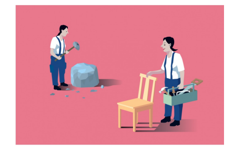
Organocatálisis asimétrica
una herramienta ingeniosa para construir moléculas

Marcos Hernández Rodríguez
Instituto de Química, UNAM

1

Premio Nobel en Química 2021
Por el desarrollo de la Organocatálisis Asimétrica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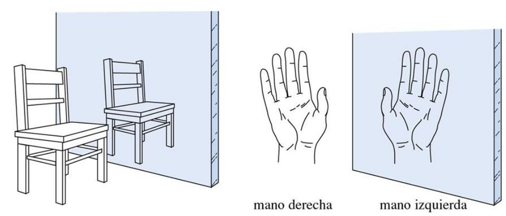
Asimétrica

3

Quiralidad

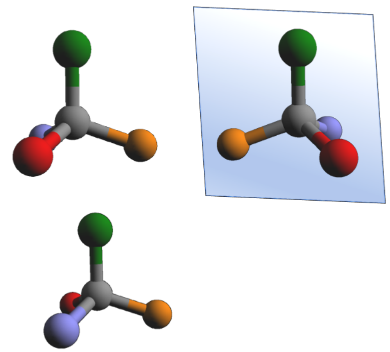


Objeto aquiral

Objeto quiral

4

Enantiomeros



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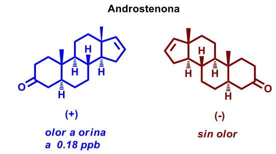
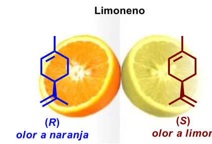
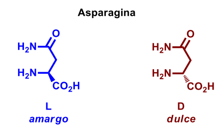
Propiedades biológicas de los enantiómeros







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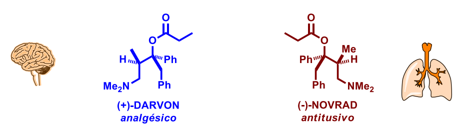
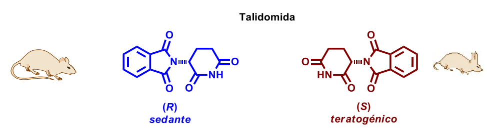
Propiedades biológicas de los enantiómeros





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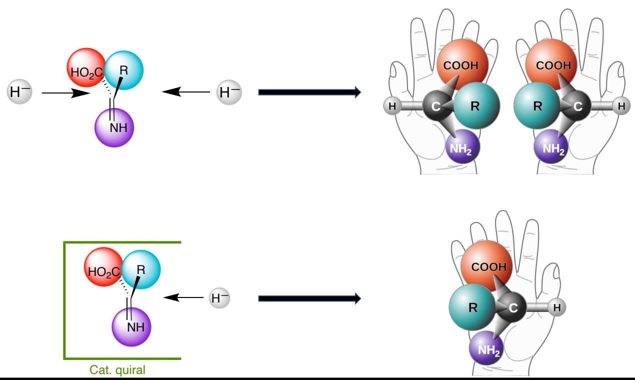
Tal vez la leche a través del espejo
no es buena para beber

http://plus.maths.org/issue24/features/symmetry/

8

Síntesis asimétrica



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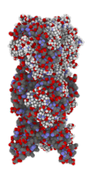
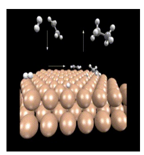
Organocatálisis

10

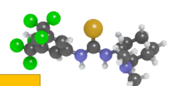
Catálisis

Enzimas

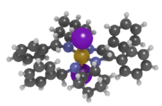




Superficies metálicas



Organocatálisis



Complejos metálicos

11

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Definiciones

Catálisis

Sustancia que incrementa la velocidad de reacción sin modificar el cambio de energía de Gibbs en la reacción. El catalizador es tanto reactante como producto en la reacción.

Pure & Appl.Chem. **1996**, *68*, 149

Organocatálisis

Uso de méculas orgánicas pequeñas para catalizar transformaciones orgánicas.

D. W. C. MacMillan. *Nature*, **2008**, *455*, 304

Catálisis con moléculas pequeñas donde el elemento inorgánico no es parte activa del ciclo catalítico.

B. List, *Chem. Rev.* **2007**, *107, 5413*

12

Proline-Catalyzed Direct Asymmetric Aldol Reactions

Benjamin List, Richard A. Lerner, and Carlos F. Barbas

View Author Information

Cite this: *J. Am. Chem. Soc.* 2000, 122, 10, 2395–2396
Publication Date: February 26, 2000
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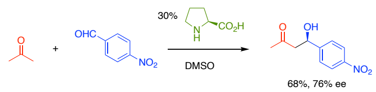

New Strategies for Organic Catalysis: The First Highly Enantioselective Organocatalytic Diels–Alder Reaction

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

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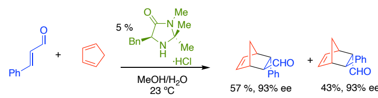

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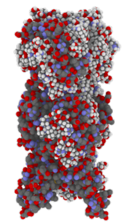
Enzimas

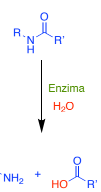


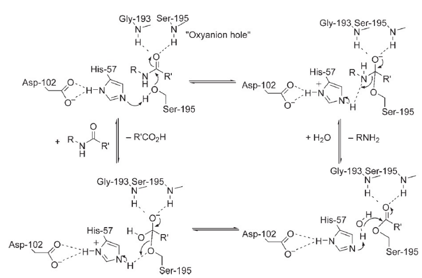
Solo 25-33 % de las enzimas contienen metales en su sitio activo.

K. J. Waldron, N. J. Robinson, *Nature Reviews Microbiology*, **2009**, *7*, 25.

14

Proteasas de serina





C. W. Wharton en *Comprehensive Biological Catalysis,* **1998** *Vol.* **1** (Ed.: M. Sinnott), Academic Press, London, 1998, 345–379.

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ANGEWANDTE CHEMIE INTERNATIONAL EDITION

Review

Organic Synthesis—Where now?

Prof. Dr. Dieter Seebach,

First published: November 1990 | https://doi.org/10.1002/anie.199013201 | Citations: 493

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Abstract

This review article is an attempt to sketch the important developments in organic synthesis during the past 25 years, and to project them into the future.—The primary motivations that once induced chemists to undertake natural product syntheses no longer exist. Instead of target structures themselves, molecular function and activity now occupy center stage. Thus, inhibitors with an affinity for all the important natural enzymes and receptors have moved to the fore as potential synthetic targets.—New synthetic *methods* are most likely to be encountered in the fields of biological and organometallic chemistry. Enzymes, whole organisms, and cell cultures for enantioselective synthesis of specific substances have already been incorporated into the synthetic arsenals of both research laboratories and industry. In addition, designing appropriate analogues to transition states and intermediates should soon make it possible, with the aid of the mammalian immune system and gene technology, to prepare catalytically active monoclonal antibodies for almost any reaction; perhaps, more important, such processes will increasingly come to be applied on an industrial scale.-The discovery of truly new reactions is likely to be limited to the realm of transition-metal organic chemistry, which will almost certainly provide us with additional "miracle reagents" in the years to come. As regards main group elements ("organoelemental chemistry"), we can surely anticipate further stepwise improvements in experimental procedures and the broader application of special techniques, leading to undreamed of efficiency and selectivity with respect to known procedures. The primary center of attention for all synthetic methods will continue to shift toward catalytic and enantioselective variants; indeed, it will not be long before such modifications will be available with every standard reaction for converting achiral educts into chiral products.

