REACCIÓN DE DIELS-ALDER

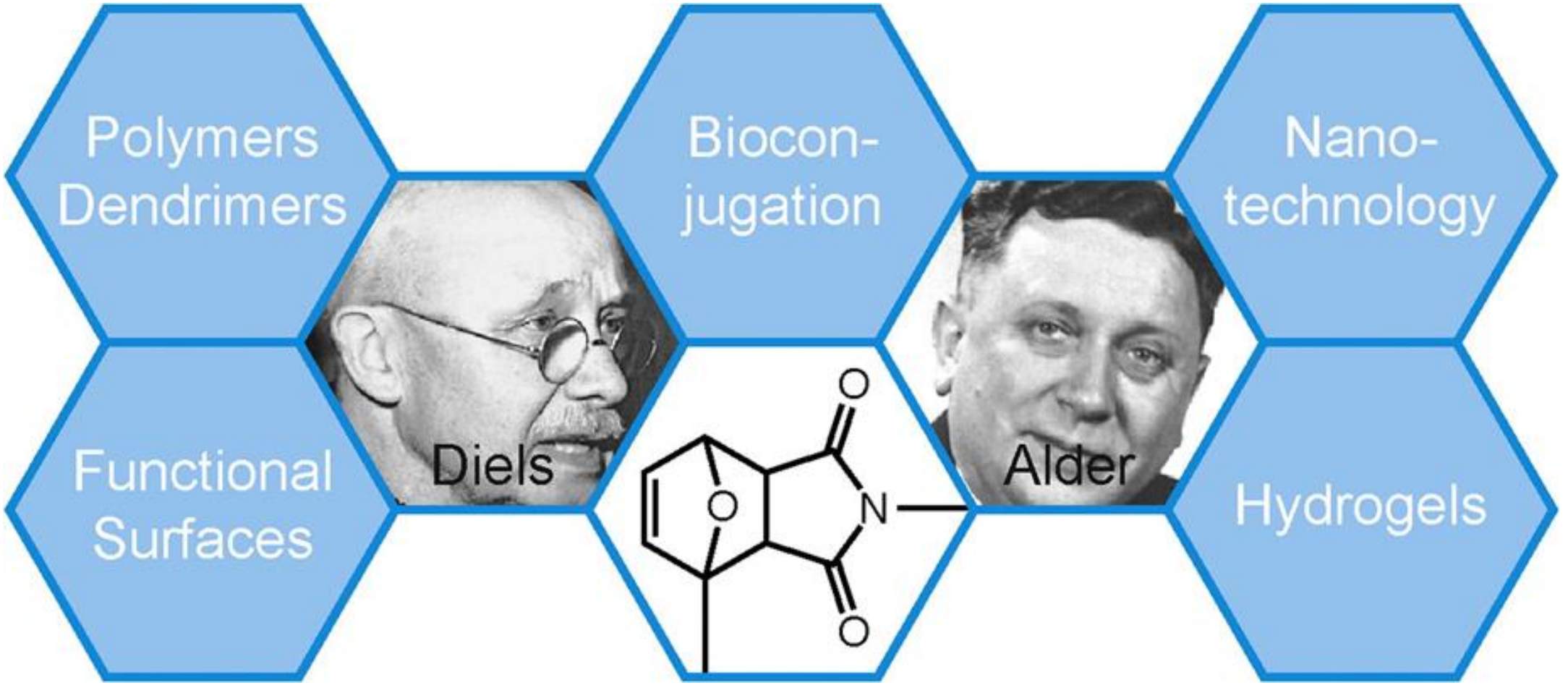
Otto Paul Hermann Diels
Tutor de Kurt Alder

1876-1954

Kurt Alder
Estudiante de doctorado

1902-1958

Chemical & Engineering News, December 4, 1950


Polymers
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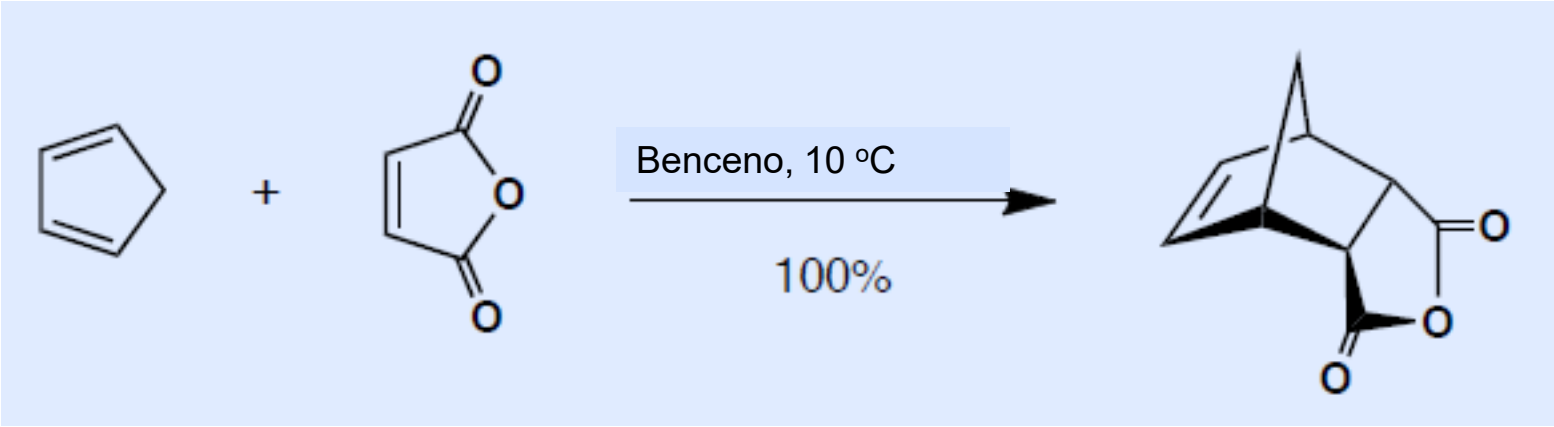
EL DESCUBRIMIENTO DE LA REACCIÓN DE DIELS-ALDER

El trabajo de Diels y Alder se describe en una serie de 28 artículos publicados en *Justus Liebigs Annalen der Chemie* y *Berichte der deutschen chemischen Gesellschaft* de 1928 a 1937. Los primeros 19 artículos fueron escritos por Diels y Alder, mientras que los artículos posteriores fueron escritos por Diels y varios colaboradores



Diels, O.; Alder, K."Synthesen in der hydroaromatischen Reihe, I". Justus Liebigs Annalen der Chemie. **1928**, *460: 98–122.*

III. Fraktion (2,2 g), Siedep.$_{13}$ = 160°. Erstarrt beim Impfen mit o-Acetyl-o-chlor-p-kresol (XXIV, S. 76) und kann durch den Mischschmelzp. 91° mit dem reinen Produkt (S. 84) als solches identifiziert werden.

Es wurden also gebildet: etwa 40 Proc. des theoretisch möglichen o-Acetyl-m-kresols und etwa 60 Proc. o-Acetyl-o-chlor-p-kresol.

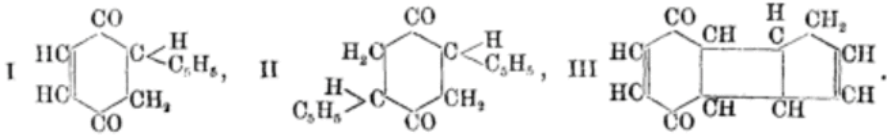
Synthesen in der hydroaromatischen Reihe;

von *Otto Diels* und *Kurt Alder.*

I. Mitteilung:
Anlagerungen von „Di-en"-kohlenwasserstoffen.

(Eingelaufen am 13. Dezember 1927.)

In einer Untersuchung über Cyclopentadienchinon berichtet W. Albrecht[1]) über die Anlagerung von Cyclopentadien an p-Chinon. Den dabei entstehenden, von ihm als „Cyclopentadienchinon" und „Di-cyclopentadienchinon" bezeichneten Verbindungen legt er die Formeln I und II bei:



Er nimmt also an, daß sich Cyclopentadien mit der *Methylengruppe* an die Doppelbindungen des Chinons anlagert und daß die Reaktionsprodukte *noch beide Doppelbindungen des Cyclopentadiens* enthalten.

H. Staudinger[2]) neigt dagegen der Ansicht zu, daß sich Chinon und Cyclopentadien zu einem *Cyclo-butan-deri-*

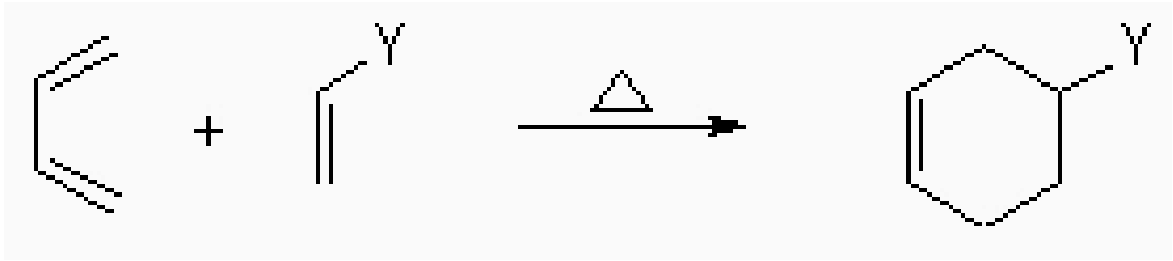
[1]) A. **348**, 31 (1906). — Walter Albrecht, Über Cyclopentadienchinone. **Inauguraldissertation, München 1902.**

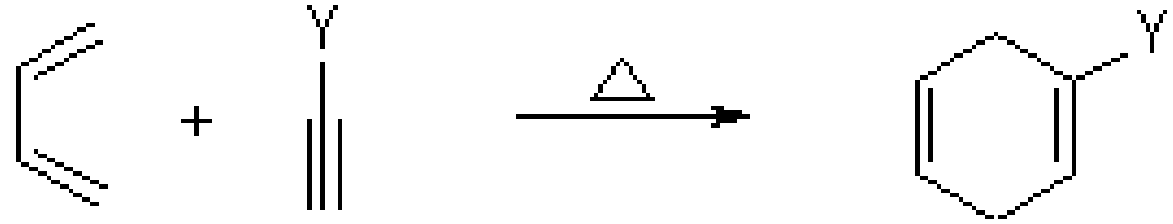
[2]) Die Ketene. Stuttgart 1912, S. 59, Anm. 2.

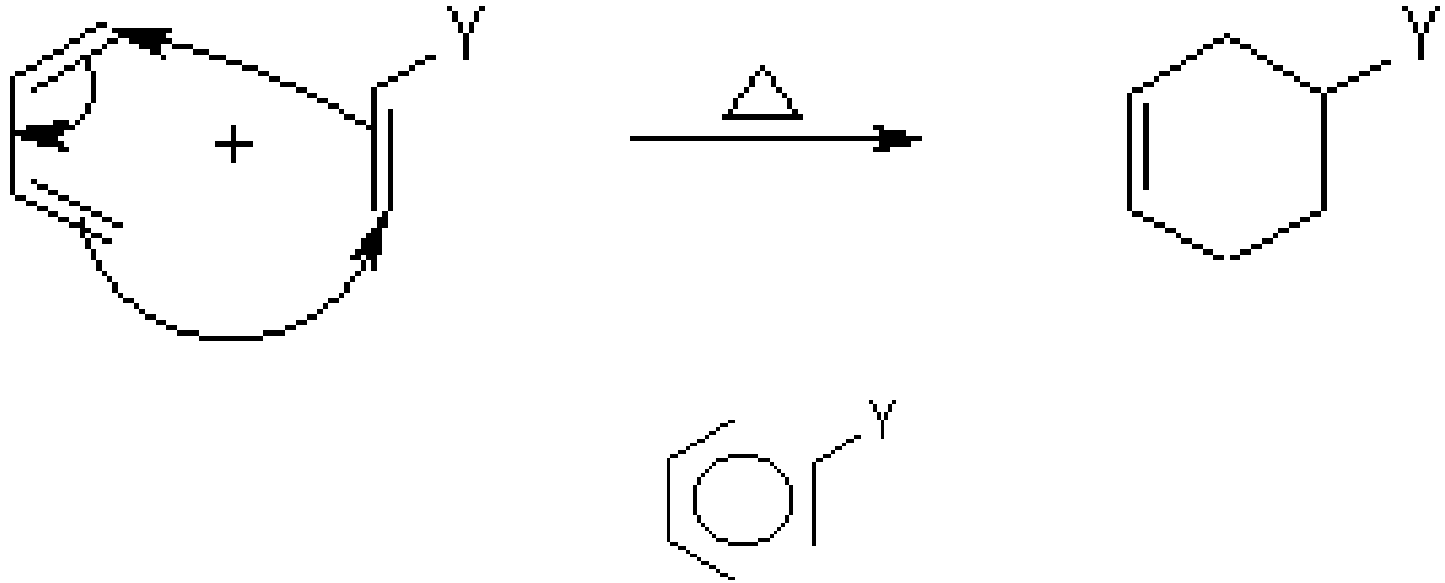
Our results will play a role not only in the discussion of theoretically interesting questions . . . . but probably also will yield greater significance in a practical sense. Thus it appears to us that the possibility of synthesis of complex compounds related to or identical with natural products such as terpenes, sesquiterpenes, perhaps also alkaloids, has been moved to the near prospect.
. . . . . We explicitly reserve for ourselves the application of the reaction discovered by us to the solution of such problems.

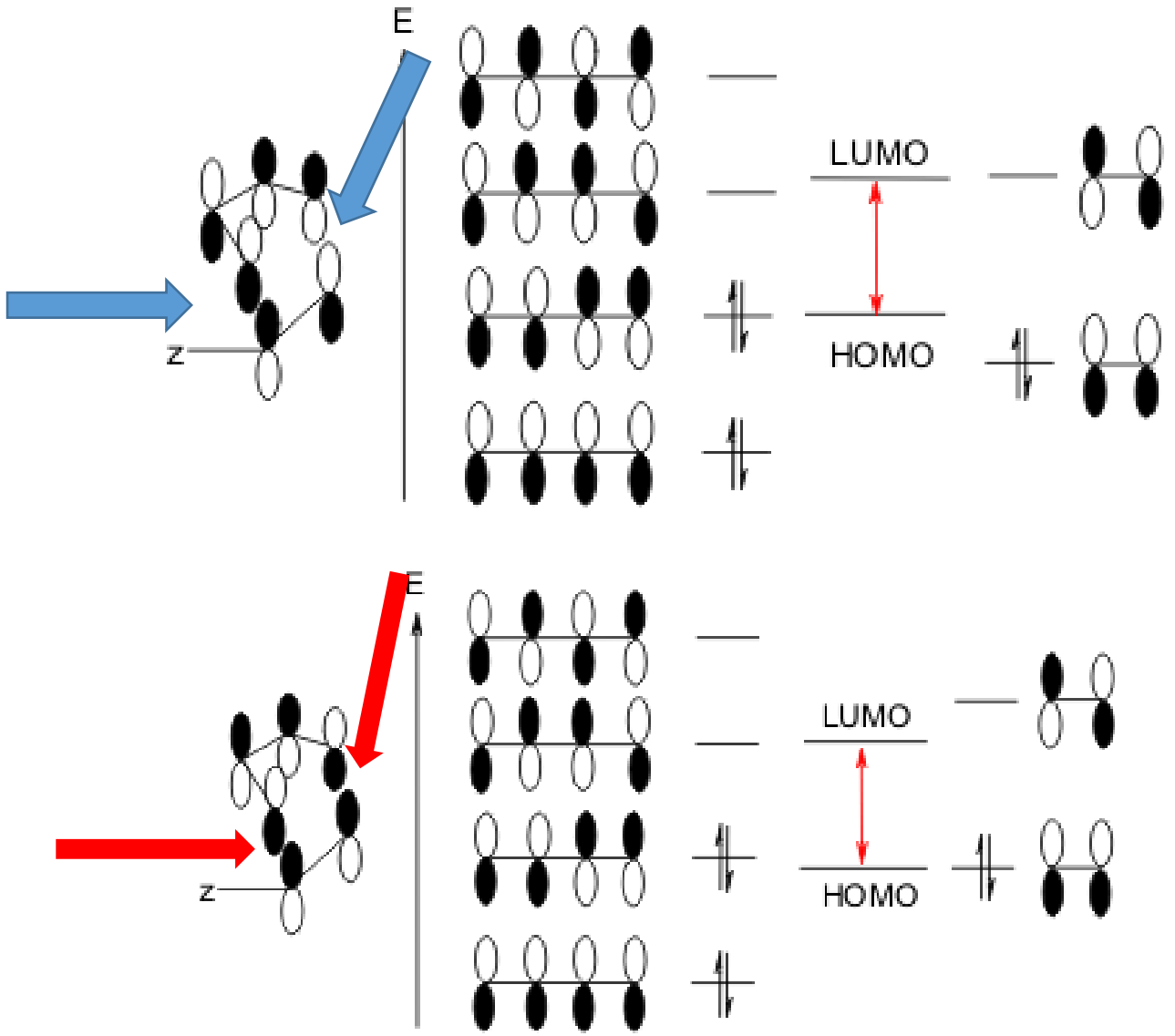
Otto Diels and Kurt Alder *Justus Liebigs Annalen der Chemie,* **1928**, *460***,** 98

Nuestros resultados tendrán un papel importante no sólo en la discusión de cuestiones teóricamente interesantes, pero probablemente también tendrá una mayor importancia en el sentido práctico. Así nos parece que la posibilidad de una síntesis de compuestos complejos relacionados con ,o bien idénticos, a productos naturales tales como terpenos, sesquiterpenos, quizás también alcaloides, se ha aplicado hacia esta perspectiva…. Nos reservamos explícitamente la aplicación de la reacción descubierta por nosotros para la solución de tales problemas .





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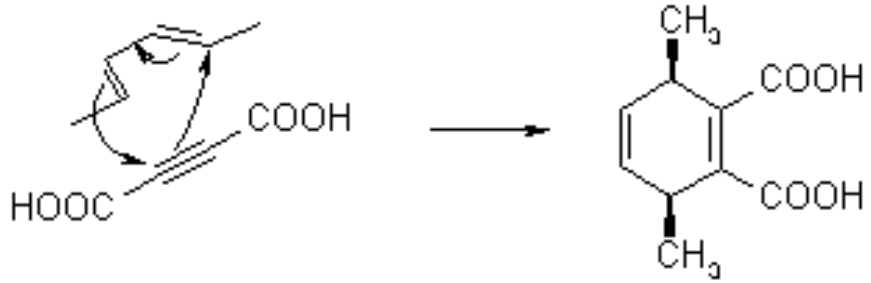
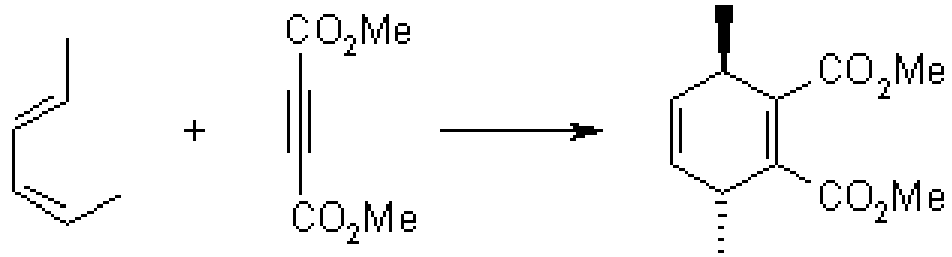

COOH
HOOC
CH3
COOH
COOH
CH3


CO2Me
CO2Me
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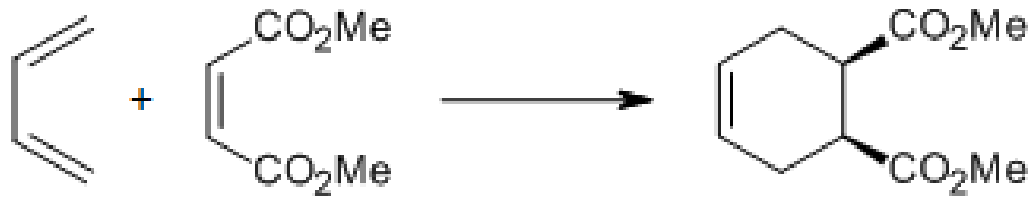
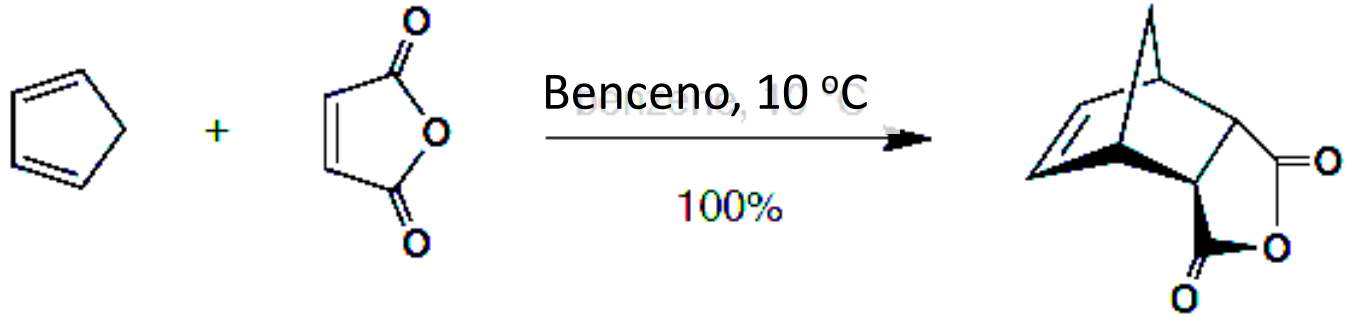
CO2Me

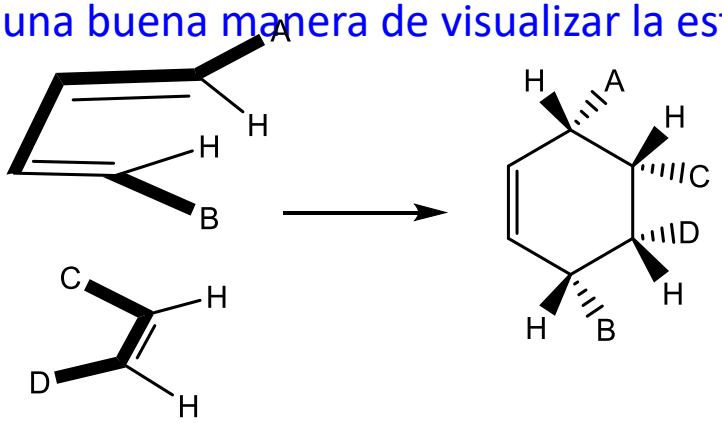

CO2Me
CO2Me
CO2Me
CO2Me

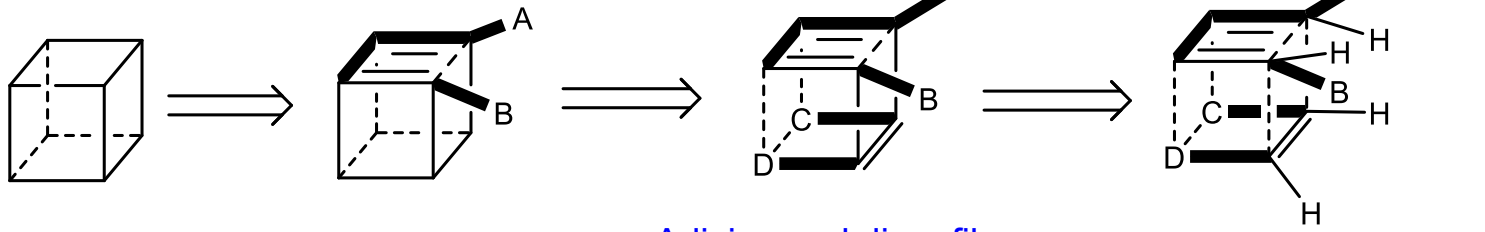

MeO2C
CO2Me
CO2Me
CO2Me

EL DESCUBRIMIENTO DE LA REACCIÓN DE DIELS-ALDER



MÉTODO CUBO Es una buena manera de visualizar la estereoquímica relativa





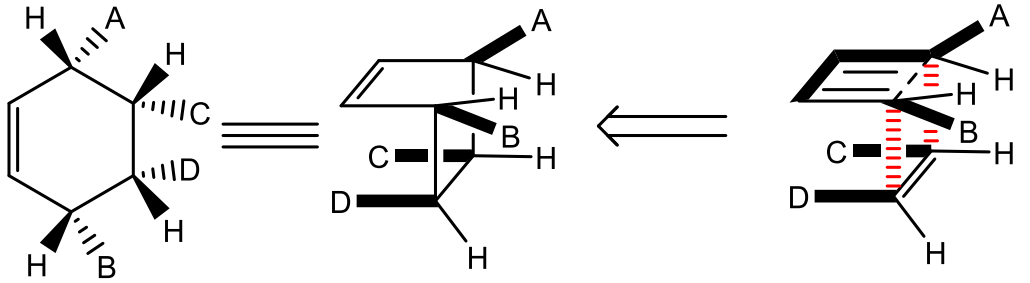
Dibujar un cubo

Adicionar el dieno

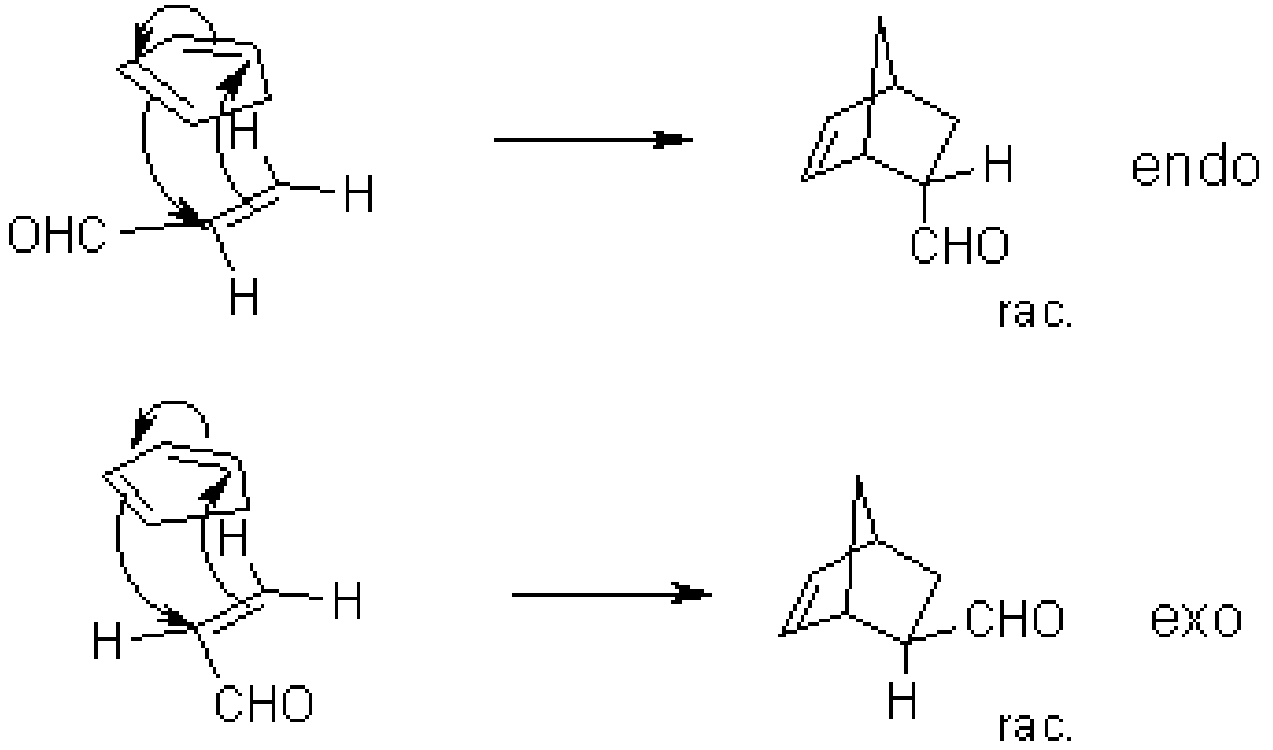
Adicionar el dienofilo (el sustituyente endo tiene sustituyentes directamente abajo del dieno)

