Reaction- and Stereocontrol through Organocatalytic Activation Strategies

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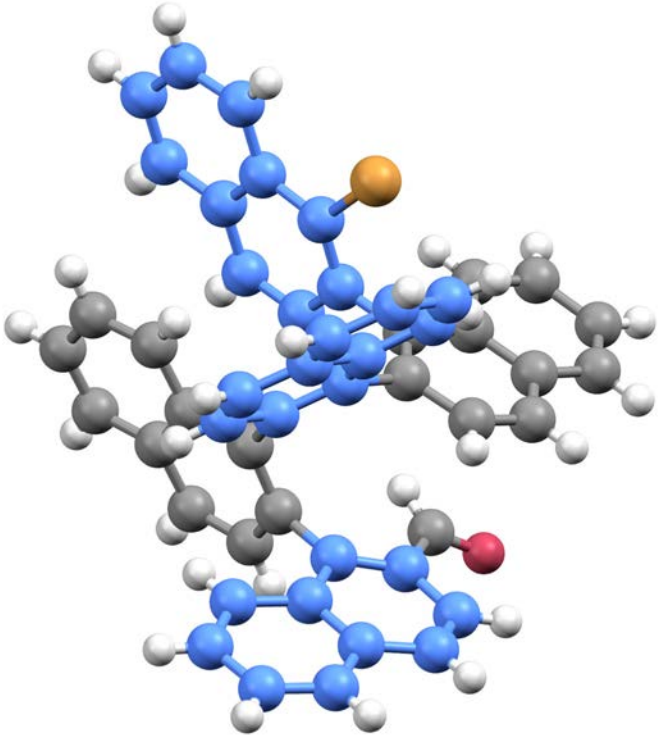
University of Basel

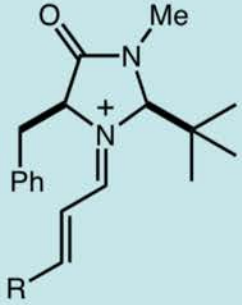
Therecat Network
Basel 25th September 2019



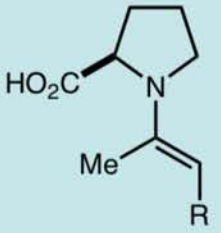
For introduction see:
http://chemlabs.princeton.edu/macmillan/

Organocatalytic Activation Modes

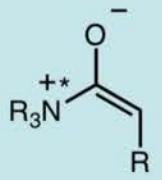
Established Reaction Modes



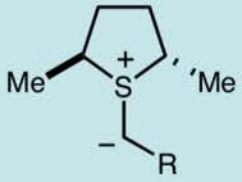
Iminium



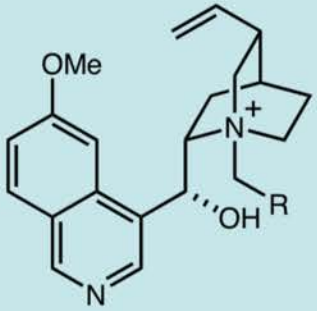
Enamine



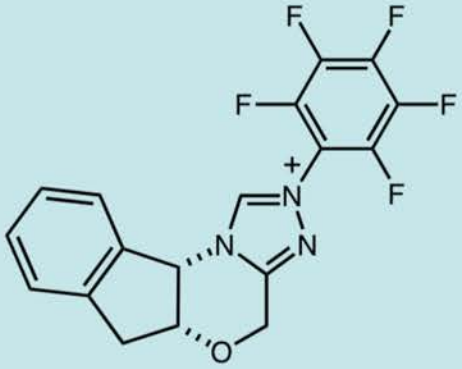
Ammonium



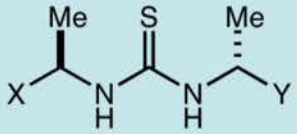
Ylide

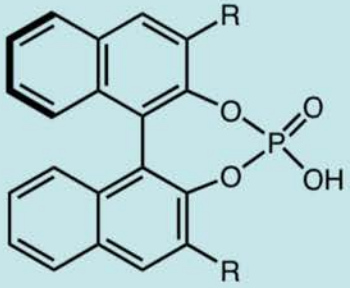


Phase Transfer



Carbene



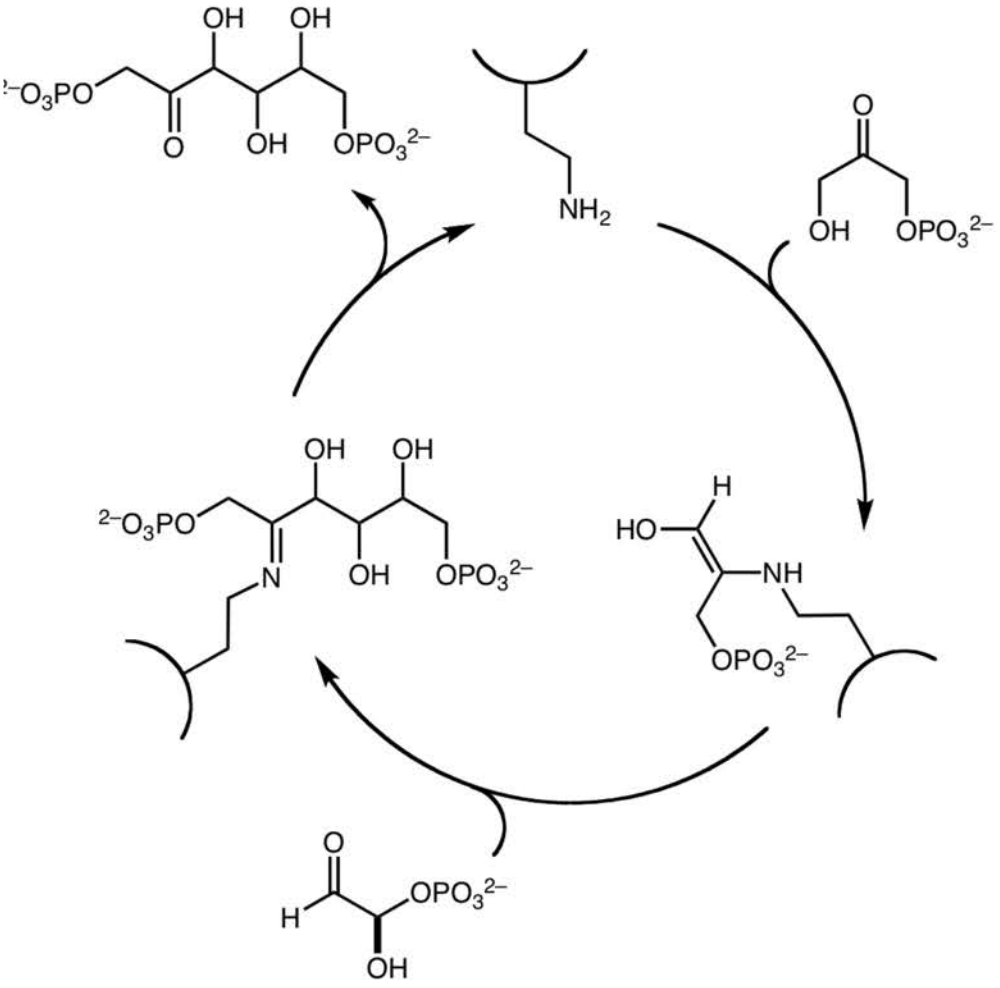


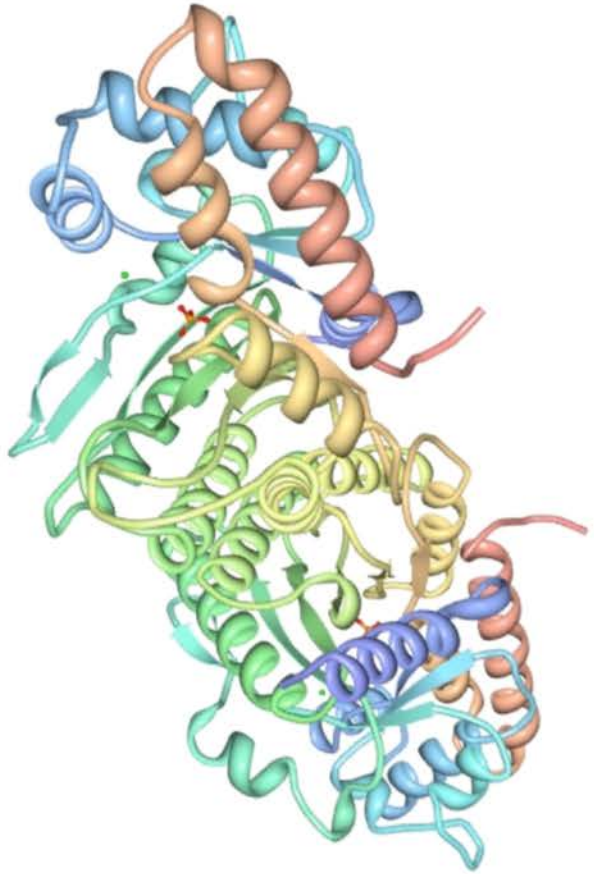
Hydrogen Bonding

- These systems have been developed widely during the previous decade 2000-2009

Enamine Catalysis: Inspiration from Biology

- Mechanism of class I aldolases is proposed to involve enamine intermediates





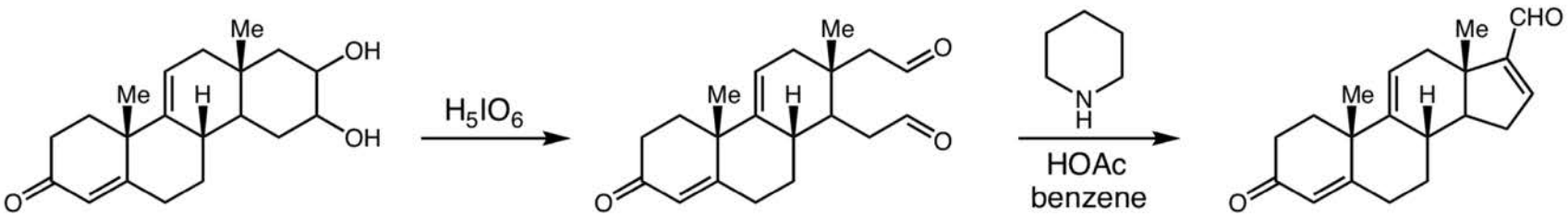
Fructose bisphosphate aldolase

Lysine reside is required for catalytic activity

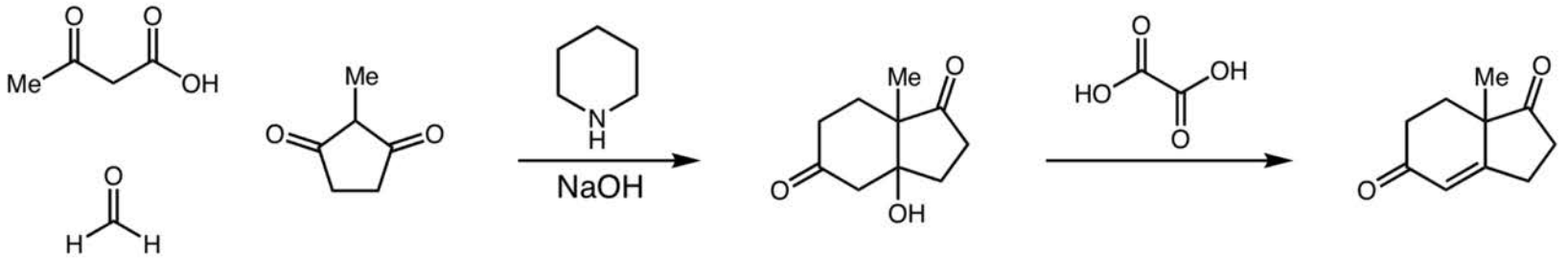
Rutter, W. J. *Fed. Proc. Am. Soc. Exp. Biol.* **1964**, *23*, 1248

Enamine Catalysis: Early Adoption in Total Synthesis

- Woodward-Wieland-Miescher enamine cyclization for steroid synthesis



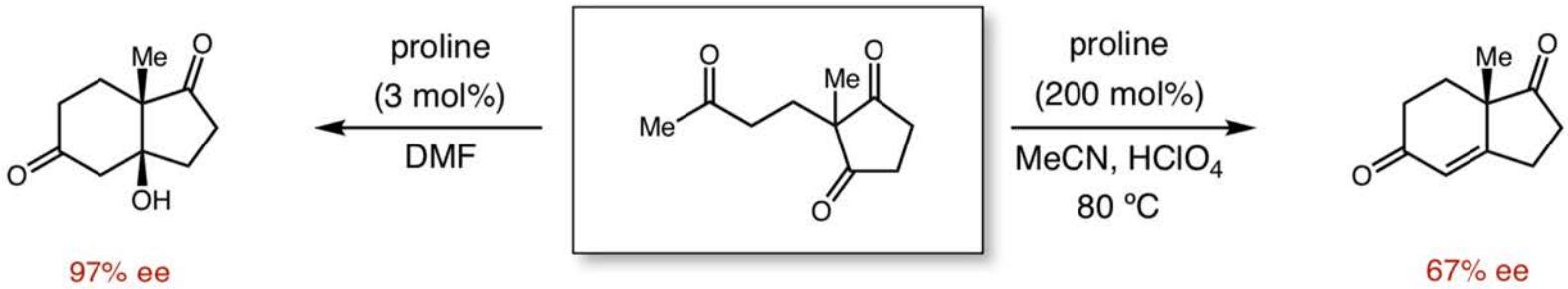
Woodward, R. B.; Sondheimer, F.; Taub, D.; Heusler, K.; McLamore, W. M. *J. Am. Chem. Soc.* **1952**, *74*, 4223



Wieland, P.; Miescher, K. *Helv. Chim. Acta* **1950**, *33*, 2215

Hajos-Parrish-Eder-Sauer-Wiechart: Asymmetric Breakthrough

- Use of proline to deliver the Weiland-Miescher ketone in an asymmetric fasion



97% ee

67% ee

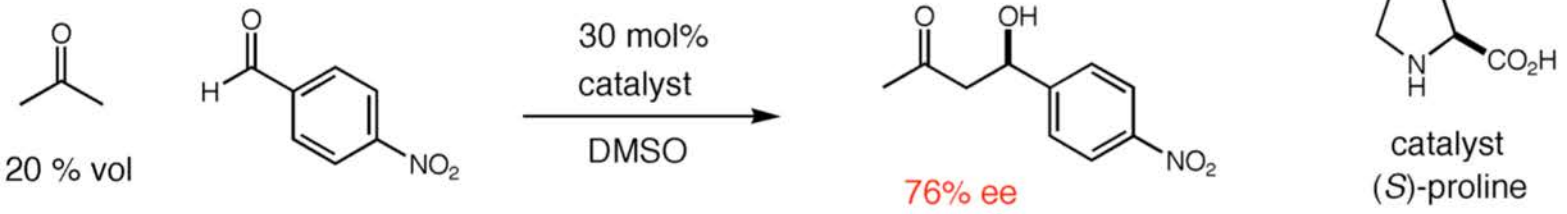
J. Org. Chem. **1974**, *39*, 1615.

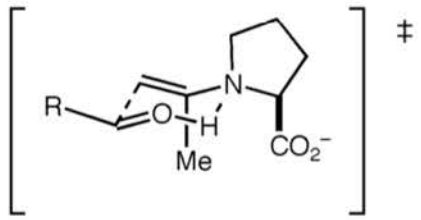
Angew. Chem. Int. Ed. **1971**, *10*, 496.

German Patent DE2102623 (July 29, 1971)

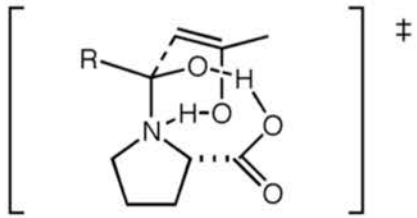
German Patent DE2014757 (Oct 7, 1971)

Enamine Aldol: Proposed Transition States to Date

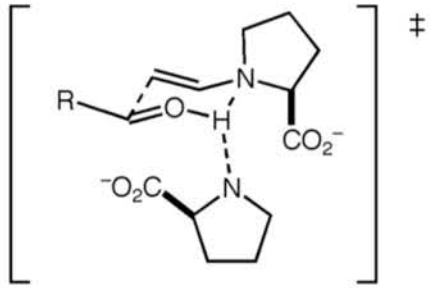




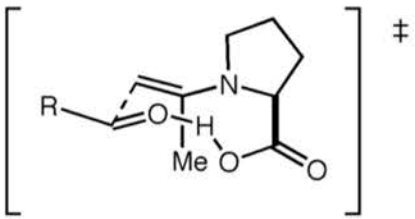
Hajos–Parrish (1971)



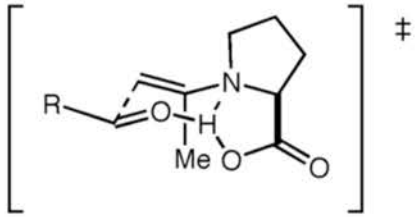
Hajos–Parrish (1971)



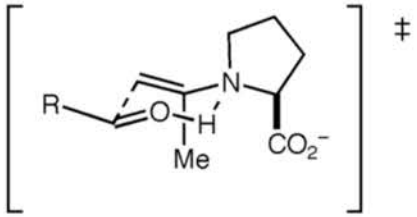
Agami (1987)



Barbas–List (2000)



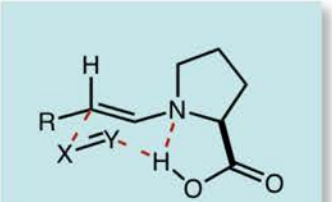
Houk (2002)

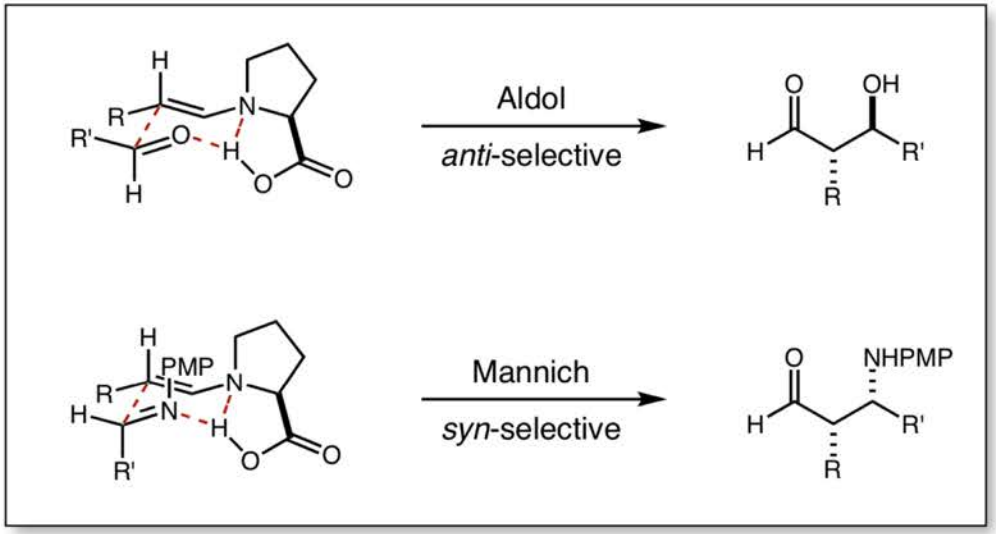


MacMillan (2003)

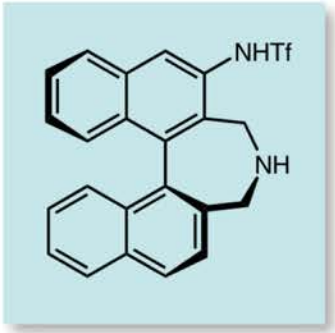
Predictable Stereochemistry for Aldol and Mannich

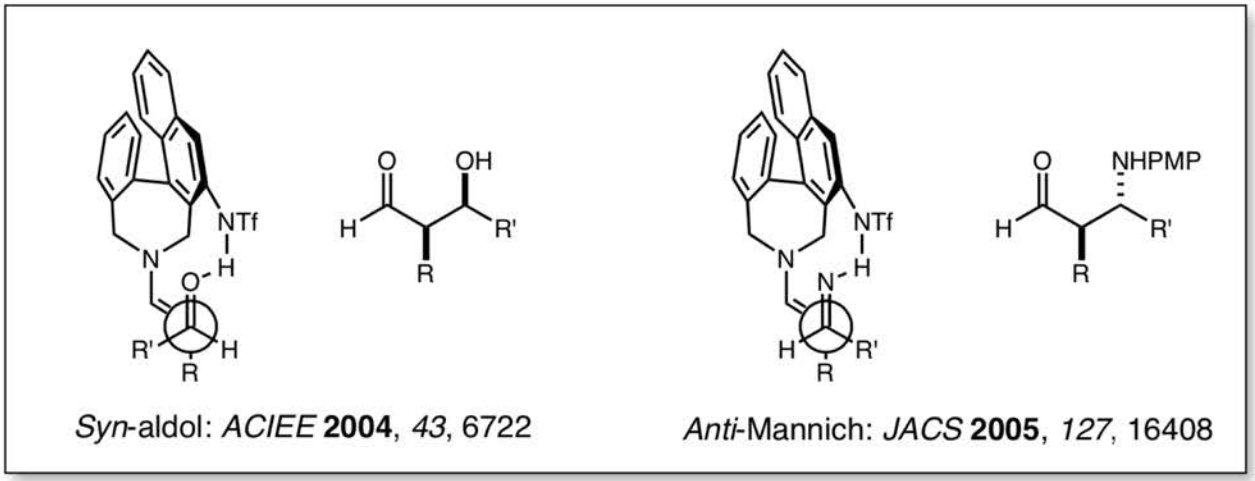
- Use of proline or proline-type catalysts leads to *anti*-aldol or *syn*-Mannich





