

Gold-Catalyzed [3+3] Cycloaddition Reaction

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Checker: Chang-Bin Yu

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Zhang, J. *et al. Angew. Chem. Int. Ed.* **2014**, 53, 4350.

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作者简介

1997年本科毕业于天津大学化学系应用化学专业；

2002年取得有机化学博士学位，师从麻生明院士；

2002-2003年，在中科院上海有机所以临时工作人员身份工作一年；

2003年10月赴德国科隆大学化学系从事博士后研究，洪堡学者奖学金获得者；

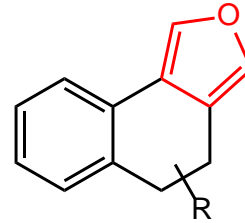
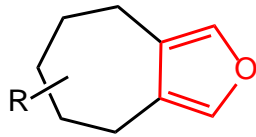
2005年赴美国芝加哥大学化学系从事博士后研究；

2006年12月加入华东师范大学化学系工作。

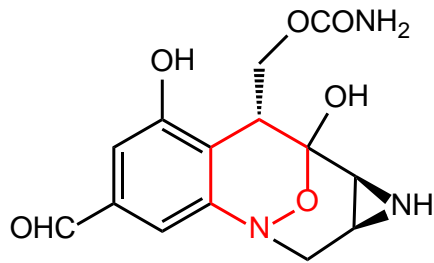


张俊良教授
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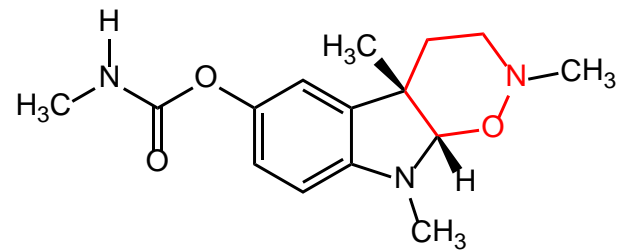
Introduction



3,4-fused bicyclic furans

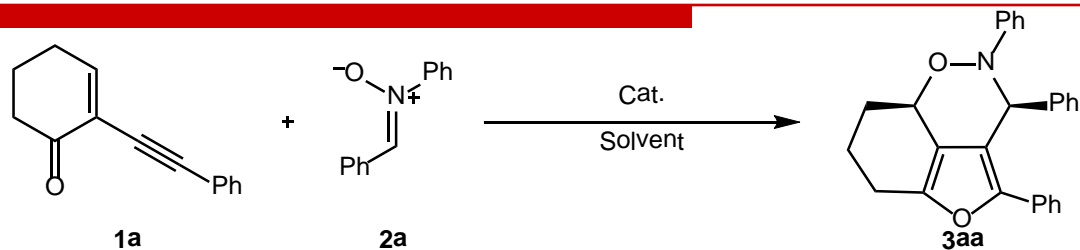


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Geneserine

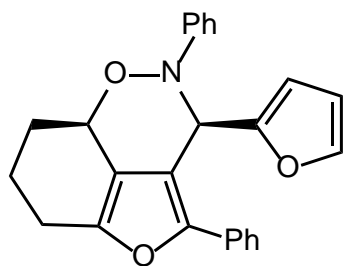
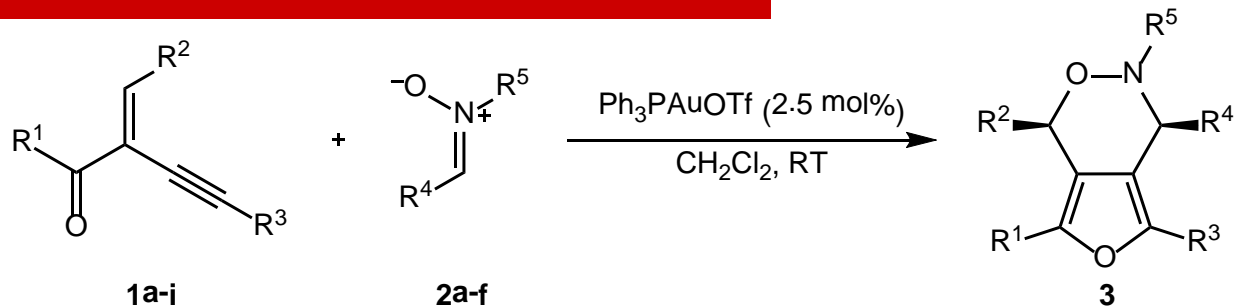
Gold(I)-Catalyzed [3+3] Cycloaddition Reaction



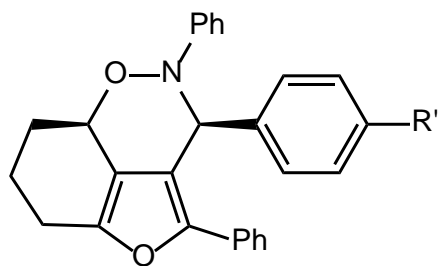
Entry	Cat. (5 mol%)	Solvent	T (°C)	Time (h)	Yield [%]
1	Sc(OTf) ₃	CH ₂ Cl ₂	40	30	trace
2	Sn(OTf) ₂	CH ₂ Cl ₂	40	30	trace
3	Cu(OTf) ₂	CH ₂ Cl ₂	40	30	trace
4	Yb(OTf) ₃	CH ₂ Cl ₂	40	30	trace
5	Y(OTf) ₃	CH ₂ Cl ₂	40	26	trace
6	In(OTf) ₃	CH ₂ Cl ₂	40	26	trace
7	Ni(ClO ₄) ₂ ·6H ₂ O	CH ₂ Cl ₂	40	30	trace
8	AgOTf	CH ₂ Cl ₂	rt	20 min	80
9	Ph ₃ PAuCl	CH ₂ Cl ₂	rt	72	0
10^a	Ph₃PAuCl/AgOTf	CH₂Cl₂	rt	20 min	93
11 ^a	Ph ₃ PAuCl/AgOTf	DCE	rt	20 min	92
12 ^a	Ph ₃ PAuCl/AgOTf	MeCN	rt	30 min	84
13 ^a	Ph ₃ PAuCl/AgOTf	THF	rt	15	9
14 ^a	Ph ₃ PAuCl/AgOTf	PhMe	rt	30	55
15	AuCl ₃	CH ₂ Cl ₂	rt	30 min	76