Tomar en cuenta otros sustituyentes presentes

Deberá ser capaz de ver la estereoquímica relativa



Hacer la reacción (dibujar los nuevos enlaces)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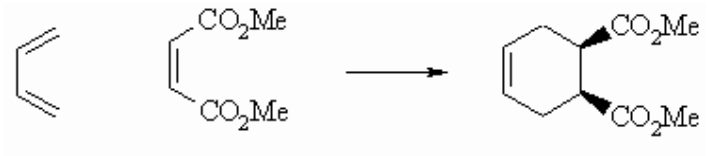
CO2Me
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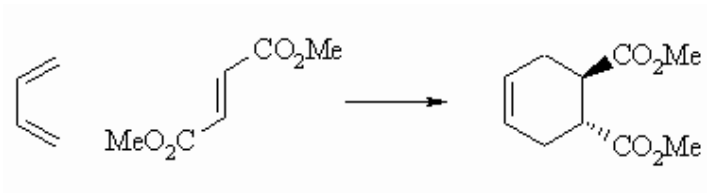
CO2Me
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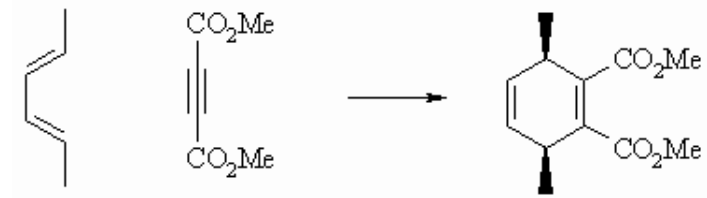
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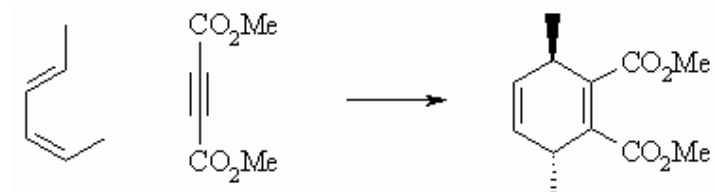
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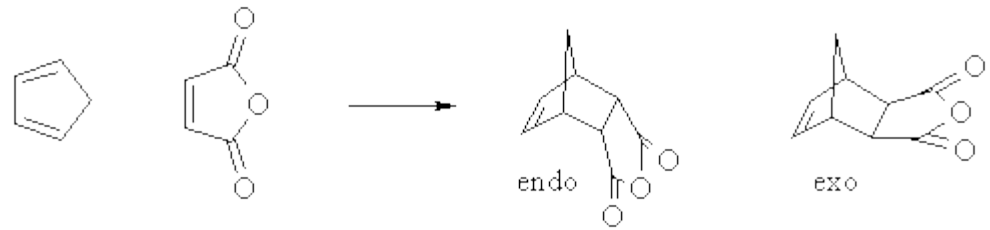
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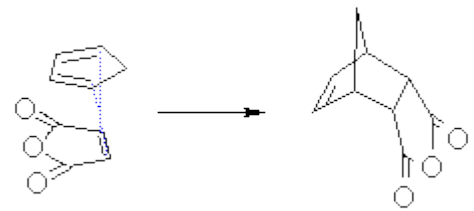

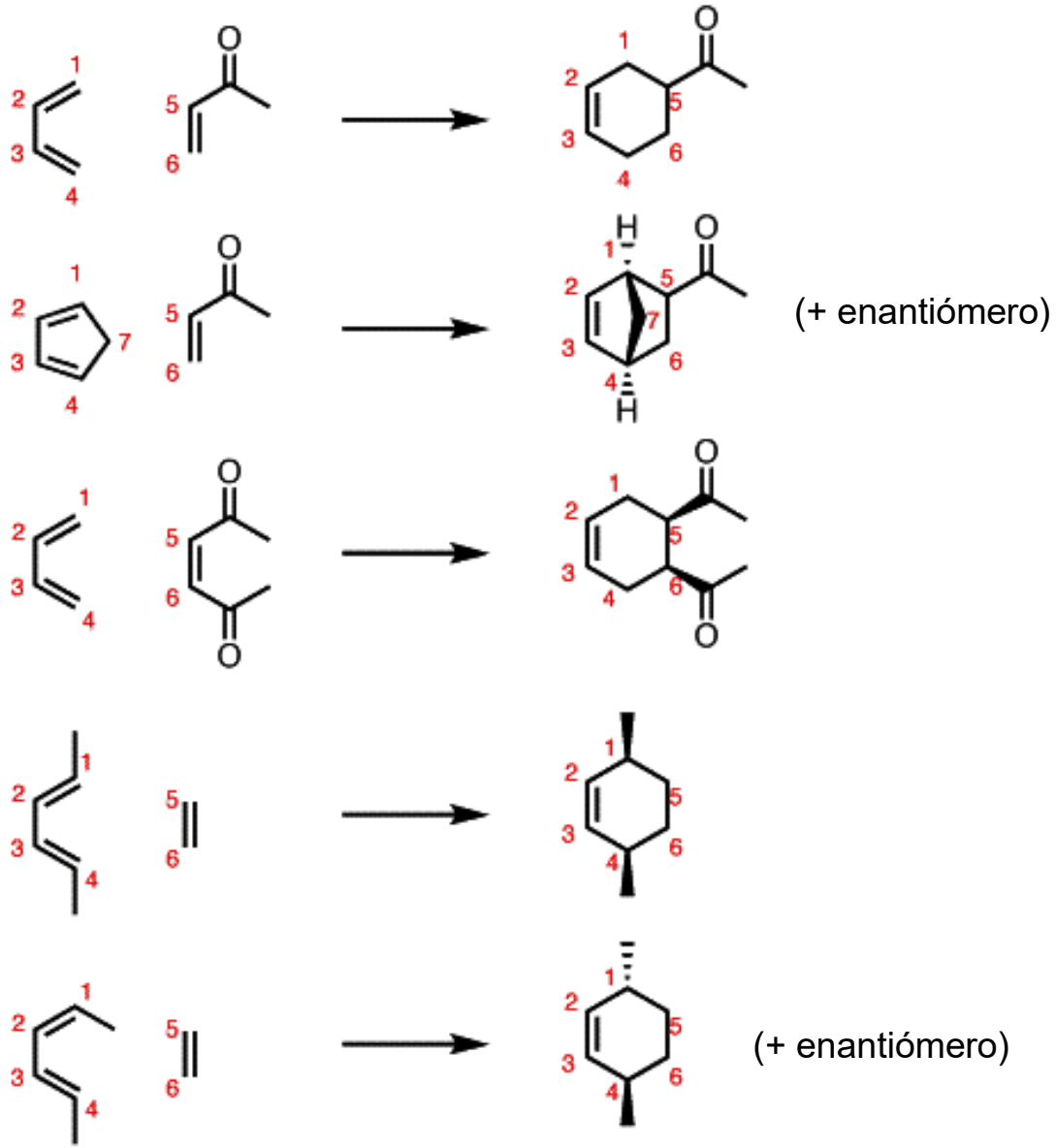

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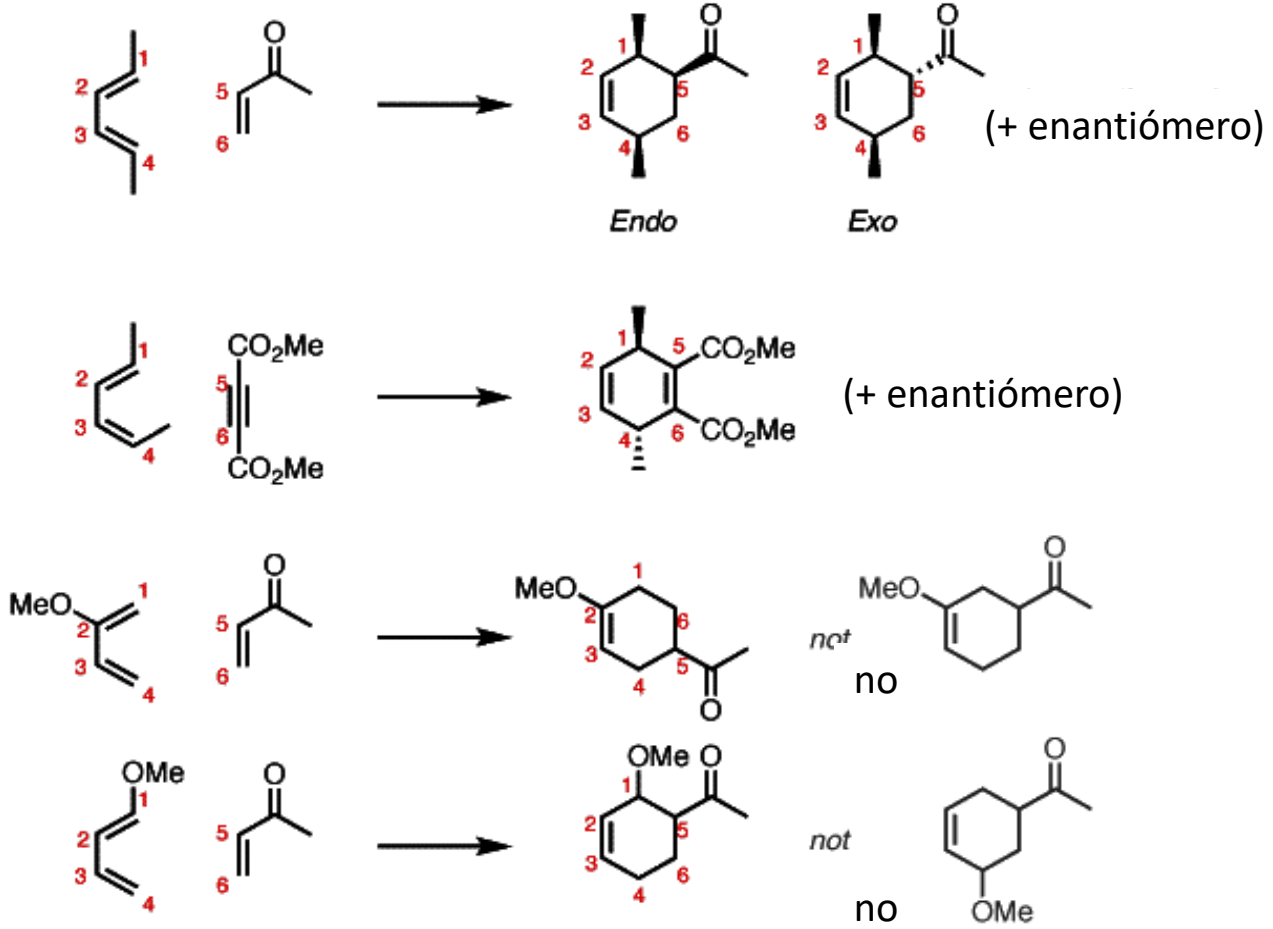
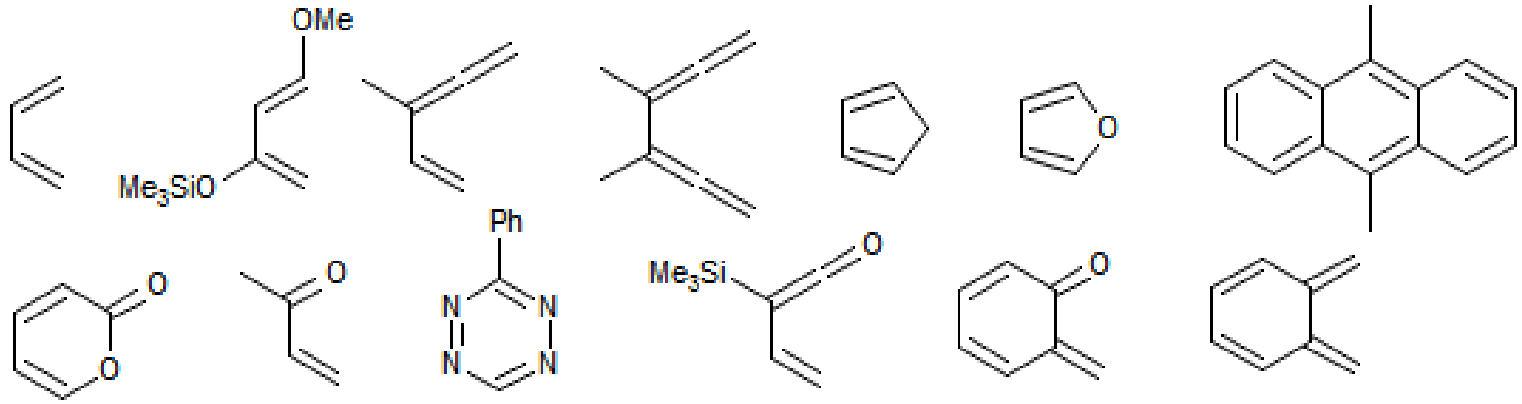
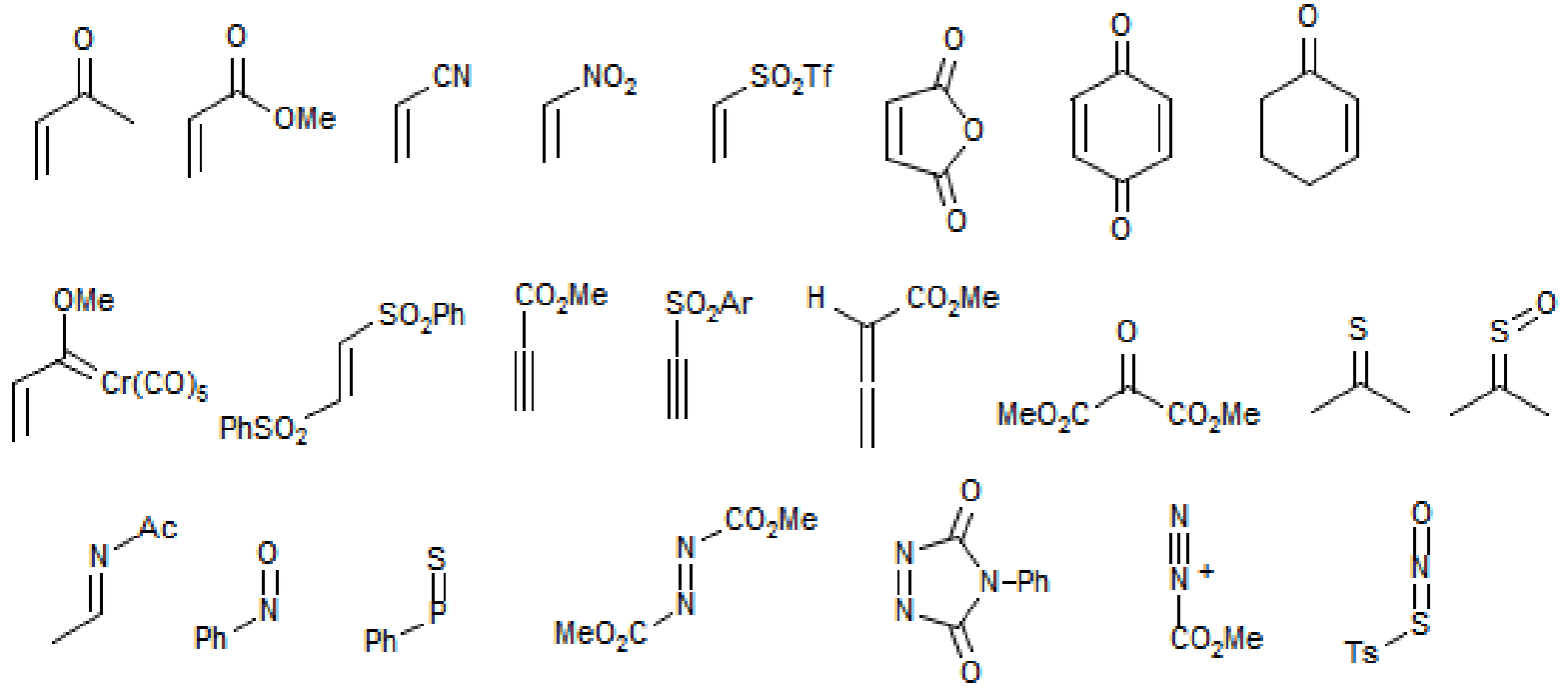
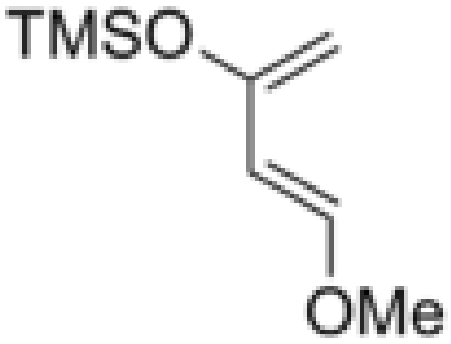


Algunos tipos de dienos que presentan la reacción de Diel-Alder

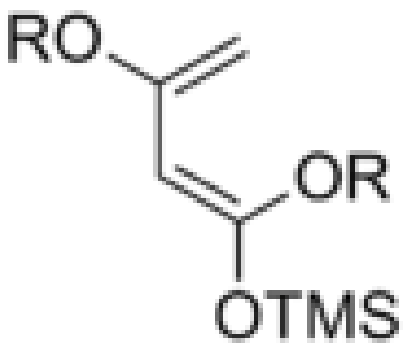


Algunos tipos de dienofilos que presentan la reacción de Diel-Alder

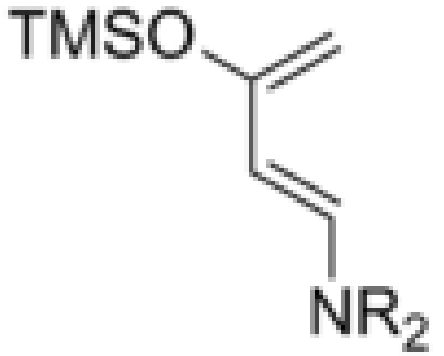




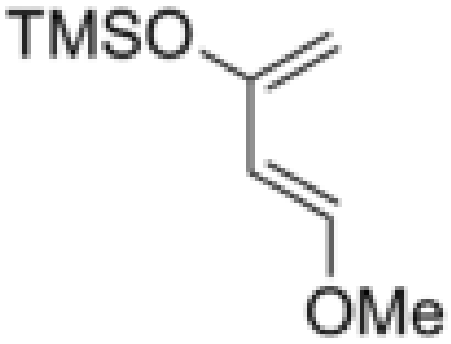
Dieno de Danishefsky



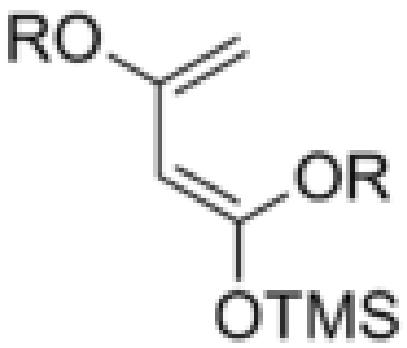
Dieno de Brassard



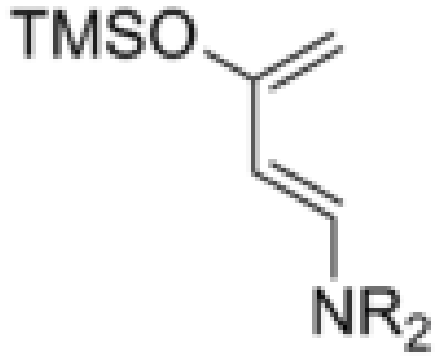
Dieno de Rawal



Dieno de Danishefsky

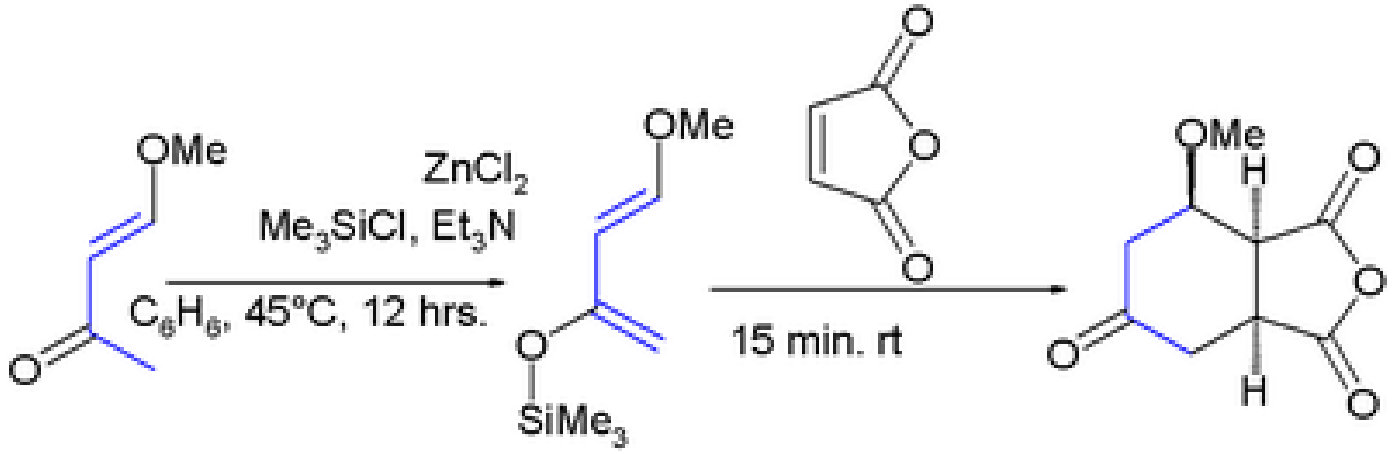


Dieno de Brassard



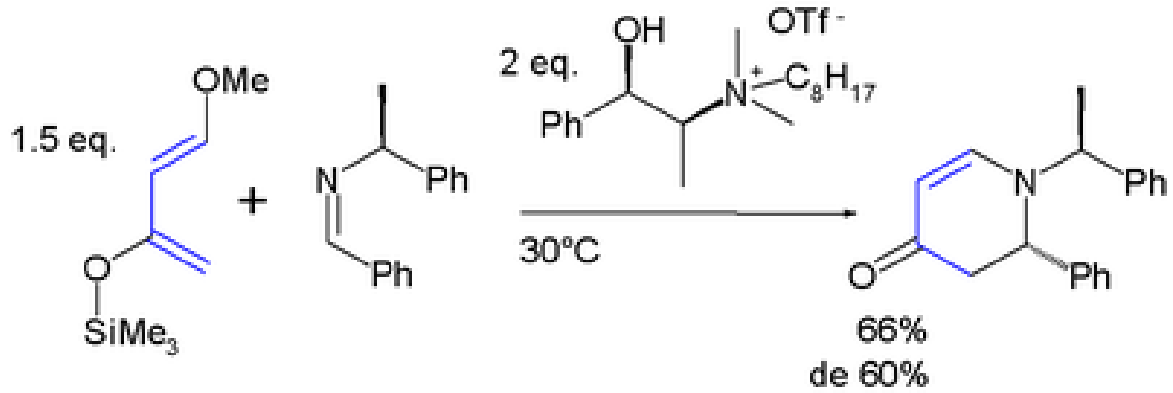
Dieno de Rawal

Dieno de Danishefsky

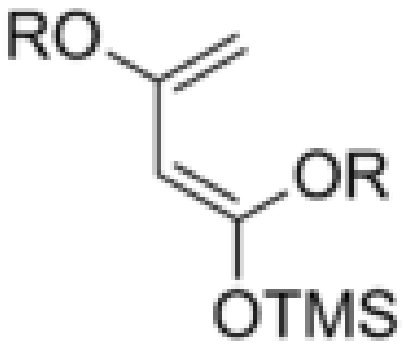


Preparation and Diels-Alder Reaction of a Highly Nucleophilic Diene. Org. Synth., Coll. Vol. 7, p.312 (1990); Vol. 61, p.147 (1983

Esta es una reacción asimétrica con un líquido iónico quiral como disolvente quiral. El rendimiento químico informado es del 66% con un exceso de diastereoisómero del 60%.



Asymmetric aza-Diels-Alder reaction of Danishefsky's diene with imines in a chiral reaction medium Pegot B, Nguyen Van Buu O, Gori D, Vo-Thanh G *Beilstein Journal of Organic Chemistry*, 2006-10-11 at the Wayback Machine

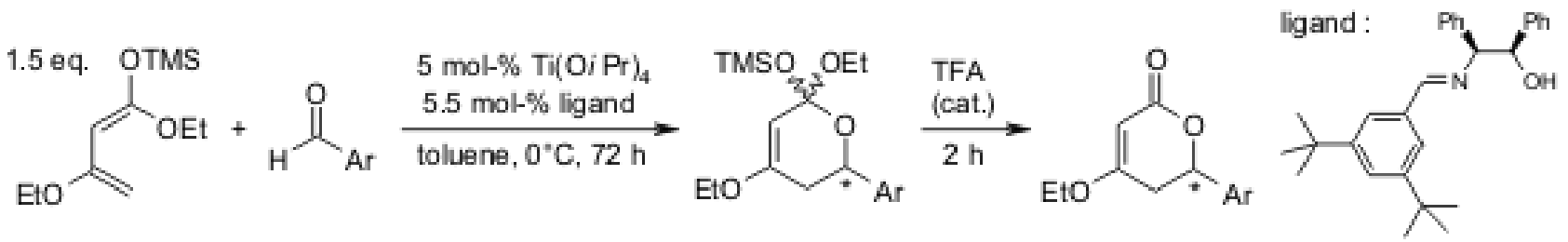


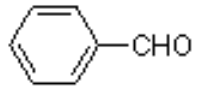
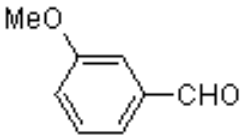
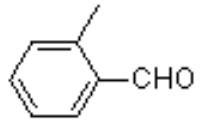
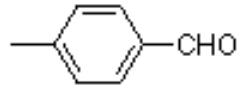
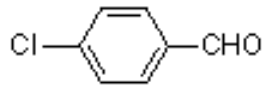
Dieno de Brassard

DIENO DE BASSARD

A Mild and Efficient Asymmetric Hetero-Diels-Alder Reaction of the Brassard Diene with Aldehydes

Q. Fan, L. Lin, J. Liu, Y. Huang, X. Feng, *Eur. J. Org. Chem.*, **2005**, 3542-3552.



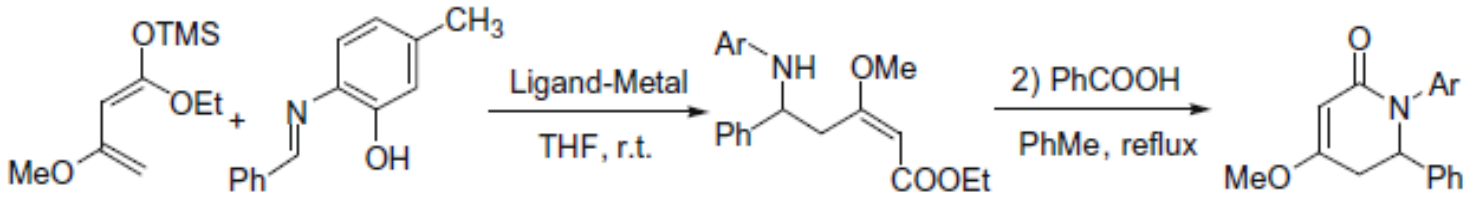
Aldehyde	Yield (%, isol.)	ee (%)
	71	93
	45	96
	24	92
	36	90
	87	97
	56	91

Savard, J.; Brassard, P. (1979). "Regiospecific syntheses of quinones using vinylketene acetals derived from unsaturated esters". *Tetrahedron Letters*. **20** (51): 4911–4914. doi:10.1016/S0040-4039(01)86747-2.

Enantioselective aza-Diels–Alder reaction of Brassard's diene with aldimines catalyzed by chiral N,N0-dioxide–Yb(OTf)3 complex

Zhenling Chen, Lili Lin, Donghui Chen, Jiangting Li, Xiaohua Liu, Xiaoming Feng

Tetrahedron Letters **2010,** *51,* 3088–3091



Entry	L	Metal	Total yield of **4a**[b] (%)	ee[c] (%)
1	**L1**	$Sc(OTf)_3$	26	36
2	**L1**	$Sm(OTf)_3$	41	57
3	**L1**	$Y(OTf)_3$	46	64
4	**L1**	$La(OTf)_3$	30	68
5	**L1**	$Yb(OTf)_3$	56	73
6	**L2**	$Yb(OTf)_3$	33	59
7	**L3**	$Yb(OTf)_3$	32	−9
8	**L4**	$Yb(OTf)_3$	43	72
9	**L5**	$Yb(OTf)_3$	44	63
10[d]	**L1**	$Yb(OTf)_3$	58	76
11[e]	**L1**	$Yb(OTf)_3$	47	70

[a] Unless otherwise noted, all reactions were carried out with *N,N'*-dioxide (5 mol %), metal (5 mol %), imine **2a** (0.1 mmol), and Brassard diene **1** (0.185 mmol) in THF (0.5 mL) at rt for 22 h, then isolation was followed by adding PhCOOH (0.1 mmol) at 110 °C in PhMe for 12 h.

[b] Yield after flash chromatography.

[c] ee of **4a** determined by HPLC.

[d] The ratio of **L1**:$Yb(OTf)_3$ was 1.1:1.

[e] The ratio of **L1**:$Yb(OTf)_3$ was 1.2:1.

