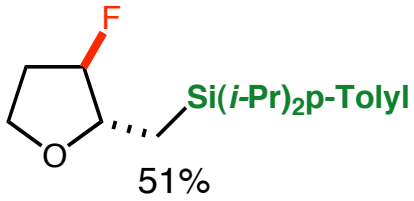
Access to both SYN and ANTI Fluorinated Heterocycles

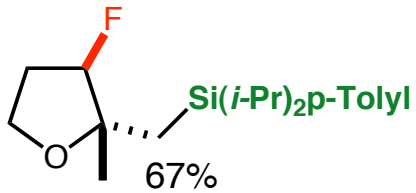












- SM accessible via RCM-ring opening
- Fluoroetherification with Si(*i*-Pr)$_3$

>>> Selectfluor in MeCN

- Fluoroetherification with Si(*i*-Pr)$_2$*p*-Tolyl

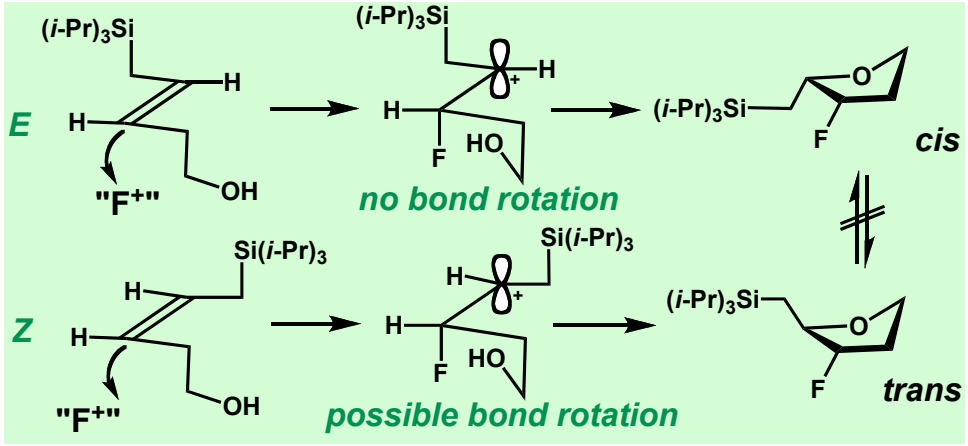
>>> NFSI in MeCN

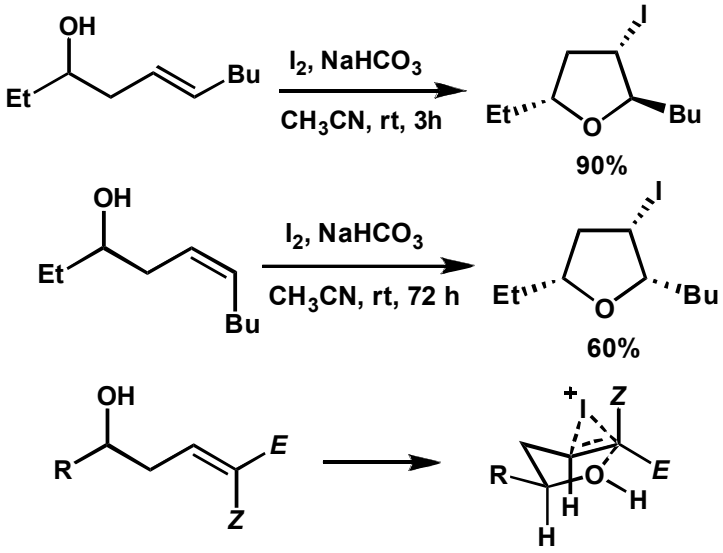
- *Syn* suprafacial
- *Z*-allylsilanes → *Anti* selectivity

Erosion is observed [> 20 :1 to 10:1]
Si(iPr)$_2$pTolyl is oxidatively cleavable
HBF$_4$ then H$_2$O$_2$ TBAF

Endo Fluoroetherification and Fluoroamination

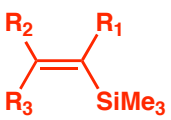
Access to both SYN and ANTI Fluorinated Heterocycles

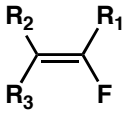




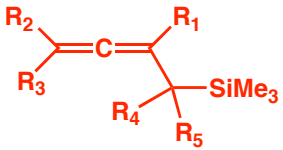
What have we learned? What is coming next?

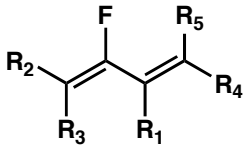
Synthesis of Fluorinated Compounds from Organosilanes



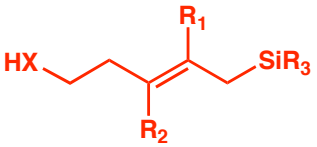


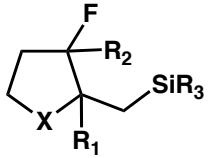
moderate to excellent level E/Z



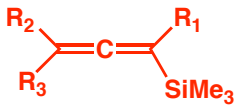


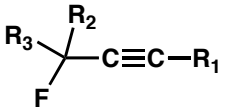
moderate to excellent level E/Z



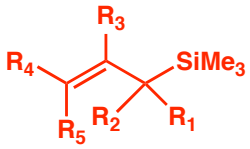


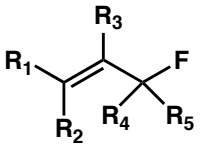
syn/anti stereochemistry is programmable



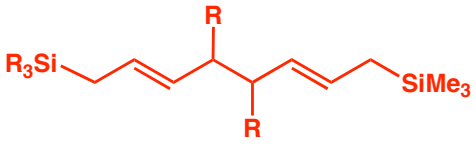


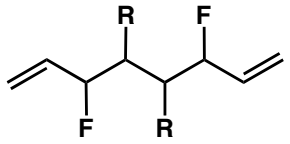
S_E2' Transfer of chirality





S_E2' Transfer of chirality
asymmetric fluorination [catalytic variant]
diastereoselective fluorodesilylation
fluorous variant
hot variant [radiochemistry]



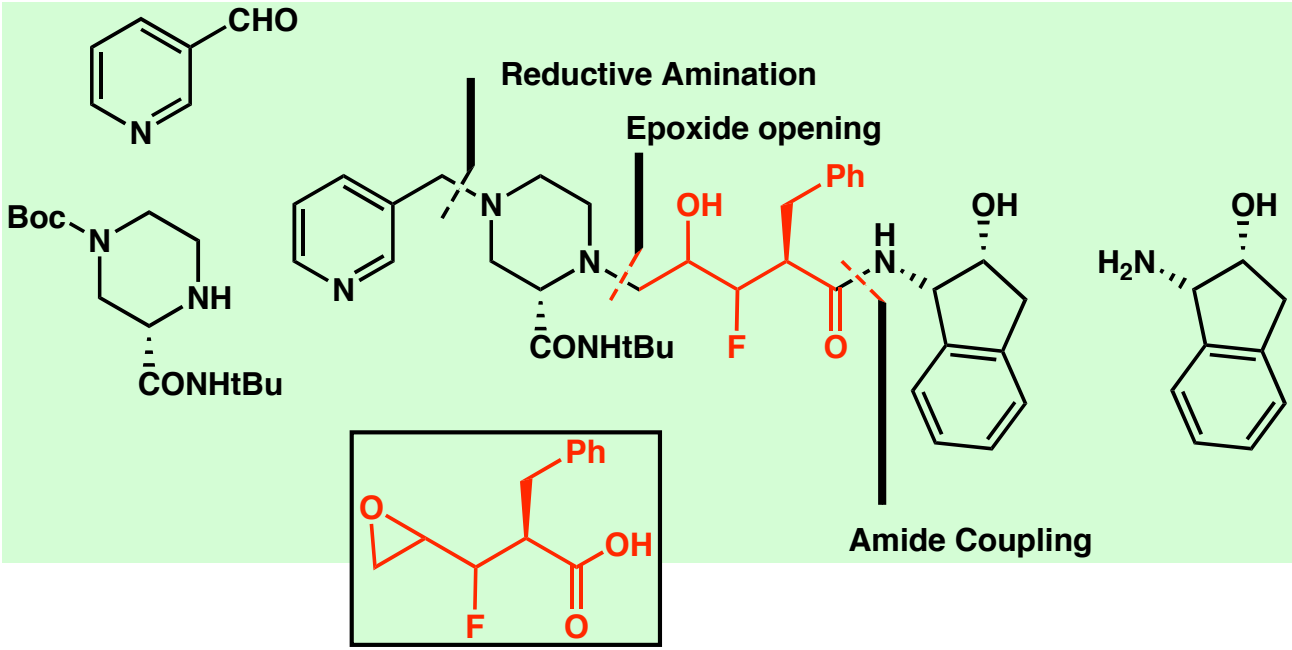


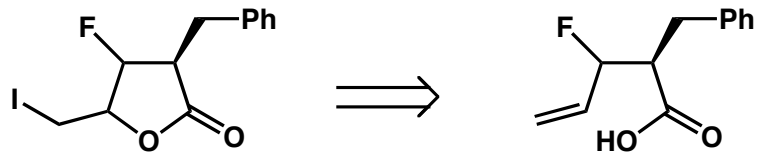
Two-directional approach

1. Allylic fluorides and the *inside fluoro effect*
2. Allylic fluorides and Pd(0)-catalysed reactions
3. Fluorine Chemistry and Au Catalysis

Allylic Fluorides are Responsive to Iodocyclisations

Access to β-Fluorinated Lactones

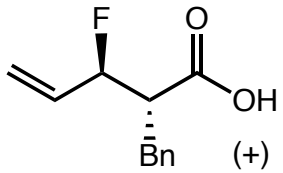
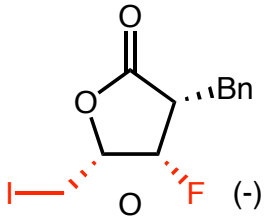
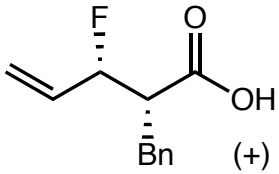
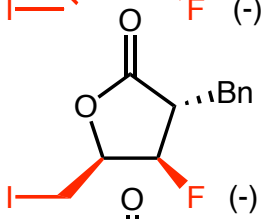
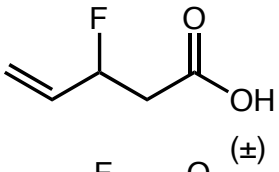
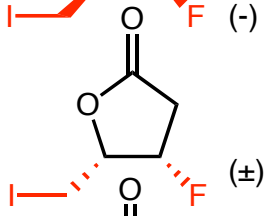
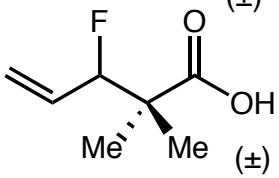
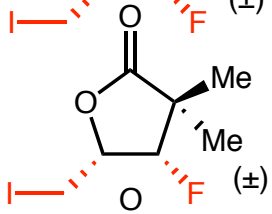
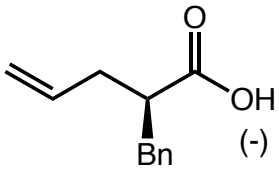
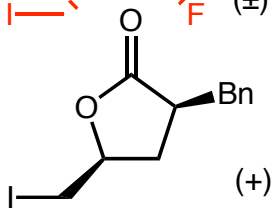




A. G. Myers et al. *J. Am. Chem. Soc.* **2001**, *123*, 7207

Synthesis of β-Fluorinated γ-lactones

The fluorine substituent is a SYN stereodirecting group

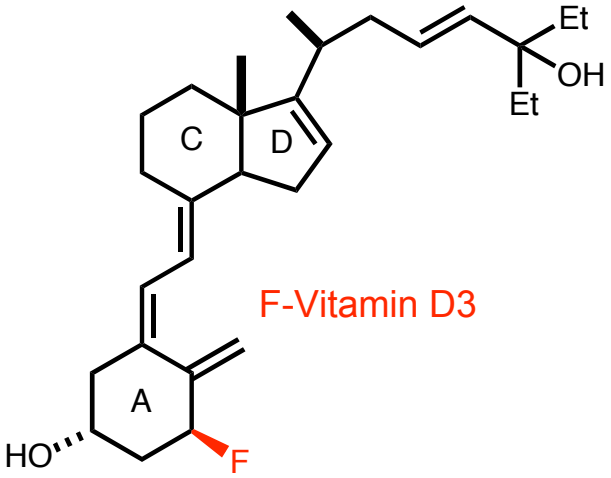
Alkenoic acid	lactone		yield	d.r.
		A B	86% 94%	> 20:1 > 20:1
		A B	95% 74%	> 20:1 > 20:1
		A B	24% 25%	> 20:1 > 20:1
		A B	48% 72%	> 20:1 > 20:1
		A B	100% 100%	2:1 2:1

A: I_2, DCM-aq. $NaHCO_3$, rt; B: I_2, CH_3CN, rt

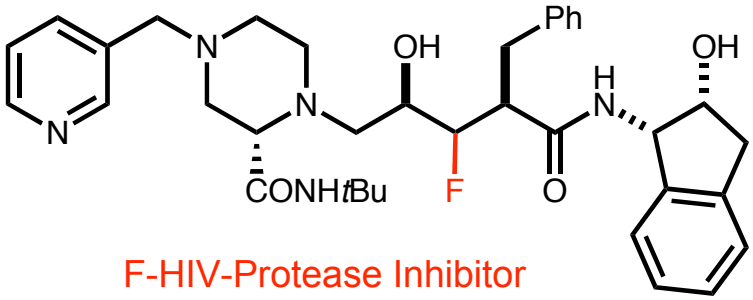
With M. Tredwell in *Angew. Chem. Int. Ed.* **2008**, *47,* 357-360.

