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IN TORUŃ
Faculty of Chemistry

HIGHLY ASYMMETRIC REDUCTION OF NEW BENZOFURYL AND BENZOTHIOPHENYL α-AMINO KETONES

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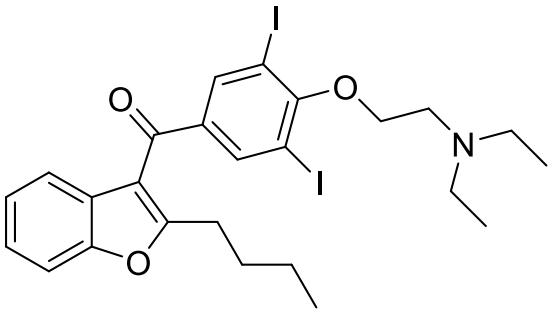
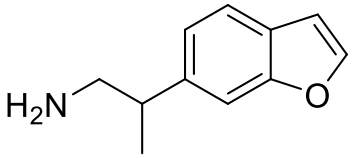
08.11.2019

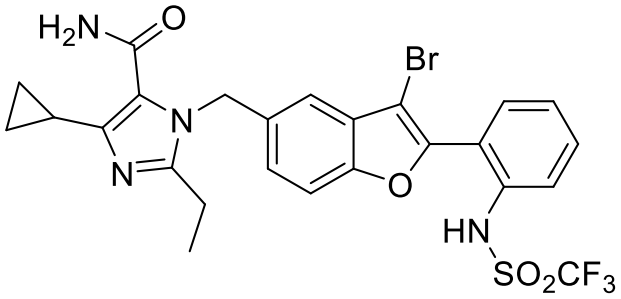
BENZOFURYL AND BENZOTHIOPHENYL DRUGS



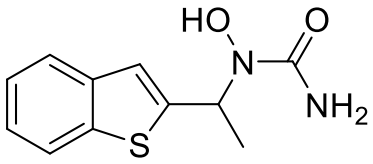
Amiodarone



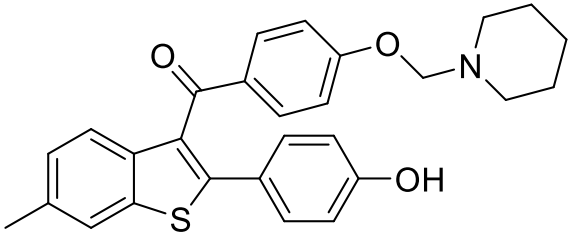
6-APB



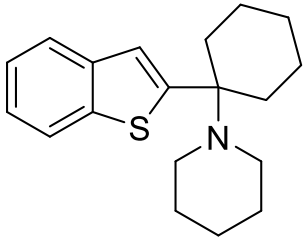
Saprisartan



Zileuton



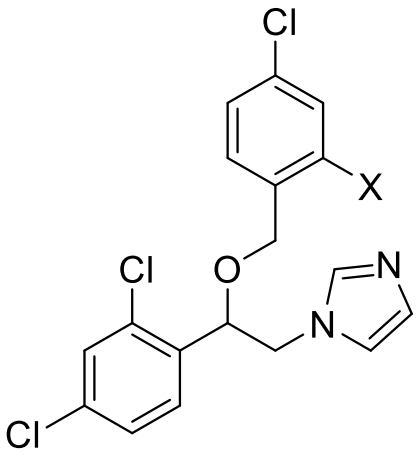
Raloxifene



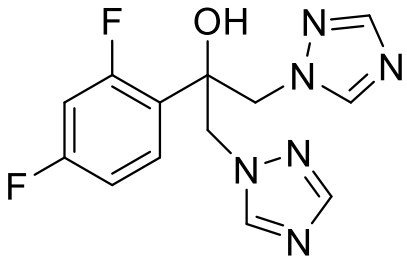
Benocyclidene

H. K. Shamsuzzaman, *Eur. J. Med. Chem*. **2015**, *97*, 483-504.
R. S. Keri et al., *Eur. J. Med. Chem*. **2017**, *138*, 1002-1033.