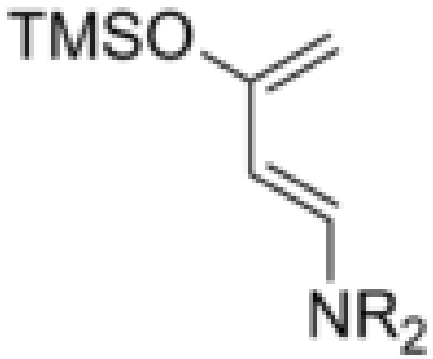
Sc Escandio
Sa Samario
Y Itrio
La Lantano
Yb Iterbio

Divergent Asymmetric Total Synthesis of All Four Pestalotin Diastereomers from (R)-Glycidol

Mizuki Moriyama, Kohei Nakata, Tetsuya Fujiwara and Yoo Tanabe

Molecules **2020**, *25*(2), 394; https://doi.org/10.3390/molecules25020394

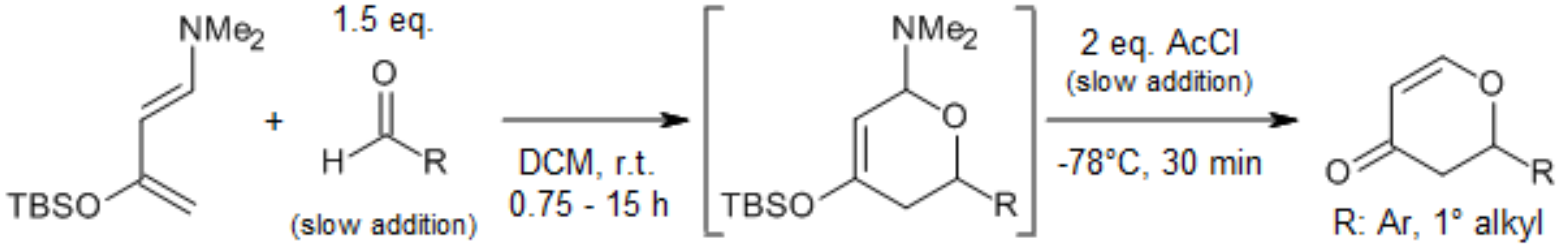
SEMINARIO

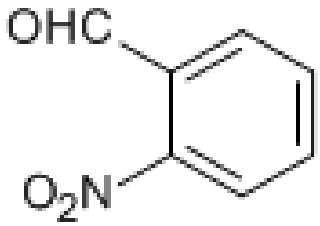
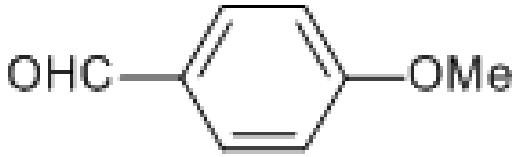


Dieno de Rawal

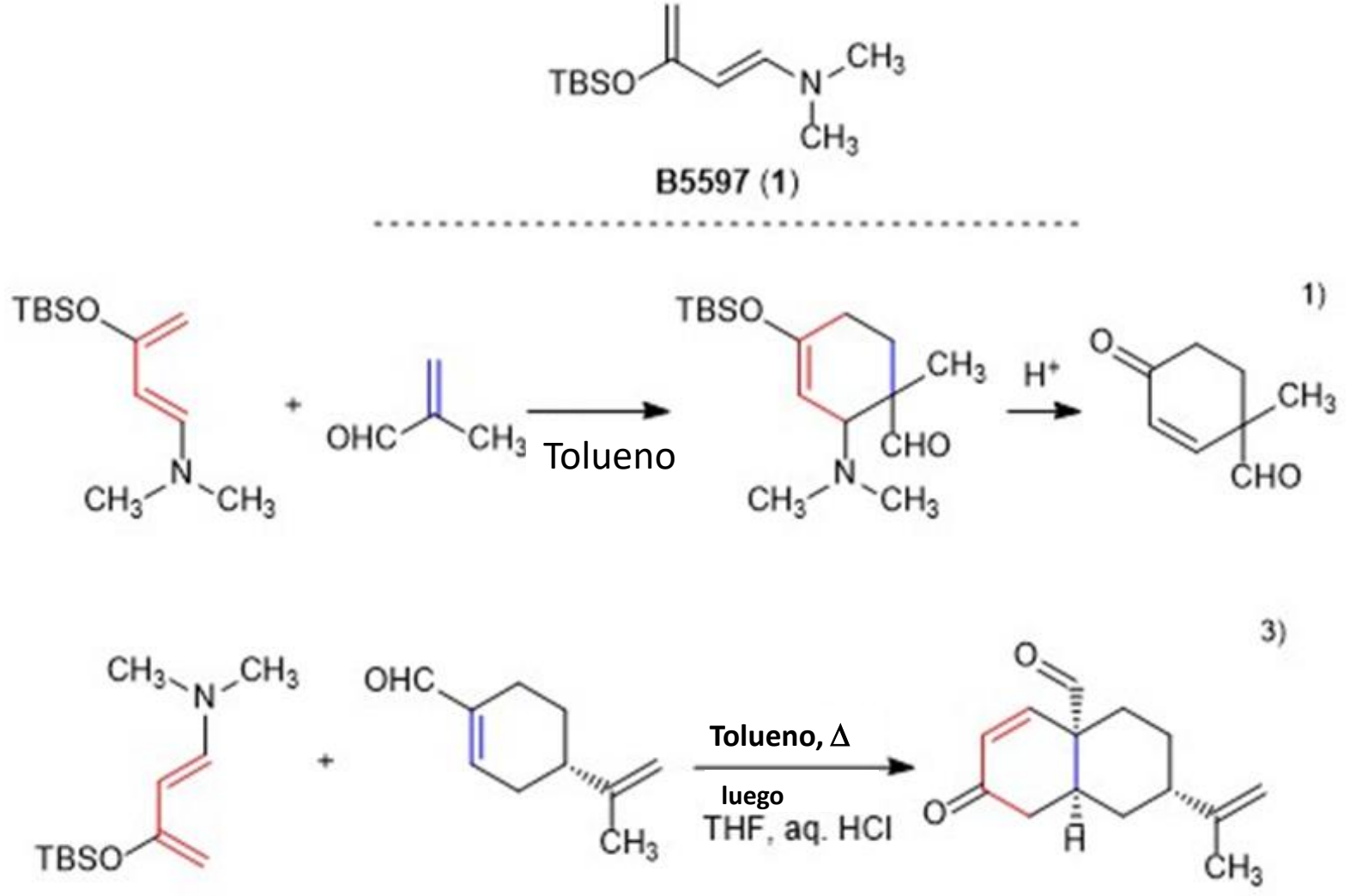
Hetero Diels-Alder Reactions of 1-Amino-3-siloxy-1,3-butadienes under Strictly Thermal Conditions

Y. Huang, V. H. Rawal, *Org. Lett.*, **2000**, *2*, 3321-3323.



aldehyde	t (h)	yield (%, isol.)
	0.75	81
	15	71
	2	73
	2.5	82

Viresh H. Rawal
(1958 -)
Químico norteamericano
nació en la India



1) Preparation and Diels–Alder Reactivity of 1-Amino-3-siloxy-1,3-butadienes
S. A. Kozmin, V. H. Rawal, **J. Org. Chem. 1997**, **62**, 5252.

2) On the Reactivity of 1-Amino-3-siloxy-1,3-dienes: Kinetics Investigation and Theoretical Interpretation
S. A. Kozmin, M. T. Green, V. H. Rawal, **J. Org. Chem. 1999**, **64**, 8045.

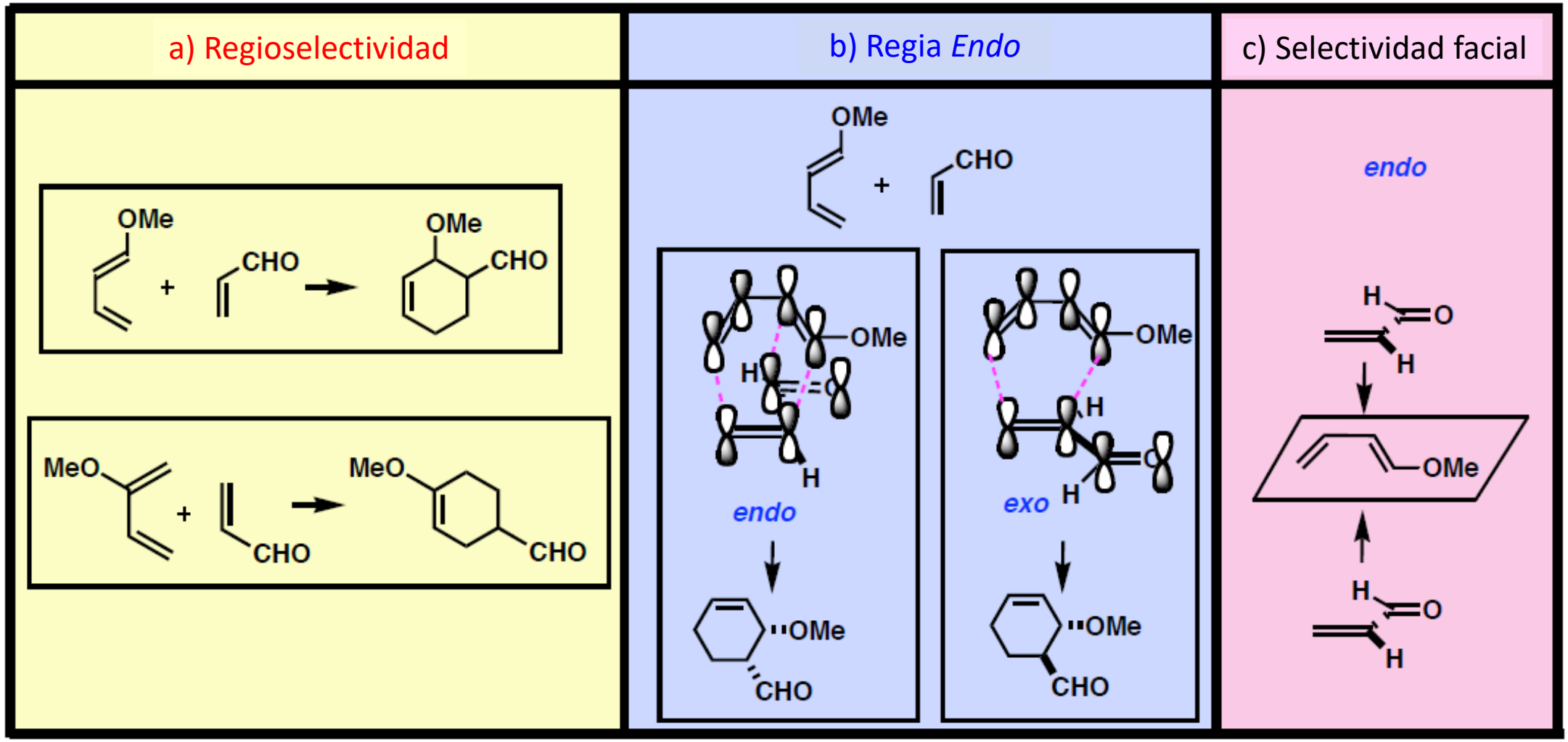
3) A Nine-Step Total Synthesis of (−)-Platencin
K. Tiefenbacher, J. Mulzer, **J. Org. Chem. 2009**, **74**, 2937

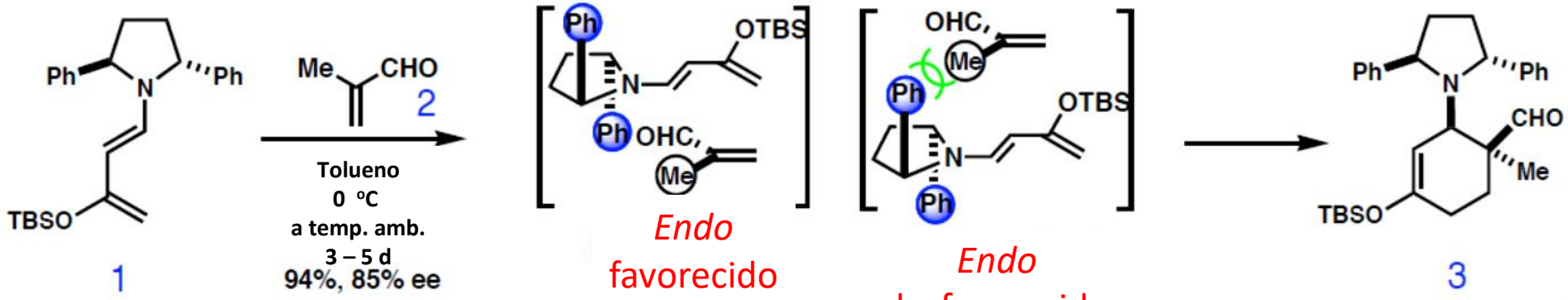
Dieno de Danishefsky

Dieno de Rawal

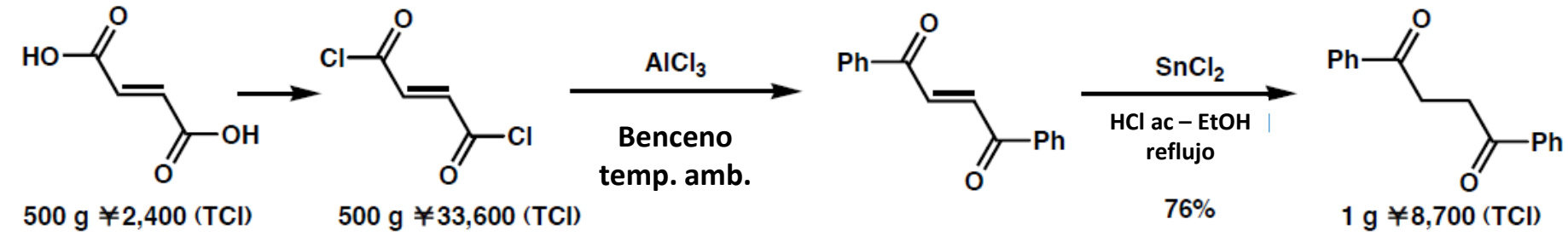
Ventajas del grupo amino

1. La cicloadición proporcionará acceso a la síntesis de alcaloides que contienen N
2. Mayor nucleofilia = mayor reactividad que el dieno Danishefsky
3. Brinda la oportunidad para la introducción de quiralidad


a) Regioselectividad
OMe
CHO
OMe
CHO
MeO
CHO
MeO
CHO
b) Regia *Endo*
OMe
CHO
OMe
H
H
endo
OMe
CHO
OMe
H
H
exo
OMe
CHO
c) Selectividad facial
endo
H
O
H
OMe
H
O
H



V. H. Rawal *et al.*, *J. Am. Chem.* Soc., **119**, 7165 (1997)



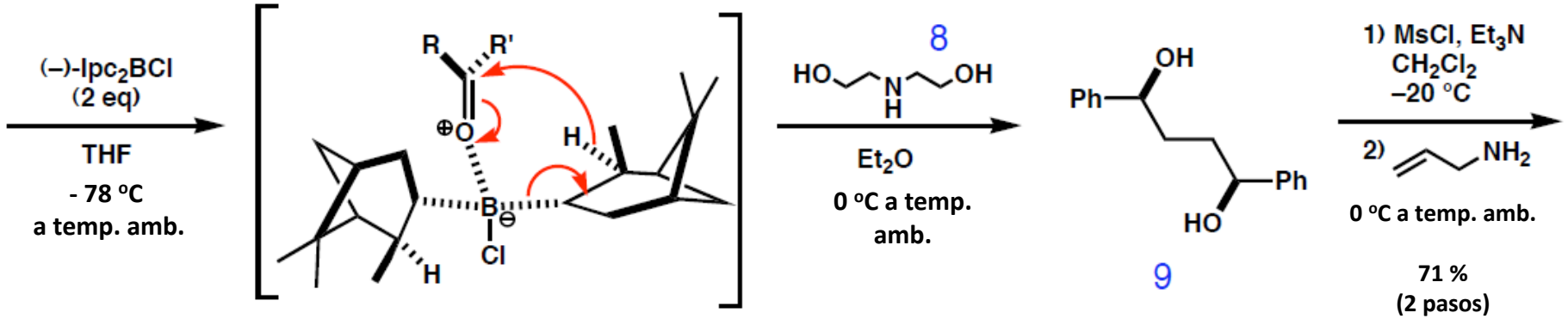
500 g ¥2,400 (TCI) — 4

500 g ¥33,600 (TCI) — 5

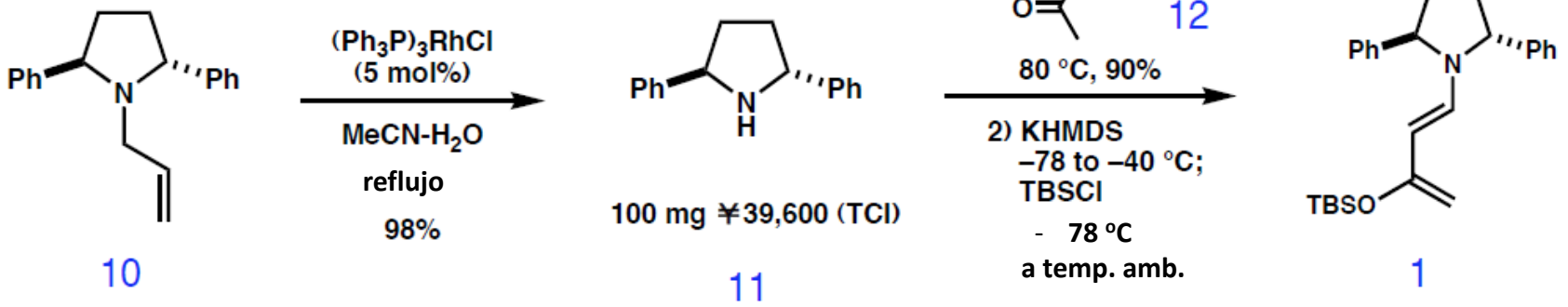
6

1 g ¥8,700 (TCI) — 7

Tokyo Chemical Industry (TCI)



9

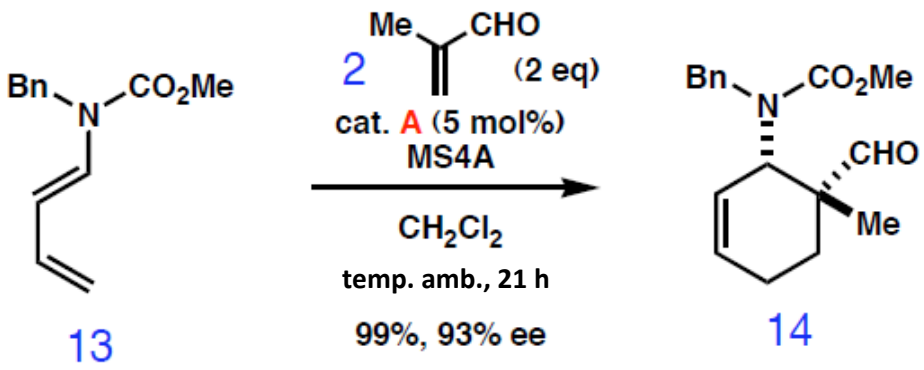


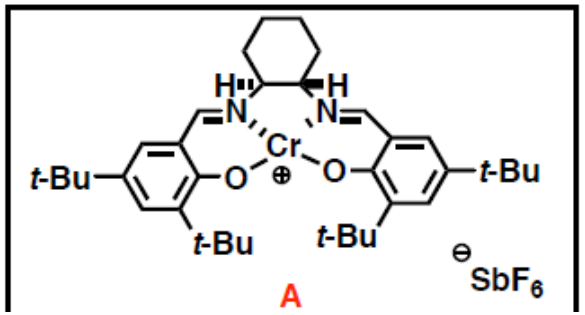
10

100 mg ¥39,600 (TCI) — 11

1

REACCIÓN DE DIELS-ALDER (DA), CATALÍTICA ASIMÉTRICA
REACCIÓN DE DA CATALIZADA CON ÁCIDO DE LEWIS QUIRAL

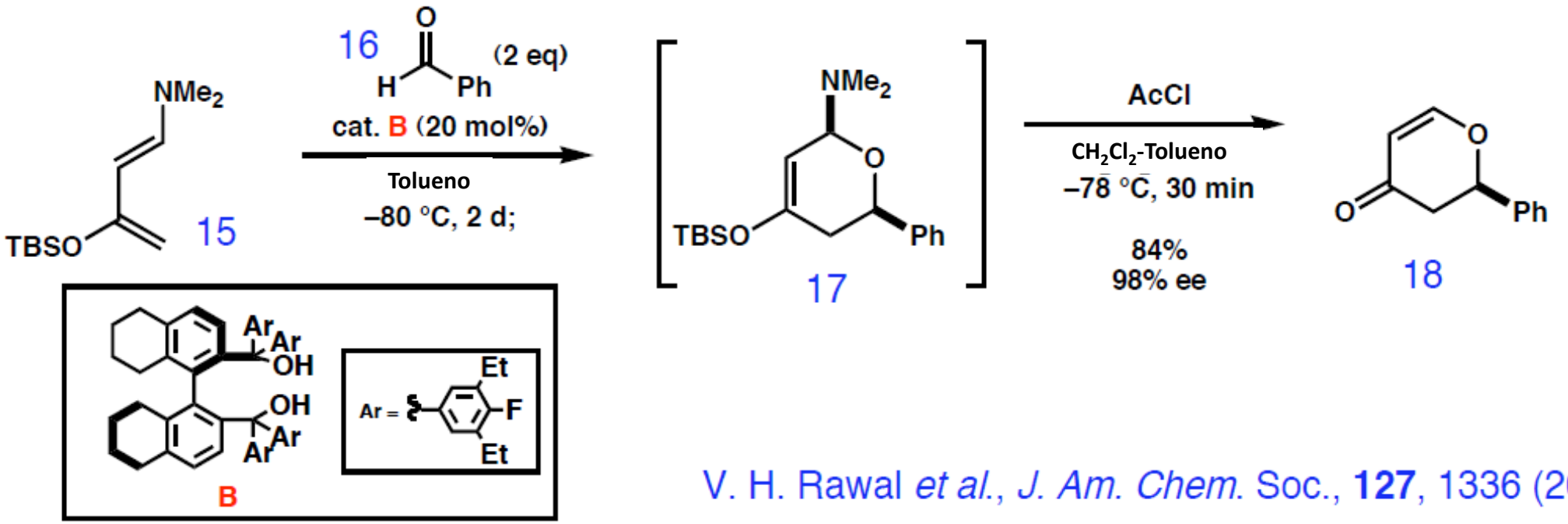




Catalizador de Jacobsen
Salen-Cr (III)

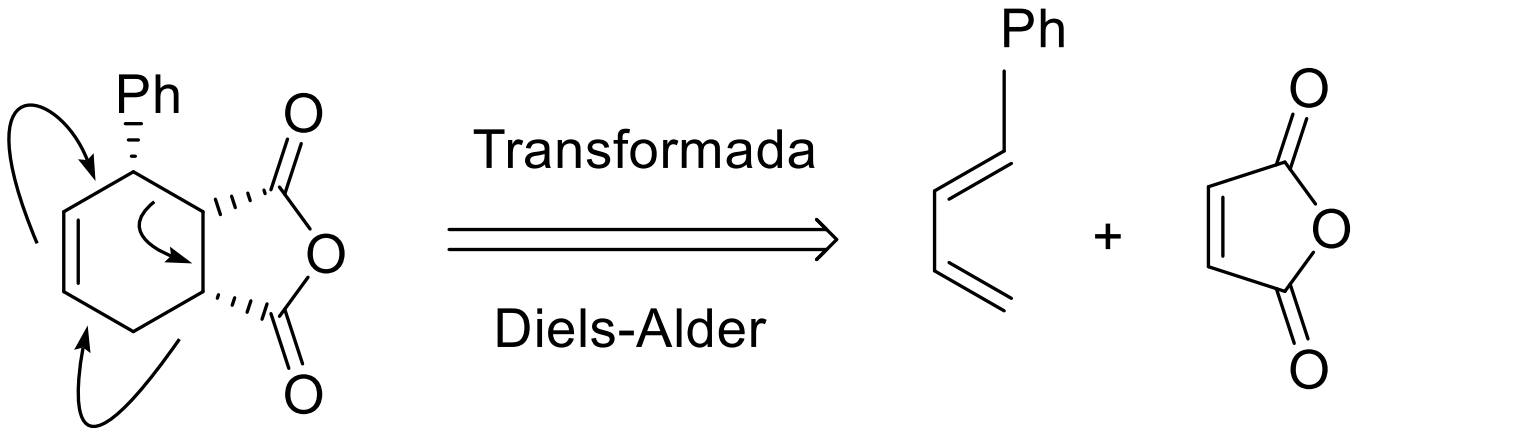
V. H. Rawal *et al.*, *J. Am. Chem.* Soc., **124**, 5950 (2002)

REACCIÓN HETERO DIELS-ALDER A TRAVÉS DE PUENTES DE HIDRÓGENO CATALIZADA CON BIARILDIOLES QUIRALES

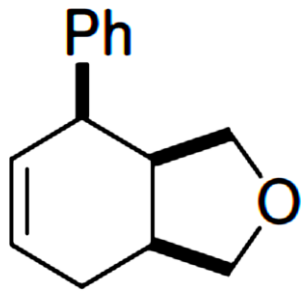


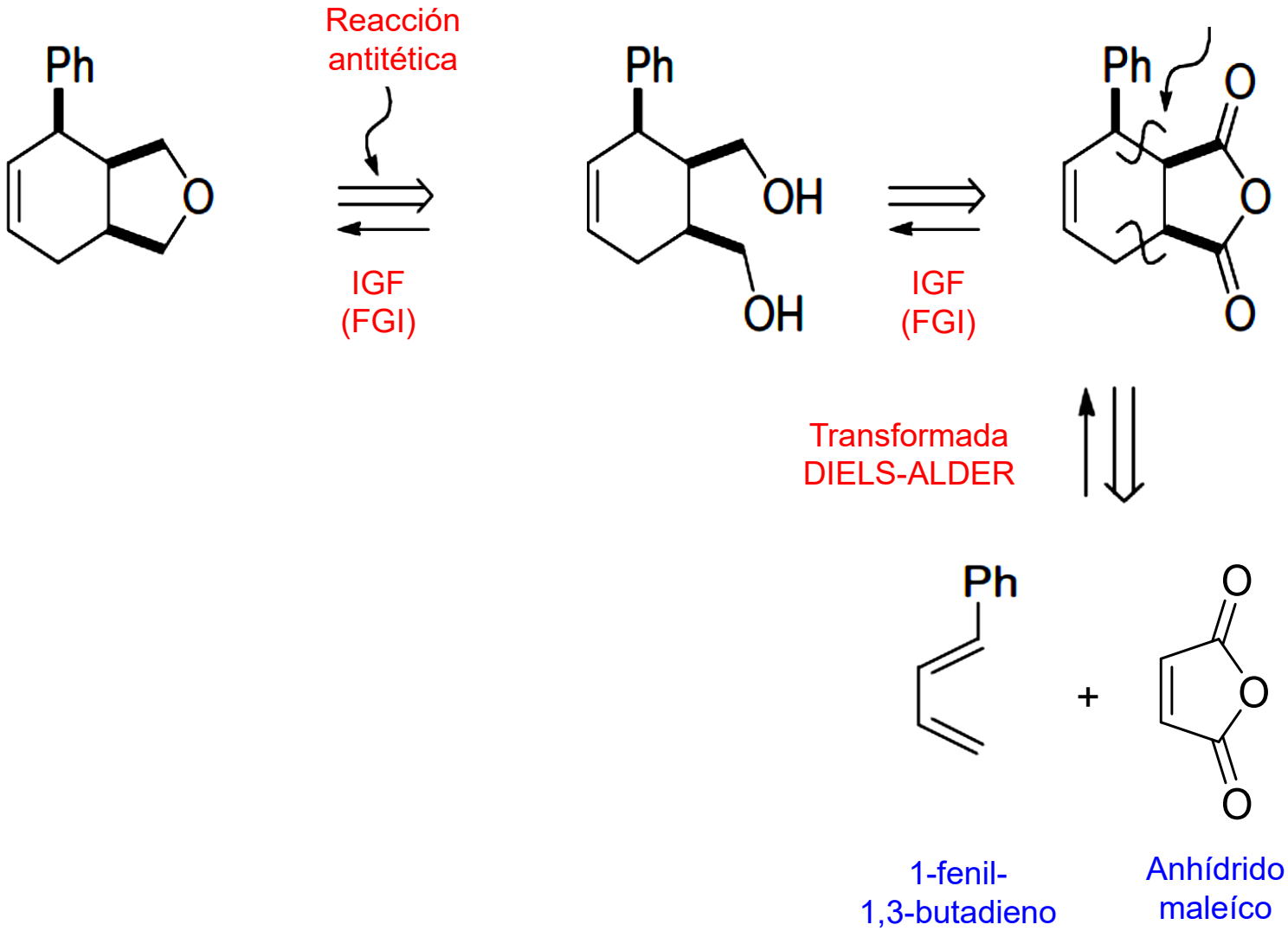
V. H. Rawal *et al.*, *J. Am. Chem.* Soc., **127**, 1336 (2005)

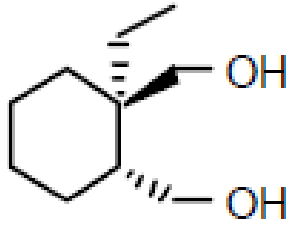
Aquí la reacción de Diels-Alder es apropiada debido a que es una reacción estereoespecífica

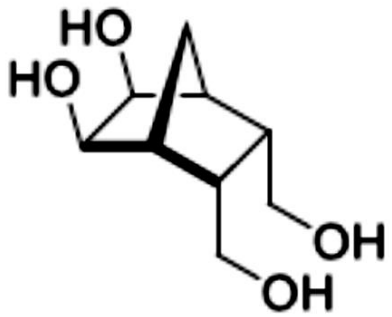


Dieno conjugado ***Dienófilo Doble enlace-cis***


Ph
O

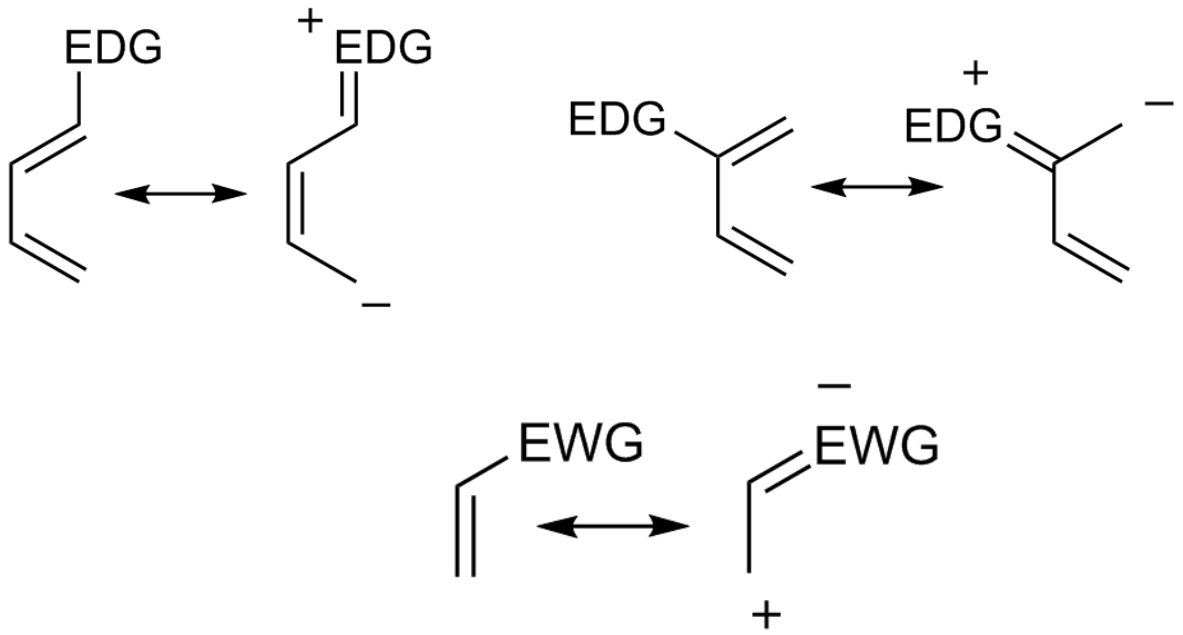

Ph
O
Reacción
antitética
IGF
(FGI)
Ph
OH
OH
IGF
(FGI)
Ph
O
O
O
Transformada
DIELS-ALDER
Ph
+
O
O
O
1-fenil-
1,3-butadieno
Anhídrido
maleíco


OH
OH


HO
HO
OH
OH

Regioselectividad

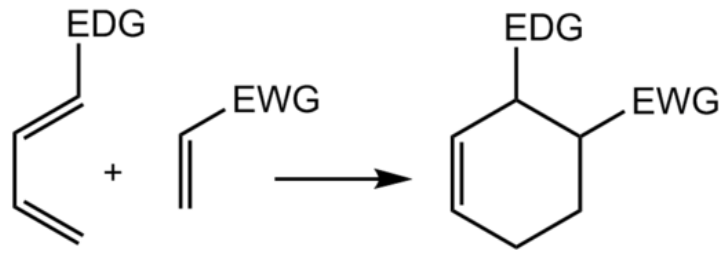
La teoría orbital molecular de frontera también se ha utilizado para explicar los patrones de regioselectividad observados en las reacciones de Diels-Alder de sistemas sustituidos. El cálculo de la energía y los coeficientes orbitales de los orbitales fronterizos de los componentes proporciona una imagen que está de acuerdo con el análisis más directo de los efectos de resonancia de los sustituyentes, como se ilustra a continuación.