¿Por qué la síntesis orgánica pasó por alto la organocatálisis?

"Es muy probable que los nuevos métodos sintéticos se encuentren en los campos de la química biológica y organometálica".

D. Seebach, *Angew. Chem. Int. Ed.*, **1990**, 29, 1320.

"Es imposible pasar por alto un campo que todavía no existe, de la misma manera en que no se puede trabajar en un problema que no se ha definido."

D.W.C. MacMillan

16

Premio nobel 2001

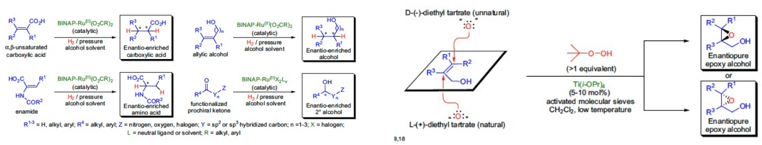
Knowles y Noyori:
Hidrogenación catalítica quiral

Photo from the Nobel Foundation archive.
William S. Knowles
Prize share: 1/4

Photo from the Nobel Foundation archive.
Ryoji Noyori
Prize share: 1/4

Photo from the Nobel Foundation archive.
K. Barry Sharpless
Prize share: 1/2

Sharpless:
Oxidación catalítica quiral



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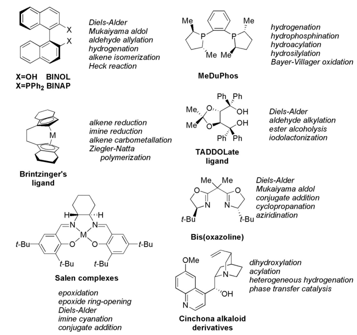
Ligandos quirales



T. K. Yoon, E. N. Jacobsen, *Science*, **2002**, *299*, 1691.

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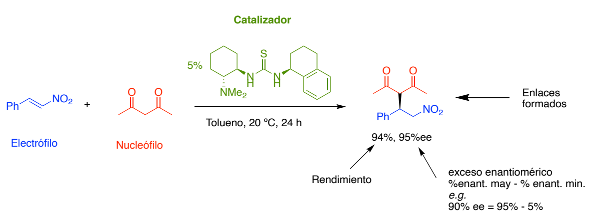
Convención



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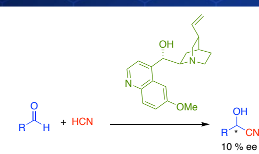
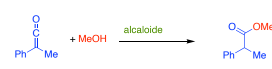
Antecedentes organocatálisis

1912 Bredig y Fiske



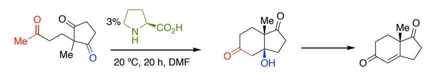
G. Bredig, W. S. Fiske, *Beiträge zur chemischen Physiologie und Pathologie. In Biochemische Zeitschrift*, **1912**, *46*, 7

1960 Pracejus



H. Pracejus, *Justus Liebigs Ann. Chem.* **1960**, *634*, 9.

1970
Hajos-Parrish,
Eder, Sauer, Wiechert

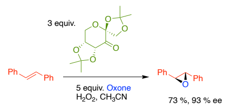


Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1974**, *39*, 1615.
Eder, U.; Sauer, G.; Wiechert, R. *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 496

20

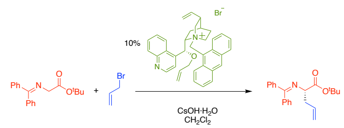
Antecedentes organocatálisis

1996 Shi



Y. Shi, *J. Am. Chem. Soc.* **1996**, *118*, 9806

1997 Corey



E. J. Corey, F. Xu, M. C. Noe, *J. Am. Chem. Soc.*, **1997**, *119*, 12414.

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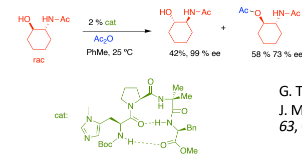
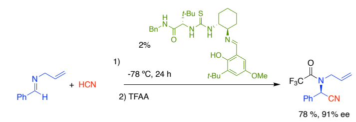
Antecedentes organocatálisis

Miller 1998



G. T. Copeland, E. R. Jarvo, S. J. Miller, *J. Org. Chem.*, **1998**, *63*, 6784

Jacobsen 1998



M. S. Sigman, E. N. Jacobsen, *J. Am. Chem. Soc.* **1998**, *120*, 4901

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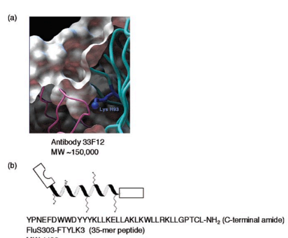
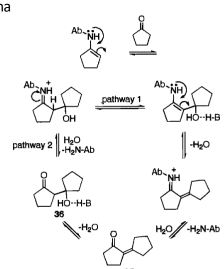
Benjamin List

Anticuerpos de aldolasa
catalizan reacciones de condensación aldólica vía enamina





J. Wagner, R. A. Lerner, C. F. III Barbas, *Science*, **1995**, *270*, 1797
T. Hoffmann, G. Zhong, B. List, D. Shabat, J. Anderson, S. Gramatikova, R. A. Lerner, C. F. Barbas, *J. Am. Chem. Soc.* **1998**, *120*, 2768

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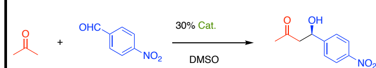
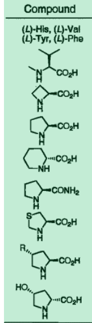
Benjamin List



B. List, R. A. Lerner, C. F. Barbas, *J. Am. Chem. Soc.* **2000**, *122*, 2395

Compound	Entry	Yield	ee[a]
(L)-His, (L)-Val (L)-Tyr, (L)-Phe	1	< 10%	n. d.[b]
	2	< 10%	n. d.
	3	55%	40%
	4	68%	76%
	5	< 10%	n. d.
	6	< 10%	n. d.
	7	67%	73%
	8a R = OH 8b R = OtBu 8c R = OAc	85% > 50%[c] 70%	78% 62% 74%
	9	> 50%[c]	62%[d]



