Séminaire bibliographique **Cyril Bressy**

Réarrangement énantiosélectif des époxydes *meso* Catalysé par des bases chirales

8 février 2007

Revues sur le sujet

« *Asymmetric synthesis using homochiral lithium amide bases* »
Cox, P.J.; Simpkins, N.S.
Tetrahedron: Asymmetry **1991**, *2*, 1-26.

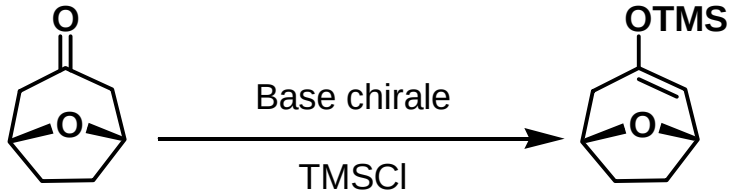
« *Enantioselective desymmetrisation of achiral epoxides* »
Hodgson, D.M.; Gibbs, A.R. ; Lee, G.P.
Tetrahedron **1996**, *52*, 14361-14384.

« *Recent advances in asymmetric synthesis using chiral lithium amide bases* »
O'Brien, P.
J. Chem. Soc., Perkin Trans I, **1998**, 1439-1457.

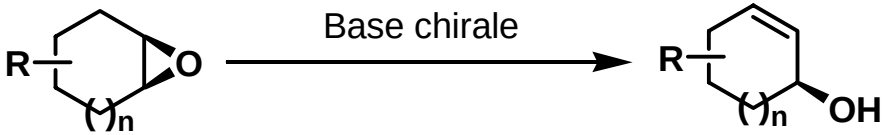
« *Recent developments in enantioselective deprotonation mediated by sub-stoichiometric quantities of chiral bases* »
Eames, J.
Eur. J. Org. Chem. **2002**, 393-401.

Gamme de transformations possibles
Avec l'emploi de bases chirales

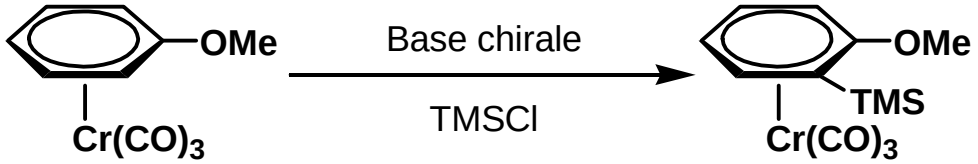
Déprotonation de cétones



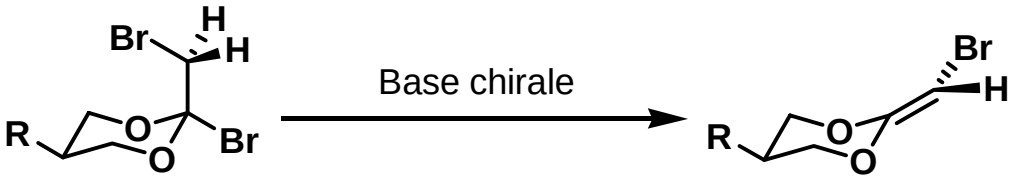
Réarrangement d'époxydes



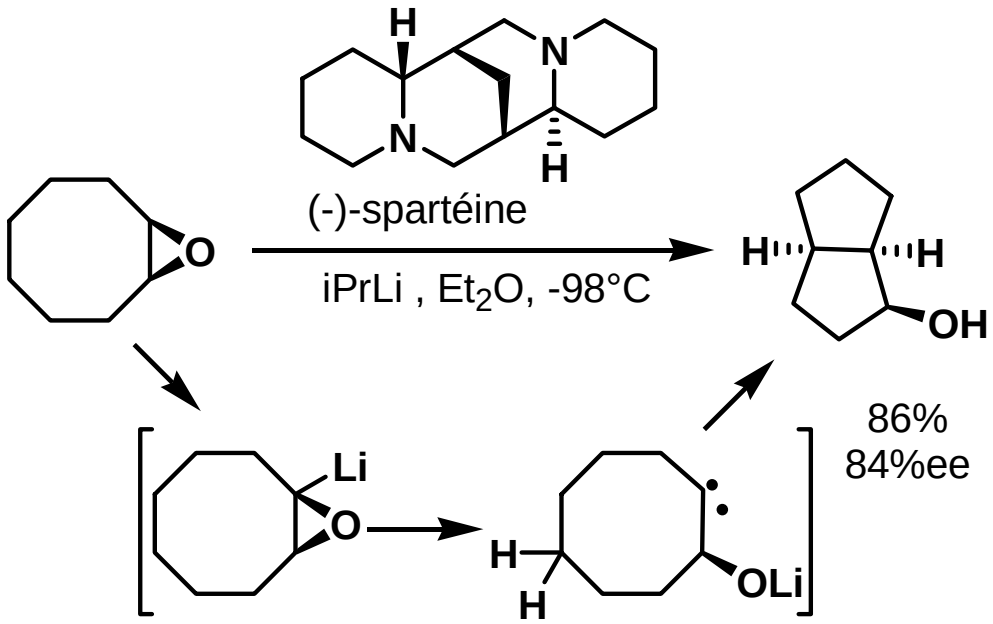
Fonctionnalisation des
Arènes-chrome tricarbonyle