- Maruoka's binaphthyl catalyst is a significant advance to access opposite stereoisomers

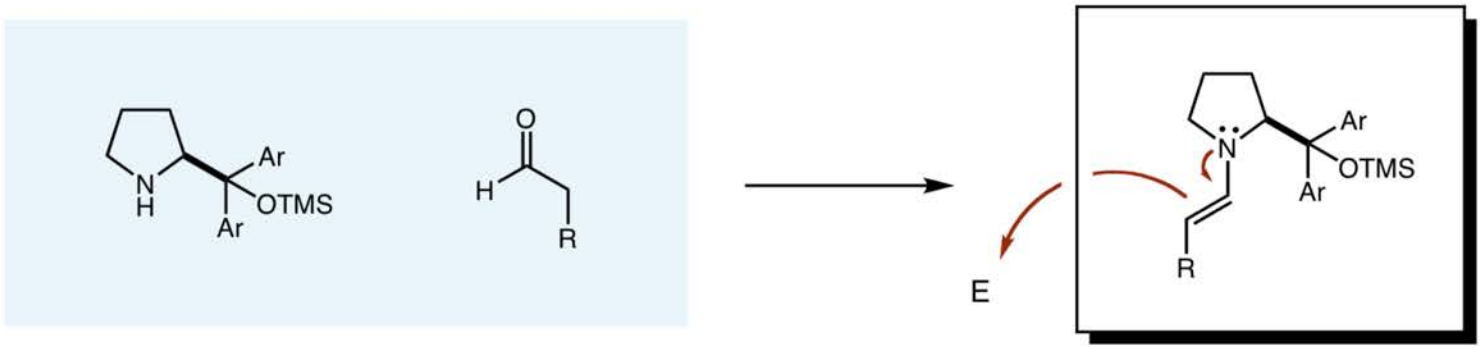


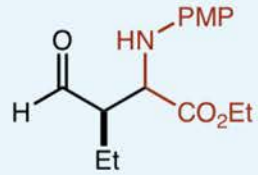


Syn-aldol: *ACIEE* **2004**, *43*, 6722

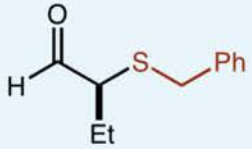
Anti-Mannich: *JACS* **2005**, *127*, 16408

Enamine Chemistry with Jørgensen's Catalyst



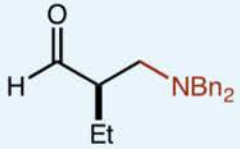


83%, 94% ee, 4:1 dr

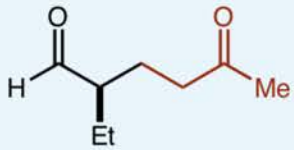


85%, 96% ee

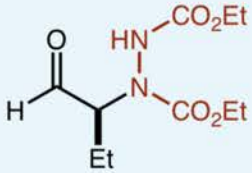
74%, 93% ee



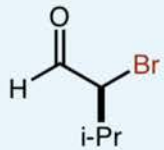
84%, 90% ee



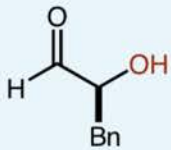
83%, 93% ee



79%, 90% ee



74%, 94% ee

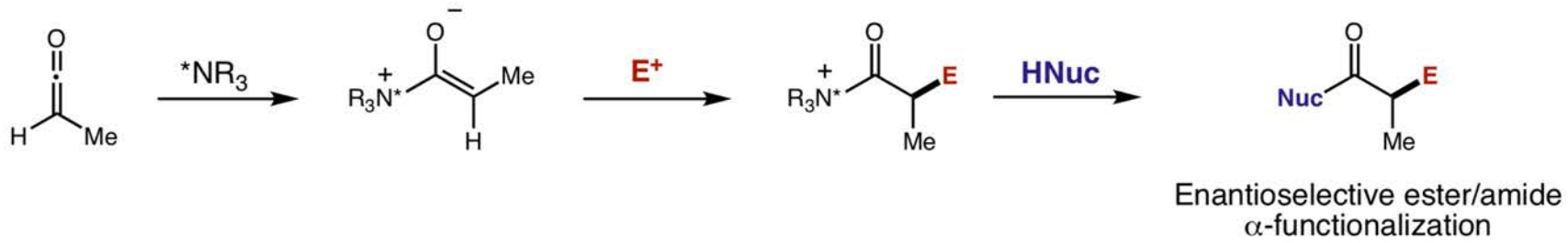


70%, 87% ee

Franzén, J.; Marigo, M.; Fielenbach, D.; Wabnitz, T. C.; Kaersgaard, A.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 18296.
Chi, Y.; Gellman, S. H. *J. Am. Chem. Soc.* **2006**, *128*, 6804.

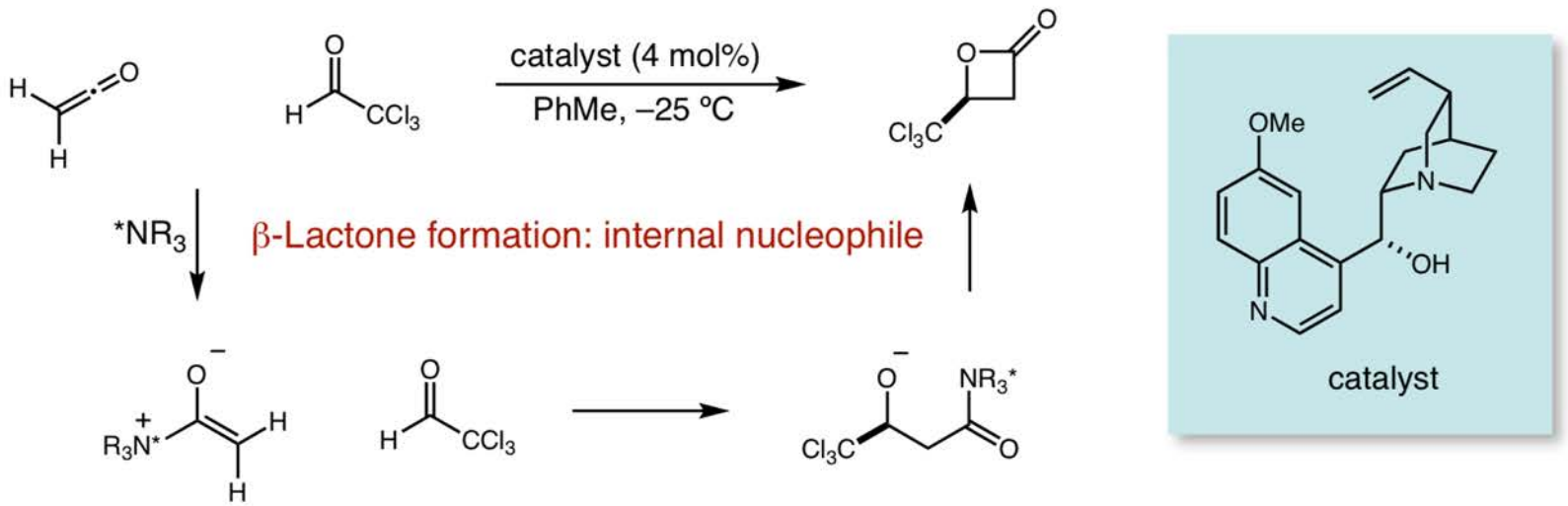
Ketenes as Precursors for Ammonium Enolates

- Attack of nucleophilic tertiary amine on ketene leads directly to ammonium enolate



Enantioselective ester/amide
α-functionalization

- First asymmetric example by Wynberg in 1982 (first racemic by Sauer in 1947)

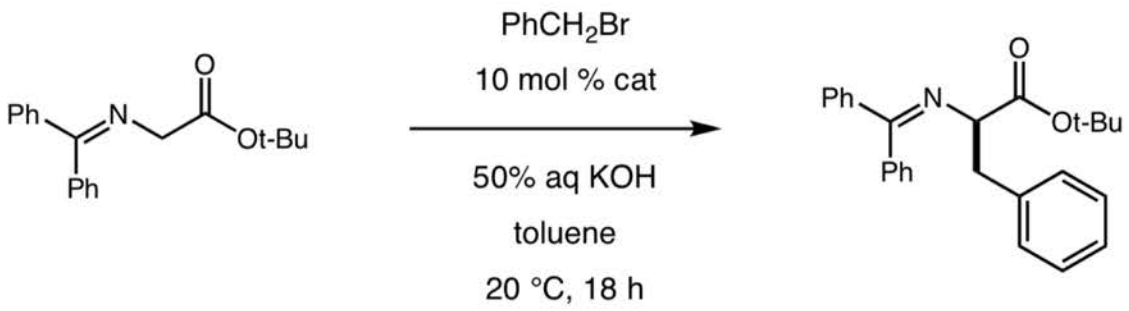


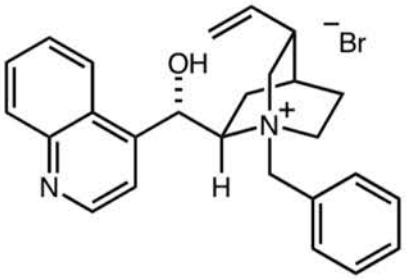
Wynberg, H.; Staring, E. G. J. *J. Am. Chem. Soc.* **1982**, *104*, 166

Sauer, J. C. *J. Am. Chem. Soc.* **1947**, *69*, 2444

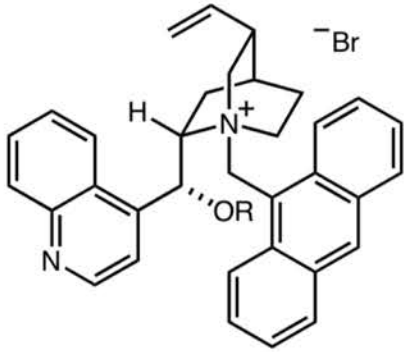
Advances in Catalyst Design

■ Catalysts have been benchmarked using the benzylation of glycine imine:

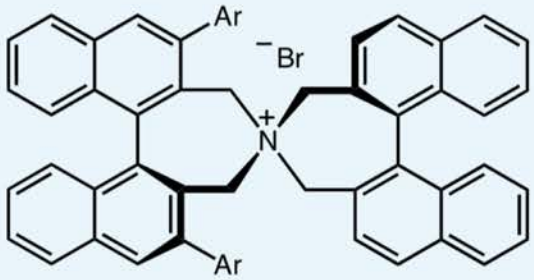


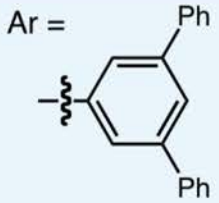


Ar = Ph
O'Donnell 1989
10 mol %
75% yield, 66% ee



R = allyl
Lygo, Corey 1997
10 mol %
87% yield, 94% ee



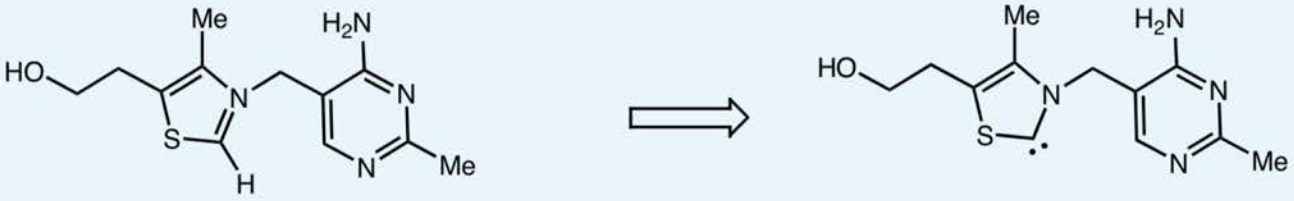


Maruoka 1999
1 mol %
91% yield, 98% ee

Shirakawa, S.; Marouka, K. *Catalytic Asymmetric Synthesis.* Hoboken: Wiley, 2010.

Carbenes as Organocatalysts

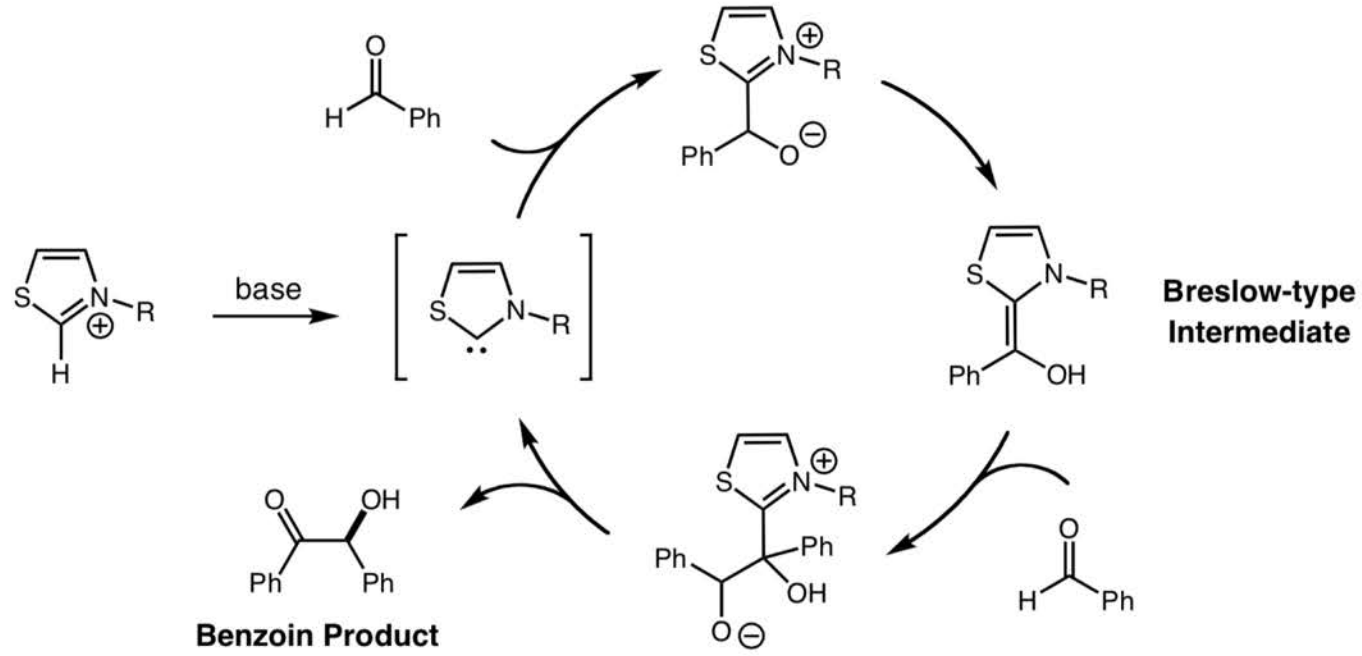
- Carbenes were long suspected as catalytic intermediates



Thiazolium Salt of Thiamine Coenzyme (vitamin B_1)

Nature's Carbene Organocatalyst

- For many years a carbene catalyst for the enantioselective benzoin condensation was elusive



Carbenes as Organocatalysts

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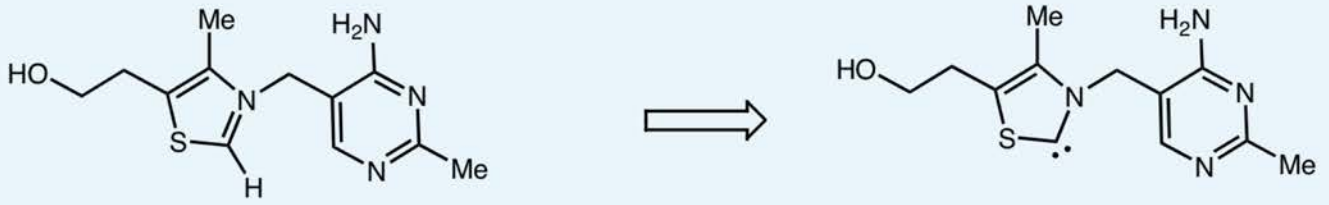
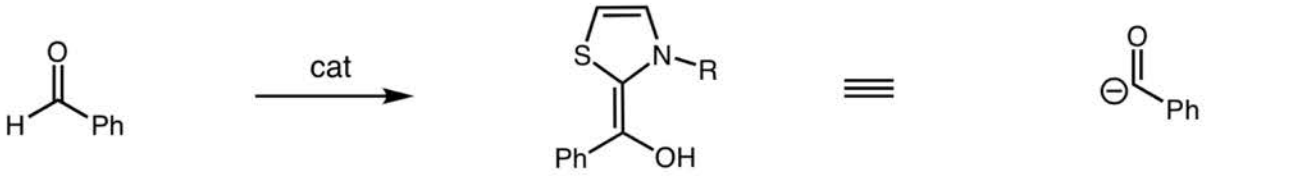


Thiazolium Salt of Thiamine Coenzyme (vitamin B_1) — Nature's Carbene Organocatalyst

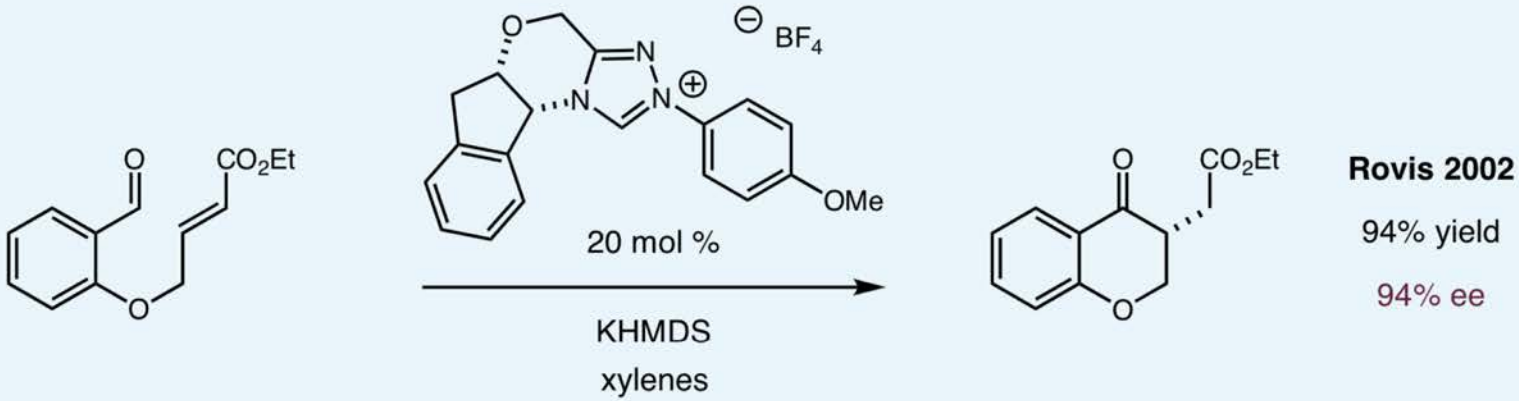
- For many years a carbene catalyst for the enantioselective benzoin condensation was elusive
- The newly proposed intermediate exhibits umpolung reactivity



electrophilic — **Breslow-type Intermediate** — **acyl anion synthon**

Recent Advance in Carbene Catalysis

■ After the initial disclosures in the 1990's the Stetter reaction has been championed by Rovis



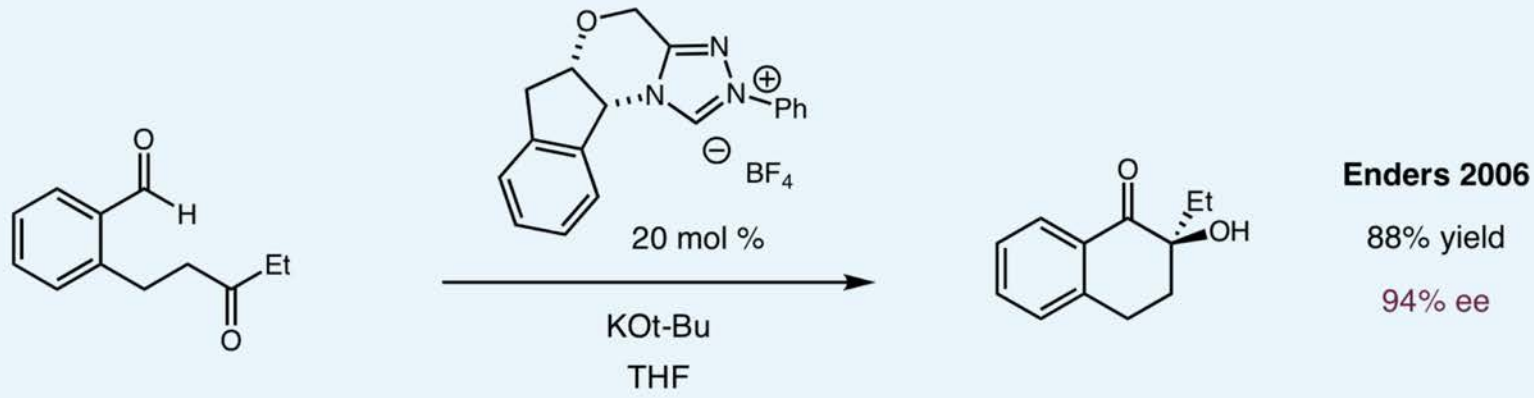
Rovis 2002

94% yield

94% ee

Kerr, M. S.; Read de Alaniz, J.; Rovis, T. *J. Am Chem. Soc.* **2002**, *124*, 10298.

■ The Rovis catalyst design has been have been proven to be excellent for many more reactions



Enders 2006

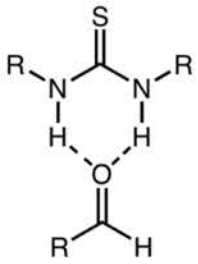
88% yield

94% ee

Enders, D.; Niemeier, O.; Raabe, G. *Synlett* **2006**, 2431.