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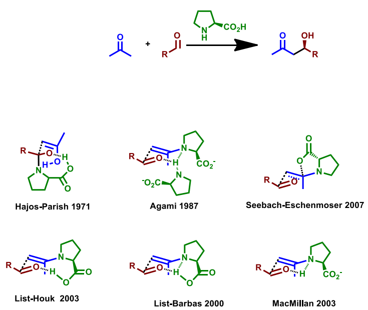
Estados de transición propuestos



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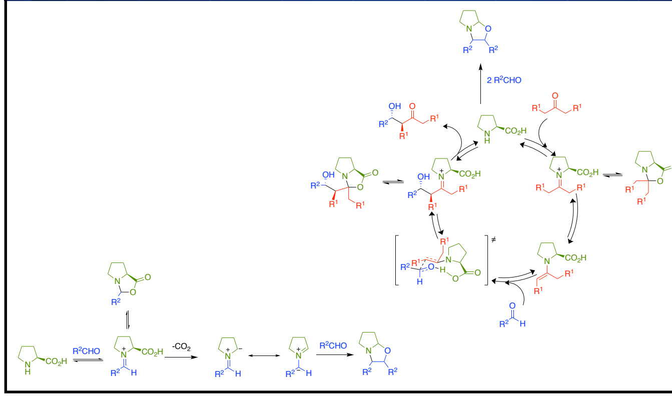
Ciclocatalítico prolina



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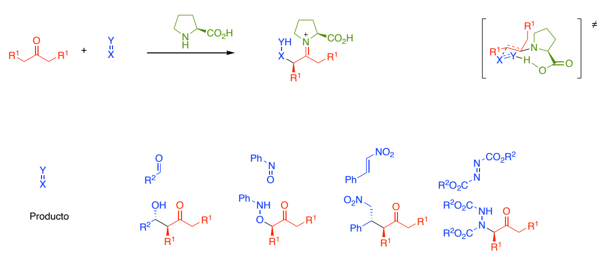
Generalización de la organocatálisis vía enamina



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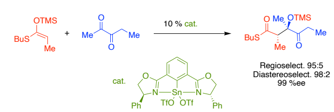
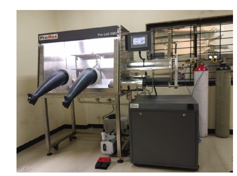
David W. C. MacMillan





D. A. Evans, D. W. C. MacMillan, *J. Am. Chem. Soc.* **1997**, *119*, 10859

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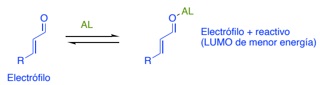
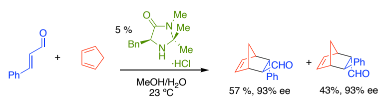
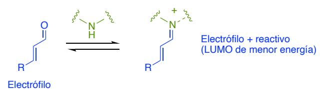
David W. C. MacMillan







K. A. Ahrendt, C. J .Borths, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2000**, *122*, 4243

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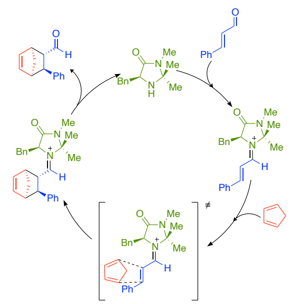
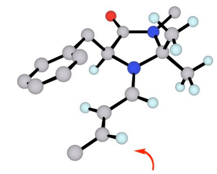
David W. C. MacMillan





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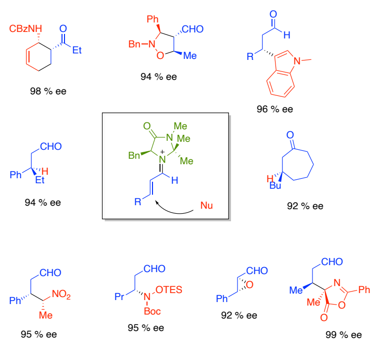
Generalización de la activación vía iminio



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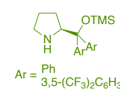
Catalizador Hayashi-Jørgensen



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Enantioselective Organocatalyzed α Sulfenylation of Aldehydes†

Mauro Marigo, Tobias C. Wabnitz Dr., Doris Fielenbach Dr., Karl Anker Jørgensen Prof. Dr.

First published: 18 January 2005 | https://doi.org/10.1002/anie.200462101 | Citations: 818

† This work was made possible by a grant from The Danish National Research Foundation. M.M. and T.C.W. thank the EU (HMPT-CT-2001-00317) for financial support.

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Abstract

The facile elaboration of optically active α-sulfanyl-substituted aldehydes makes their direct preparation from unmodified aldehydes and 1-benzylsulfanyl-1,2,4-triazole particularly valuable. The substituted aldehydes are formed with excellent enantioselectivities in the presence of sterically demanding chiral pyrrolidine derivatives as organocatalysts (see scheme). R, R′=H, alkyl, allyl, benzyl, Ph.

Angewandte Chemie International Edition
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Diphenylprolinol Silyl Ethers as Efficient Organocatalysts for the Asymmetric Michael Reaction of Aldehydes and Nitroalkenes†

Yujiro Hayashi Prof. Dr., Hiroaki Gotoh, Takaaki Hayashi, Mitsuru Shoji Dr.,

First published: 23 June 2005 | https://doi.org/10.1002/anie.200500599 | Citations: 921

† We thank Prof. K. Saigo and Dr. Y. Ishida (The University of Tokyo) for the use of a high-pressure mercury lamp. This work was partially supported by a Grand-in-Aid for Scientific Research on Priority Area (A): "Creation of Biologically Functional Molecules", from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

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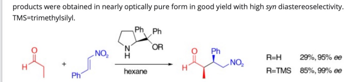
Abstract

The direct, catalytic, asymmetric Michael addition of aldehydes to nitroolefins in the presence of a chiral diphenylprolinol silyl ether organocatalyst is described (see scheme). The desired 1,4-addition products were obtained in nearly optically pure form in good yield with high *syn* diastereoselectivity. TMS=trimethylsilyl.