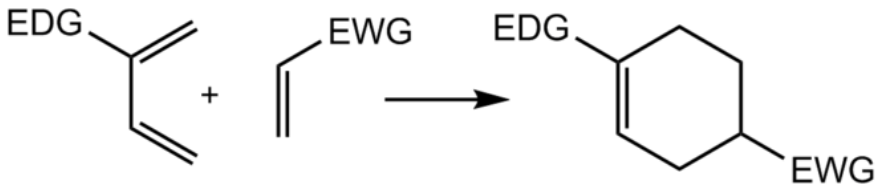
Regioselectividad

En general, la regioselectividad encontrada tanto para la reacción de Diels-Alder normal como para la demanda inversa de electrones sigue la regla ***orto-para***, llamada así, porque el producto ciclohexeno tiene sustituyentes en posiciones análogas a las posiciones *orto* y *para* de arenos disustituidos.

1

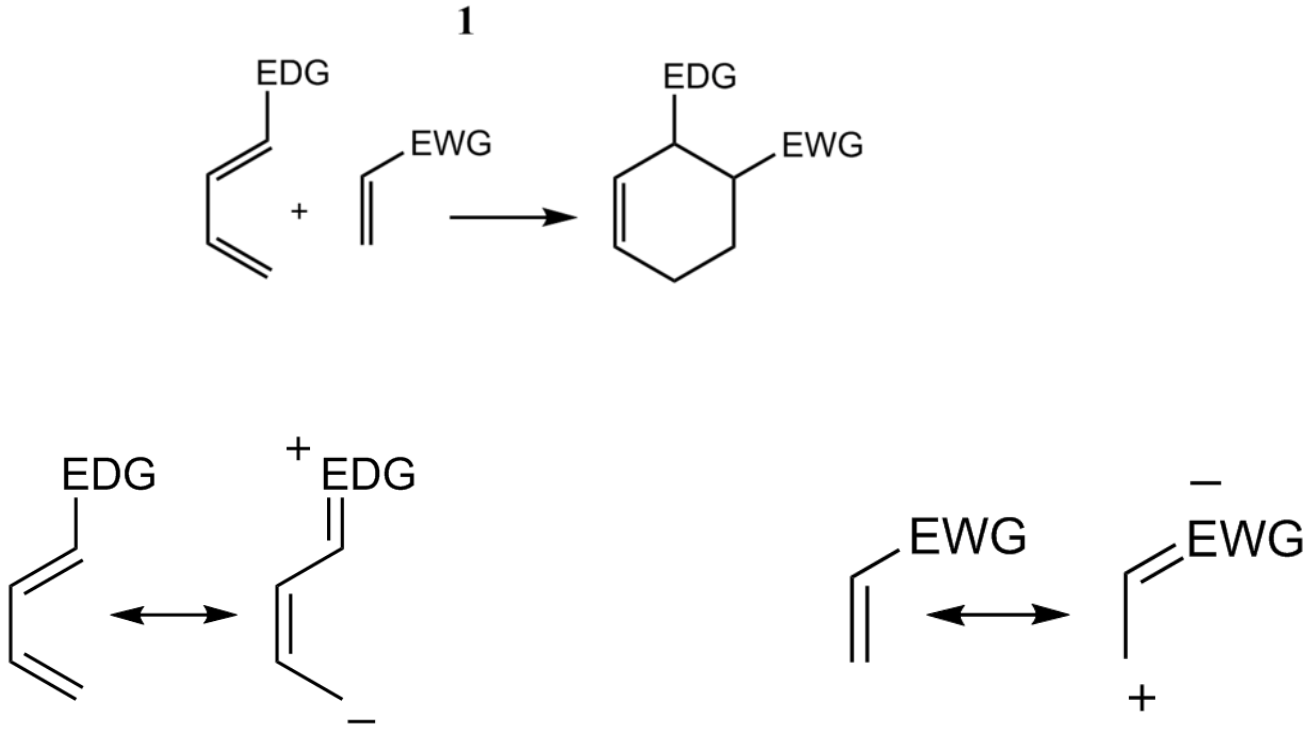


2



Regioselectividad

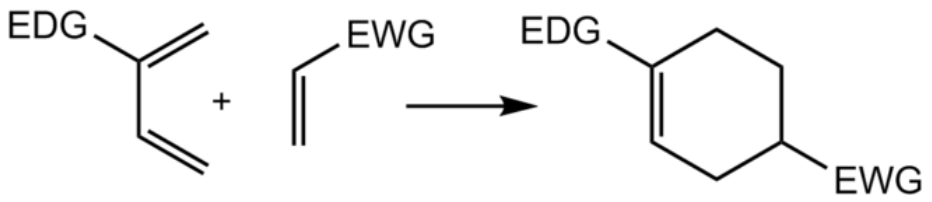
Por ejemplo, en el caso de una demanda normal, un dieno con un grupo donador de electrones (EDG) en C1 tiene su mayor coeficiente HOMO en C4, mientras que el dienófilo con un grupo de extracción de electrones (EWG) en C1 tiene el mayor coeficiente LUMO en C2 El emparejamiento de estos dos coeficientes da el producto "***orto***" como se ve en el caso 1 en la figura siguiente. y polarización.



Regioselectividad

Un dieno sustituido en C2 como en el caso 2 a continuación tiene el mayor coeficiente HOMO en C1, dando lugar al producto "*para*".

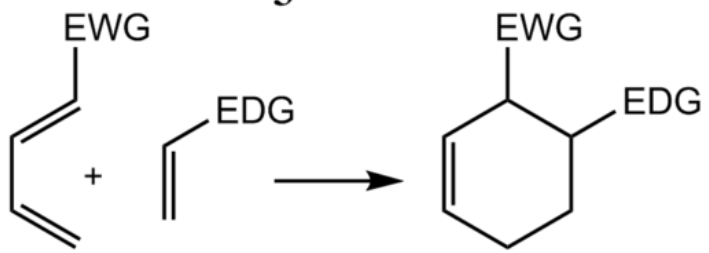
2



Regioselectividad

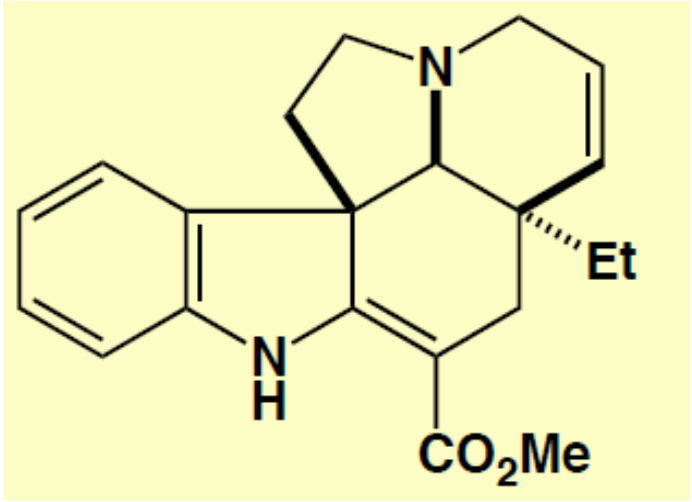
Análisis similares para los escenarios de demanda inversa correspondientes dan lugar a productos análogos, como se ve en los casos 3 y 4. Examinando las formas mesoméricas canónicas anteriores, es fácil verificar que estos resultados están de acuerdo con las expectativas basadas en la consideración de la densidad electrónica y polarización.

3



4

SÍNTESIS TOTAL DE LA (±)-TABERSONINA



(±)-TABERSONINA

V. H. Rawal *et al.*, *J. Am. Chem. Soc.*, **124**, 4628 (2002)

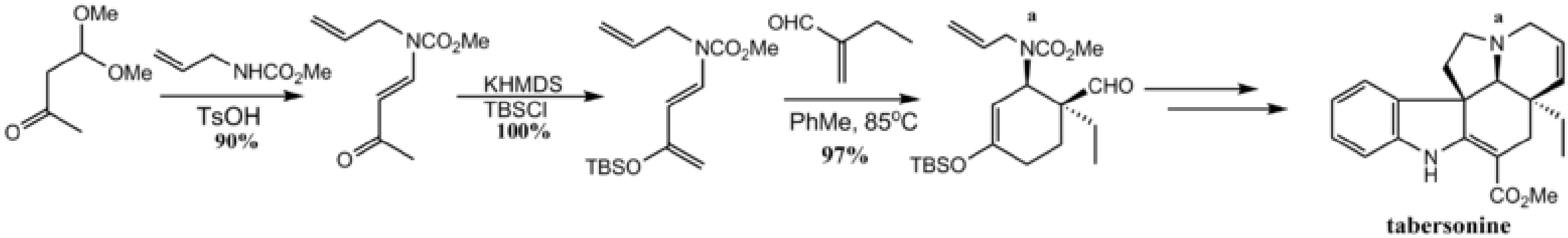
A General Strategy to *Aspidosperma* Alkaloids: Efficient, Stereocontrolled Synthesis of Tabersonine
Sergey A. Kozmin and Viresh H. Rawal
J. Am. Chem. Soc. **1998**, *120*, 51, 13523–13524

An Efficient Approach to *Aspidosperma* Alkaloids via [4 + 2] Cycloadditions of Aminosiloxydienes: Stereocontrolled Total Synthesis of (±)-Tabersonine. Gram-Scale Catalytic Asymmetric Syntheses of (+)-Tabersonine and (+)-16-Methoxytabersonine. Asymmetric Syntheses of (+)-Aspidospermidine and (−)-Quebrachamine
Sergey A. Kozmin, Tetsuo Iwama, Yong Huang and Viresh H. Rawal
J. Am. Chem. Soc. **2002**, *124*, 17, 4628–4641

SEMINARIO

A General Strategy to Aspidosperma Alkaloids: Efficient, Stereocontrolled Synthesis of Tabersonine

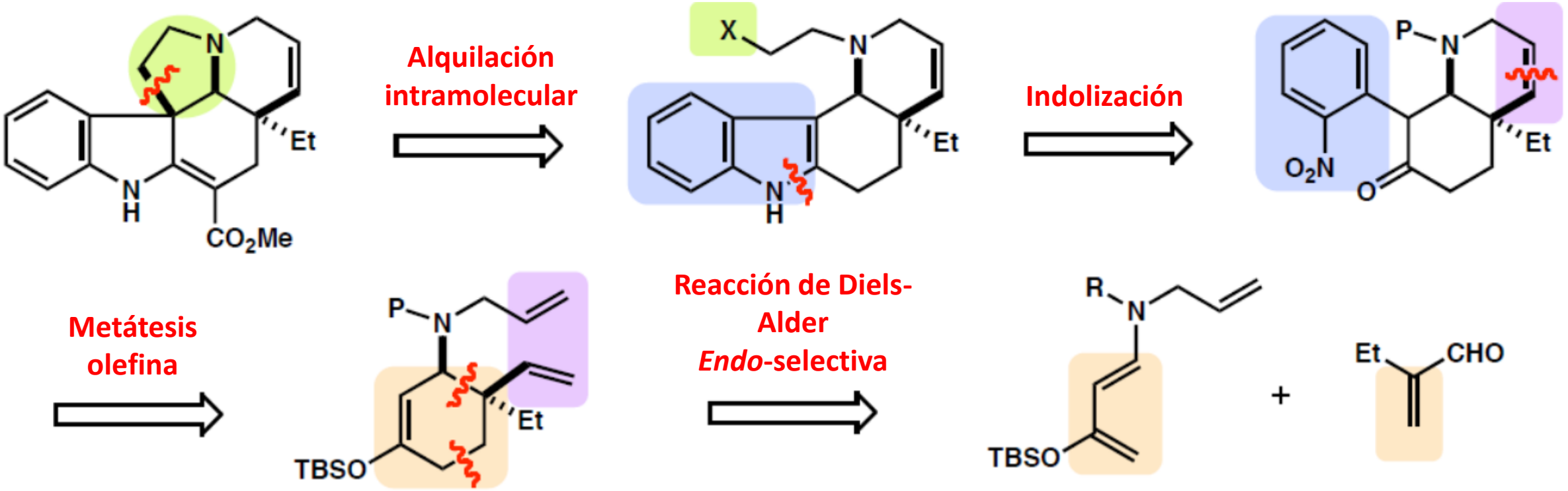
Kozmin, S. A.; Rawal, V. H. *Journal of the American Chemical Society* **1998**, *120*(51): 13523–13524. doi:10.1021/ja983198k.

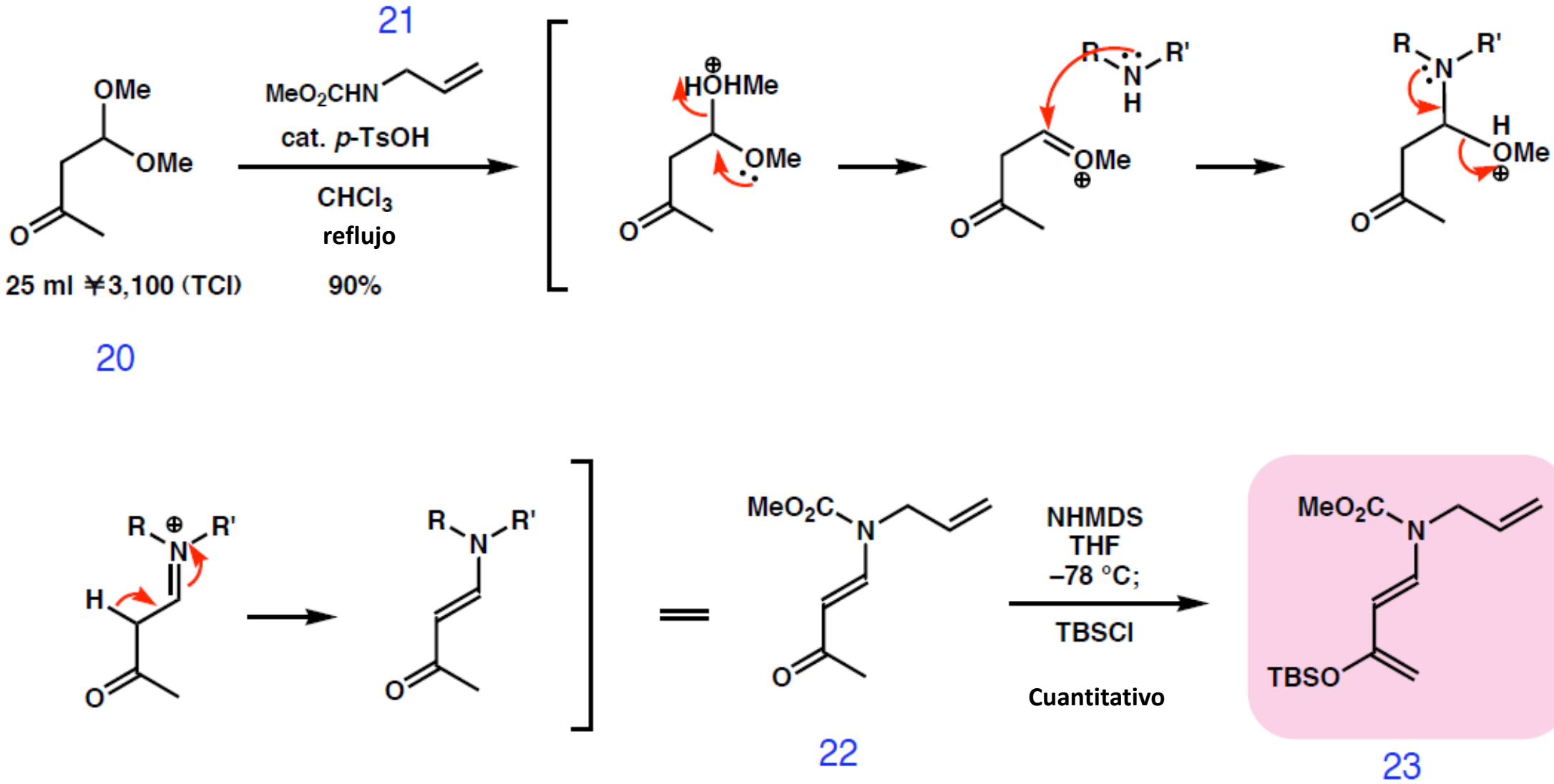


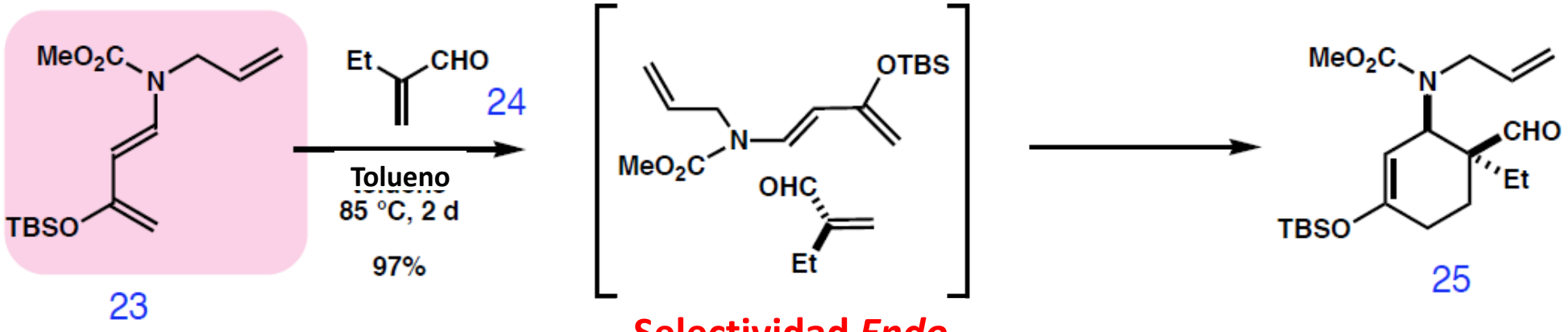
tabersonine

SEMINARIO

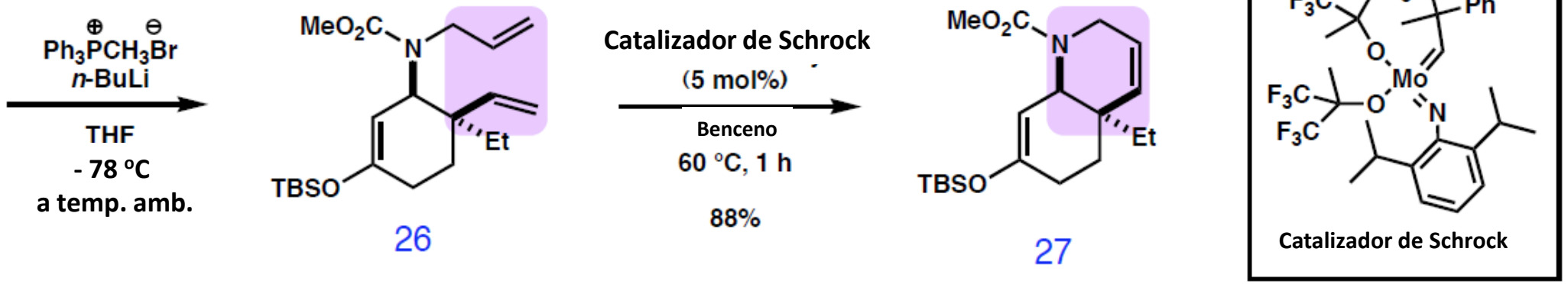
ANÁLISIS RETROSINTÉTICO

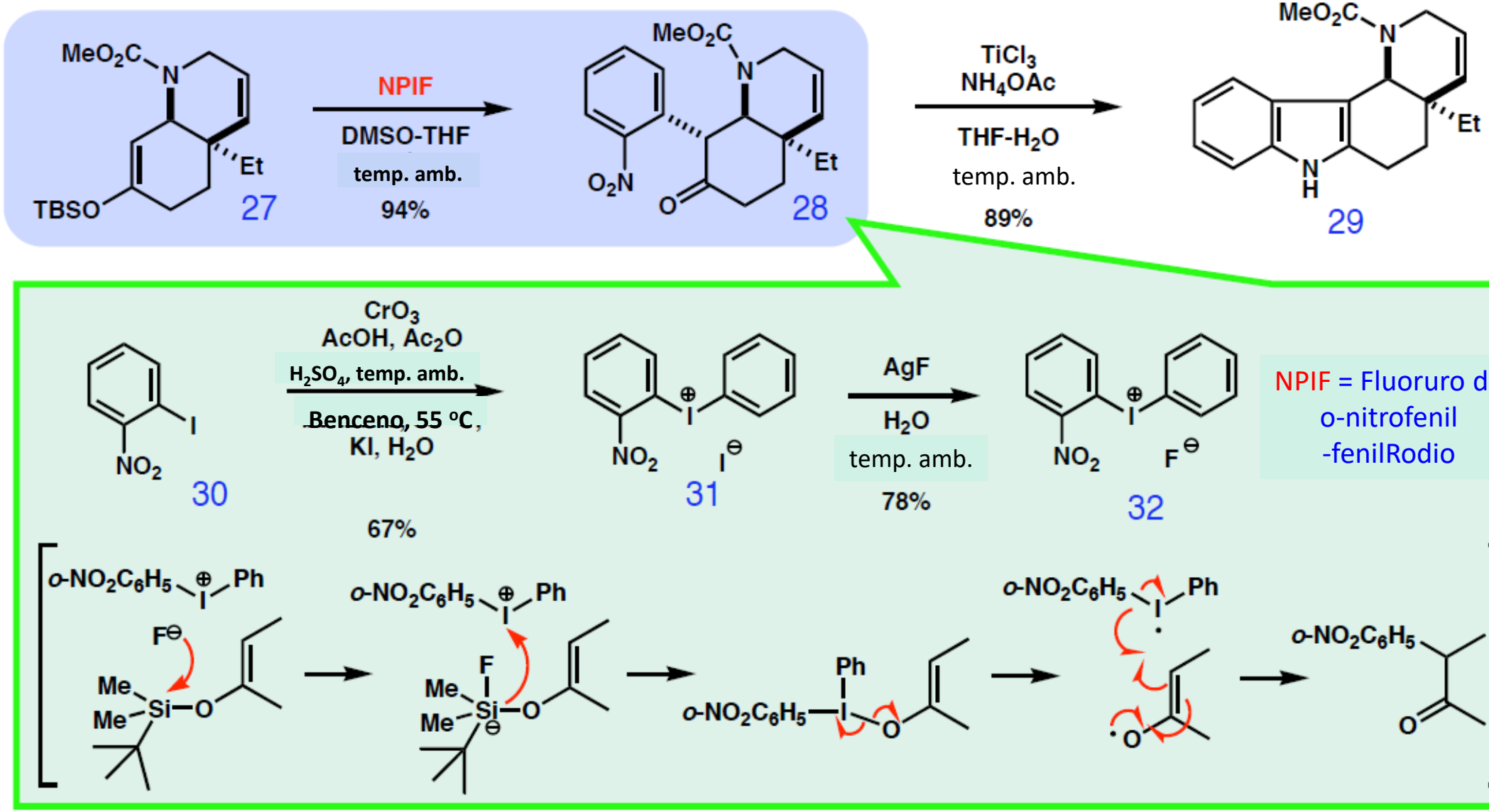


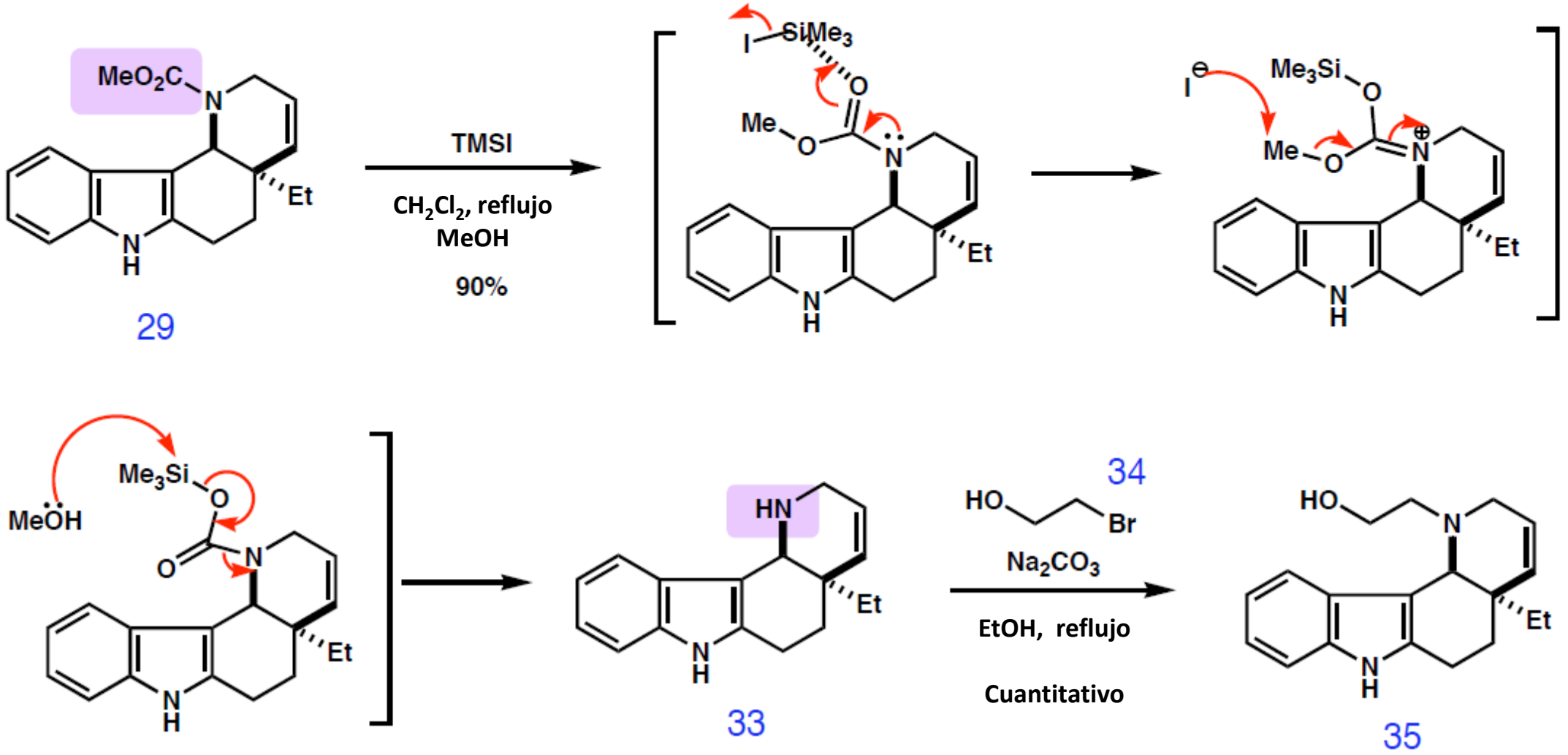

21
OMe
OMe
O
MeO2CHN
cat. p-TsOH
CHCl3
reflujo
25 ml ¥3,100 (TCI)
90%
20
HOHMe
OMe
R
N
R'
H
MeO2C
TBSO
NHMDS
THF
–78 °C;
TBSCl
Cuantitativo
22
23