Fluorination of Less Activated Substrates

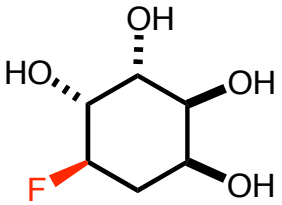
When possible, late fluorination for application in PET ….



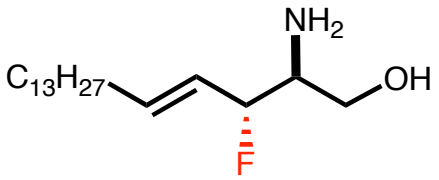
F-Vitamin D3



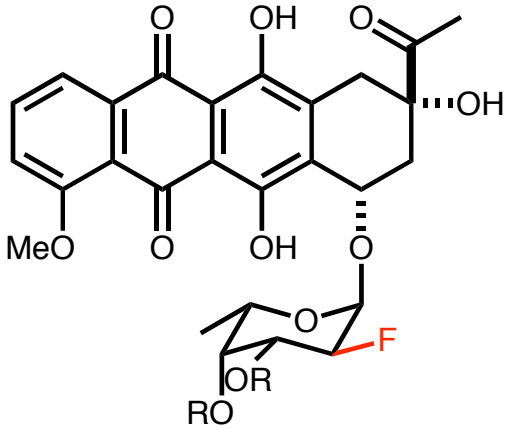
F-HIV-Protease Inhibitor



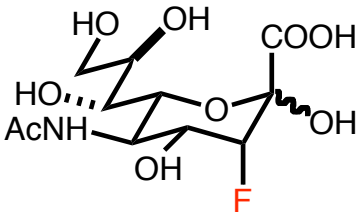
F-Cyclitols



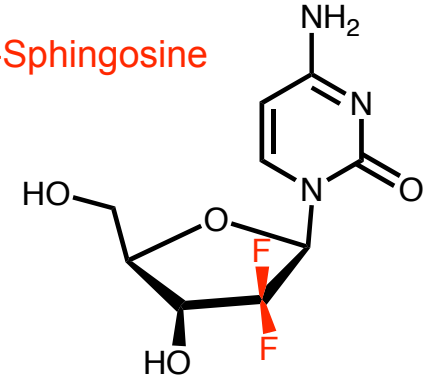
F-Sphingosine



F-Daunomycinone



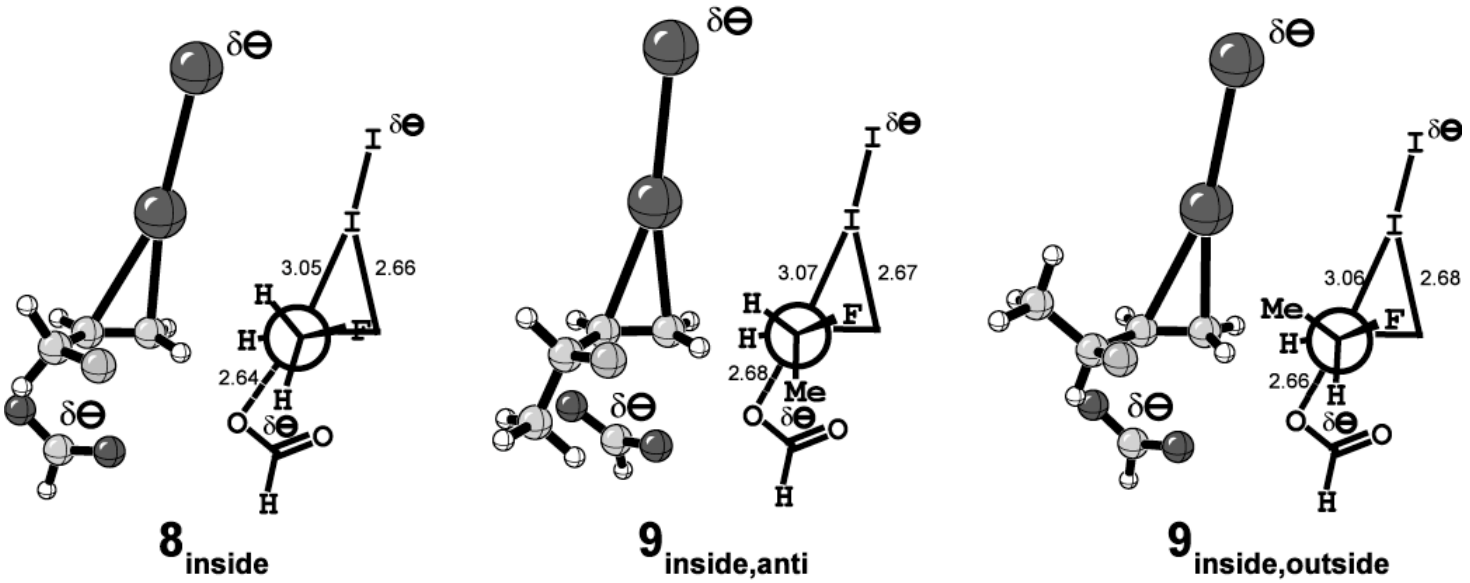
F-Sialic acid

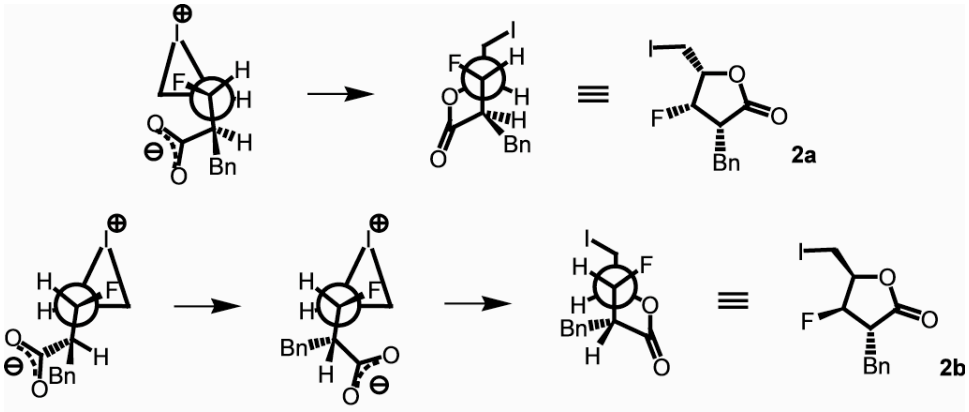


gemcitabine

Synthesis of β-Fluorinated γ-lactones

The fluorine substituent is a SYN stereodirecting group



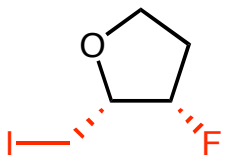


- I_2-π Complex is loosely associated
- Proximal orientation of $HCOO^-$ is preferred
- Distal orientation is ~ 4 kcal/mol less stable
- Fluorine resides preferentially *inside*
- F *inside* is preferred over F *outside* by 1 kcal/mol
- F *inside* is preferred over F *anti* by 3 kcal/mol
- $HCOO^-$ approaches at 110°; backside attack of $\sigma^*_{C\text{-}I}$ bond

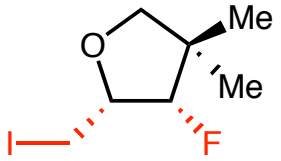
Angew. Chem. Int. Ed. **2008**, *47,* 357-360.

β-Fluoro-Tetrahydrofurans, -Pyrrolidines and -Lactams

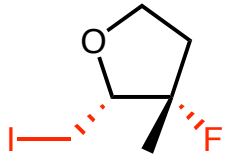
The fluorine substituent is a SYN stereodirecting group