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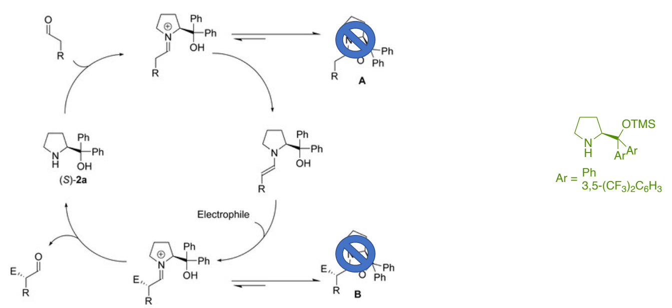
Catalizador Hayashi-Jorgensen



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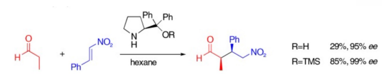
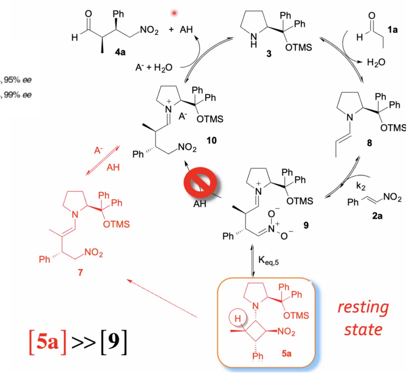
Catalizador Hayashi-Jorgensen





J. Burés, A. Armstrong, D. G. Blackmond, *J. Am. Chem. Soc.* **2012**, *134*, 15, 6741

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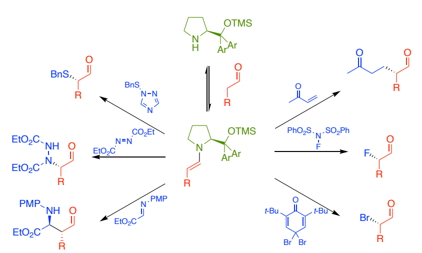
Catalizador Hayashi-Jorgensen



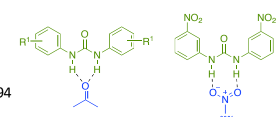
J. Franzén, M. Marigo, D. Fielenbach, T. C. Wabnitz, A. Kjærsgaard, K. A. Jørgensen, *J. Am. Chem. Soc.*, **2005**, *127*, 18296.

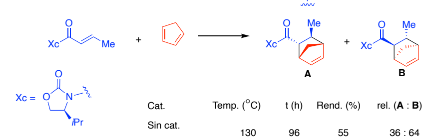
35

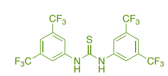
Organocatálisis por enlace de hidrógeno

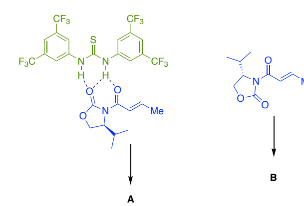
Etter 1988

Curran 1994





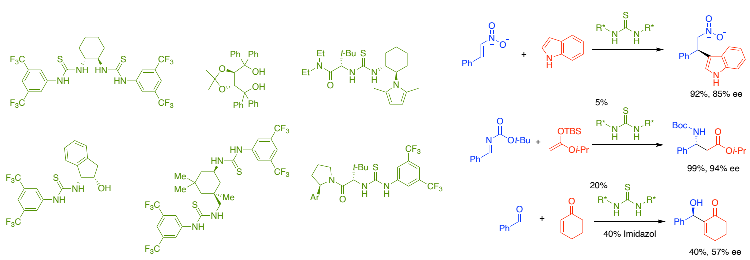
Cat.	Temp. (°C)	t (h)	Rend. (%)	rel. (A : B)
Sin cat.	130	96	55	36 : 64
	23	48	78	81 : 19



P. R. Schreiner, A. Wittkopp, *Org. Lett.*, **2002**, *4*, 217

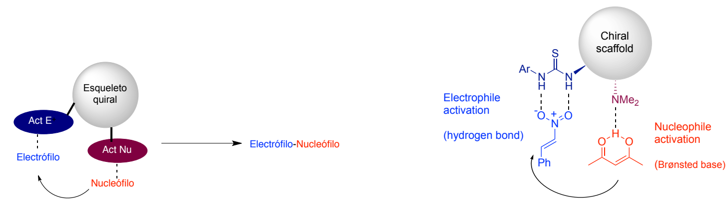
36

Organocatálisis por enlace de hidrógeno



37

Organocatálisis bifuncional



T. Okino, Y. Hoashi, Y. Takemoto, *J. Am. Chem. Soc.* **2003**. *125*, 12672
W-Y., Siau, J. Wang, *Catal. Sci. Technol.*, **2011**, *1*, 1298

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Organocatálisis bifuncional

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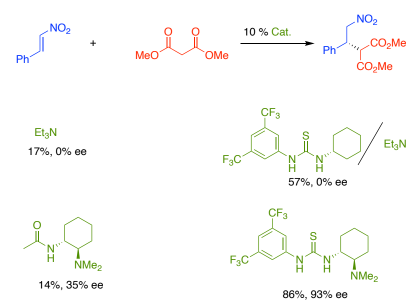
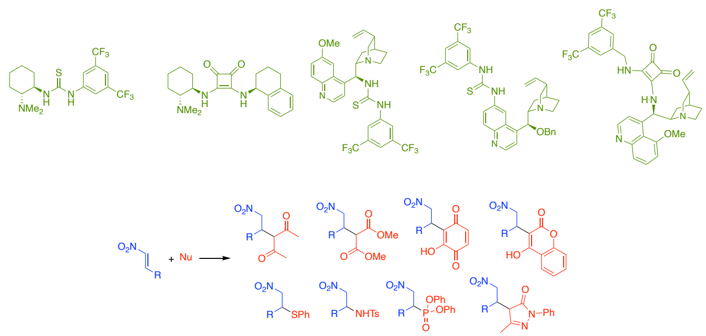
Organocatálisis bifuncional enlace de hirógeno/base de Brønsted



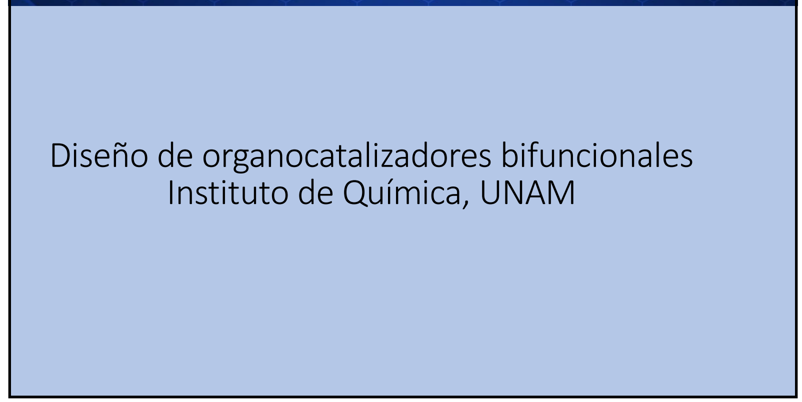
T. Okino, Y. Hoashi, Y. Takemoto, *J. Am. Chem. Soc.* **2003**. *125*, 12672

40

Organocatálisis bifuncional

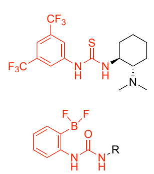


41



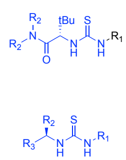
42

Síntesis tioureas con grupos quirales con CF_3

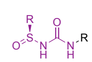


J. Am. Chem. Soc., **2012**, *134*, 8798

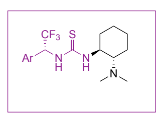
Good HB-donor
(+ yield)



Chiral groups
(+ selectivity)