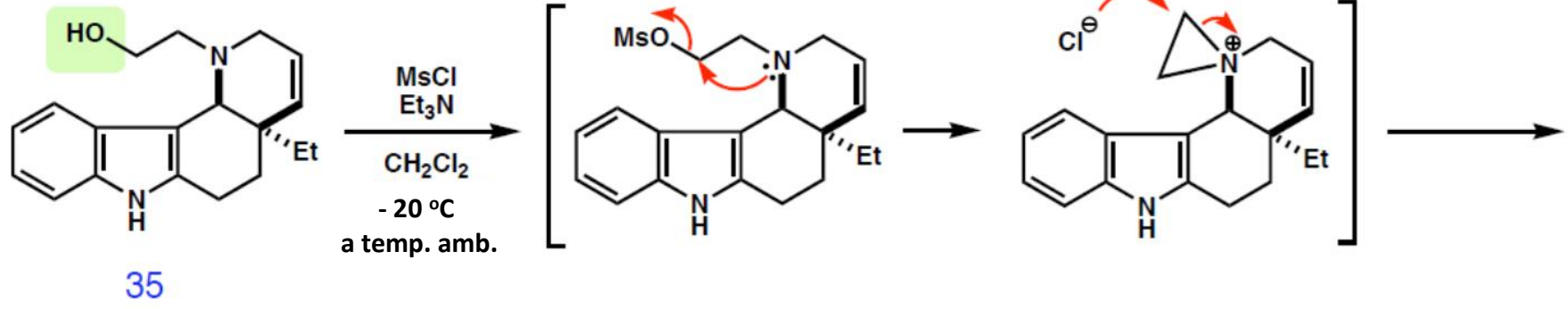


Selectividad *Endo*

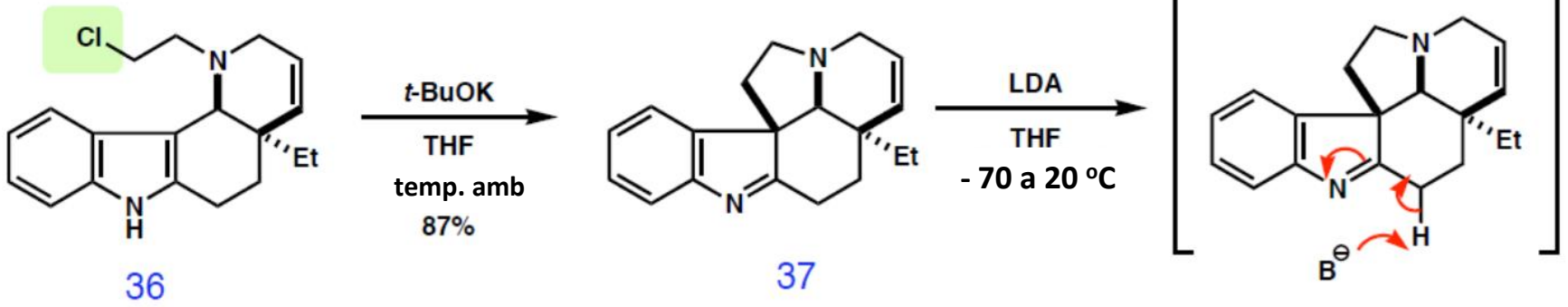



MeO2C
N
Et
TBSO
27
NPIF
DMSO-THF
temp. amb.
94%
O2N
O
28
TiCl3
NH4OAc
THF-H2O
temp. amb.
89%
NH
29
CrO3
AcOH, Ac2O
H2SO4, temp. amb.
Benceno, 55 °C,
KI, H2O
67%
NO2
I
30
31
AgF
H2O
temp. amb.
78%
F
32
NPIF = Fluoruro de o-nitrofenil -fenilRodio
o-NO2C6H5
Ph
Me
Si
O

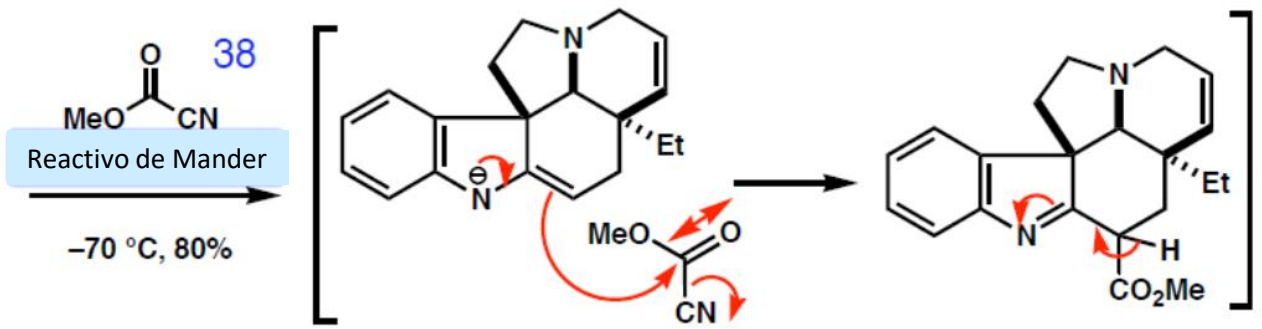

MeO2C
N
Et
N
H
29
TMSI
CH2Cl2, reflujo
MeOH
90%
I
SiMe3
O
Me
O
N
Et
N
H
I
Me3Si
O
Me
O
N
Et
N
H
Me3Si
O
MeOH
O
N
Et
N
H
HN
Et
N
H
33
34
HO
Br
Na2CO3
EtOH, reflujo
Cuantitativo
HO
N
Et
N
H
35

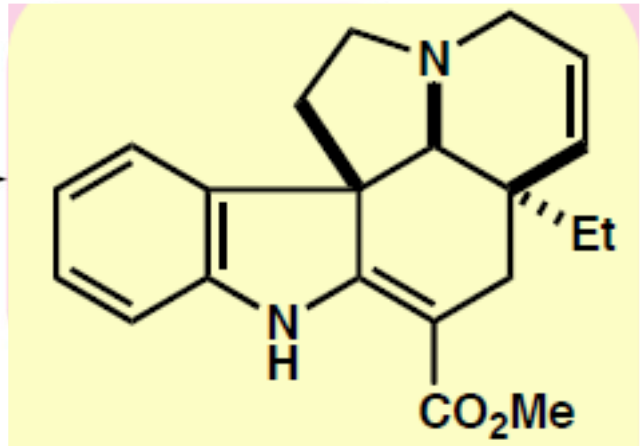


35



36 37



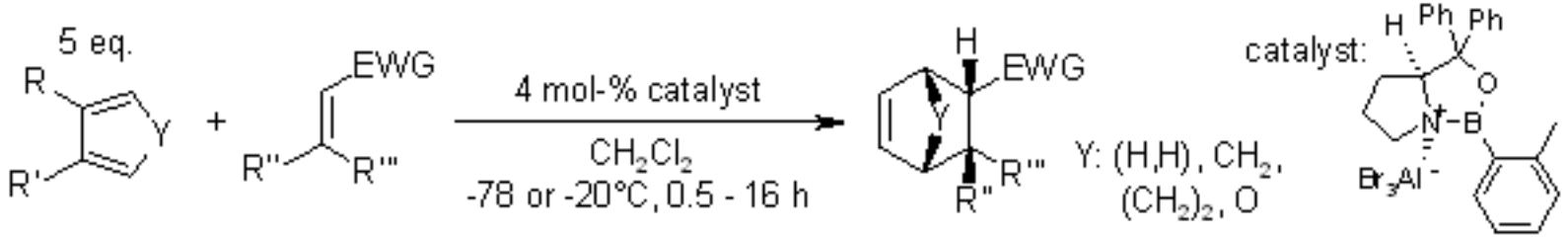


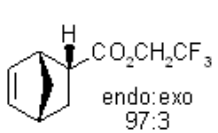
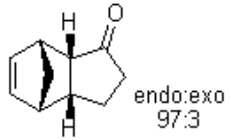
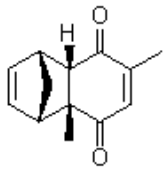
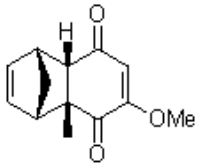
Cloroformato de metilo → N-alquilación

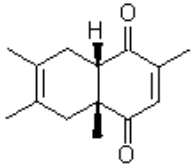
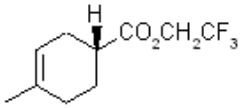
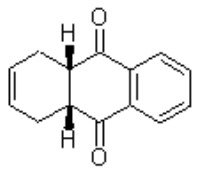
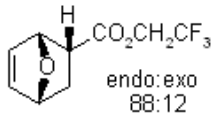
12 pasos
Rendimiento global 30.5 %

Chiral Oxazaborolidine-Aluminum Bromide Complexes Are Unusually Powerful and Effective Catalysts for Enantioselective Diels-Alder Reactions

D. Liu, E. Canales, E. J. Corey, *J. Am. Chem. Soc.*, **2007**, *129*, 1498-1499.

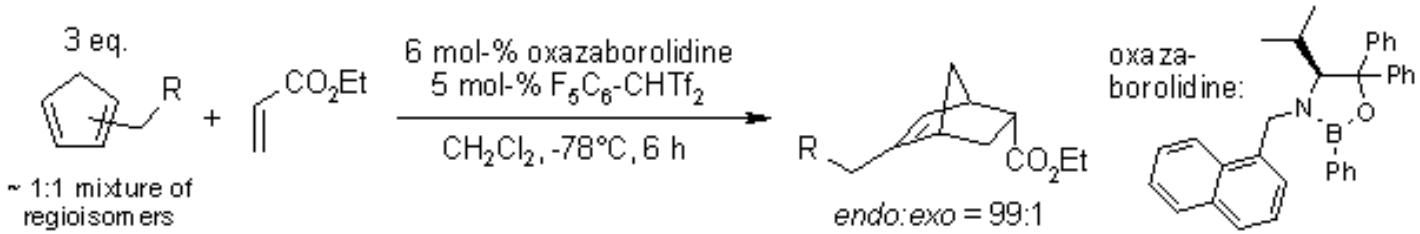


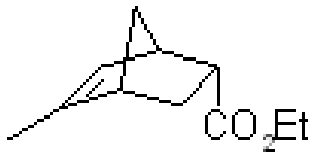
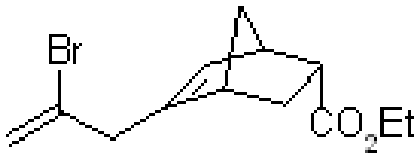
product	T (°C)	t (h)	yield (%, isol.)	ee (%)
 endo:exo 97:3	-78	8	98	99
 endo:exo 97:3	-40	1	95	92
	-78	0.5	99	99
	-78	12	99	88

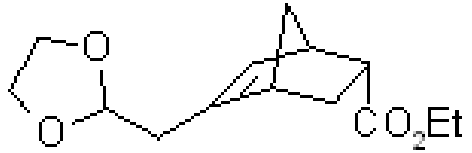
product	T (°C)	t (h)	yield (%, isol.)	ee (%)
	-78	16	97	96
	-20	16	96	91
	-78	16	99	84
 endo:exo 88:12	-78	8	99	99

Regioselective and Asymmetric Diels-Alder Reaction of 1- and 2-Substituted Cyclopentadienes Catalyzed by a Brønsted Acid Activated Chiral Oxazaborolidine

J. N. Payette, H. Yamamoto, *J. Am. Chem. Soc.*, **2007**, *129*, 9536-9537.

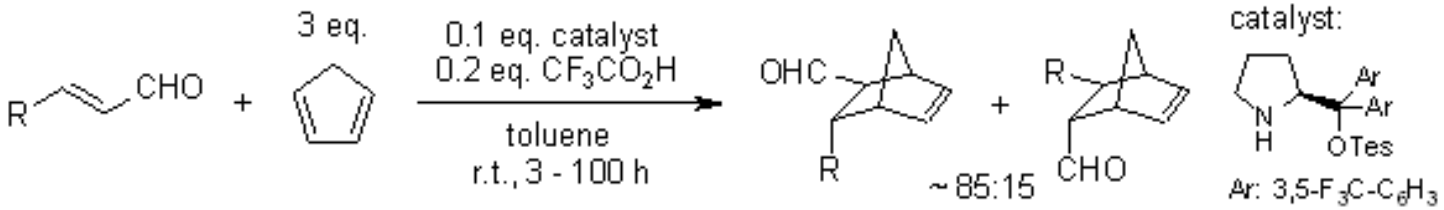


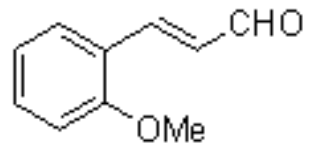
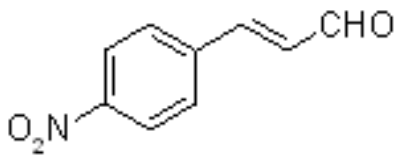
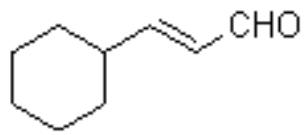
product	yield (%, isol.)	ee (%)
	96	99
	85	96

product	yield (%, isol.)	ee (%)
	81	99
	98	98

Diarylprolinol Silyl Ether as Catalyst of an *exo*-Selective, Enantioselective Diels-Alder Reaction

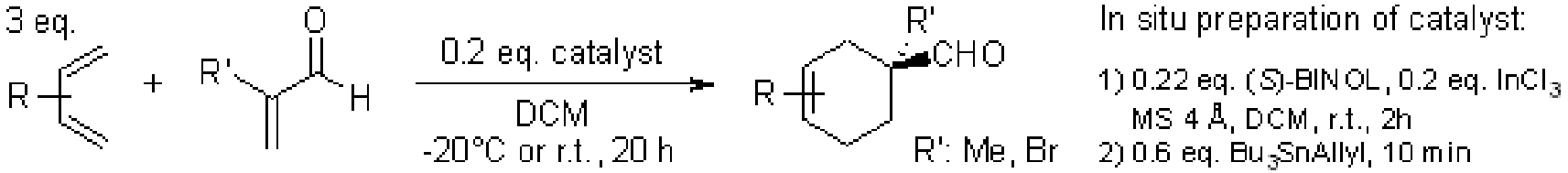
H. Gotoh, Y. Hayashi, *Org. Lett.*, **2007**, *9*, 2859-2862.



unsaturated aldehyde	t (h)	*exo*:*endo*	yield (%, isol.) (mixture)	ee (%) *exo*	ee (%) *endo*
	78	78:22	71	96	96
	6	87:13	93	96	82
	17	85:15	78	97	93
	3	78:22	65	94	91

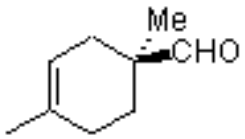
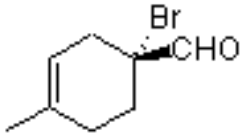
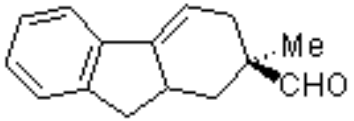
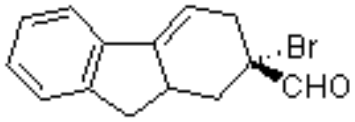
Catalytic Enantioselective Diels-Alder Reaction via a Chiral Indium(III) Complex

Y.-Chua Teo, T.-P. Loh, *Org. Lett.*, **2005**, *7*, 2539-2541.



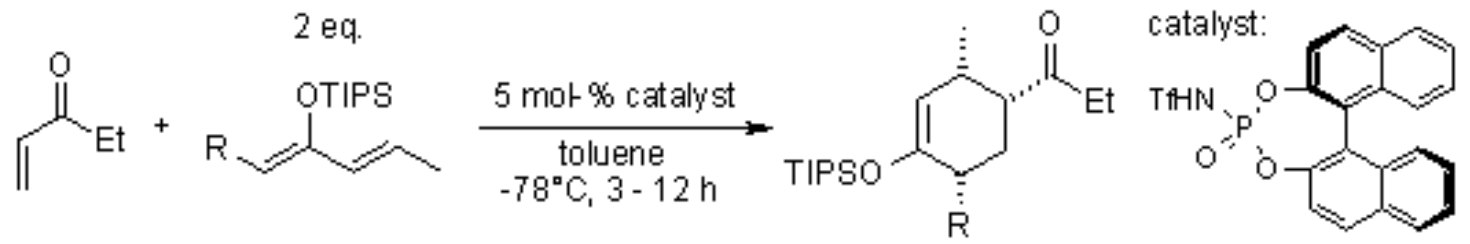
In situ preparation of catalyst:

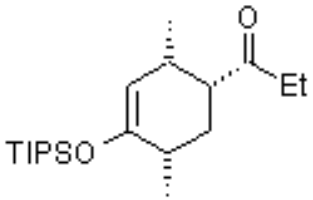
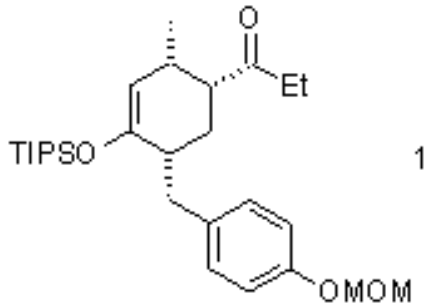
1) 0.22 eq. (S)-BINOL, 0.2 eq. $InCl_3$
MS 4 Å, DCM, r.t., 2h
2) 0.6 eq. $Bu_3SnAllyl$, 10 min

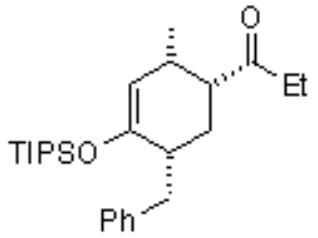
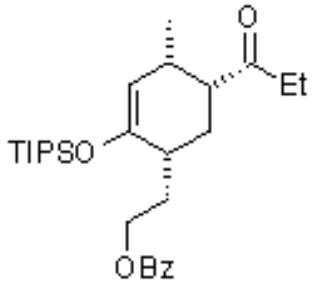
product	T (°C)	yield (%, isol.)	ee (%)
	r.t.	35	90
	-20	70	96
	-20	71	98
	-20	72	98

Design of Chiral *N*-Triflyl Phosphoramide as a Strong Chiral Brønsted Acid and Its Application to Asymmetric Diels-Alder Reaction

D. Nakashima, H. Yamamoto, *J. Am. Chem. Soc.*, **2006**, *128*, 9626-9627.

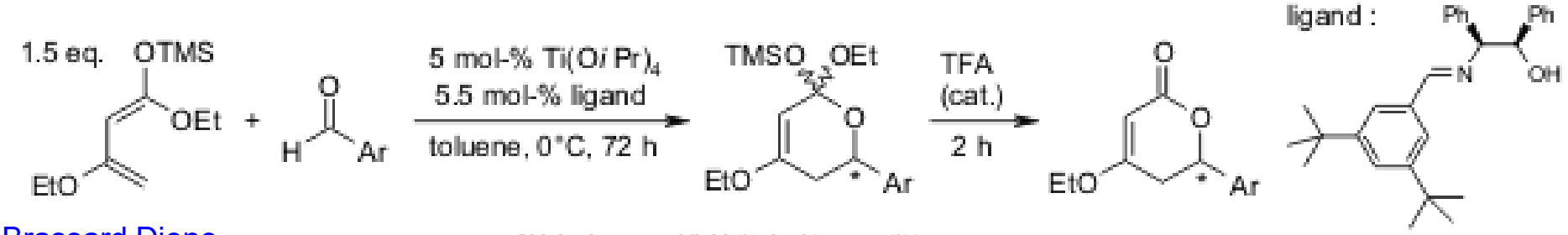


product	t (h)	yield (%, isol.)	ee (%)
	3	95	92
	12	99	85

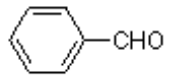
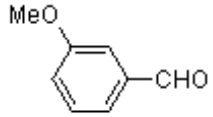
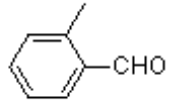
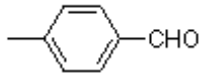
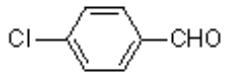
product	t (h)	yield (%, isol.)	ee (%)
	12	99	87
	12	99	91

A Mild and Efficient Asymmetric Hetero-Diels-Alder Reaction of the Brassard Diene with Aldehydes

Q. Fan, L. Lin, J. Liu, Y. Huang, X. Feng, *Eur. J. Org. Chem.*, **2005**, 3542-3552.

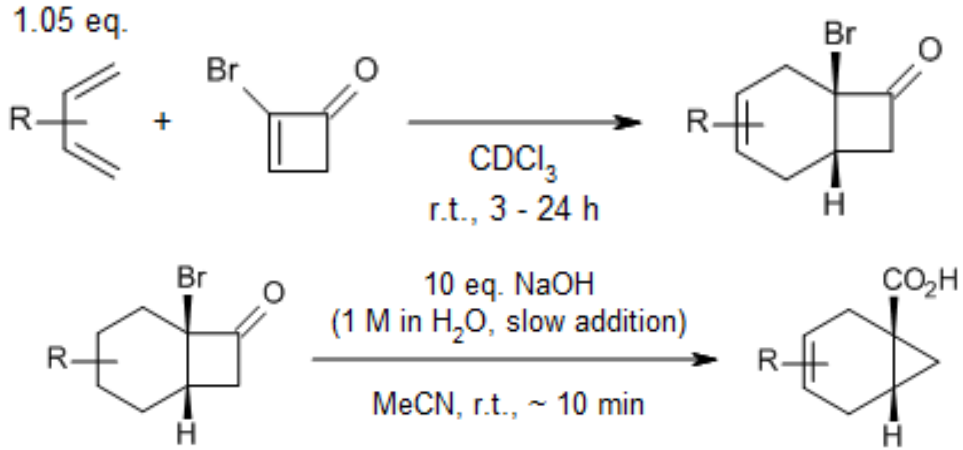


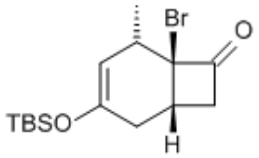
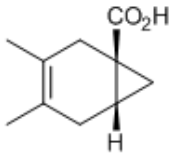
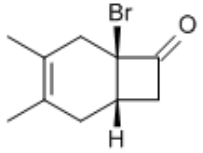
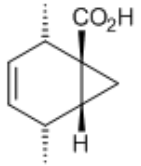
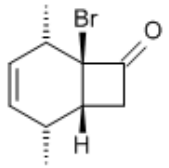
Brassard Diene

Aldehyde	Yield (%, isol.)	ee (%)
	71	93
	45	96
	24	92
	36	90
	87	97
	56	91

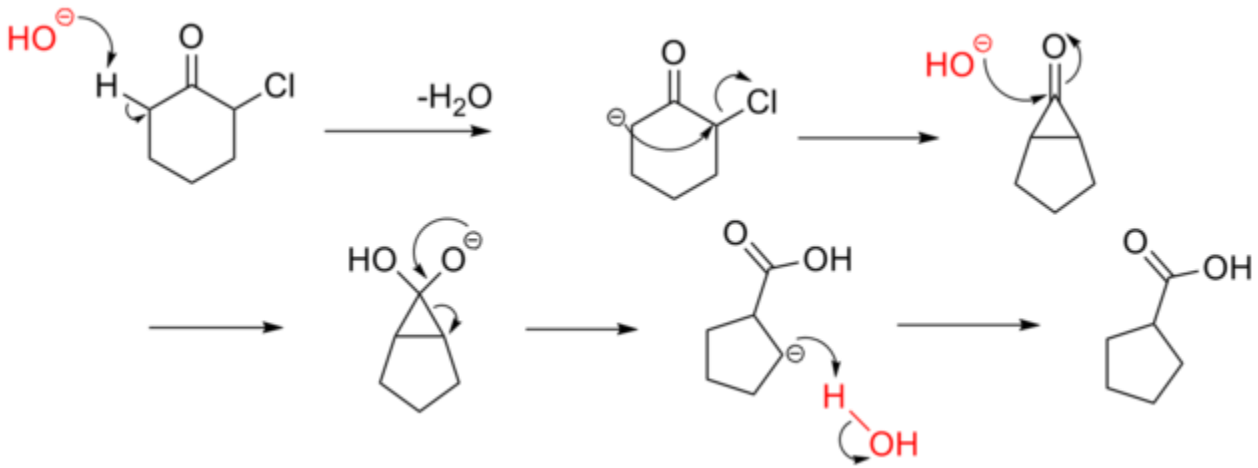
Halocycloalkenones as Diels-Alder Dienophiles. Applications to Generating Useful Structural Patterns

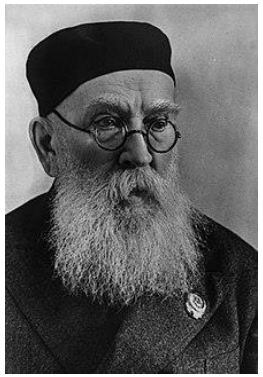
A. G. Ross, S. D. Townsend, S. J. Danishefsky, *J. Org. Chem.*, **2013**, *78*, 204-210.



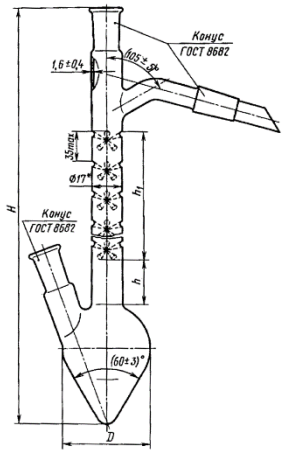
product	t (h)	yield (%, isol.)	product	yield (%, isol.)
	6	88		72
	18	92		56
	18	97		

REARREGLO DE FAVORSKY





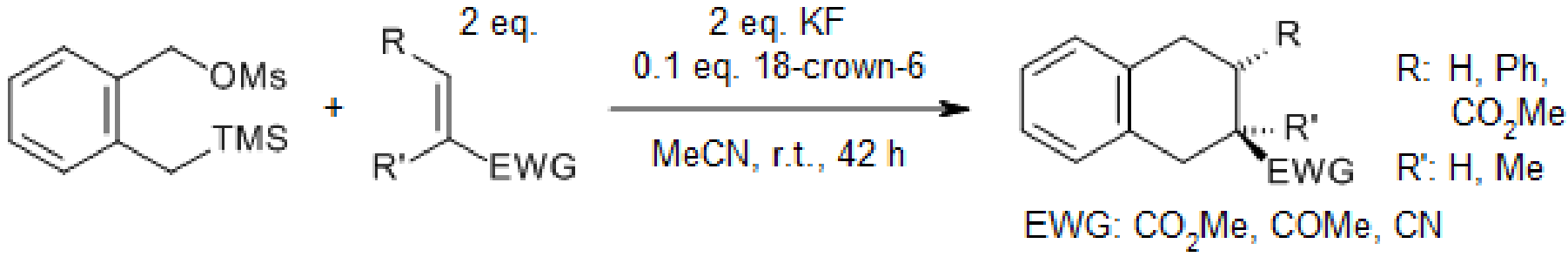
Alexey Yevgrafovich Favorsky
Químico ruso
(1860 – 1945)

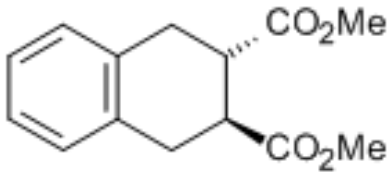
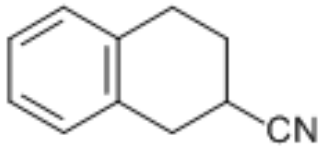
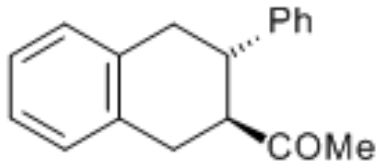
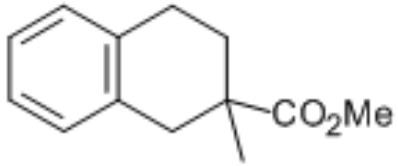


Matraz de Favorsky

2-[(Trimethylsilyl)methyl]benzyl Methanesulfonates: Useful Precursors for the Generation of *o*-Quinodimethanes

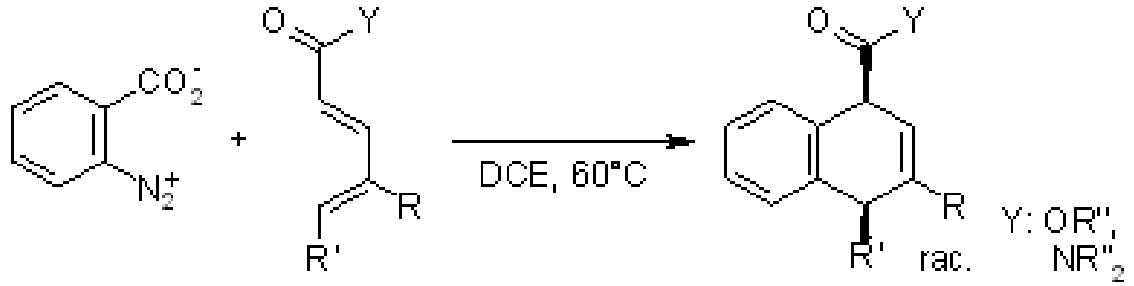
H. Shirakawa, H. Sano, *Synthesis*, **2014**, *46*, 1788-1792.