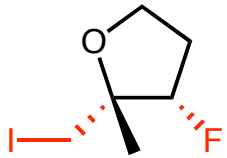
52% d.r. = 12:1



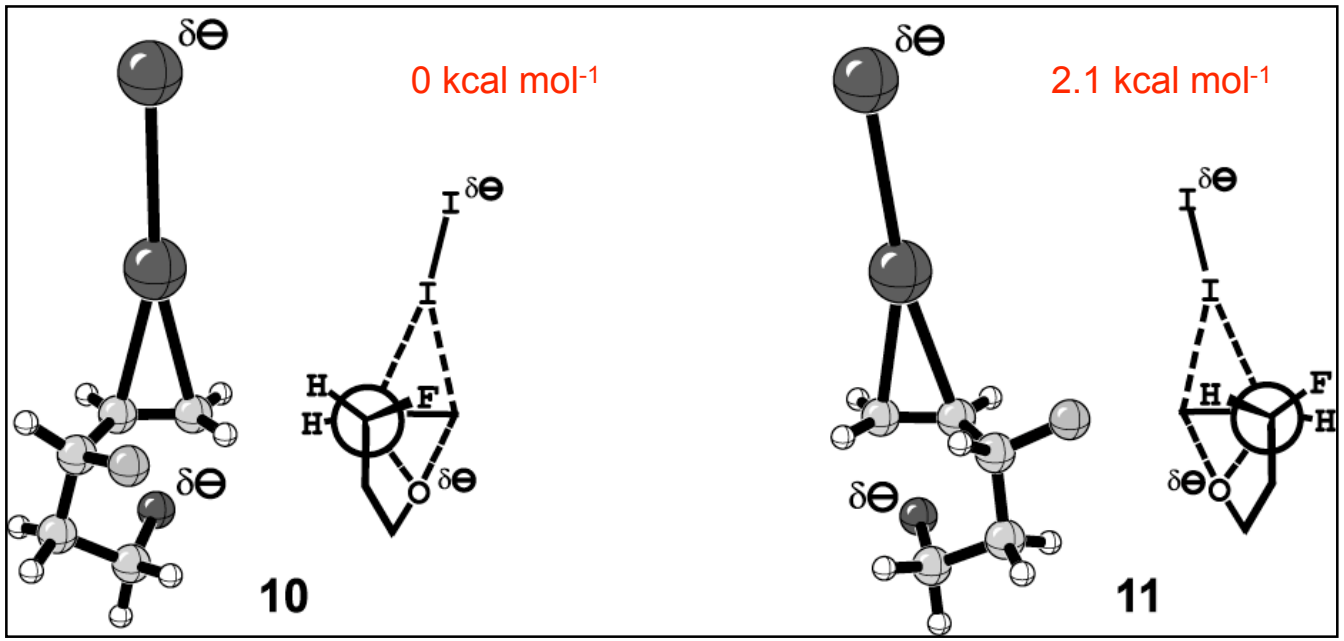
92% d.r. > 20:1

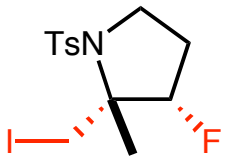


88% d.r. = 9:1

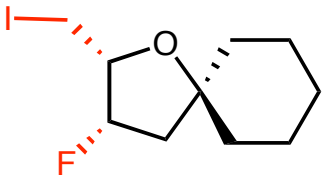


69% d.r. = 9:1





65% d.r. = 10:1



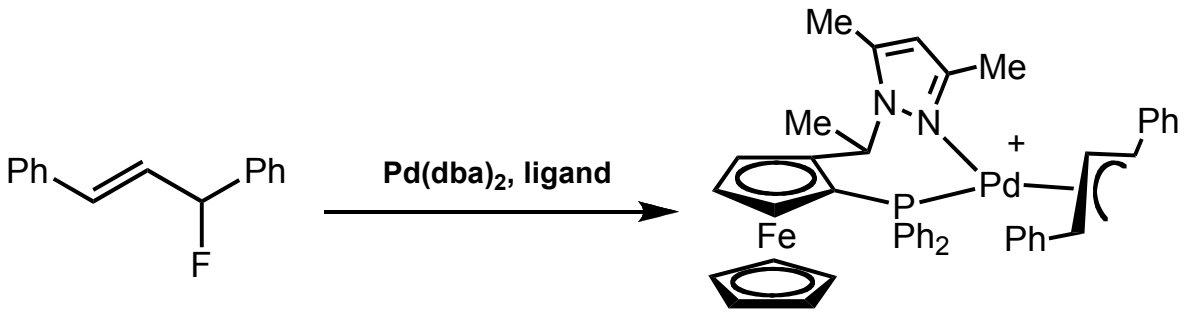
69% d.r. = 12:1

Reaction conditions: I_2, MeCN or I_2, DCM/aq. $NaHCO_3$

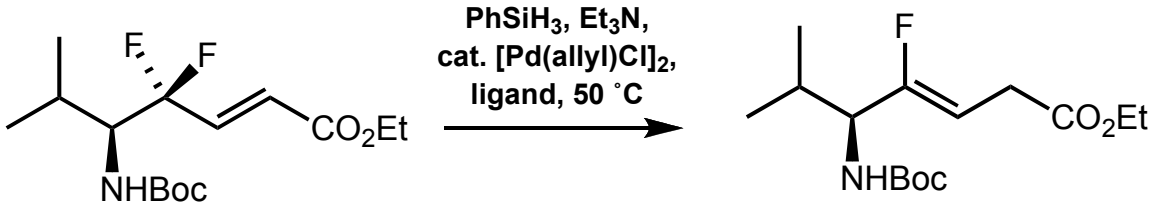
Angew. Chem. Int. Ed. **2008**, *47,* 357 and with L. Combettes *unpublished results.*

Allylic Fluorides are Responsive to Pd-Catalyzed Substitution

Leaving Group Ability of Fluorine



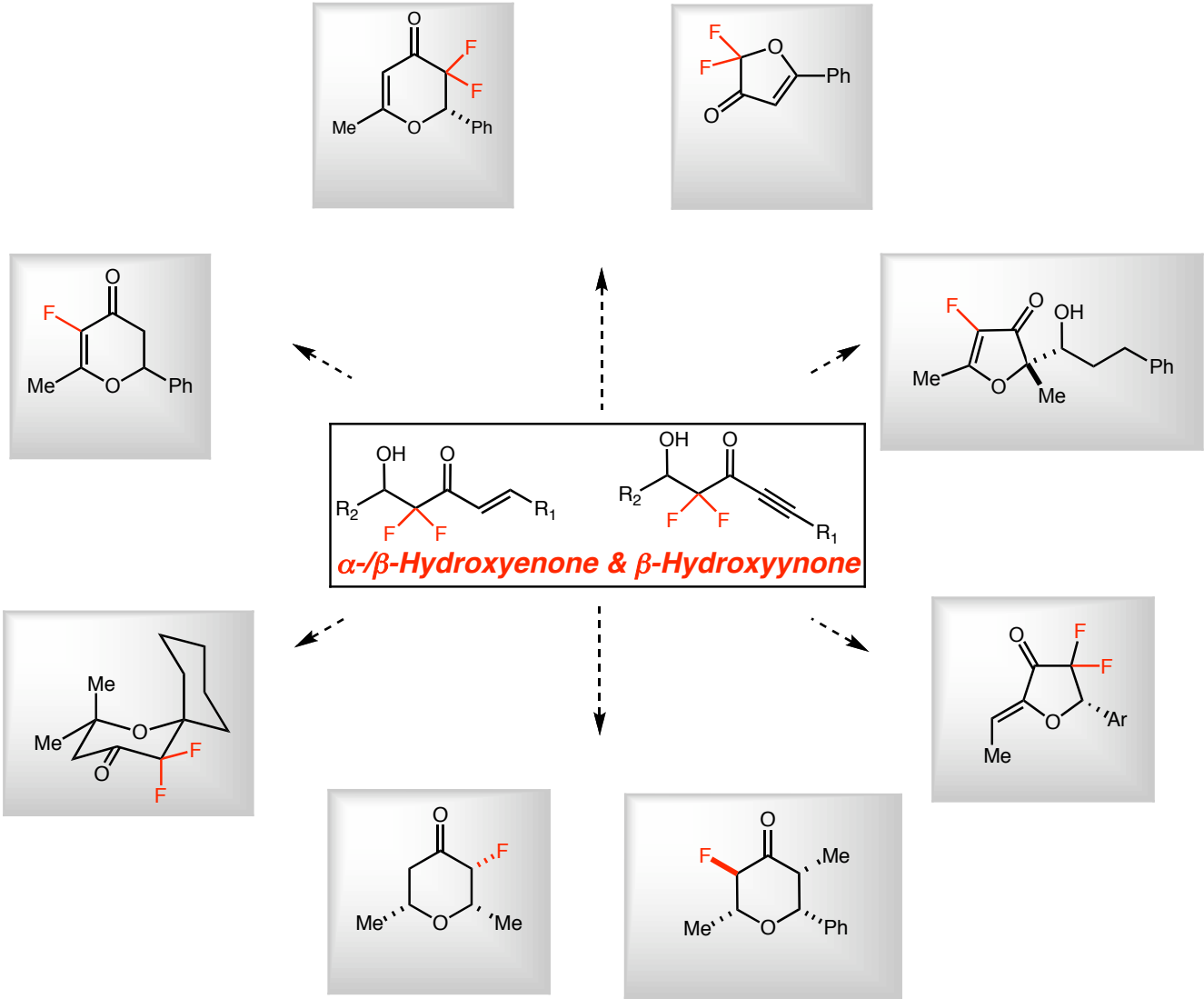
Togni et al. *Eur. J. Inorg. Chem.* **2006** 1397



Fujii. N et al. *Tetrahedron* **2008** 4332

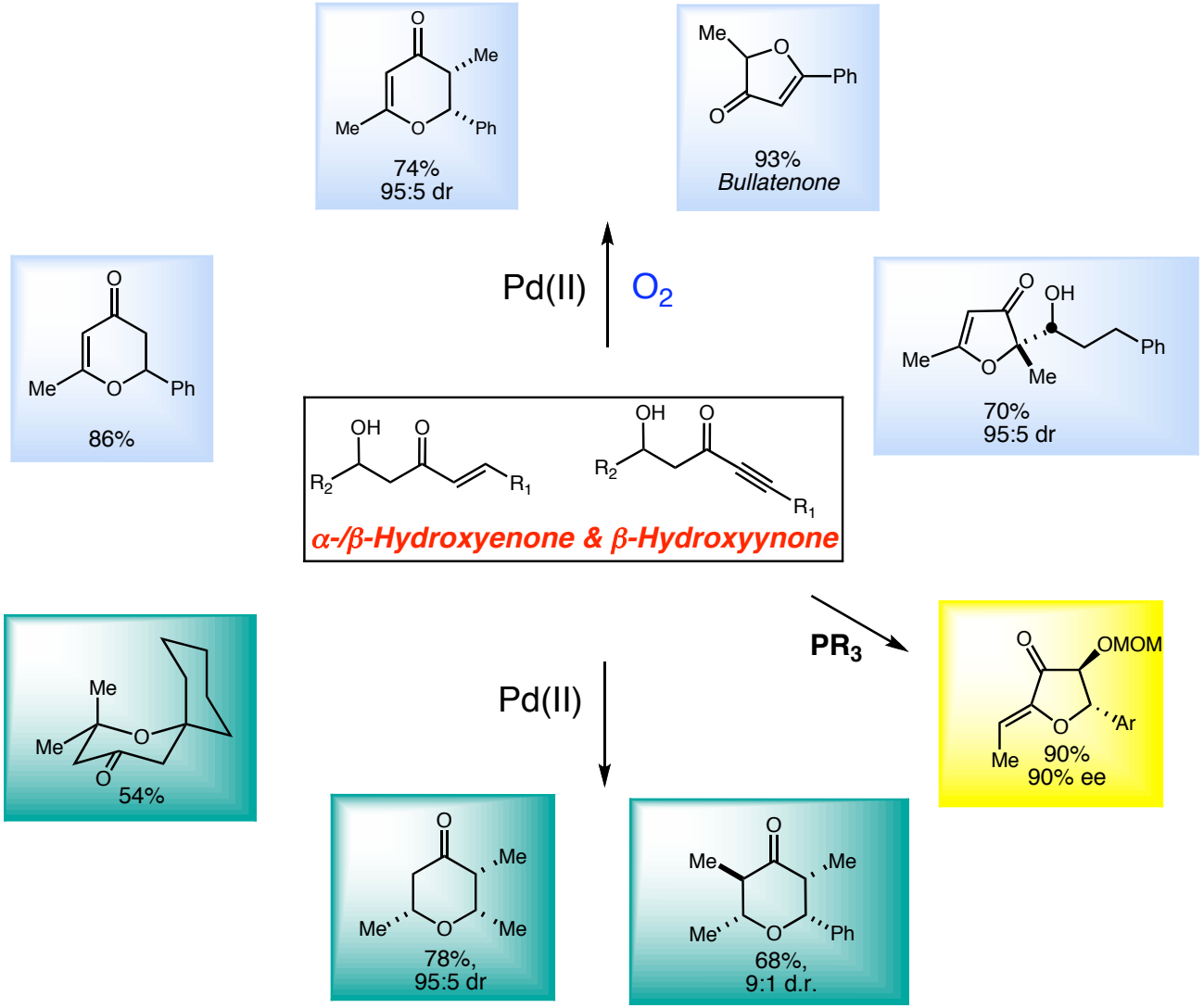
Pd- and Phosphine-Catalysed Ring Closures