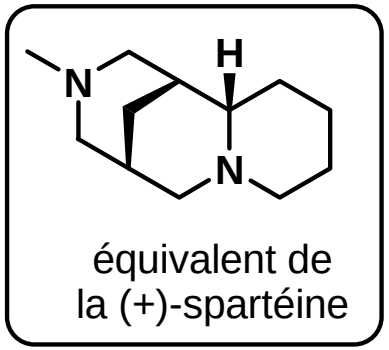


Déhydrobromation



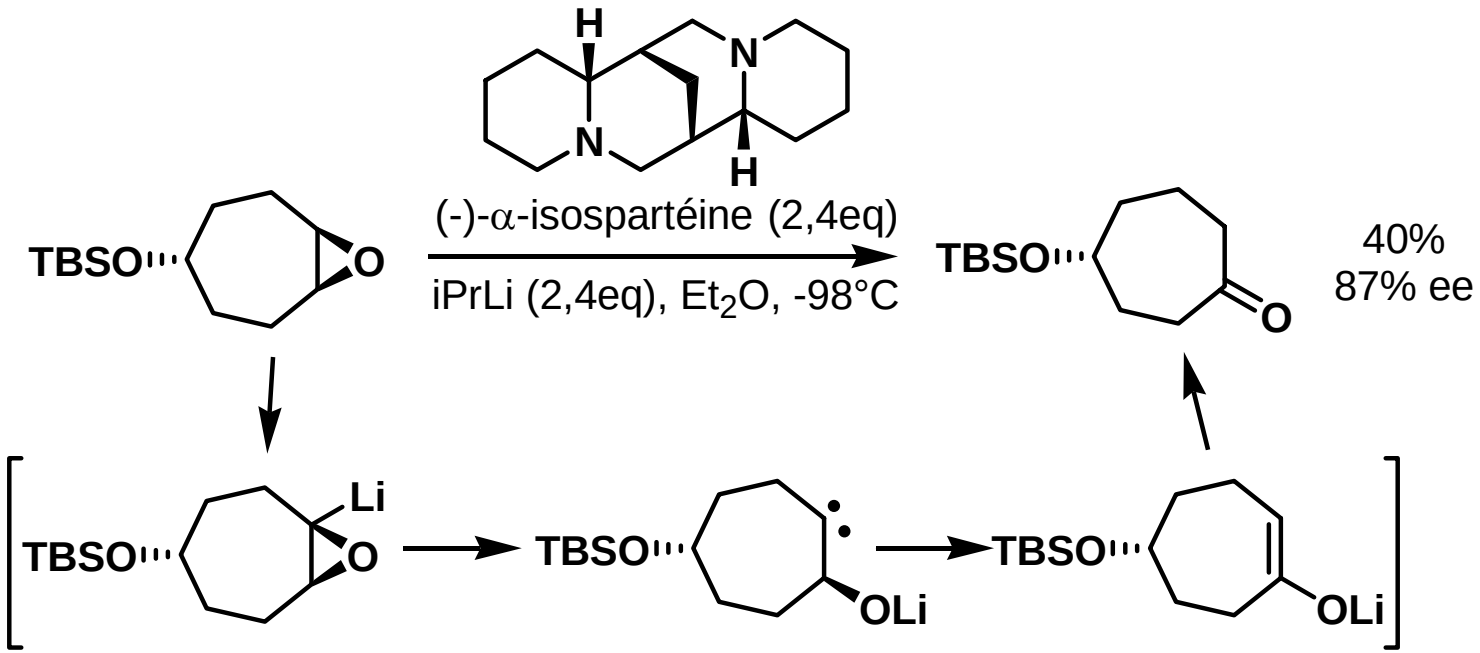
Réactivité des époxydes en présence de bases
α-déprotonation (1)





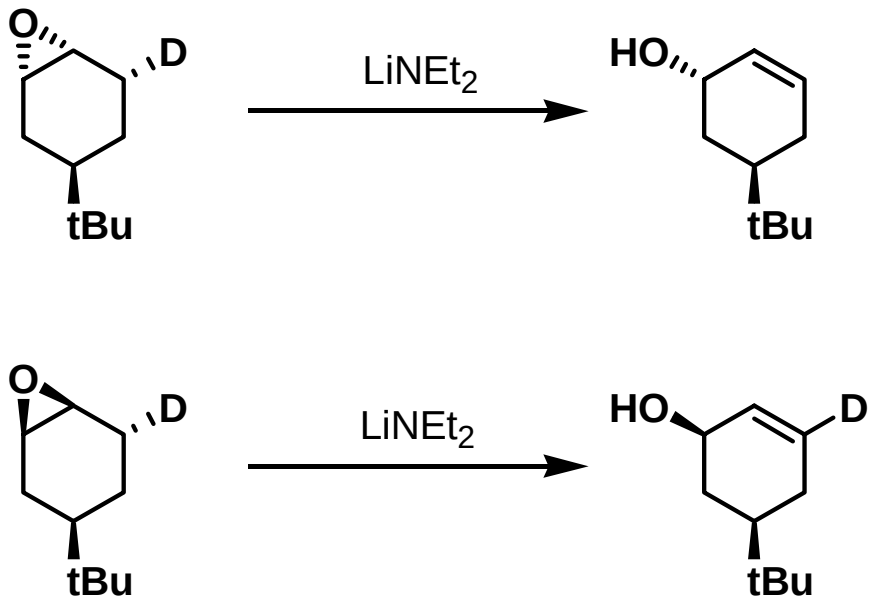
Hodgson, D.M. ; Lee, G.P. *Chem. Commun* **1996**, 1015-1016.
Dearden, M.J. ; Firkin, C.R. ; Hermet, J-P.R. O'Brien, P. *J. Am. Chem. Soc.* **2002**, *124*, 11870-11871.

Réactivité des époxydes en présence de bases
α-déprotonation (2)



Hodgson, D.M. ; Robinson, L.A. ; Jones, M.L. *Tetrahedron Lett.* **1999**, 40, 8637-8640.

