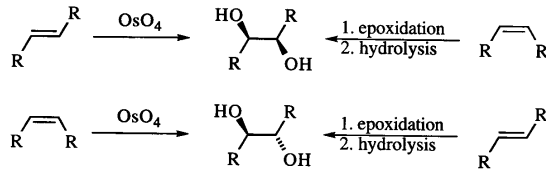
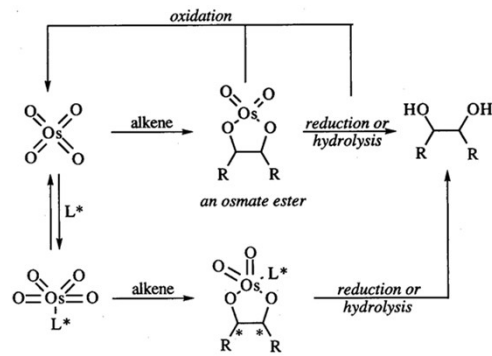


Diidrossilazioni Osmio Catalizzate



Meccanismo generale



2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

Processo stereoselettivo - LEGANTI CHIRALI

9.8 Enantioselective Dihydroxylations of Olefins

297

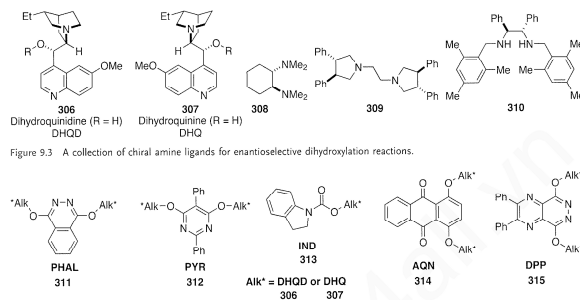


Figure 9.3 A collection of chiral amine ligands for enantioselective dihydroxylation reactions.

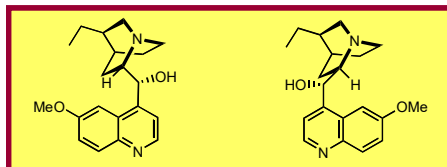
Olefin class	R ¹	R ²	R ¹ , R ²	R ¹ , R ²	R ¹ , R ²	R ¹ , R ²
Preferred ligand	R = Aromatic: DPP, PHAL Aliphatic: AGN Branched: PYR	R ¹ , R ² = Aromatic: DPP, PHAL Aliphatic: AGN Branched: PYR	R ¹ , R ² = Acyclic: IND Cyclic: PYH, DPP, AQN	R ¹ , R ² = Aromatic: DPP, PHAL Aliphatic: AGN	PHAL, DPP AGN	PYR, PHAL

Figure 9.4 The various ligands and their associated scope in Sharpless' dihydroxylation reaction.