C-O Ring Closure of Difluorinated Enones &Ynones



Pd- and Phosphine-Catalysed Ring Closures

C-O Ring Closure of Enones & Ynones

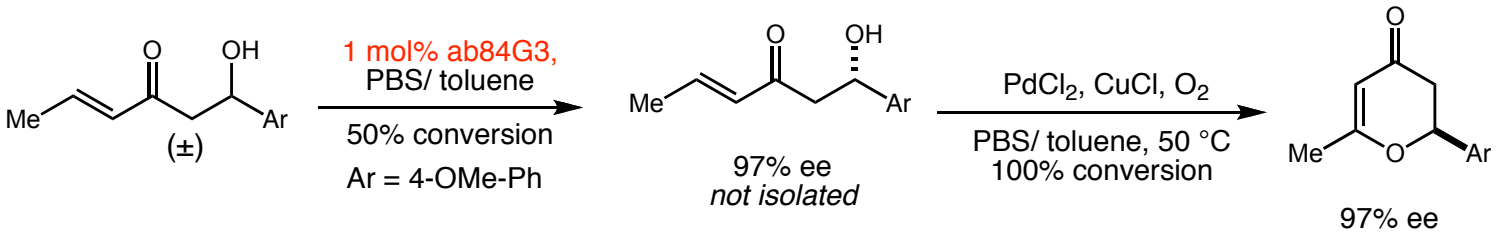


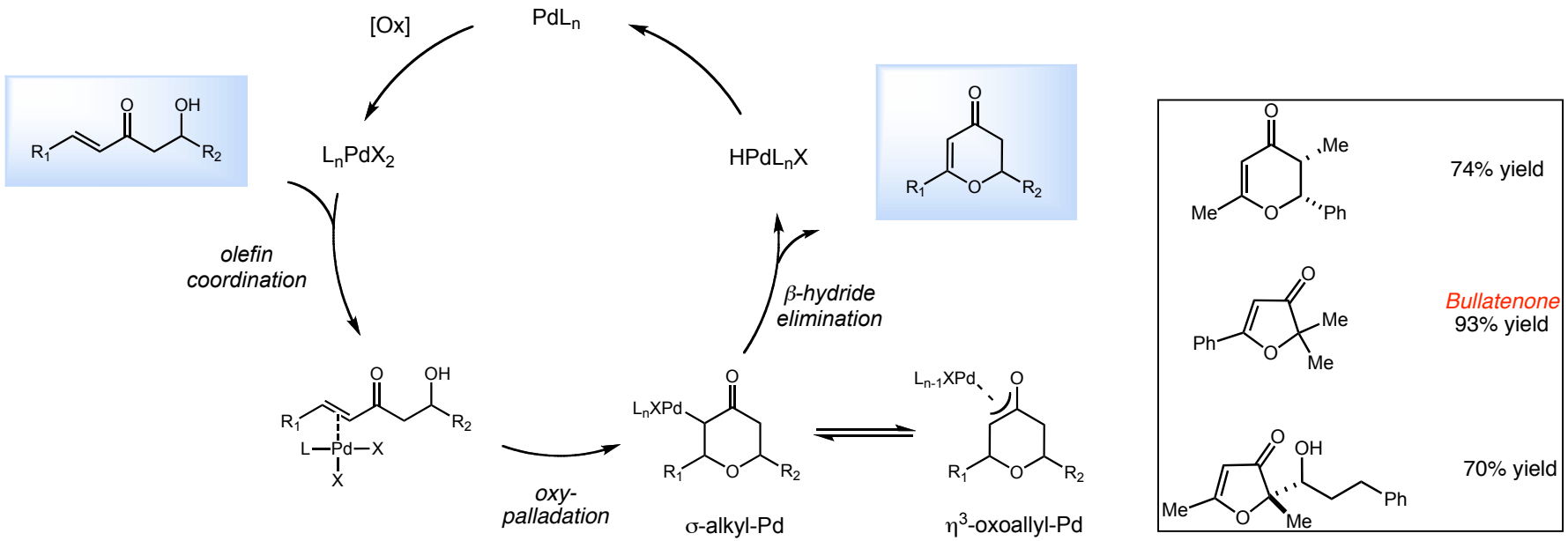
With M. Reiter, F. Silva, M. Sawicki in *Org. Lett.* **2004**, *6*, 91; *J. Am. Chem. Soc.* **2005**, *127*, 1481; *J. Org. Chem.* **2005**, *70*, 8478; *J. Org. Chem.* **2006**, *71*, 8390; *Chemistry A European Journal* **2006**, *12*, 7190; *Org. Lett.* **2006**, *8*, 5417.

Fluorinated Dihydro- and Tetrahydropyranones

De Novo Synthesis of Fluorinated O-Heterocycles & Carbohydrates

- One-pot bioorganic synthesis of enantioenriched dihydropyranones

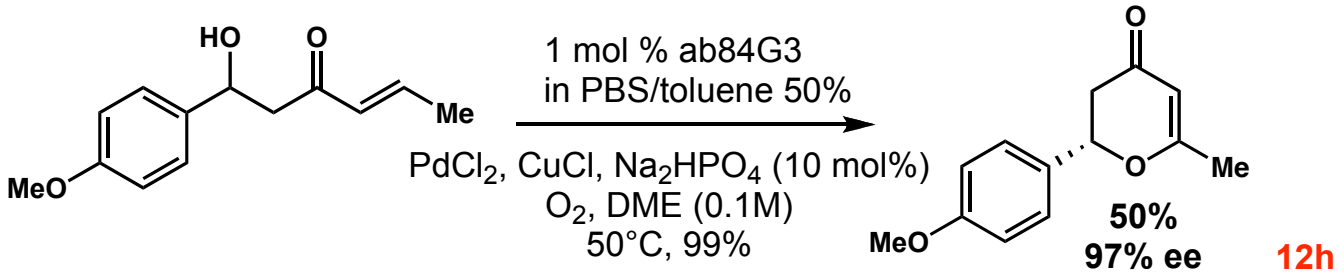


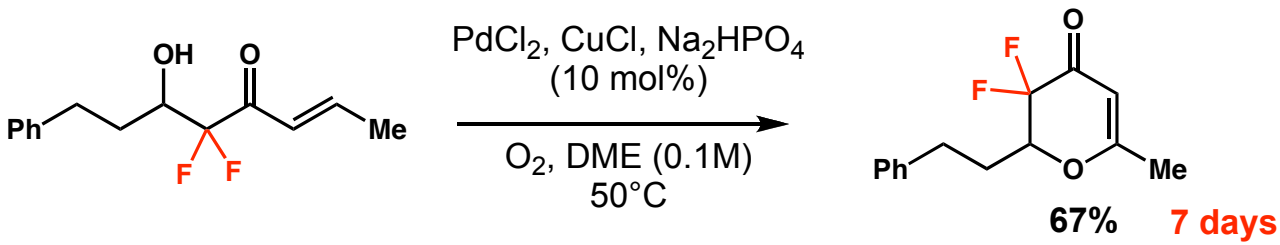


With M. Reiter and F. Silva in *Org. Lett.* **2004**, *6*, 91 & *J. Am. Chem. Soc.* **2005**, *127*, 1481 & *J. Org. Chem.* **2005**, *70*, 8478

Fluorinated Dihydropyranones

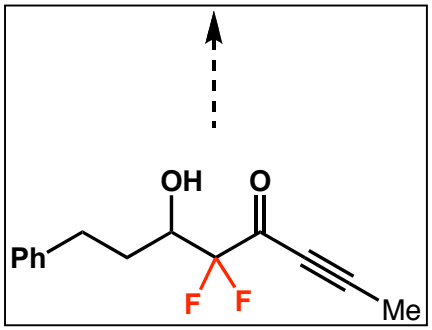
from α,α-Difluoro-β-Hydroxylated Ynones





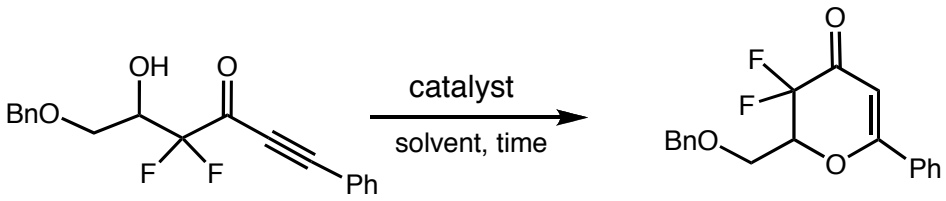
With M. Reiter *J. Am. Chem. Soc.* **2005,** 1481; *Org. Lett.* **2004,** 91.

- The fluorine substituents affect significantly reactivity
- More efficient catalytic ring closures are needed
- Explore non-oxidative ring closures



Gold and Fluorine

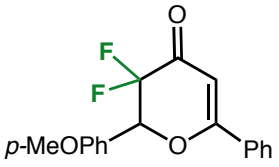
6-Endo-dig Non Oxidative Ring Closure of α,α-Difluoro-β-Hydroxylated Ynones



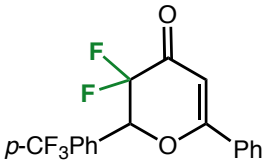
Catalyst	Loading [mol%]	Conditions	Yield [%]
$(MeCN)_2PdCl_2$	10	DCM, 18h	-[a]
$(MeCN)_4Pd(BF_4)_2$	8	DCM, 18h	15
Amberlyst-15	-[b]	DCM, 18h	-[a]
NaH	100	DCM, 5h	-[c]
HCl	100	CH_3CN, 40h	-[a]
TfOH	50	DCM, 29h	-[c]
$PtCl_2$	5	DCM, 18h	-[a]
$InCl_3$	5	DCM, 18h	-[a]
$AgNO_3$	5	THF, 18h	-[a]
$AgSbF_6$	5	DCM, 18h	25
$AuCl_3$	5	DCM, 18h	79
AuCl	5	DCM, 18h	93
$Au(PPh_3)OTf$	5	DCM, 18h	90

Gold and Fluorine

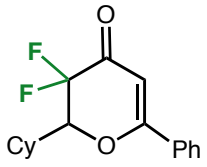
6-Endo-dig Non Oxidative Ring Closure of α,α-Difluoro-β-Hydroxylated Ynones



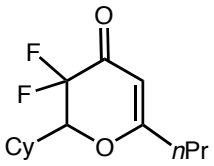
92%



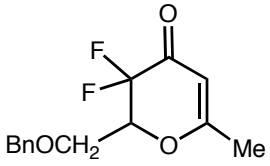
94%



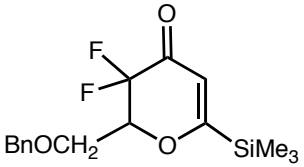
94%



90%



83%



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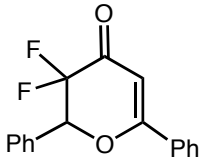
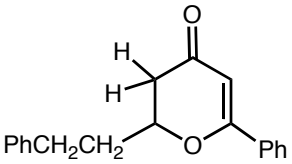
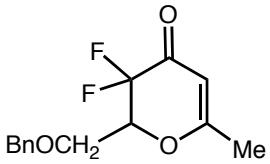