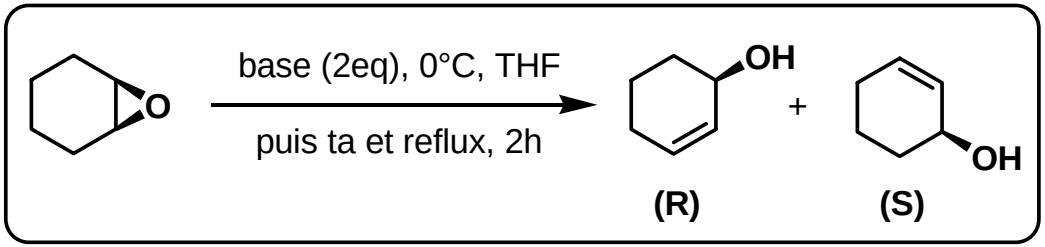
Réactivité des époxydes en présence de bases
β-déprotonation

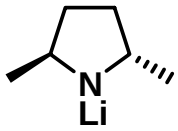


Syn-élimination

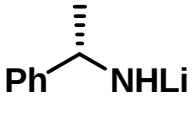
Thummel, R.P. ; Rickborn, B. *J. Am. Chem. Soc.* **1970**, *92*, 2064-2067.

Premier cas de réarrangement énantiosélectif

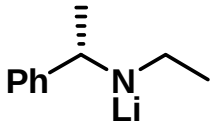




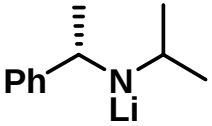
44%
3% ee (R)



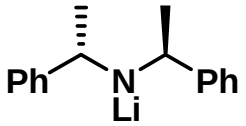
51%
3% ee (S)



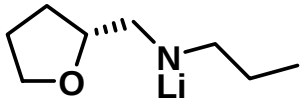
69%
11% ee (R)



95%
9% ee (R)



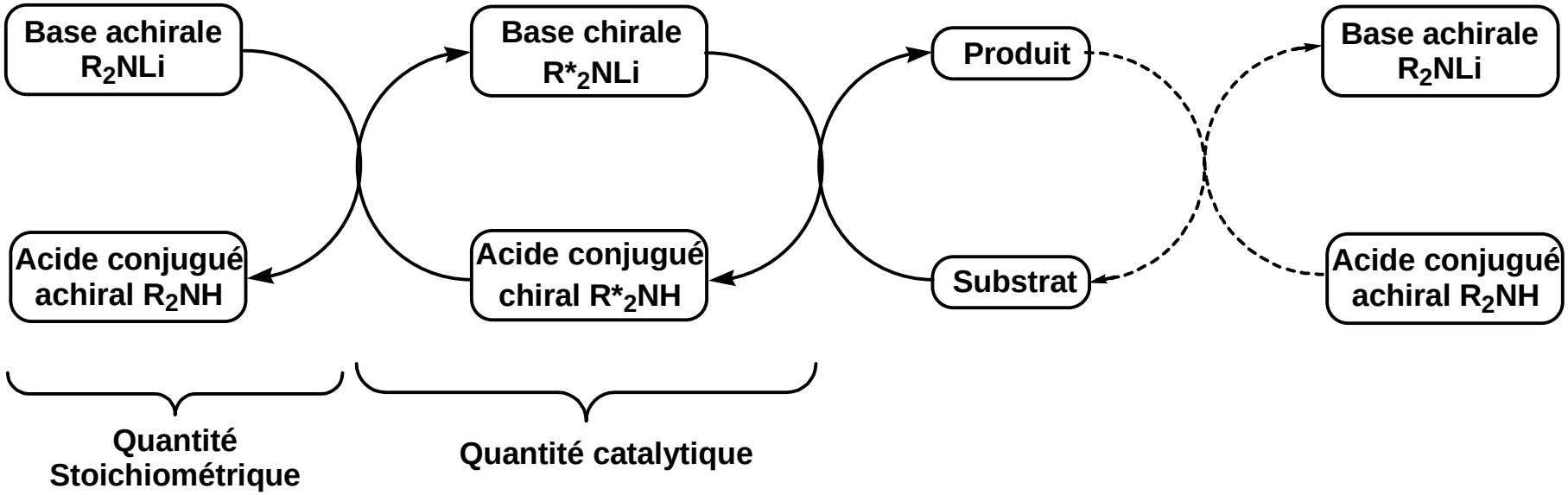
65%
31% ee (R)



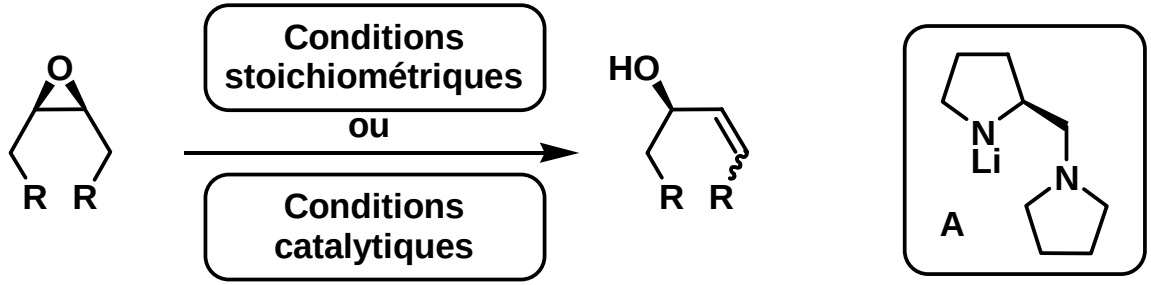
76%
18% ee (S)

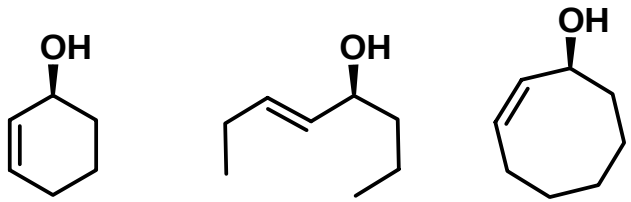
Whitesell, J.K. ; Felman, S.W. *J. Org. Chem.* **1980**, *45*, 755-756.