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

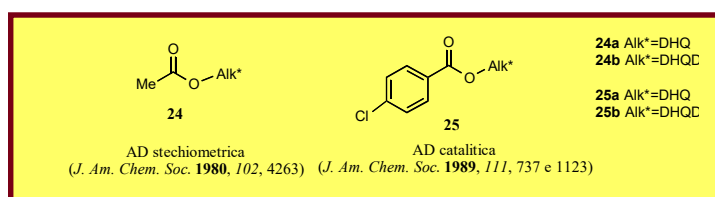
2

ALCALOIDI DELLA CINCONA



Diidrochinina (DHQ) Diidrochinidina (DHQD)
pseudoenantiomeri

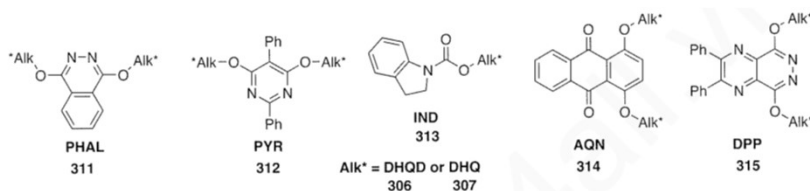
LEGANTI CHIRALI - PRIMA GENERAZIONE



2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

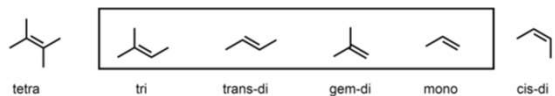
3

LEGANTI CHIRALI - SECONDA GENERAZIONE



Olefin class	R	R^1, R^2	R^1, R^2	R^1, R^2	R^1, R^2, R^3	R^1, R^2, R^3, R^4
Preferred ligand	$R =$ Aromatic: DPP, PHAL Aliphatic: AQN Branched: PYR	$R^1, R^2 =$ Aromatic: DPP, PHAL Aliphatic: AQN Branched: PYR	$R^1, R^2 =$ Acyclic: IND Cyclic: PYR, DPP, AQN	$R^1, R^2 =$ Aromatic: DPP, PHAL Aliphatic: AQN	PHAL, DPP AQN	PYR, PHAL

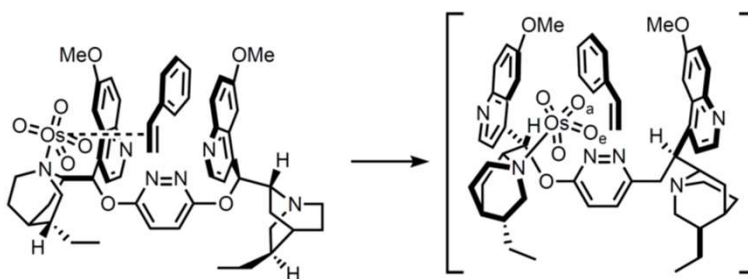
4 of 6 Olefin substitution classes are successfully dihydroxylated:



2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

4

intermedio reazione con stirene (U-shaped)

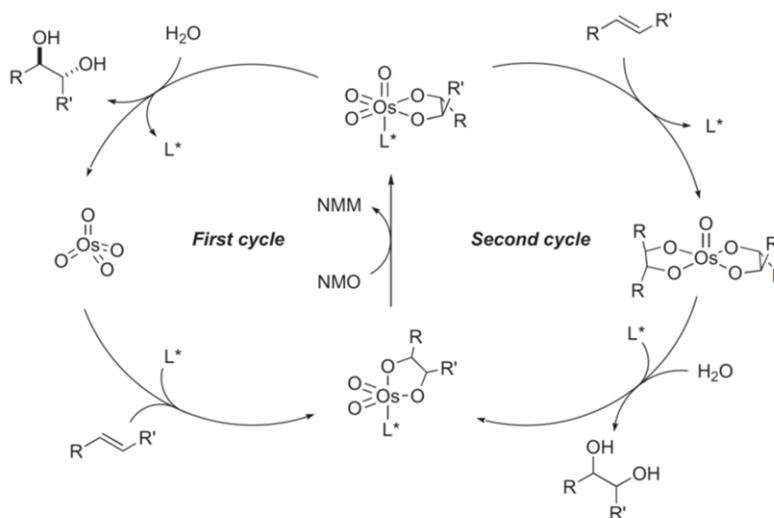


Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *Tetrahedron Lett.* **1995**, 36, 3481–3484.

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

5

Ciclo Catalitico Co-ossidante NMO (*N*-metil-morfolina-*N*-ossido)