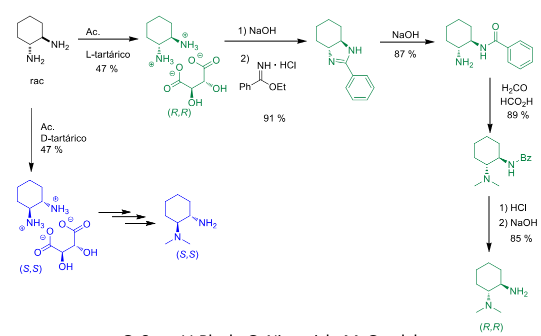


J. Am. Chem. Soc., **2012**, *134*, 9058



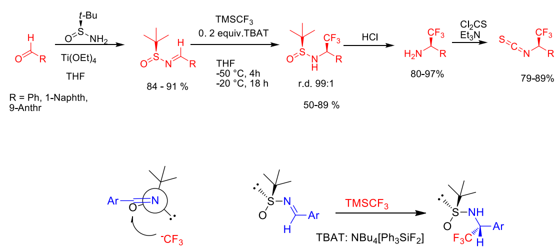
Chiral groups enhaced acidity
(+ yield, + selectivity)

43



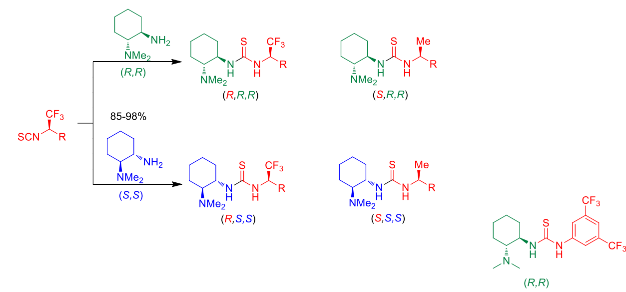
G. Suez, V. Bloch, G. Nisnevich, M. Gandelman,
Eur. J. Org. Chem. **2012**, 2118

44



M. Hernández-Rodríguez,* T. Castillo-Hernández, K. E. Trejo-Huizar, *Synthesis,* **2011**, 2817

45



E. I. Jiménez, W. E. Vallejo-Narvaez, C. Román-Chavarría, J. Vazquez-Chavez, T. Rocha-Rinza, M. Hernández-Rodríguez*, *J. Org. Chem.*, **2016**, *81*, 7419

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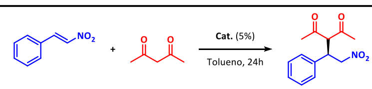
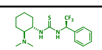
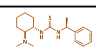
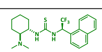
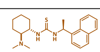
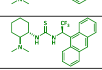
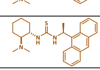
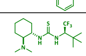
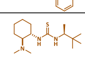
Evaluación de los catalizadores



#	Estructura	Cat.	Rend (%)	ee (%)	#	Estructura	Cat.	Rend (%)	ee (%)
1		C-1a	96	−89	9		C-5a	79	−81
2		C-1b	86	68	10		C-5b	87	86
3		C-2a	94	−92	11		C-6a	84	−76
4		C-2b	88	67	12		C-6b	94	87
5		C-3a	87	−84	13		C-7a	75	−60
6		C-3b	76	46	14		C-7b	86	74
7		C-4a	90	−94	15		C-8a	94	−62
8		C-4b	88	69	16		C-8b	87	86

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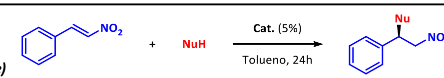
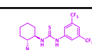
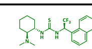
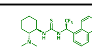
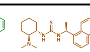
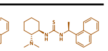
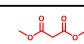
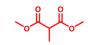
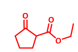
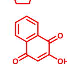


Rend (ee)

#	NuH					
1		83 (88)	69 (−87)	66 (68)	34 (−76)	78 (88)
2		88 (92)	57 (−91)	61 (72)	18 (−83)	64 (90)
3*		73 (64)	96 (−76)	77 (25)	59 (−80)	79 (50)
4		96 (88)	84 (−96)	98 (87)	86 (−85)	94 (90)

**dr 7:1 para todos los cat.*

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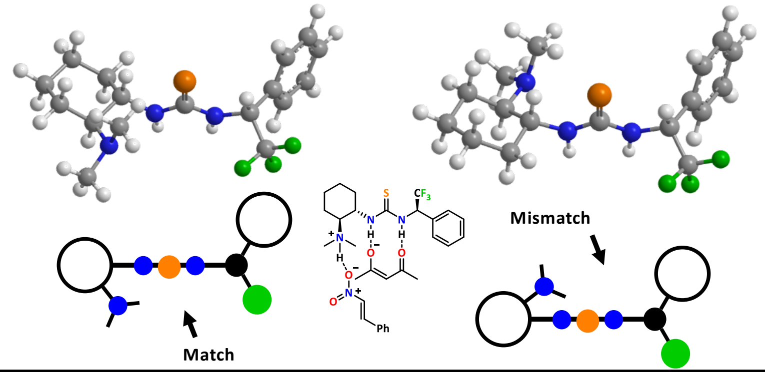
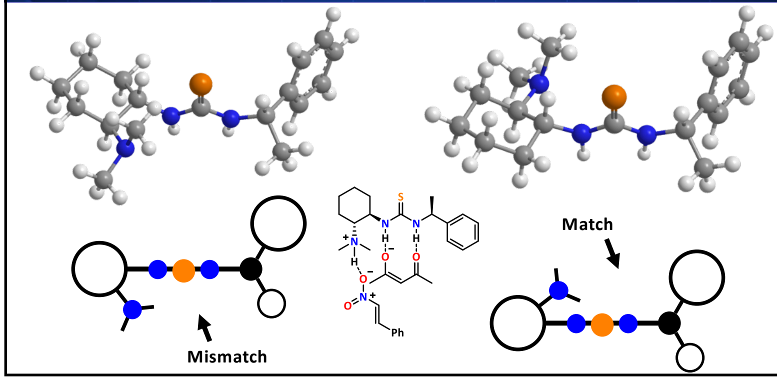
Match and mismatch