Conditions pour la catalyse par des bases chirales



Premier cas de catalyse: travaux d'Asami (1)

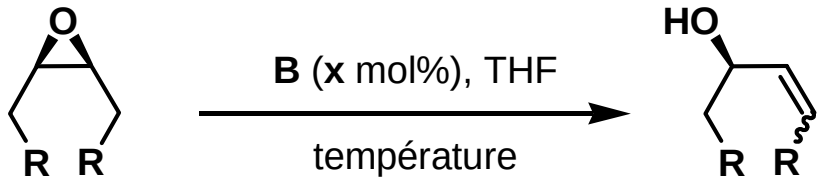




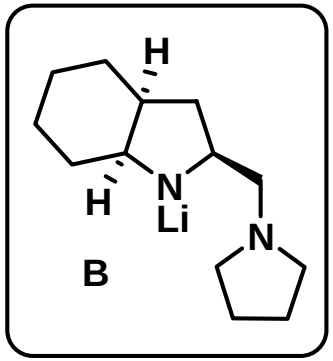
Conditions stoichiométriques	80% 81% ee	66% 60% ee	45% 58% ee	1,5eq de **A**, DBU (1,65eq), THF, ta
sans DBU	63% 48% ee			
Conditions catalytiques	71% 75% ee	54% 60% ee	27% 54% ee	0,2eq de **A**, LDA (1eq), DBU (6eq), THF, ta

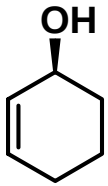
Asami, M. ; Ishizaki, T. ; Inoue, S. *Tetrahedron Asymmetry* **1994**, *5*, 791-796

Travaux d'Asami (2)

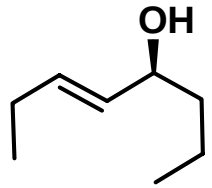


sans DBU

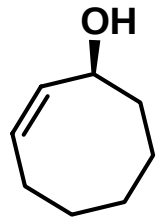




X mol% de B	temp	durée	Rdt	ee
150	ta	6h	86%	89%
20 (+1,8eq de LDA)	ta	6h	95%	88%
20 (+1,8eq de LDA)	0°C	18h	89%	94%



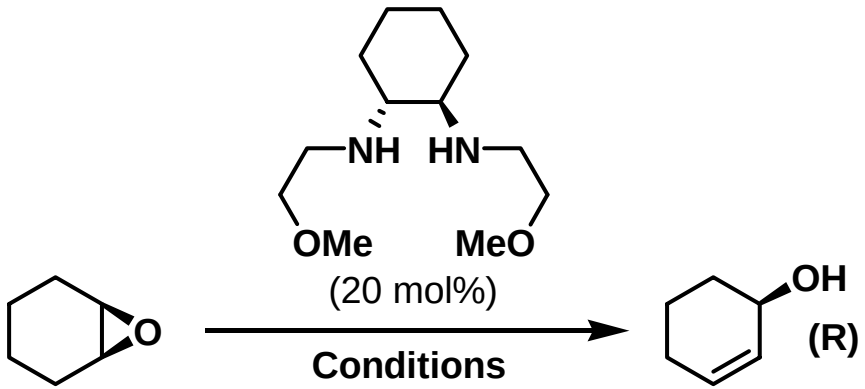
84%,
86% ee,
0°C



73%,
53% ee,
0°C

Asami, M. ; Suga, T. ; Honda, K. ; Inoue, S. *Tetrahedron Lett.* **1997**, *38*, 6425-6428

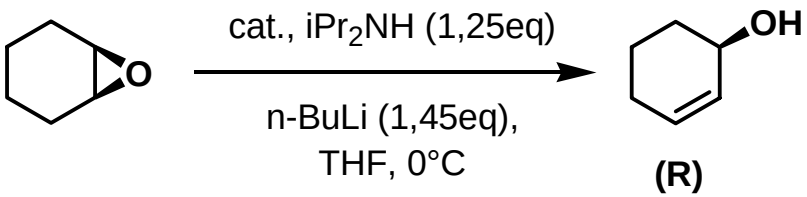
Travaux d'Alexakis



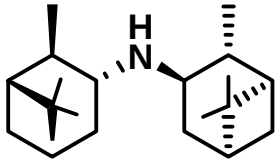
Conditions	Rdt	ee
n-BuLi (1eq) hexanes / PhH 5°C puis ta, 48h	47%	67%
LDA (1,5eq) hexanes /THF 0°C puis ta, 22h	66%	32%
LDA (1,5eq) hexanes /THF, DBU (6eq), 0°C puis ta, 43h	35%	13%

Tierney, J.P. ; Alexakis, A. ; Mangeney, P. *Tetrahedron: Asymmetry* **1997**, *8*, 1019-1022

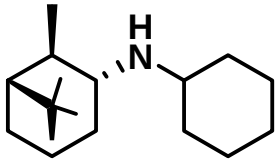
Travaux de Malhotra



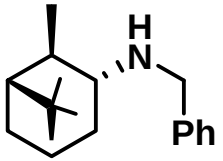
Catalyseur :