^a 2.5 mol% catalyst was used

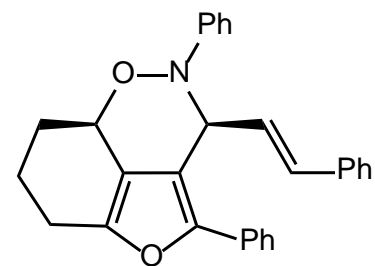
Zhang, J. *et al. Angew Chem. Int. Ed.* **2009**, *48*, 5505.



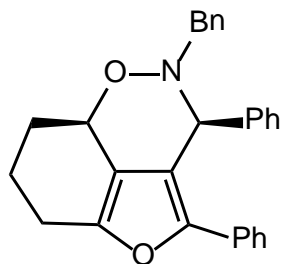
3ab 91%, 97:3



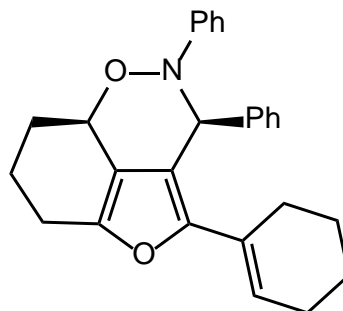
$\text{R}' = \text{NO}_2$ **3ac** 77%, 99:1
 $\text{R}' = \text{OMe}$ **3ad** 95%, >99:1



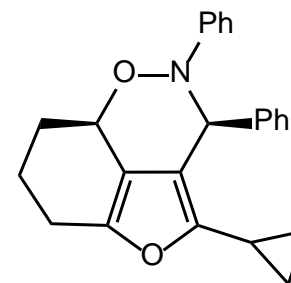
3ae 88%, 99:1



3af 53%, 93:7

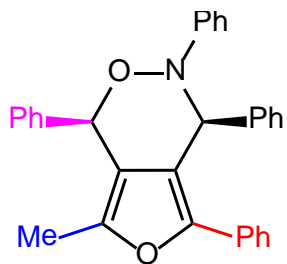


3ba 90%, 98:2

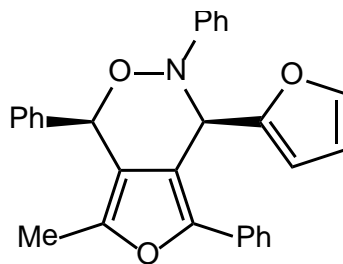


3ca 85%, >99:1

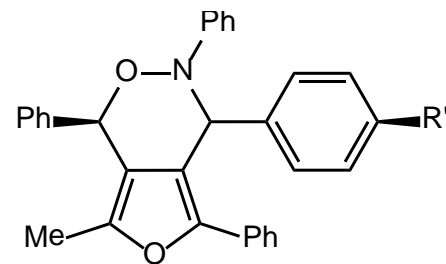
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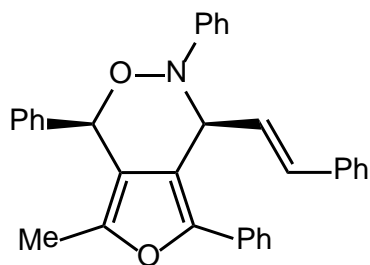
3da 98%, >99:1



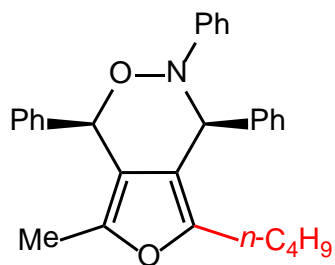
3db 88%, 98:2



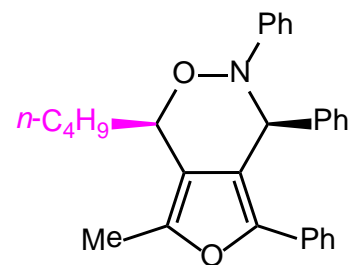
R' = NO₂ **3dc** 80%, 97:3
R' = OMe **3dd** 80%, 98:2