49

Match and mismatch



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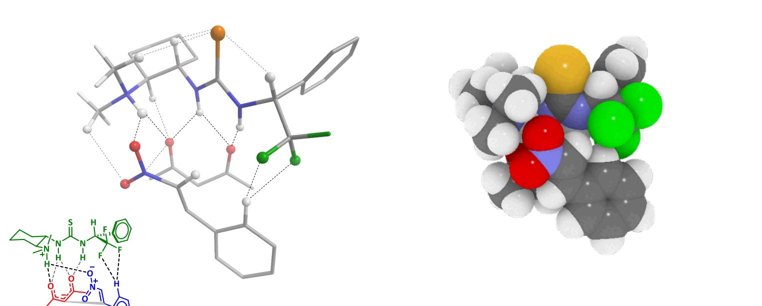
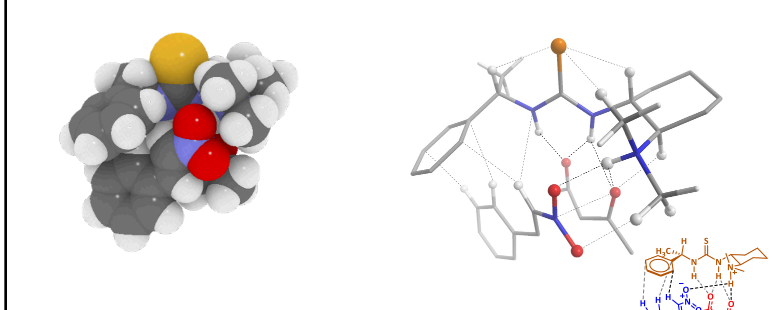
QTAIM (Quantum theory of atoms in molecules) of the TS



M062x/6-31+G(d)

51

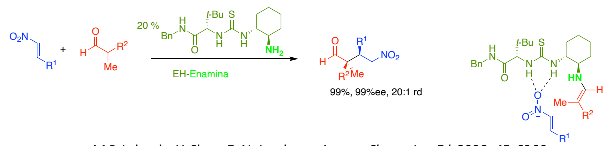
QTAIM (Quantum theory of atoms in molecules) of the TS



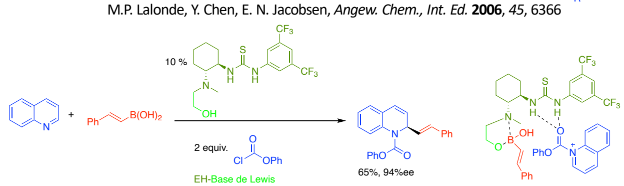
SMD-(Tolueno)-M06-2x/6-31+G(d)

52

Organocatalizadores bifuncionales con otros grupos



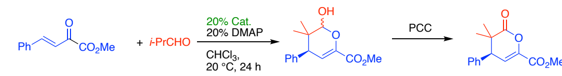
M.P. Lalonde, Y. Chen, E. N. Jacobsen, *Angew. Chem., Int. Ed.* **2006**, *45*, 6366

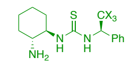
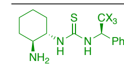


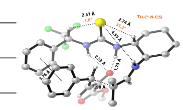
Y. Yamaoka, H. Miyabe, Y. Takemoto, *J. Am. Chem. Soc.* **2007**, *129*, 6686

53

Enamine-HB activation



Catalyst		Yield (%)	ee (%)
	A_F X = F	73	72
	A X = H	65	48
	B_F X = F	70	-64
	B X = H	65	-62

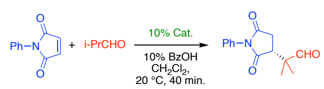


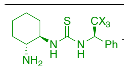
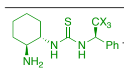
A_F

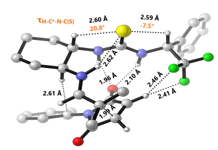
J. Vazquez-Chavez, S. Luna-Morales, D. A. Cruz-Aguilar, H. Díaz-Salazar, W. E. Vallejo-Narvaez, R. Silva-Gutiérrez, S. Hernández-Ortega, T. Rocha-Rinza, M. Hernández-Rodríguez*, *Org. Biomol. Chem.*, **2019**, *7*, 10045

54

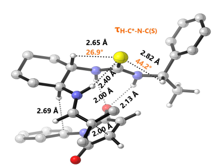
Enamine-HB activation



Catalyst		Yield (%)	ee (%)
	A_F X = F	99	78
	A X = H	88	97
	B_F X = F	96	-82
	B X = H	99	-99



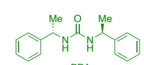
B_F



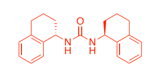
B

55

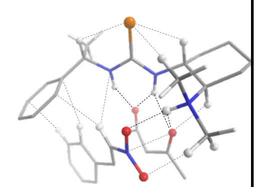
X-ray structures of thioureas

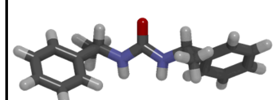


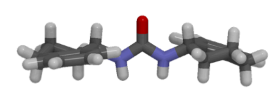
PEA



AT







B. M Novak, *et. al. Eur. J. Org. Chem.* **2015**, 7511–7518.
M. Hernández-Rodríguez, M. *et. al. New J. Chem.* **2013**, *37*, 2610–2613.

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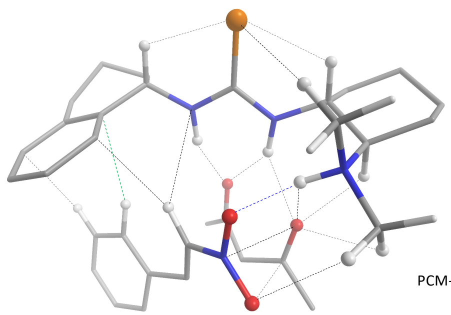
QTAIM of the TS of the bifunctional catalyst with AT



PCM-(Toluene)-B97-D/TZVP

E. I. Jiménez, W. E. Vallejo-Narvaez, T. Rocha-Rinza, M. Hernández-Rodríguez*
Catal. Sci. Tech. **2017**, *7*, 4470.

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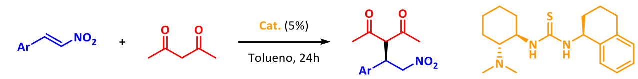

#	*Ar*	*Rend (%)*	*ee (%)*
1	C_6H_5	89	94
2	$4\text{-}CH_3C_6H_4$	85	95
3	$4\text{-}OCH_3C_6H_4$	72	93
4	$4\text{-}ClC_6H_4$	95	93
5	$4\text{-}NO_2C_6H_4$	75	93
6	$2\text{-}BrC_6H_4$	90	92
7	1-Naftilo	82	94
8	2-Tiofeno	90	93

E. I. Jiménez, W. E. Vallejo-Narvaez, T. Rocha-Rinza, M. Hernández-Rodríguez*
Catal. Sci. Tech. **2017**, *7*, 4470.

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Enantioselective catalyst design

Intuition- and concept-guided design

Experimental

Diastereomeric TSs modeling

Theoretical

Quantitative structure-selectivity relationships (QSSR)

Selectivity = f (catalyst parameters)

Experimental and theoretical

A. F. Zahrt, S. V. Athavale, S. E. Denmark*, *Chem. Rev.* **2020**, *120*, 1620

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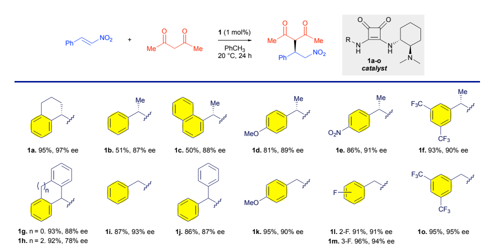
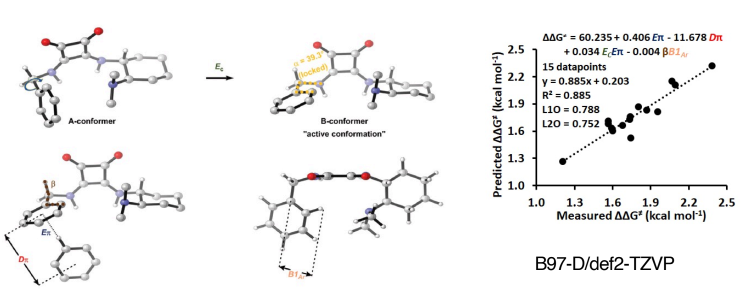
Multivariate Linear Free Energy Relationship (MLR)



H. Díaz-Salazar, E. I. Jiménez, W. E. Vallejo Narvaez, T. Rocha-Rinza, M. Hernández-Rodríguez*, *Org. Chem. Front.*, **2021**, *8*, 3217.