Hydrogen-Bonding Catalysis

H-bond catalysis



~30 new reactions

Jacobsen–Akiyama

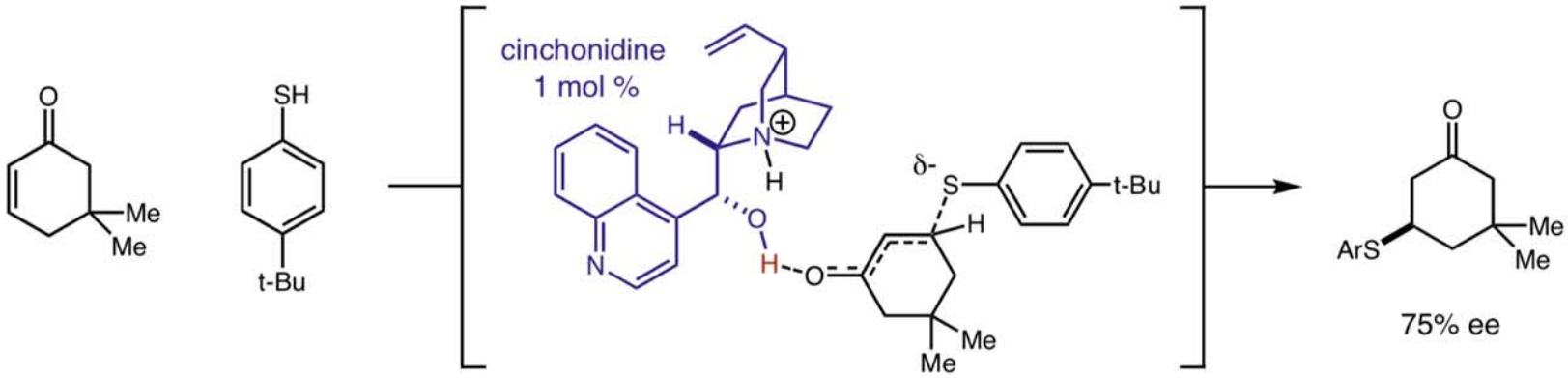
J. Am. Chem. Soc. **1981**, *103*, 417–430

Addition of Aromatic Thiols to Conjugated Cycloalkenones, Catalyzed by Chiral β-Hydroxy Amines. A Mechanistic Study on Homogeneous Catalytic Asymmetric Synthesis[1]

Henk Hiemstra and Hans Wynberg*

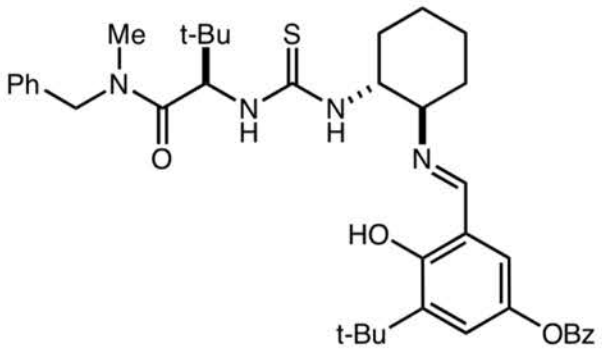
Contribution from the Laboratory of Organic Chemistry, The University of Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands. *Received February 25, 1980*

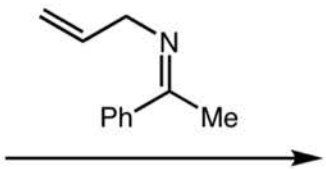
■ Early examples using cinchonia alkaloidsas H-bonding catalysts

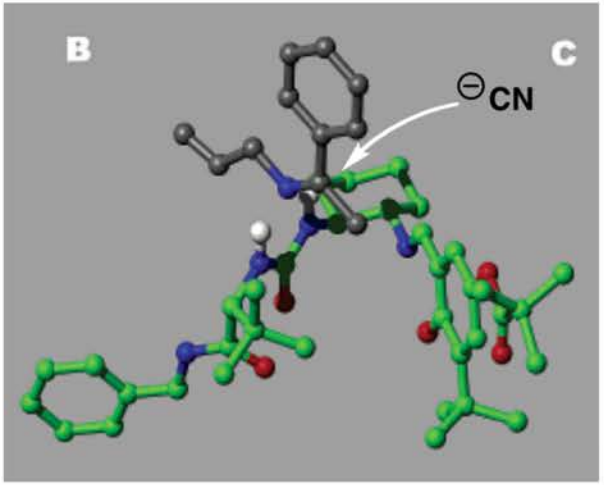


Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713. Hiemstra, H.; Wynberg, H. *J. Am. Chem. Soc.* **1981**, *103*, 417.

Urea Stereochemical Model

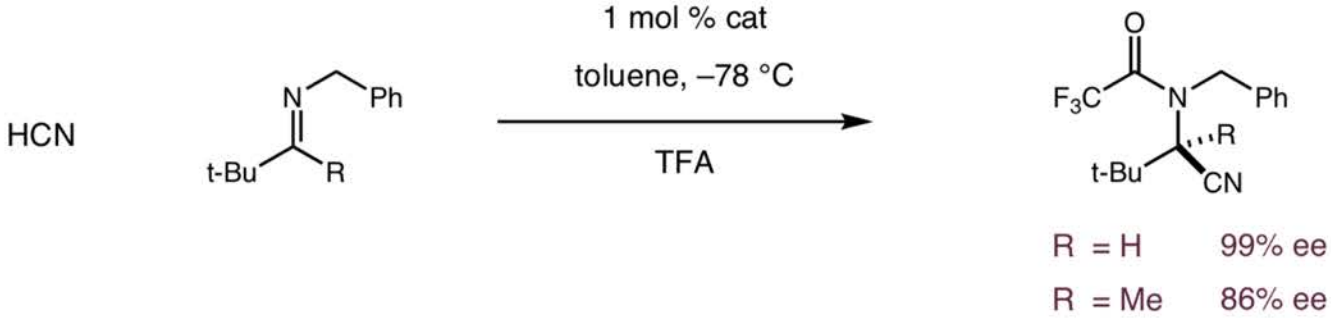






- With a better understanding of how these catalysts work new reaction methods can be developed

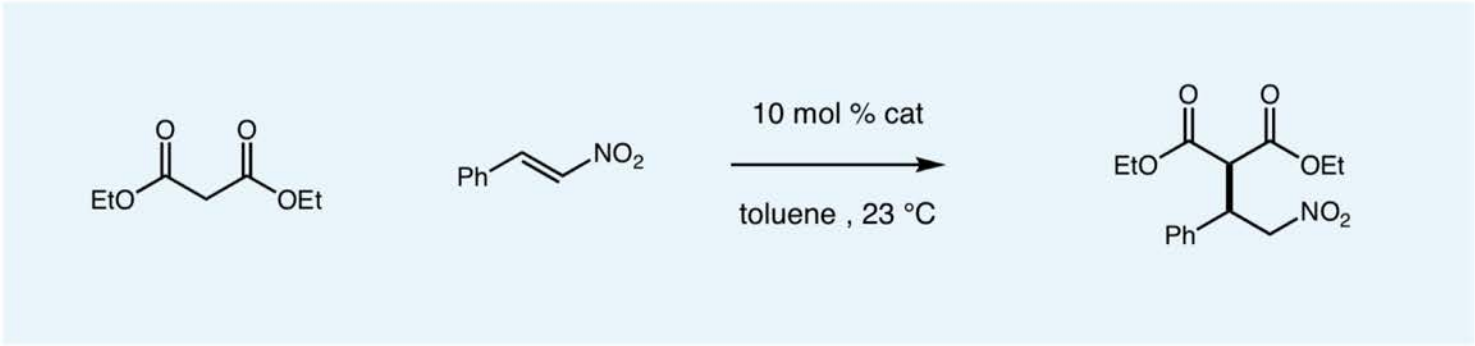
Strecker reaction with aldimine or ketoimine



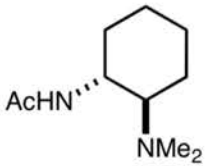
Vachal, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *120*, 10012.

Bifunctional Urea Catalysts

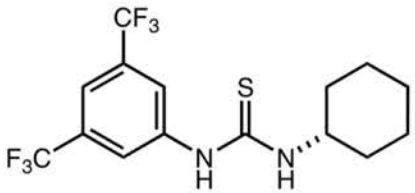
■ Enantioselective Michael Addition



■ Both thiourea and tertiary amine are needed

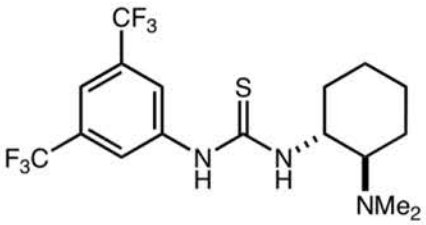


14%, 35% ee

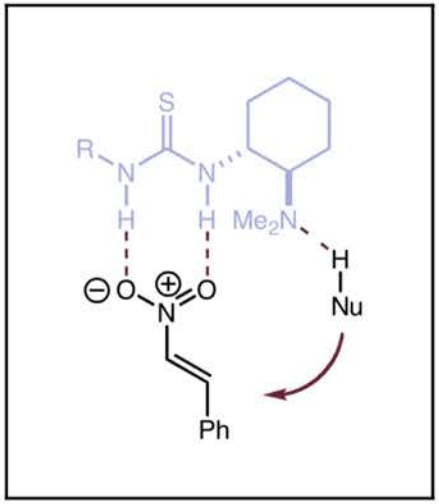


10 mol % NEt_3

57%, 0% ee

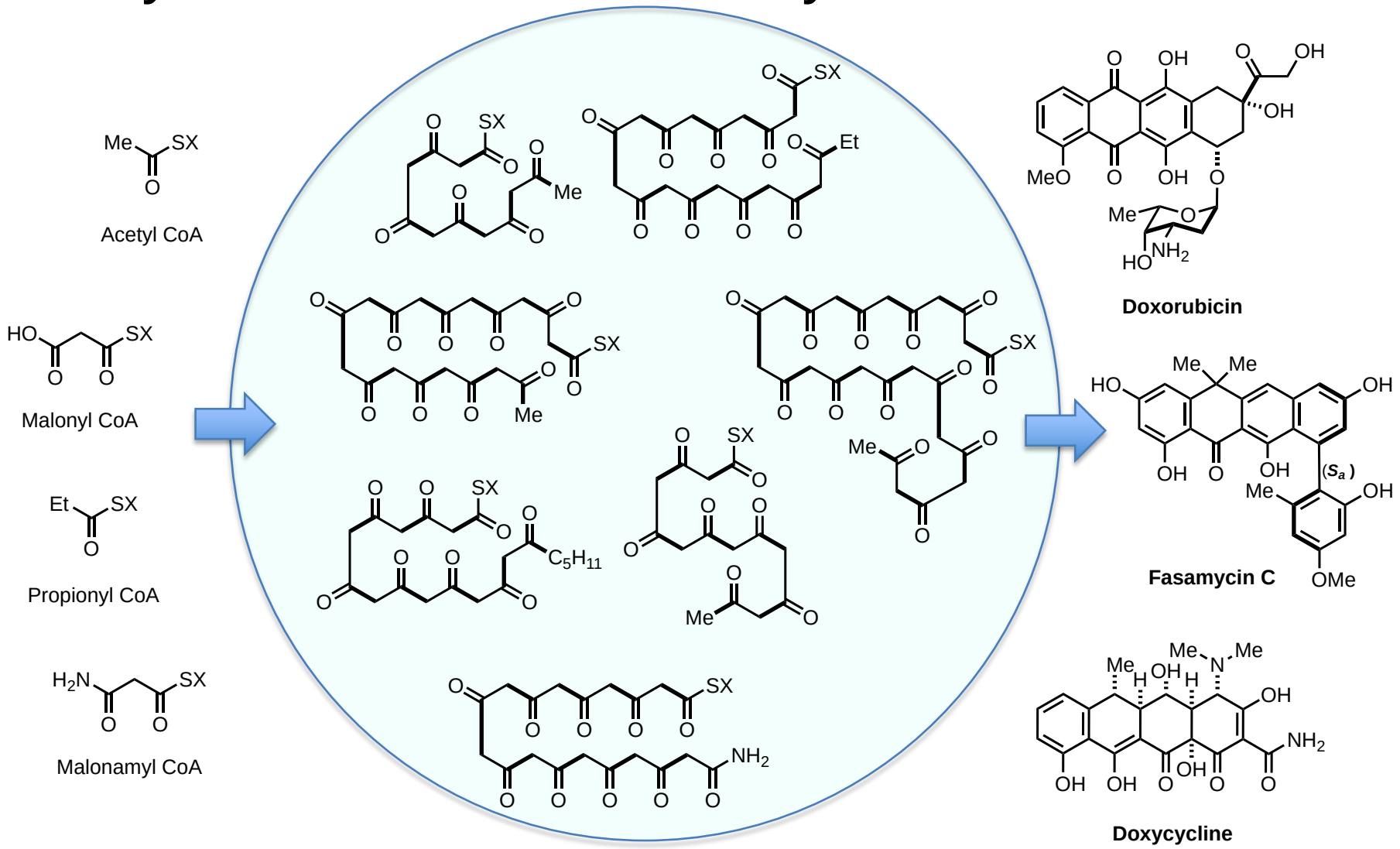


86%, 93% ee



Okino, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* **2003**, *128*, 12672.

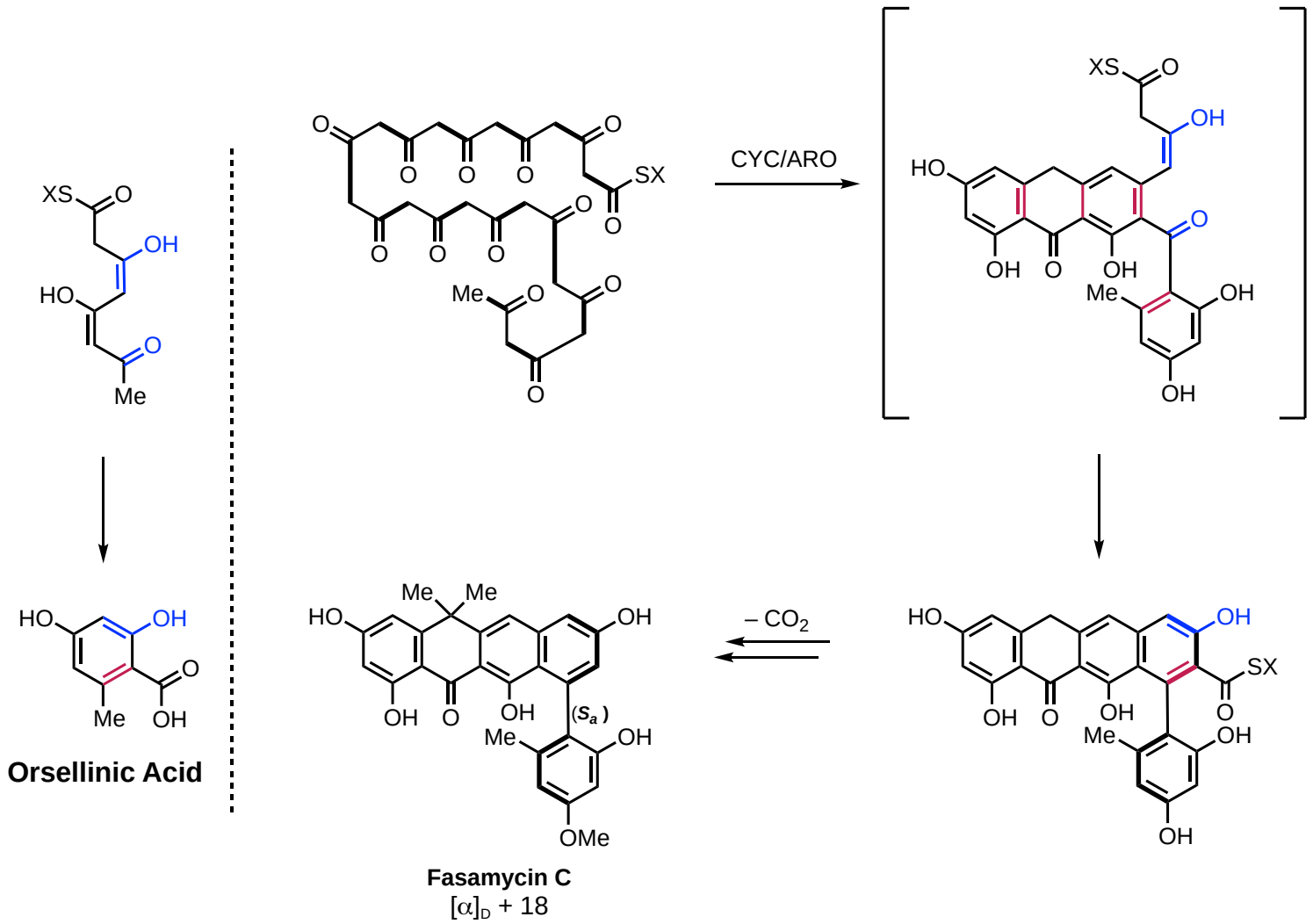
Biosynthesis of Aromatic Polyketides



C. Hertweck, *Angew. Chem. Int. Ed.* **2009**, *48*, 4688; A. Das, **C. Koshla**, *Acc. Chem. Res*. **2009**, *42*, 631; J. M. Crawford, **C. A. Townsend**, *Nat. Rev. Microbiol*. **2010**, *8*, 879; **J. Staunton**, K. J. Weissman, *Nat. Prod. Rep*. **2001**, *18*, 380.

Seminal biomimetic studies (stochiometric): **T. M. Harris**, C. M. Harris, *Tetrahedron* **1977**, *33*, 2159; **M. Yamaguchi**, T. Okuma, A. Horiguchi, C. Ikeura, T. Minami, *J. Org. Chem.* **1992**, *57*, 1647; Convergent synthesis: **A. G. Myers** group, *Science* **2005**, *308*, 395.

Biosynthesis of Fasamycin C

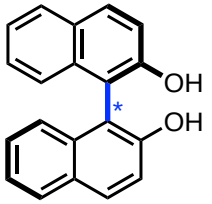


Orsellinic Acid

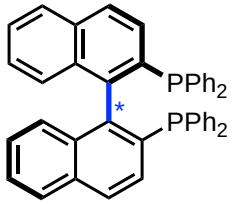
Fasamycin C
$[\alpha]_D$ + 18

Z. Qin, J. T. Munnoch, R. Devine, N. A. Holmes, R. F. Seipke, K. A. Wilkinson, **B. Wilkinson**, **M. I. Hutchings**, *Chem. Sci*. **2017**, *8*, 3218; Z. Feng, D. Kallifidas, **S. F. Brady**, *PNAS* **2011**, *108*, 12629; F. Zeng, D. Chakraborty, S. B. Dewell, B. V. Reddy, **S. F. Brady**, *J. Am. Chem. Soc*. **2012**, *134*, 2981.

