A SYN-SELECTIVE AZA-ALDOL REACTION OF BORON AZA-ENOLATES GENERATED FROM N-SULFONYL-1,2,-3-TRIAZOLES AND 9-BBN-H

Tomoya Miura, Takayuki Nakamuro, Sho Miyakawa, Mashiro Murakami

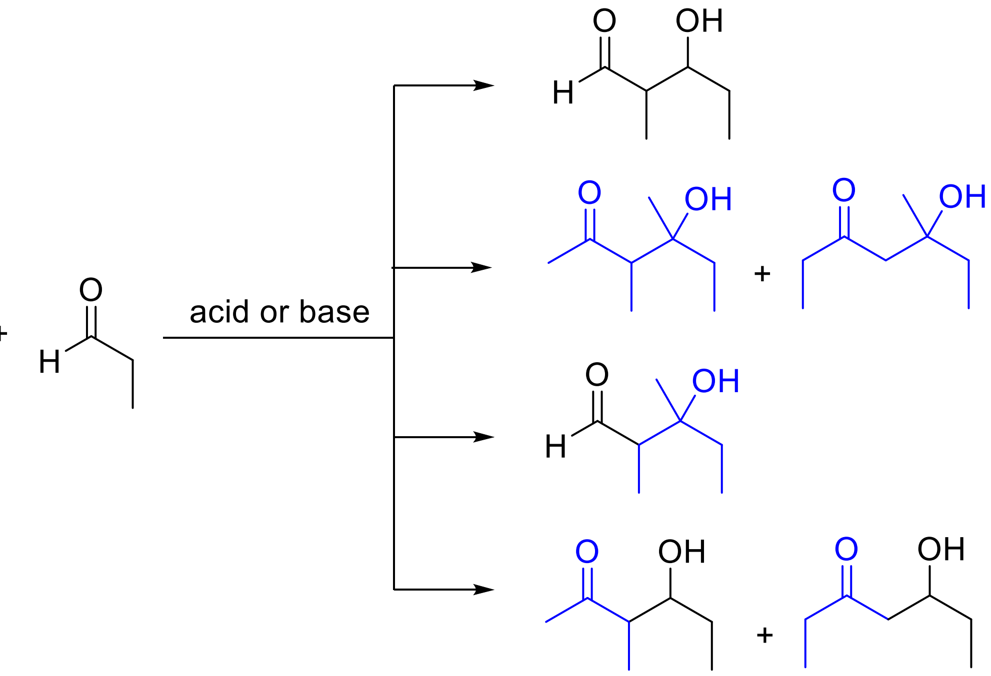
Angew. Chem. Int. Ed., **2016**, 55, *early view*