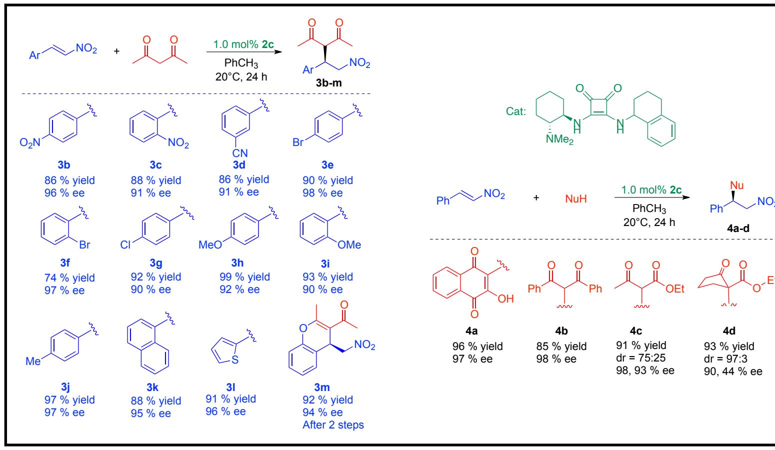
60

Multivariate Linear Free Energy Relationship (MLR)



H. Díaz-Salazar, E. I. Jiménez, W. E. Vallejo Narvaez, T. Rocha-Rinza, M. Hernández-Rodríguez*, *Org. Chem. Front.*, **2021**, *8*, 3217.

61



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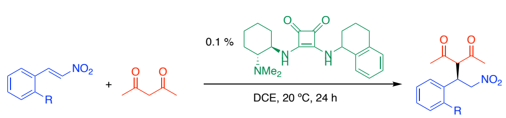
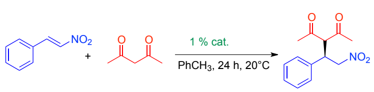
Escalamiento de reacciones



R = H, 96 % (96 % ee), 1.24 g
R = Br, 77 % (95 % ee), 1.26 g



Ciclo	Rend. (%)	ee (%)
1	95	97
2	93	90
3	87	85
4	70	80

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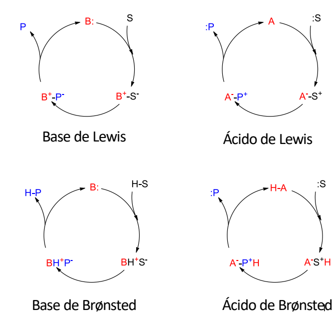
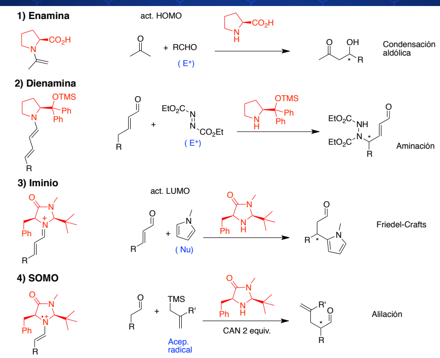
Clasificación de los organocatalizadores



J. Seayad, B. List, *Org. Biomol. Chem.* **2005**, 719

64

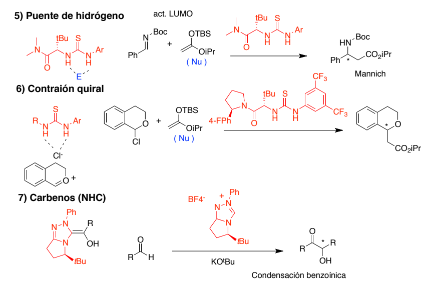
Otros tipos de activación



D. W. C. MacMillan, *Nature*, **2008**, *455*, 304

65

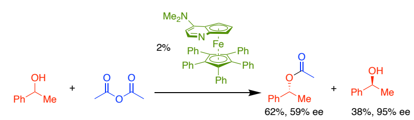
Otros tipos de activación



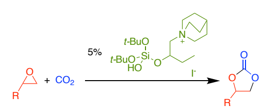
D. W. C. MacMillan, *Nature*, **2008**, *455*, 304

66

Organocatalizadores con metales en su estructura



J. C. Ruble, H. A. Latham, G. C. Fu, *J. Am. Chem. Soc.*, **1997**, *119*, 1492



J. Pérez-Pérez, U. Hernández-Balderas, D. Martínez-Otero, V. Jancik, *New J. Chem.*, **2019**,*43*, 18525

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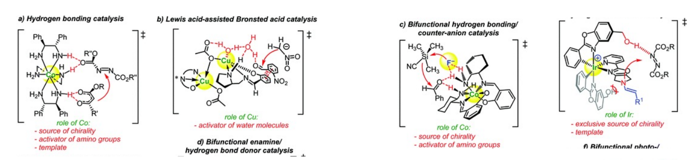
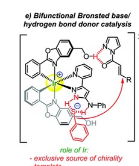
Organocatalizadores con metales en su estructura



Organocatálisis disfrazada.
Catálisis mediante la esfera de ligandos de complejos metálicos.