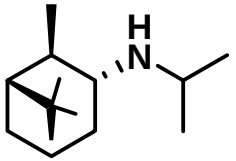
DIPAM
20 mol%
77%, 95% ee



ChxIPAM
20 mol%
70%, 78% ee



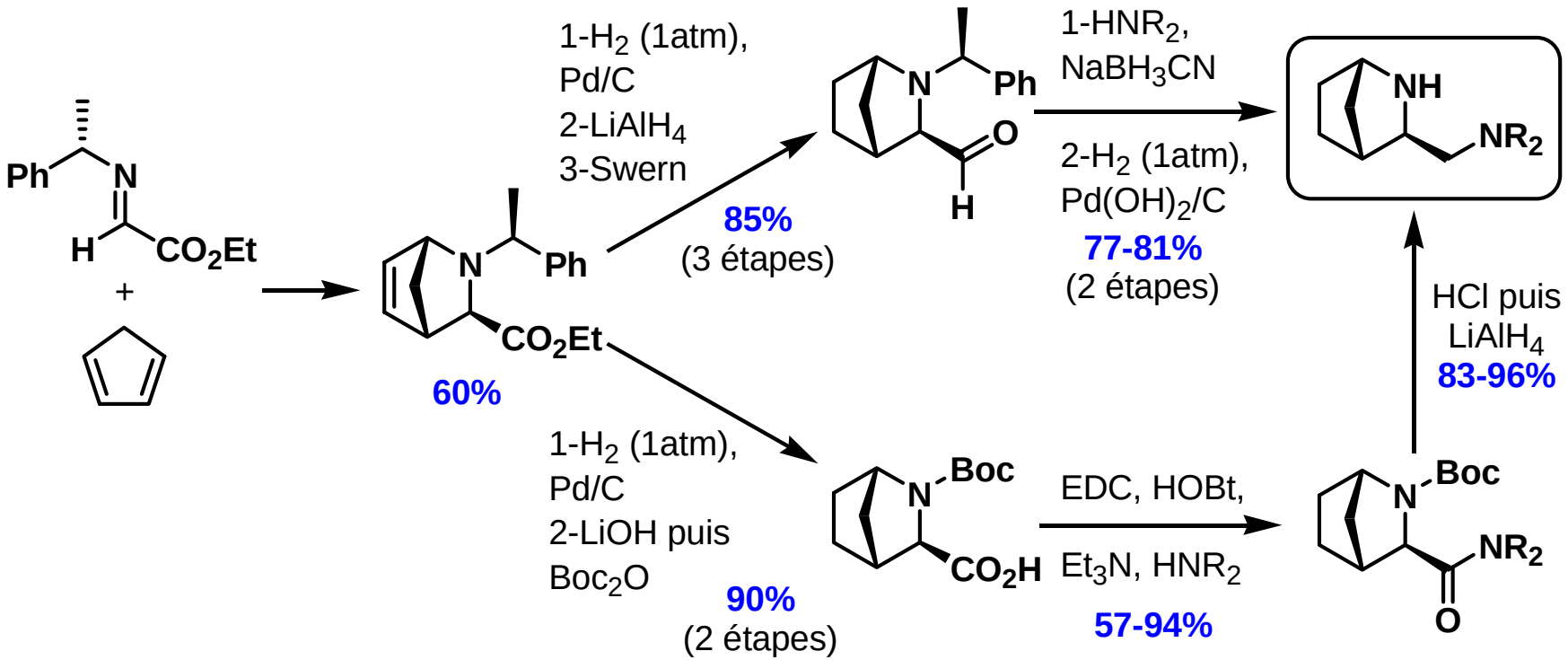
BzIPAM
20 mol%
57%, 48% ee



iPIPAM
20 mol%
58%, 52% ee

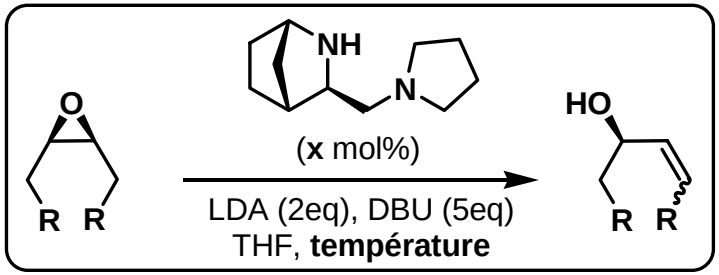
Malhotra, S.V. *Tetrahedron: Asymmetry* **2003**, *14*, 645-647

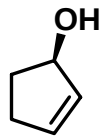
Travaux d'Andersson (1)



Södergren, M.J. ; Andersson, P.G. *J. Am. Chem. Soc.* **1998**, *120*, 10760-10761.