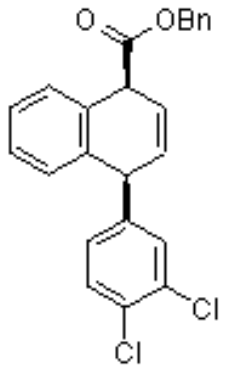
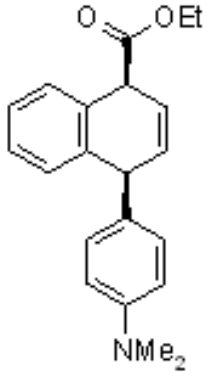
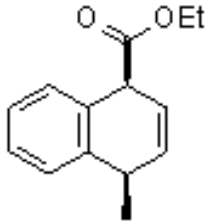
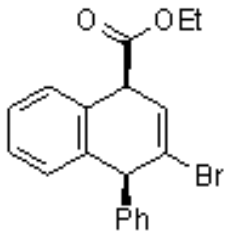


product	yield (%, isol.)	product	yield (%, isol.)
	81		86
	74		66

Synthesis of Dihydronaphthalenes via Aryne Diels-Alder Reactions: Scope and Diastereoselectivity

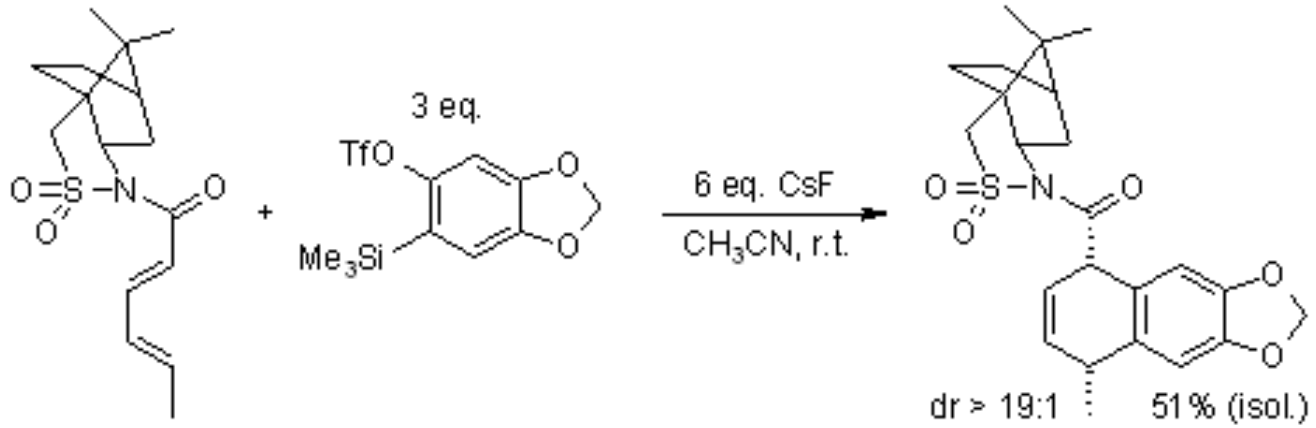
C. Dockendorff, S. Sahli, M. Olsen, L. Milhau, M. Lautens, *J. Am. Chem. Soc.*, **2005**, *127*, 15028-15029.



product	Yield (%, isol.)	product	Yield (%, isol.)	product	Yield (%, isol.)
	78		0		74
					80

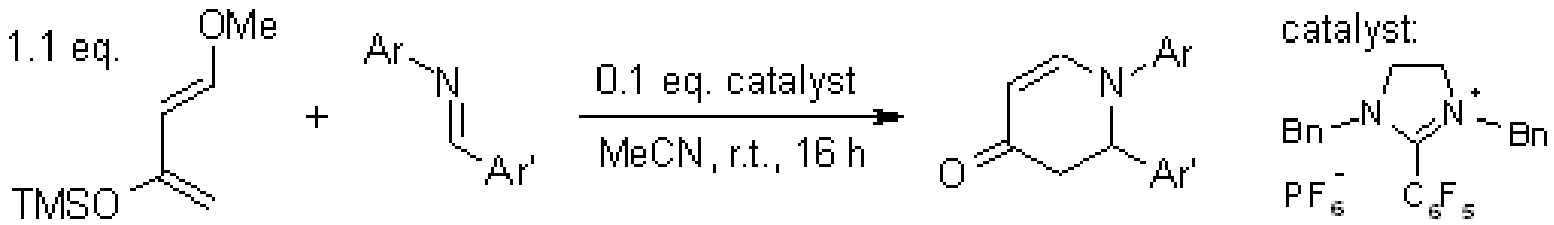
Synthesis of Dihydronaphthalenes via Aryne Diels-Alder Reactions: Scope and Diastereoselectivity

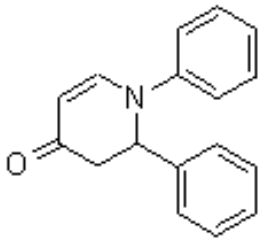
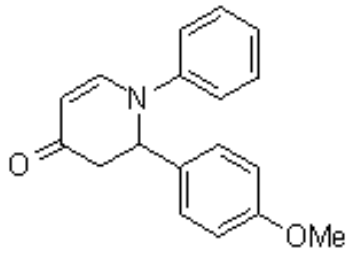
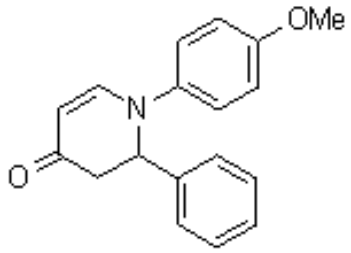
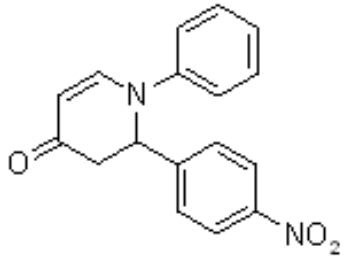
C. Dockendorff, S. Sahli, M. Olsen, L. Milhau, M. Lautens, *J. Am. Chem. Soc.*, **2005**, *127*, 15028-15029.



Imidazolinium salts as catalysts for the aza-Diels-Alder reaction

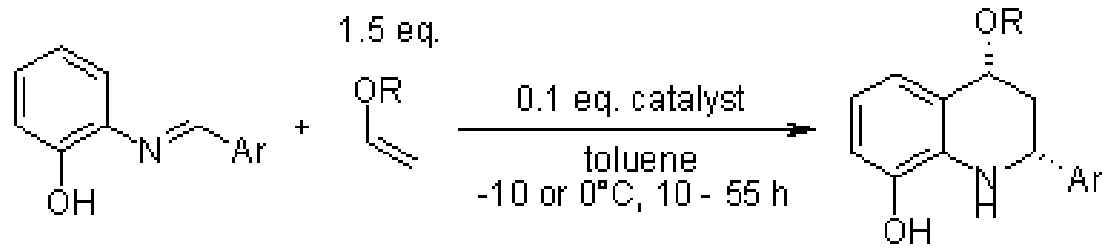
V. Jurcik, R. Wilhelm, *Org. Biomol. Chem.*, **2005**, *3*, 239-244.

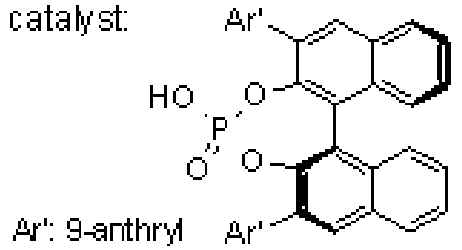


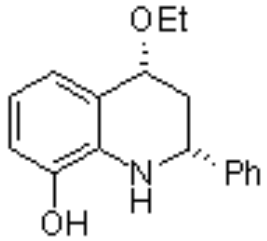
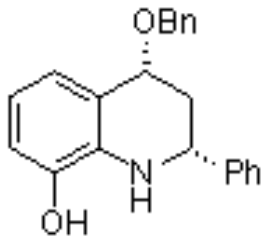
Product	Yield (%, isol.)	Product	Yield (%, isol.)
	95		45
	92		50

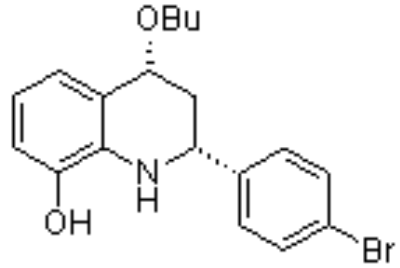
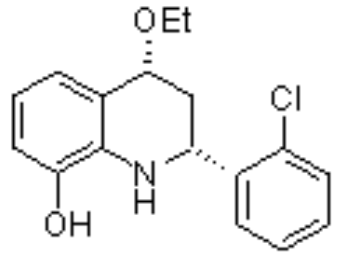
Chiral Brønsted Acid-Catalyzed Inverse Electron-Demand Aza Diels-Alder Reaction

T. Akiyama, H. Morita, K. Fuchibe, *J. Am. Chem. Soc.*, **2006**, *128*, 13070-13071.



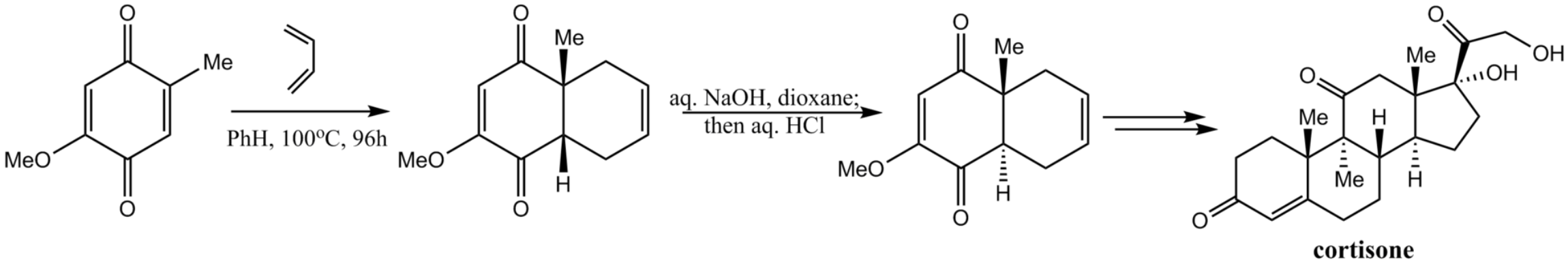


product	T (°C)	yield (%, isol.)	cis/trans	ee (%)
	-10	89	99:1	94
	0	76	99:1	91

product	T (°C)	yield (%, isol.)	cis/trans	ee (%)
	-10	86	99:1	89
	0	72	96:4	87

The Total Synthesis of Steroids

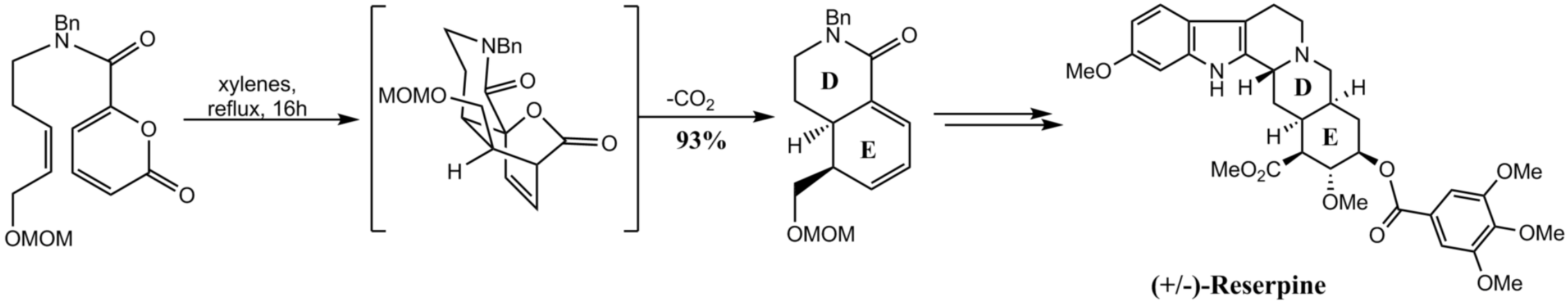
Woodward, R. B.; Sondheimer, F.; Taub, D.; Heusler, K.; McLamore, W. M. *Journal of the American Chemical Society*, **1952**, *74*(17): 4223–4251. doi:10.1021/ja01137a001.



cortisone

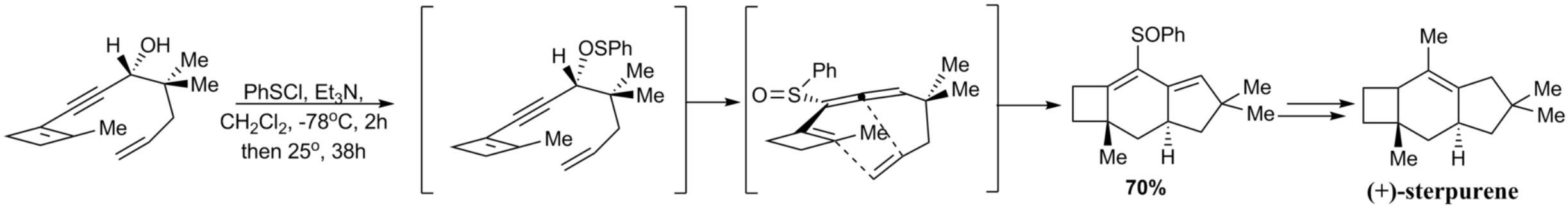
General methodology for cis-hydroisoquinoline synthesis: Synthesis of reserpine

Wender, P. A.; Schaus, J. M.; White, A. W. (). *Journal of the American Chemical Society* **1980**, *102* (19): 6157–6159. doi:10.1021/ja00539a038



A short enantioselective synthesis of (+)-sterpurene: Complete intramolecular transfer of central to axial to central chiral elements

Gibbs, R. A.; Okamura, W. H. (). . *Journal of the American Chemical Society* **1988**, *110* (12): 4062–4063. doi:10.1021/ja00220a069



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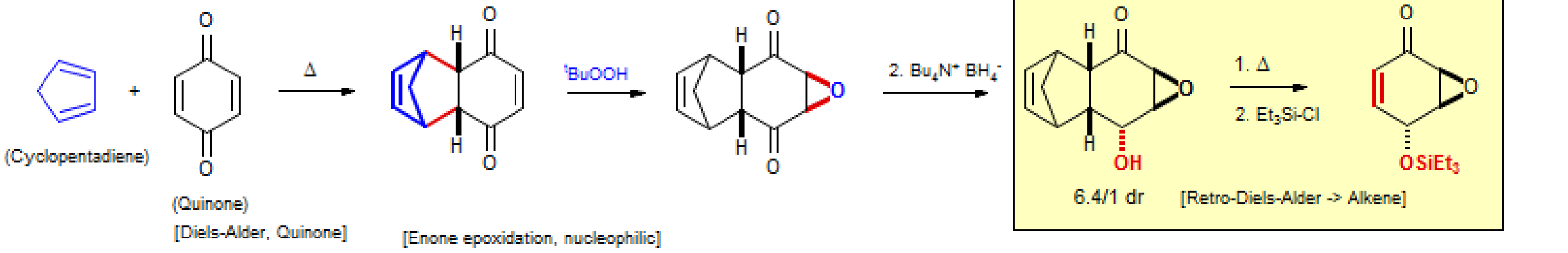
Epoxydon, Epi-

Genski, T.; Taylor, R. J. K. *Tetrahedron Lett.* **2002**, *43*, 3573.

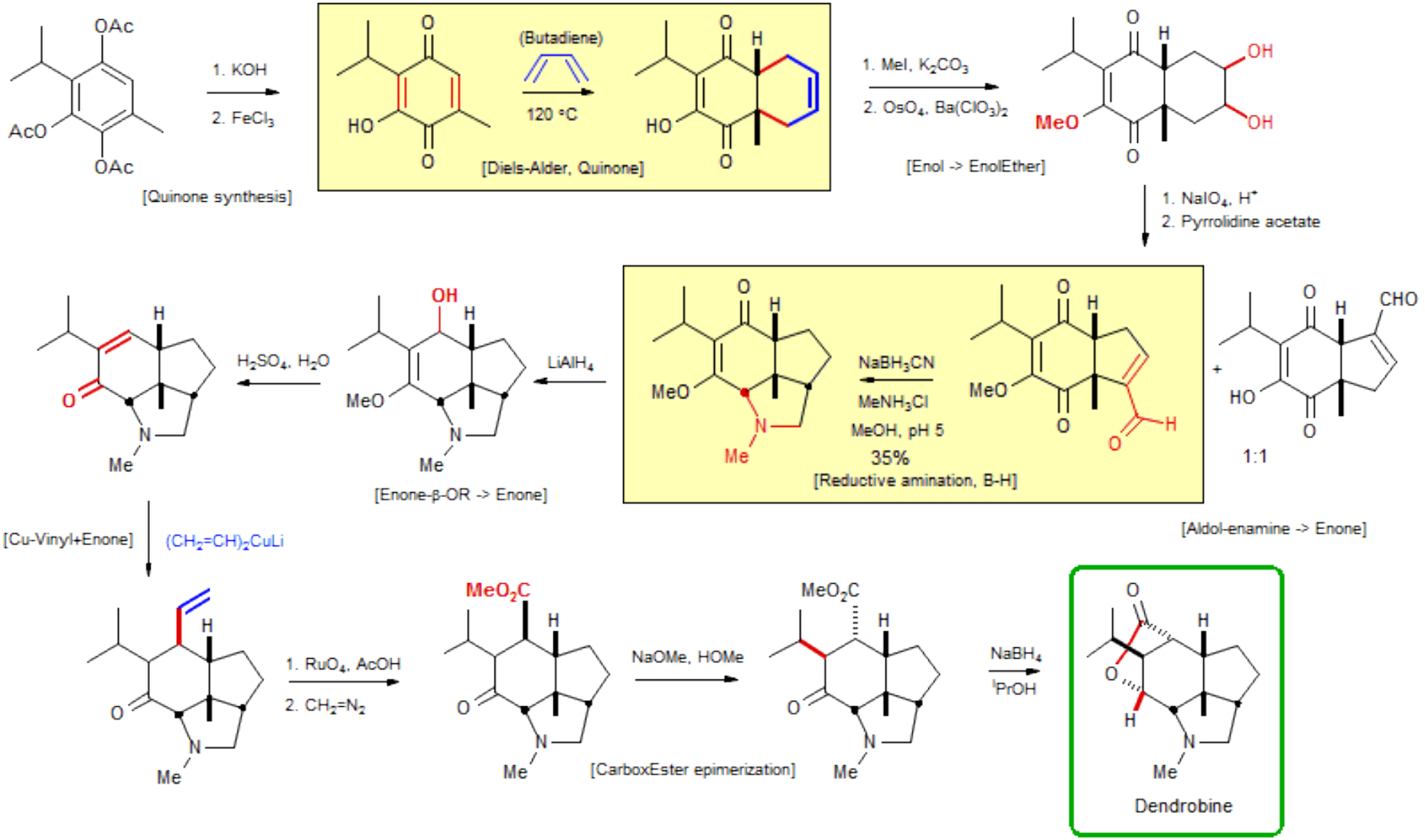


Dendrobine

74-07

COMM

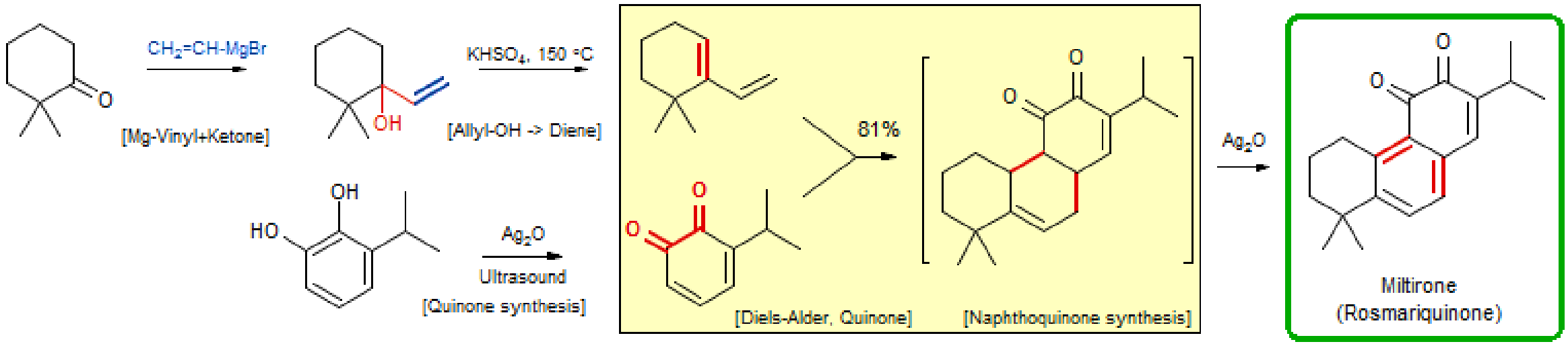
Kende, A. S.; Bentley, T. J.; Mader, R. A.; Ridge, D. *J. Am. Chem. Soc.* **1974**, *96*, 4332-4334.



Miltirone

90-07

Lee, J.; Mei, H. S.; Snyder, J. K *J. Org. Chem.* **1990**, *55*, 5013 (see also *J. Org. Chem.* **1985**, *50*, 4996).



Intramolecular Diels-Alder Reactions

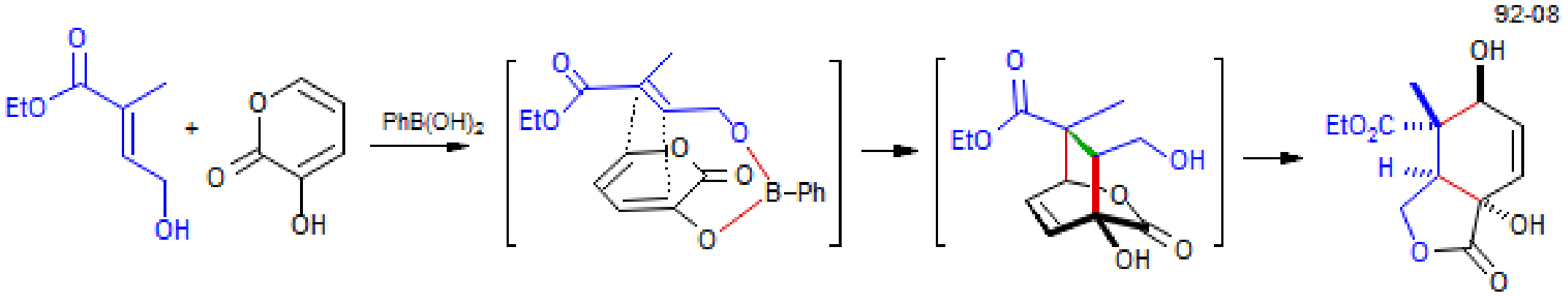
The Intramolecular Diels-Alder Reaction,
E. Ciganek, *Org. React.* **1984**, 32.
Stereochemical Aspects of the Intramolecular Diels-Alder Reactions,
Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187.
Cytochalasan Synthesis: Macrocycle Formation via Intramolecular Diels-Alder Reactions,
Thomas, E. J. *Acc. Chem. Res.* **1991**, *24*, 229.
Pericyclization of Vinylallenes in Organic Synthesis: On the Intramolecular Diels-Alder Reaction,
Okamura, W. H.; Curtin, M. L. *Synlett* **1990**, *1*, 1.
Transannular Diels-Alder Reaction on Macrocycles. A General Strategy for the Synthesis of Polycyclic Compounds,
Deslongchamps, P. *Pure Appl. Chem.* **1992**, *64*, 1831-47.
Second Generation of Steroid Synthesis via o-Quinodimethane,
Nemoto, H.; Fukumoto, K. *Tetrahedron* **1998,** *54*, 5425-64.
Harvesting Diels and Alder's Garden: Synthetic Investigations of Intramolecular [4 + 2] Cycloadditions,
Fallis, A. G. *Acc. Chem. Res.* **1999**, *32*, 464-74.
The Type 2 Intramolecular Diels-Alder Reaction: Synthesis and Chemistry of Bridgehead Alkenes,
Bear, B. R.; Sparks, S. M.; Shea, K. J. *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 820-49.
The Transannular Diels-Alder Strategy: Applications to Total Synthesis,
Marsault, E.; Toro, A.; Nowak, P.; Deslongchamps, P. *Tetrahedron* **2001**, *57*, 4243-60.
On the Origins of Diastereofacial Selectivity of [4+2] Cycloadditions in Cage-Annulated and Polycarbocyclic Diene/Dienophile Systems,
Marchand, A. P.; Coxon, J. M. *Acc. Chem. Res.* **2002**, *35*, 271-7.

Intramolecular Diels-Alder Reactions

Temporary linkage between diene and dienophile for regiocontrol

Taxol Ring D

Nicolaou, K. C.; Liu, J. J.; Hwang, C.-K.; Pai, W. M.; Guy, R. K. *Chem. Commun.* **1992**, 1118



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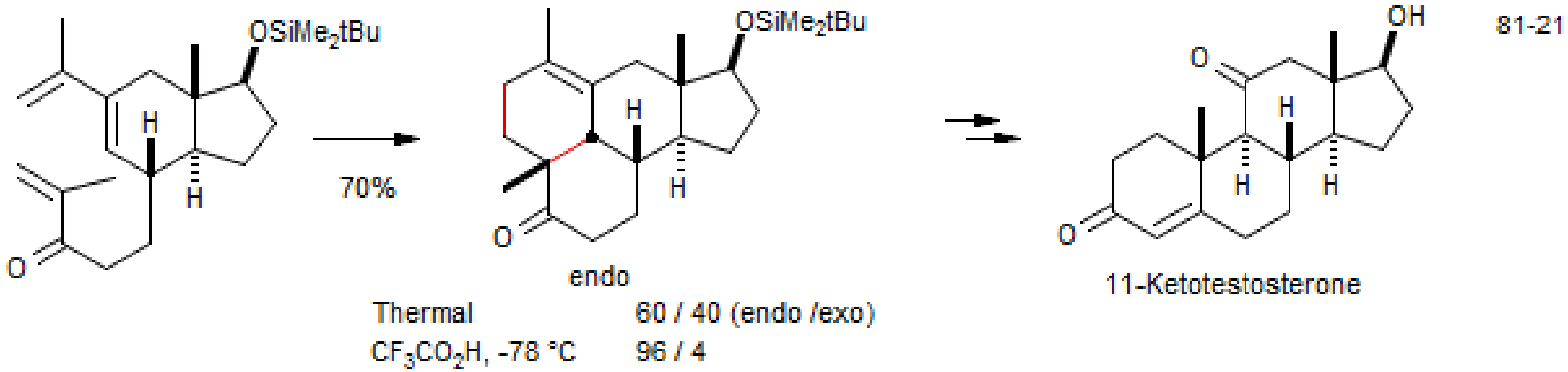
Intramolecular Diels-Alder Reactions

Increased *endo* proference with acid catalysis.

Testosterone, 11-keto

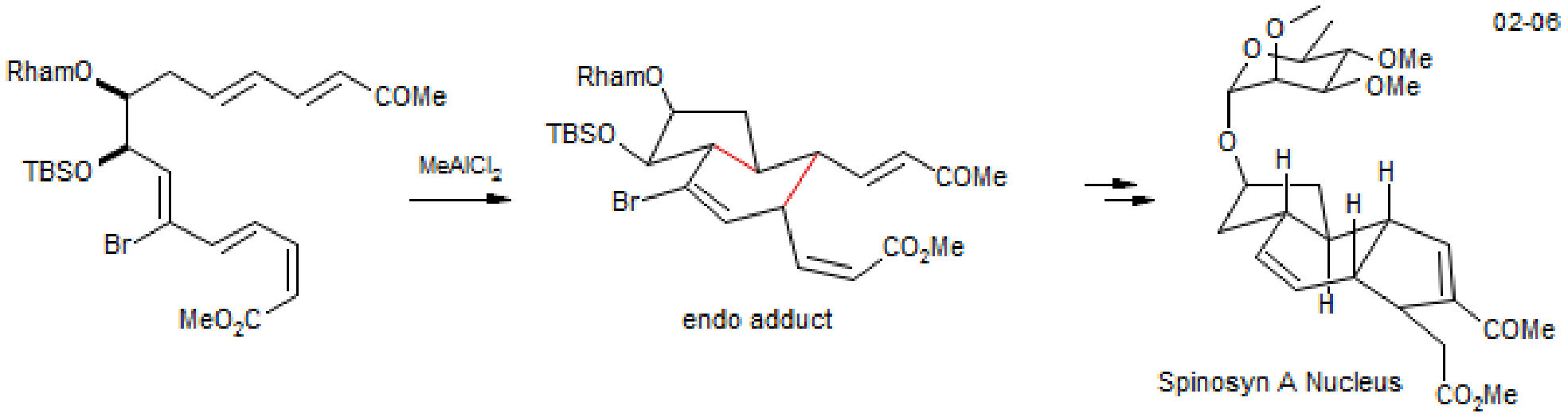
Stork, G.; Clark, G.; Shiner, C. S. *J. Am. Chem. Soc.* **1981**, *103*, 4948.