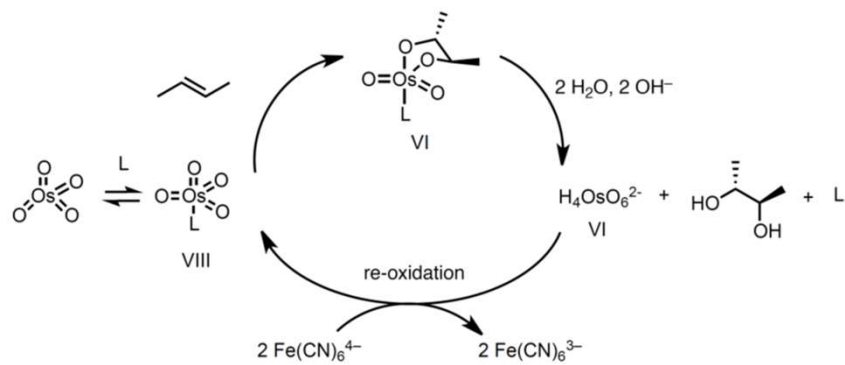


2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

6

Ciclo catalitico – Co-ossidante $K_2Fe(CN)_6/K_2CO_3$

Catalytic Cycle:

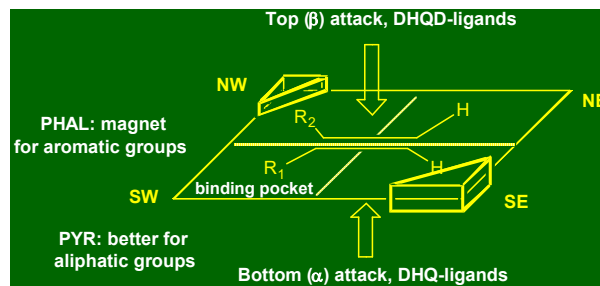


Sharpless, K.B. *et al. Tetrahedron Lett.*, **1990**, 31, 2999 e **1991**, 32, 3965

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

7

DIIDROSSILAZIONI ASIMMETRICHE MODELLO EMPIRICO (PHAL E PYR)

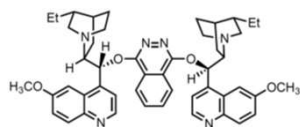


Vanhessche, P.M.; Sharpless, K.B. *J. Org. Chem.*, **1996**, 61, 7978

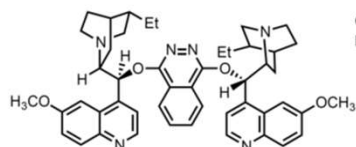
2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

8

DIIDROSSILAZIONI ASIMMETRICHE AD MIX alfa o beta



(DHQ)₂-PHAL
ligand for AD-mix-α
(slightly less
enantioselective)



(DHQD)₂-PHAL
ligand for AD-mix-β

Sigma Aldrich

AD-mix-beta Components

Mixture contains:

(DHQD)₂PHAL (Cat. No. 392731) 0.0016 mole

Potassium carbonate, powder 0.4988 mole

Potassium ferricyanide 0.4988 mole

Potassium osmate dihydrate 0.0007 mole

392766-10G 25.40 €

392766-50G 83.60 €

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

9

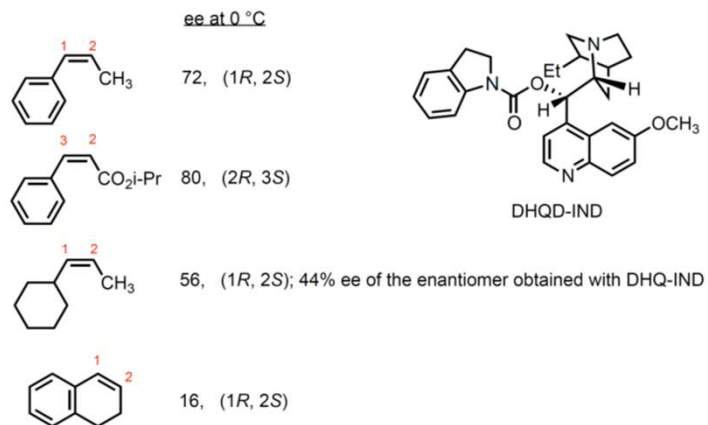
DIIDROSSILAZIONI ASIMMETRICHE - AD MIX alfa o beta