Serene Tai

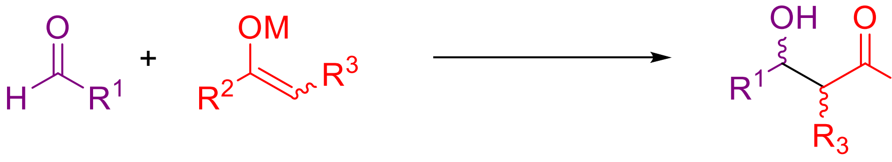
Current Literature 6/18/2016

OL REACTIONS

assical aldol addition



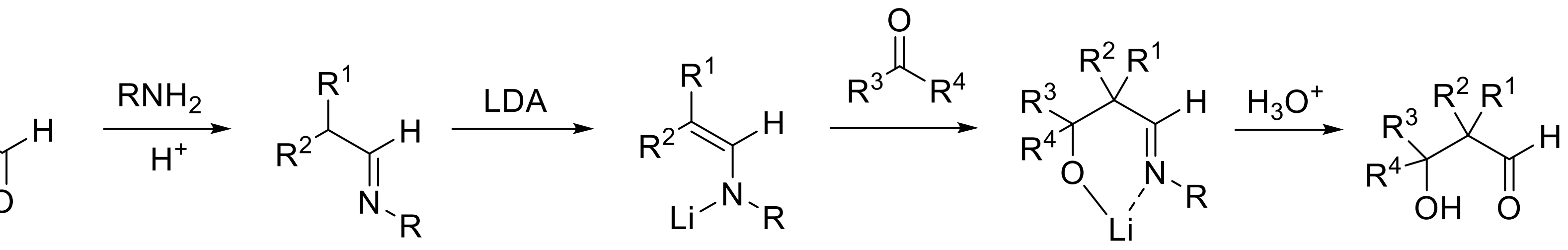
Directed aldol addition



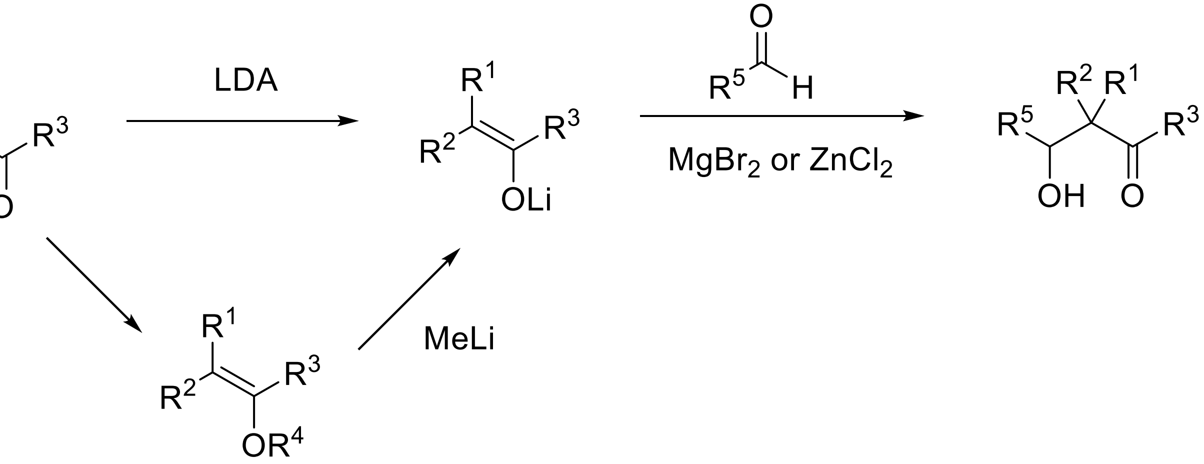
M = Li, B, Ti, Si, Al, Mg, Zn, Zr...

ECTED CROSS-ALDOL REACTION

hium enamide-aldol reaction (Wittig 1963)



hium enolate-aldol reaction (House 1973)



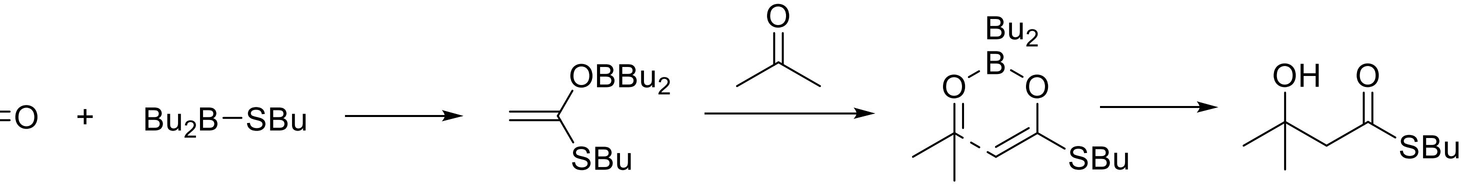
R^4 = $SiMe_3$ or $COCH_3$

Angew. Chem. Int. Ed. Engl. **1963**, *2*, 683-684

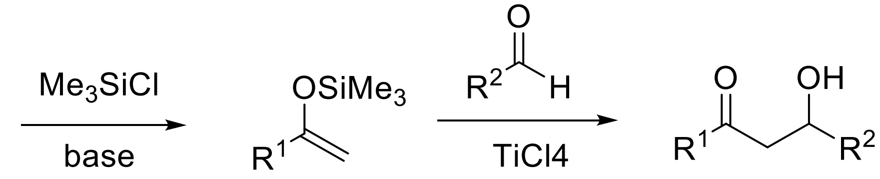
J. Am. Chem. Soc. **1973**, *95*, 3310-3324