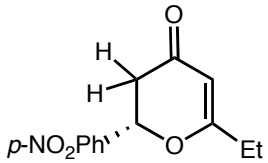
92%



89%

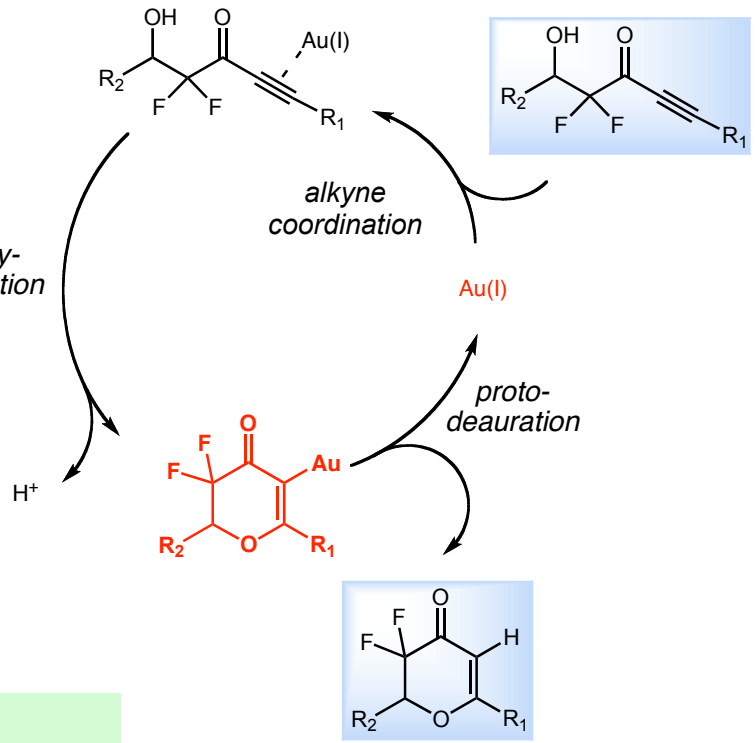


75%



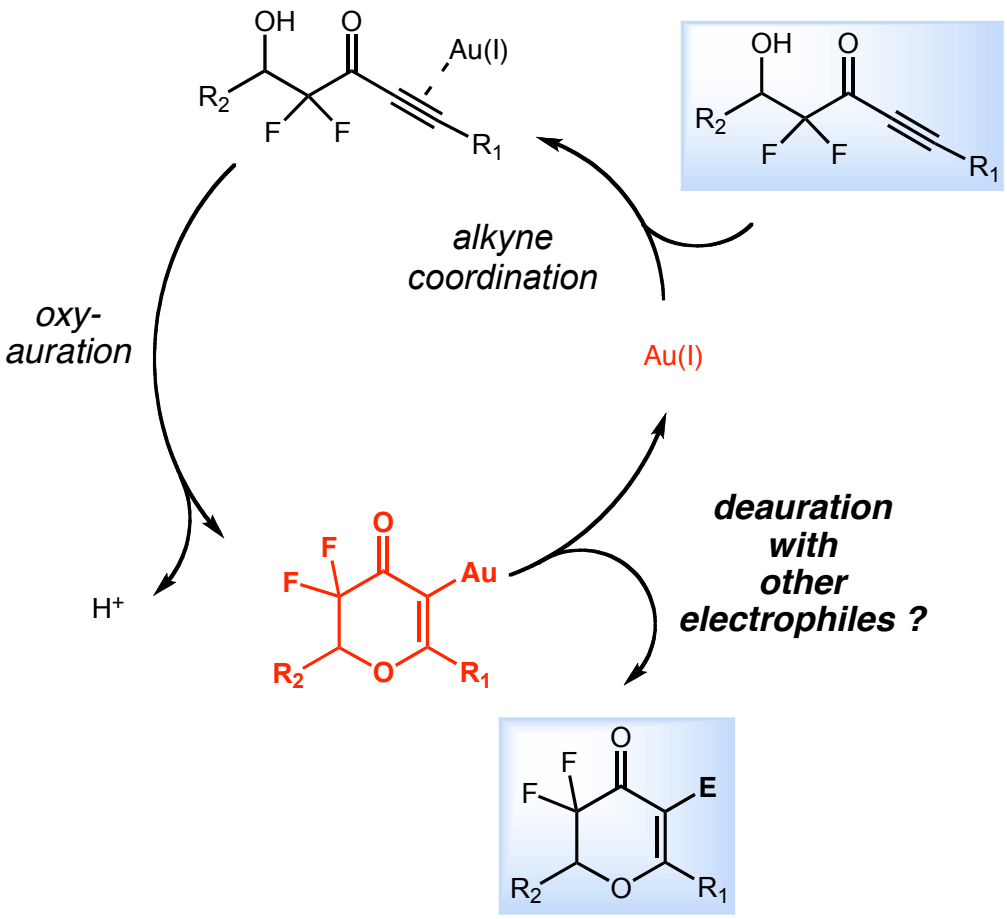
65%

AuCl or $AuCl_3$ in DCM
RT, 18 h
Validation with fluorinated & non-fluorinated ynones
No erosion of enantiomeric excess upon cyclisation



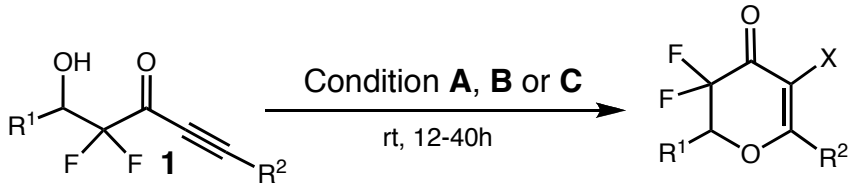
Gold and Fluorine

6-Endo-dig Ring Closure of α,α-Difluoro-β-Hydroxylated Ynones



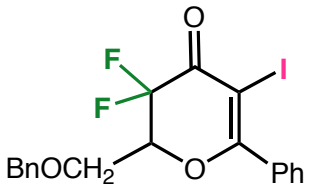
Gold and Fluorine

6-Endo-dig Ring Closure of β-Hydroxylated Ynones: Iodo- & bromoalkoxylation



A: 5 mol% AuCl, 1.2 eq. NIS, acetone
B: 5 mol% AuCl, 1.2 eq. NBS, DCM
C: 5 mol% AuCl, 1.2 eq. NCS, DCM

X = I
X = Br
X = Cl



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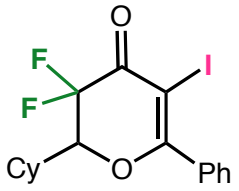

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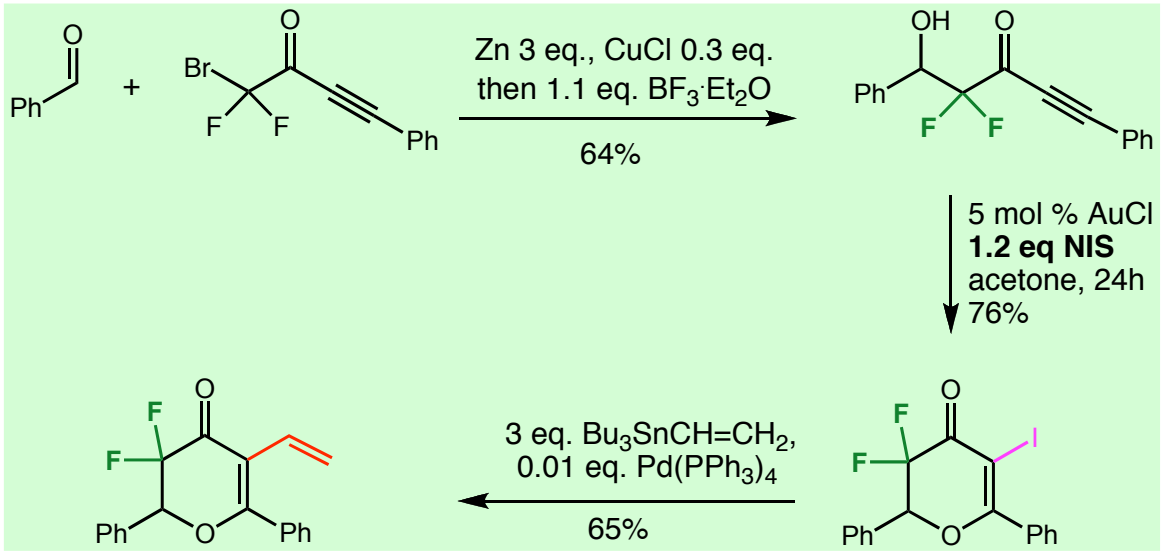
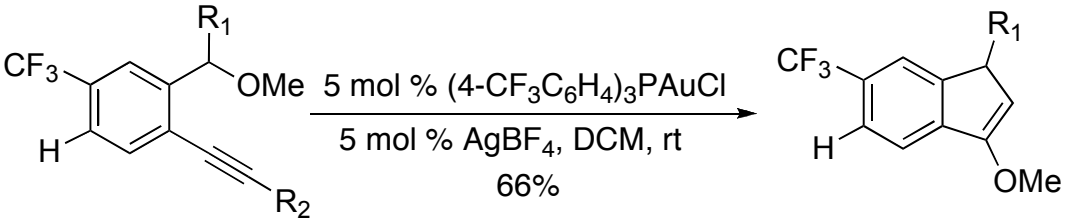


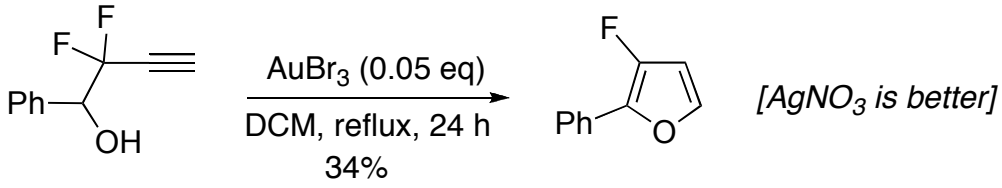
Gold and Fluorine

Fluorinated Building Blocks or Fluorinations are Scarcely Explored…

Gold Catalysis with Fluorinated Building Blocks

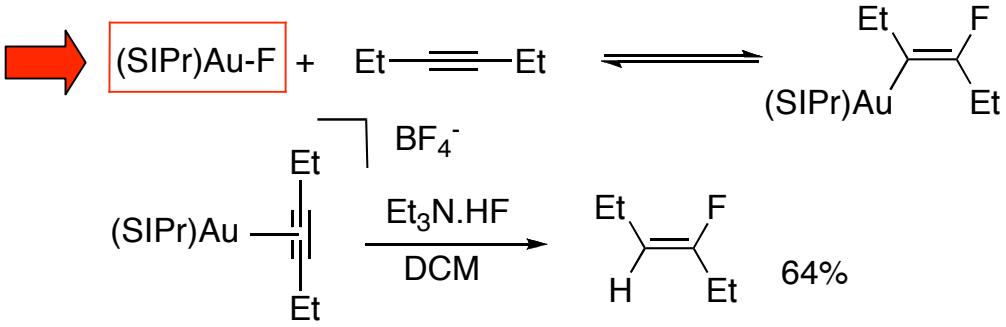


Toste *et al.*
J. Am. Chem. Soc. **2006**, *128,* 12062



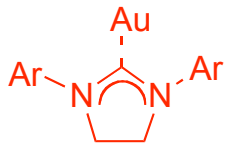
Hammond *et al.*
J. Org. Chem. **2007**, *72,* 8559.

Gold Catalysis and Fluorination



J. P. Sadighi *et al.*
J. Am. Chem. Soc. **2007**, *129,* 7736.

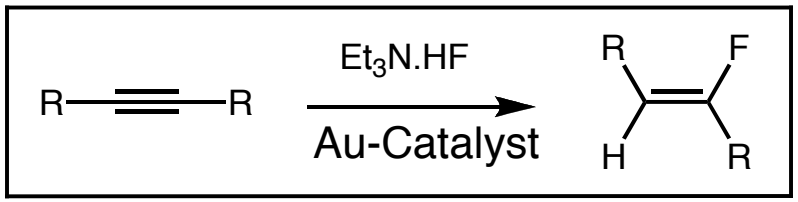
SIPr = 1,3bis(2,6-*di*isopropylphenyl)imidazolin-2-ylidene



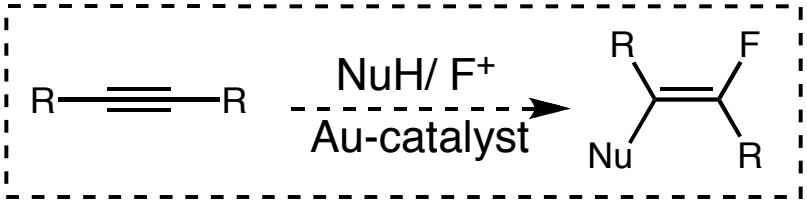
Gold & Fluorine

Alkoxyfluorination of α,α-Difluoro-β-Hydroxylated Ynones

Known Approach: Gold and "F^-" source

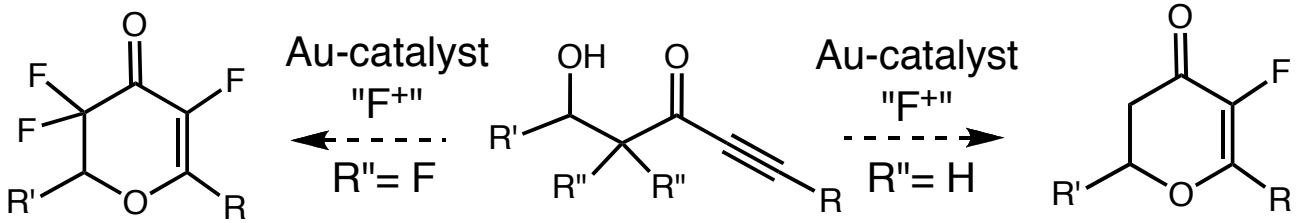


New Approach: Gold and "F^+" source



- Compatibility of gold catalysis with "F^-"
- Rare nucleophilic approach to fluoro alkenes
- No regiocontrol for unsymmetrical alkynes

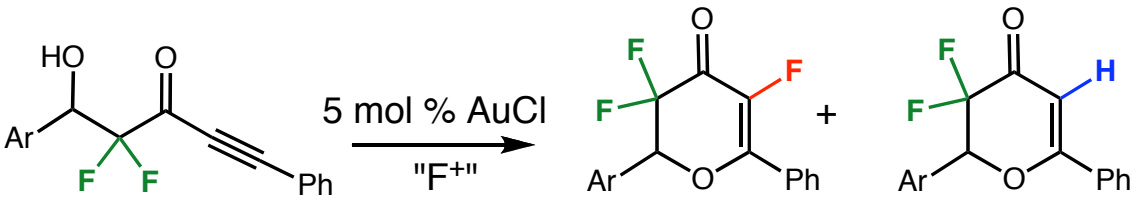
- Compatibility of gold catalysis with "F^+" ?
- Which electrophilic fluorinating reagent ?
- Mechanism & Intermediacy of Organogold Species ?