Intramolecular Diels-Alder Reactions

Spinosyn A Nucleus:

Mergott, D. J.; Frank. S. A.; Rousch, W. R. *Org. Lett.* **2002**, *4*, 3157



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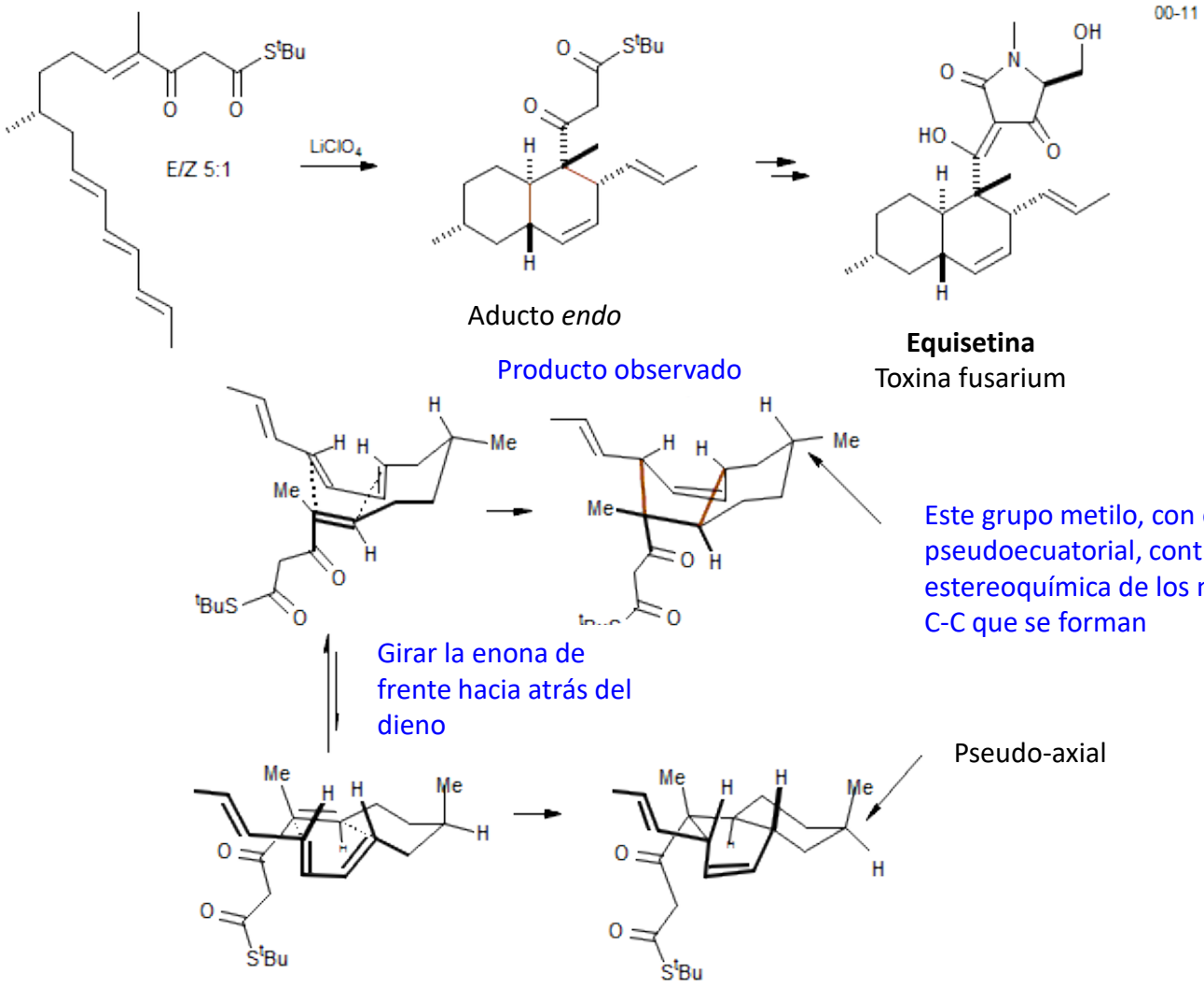
Intramolecular Diels-Alder Reactions

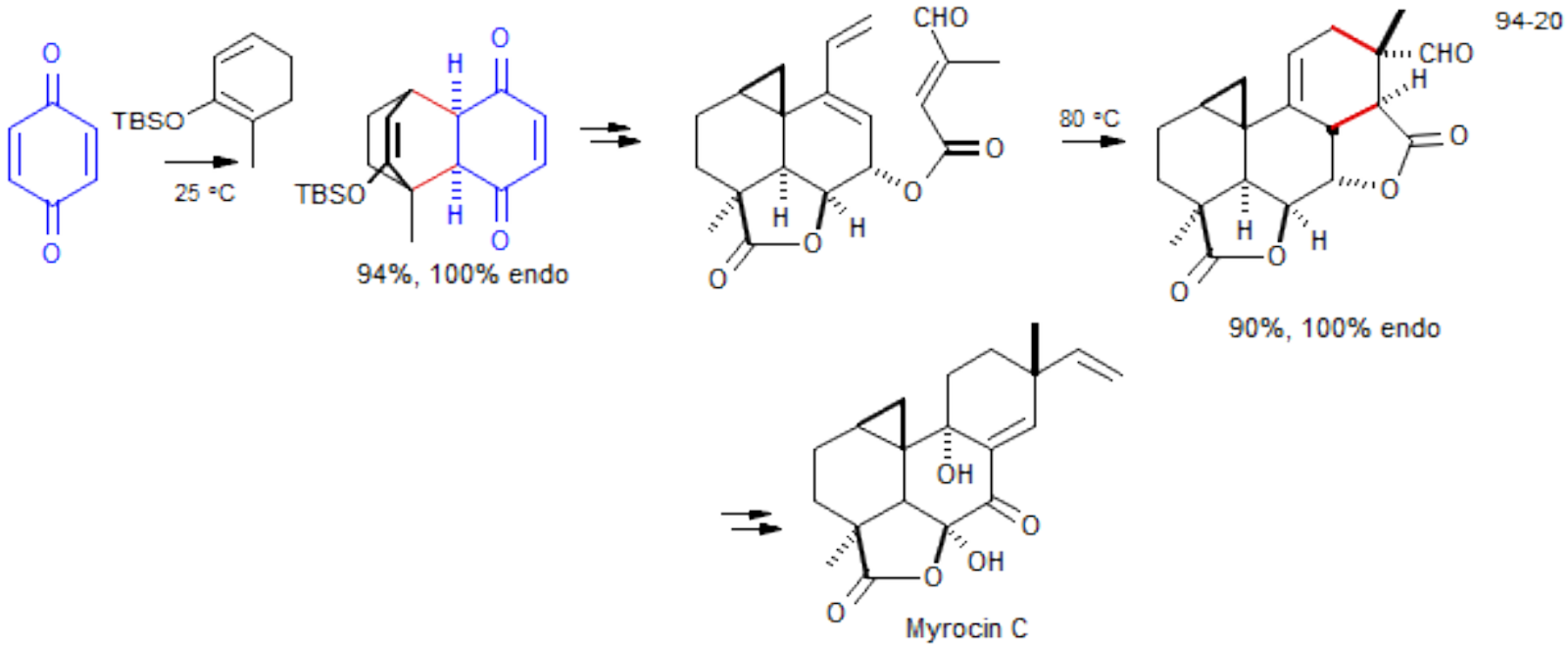
Equisetina

Burke, L T; Dixon, D J.; Ley, S. V.; Rodrigues, F. *Org. Lett.* **2000**, *2*, 3611



Myrocin C

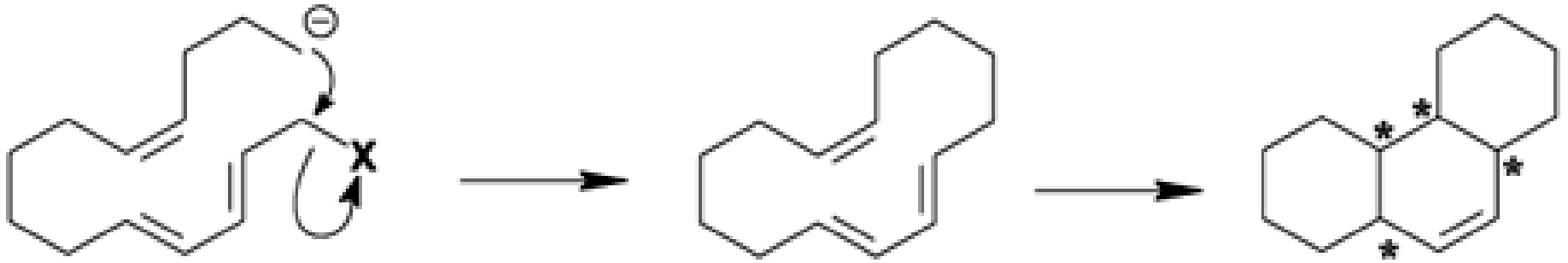
Chu-Moyer, Danishefsky, Schulte *J. Am. Chem. Soc.* **1994**, *116*, 11213



TRANSANNULAR DIELS-ALDER (TADA) REACTION

Deslongchamps, P. *Aldrichimica Acta* **1991**, *24*, 43-56.

Deslongchamps, P. *Pure & Appl. Chem*. **1992**, *64*, 1831-1847.



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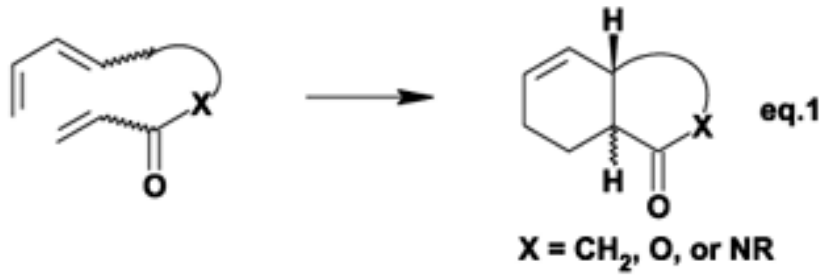
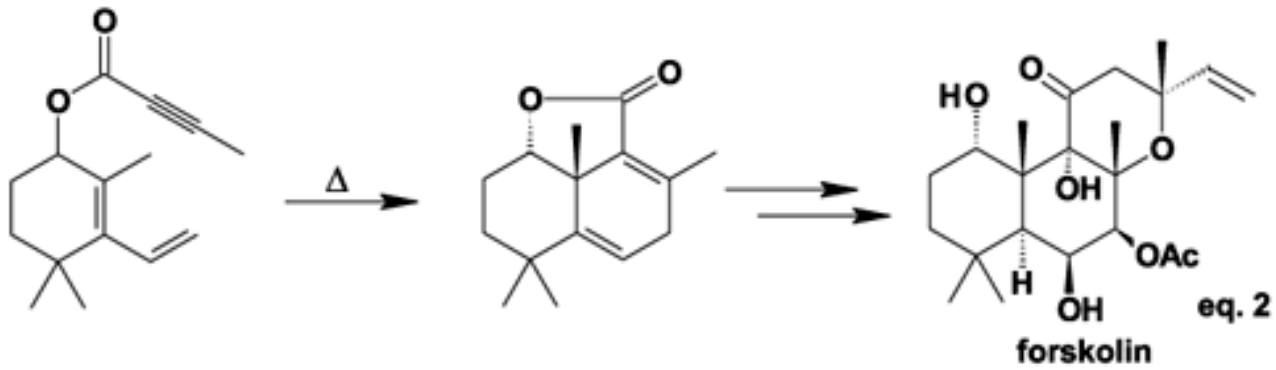
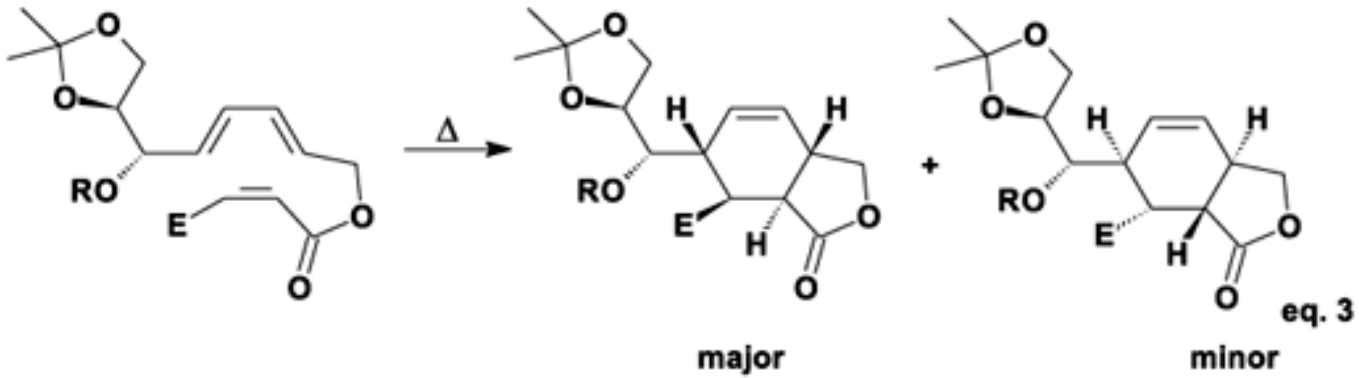


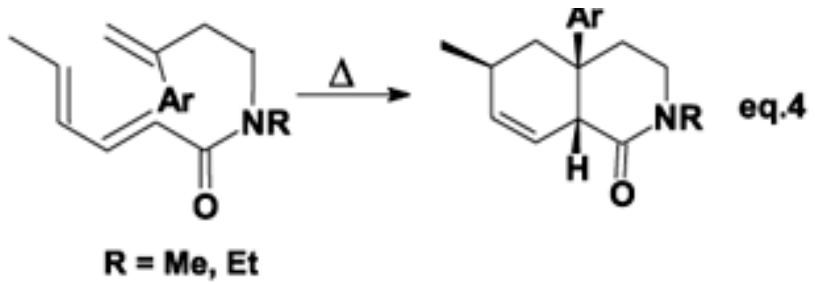
Delpech, B.; Calvo, D.; Lett, R. *Tetrahedron Lett.* **1996**, *37*, 1015-1018.



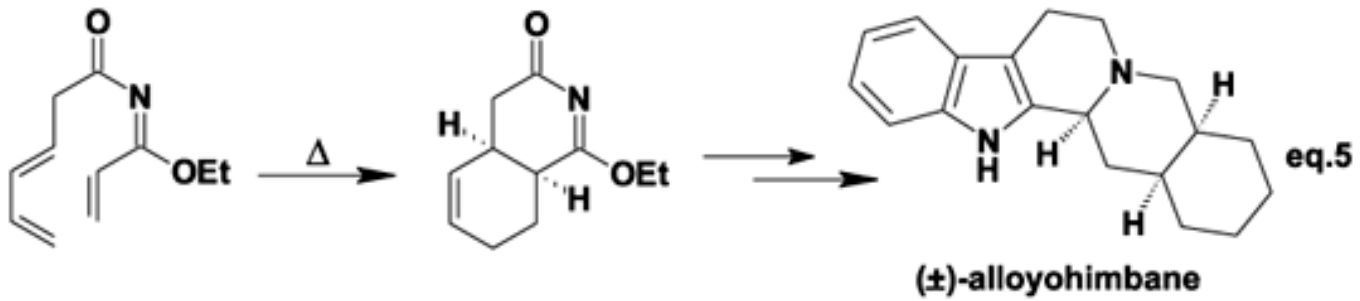
Lilly, M. J.; Sherburn, M. S. *Chem. Commun.* **1997**, 967-968.



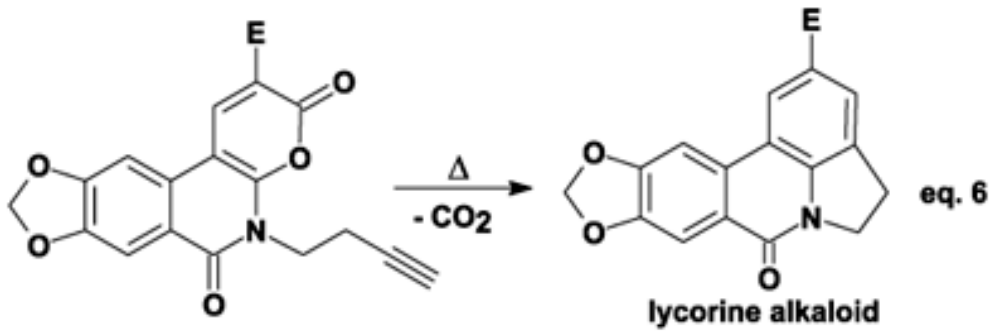
Lilly, M. J.; Sherburn, M. S. *Chem. Commun.* **1997**, 967-968.



Handa, S.; Jones, K.; Newton, C. G. *J. Chem. Soc., Perkin Trans 1* **1995**, 1623-1633.



Sparks, S. M.; Shea, K. J. *Tetrahedron Lett.* **2000**, *41*, 6721-6724.



Pérez, D.; Burés, G.; Guitián, E.; Castedo, L. *J. Org. Chem.* **1996**, *61*, 1650-1654.

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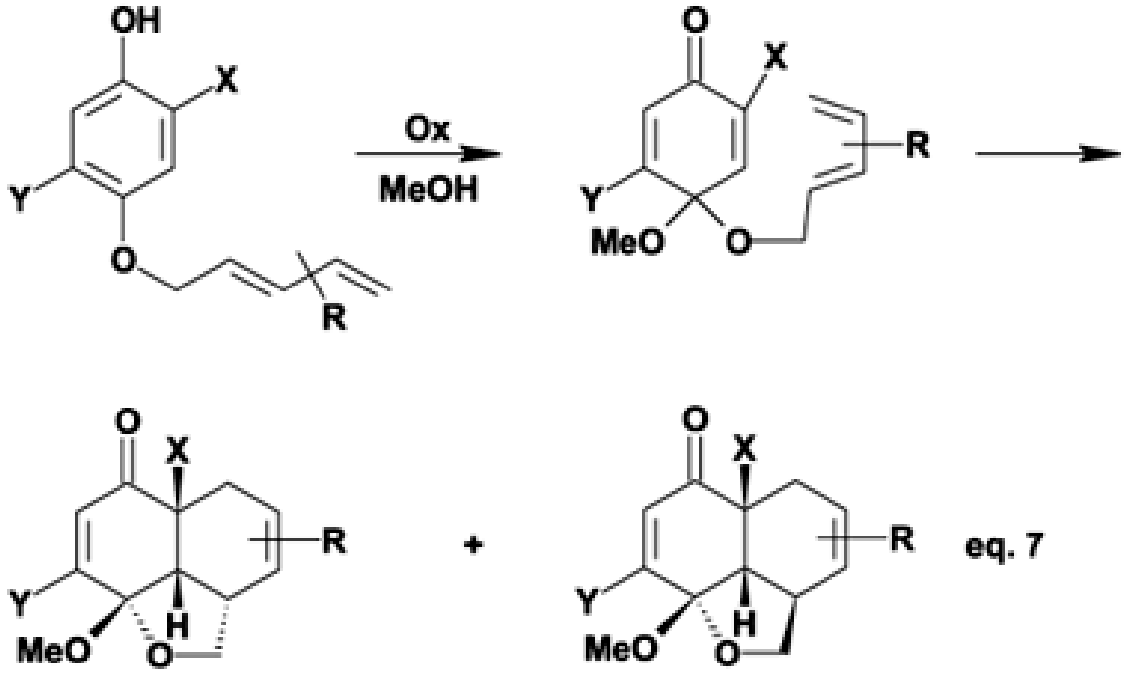
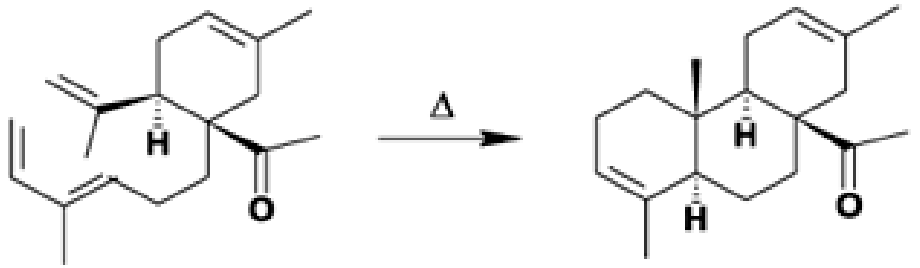


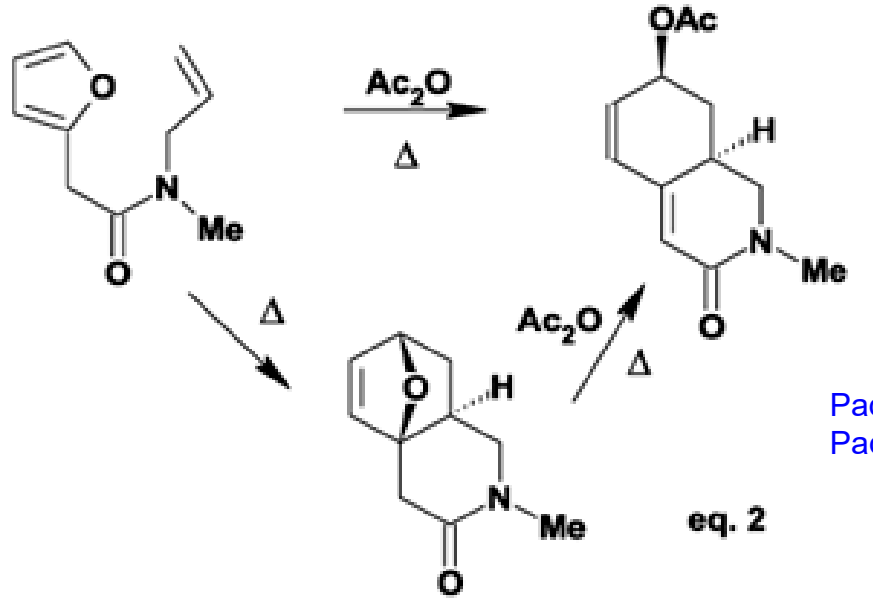
Tsai, Y-F.; Peddinti, R. K.; Liao, C-C. *Chem. Commun.* **2000**, 475-476;

Carlini, R.; Higgs, K.; Older, C.; Randhawa, S.; Rodrigo, R. *J. Org. Chem.* **1997**, *62*, 2330-2331.



eq. 1

Abad. A.; Agulló, C.; Cuñat, A. C.; Navarro, I.; de Arellano, M. C. R. *Synlett* **2001**, 349-352.



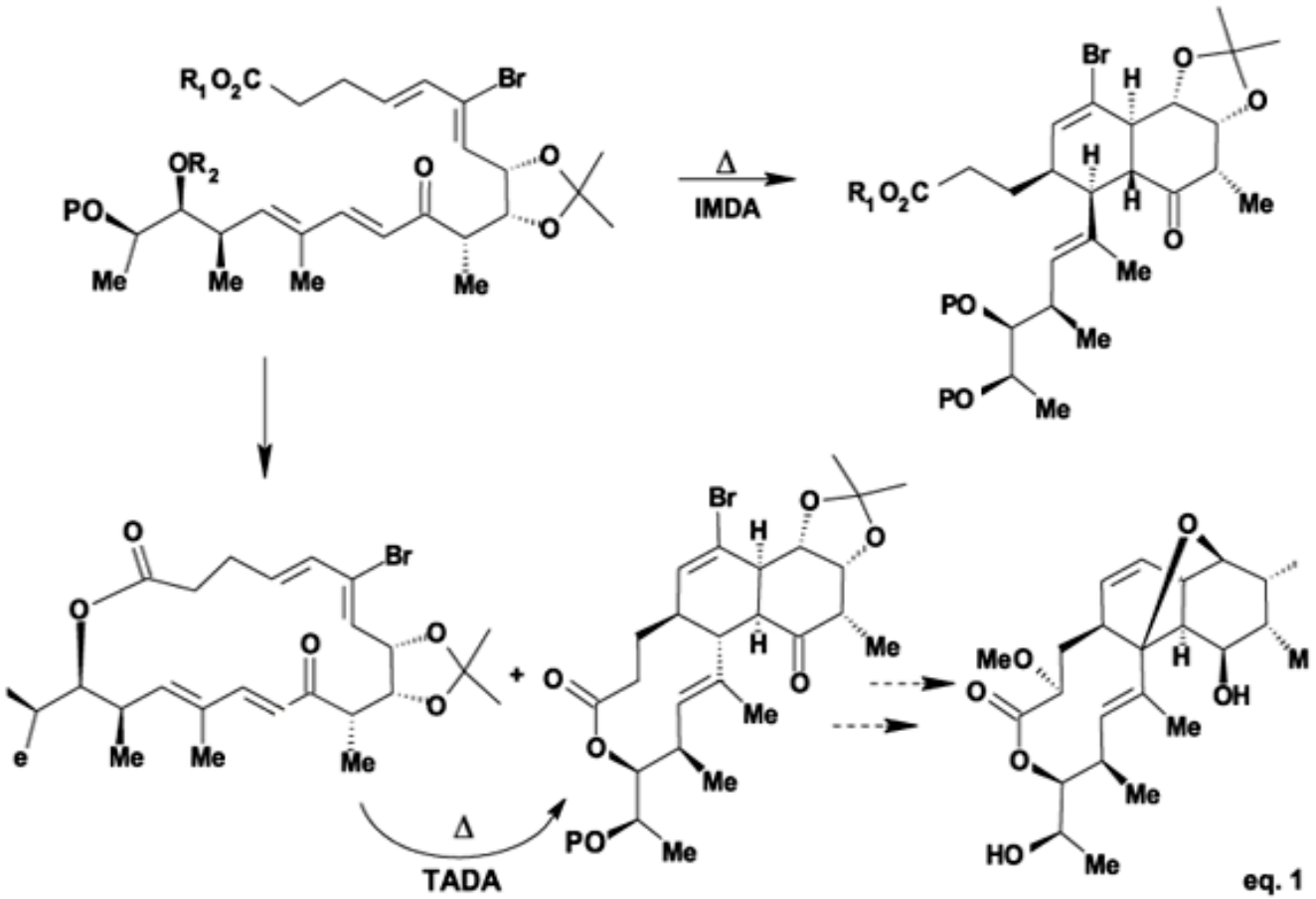
eq. 2

Padwa, A.; Reger, T. S. *Can. J. Chem.* **2000**, *78*, 749-756;
Padwa, A.; Brodney, M. A.; Dimitroff, M.; Liu, B.; Wu, T. *J. Org. Chem.* **2001**, *66*, 3119-3128.

Scheme 4.

Síntesis de Nodusmicina

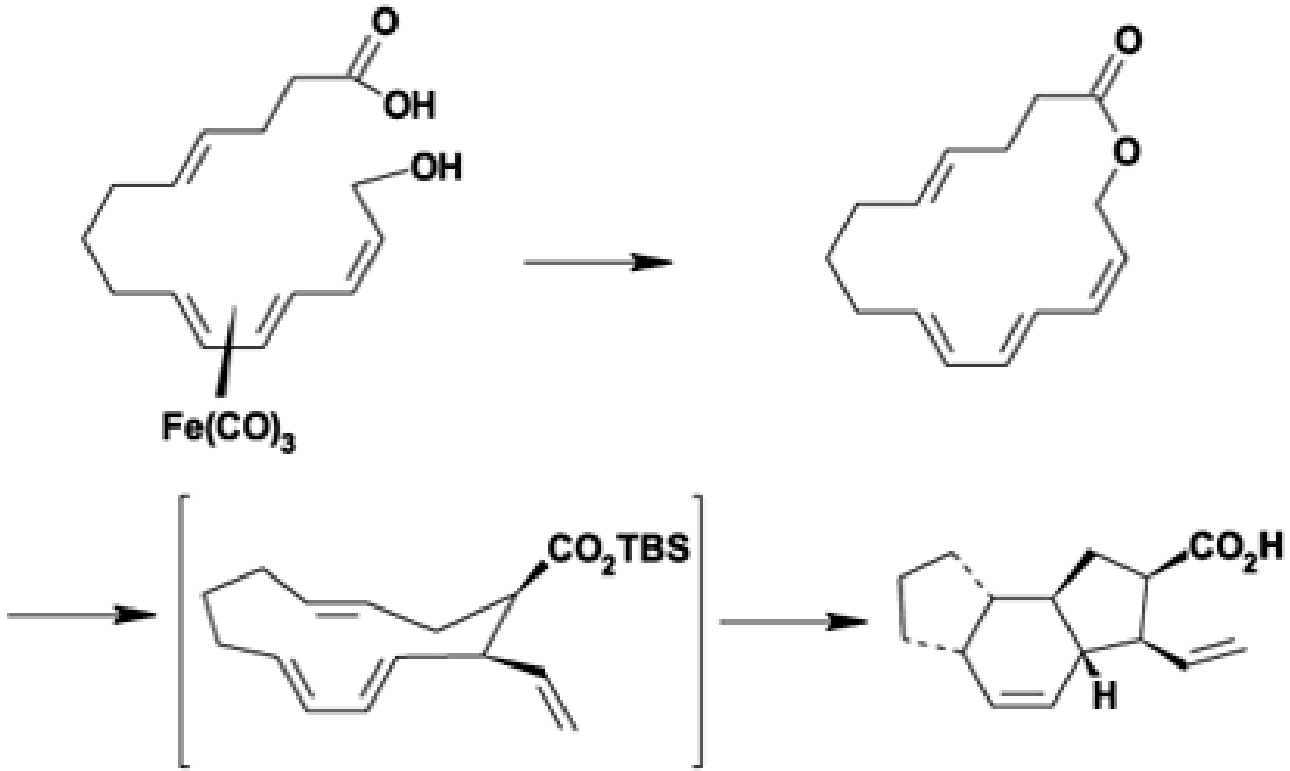
H. A. Whaley, C. G. Chidester, S. A. Mizsak, R. J. Wnuk, *Tetrahedron Lett.* **1980**, *21*, 3659-3662.