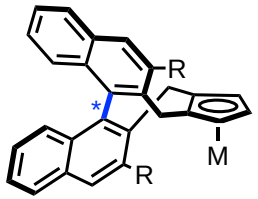
Selected Atropisomers



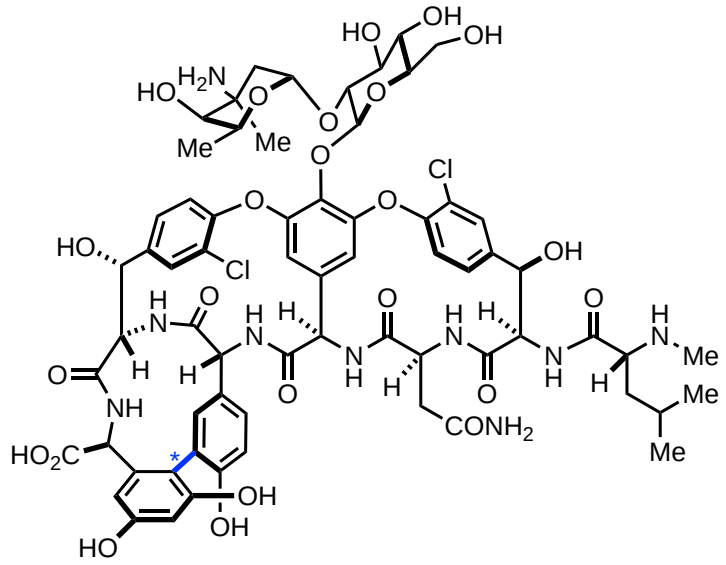
(+)-(R_a)-BINOL



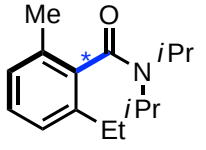
(+)-(R_a)-BINAP



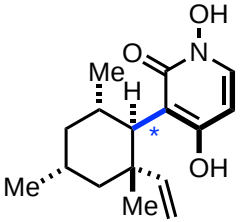
Cp^x ligands



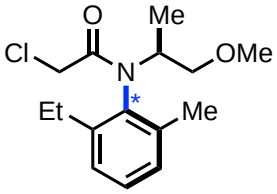
Vancomycin



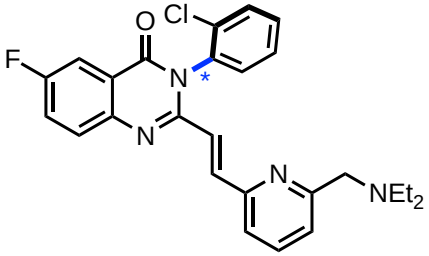
tertiary Aromatic Amides



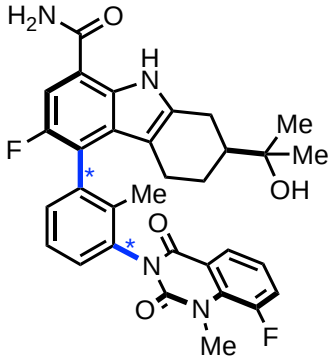
Cordypyridone B



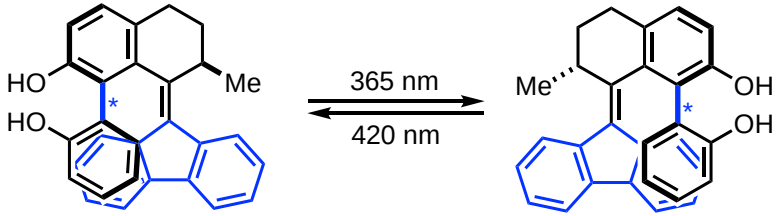
Metolachlor



3-Aryl-quinazolin-4-ones



BMS-986142

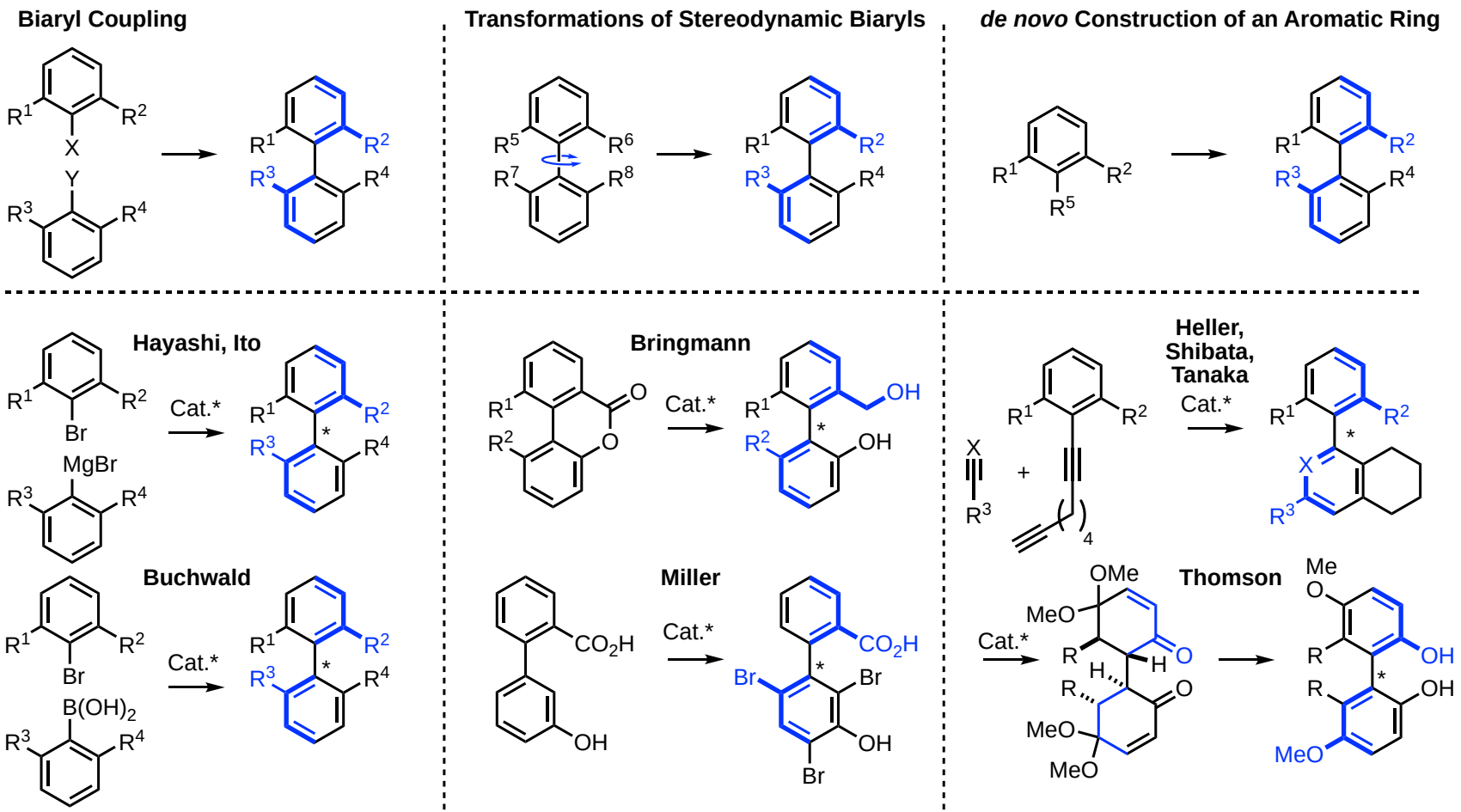


Photoresponsive Switch (Molecular Nanoscience)

A. Miyashita, A. Yasuda, H. Takaya, K. Toriumi, T. Ito, T. Souchi, R. Noyori, *J. Am. Chem. Soc.* **1980**, *102*, 7932; J. Clayden, W. J. Moran, P. J. Edwards, S. R. LaPlante, *Angew. Chem. Int. Ed.* **2009**, *48*, 6398; T. Nguyen, *Chem. Eng. News* **2018**, 96. G. Beutner et al., *Org. Lett.* **2018**, *20*, 3736.

B. Ye, N. Cramer, *Science* **2012**, *338*, 504; M. Schäfer, T. R. Schneider, G. M. Sheldrick, *Structure* **1996**, *4*, 1509; M. Isaka, M. Tanticharoen, *J. Org. Chem.* **2001**, *66*, 4803, S. F. Pizzaloto, P. Stacko, J. C. M. Kistemaker, T. van Leeuwen, E. Otten, B. L. Feringa, *J. Am. Chem. Soc.* **2018**, 17278.

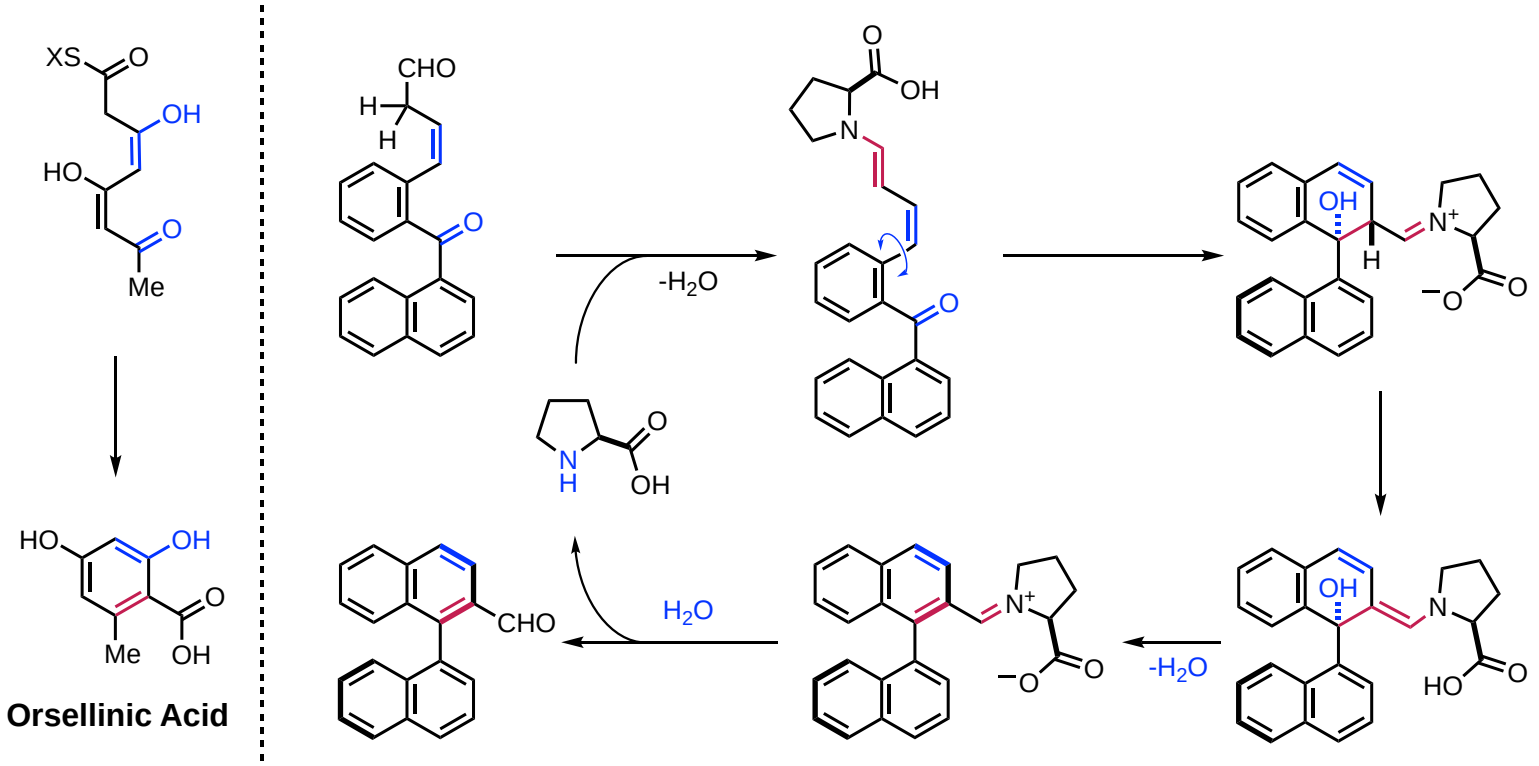
Atroposelective Catalysis – Biaryl Synthesis



Abe, Asano, Akiyama, Baudoin, Bencivenni, Bella, Berson, Boger, Bonne, Bressy, Bringmann, Brussee, Buchwald, Bugaut, Chen, Clayden, Colobert, Cram, Cramer, Evans, Gong, Gu, Gustafson, Hattori, Hayashi, Heller, Itami, Ito, Katsuki, Kozlowski, Kürti, Lassaletta, Leroux, Li, Lipshutz, List, Maruoka, Matsubara, Merlic, Meyers, Miller, Mislow, Miyano, Nakajima, Nishii, Nicolaou, Oh, Pappo, Rodriguez, Sasai, Seidel, Shi, Shibata, Smith, Studer, Suginome, Takizawa, Tan, Tanabe, Tanaka, Tang, Thomson, Tomioka, Toste, Uang, Uemura, Wallace, Wang, Wencel-Delord, Wulff, Xu, Yamamoto, Yan, Yeung, You, Zhao, Zhu ...

Stereoselective Aldol Condensation

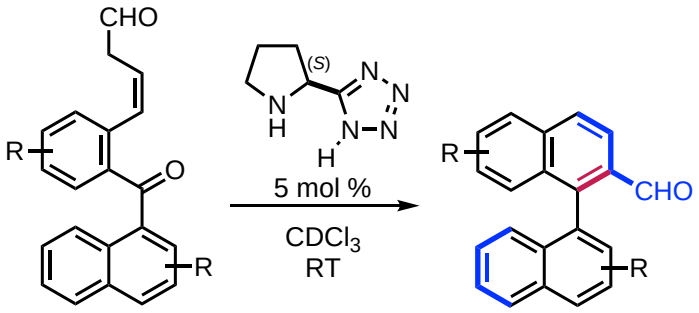
Arene-Forming



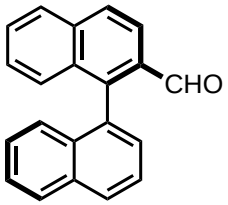
with **Achim Link**

Angew. Chem. Int. Ed. **2014**, *53*, 5458.

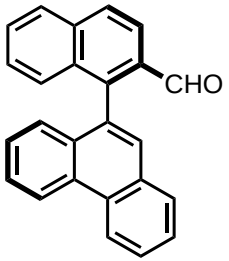
Scope



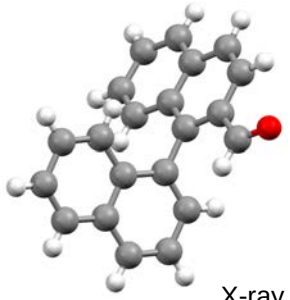
(S_a)



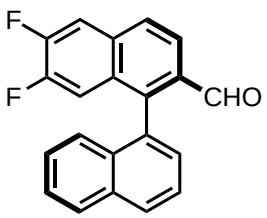
74 % yield
e.r. 99:1
(S_a) by X-ray



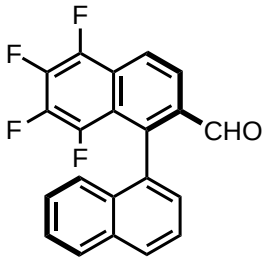
76 % yield
e.r. 99:1



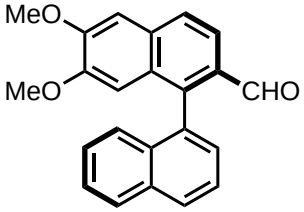
X-ray



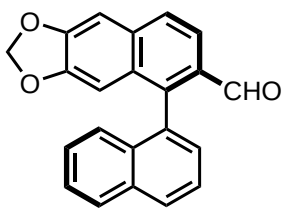
89 % yield
e.r. 98:2



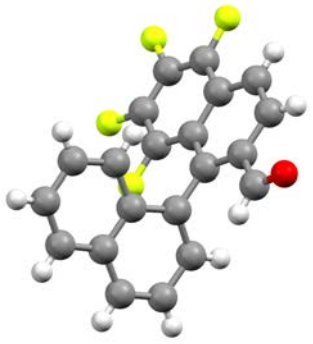
66 % yield
e.r. 96:4
(S_a) by X-ray



74 % yield
e.r. 98:2



67 % yield
e.r. 99:1

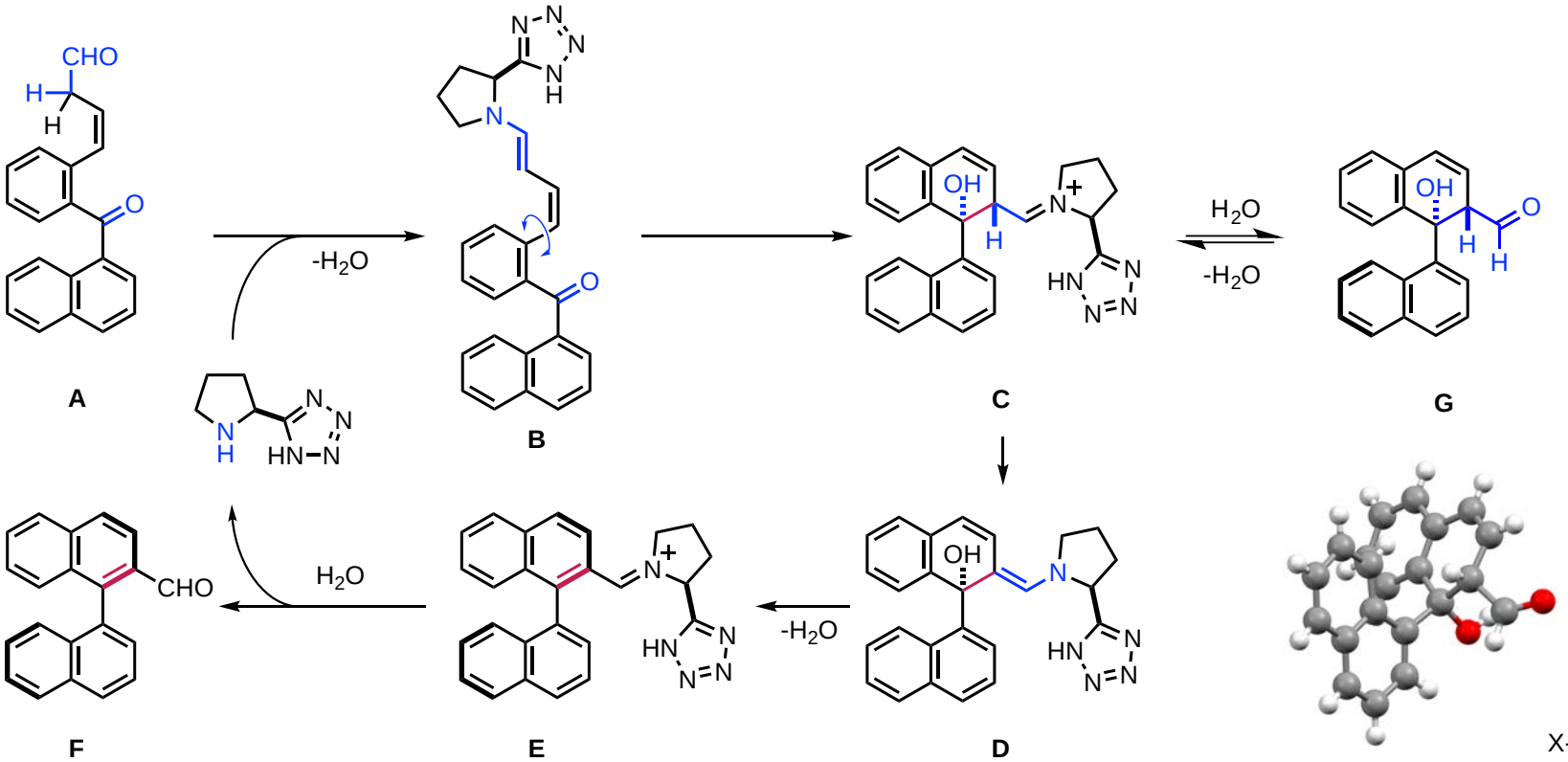


X-ray

Pyrrolidinyl-tetrazole catalyst: A. J. A. Cobb, D. M. Shaw, **S. V. Ley**, *Synlett* **2004**, 558; H. Torii, M. Nakadai, K. Ishihara, S. Saito, **H. Yamamoto**, *Angew. Chem. Int. Ed.* **2004**, *43*, 1983; A. Hartikka, **P. I. Arvidsson**, *Tetrahedron: Asymm.* **2004**, *15*, 1831.

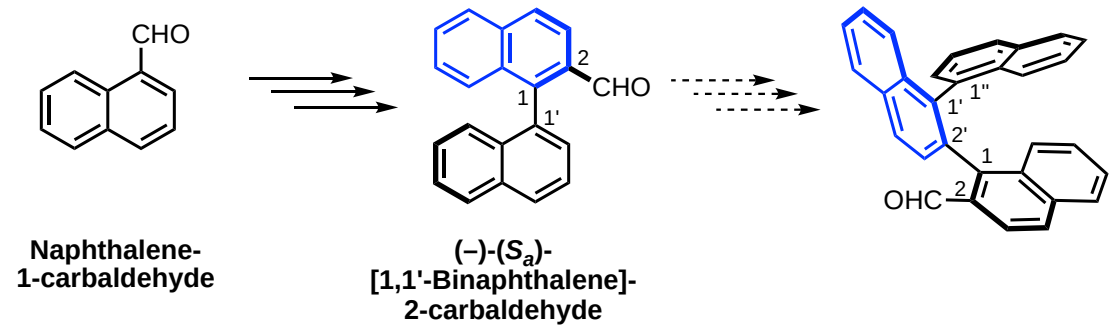
with **Achim Link**
X-ray: M. Neuburger
Angew. Chem. Int. Ed. **2014**, *53*, 5458.

