Department of Chemistry
The University of Hong Kong

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Copper-catalyzed Asymmetric Reductions of *2H*-azirines

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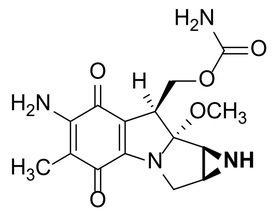
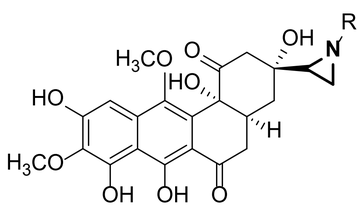
1. Background

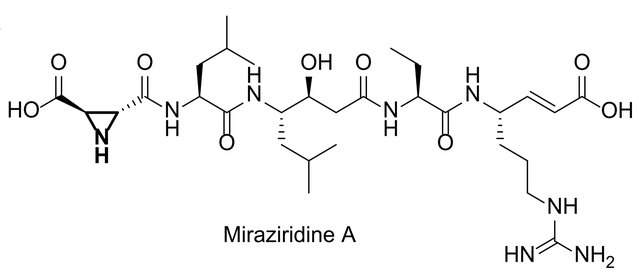
Aziridines, are crucial motifs embedded in numerous natural products. In the meanwhile, they are of great value for building block utility in organic synthesis. Nevertheless, the enantio-enriched N-H aziridine preparation has been scarcely reported.



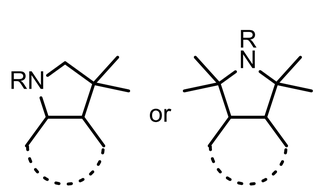
Mitomycin C



Azicemicin A: R = CH_3
Azicemicin B: R = H

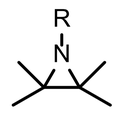


Miraziridine A



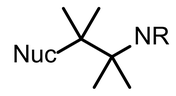
1,3-dipolarophile:
C = O, C = C...

1,3-dipolarophile ← *Ring-expansion*



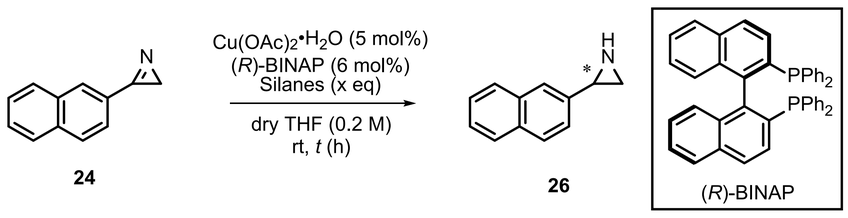
R = H, or PGs

Ring-opening → **Nucleophile**



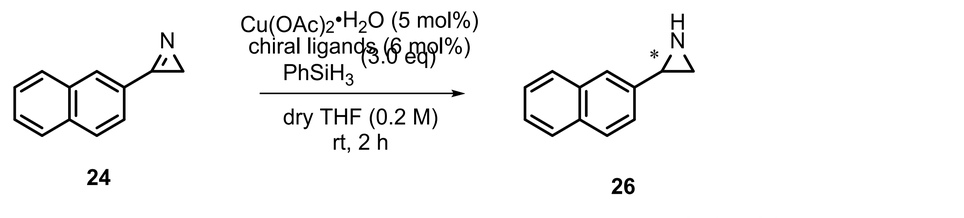
Nuc: O, N, Halogen...

2. Effect of reductive silanes

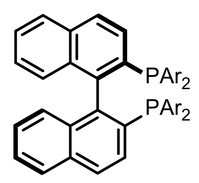


Entry	Silanes	Equiv (x eq)	*t* (h)	Yield/%[b]	ee/%[c]
1	PMHS	1.5	2.0	64	37
2	DEMS	3.0	2.0	48	38
3	$(EtO)_3SiH$	3.0	2.5	77	39
4	Et_3SiH	6.0	-	-	-
5	$PhMe_2SiH$	6.0	14.0	24	38
6	Ph_2MeSiH	9.0	4.0	39	31
7	**$PhSiH_3$**	**3.0**	**2.0**	**87**	**35**

3. Effect of nonracemic ligands - axial chirality



BINAP

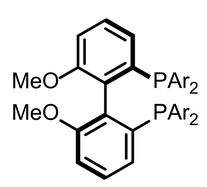


L1: (*R*)-BINAP (Ar = Ph) — **87% yield, 35% ee**

L2: (*R*)-XylBINAP (Ar = 3,5-xylyl) — **89% yield, 53% ee**

L3: (*R*)-TolBINAP (Ar = p-tol) — **87% yield, 53% ee**

MeO-BIPHEP

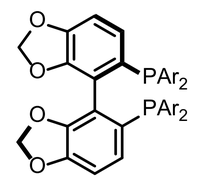


L4: (*R*)-MeO-BIPHEP (Ar = Ph) — **73% yield, 35% ee**

L5: (*R*)-DM-MeO-BIPHEP (Ar = 3,5-xylyl) — **99% yield, 45% ee**

L6: (*R*)-DTBM-MeO-BIPHEP (Ar = 3,5- (*t*-Bu)-4-MeO-C_6H_2) — **68% yield, 11% ee**