Nodusmicina

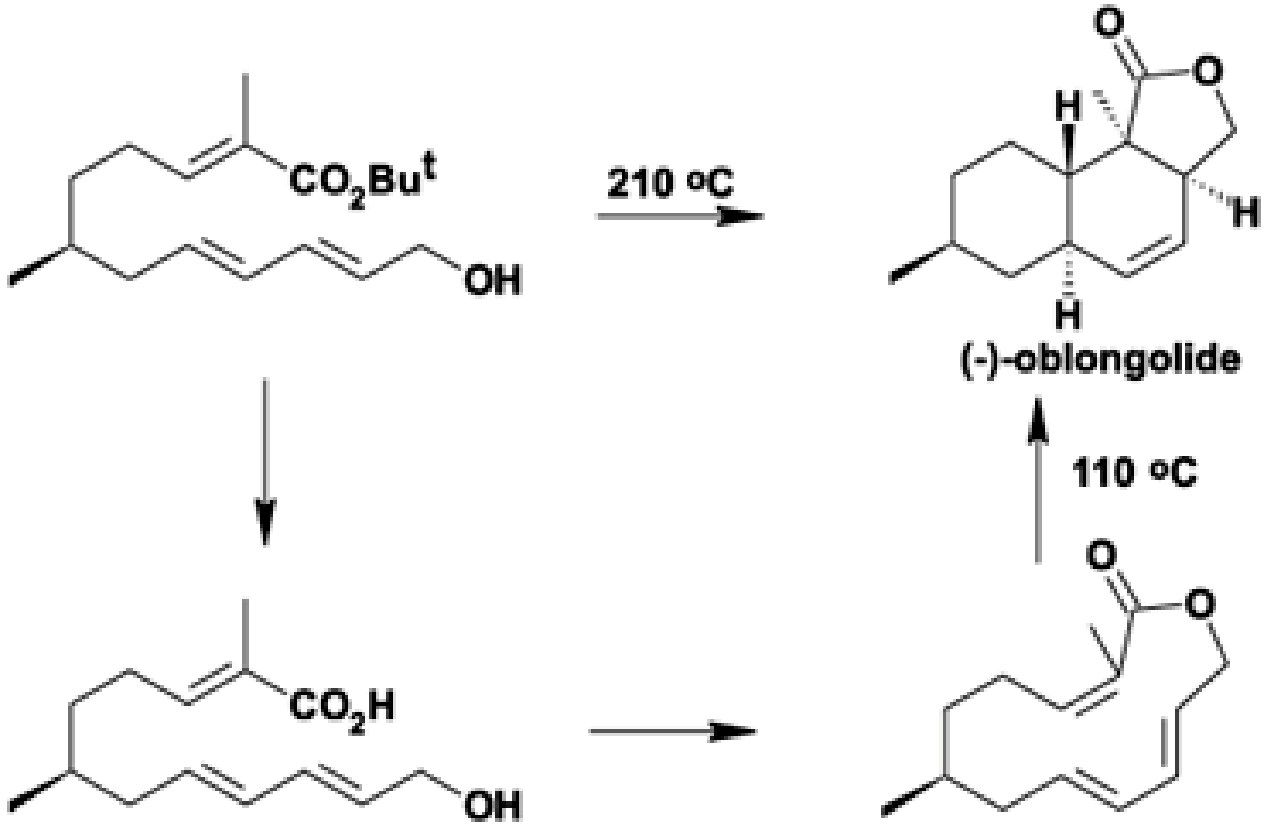
Transposición de Ireland-Claisen y contracción anular para formar un macrociclo ideal de 12 miembros *a* través de una reacción Diels-Alder transanular llevada a cabo *in situ*

Frank, S. A.; Works, A. B.; Roush, W. R. *Can J. Chem.* **2000**, *78*, 757-771.



Shing and Yang efectuaron la síntesis de (-)-oblongolido tanto por reacciones IMDA como por TADA

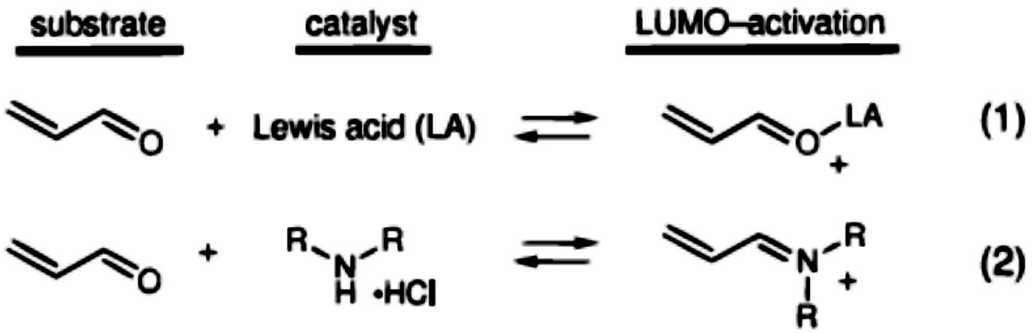
Shing, T. K. M.; Yang, J. *J. Org. Chem.* **1995**, *60*, 5785-5789.

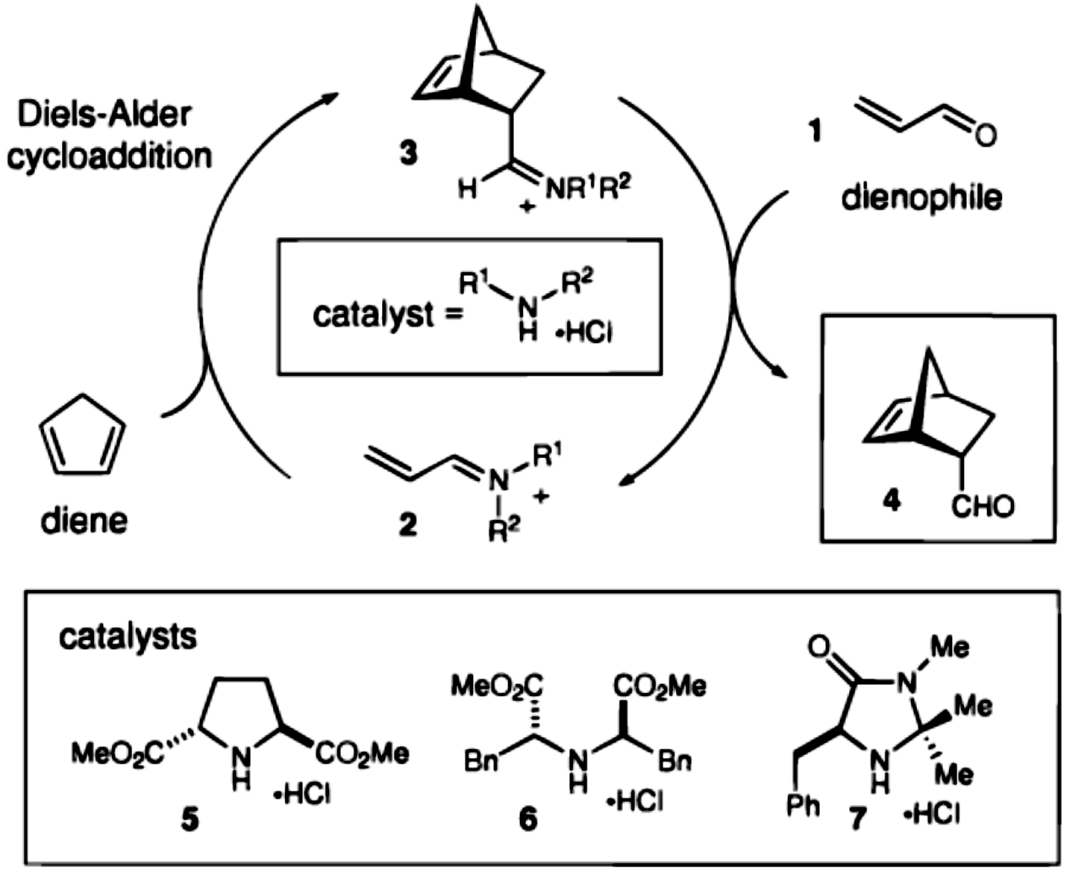


New Strategies for Organic Catalysis: The First Highly Enantioselective Organocatalytic Diels−Alder Reaction

Kateri A. Ahrendt , Christopher J. Borths , and David W. C. MacMillan *

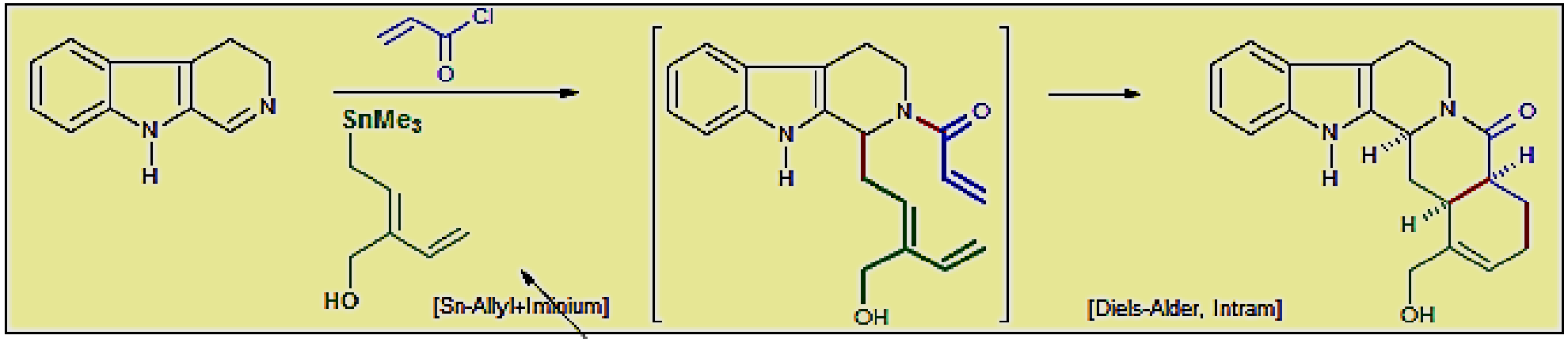
J. Am. Chem. Soc., **2000**, *122* (17), pp 4243–4244
DOI: 10.1021/ja000092s





Nitraraine

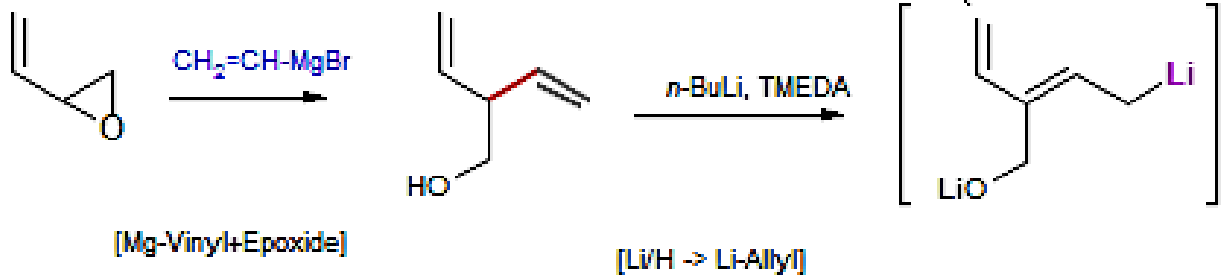
Yamaguchi, R.; Hamasaki, T.; Sasaki, T.; Ohta, T. Utimoto, K.; Kozima, S.; Takaya, S. *J. Org. Chem.* 1993, *58*, 1136.



[Li-Allyl -> Sn-Allyl]

96/4 E/Z

Me_3SnCl

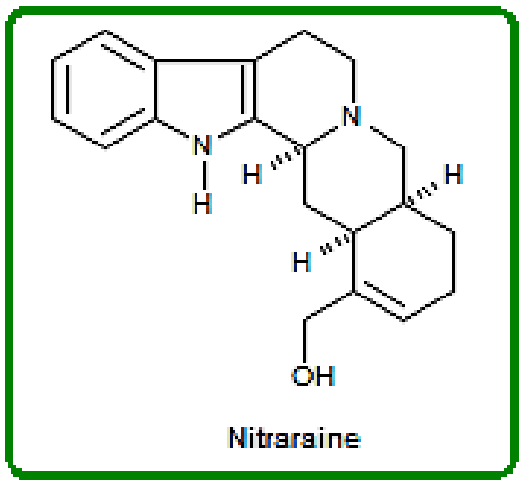


[Mg-Vinyl+Epoxide]

[Li/H -> Li-Allyl]

1. $Me_2{}^tBuSiCl$
2. $LiAlH_4$
3. $Bu_4N^+ F^-$

[CarboxAmide -> Amine]



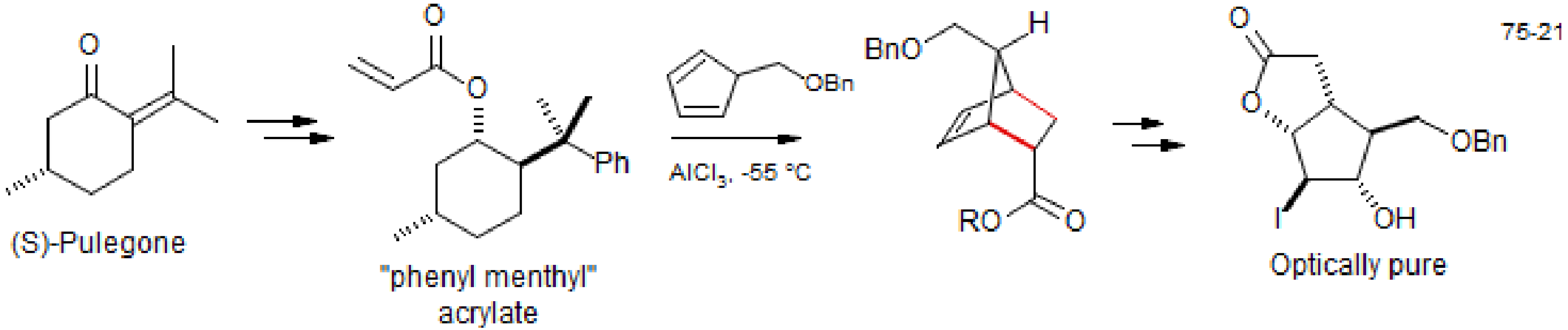
Nitraraine

The Asymmetric Diels-Alder Reaction

Asymmetric Diels-Alder and Ene Reactions in Organic Synthesis,
Oppolzer, W. *Angew. Chem. Int. Ed.* **1984**, *23*, 876.
Catalytic Asymmetric Diels-Alder Reactions,
Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007.
Reagent-Controlled Asymmetric Diels-Alder Reactions,
Oh, T.; Reilly, M. *Org. Prep. Proc. Int.* **1994**, *26*, 129.
Diastereofacial Selectivity in the Diels-Alder Reaction,
Coxon, J. A.; McDonald D. Q.; Steel, P. J.
Advances in Detailed Reaction Mechanisms,
Vol. 3. James M. Coxon, Ed., Jai Press: Greenwich, CT 1994.
Chiral Heterosubstituted 1,3-Butadienes: Synthesis and [4 + 2] Cycloaddition Reactions,
Barluenga, J.; Su'arez-Sobrino, A.; L'opez, L. A. *Aldrichimica Acta* **1999**, *32*, 4-15.
Stereoelectronic Control in Diels-Alder Reaction of Dissymmetric 1,3-Dienes,
Mehta, G.; Uma, R. **2000**, *33*, 278-86.
The Sulfinyl Group as a Chiral Inductor in Asymmetric Diels-Alder Reactions,
Ruano, J.L.G.; Carretero, J.C.; Carreno, M.C.; Cabrejas, L.M.M.; Urgano, A. *Pure Appl. Chem.* **1996**, *68*, 925-30.
Chiral Sulfinylethenes as Efficient Dienophiles for Asymmetric Diels-Alder Reactions,
Arai, Y.; Koizumi, T. *Sulfur Reports*, **1993**, *15*, 41-65.
Asymmetric [4+2] Cycloadditions Mediated by Sulfoxides,
Ruano, J. L. G.; De la Plata, B. C. *Top. Curr. Chem.***1999**, *204*, 1-126.
Catalytic Enantioselective Diels ± Alder Reactions: Methods, Mechanistic Fundamentals, Pathways, and Applications
Corey, E. J. *Angew. Chem. Int. Ed.* **2002**, *41*, 1650-1667.
Chiral Auxiliaries in Cycloadditions,
Rück-Braun, K.; Kunz, H. Wiley: New York, 1999

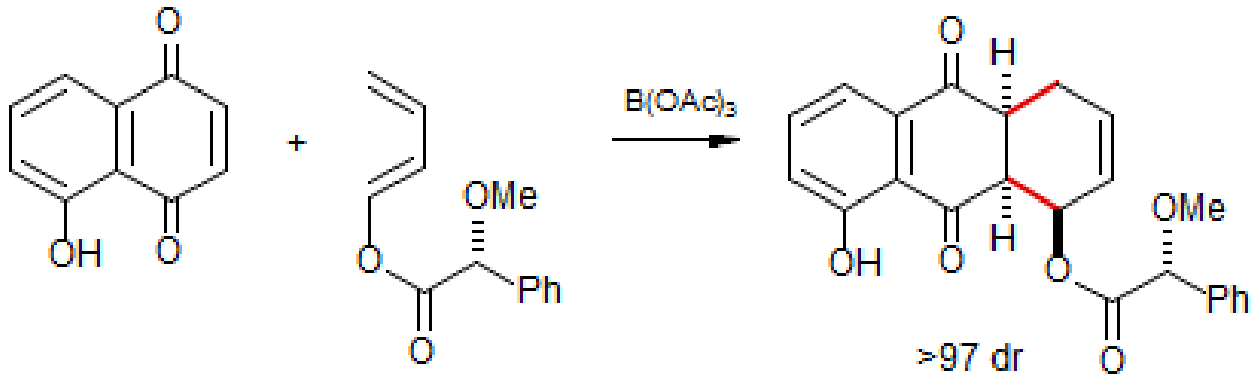
Diels-Alder Chiral Auxiliaries

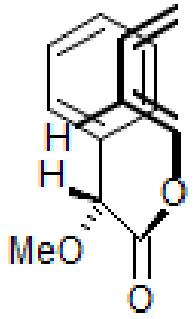
Corey, E. J.; Ensley, H. E. *J. Am. Chem. Soc.* **1975**, *97*, 6908.



Diels-Alder Chiral Auxiliaries

Trost, B. M.; O'Krongly, D.; Belletire, J. L. *J. Am. Chem. Soc.* **1980**, *102*, 7595.

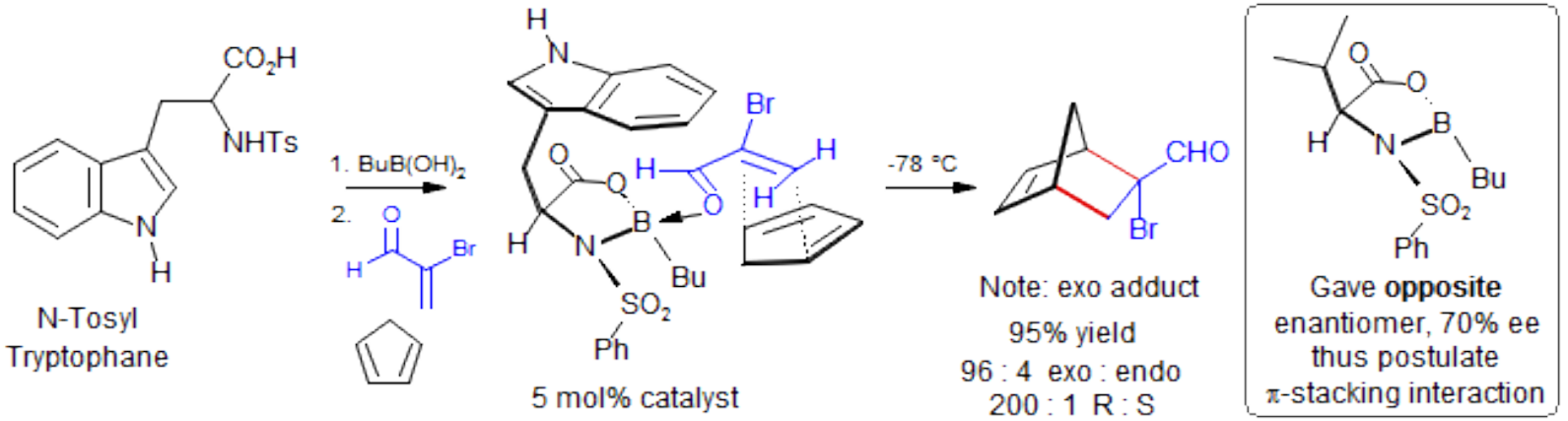




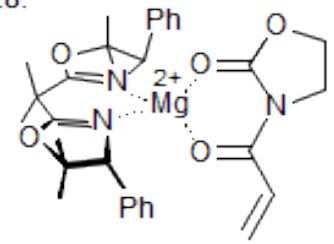
π-Stacking model - dienophile approaches from the top

Asymmetric Catalysis in Diels Alder Reactions

Corey, E. J.; Lo, T.-P. *J. Am. Chem. Soc.*, **1991**, *113*, 8966.

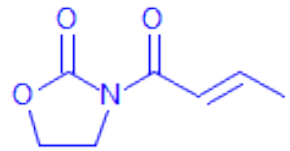


Magnesium complex: Corey, E. J.; Ishihara, K. *Tet. Lett.*, **1992**, *33*, 6807. Similar Fe complex: Corey, *JACS*, **1991**, *113*, 728.



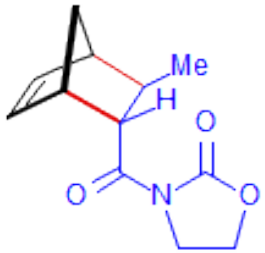
10% catalyst
Cyclopentadiene
92% ee
97/3 endo/exo
82% yield

The cupric salts are square planar, and give the opposite enantiomer: Evans, Miller, Lectka, von Matt *J. Am. Chem. Soc.* **1999**, *121*, 7559.

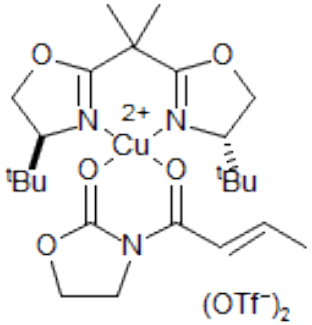


-15 °C

10% catalyst

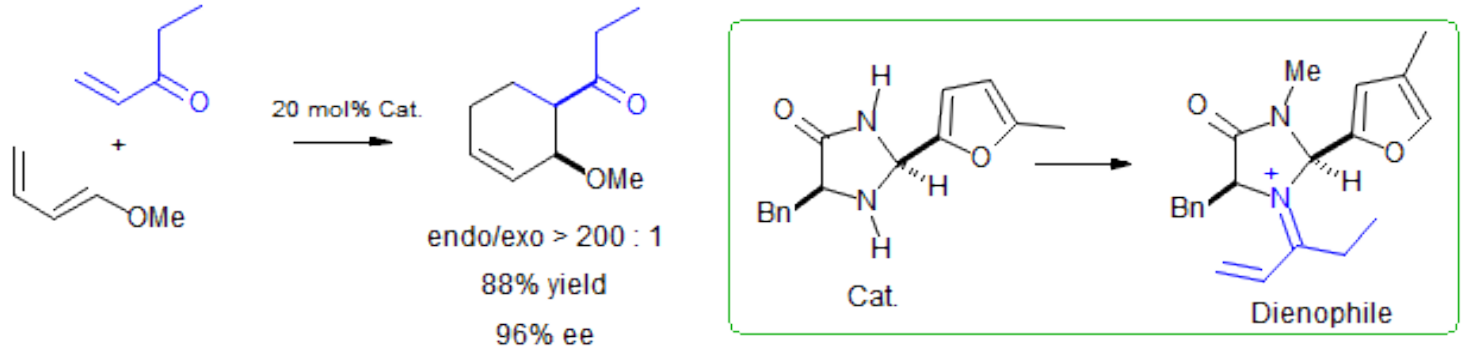


97% ee
96/4 endo/exo



Chiral Organocatalysis of Diels-Alder Reactions

Northrup, A. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 2458.

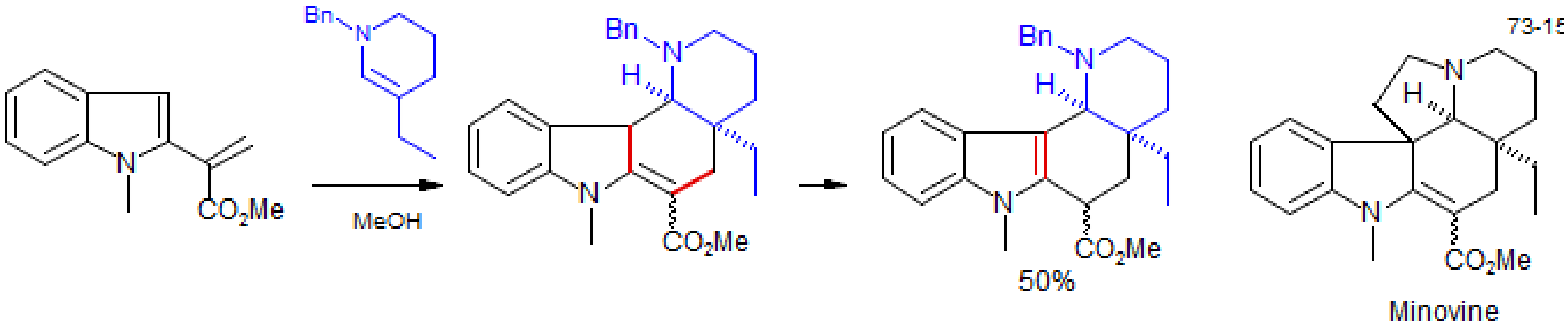


- Methyl and isopropyl ketones as well as cyclopentenone and cyclohexenone worked poorly
- Variety of dienes worked well
- Reactions can be run in aqueous or ethanolic media

Inverse Electron Demand Diels-Alder Reactions

Recent Applications of the Inverse Electron Demand Diels-Alder Reaction,

Biogenetically modeled synthesis via an indole acrylic ester. Total synthesis of (+-)-minovine
Frederick E. Ziegler; Ernest B. Spitzner
Journal of the American Chemical Society 1973, 95, 21, 7146-7149

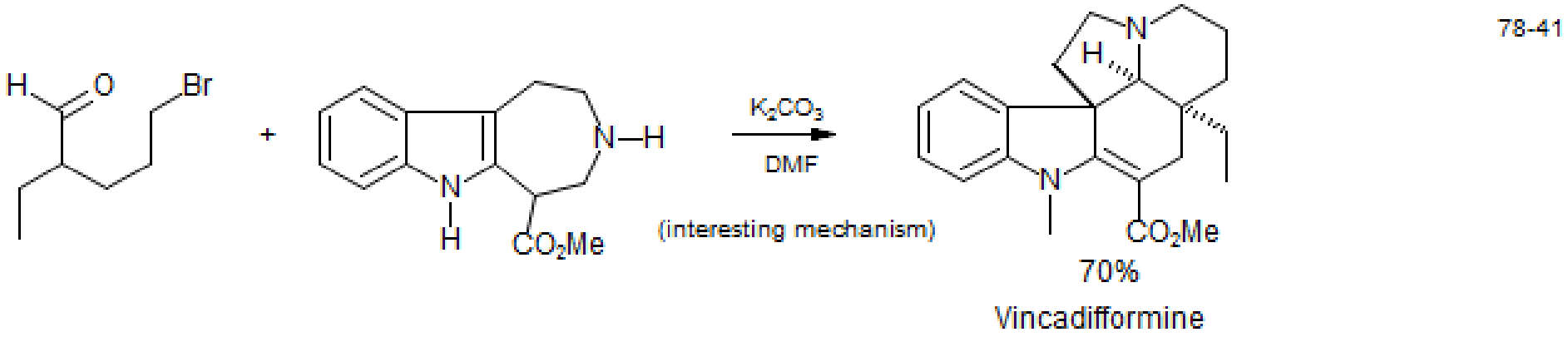


Inverse Electron Demand Diels-Alder Reactions

Vincadifformine

Kuehne, M. E.; Roland, D. M.; Hafter, R. *J. Org. Chem.* **1978**, *43*, 3705

78-41



SEMINARIO

Inverse Electron Demand Diels-Alder Reactions

Synthesis of a nicotine analog

Che, Siegl, Seitz *Tetrahedron Assym.* **1999**, 573.