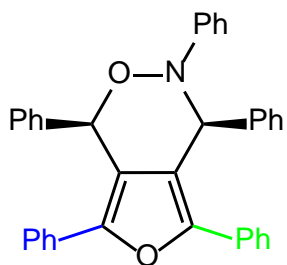
3de 79%, 97:3



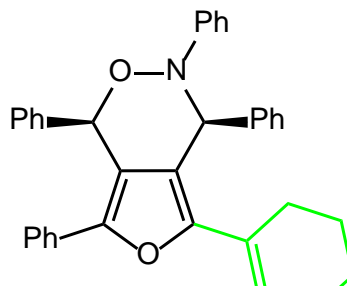
3ea 94%, >99:1



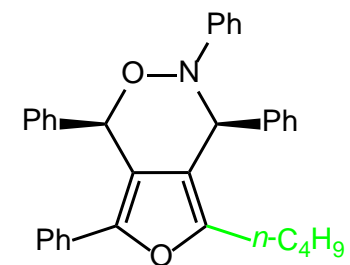
3fa 87%, 90:10



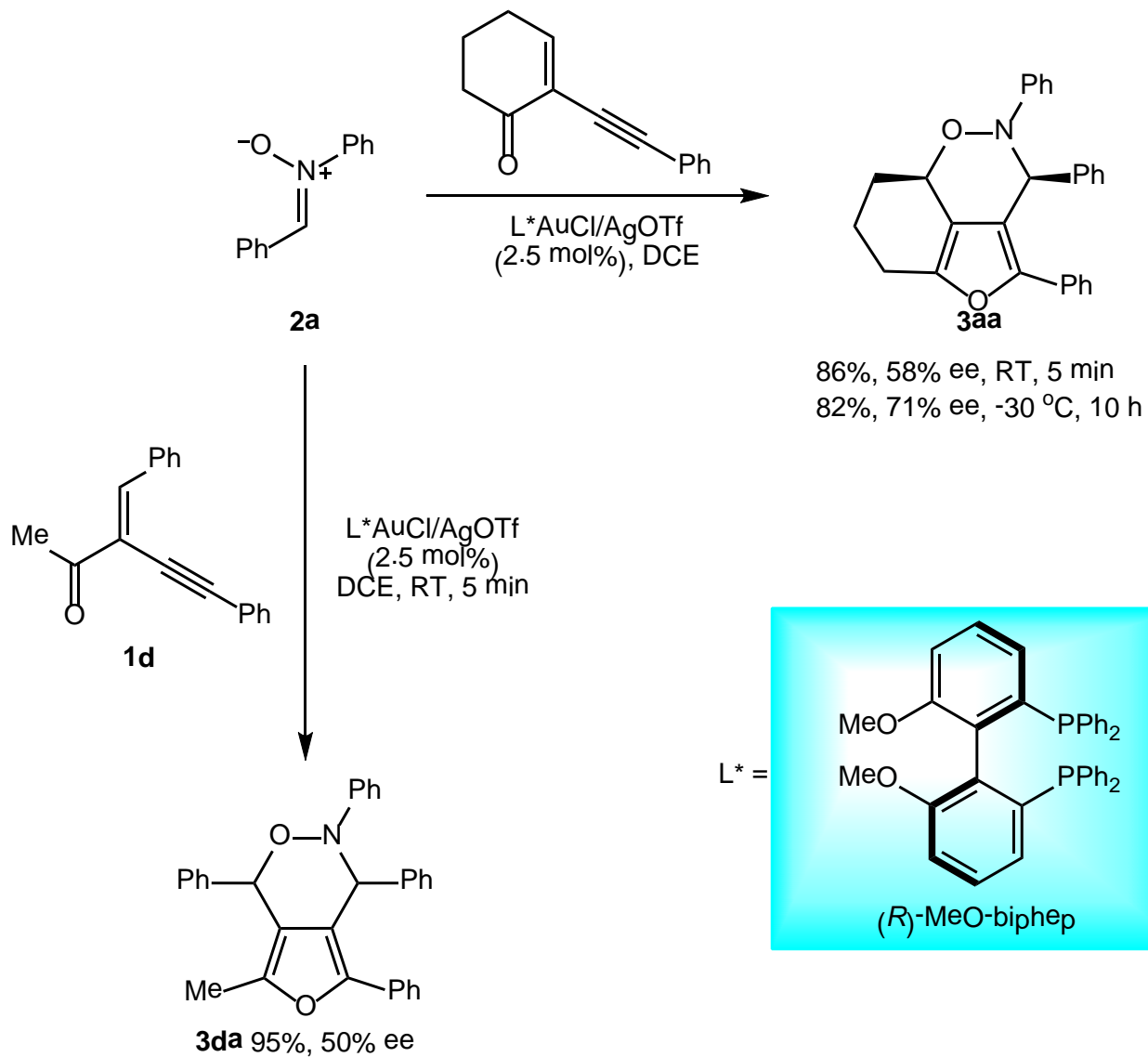
3ga 86%, 87:13

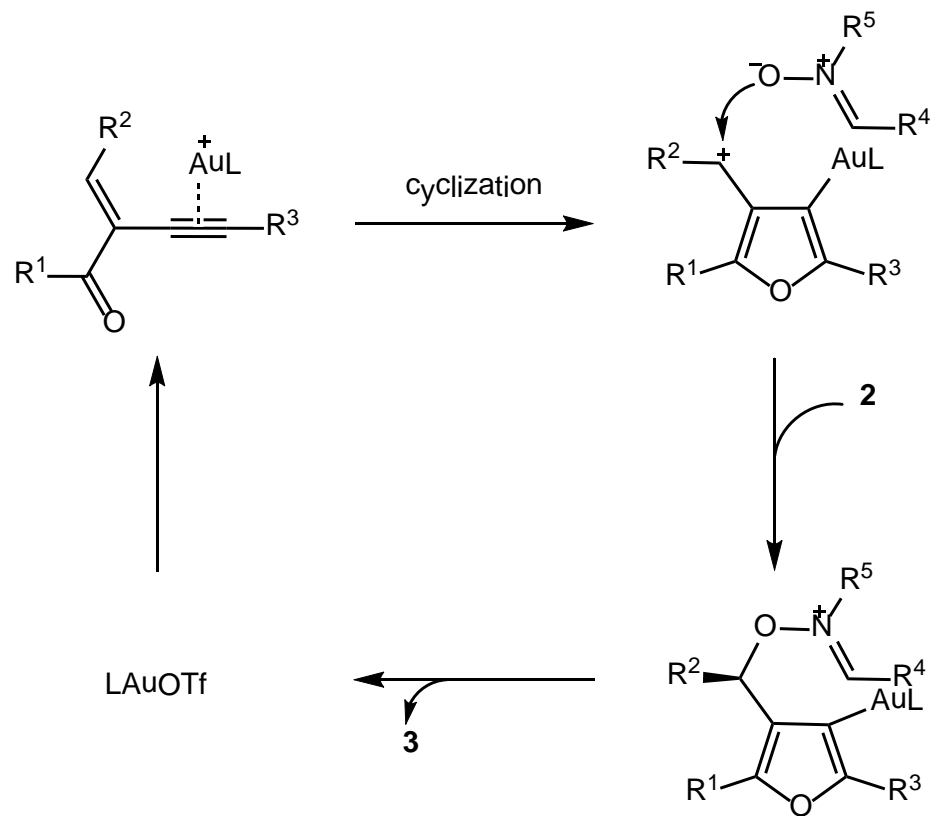


3ha 80%, 85:15

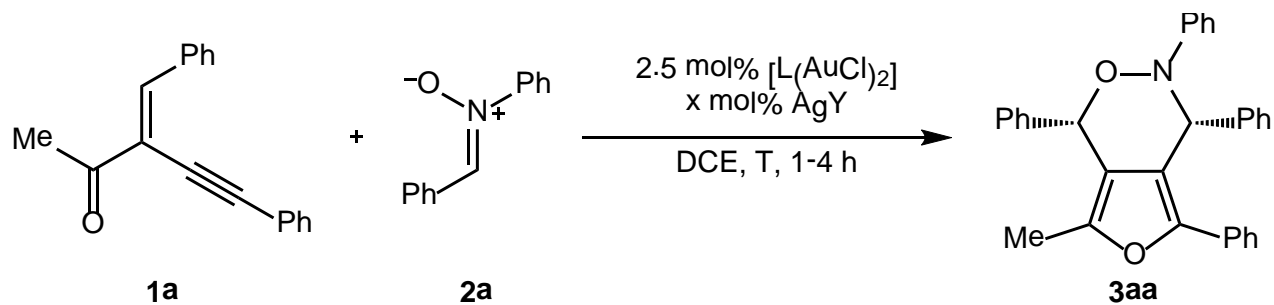


3ia 82%, 86:14

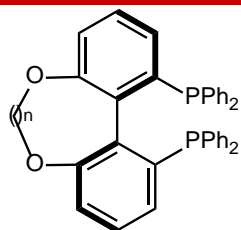




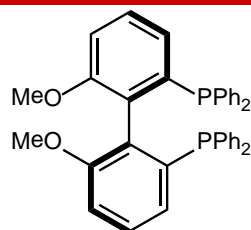
Enantioselective Gold(I)-Catalyzed [3+3] Cycloaddition Reaction



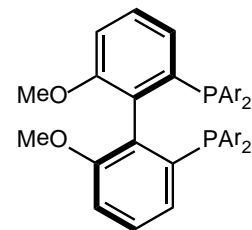
Zhang, J. *et al. Angew. Chem. Int. Ed.* **2010**, 49, 6669.



(*R*)-C_{*n*}-tunePhos
n = 1-3
L1



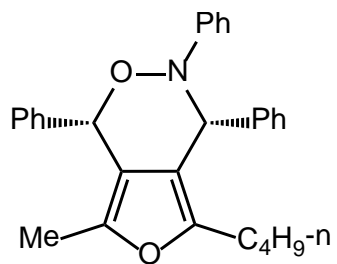
(*R*)-MeO-biphep



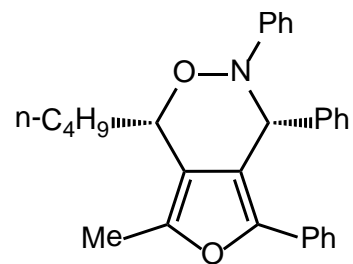