KAIYAMA ALDOL REACTION (1973)

ron enolate-aldol reaction



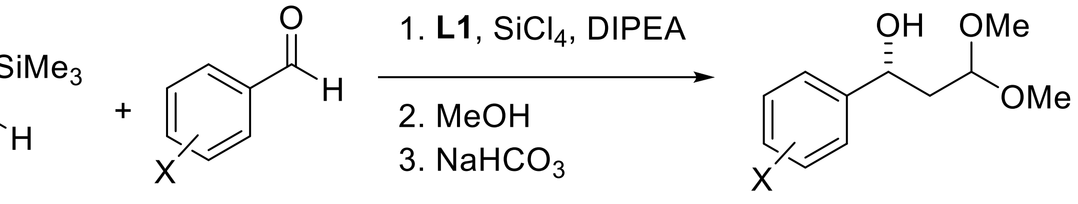
yl enol ether-aldol reaction

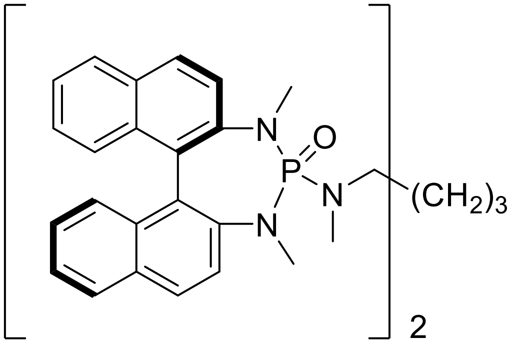


J. Am. Chem. Soc. **1973**, *95*, 967-968
Chem. Lett. **1973**, 1011-1014; **1974**, 15; **1975**, 98

DEHYDE-ALDEHYDE ALDOL REACTION

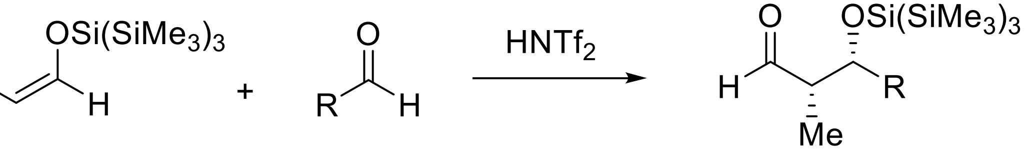
wis base catalyzed





L1

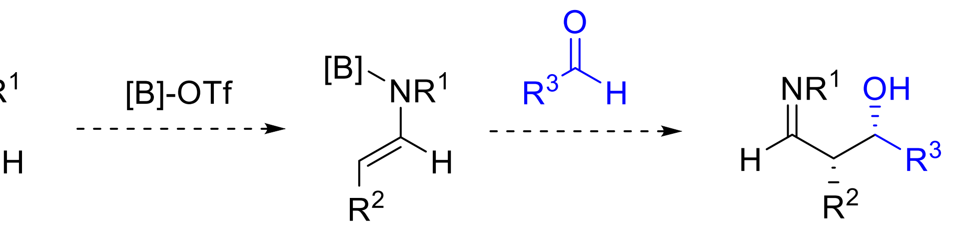
wis acid catalyzed



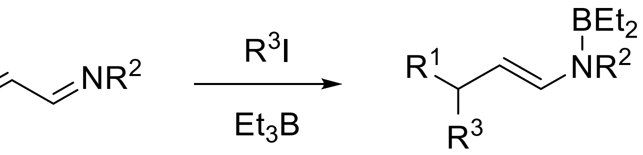
syn/anti = 80:20 to >95:5

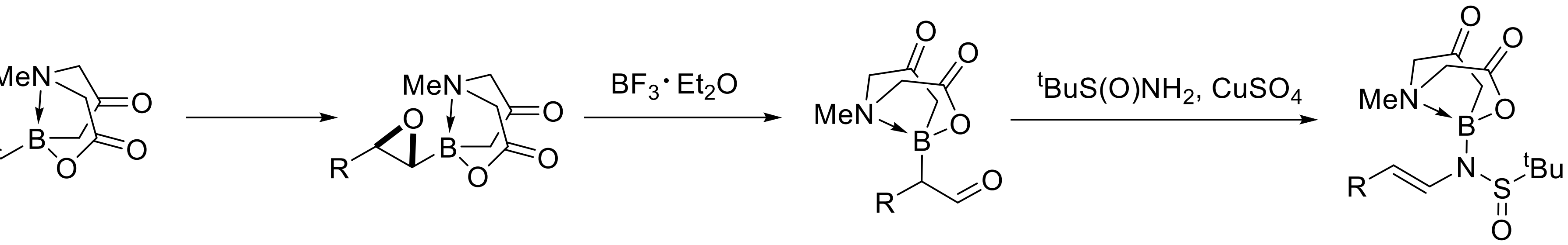
J. Org. Chem. **2005**, *70*, 10190-10193
J. Am. Chem. Soc. **2006**, *128*, 48-49