Mechanistic Investigation



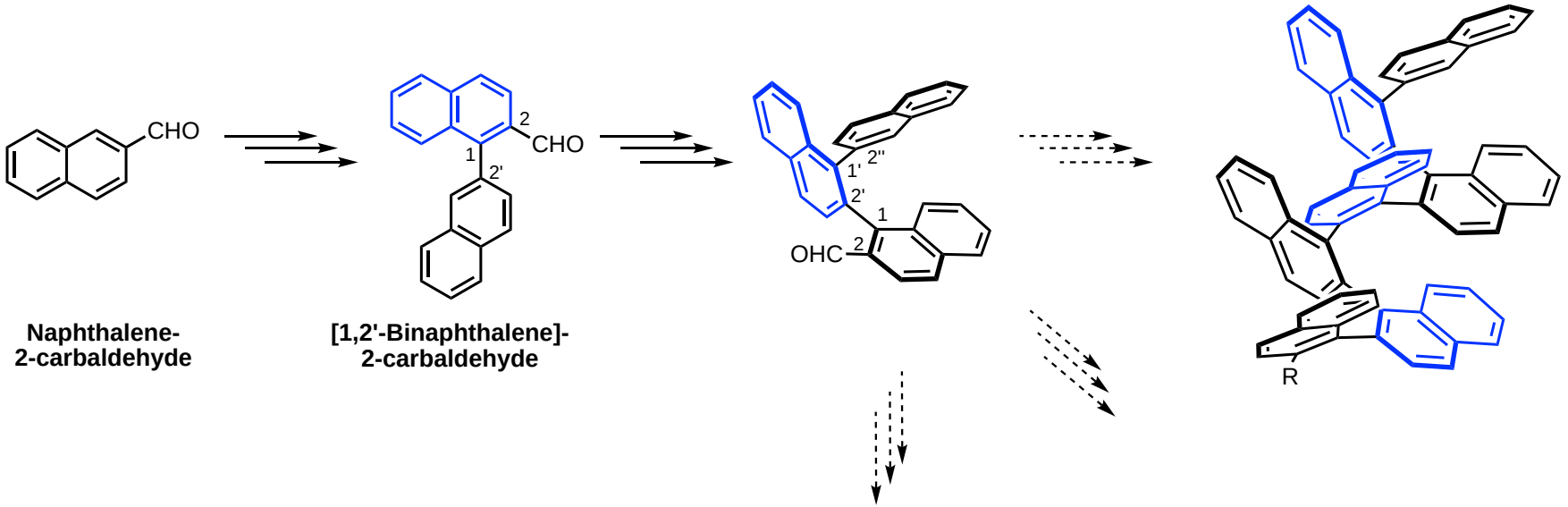
with **Reto M. Witzig** and **Achim Link**
unpublished results

Atroposelective Oligonaphthylene Synthesis



Naphthalene-1-carbaldehyde

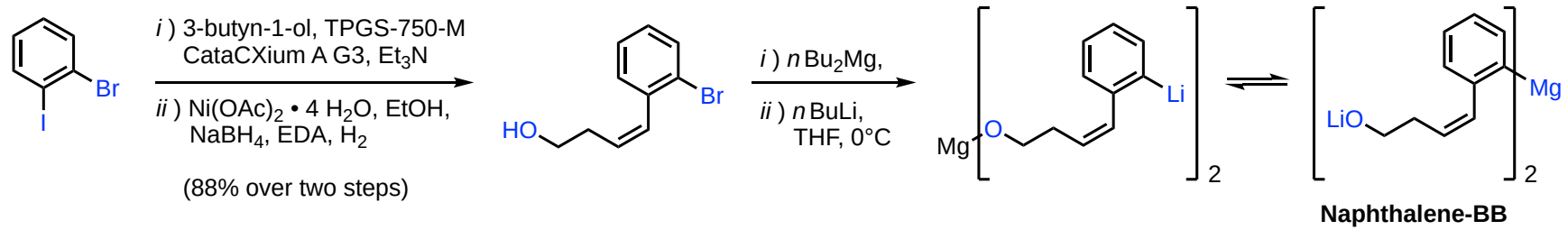
(–)-(S_a)-[1,1'-Binaphthalene]-2-carbaldehyde

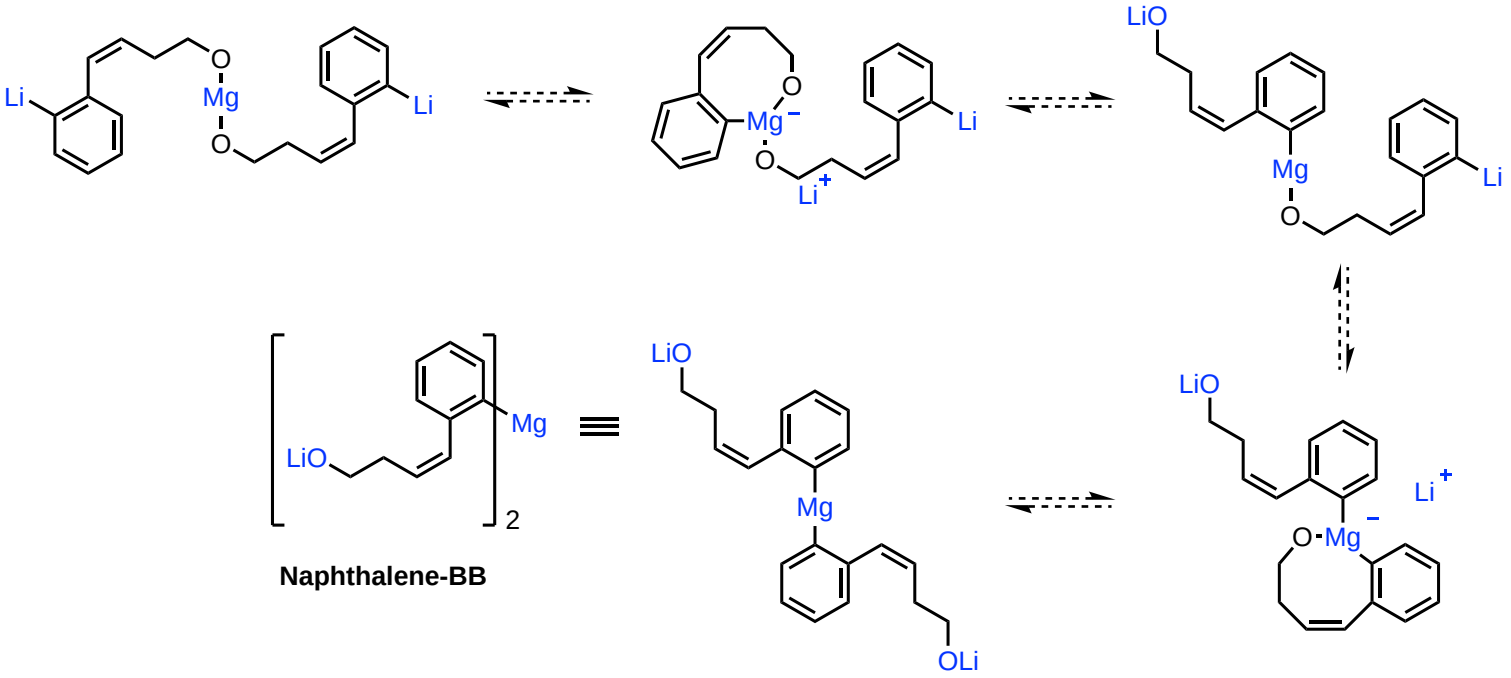


Naphthalene-2-carbaldehyde

[1,2'-Binaphthalene]-2-carbaldehyde

Synthesis of the Naphthalene Building Block

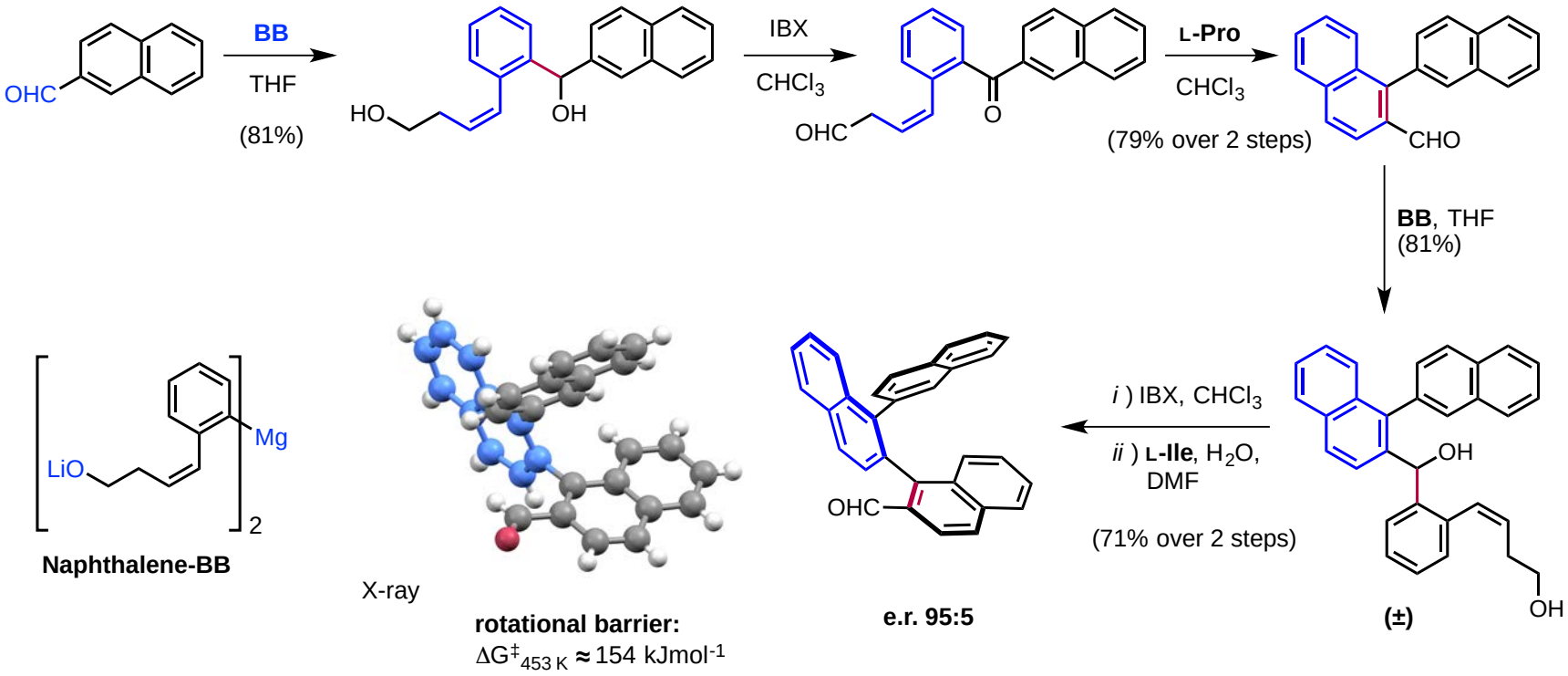




Transmetallation: S. Kato, N. Nonoyama, K. Tomimoto, T. Mase, *Tetrahedron Lett.* **2002**, *43*, 7315.

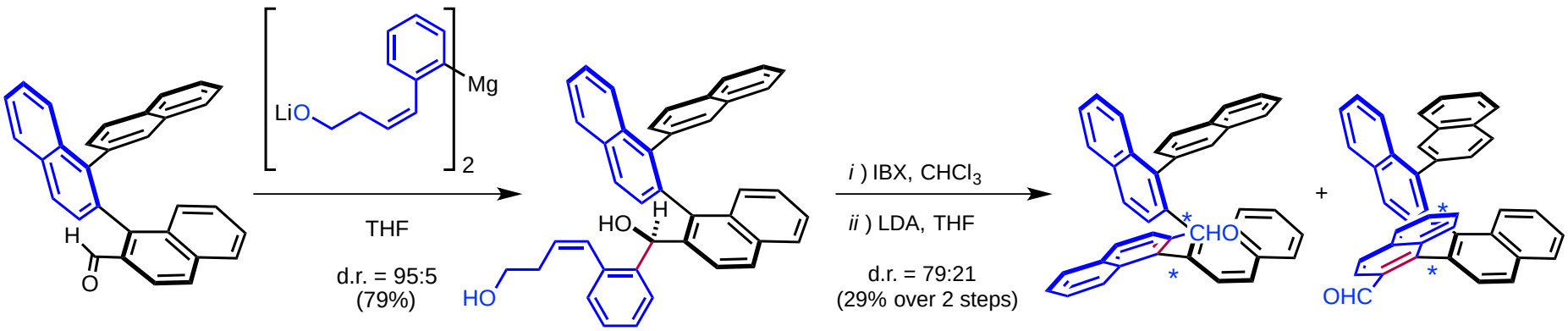
with **Dominik Lotter**
Angew. Chem. Int. Ed. **2016**, *55*, 2920.
micellar: with M. Jakobi, M. Parmentier, F. Gallou (Novartis)

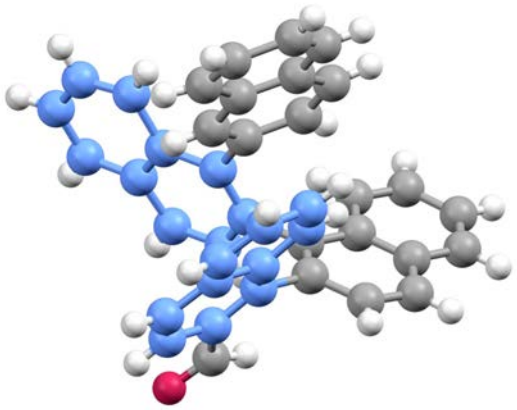
Atroposelective Oligonaphthylene Synthesis

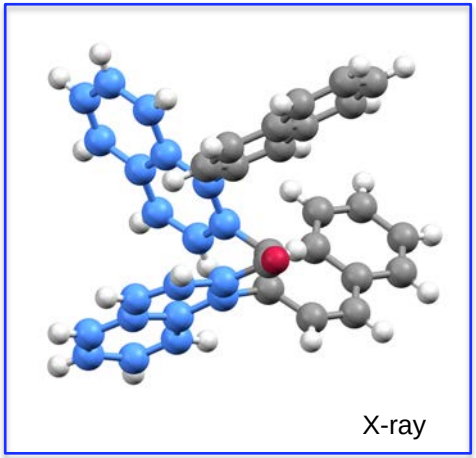


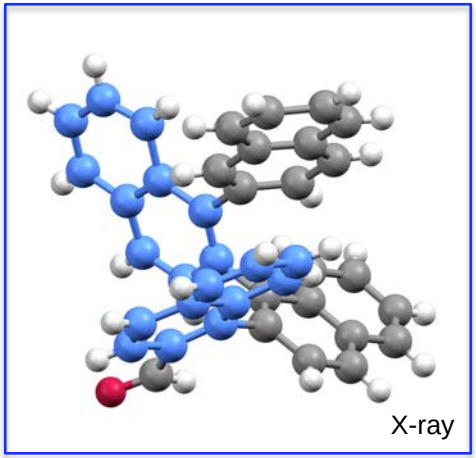
with **Dominik Lotter**
X-ray: M. Neuburger
Angew. Chem. Int. Ed. **2016**, *55*, 2920.

Oligo-1,2-naphthylene Diastereoisomers





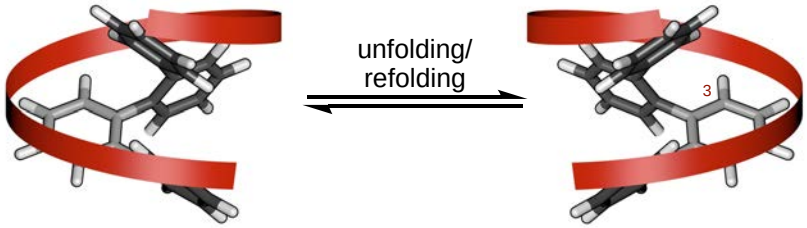




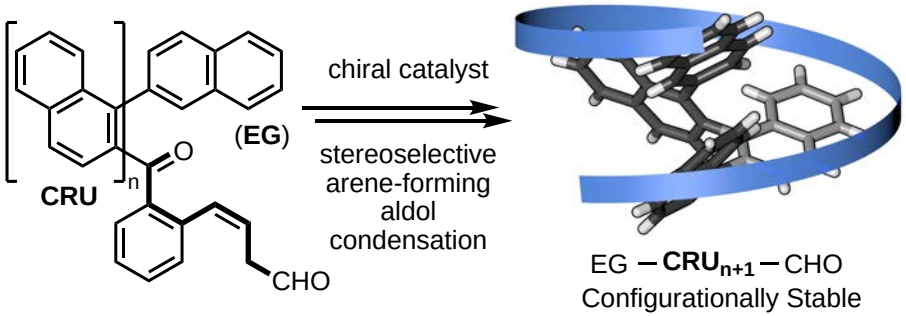
with **Dominik Lotter**
X-ray: M. Neuburger
Angew. Chem. Int. Ed. **2016**, *55*, 2920.

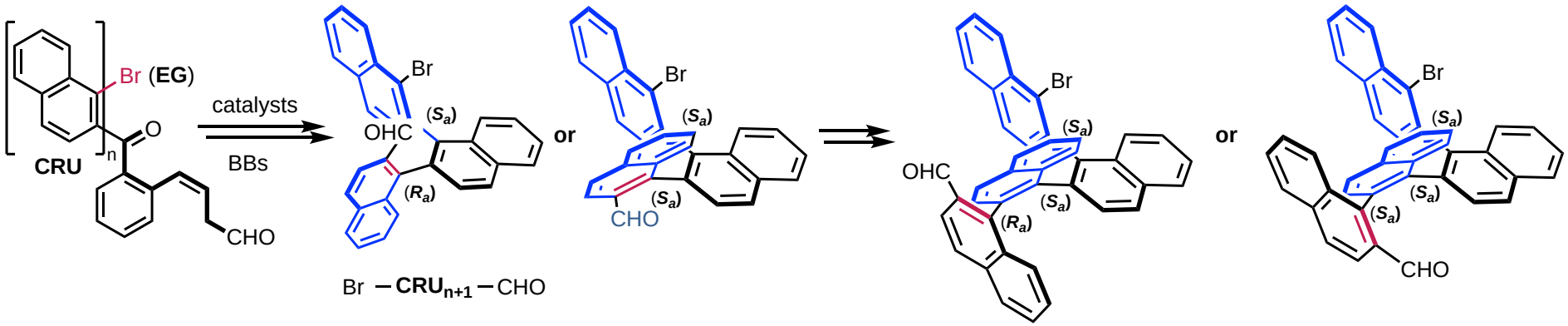
Catalyst-Controlled Stereodivergent Synthesis

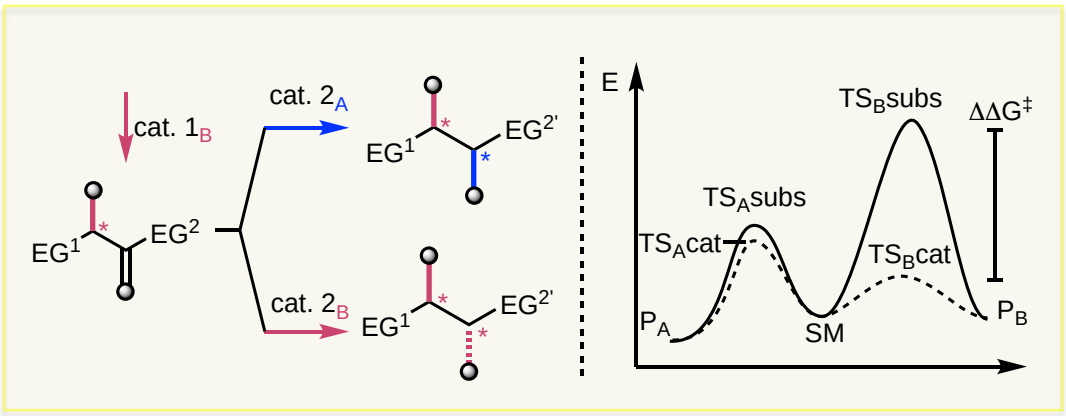
Helix-sense Inversion of *ortho*-Phenylenes



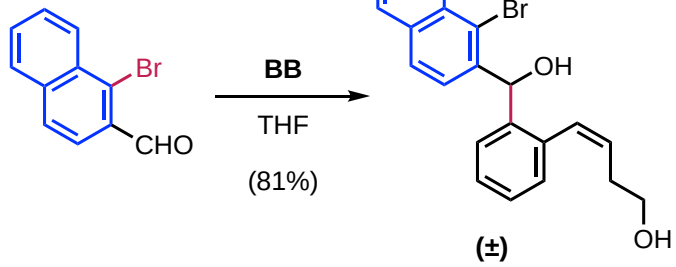
Configurational Stability of 1,2-Naphthylenes



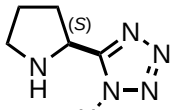




Stereodivergent Synthesis of Atropodiastereomers



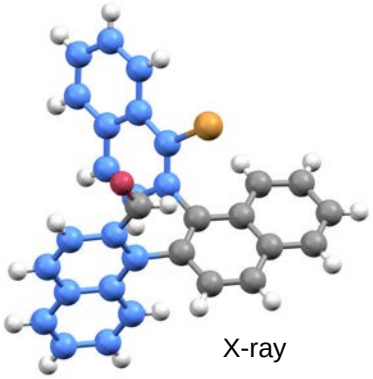
i) IBX, $CHCl_3$, DMSO
ii)



$CHCl_3$, DMF, H_2O

iii) Amberlite IRA-96, $CHCl_3$, **e.r. = 99:1**
iv) **BB**, THF, d.r. = 99:1

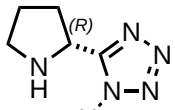
(58% yield over 4 steps)



X-ray

i) IBX, MeCN
ii$_a$) substrate diastereocontrol (KOH, $CDCl_3$, RT)
d.r. = 80:20 (65% yield)

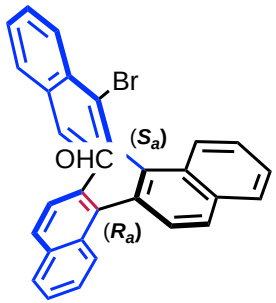
ii$_b$)

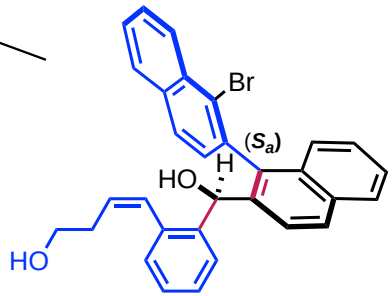


$CDCl_3$, DMF, citrate buffer

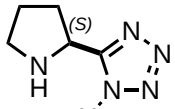
d.r. = 96:4 (R_a,S_a)

(64 % yield over 2 steps)





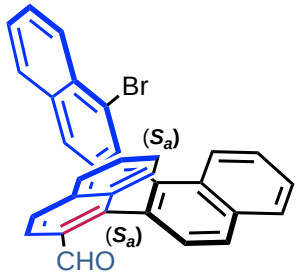
i) IBX, MeCN
ii$_c$)

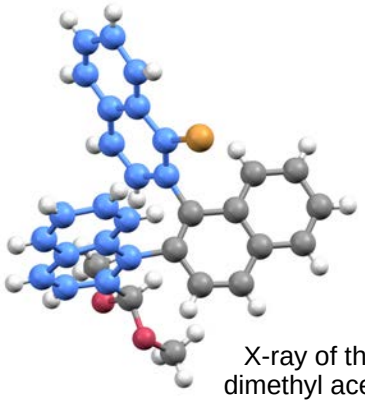


$CDCl_3$, DMF, citrate buffer

d.r. = 97:3 (S_a,S_a)

(75% yield over 2 steps)