(*R*)-MeO-dtbm-biphep
Ar = 3,5-*t*-C₄H₉-4-MeOC₆H₂
L2

Entry	Ligand (L)	AgX (mol%)	T (°C)	Yield [%] ee (%)
1	(<i>R</i>)-MeO-biphep	AgOTf (2.5)	-10	95 (56)
2	(<i>R</i>)-C ₁ -tunePhos (L1)	AgOTf (5)	-10	94 (76)
3	L1	AgOTf (3.75)	-10	99 (89)
4	L1	AgOTf (2.5)	-10	97 (95)
5	L1	AgOTf (2.5)	-20	95 (94)
6 ^a	L1	AgOTf (2.5)	-10	81 (96)
7	L1	AgPF ₆ (2.5)	-10	92 (93)
8	L1	AgBF ₄ (2.5)	-10	91 (93)
9	L1	AgSbF ₆ (2.5)	-10	99 (94)
10	(<i>R</i>)-C ₂ -tunePhos	AgOTf (2.5)	-10	91 (81)
11	(<i>R</i>)-C ₃ -tunePhos	AgOTf (2.5)	-10	94 (88)
12	L2	AgOTf (2.5)	0	94 (99)
13	(<i>S</i>)-binap	AgOTf (2.5)	-10	99 (29)
14	(<i>R</i>)-toly-binap	AgOTf (2.5)	-10	99 (-38)

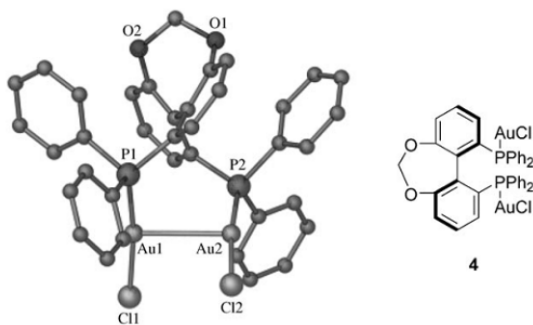
^a CHCl₃ was used as solvent.