V. A. Larionov, B. L. Feringa, Y. N. Belokon, *Chem. Rev.*, **2021**, *50*, 9715



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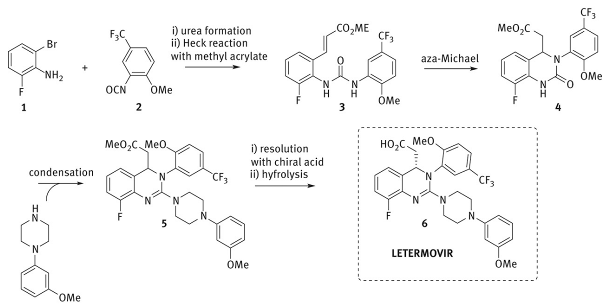
Impacto de la organocatálisis en la síntesis de fármacos

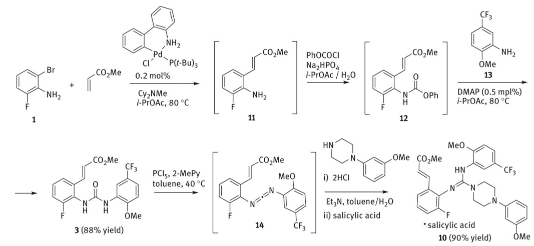
Síntesis antiviral Letermovir



K. Goossen, O. Kuhn, M. Berwe, J. Krüger, H.-C. Militzer, Process for the preparation of dihydroquinazolines. US20090221822

69

Letermovil



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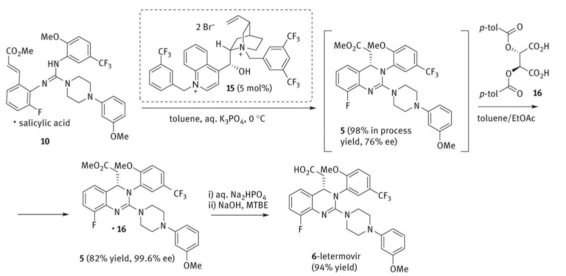
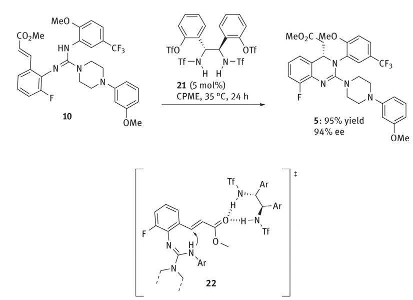
Letermovil



B. Xiang, K. M. Belyk, R. A. Reamer, N. Yasuda, *Angew Chem Int Ed*. **2014,** *53*, 8375

71

Letermovil



C. K. Chung, Z. Liu, K. W. Lexa, T. Andreani, Y. Xu, Y. Ji, et al. *J Am Chem Soc.*, **2017,** *139,* 10637

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Green Chemistry Challenge: 2017 Greener Synthetic Pathways Award

Merck & Co., Inc.

Letermovir: A Case Study in State-of-the-Art Approaches to Sustainable Commercial Manufacturing Processes in the Pharmaceutical Industry

Merck & Co., Inc., Rahway, New Jersey, is being recognized for successfully applying green chemistry design principles to Letermovir, an antiviral drug candidate, that is currently in phase III clinical trials. The improvements to the way the drug is made, including use of a better chemical catalyst, increases the overall yield by more than 60%, reduces raw material costs by 93%, and reduces water usage by 90%.

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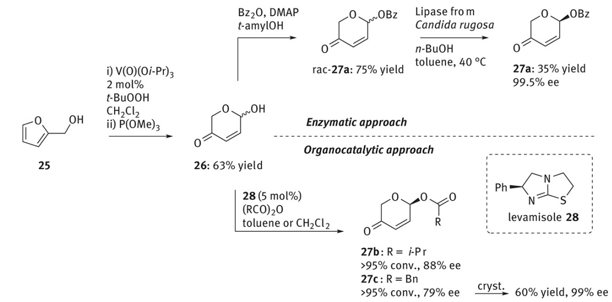
Censavudine (antiviral para tratar el VIH)



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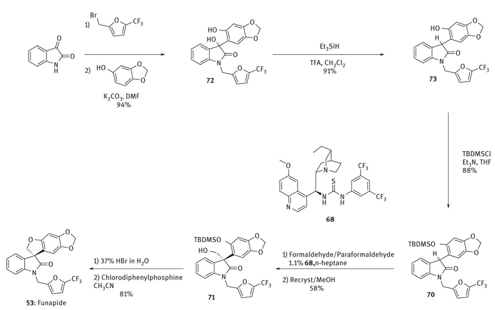
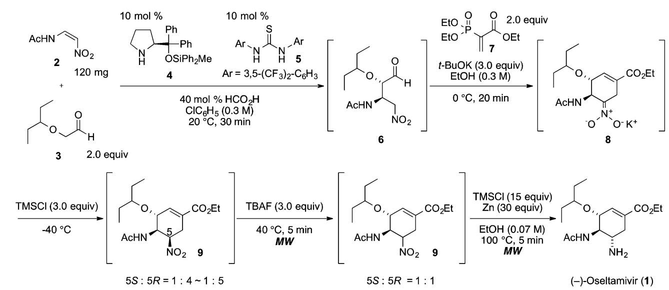
Funapide (tratamiento neuralgia postherpética)



J. A. Sclafani, J. Chen, D. V. Levy, H. Reese, M. Dimitri, P. Mudipalli P, et al. *Org Process Res Dev.* **2017**, *21,* 1616

75

Turbo síntesis de oseltamivir



Five reaction steps in one-pot sequence, Total yield 15%, Total time 60 minutes

Y. Hayashi, S. Ogasawara, *Org. Lett.*, **2016**, *18*, 3426

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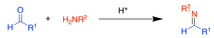
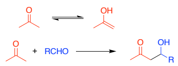
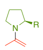
¿En docencia donde se puede hablar de organocatálisis?

1. Química de carbonilos



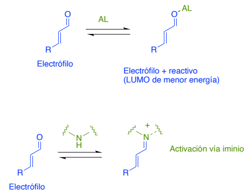
2. Tautomería ceto/enol, condensación aldólica





ciclo catalítico vía enamina

3. Reacción de Diels-Alder acelerada por ácidos de Lewis



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¿En docencia donde se puede hablar de organocatálisis?

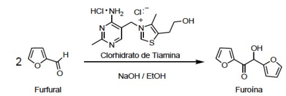
Práctica de laboratorio de Química Orgánica V en Facultad de Química, UNAM

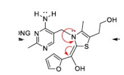
Experimento No. 4. Reacciones de azoles 1,3. Obtención de furoína.

Objetivos.
1. Que el alumno lleve a cabo la condensación benzoínica, utilizando como catalizador a la tiamina (vitamina B_1).
2. Ilustrar una reacción característica de los azoles-1,3.
3. Ilustrar como actúa una coenzima.

Antecedentes.
1. Reacción de condensación aldólica.
2. Fundamento químico y mecanismo de reacción.
3. Propiedades de reactivos y producto.
4. Interés en química los azoles-1,3.

Información.
Esta reacción de condensación del furfural es muy importante, ya que gracias a la sal de tiazolio ocurre una inversión en la polaridad del grupo carbonilo (umpolung). Una vez que se adiciona el anión de la sal de tiazolio al grupo carbonilo, ocurre un equilibrio ácido-base a través del cual se genera un carbanión (sobre el átomo de carbono del que era el grupo carbonilo), y este es el que actúa ahora sobre el grupo carbonilo de la otra molécula de furfural para formar el enlace carbono-carbono y que se forme así la furoína.





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Colaboradores:
Prof. Tomás Rocha Rinza
Dr. Wilmer E. Vallejo Narváez

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