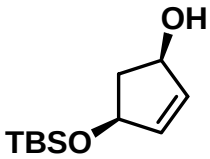
Travaux d'Andersson (2)





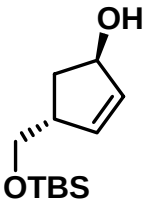
20 mol%, ta
67%, **49% ee**

120 mol%, ta
78%, **95% ee**

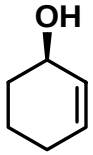


5 mol%, 0°C
60%, **67% ee**

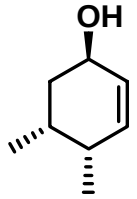
120 mol%, 0°C
85%, **95% ee**



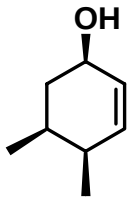
20 mol%, ta
42%, **95% ee**



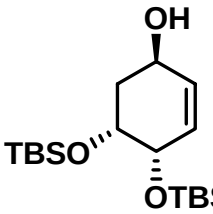
5 mol%, 0°C
91%, **96% ee**



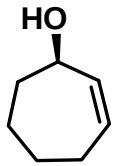
5 mol%, 0°C
95%, **94% ee**



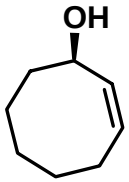
5 mol%, 0°C
95%, **97% ee**



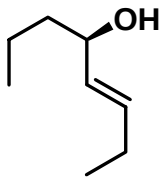
5 mol%, 0°C
60%, **97% ee**



5 mol%, 0°C
89%, **96% ee**



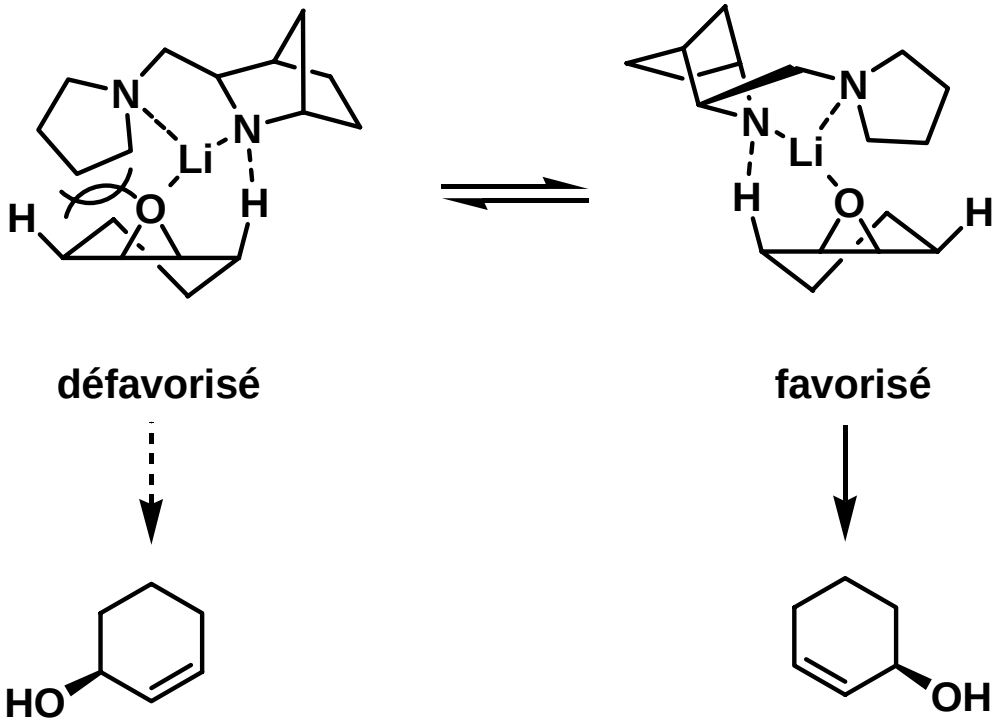
5 mol%, 0°C
81%, **78% ee**



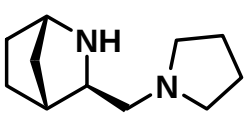
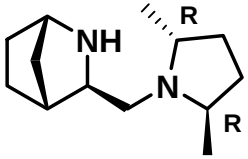
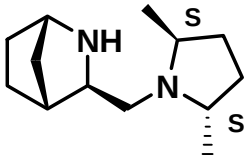
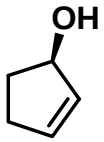
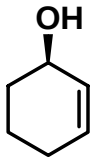
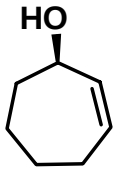
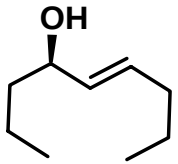
5 mol%, 0°C
82%, **66% ee**

Södergren, M.J. ; Bertilsson, S.K. ; Andersson, P.G. *J. Am. Chem. Soc.* **2000**, *122*, 6610-6618.

Travaux d’Andersson (3)



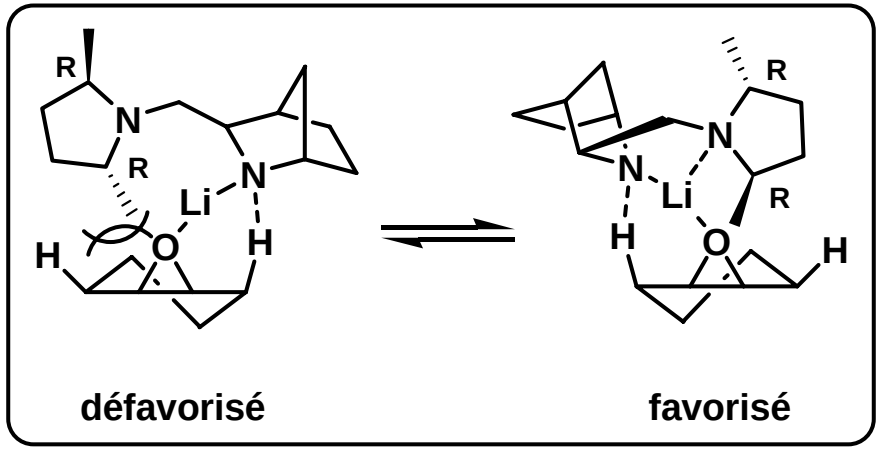
Travaux d'Andersson (4)