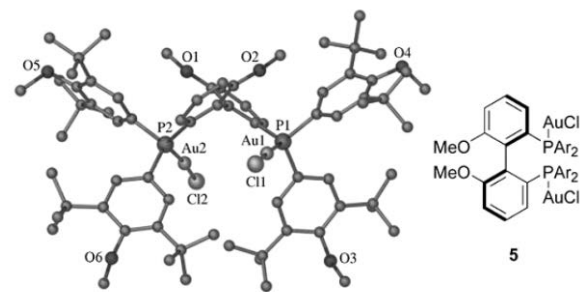
3aa L1 77%, 55% ee
L2 59%, 32% ee



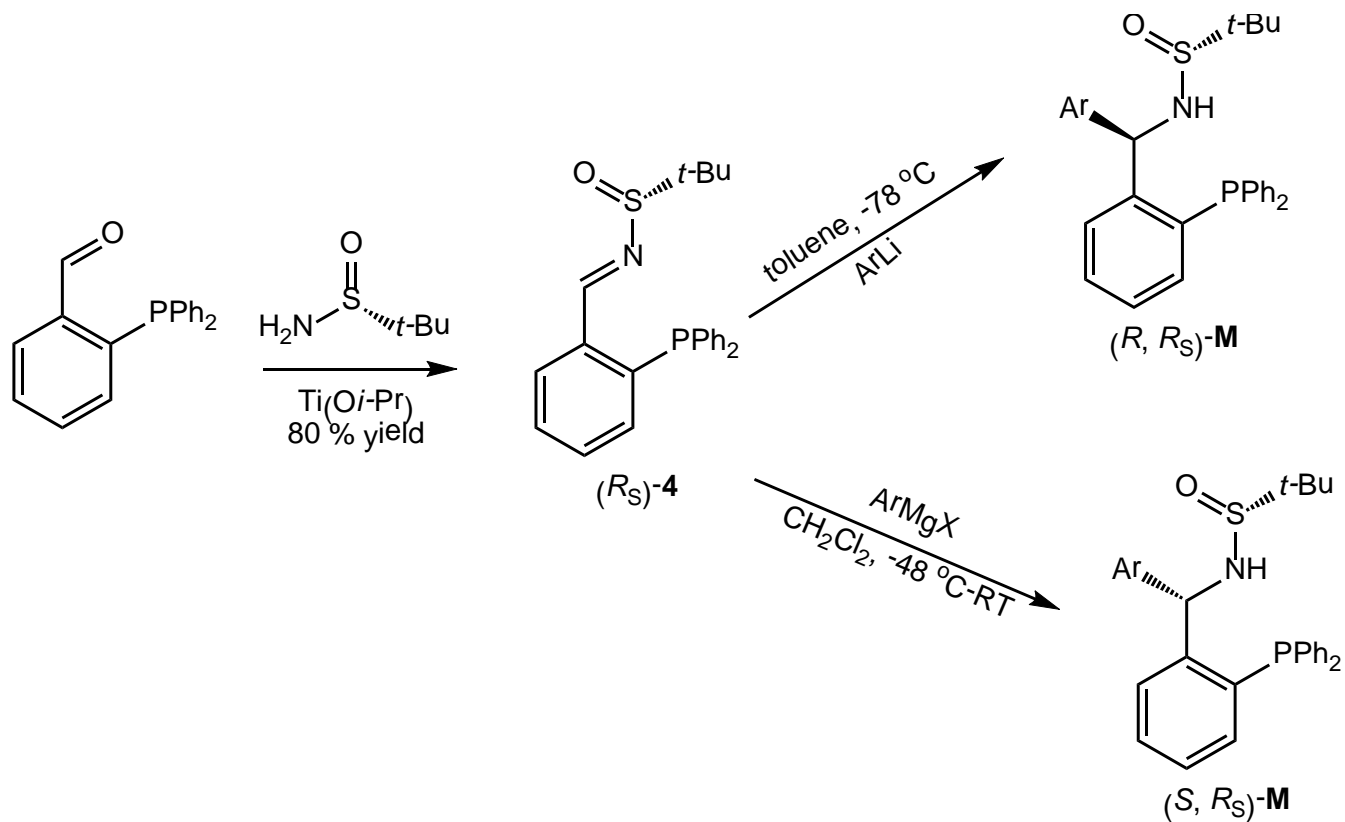
3ab L1 92%, 75% ee
L2 84%, 64% ee



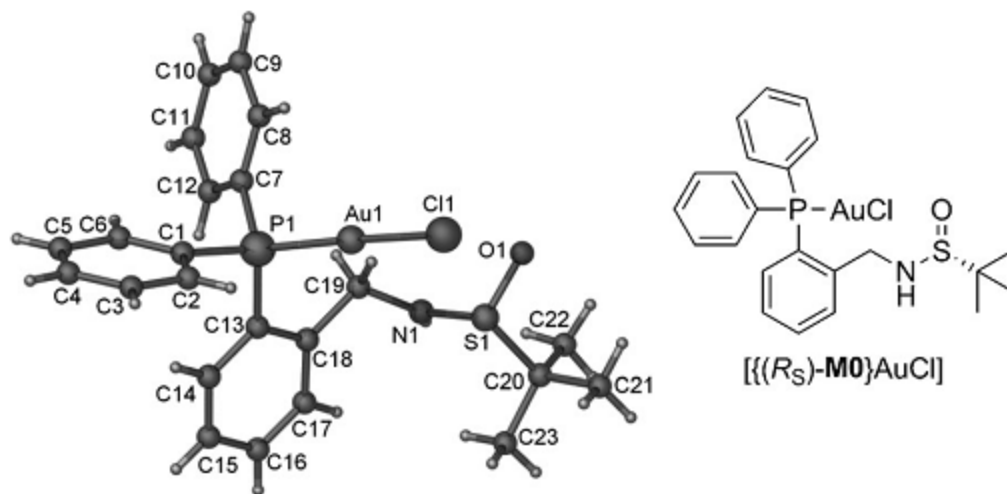
Au1-Au2 = 2.944 Å

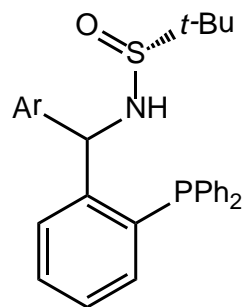
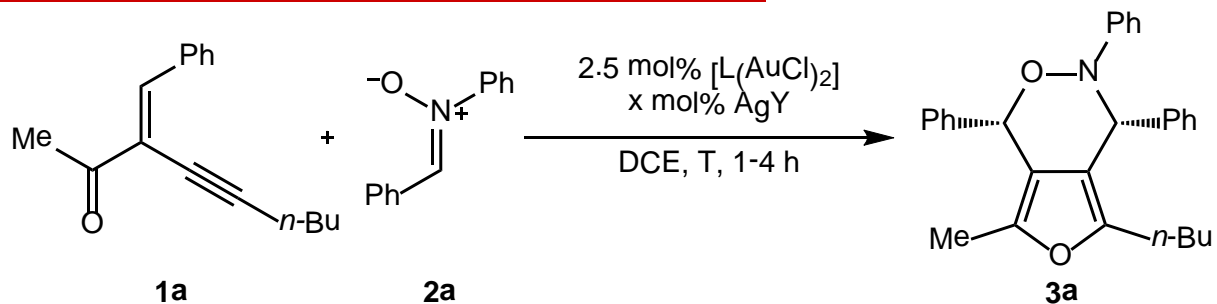