J. P. Sadighi *J. Am. Chem. Soc.* **2007**, *129*, 7736.

Gold & Fluorine

Alkoxyfluorination of α,α-Difluoro-β-Hydroxylated Ynones



Ar = *p*-MeOPh **1d** **3d** **2d**

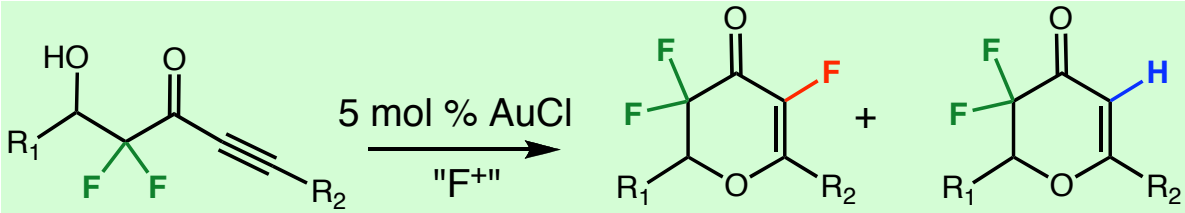
Entry	F^+ Reagent (eq.)	Conditions	**1d** [%]	**3d** [%]	**2d** [%]
1	NFSI (2.5)	DCM, rt, 18h	73	0	27
2	NFSI (1.5)	DCM, reflux, 18h	93	0	7
3	Pyridinium (2.0)	MeCN, rt, 6 d	68	0	32
4	Selectfluor (1.5)	MeCN, rt, 55h	0	40	60
5	Selectfluor (2.5)	MeCN, rt, 48h	0	45	55
6	Selectfluor (2.5)	DCM, $NaHCO_3$, rt, 66h	100	0	0

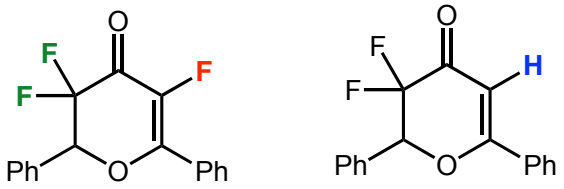
Ratio determined by ^{19}F NMR

With M. Schuler, F. Silva, C. Bobbio and A. Tessier *Angew. Chem. Int. Ed.* **2008** *Early View*

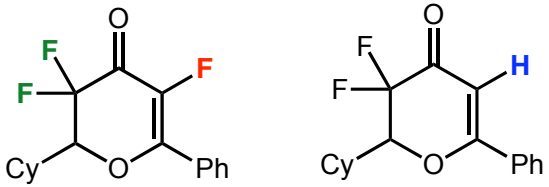
Gold & Fluorine

Alkoxyfluorination of α,α-Difluoro-β-Hydroxylated Ynones





20/33



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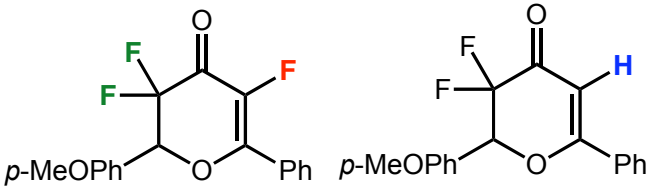
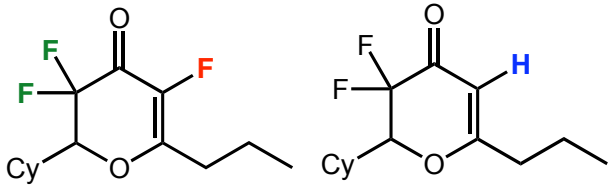


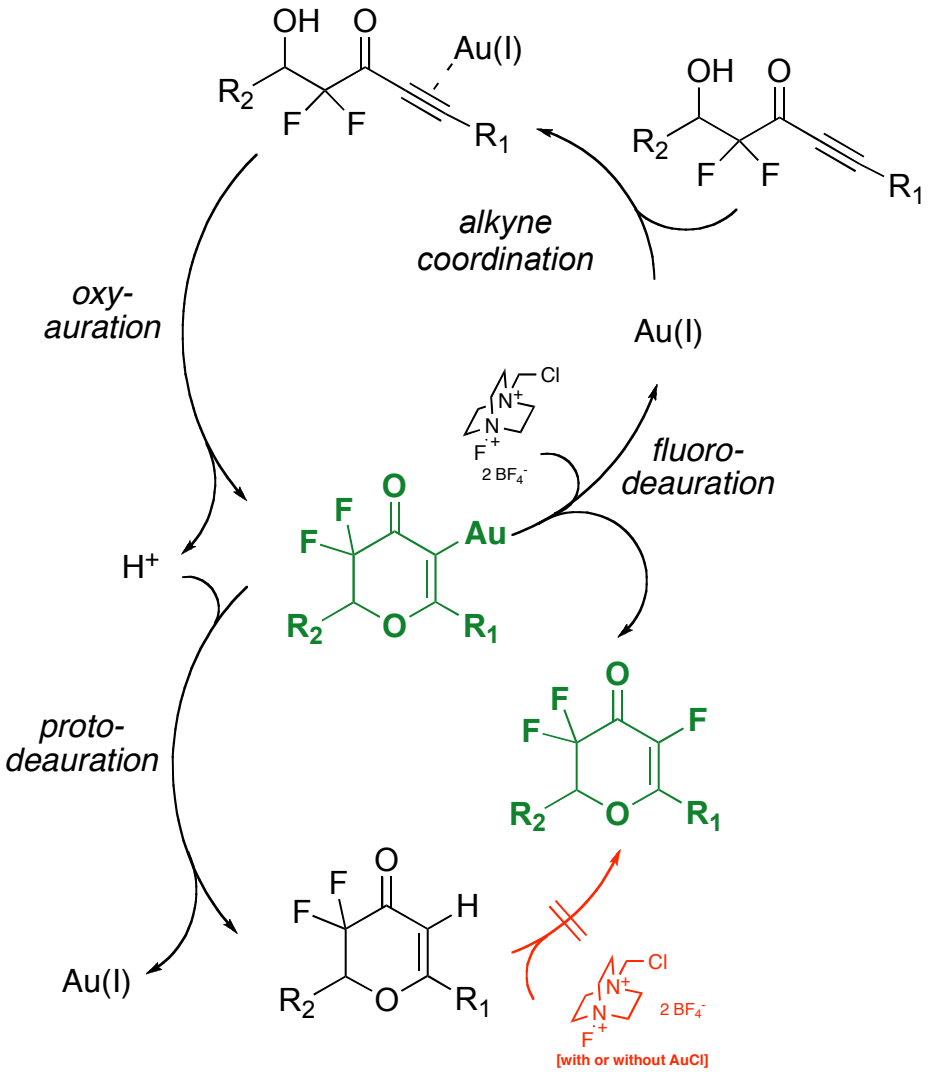
26/33

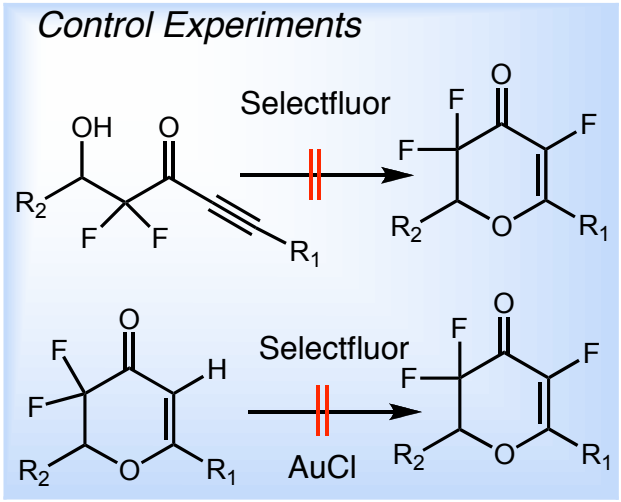


27/37

Gold & Fluorine

Alkoxyfluorination of α,α-Difluoro-β-Hydroxylated Ynones



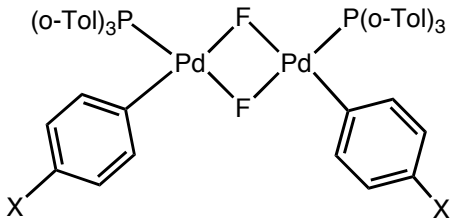


- No reaction occurred between Selectfluor and Ynones in the absence of AuCl
- The protodeaurated dihydropyranone does not react with Selectfluor in the absence or in the presence of AuCl
- Electrophilic fluorination of vinylgold intermediate

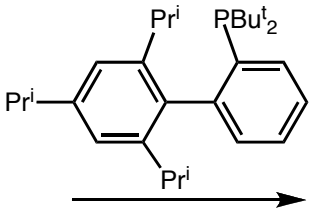
Pd(0)-Pd(II)-Pd(IV) & Fluorine

Grushin - Sanford - Ritter

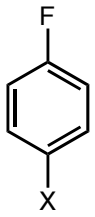
Grushin



Problems with Pd(II) Ar-F formation

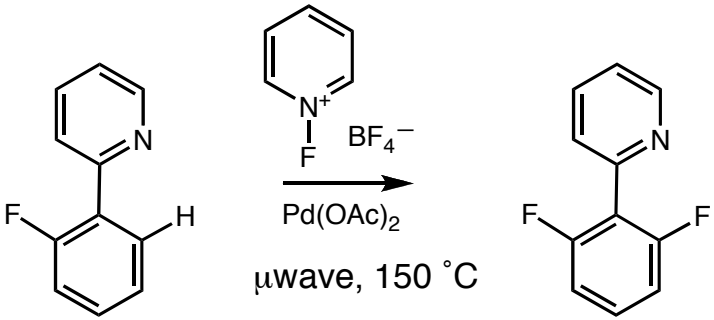


X = NO_2, 10%

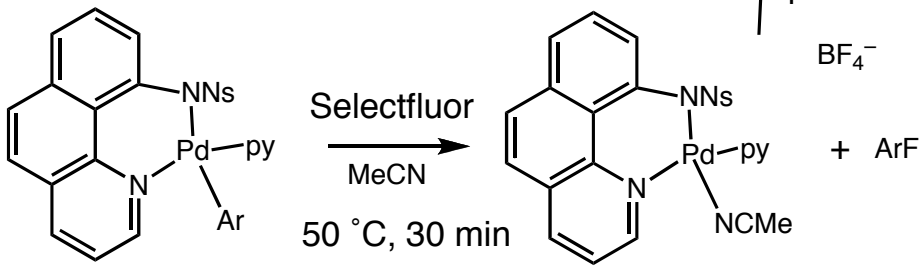


X = H, Me, OMe
no product

Sanford & Ritter



Sanford; catalytic in Pd



[ex. $ArB(OH)_2$]