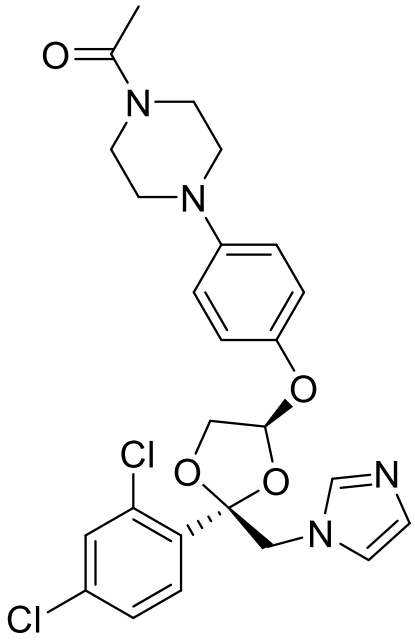
MAIN AZOLE-ANTIFUNGAL AGENTS



X = H Econazole
X = Cl Miconazole

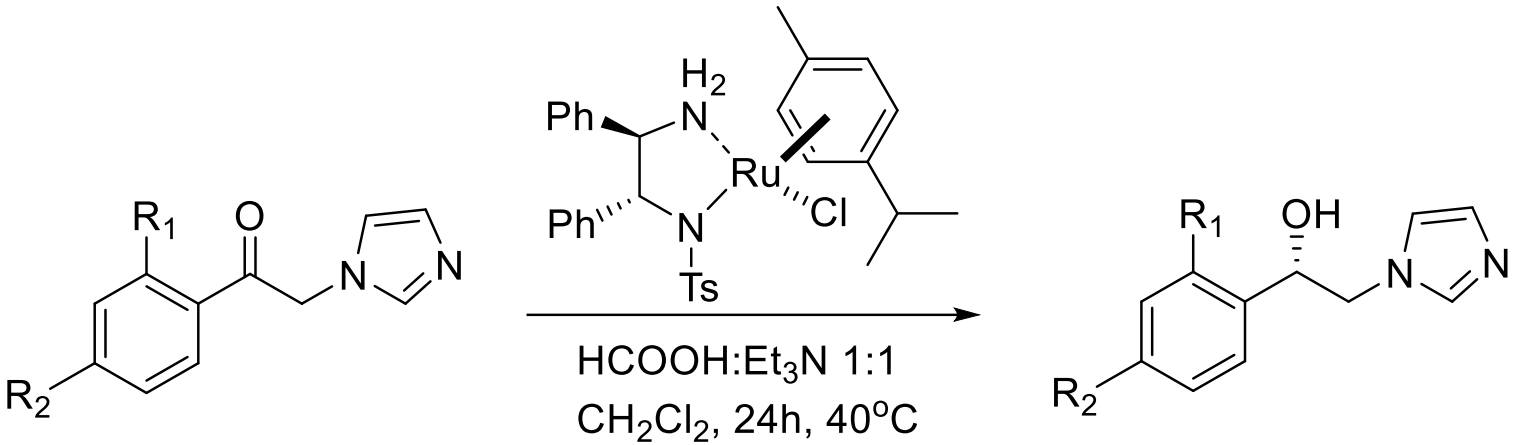


Fluconazole



Ketoconazole

ASYMMETRIC TRANSFER HYDROGENATION OF 1-ARYL-2-(IMIDAZOL-1-YL)ETHANONES

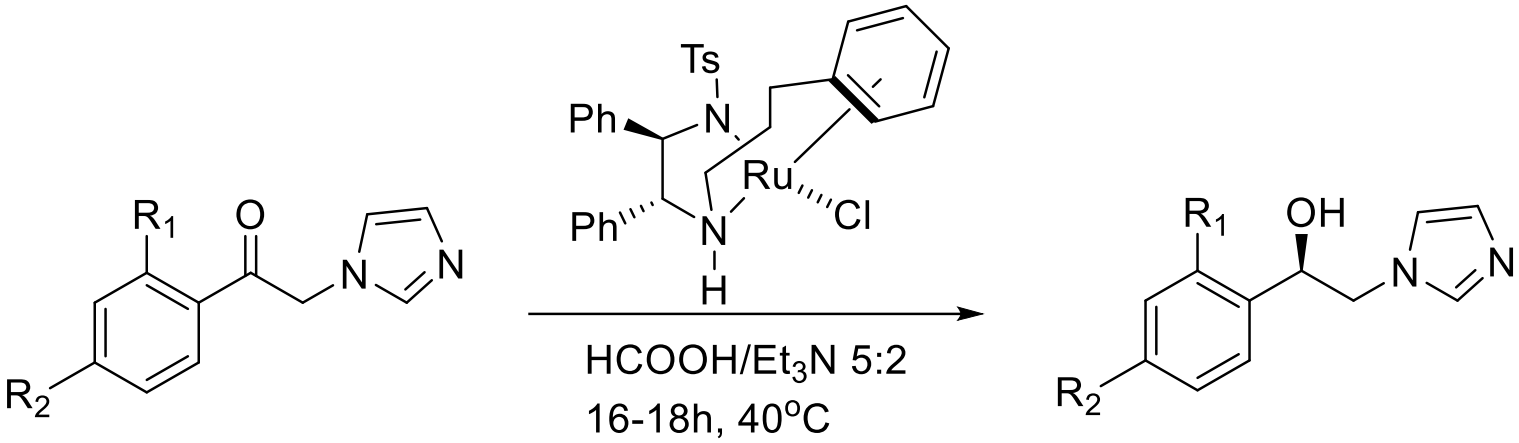


R_1 = H R_2 = H
R_1 = Cl R_2 = Cl

99% yield, 97% ee
98% yield, 91% ee

I. C. Lennon, J. A. Ramsden, *Org. Process Res. Dev*. **2005**, *9*, 110-112.

ASYMMETRIC TRANSFER HYDROGENATION OF 1-ARYL-2-(IMIDAZOL-1-YL)ETHANONES

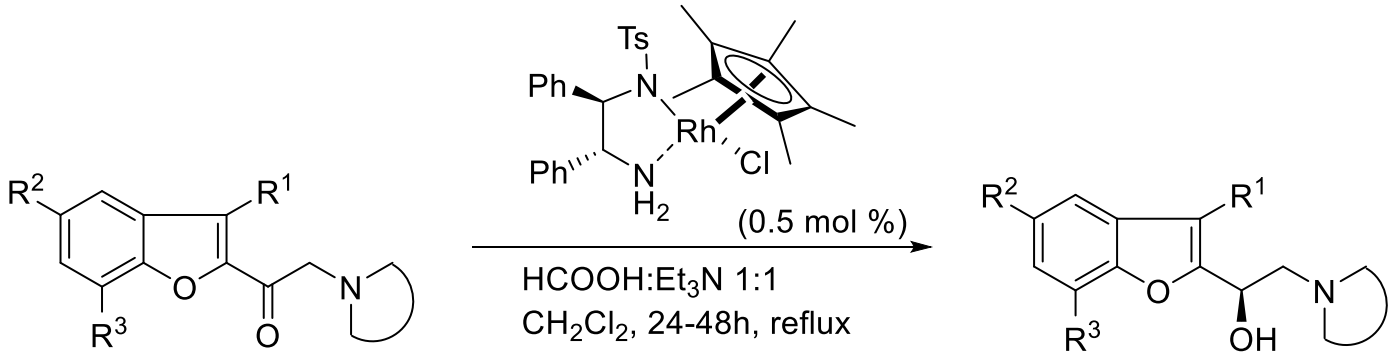


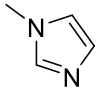
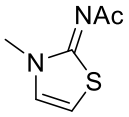
R_1 = H R_2 = H
R_1 = Cl R_2 = Cl

99% yield, 99% ee
98% yield, 71% ee

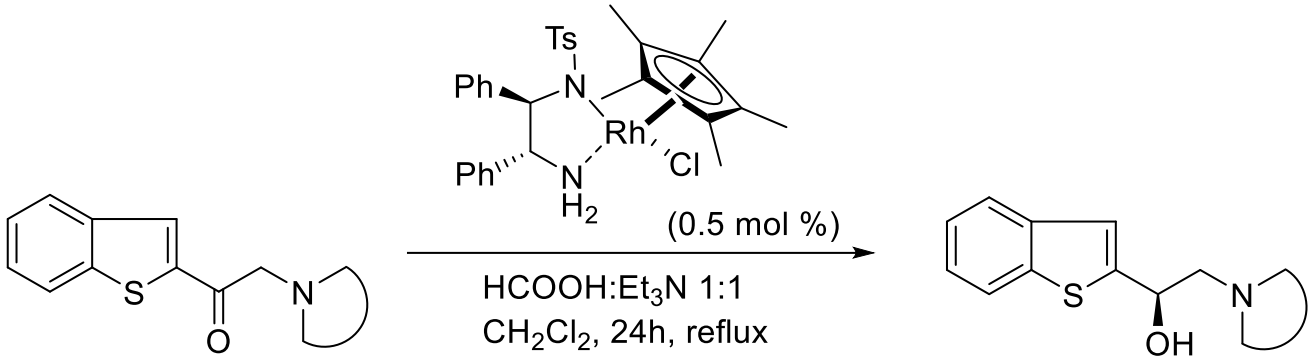
D. J. Morris, A. M. Hayes, M. Wills, *J. Org. Chem*. **2006**, *71*, 7035-7044.

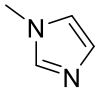
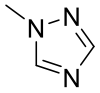