Au1-Au2 = 5.316 Å



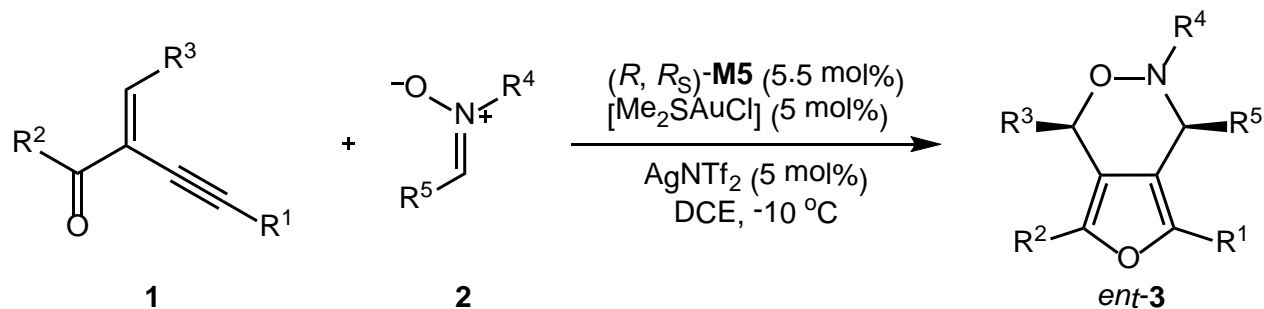
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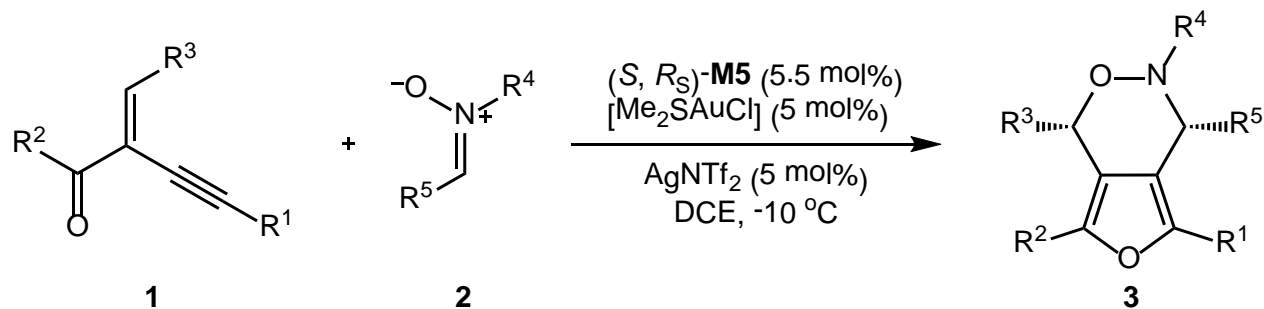


- M1** Ar = Ph
M2 Ar = 4-EtOC₆H₄
M3 Ar = 4-MeOC₆H₄
M4 Ar = 3,5-(*t*-Bu)₂-4-MeOC₆H₂
M5 Ar = 1-naphthyl