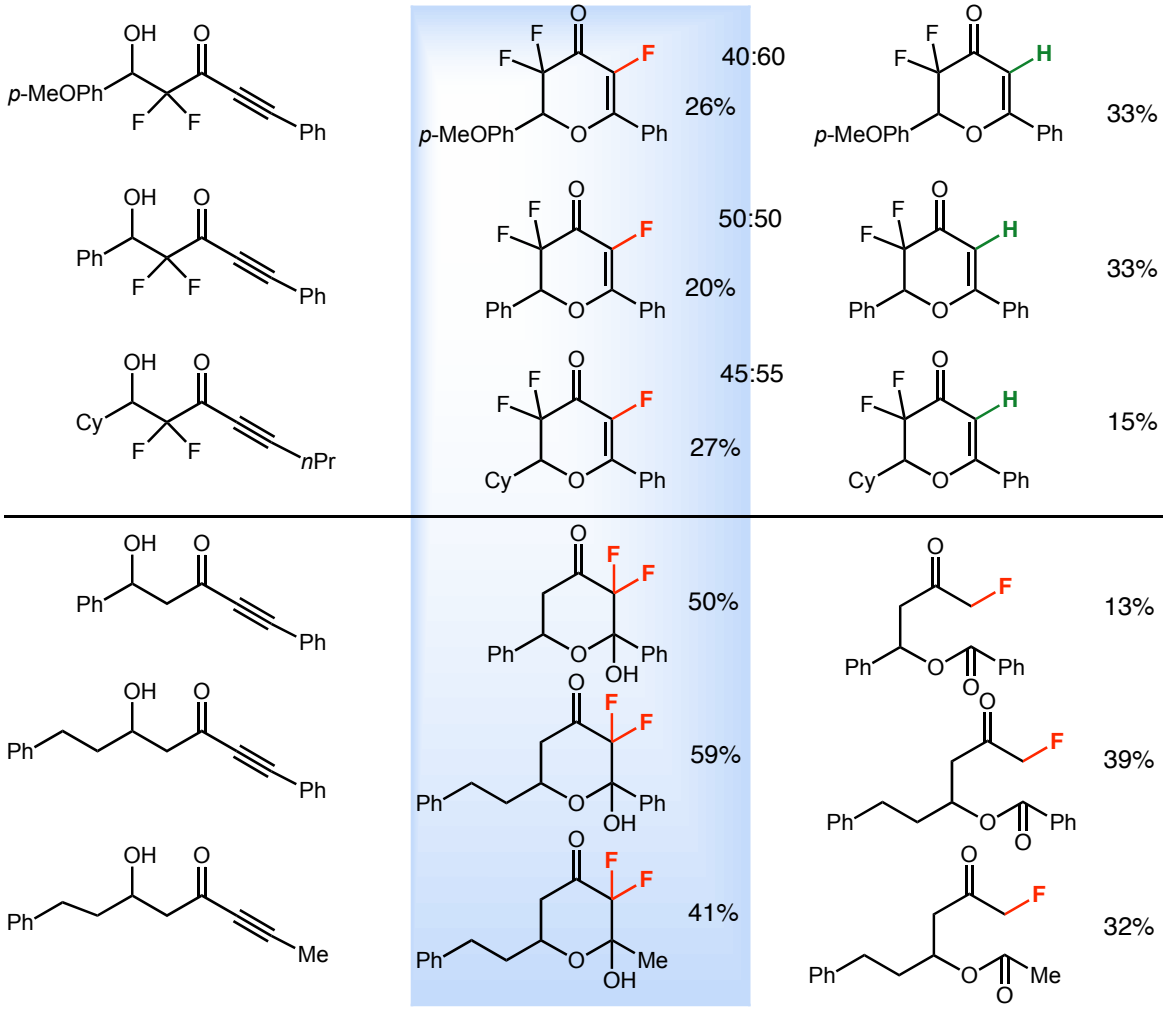
Ritter; stoichiometric in Pd

Grushin, V. V.; Marshall, W. J. *Organometallics* **2007**, *26*, 4997-5002;
Hull, K. L.; Anani W. Q.; Sanford M. S. *J Am Chem Soc* **2006**, *128*, 7134-7135.
Furuya, T.; Ritter, T. *J. Am. Chem. Soc.* **2008**, *130*, 10060-10061;
Furuya, T.; Kaiser, H. M.; Ritter, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 5993-5996.

Gold & Fluorine

Alkoxyfluorination of α,α-Difluoro-β-Hydroxylated Ynones

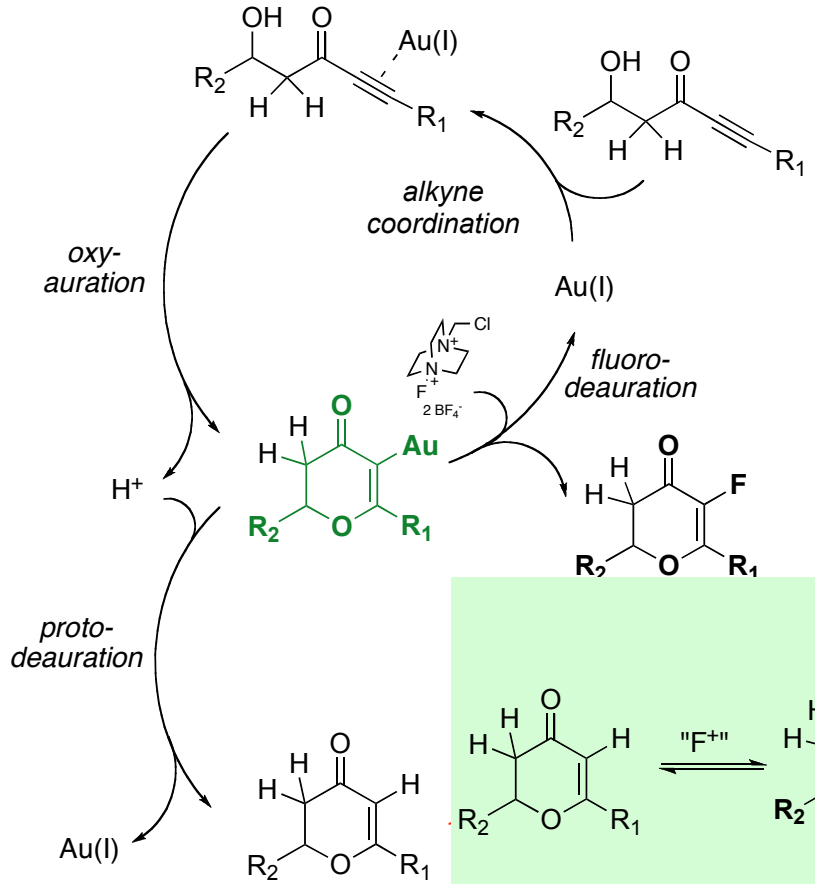
5 mol % AuCl, 24- 48 h, MeCN, 2.5 eq. Selectfluor [with or without H_2O]

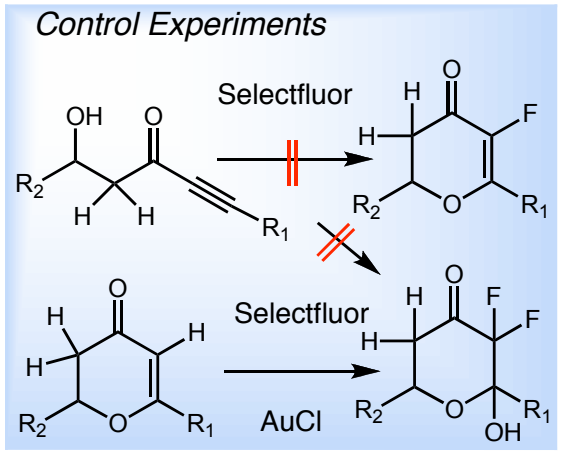


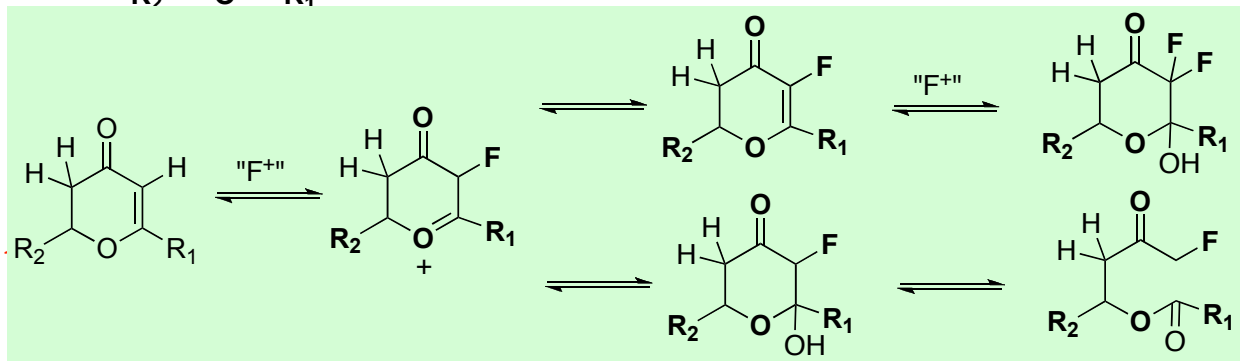
With M. Schuler, F. Silva, C. Bobbio and A. Tessier *Angew. Chem. Int. Ed.* **2008** *Early View* 48

Gold & Fluorine

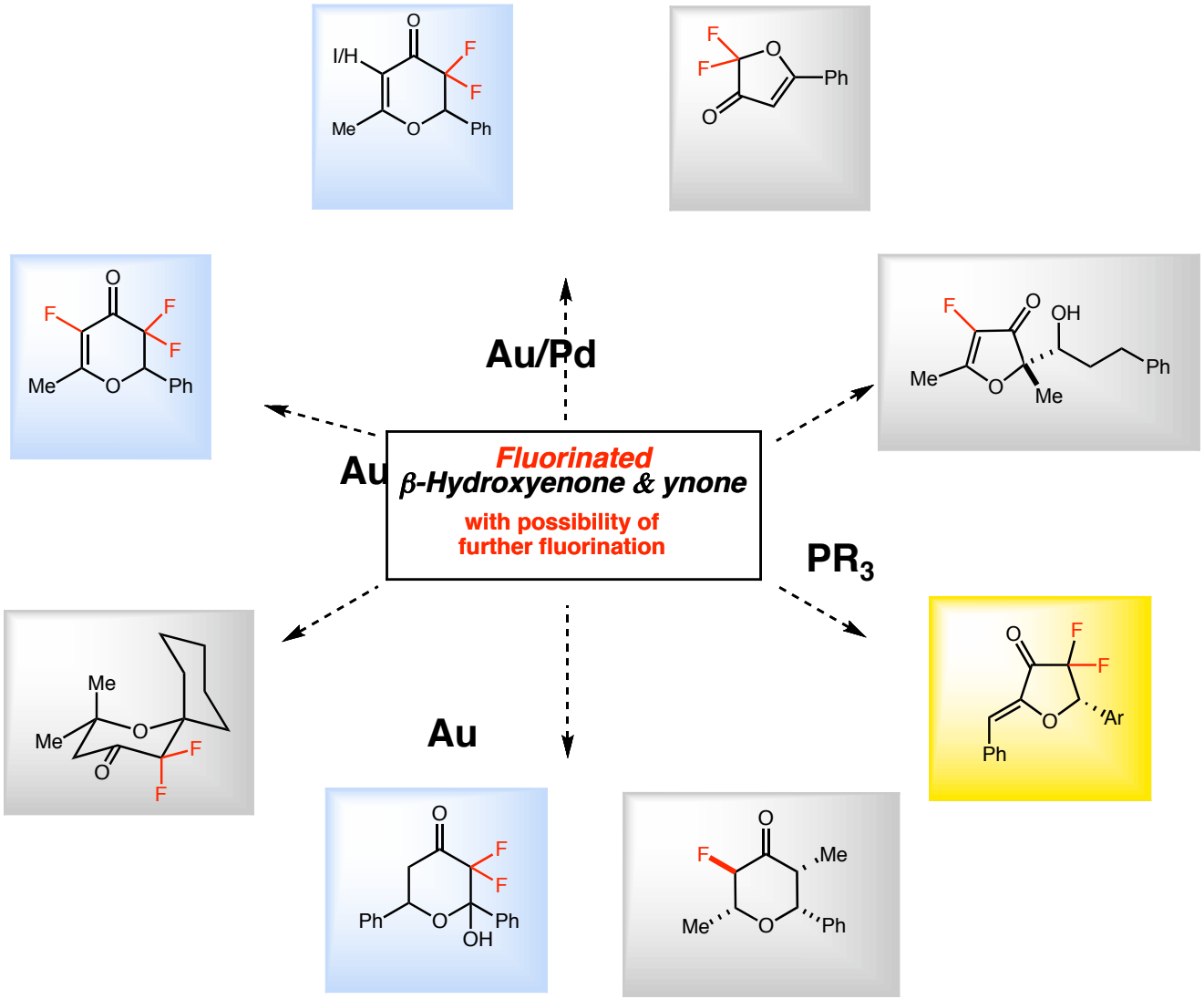
Alkoxyfluorination of α,α-Difluoro-β-Hydroxylated Ynones