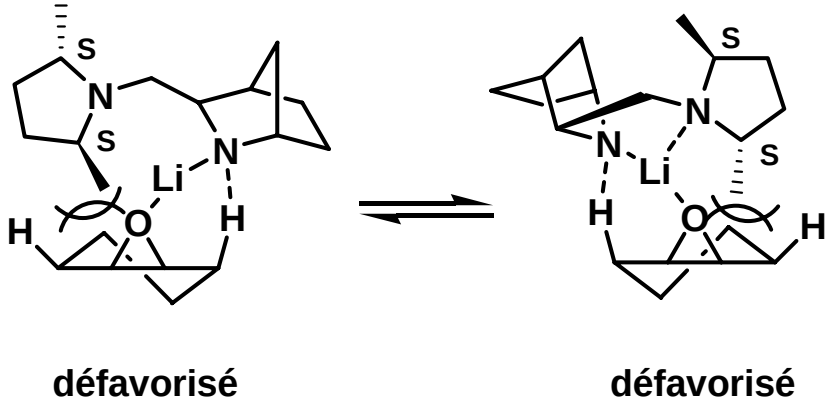
			
	67% 49% ee	81% (ta) **96% ee**	-
	91% 96% ee	95% **99% ee**	19% conv. 44% ee après 2h
	89% 96% ee	93% **>99% ee**	-
	82% 66% ee	80% **91% ee**	-

Conditions:
5 mol% de diamine,
DBU (10eq),
LDA (1,5eq),
THF, 0°C

Bertilsson, S.K. ; Södergren, M.J. ; Andersson, P.G. *J. Org. Chem.* **2002**, *67*, 1567-1573.

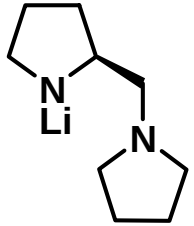
Travaux d’Andersson (5)