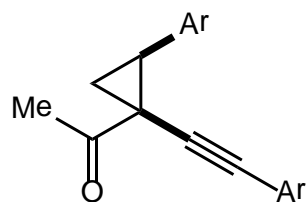
Entry	Ligand	ee of <i>ent</i> - 3a (%)	Entry	Ligand	ee of 3a (%)
1	(<i>R</i> , <i>R</i> _S)- M1	83	6	(<i>S</i> , <i>R</i> _S)- M1	89
2	(<i>R</i> , <i>R</i> _S)- M2	80	7	(<i>S</i> , <i>R</i> _S)- M2	91
3	(<i>R</i> , <i>R</i> _S)- M3	92	8	(<i>S</i> , <i>R</i> _S)- M3	73
4	(<i>R</i> , <i>R</i> _S)- M4	95	9	(<i>S</i> , <i>R</i> _S)- M4	93
5	(<i>R</i> , <i>R</i> _S)- M5	96	10	(<i>S</i> , <i>R</i> _S)- M5	94



Entry	R ¹ , R ² , R ³ (1)	R ⁴ , R ⁵ (2)	<i>ent</i> - 3	Yield (%)	ee (%)
1	<i>n</i> -Bu, Me, Ph (1a)	Ph, Ph (2a)	3a	92	96
2	1a	4-MeC ₆ H ₄ , Ph (2b)	3b	92	95
3	1a	Ph, 3,4,5-(MeO) ₃ C ₆ H ₂ (2c)	3c	85	97
4	1a	Ph, 4-MeOC ₆ H ₄ (2d)	3d	96	98
5	1a	3-ClC ₆ H ₄ , 4-MeOC ₆ H ₄ (2e)	3e	87	96
6	1a	Ph, styryl (2f)	3f	85	93
7	Cl(CH ₂) ₃ , Me, Ph (1b)	2a	3g	99	94
8	AcO(CH ₂) ₂ , Me, Ph (1c)	2a	3h	92	96
9	<i>n</i> -Pr, Me, Ph (1d)	2a	3i	85	95
10	<i>n</i> -Bu, Ph, 4-CH ₃ OC ₆ H ₄ (1e)	2a	3j	92	97
11	<i>n</i> -Bu, Me, 4-CH ₃ C ₆ H ₄ (1f)	2a	3k	94	92

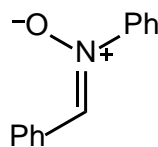


Entry	R ¹ , R ² , R ³ (1)	R ⁴ , R ⁵ (2)	3	Yield (%)	ee (%)
1	<i>n</i> -Bu, Me, Ph (1a)	Ph, Ph (2a)	3a	86	94
2	1a	4-MeC ₆ H ₄ , Ph (2b)	3b	85	97
3	1a	Ph, 3,4,5-(MeO) ₃ C ₆ H ₂ (2c)	3c	90	99
4	1a	Ph, 4-MeOC ₆ H ₄ (2d)	3d	91	93
5	1a	3-ClC ₆ H ₄ , 4-MeOC ₆ H ₄ (2e)	3e	88	98
6	1a	Ph, styryl (2f)	3f	86	95
7	Cl(CH ₂) ₃ , Me, Ph (1b)	2a	3g	99	99
8	AcO(CH ₂) ₂ , Me, Ph (1c)	2a	3h	95	99
9	<i>n</i> -Pr, Me, Ph (1d)	2a	3i	88	97
10	<i>n</i> -Bu, Ph, 4-CH ₃ OC ₆ H ₄ (1e)	2a	3j	99	97
11	<i>n</i> -Bu, Me, 4-CH ₃ C ₆ H ₄ (1f)	2a	3k	91	97

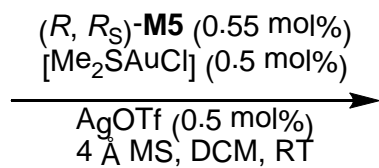


5

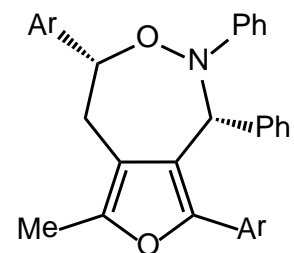
+



2a



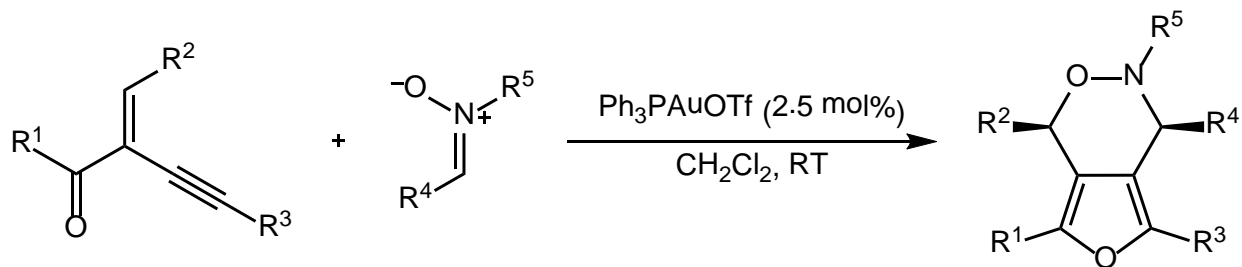
95% yield, 89% ee
with **L1**: 87% yield, 91% ee