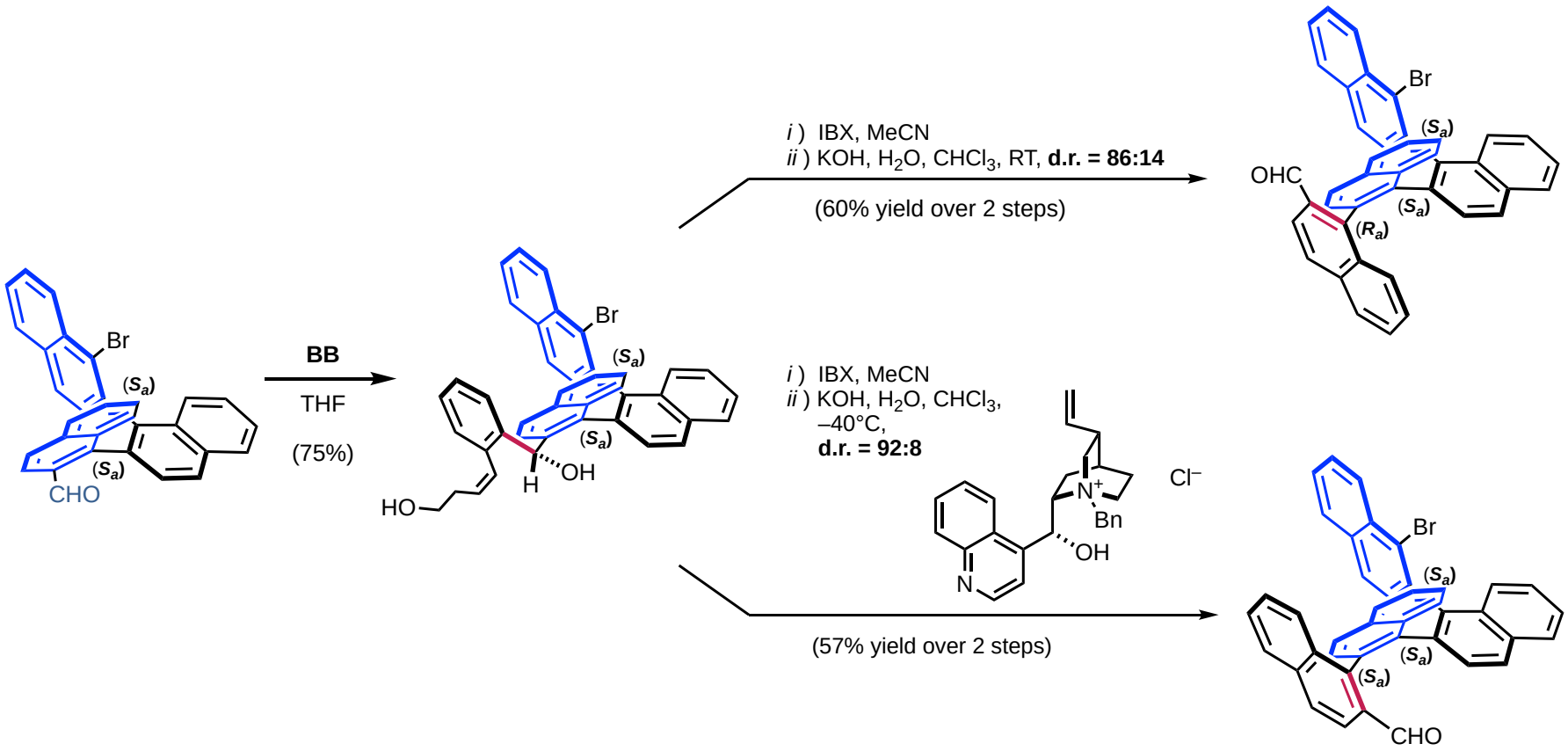




X-ray of the dimethyl acetal

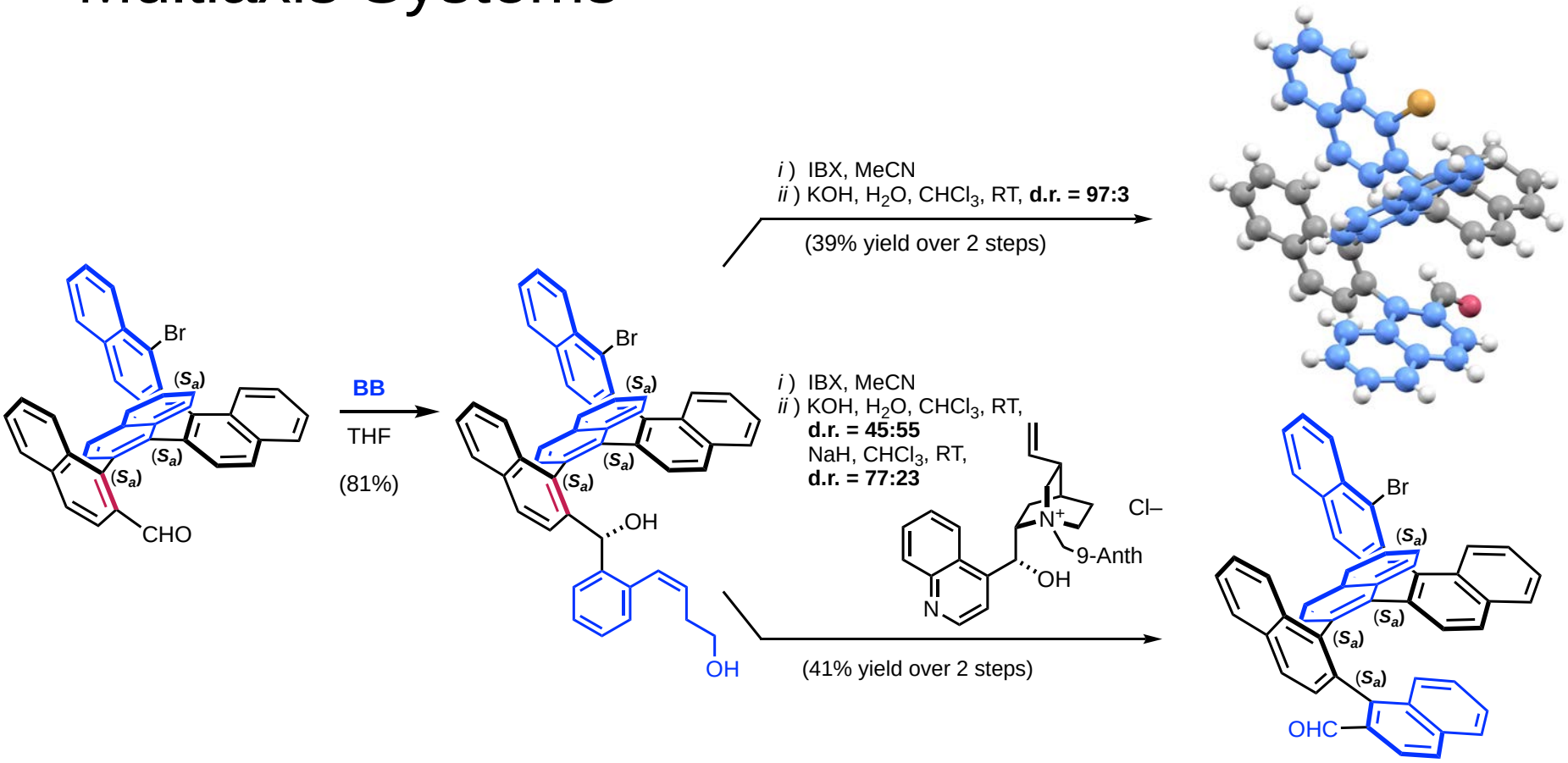
with **Dominik Lotter** and **Alessandro Castrogiovanni**, X-ray: M. Neuburger
ACS Cent. Sci. **2018**, *4*, 656.

Catalyst-Control for an Atropisomeric Stereotriad



with **Dominik Lotter** and **Alessandro Castrogiovanni**, X-ray: M. Neuburger
ACS Cent. Sci. **2018**, *4*, 656.

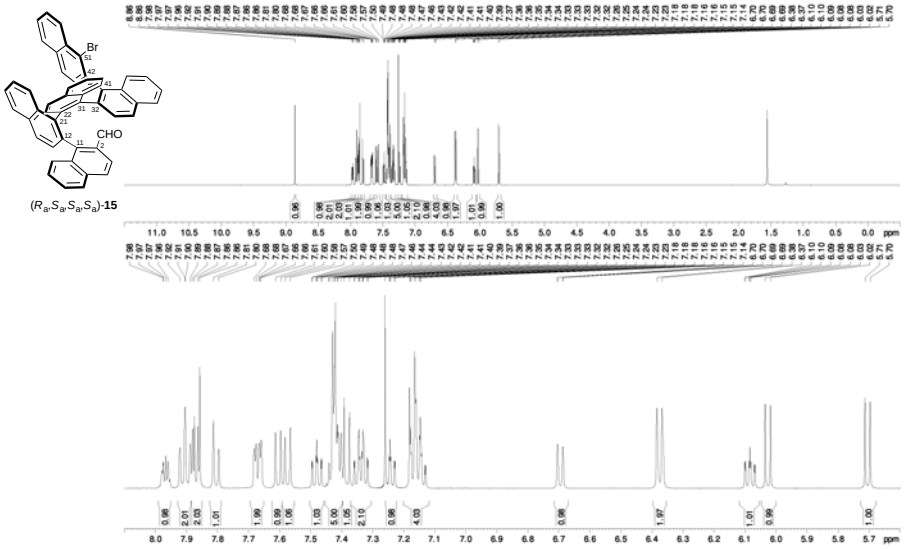
Stereodivergent Preparation of Atropisomeric Multiaxis Systems

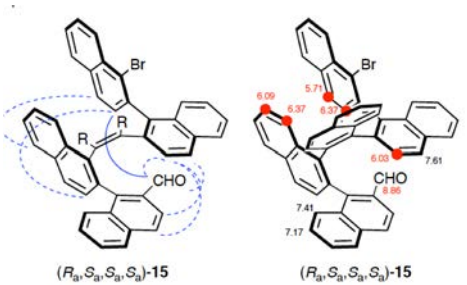


with **Dominik Lotter** and **Alessandro Castrogiovanni**, X-ray: M. Neuburger
ACS Cent. Sci. **2018**, *4*, 656.

Control over Atropisomeric Multiaxis Systems

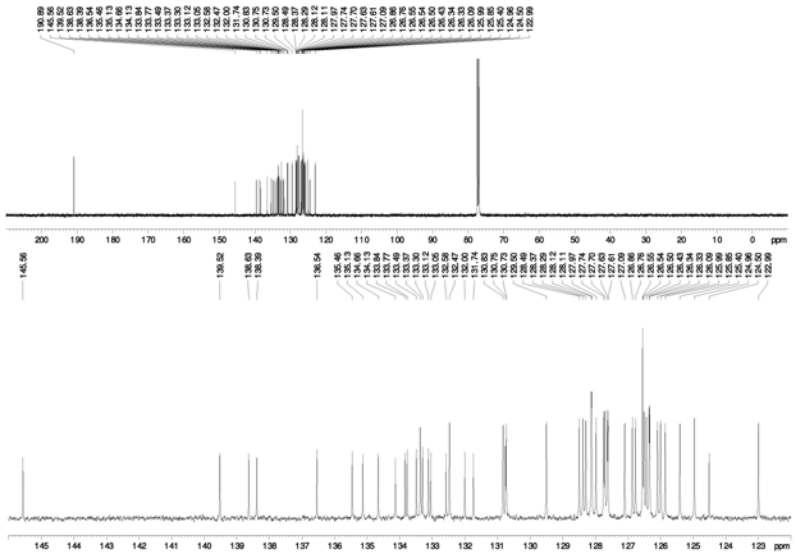
(R_a,S_a,S_a,S_a)-15, ^{1}H NMR (500 MHz, $CDCl_3$):

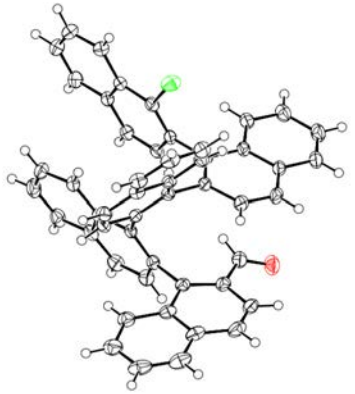




C23*H*), 7.37–7.31 (2H, m, C7*H*, C27*H*), 7.24 (1H, ddd, ^3J 8.1, 7.0, ^4J 1.1, C17*H*), 7.19–7.12 (4H, m, C8*H*, C13*H*, C28*H*, C38*H*), 6.70 (1H, d, ^3J 8.6, C39*H*), 6.40–6.36 (2H, m, C19*H*, C44*H*), 6.08 (1H, ddd, ^3J 8.4, 6.9, ^4J 1.4, C18*H*), 6.03 (1H, d, ^3J 8.5, C33*H*), 5.70 (1H, d, ^3J 8.2, C43*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 190.9 (*C1*), 145.6 (*C11*), 139.5 (*C21*), 138.6 (*C41*), 138.4 (*C31*), 136.5 (*C42*), 135.5 (*C5*), 135.1 (*C20*), 134.7 (*C32*), 134.1 (*C22*), 133.8 (*C30*), 133.8 (*C45*), 133.5 (*C15*), 133.4 (*C33*), 133.3 (*C35*), 133.1 (*C25*), 133.0 (*C2*), 132.6 (*C40*), 132.5 (*C23*), 132.0 (*C12*), 131.7 (*C50*), 130.8 (*C13*), 130.8 (*C10*), 130.7 (*C43*), 129.5 (*C29*), 128.5 (*C9*), 128.4 (*C4*), 128.3 (*C7*), 128.1 (*C46*), 128.1 (*C6*), 128.0 (*C36*), 127.7 (*C49*), 127.7 (*C14*), 127.6 (*C16*), 127.6 (*C26*), 127.1 (*C19*), 126.9 (*C48*), 126.8 (*C34*), 126.5 (*C37*, *C18*), 126.5 (*C24*), 126.4 (*C39*), 126.3 (*C38*), 126.3 (*C47*),

(R_a,S_a,S_a,S_a)-15, ^{13}C NMR (126 MHz, $CDCl_3$):

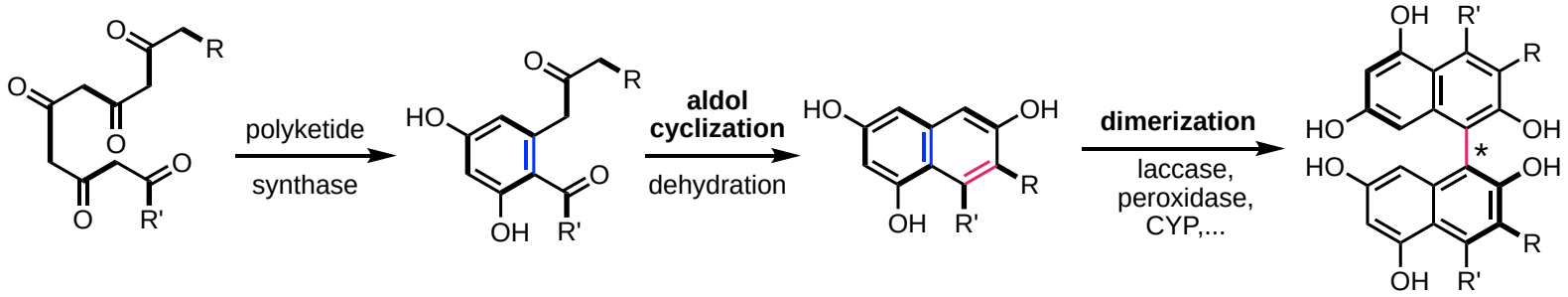




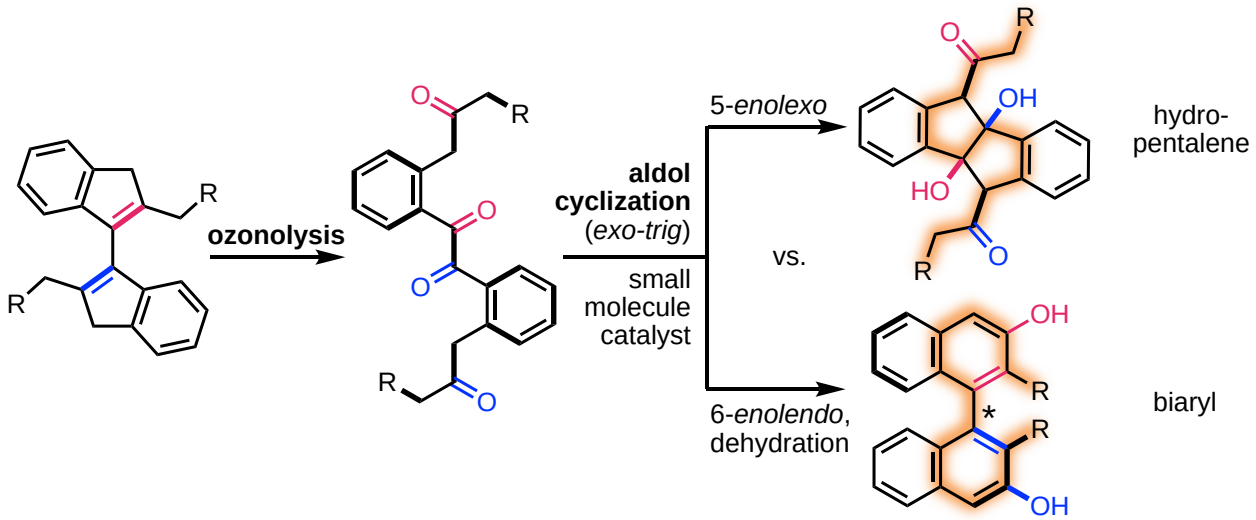
with **Dominik Lotter** and **Alessandro Castrogiovanni**, X-ray: M. Neuburger
ACS Cent. Sci. **2018**, *4*, 656.

Noncanonical Polyketide Cyclization

Biosynthesis of Atropisomeric Polyketides



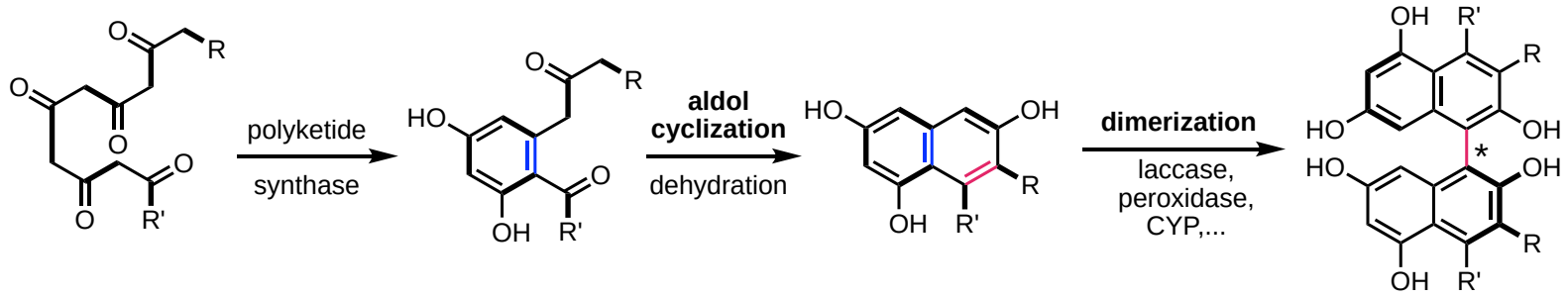
Catalytic Noncanonical Polyketide Cyclization



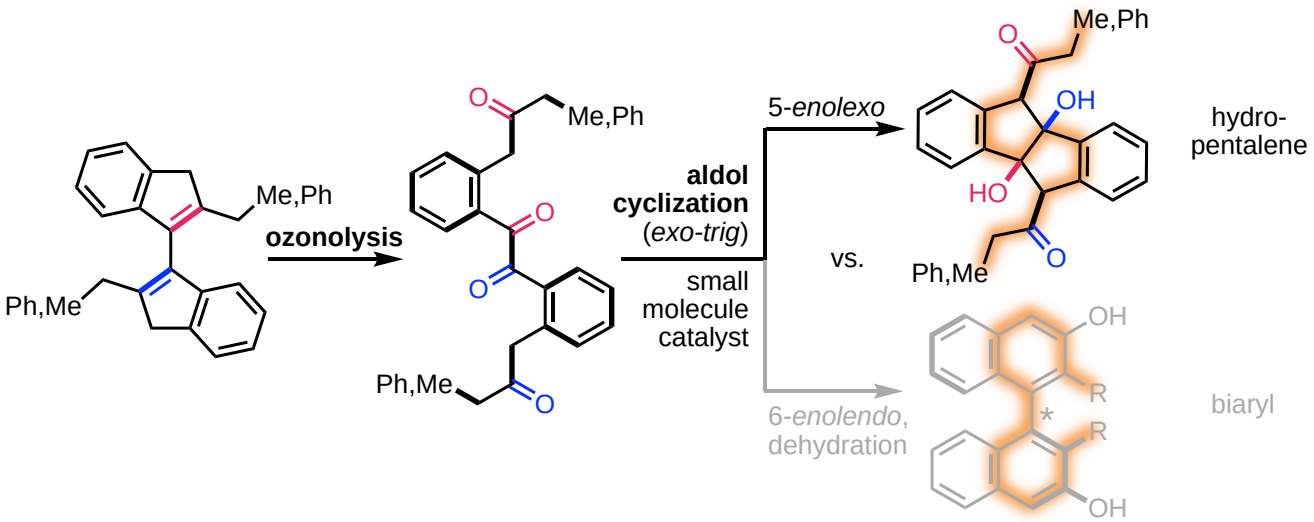
with **Reto M. Witzig** and **Vincent C. Fäseke**
submitted

Noncanonical Polyketide Cyclization

Biosynthesis of Atropisomeric Polyketides



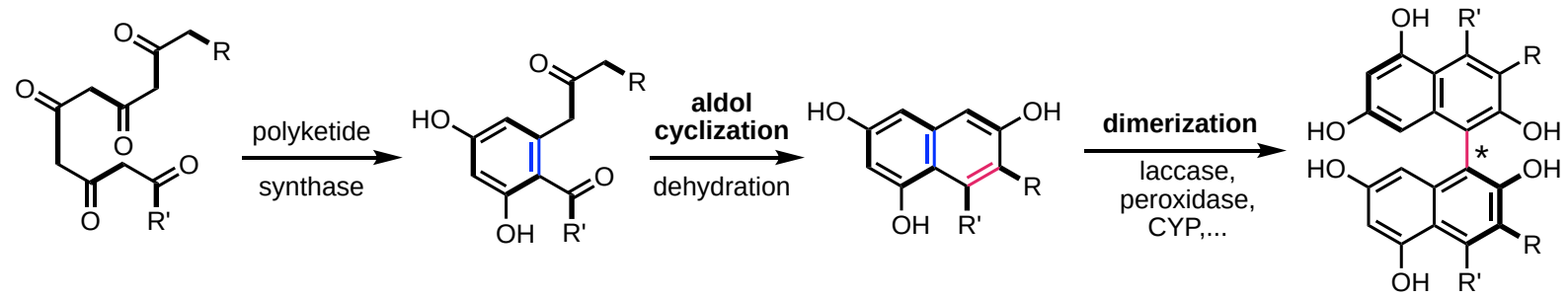
Catalytic Noncanonical Polyketide Cyclization