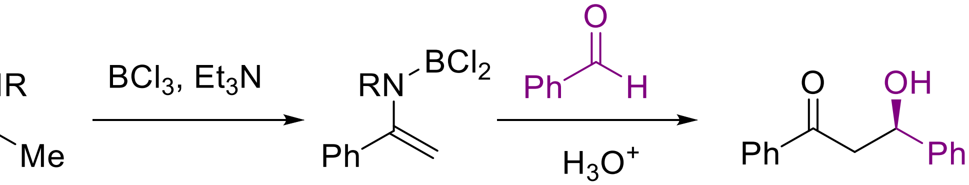
RON AZA-ENOLATES



- **Aldimines derived enolate**



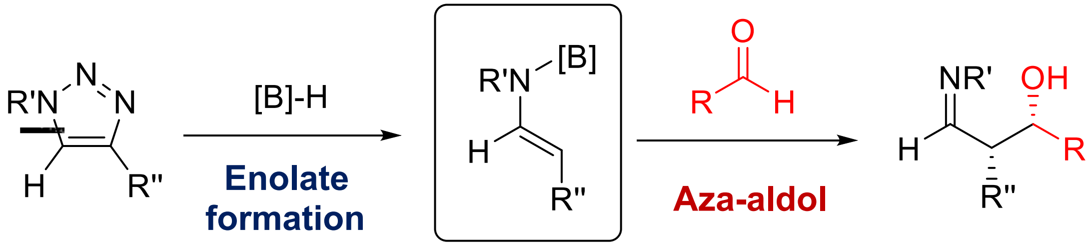




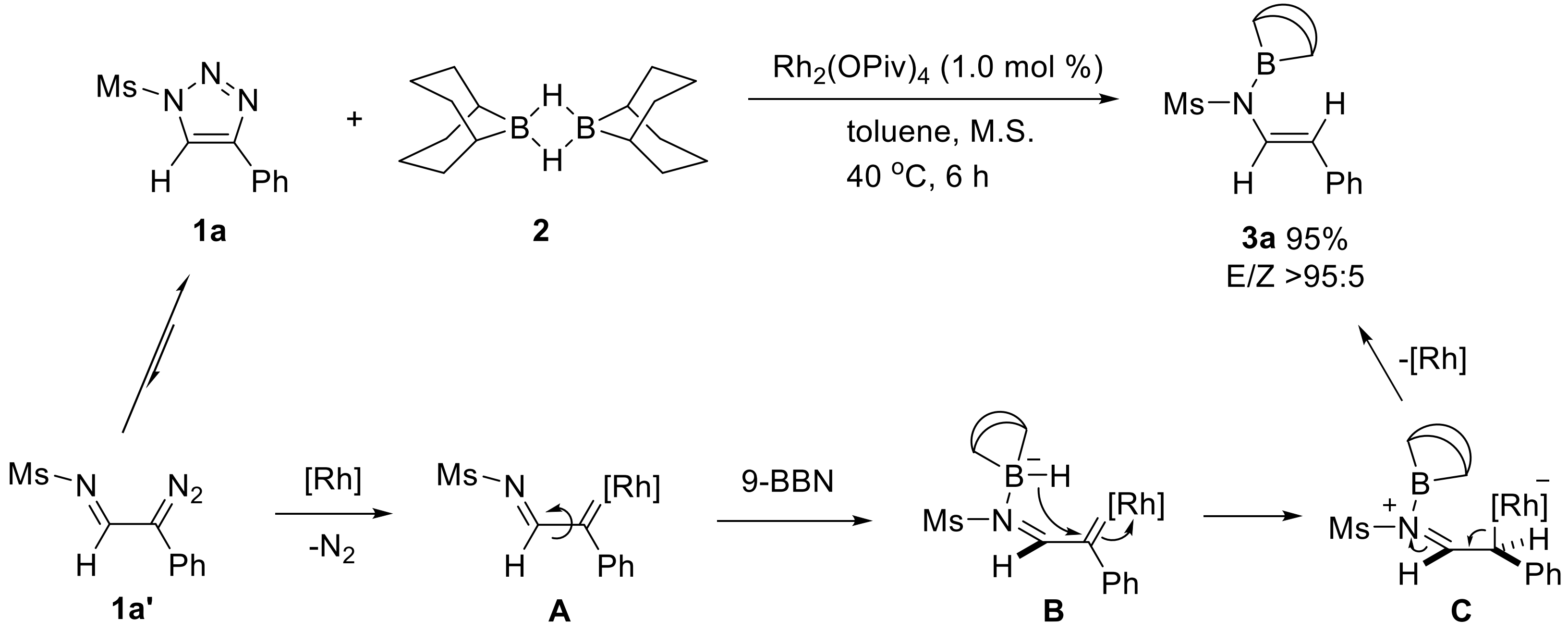
- **Ketimines derived enolate**

Org Lett. **2009**, *11*, 4632; J. Am. Chem. Soc. **2011**, *133*, 1377
Tetrahedron. Lett. **1979**, *20*, 1423