	AD-mix-β [(DHQD) ₂ -PHAL] % ee, config.	AD-mix-α [(DHQ) ₂ -PHAL] % ee, config.
	98, <i>R</i>	95, <i>S</i>
	99, <i>R, R</i>	97, <i>S, S</i>
	97, <i>R, R</i>	93, <i>S, S</i>
	99, 2 <i>S</i> , 3 <i>R</i>	96, 2 <i>R</i> , 3 <i>S</i>
	97, 2 <i>S</i> , 3 <i>R</i>	95, 2 <i>R</i> , 3 <i>S</i>
	>99.5, <i>R, R</i>	>99.5, <i>S, S</i>
	78, <i>R</i>	76, <i>S</i>

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

10

DIIDROSSILAZIONI ASIMMETRICHE – olefin cis

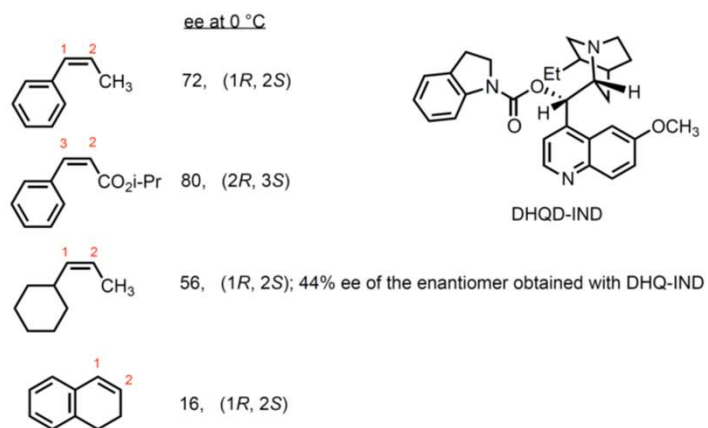


Wang, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7568–7570.

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

11

DIIDROSSILAZIONI ASIMMETRICHE – olefin cis



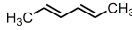
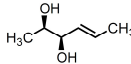
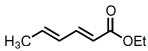
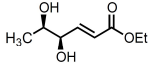
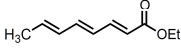
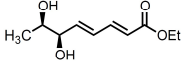
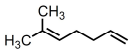
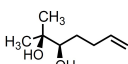
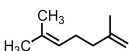
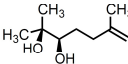
Wang, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7568–7570.

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

12

DIIDROSSILAZIONI ASIMMETRICHE – olefin cis

Regioselectivity of AD with diene substrates ((DHQD)₂PHAL as ligand):

Substrate	Product	% yield, % ee
		78, 93
		78, 92
		93, 95
		73, 98
		70, 98

in general, AD is selective for the more electron-rich double bond

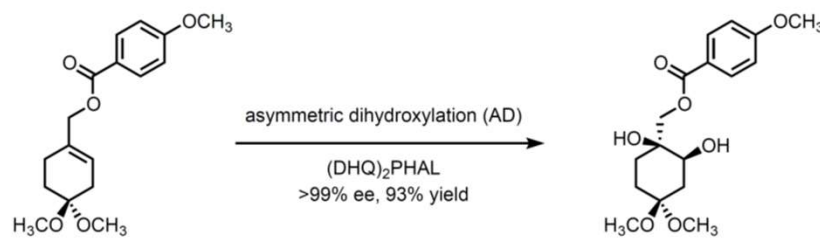
Xu, D.; Crispino, G. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7570-7571.

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

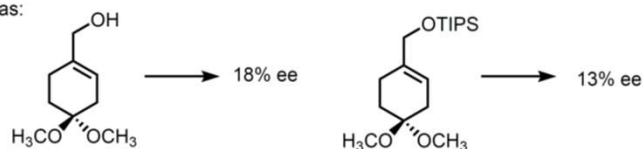
13

DIIDROSSILAZIONI ASIMMETRICHE – 4-MeO-benzoati

Allylic 4-methoxybenzoates are particularly good substrates:



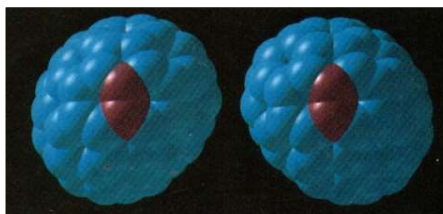
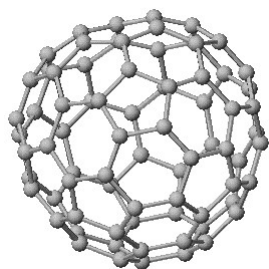
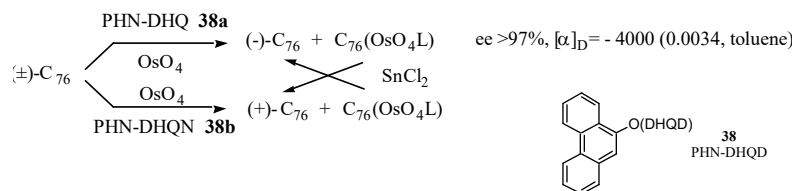
whereas:



2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

14

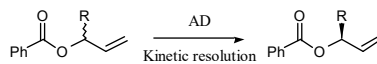
Diidrossilazioni con OsO₄ - Risoluzione cinetica C₇₆

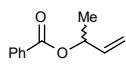
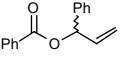


15

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

Diidrossilazioni con OsO₄ - risoluzione cinetica

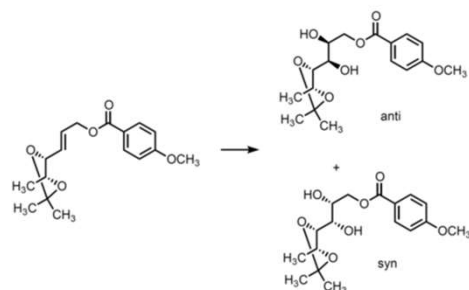


Substrate	Ligand	k _{rel} = k _{ent} /k
 52	(DHQD) ₂ PYDZ 32b	3.1
	(DHQD)-PYDZ-(S)-Anthryl 40	20
 53	(DHQD) ₂ PYDZ 32b	1.9
	(DHQD)-PYDZ-(S)-Anthryl 40	79

16

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

Diidrossilazioni con OsO₄ – reazioni su larga scala



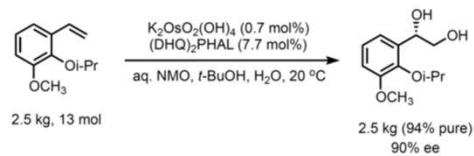
Conditions	Yield	anti : syn
OsO ₄ , NMO	88% yield (mixture)	1.9 : 1
(DHQ) ₂ PHAL (matched)	86% yield (anti)	54 : 1
(DHQD) ₂ PYDZ (mismatched)	86% yield (syn)	1 : 35

Guzman-Perez, A.; Corey, E. J. *Tetrahedron Lett.* **1997**, 38, 5941–5944.

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

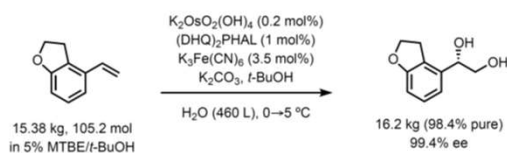
17

Diidrossilazioni con OsO₄ – doppia stereoselezione



• Olefin was added over a period of 6.5 h to the reaction mixture to prevent "second cycle" oxidation.

Ahrgren, L.; Sutin, L. *Org. Process Res. Dev.* **1997**, 1, 425–427.



Prasad, J. S.; Vu, T.; Totleben, M. J.; Crispino, G. A.; Kacsur, D. J.; Swaminathan, S.; Thornton, J. E.; Fritz, A.; Singh, A. K. *Org. Process Res. Dev.* **2003**, 7, 821–827.

2019 - G. Licini, Università di Padova. La riproduzione a fini commerciali è vietata

18