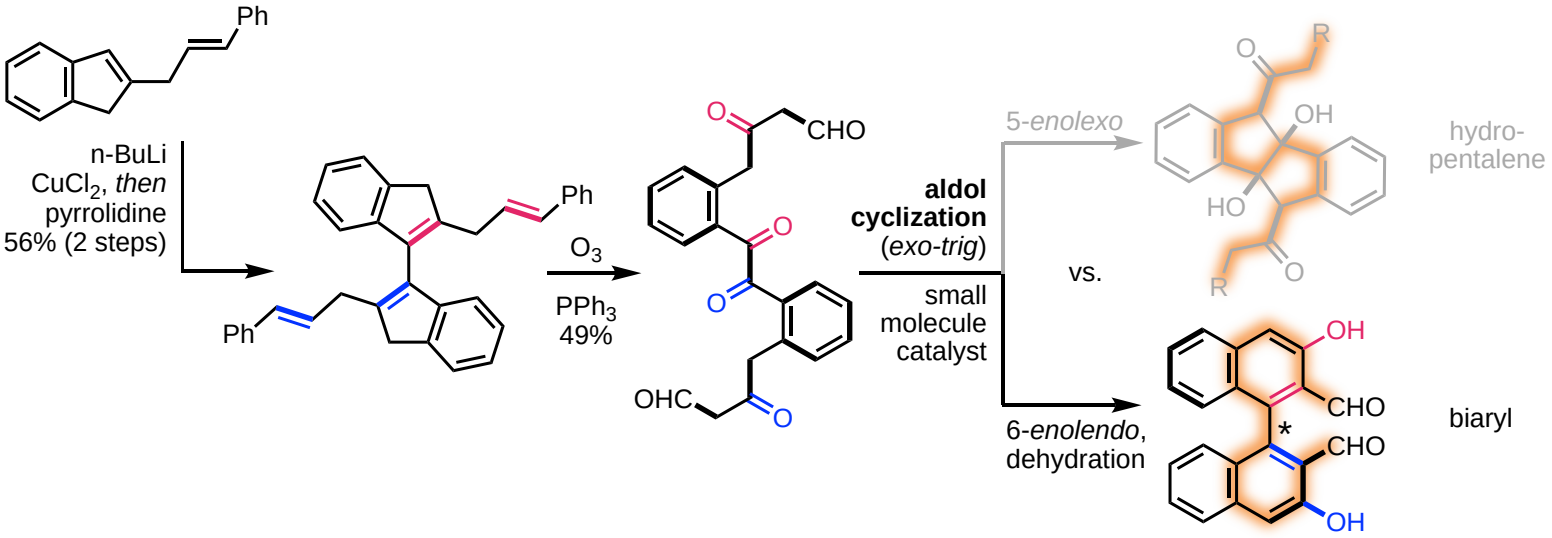
with **Reto M. Witzig** and **Vincent C. Fäseke**
submitted

Noncanonical Polyketide Cyclization

Biosynthesis of Atropisomeric Polyketides

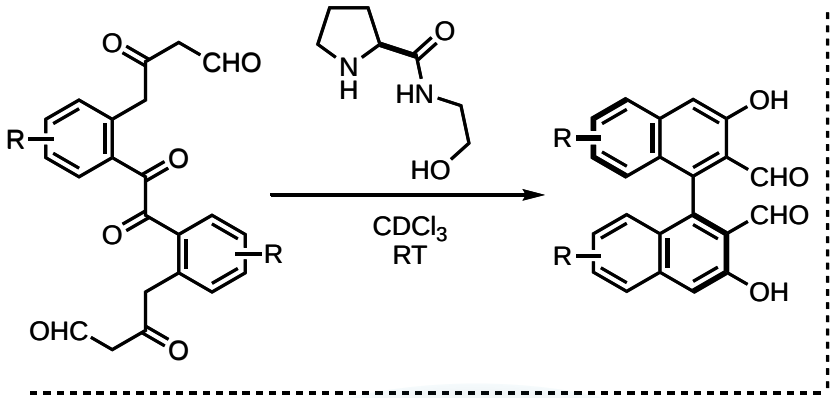


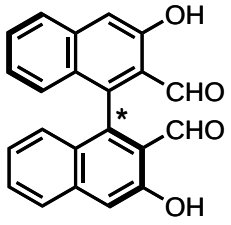
Catalytic Noncanonical Polyketide Cyclization



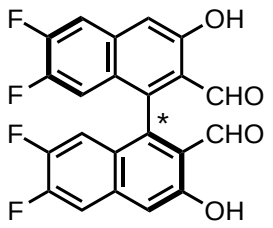
with **Reto M. Witzig** and **Vincent C. Fäseke**
submitted

Scope



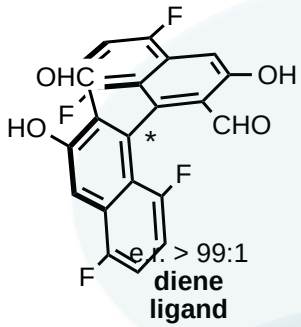


82% yield
e.r. 95:5
(S_a) by X-ray

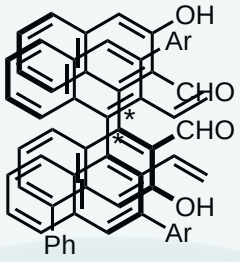


61% yield
e.r. 92:8

recryst. (e.r. > 99:1), Tf_2O, Et_3N, CH_2Cl_2
then $ArB(OH)_2$, $Pd(AcO)_2$, PPh_3,
K_2HPO_4, THF, 84 % (2 steps)

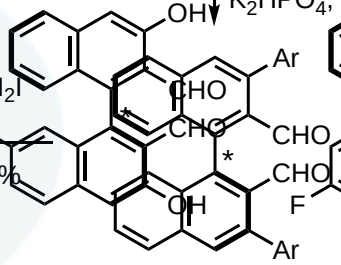


e.r. > 99:1
diene ligand
24% yield
e.r. 98:2
(S_a) by X-ray



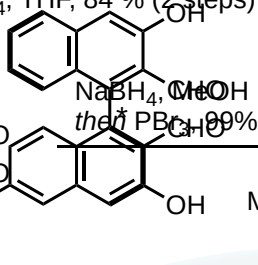
60% yield
e.r. 91:9

Ph_3PCH_2I
t-BuOK
MeO
THF, 71%



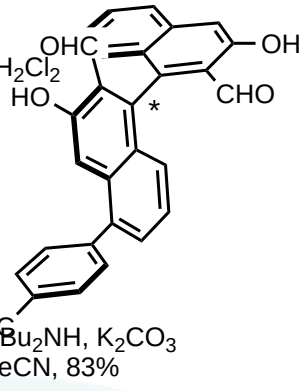
93% yield
e.r. 90:10
(S_a) by X-ray

Ar = 3,4,5-trifluorophenyl



85% yield
e.r. 94:6

$NaBH_4$, MeOH
then PBr_3, 99%

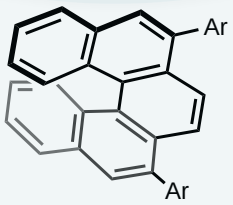


Ir-Bu_2NH, K_2CO_3
MeCN, 83%

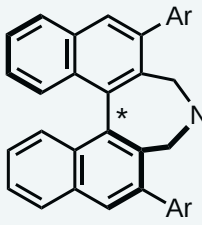
80% yield
e.r. 90:10

$NaBH_4$, MeOH,
then PBr_3

LiHMDS, HMPA,
THF, 66% (3 steps)



e.r. = 98:2
[5]helicene
$G^{\ddagger}_{333\ K}$ =109 kJmol^{-1}

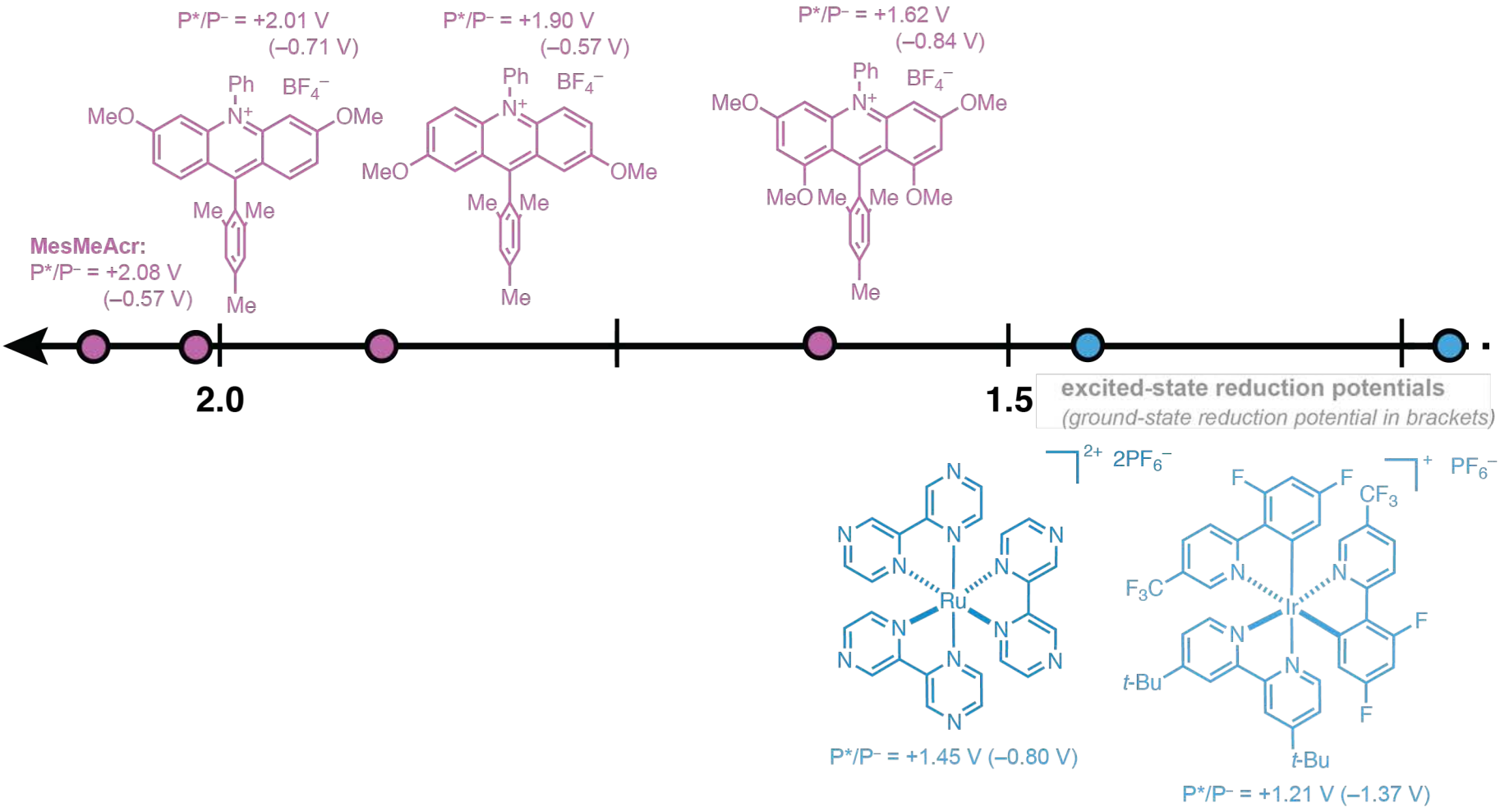


e.r. > 99:1
Maruoka ion-pairing catalyst

Configurational Stability of [5]Helicenes: P. Ravat, R. Hinkelmann, D. Steinebrunner, A. Prescimone, I. Bodoky, M. Juríček *Org. Lett.* **2017**, *19*, 3707.
T. Ooi, K. Maruoka, *Angew. Chem. Int. Ed.* **2007**, 4222.

with **Reto M. Witzig** and **Vincent C. Fäseke**
X-ray: M. Neuburger
submitted

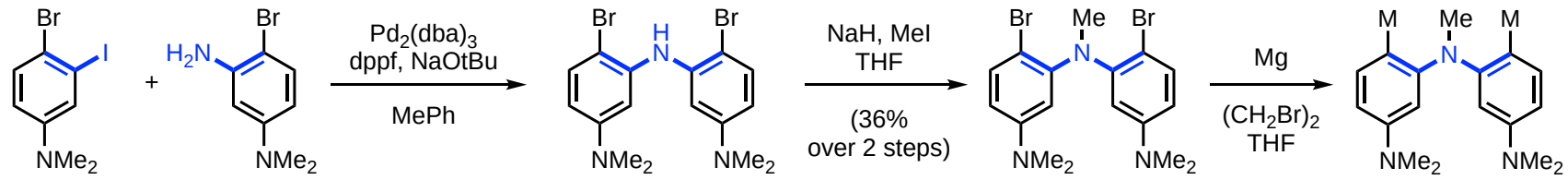
Acridinium Photoredox Catalysts

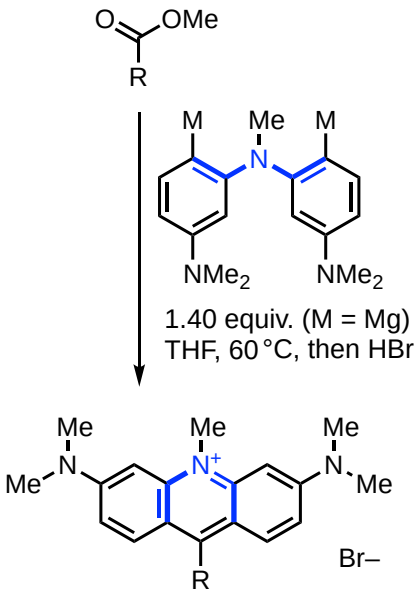


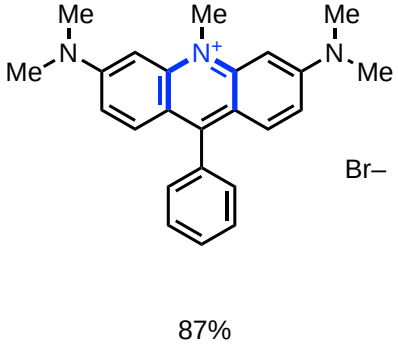
Pioneering work on acridinium photocatalysis: S. Fukuzumi and D. Nicewicz
A. Joshi-Pangu, F. Lévesque, H. G. Roth, S. F. Oliver, L.-C. Campeau, D.Nicewicz, D. A. DiRocco, *J. Org. Chem.* **2016**, 7244; and references therein.

with **Christian Fischer**
Angew. Chem. Int. Ed. **2018**, *57*, 2436.

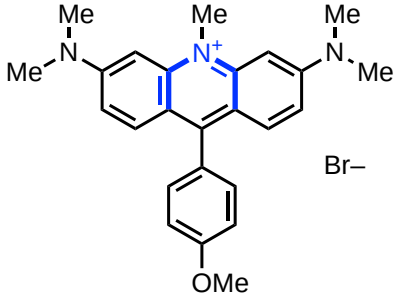
Synthesis of Aminoacridinium Dyes



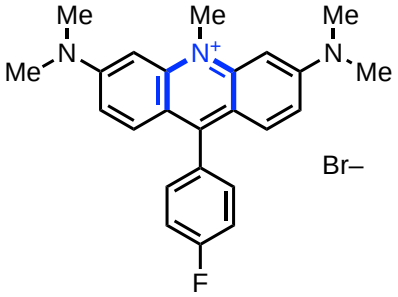




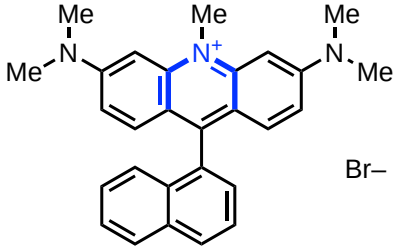
87%



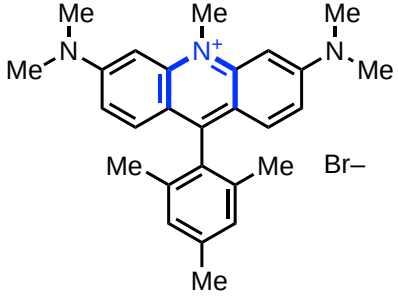
64%



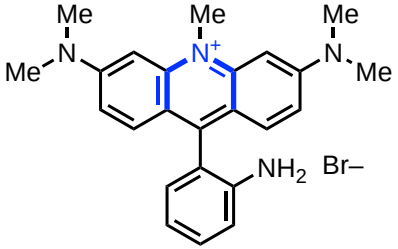
84%



75%



56%
$E_{1/2}$ (C*/C$^-$) = 1.25 V
$E_{1/2}$ (C/C$^-$) = –1.15 V
τ = 2.2 ns



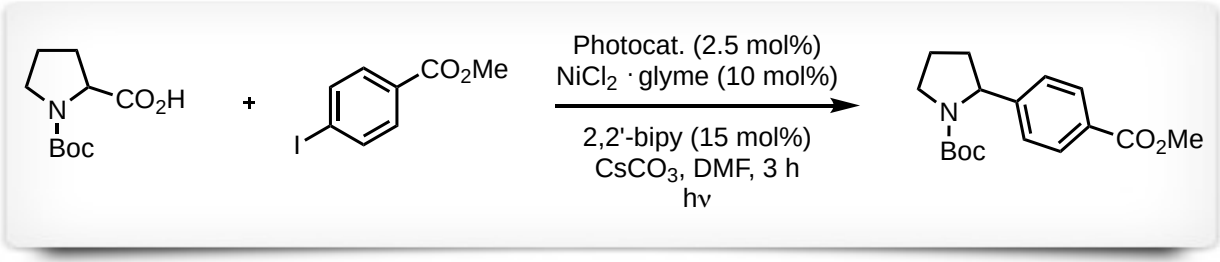
73%
(2.40 equiv.)

with **Christian Fischer**

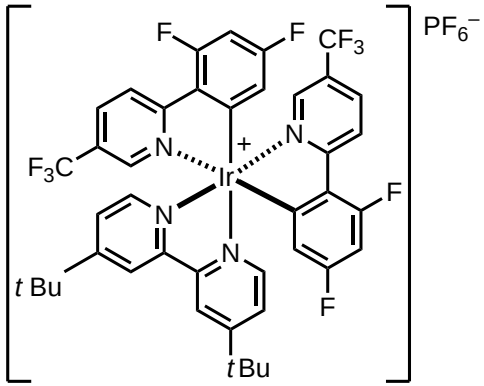
Seminal acridinium synthesis: M. Cérésole (BASF), DE-44002, **1887**.

Angew. Chem. Int. Ed. **2018**, *57*, 2436.

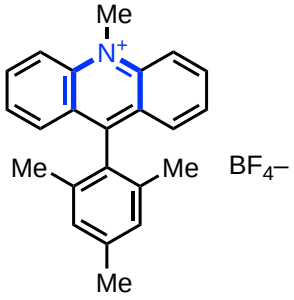
Organic Photoredox – Nickel Dual Catalysis



Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle, D. W. C. MacMillan, *Science* **2014**, *345*, 437.

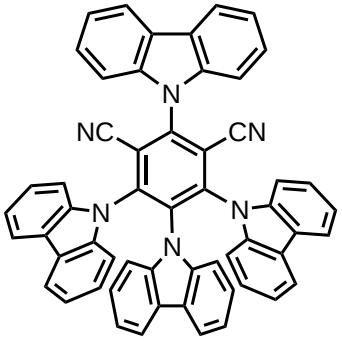


$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$
$E_{1/2}$ (C*/C⁻) = +1.21 V
$E_{1/2}$ (C/C⁻) = –1.37 V



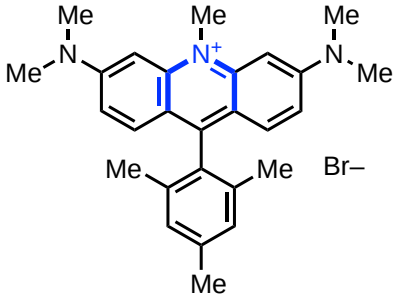
MesMeAcr ·BF_4 (Fukuzumi)
$E_{1/2}$ (C*/C⁻) = +2.06 V
$E_{1/2}$ (C/C⁻) = –1.15 V

0% yield



4CzIPN (Zhang)
$E_{1/2}$ (C*/C⁻) = +1.35 V
$E_{1/2}$ (C/C⁻) = –1.21 V

78% yield



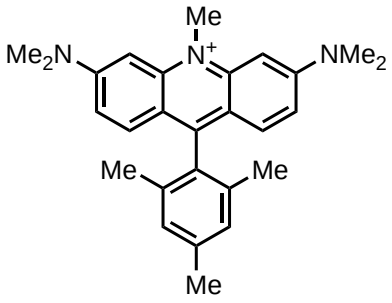
$E_{1/2}$ (C*/C⁻) = +1.25 V
$E_{1/2}$ (C/C⁻) = –1.15 V

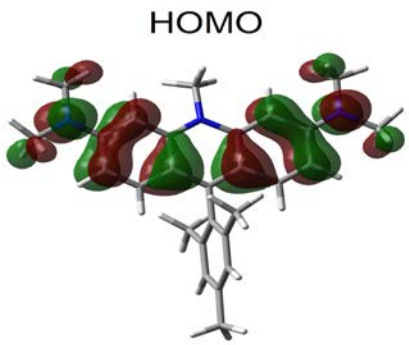
86% yield

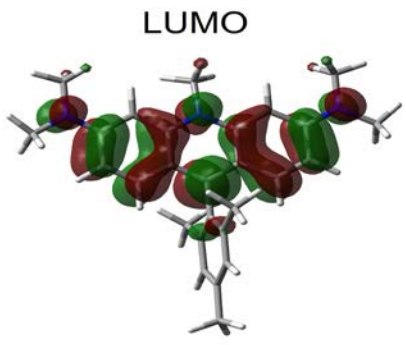
MacMillan, Yoon, Stephenson, Rovis, Molander, Rueping, Sammis, Nishibayashi, Doyle, Reiser, Ooi, Weix, Pandey, Koike, Glorius, Toste, Jamison, Akita, Knowles, Hyster, Gouverneur, Sanford, Baran, Goddard, Xia, Wenger, Meggers, Waser, Aggarwal, Fors, Nevado, Noël, Bode, Kokotos, Buchwald,...
Early work: Kellogg, Fukuzumi, Tanaka, Pac, Deronzier, Okada, Osawa,...
Organic: Nicewicz, Melchiorre, König, Gilmour, Zhang, Lakhdar, Zeitler, Tlili, DiRocco,...

with **Christian Fischer**
Angew. Chem. Int. Ed. **2018**, *57*, 2436.