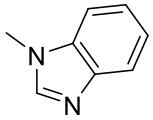
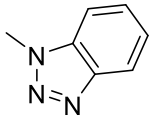
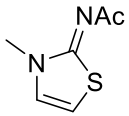
ASYMMETRIC REDUCTION OF BENZOFURYL α-AMINO KETONES



Entry	R^1	R^2	R^3		Yield (%)	Ee (%)
1	H	H	H		79	99
2	H	H	Et		75	96
3	Me	H	H		66	98
4	Me	Me	H		76	98
5	H	H	H		71	96
6	H	H	Et		77	98
7	Me	H	H		57	97
8	Me	Me	H		48	97
9	H	H	H		86	99
10	H	H	Et		69	99
11	Me	H	H		99	93
12	Me	Me	H		91	85

ASYMMETRIC REDUCTION OF BENZOTHIOPHENYL α-AMINO KETONES



Entry	N	Yield (%)	Ee (%)
1		78	99
2		95	98
3		74	94
4		98	99
5		76	98

SUMMARY

- New benzofuryl and benzothiophenyl *α*-amino ketones were prepared.
- Asymmetric transfer hydrogenation with the use of RhCl[(*R*,*R*)-TsDPEN](C_5Me_5) as the catalyst and HCOOH as a hydrogen source is an effective and convenient method for the reduction of heterocyclic *α*-amino ketones.
- Benzofuryl and benzothiophenyl *β*-amino alcohols were obtained in high yields and excellent enantioselectivities.