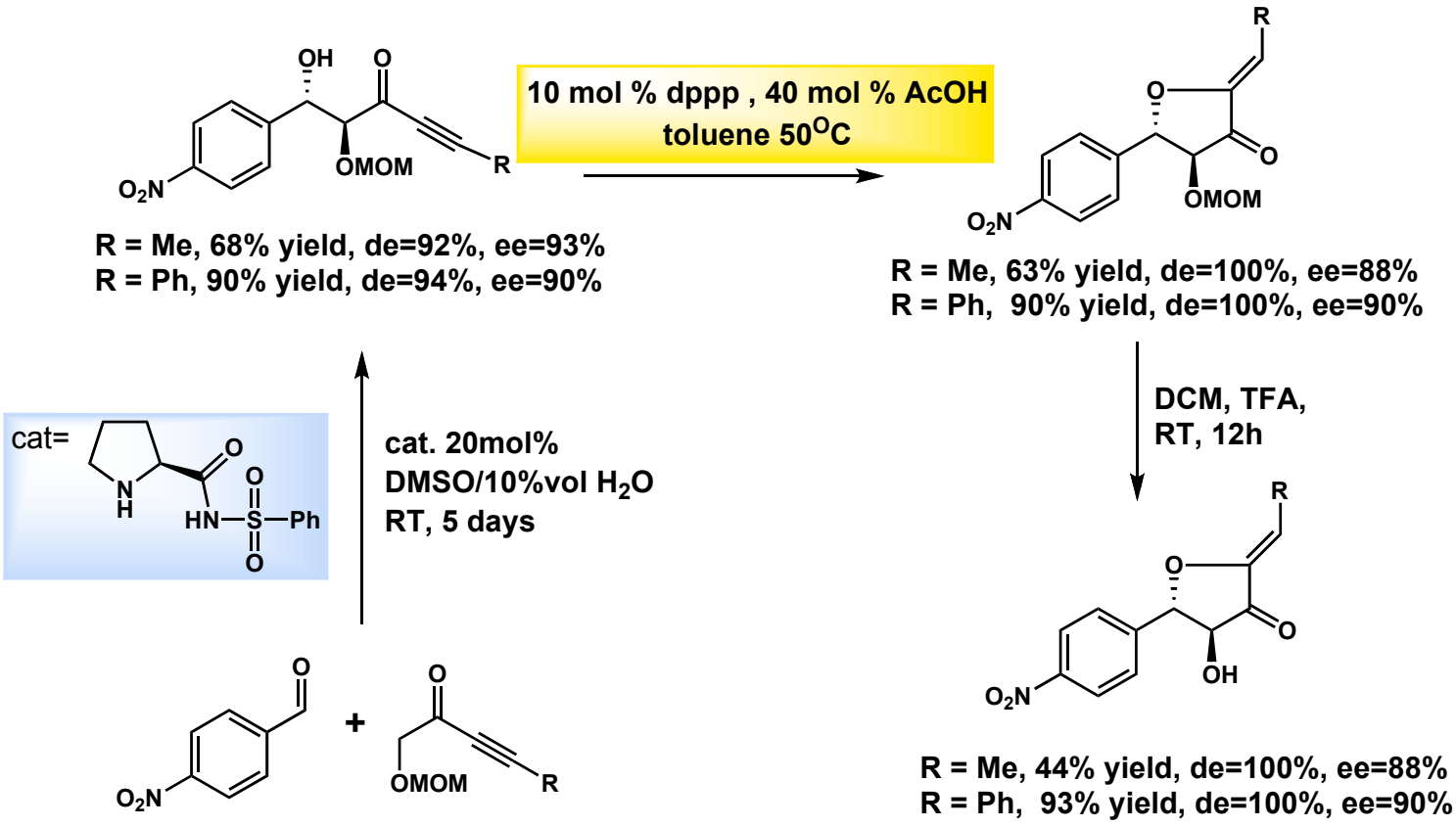


Au- and PR_3-Catalysed Synthesis of F-Targets



Double Organocatalytic Approach: Amine and Phosphine

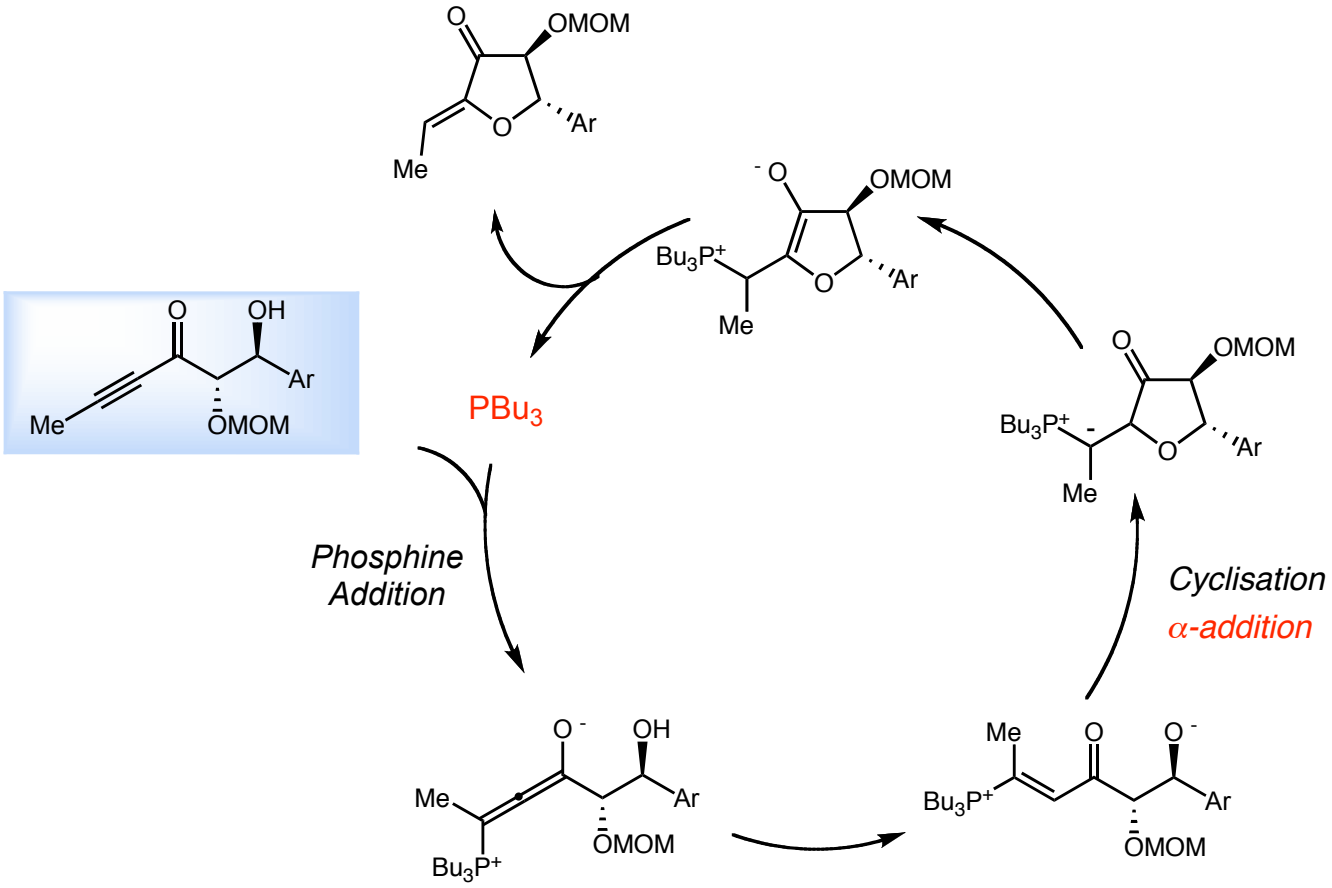
5-Exo-dig Cyclisation of HydroxylatedYnones



With F. Silva & M. Sawicki in *Org. Lett.* **2006**, *8*, 5417-5419.

Double Organocatalytic Approach: Amine and Phosphine

5-Exo-dig Cyclisation of HydroxylatedYnones



With F. Silva & M. Sawicki in *Org. Lett.* **2006**, *8*, 5417-5419.

PR_3-Catalysed Synthesis of F-Targets

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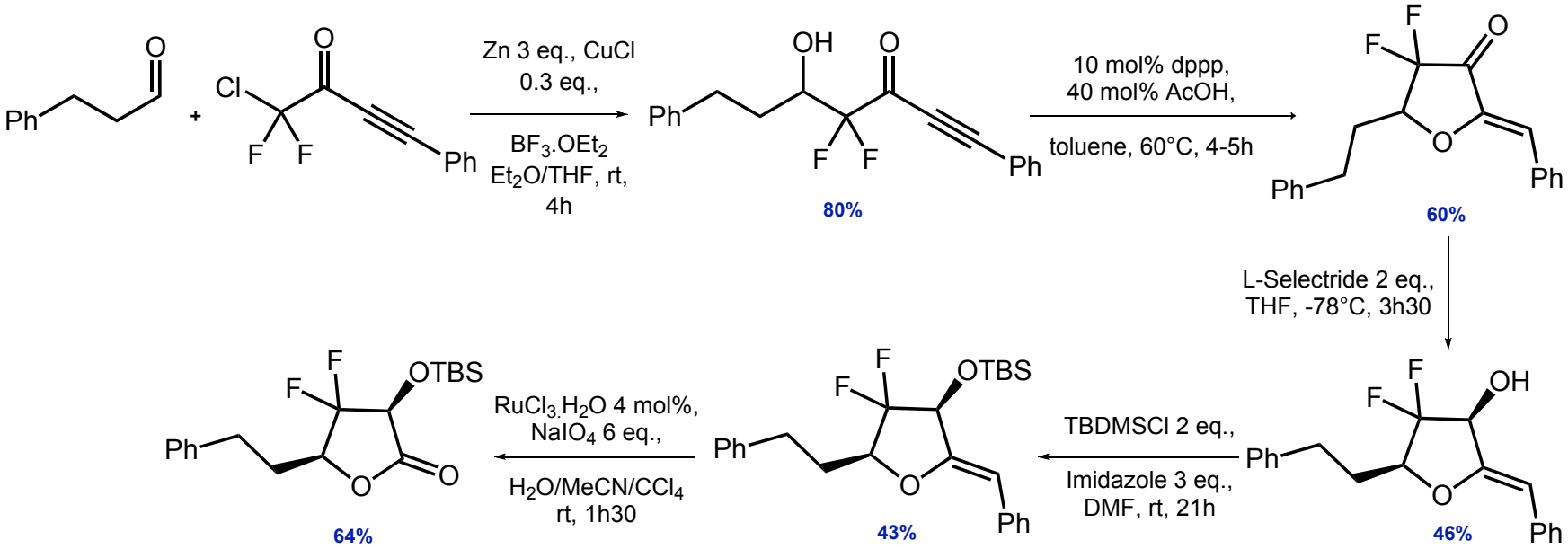

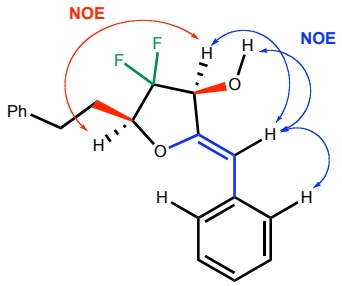

Part II, D Phil, Postdoctoral Research Assistants

Benjamin Greedy
Matthew Tredwell
Sophia Purser
Harriet Teare
Colin Lam
Susan Wilkinson
Christopher Wilson
Laurence Carroll
Guy Giuffredi
Rakesh Patel
Maud Reiter
Franck Silva

Dr Sebastien Thibaudeau
Dr Maria Pacheco Lloret
Dr Kenny Tenza
Dr Carla Bobbio
Dr Marcin Sawicki
Dr Marie Schuler
Dr Arnaud Tessier
Dr Romain Bejot

Collaborators

Professor K. N. Houk
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