IS WORK –

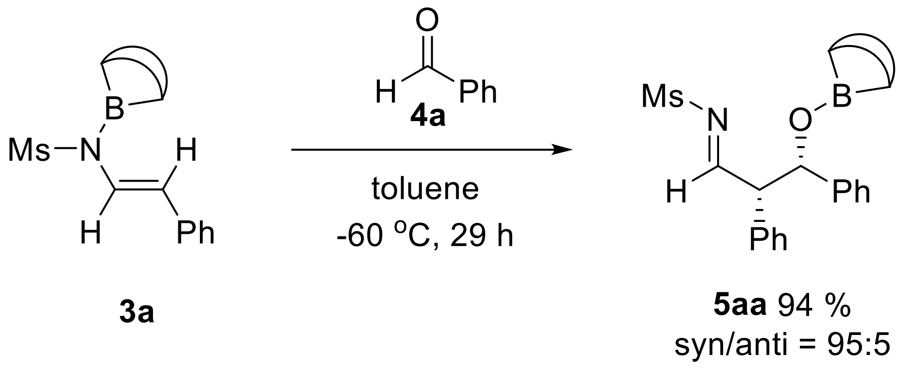


Step 1: Boron aza-enolate formation



J. Am. Soc. Chem. **2012**, *134*, 14670; **2013**, *135*, 1207

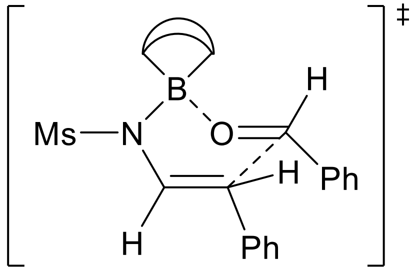
tep 2: Aza-aldol reaction



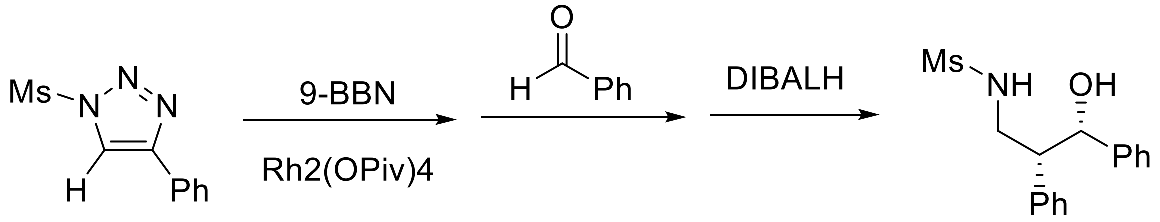
3a

5aa 94 %
syn/anti = 95:5

via:



ne-pot sequence

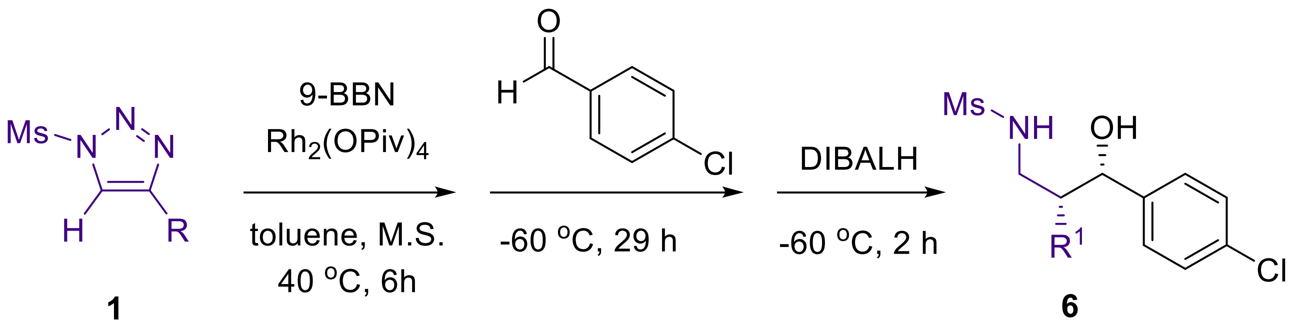


1a

6aa 77%
syn/anti >95:5

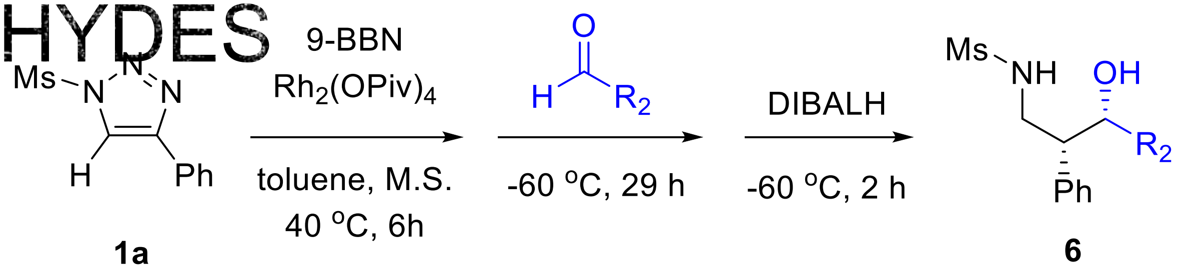
Tetrahedron. **1995,** *51*, 485

OPE OF TRIAZOLES



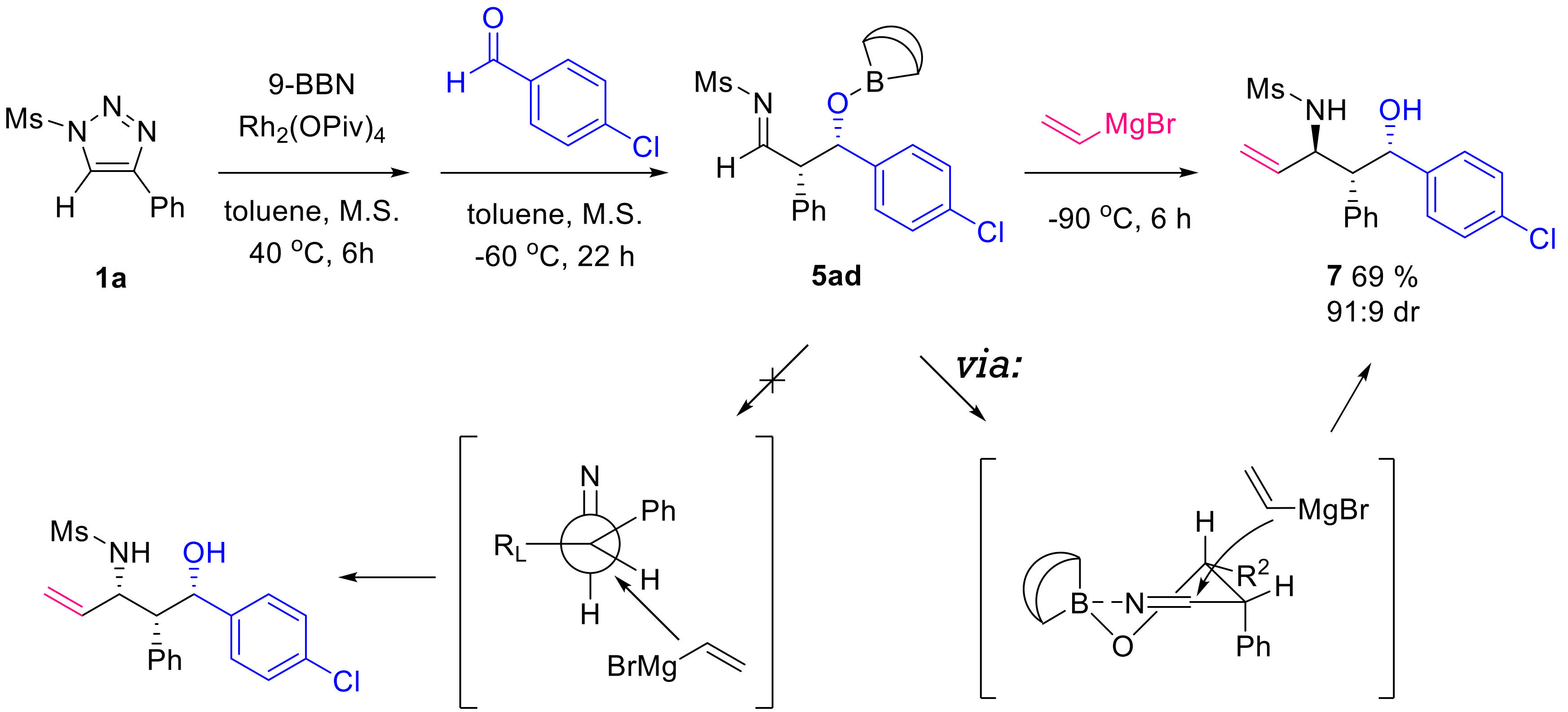
Entry	**1**	R^1	**6**	Yield [%][b]	*syn/anti*[c]
1	**1b**	*p*-MeC_6H_4	**6bd**	60[d]	>95:5
2	**1c**	*p*-$CF_3C_6H_4$	**6cd**	76[e]	92:8
3	**1d**	*p*-$MeOC_6H_4$	**6dd**	55	>95:5
4	**1e**	*p*-FC_6H_4	**6ed**	74[f]	>95:5
5	**1f**	*p*-IC_6H_4	**6fd**	76	>95:5
6	**1g**	*m*-MeC_6H_4	**6gd**	70	>95:5
7	**1h**	3-thienyl	**6hd**	69	>95:5

PE OF ALDEHYDES



Entry	**4**	R^2	**6**	Yield [%][b]	*syn/anti*[c]
1	**4b**	*p*-MeC_6H_4	**6ab**	80[d]	>95:5
2	**4c**	*p*-$NO_2C_6H_4$	**6ac** (X-ray)	67	94:6
3	**4d**	*p*-ClC_6H_4	**6ad**	76	>95:5
4	**4e**	*m*-MeC_6H_4	**6ae**	72	>95:5
5	**4f**	*m*-$MeOC_6H_4$	**6af**	79[e]	>95:5
6	**4g**	*o*-MeC_6H_4	**6ag**	80	>95:5
7	**4h**	2-furyl	**6ah**	76[d]	>95:5
8	**4i**	1-*tert*-butoxycarbonyl-3-indolyl	**6ai**	49	>95:5
9	**4j**	(*E*)-PhCH=CH	**6aj**	75[f]	93:7
10	**4k**	CH_3CH_2	**6ak**	75	89:11
11	**4l**	$PhCH_2CH_2$	**6al**	70[d]	>95:5
12	**4m**	$(CH_3)_2CHCH_2$	**6am**	65	>95:5
13	**4n**	$t\text{BuMe}_2\text{SiO}(CH_2)_3$	**6an**	67	95:5
14	**4o**	$HC{\equiv}C(CH_2)_4$	**6ao**	50[g]	>95:5
15	**4p**	cyclohexyl	**6ap**	74	>95:5