Aminoacridinium Photocatalysts

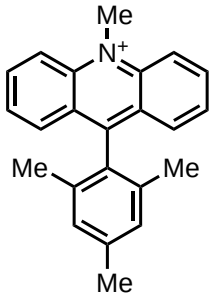


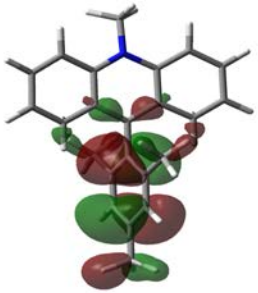


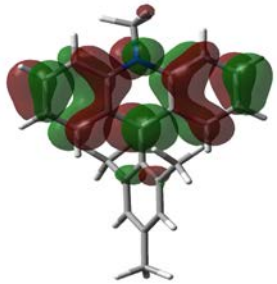


π-π* lowest energetic electronic transition

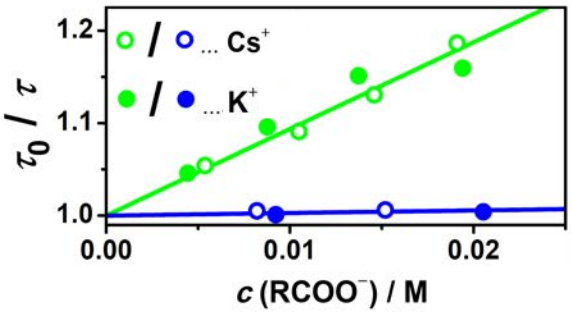
Fukuzumi catalyst







CT lowest energetic electronic transition



Green: Diaminoacridinium
Blue: Eosin Y
(with K^+/Cs^+ salts of Boc-L-Pro in DMF)

Diaminoacridinium

$E_{1/2}$ (P/P⁻) = –1.15 V
$E_{1/2}$ (P*/P⁻) = +1.25 V
E_T = 1.91 eV
τ_S = 1.59 ns
τ_T = 330 µs
Φ_{ISC} = 7%

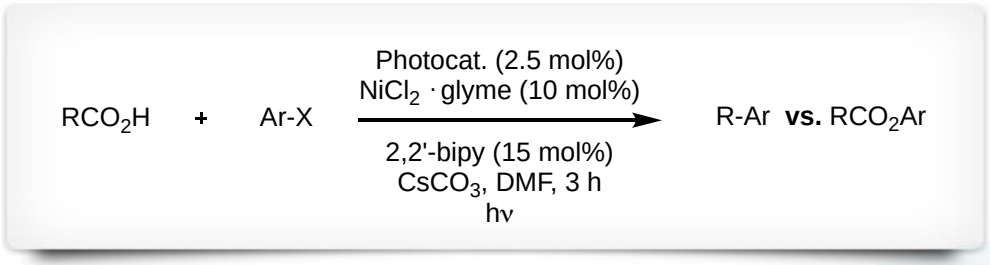
in MeCN, vs. SCE (τ_S in DMF)

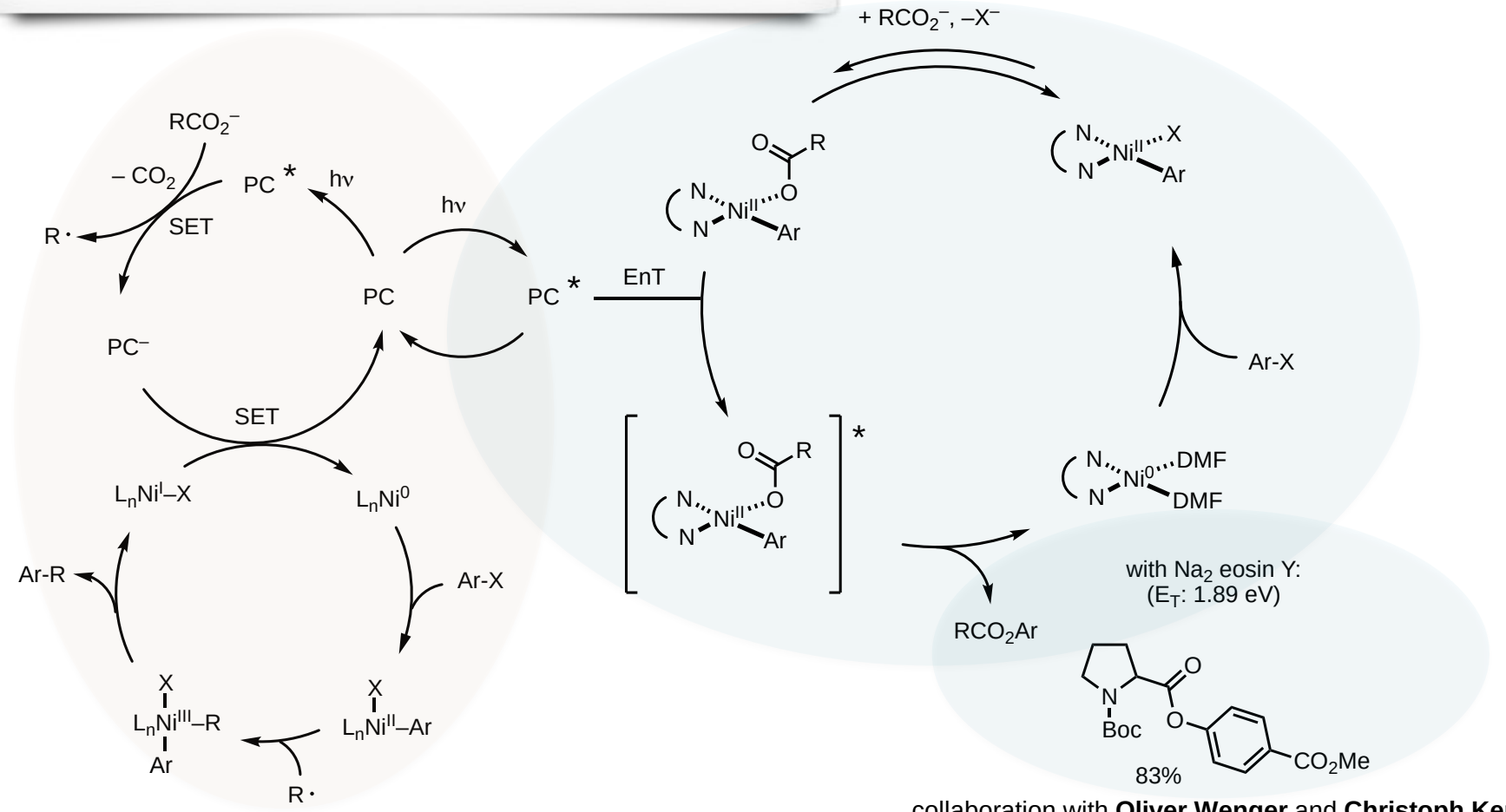
Eosin Y

$E_{1/2}$ (P/P⁻) = –1.06 V
$E_{1/2}$ (P*/P⁻) = +1.25 V
E_T = 1.89 eV
τ_S = 4.98 ns
τ_T = 24 µs
Φ_{ISC} = 80%

collaboration with **Oliver Wenger** and **Christoph Kerzig**,
with **Christian Fischer** and **Bouthayna Zilate**
submitted

Disparate Photochemical Pathways

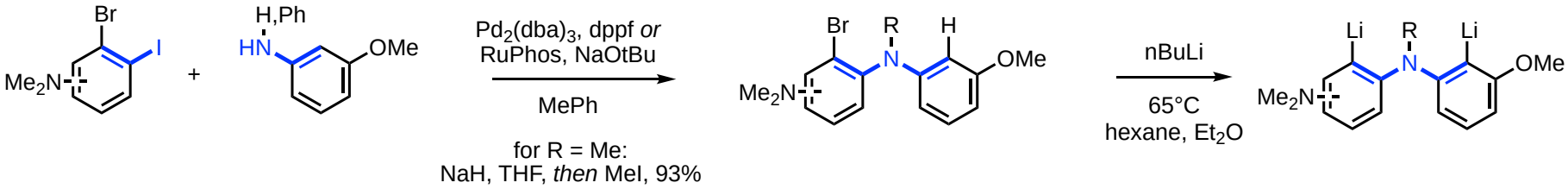


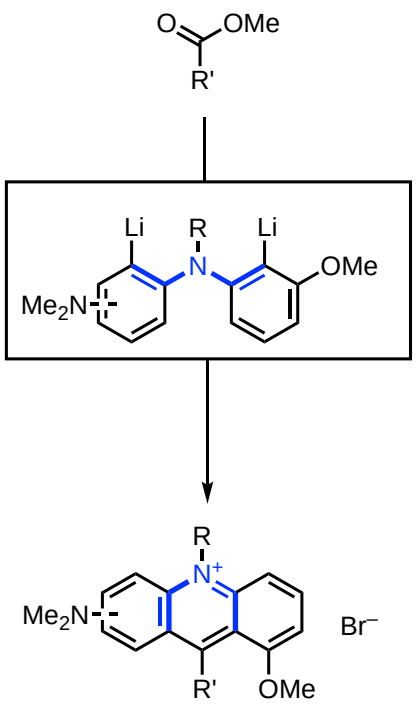


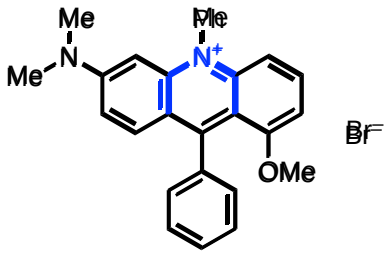
Photosensitized organometallic intermediates: E. R. Welin, C. Le, D. M. Arias-Rotondo, J. K. McCusker, D. W. C. MacMillan, *Science* **2017**, *355*, 380.

collaboration with **Oliver Wenger** and **Christoph Kerzig**, with **Christian Fischer** and **Bouthayna Zilate** experimental support by **Thomas Buchholz**, *submitted*

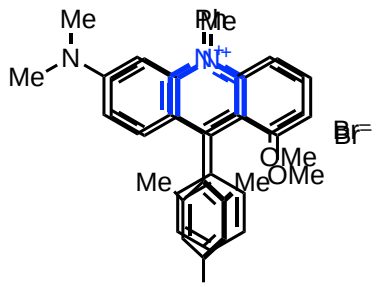
Modular Synthesis of Acridinium Fluorophores



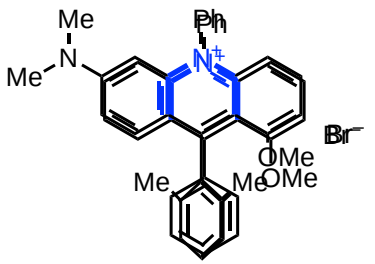




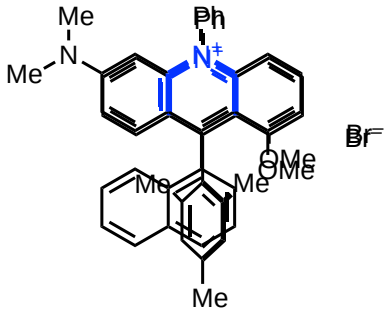
98%
τ = 4.5 ns
91%



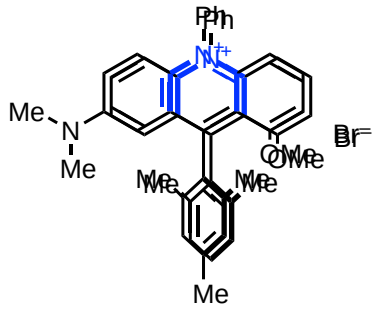
53%
τ = 16 ns
76%



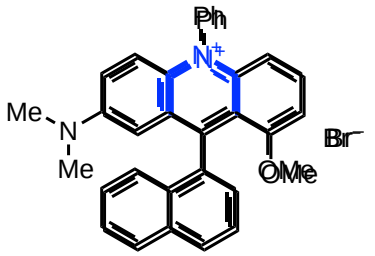
78%
78%



95%
71%
$\Delta G^{\ddagger}_{403\ K} \approx 130\ kJmol^{-1}$



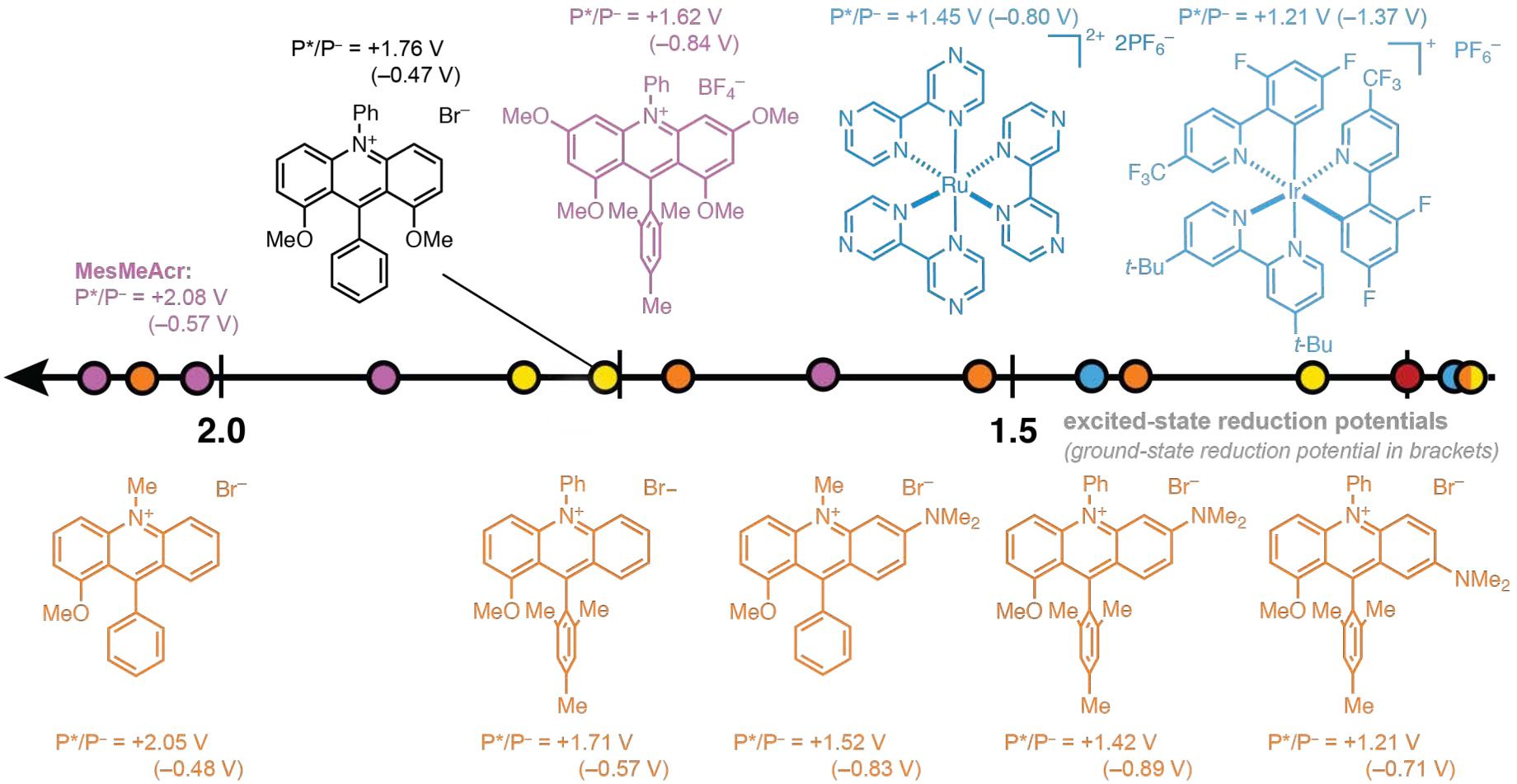
78%
71%



94%
74%
$\Delta G^{\ddagger}_{423\ K} \approx 135\ kJmol^{-1}$
$\Delta G^{\ddagger}_{333\ K} \approx 105\ kJmol^{-1}$

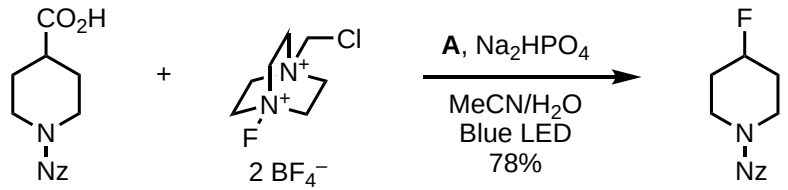
collaboration with **Oliver Wenger** and **Christoph Kerzig**,
with **Christian Fischer** and **Bouthayna Zilate**
patent filed, soon commercialized by Solvias, submitted

Modular Synthesis of Acridinium Fluorophores



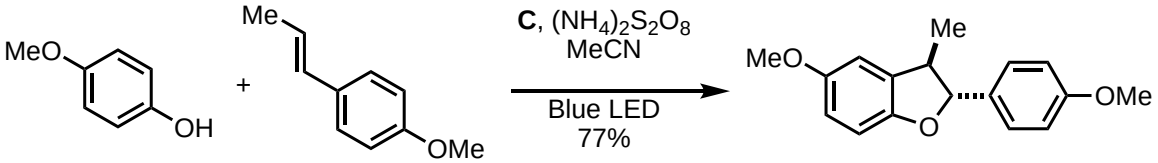
collaboration with **Oliver Wenger** and **Christoph Kerzig**,
with **Christian Fischer** and **Bouthayna Zilate**
patent filed, soon commercialized by Solvias, submitted

Tailored Organophotoredox-Catalysts

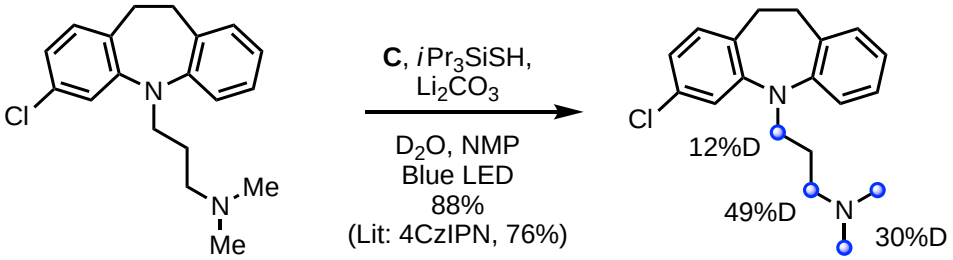


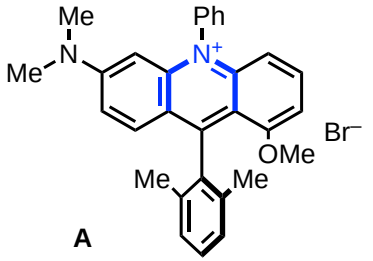
(Lit.: $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$)

(Lit.: $Ru(bpz)_3(PF_6)_2$)

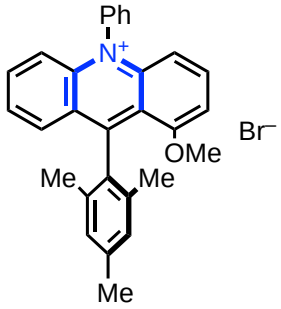


(Lit.: $Ru(bpz)_3(PF_6)_2$)

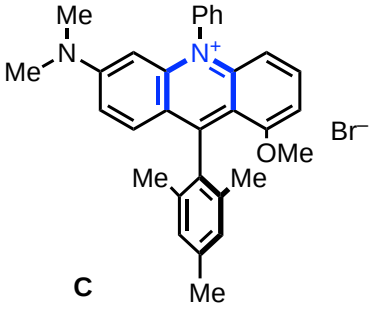




A



B



C

S. Ventre, F. R. Petronijevic, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2015**, 5654; T. R. Blum, Y. Zhu, S. A. Nordeen, T. P. Yoon, *Angew. Chem. Int. Ed.* **2014**, 11056; Y. Y. Loh, K. Nagao, A. J. Hoover, D. Hesk, N. R. Rivera, S. L. Colletti, I. W. Davies, D. W. C. MacMillan, *Science* **2017**, *358*, 1182.

with **O. Wenger, C. Kerzig, C. Fischer, B. Zilate**
submitted

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Dainis Kaldre
Frederic Bourgeois
Dragan Miladinov
Rodolphe Beaud

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M. Pfeffer (MS), S. Mittelheisser (MS)

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