6

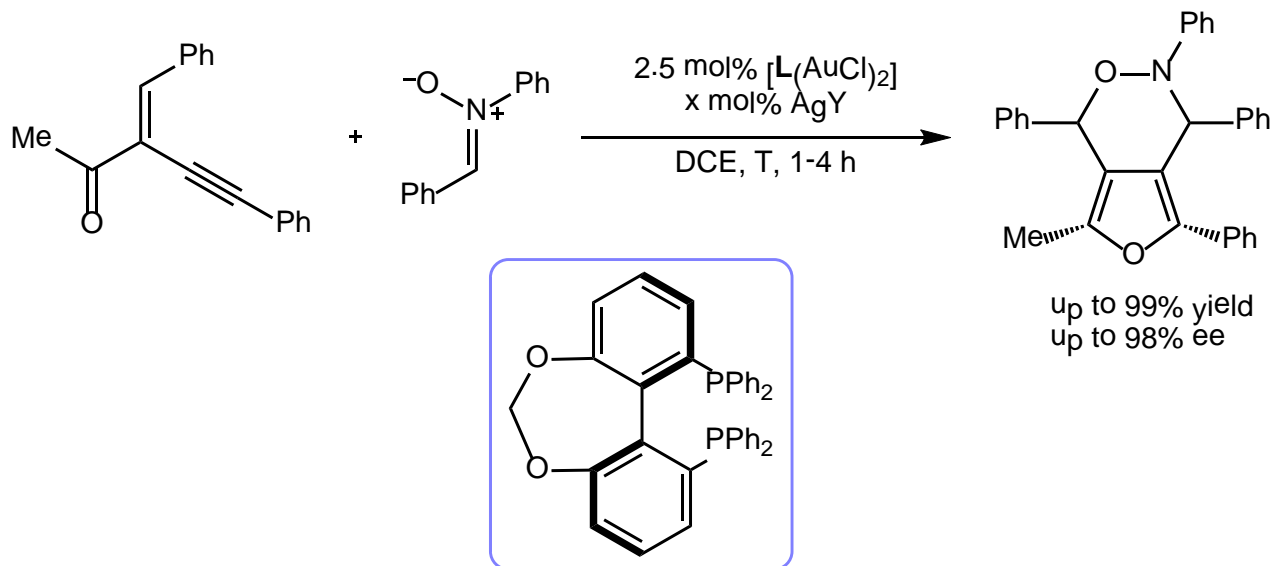
Summary

1.



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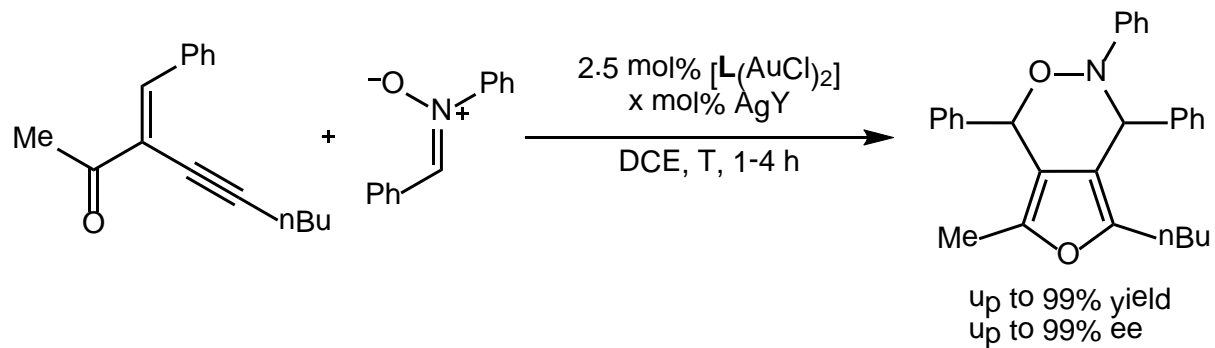
2.



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Summary

3.



M5 Ar = 1-naphthyl

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Gold complexes have shown their unrivalled power in organic synthesis over that past decade, which is due to their high capability to activate π bonds. However, the development of enantioselective gold-catalyzed processes poses considerable challenges, because gold(I) complexes strongly prefer a linear geometry, which forces the active reaction site to be far away from the chiral ligand, thus limiting its capability to transfer chirality. To date, only a few approaches have been developed that address these issues; these methods employ chiral atropisomeric biaryl phosphines or spirocyclic bisphosphines, phosphoramidites that often bear bulky or extended substituents, or helically chiral trivalent phosphines as ligands and chiral phosphoric acid derivatives as counterions.

The atropisomeric biaryl bisphosphines are among the most successful ligands in enantioselective gold(I) catalysis. However, these elaborate biaryl bisphosphine ligands are difficult to modify and can be more expensive than the noble metal itself; therefore, alternative principles for the design of new chiral ligands are highly desirable.

In summary, we have developed a new type of chiral sulfinamide monophosphine ligands, the so-called Ming-Phos ligands. Two sets of diastereomeric Ming-Phos ligands could be obtained in good yields with high diastereoselectivity from commercially available, inexpensive starting materials. Wide structural diversity can be achieved by changing the organometallic reagents. Moreover, Ming-Phos ligands performed well in two mechanistically distinct gold-catalyzed cycloaddition reactions. For the asymmetric cycloaddition reaction of 2-(1-alkynyl)-alk-2-en-1-ones with nitrones, both enantiomers could be furnished in high yields with excellent diastereo- and enantioselectivity by the employment of (*R*, *R*_S)-**M5** and (*S*, *R*_S)-**M5**, respectively.

The salient features of these new chiral ligands, including their simple structure, air stability, the practical preparation from readily available starting materials, easy modification, and good results in enantioselective transformations, render these ligands very attractive. Further studies, such as an investigation of the performance of these ligands in other metal-catalyzed asymmetric reactions, are underway in our laboratory and will be reported in due course.