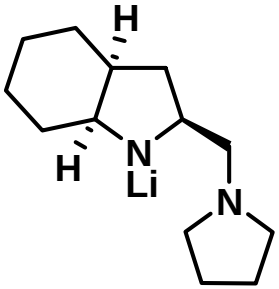
Récapitulatif

Asami 1994



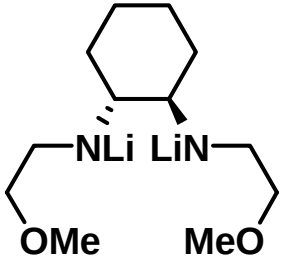
20 mol%, ta
71%, 75% ee

Asami 1997



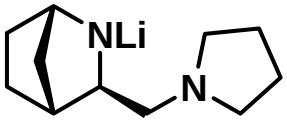
20 mol%, 0°C
89%, 94% ee

Alexakis 1997



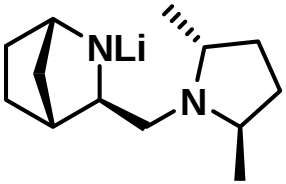
20 mol%, 5°C à ta
47%, 67% ee

Andersson 1998



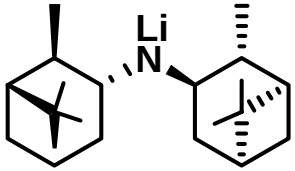
5 mol%, 0°C
91%, 96% ee

Andersson 2002



5 mol%, 0°C
95%, 99% ee

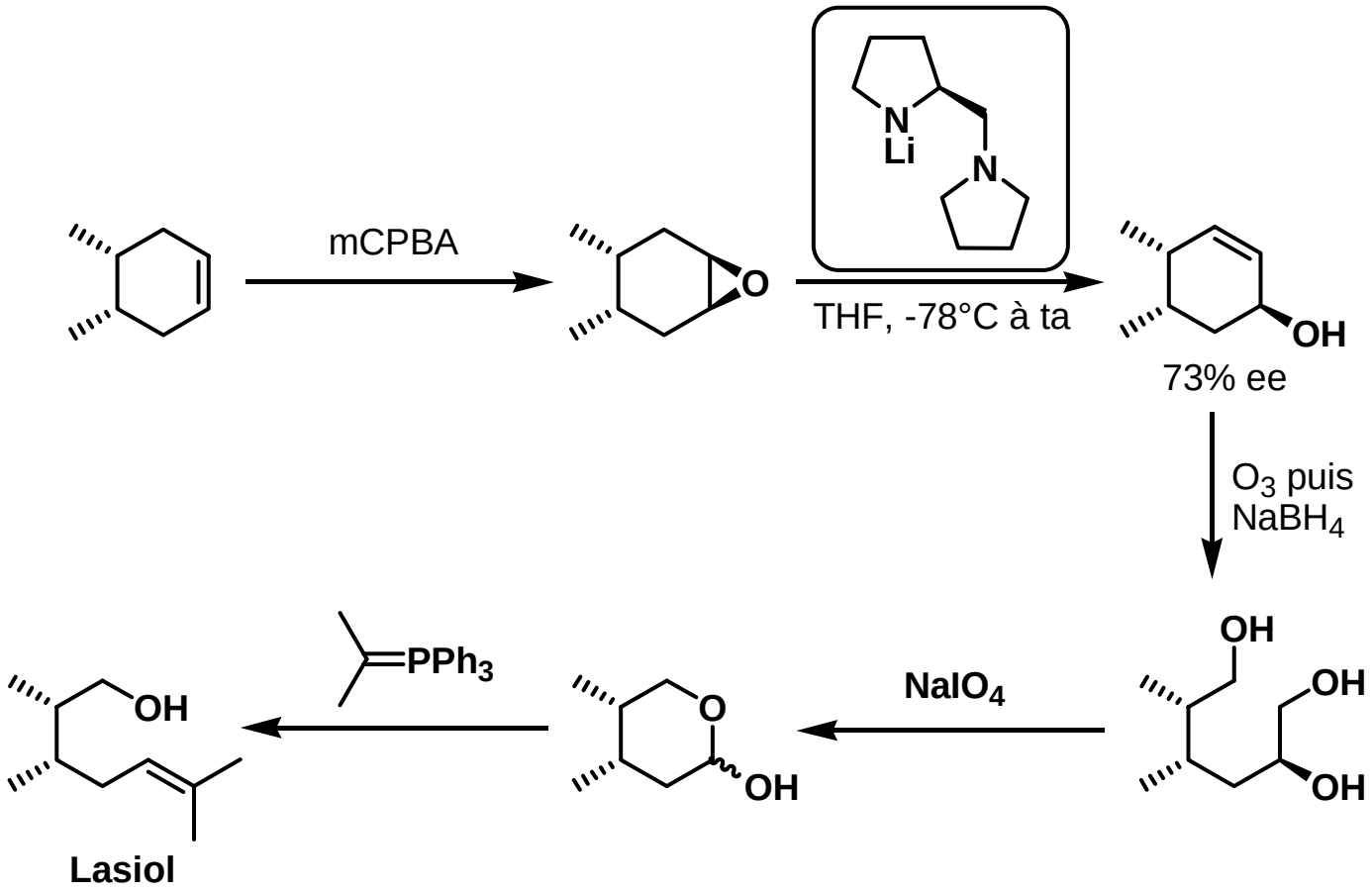
Malhotra 2003



20 mol%, 0°C
77%, 95% ee

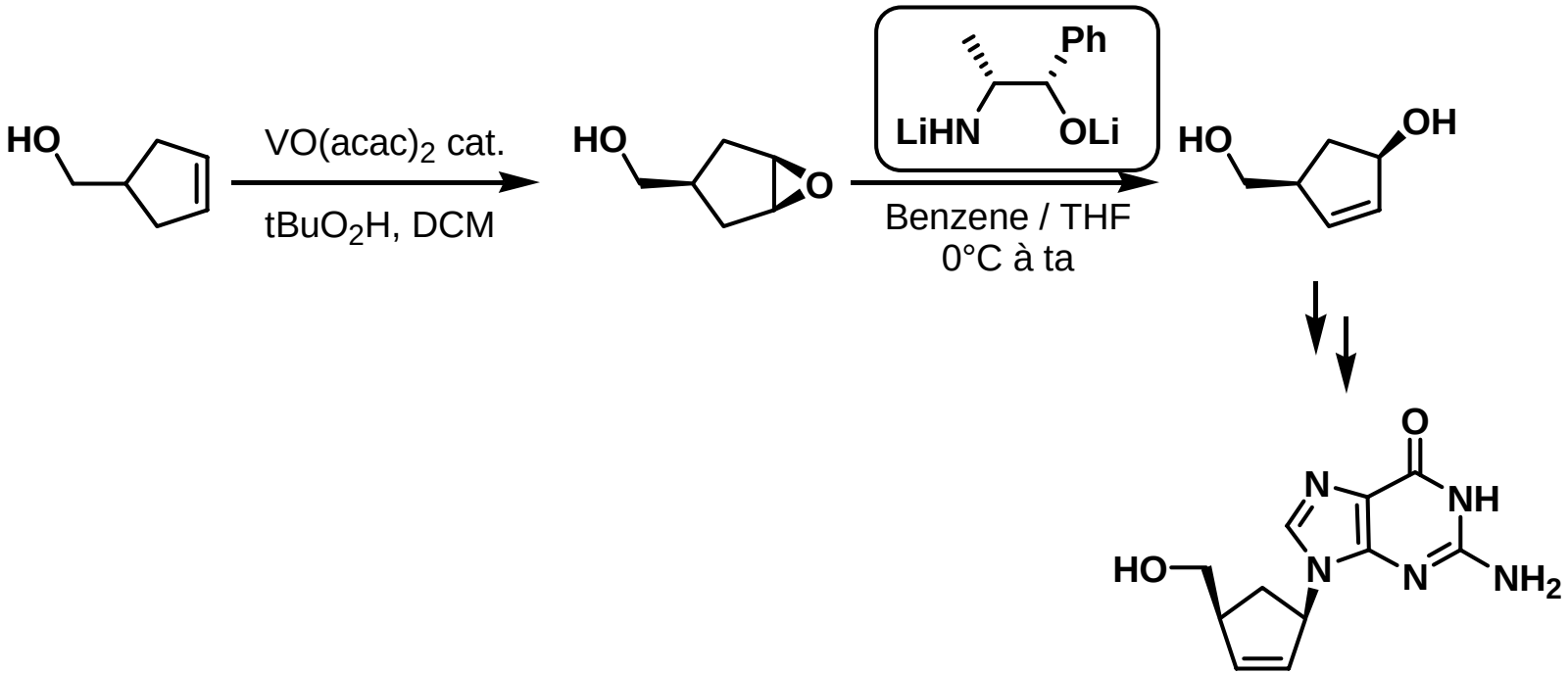
Sur la base du réarrangement de l’oxyde de cyclohexène

Synthèse du Lasiol



Kasaï, T. ; Watanabe, H. ; Mori, K. *Bioorg. Med. Chem.* **1993**, *1*, 67-70

Synthèse du Carbovir



Carbovir

Hodgson, D.M. ; Witherington, J. ; Moloney, B.A. *J. Chem. Soc., Perkin Trans 1* **1994**, 3373-3378