SEGPHOS

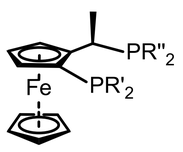


L7: (*R*)-SEGPHOS (Ar = Ph) — **89% yield, 41% ee**

L8: (*R*)-DM-SEGPHOS (Ar = 3,5-xylyl) — **66% yield, 51% ee**

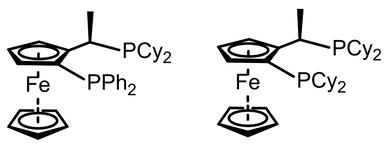
L9: (*R*)-DTBM-SEGPHOS (Ar = 3,5- (*t*-Bu)-4-MeO-C_6H_2) — **69% yield, 17% ee**

3. Effect of nonracemic ligands - planar chirality



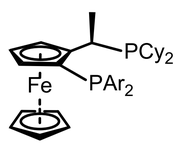
Josiphos Series

R'' = Cy

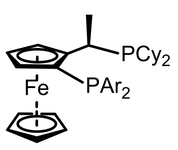


(*R*, *SP*)-Josiphos-**L16** — **52% yield, 16% ee**

(*R*, *SP*)-Josiphos-**L17** — **64% yield, 47% ee**

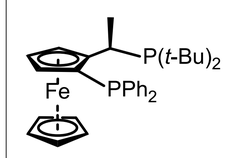


(*R*, *SP*)-Josiphos-**L18** Ar = 3,5-$(CF_3)_2$-C_6H_3 — **80% yield, 29% ee**

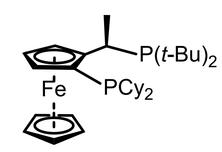


(*R*, *SP*)-Josiphos-**L19** Ar = 3,5-Me_2-4-OMe-C_6H_2 — **54% yield, 3% ee**

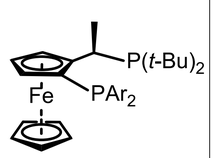
R'' = *t*-Bu



(*R*, *SP*)-Josiphos-**L20** — **41% yield, 13% ee**

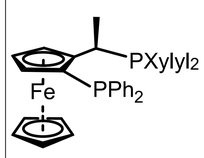


(*R*, *SP*)-Josiphos-**L21** — **77% yield, 11% ee**

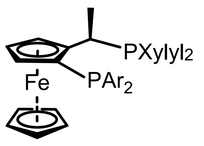


(*R*, *SP*)-Josiphos-**L22** Ar = 4-CF_3-C_6H_4 — **73% yield, 9% ee**

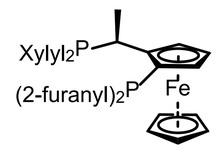
R'' = Xylyl



(*R*, *SP*)-Josiphos-**L23** — **33% yield, 70% ee**

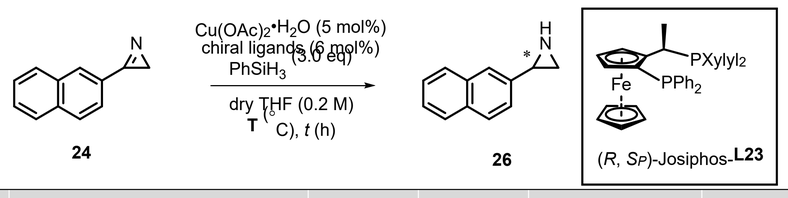


(*R*, *SP*)-Josiphos-**L24** Ar = 3,5-$(CF_3)_2$-C_6H_3 — **85% yield, 43% ee**



(*S*, *RP*)-Josiphos-**L25** — **61% yield, 32% ee**

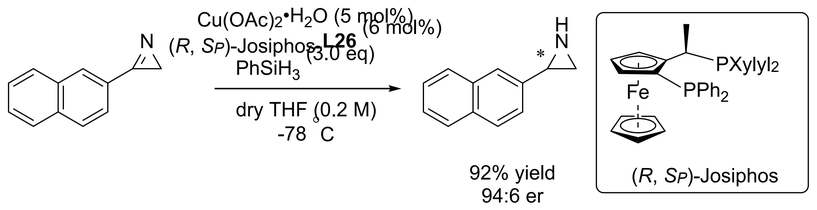
4. Effect of temperature



Entry[a]	Chiral Ligands	T (°C)	*t* (h)	Yield/%[b]	ee/%[c]
1	(*R*)-TolBINAP (**L3**)	rt	2.0	87	53
2	(*R*)-TolBINAP (**L3**)	-40	5.0	92	66
3	(*R*, S_P)-Josiphos-**L23**	rt	2.0	33	70
4	(*R*, S_P)-Josiphos-**L23**	-40	5.0	91	81
5	**(*R*, S_P)-Josiphos-L23**	**-78**	**6.0**	**92**	**88**

5. Conclusions

The investigation of reductions of *2H*-azirines mainly involves the effect of different reductive silanes, nonracemic ligands, and temperatures. Finally, the aziridine could be obtained in 92% yield and 94:6 er.



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