NERATION OF 3 CONTIGUOUS STEREOCENTERS



1a

5ad

7 69 %
91:9 dr

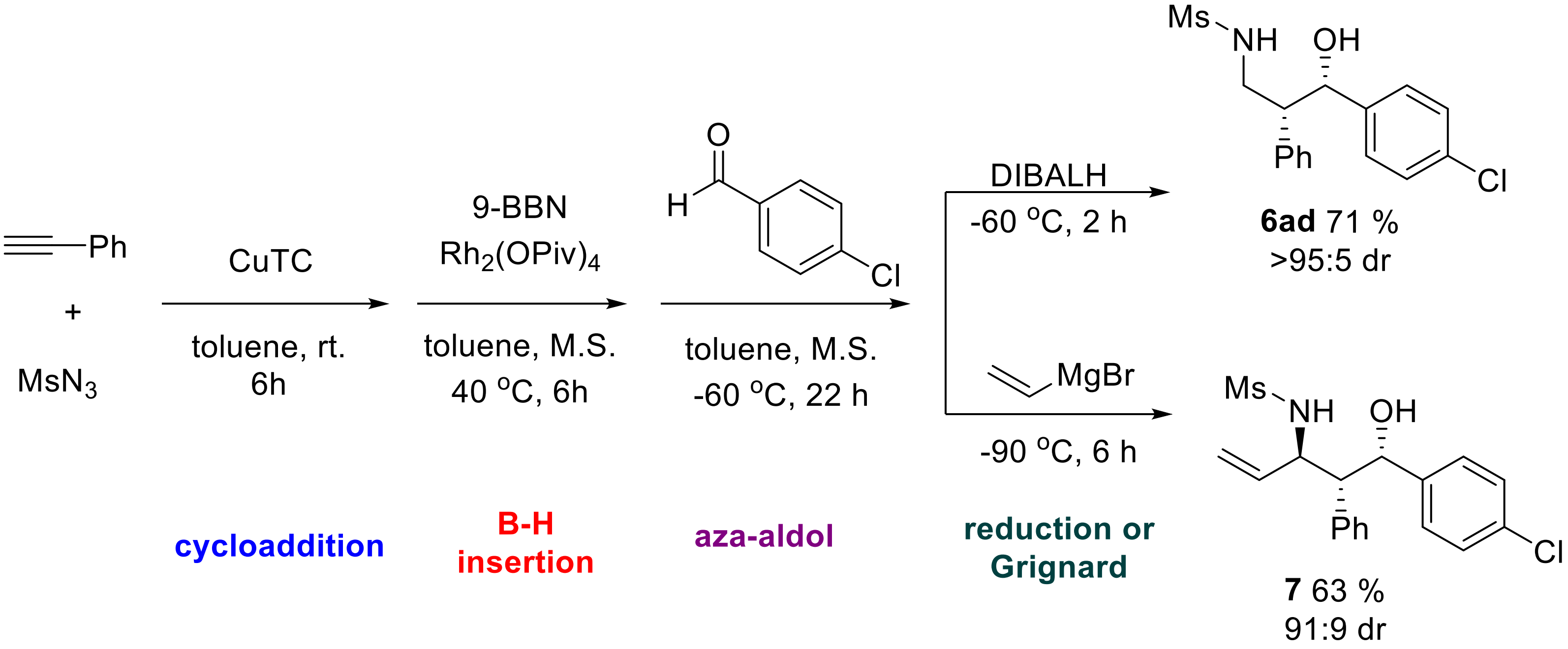
syn-syn

Felkin-Ahn Model

Chelation Model

Tetrahedron Lett. **1999,** *40*, 445

E-POT REACTION SEQUENCE



cycloaddition

B-H insertion

aza-aldol

reduction or Grignard

6ad 71 %
>95:5 dr

7 63 %
91:9 dr

NCLUSIONS

icient one-pot reaction sequence

ghly diastereoselective: (E)-enolate – syn product

roduction of contiguous stereocenters onto simple starting material – terminal alkynes

e reactions not observed