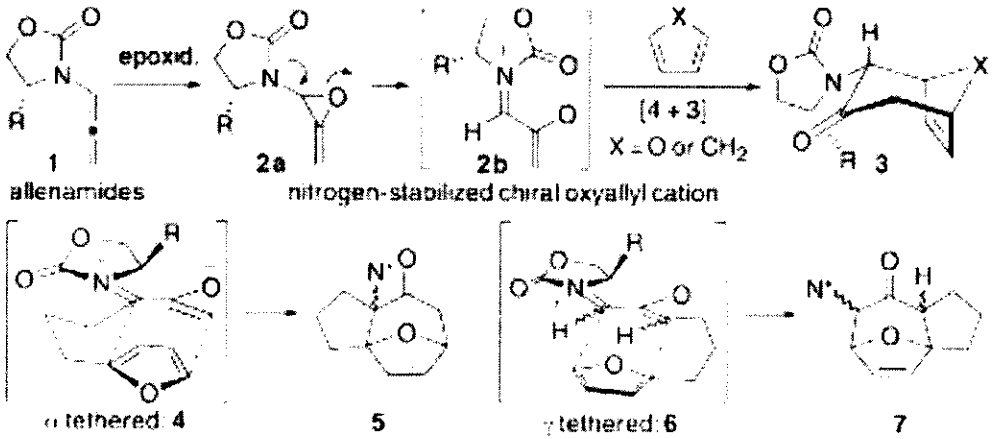
A Tandem Epoxidation/Stereoselective Intramolecular [4+3] Cycloaddition Reaction Involving Nitrogen-Stabilized Oxyallyl Cations Derived from Chiral Allenamides

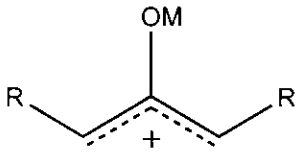
Challeppan Rameshkumar and Richard P. Hsung*



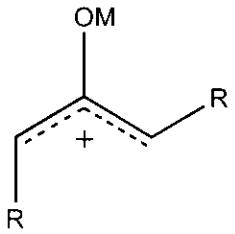
Angew. Chem. Int. Ed. Engl. **2004**, *43*, 615

Oxyallyl Cations

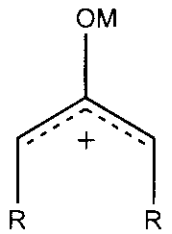
Conformation



W Conformation

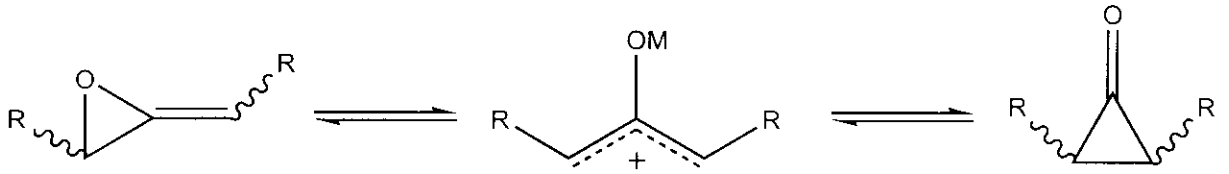


Sickle Form

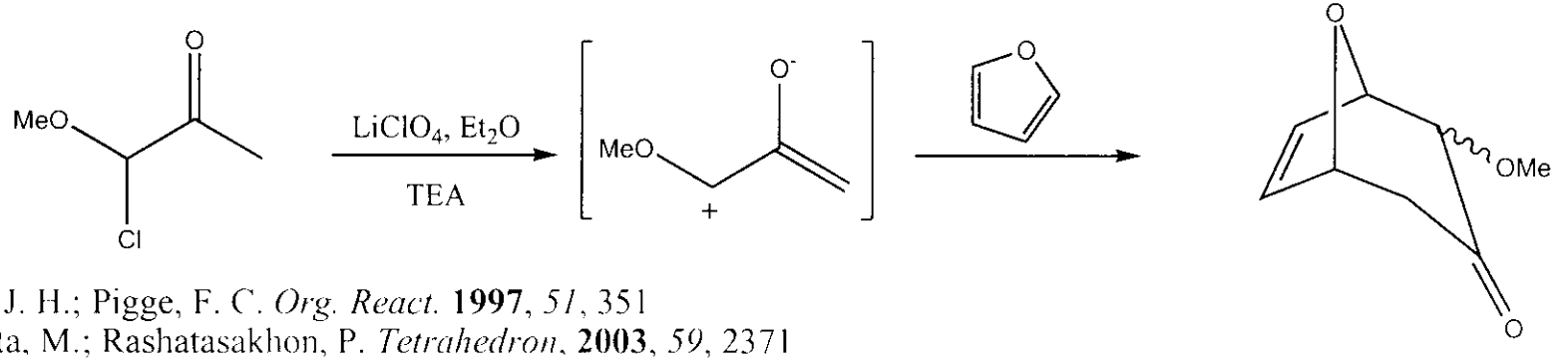


U Form

Equilibria Affecting Reactivity



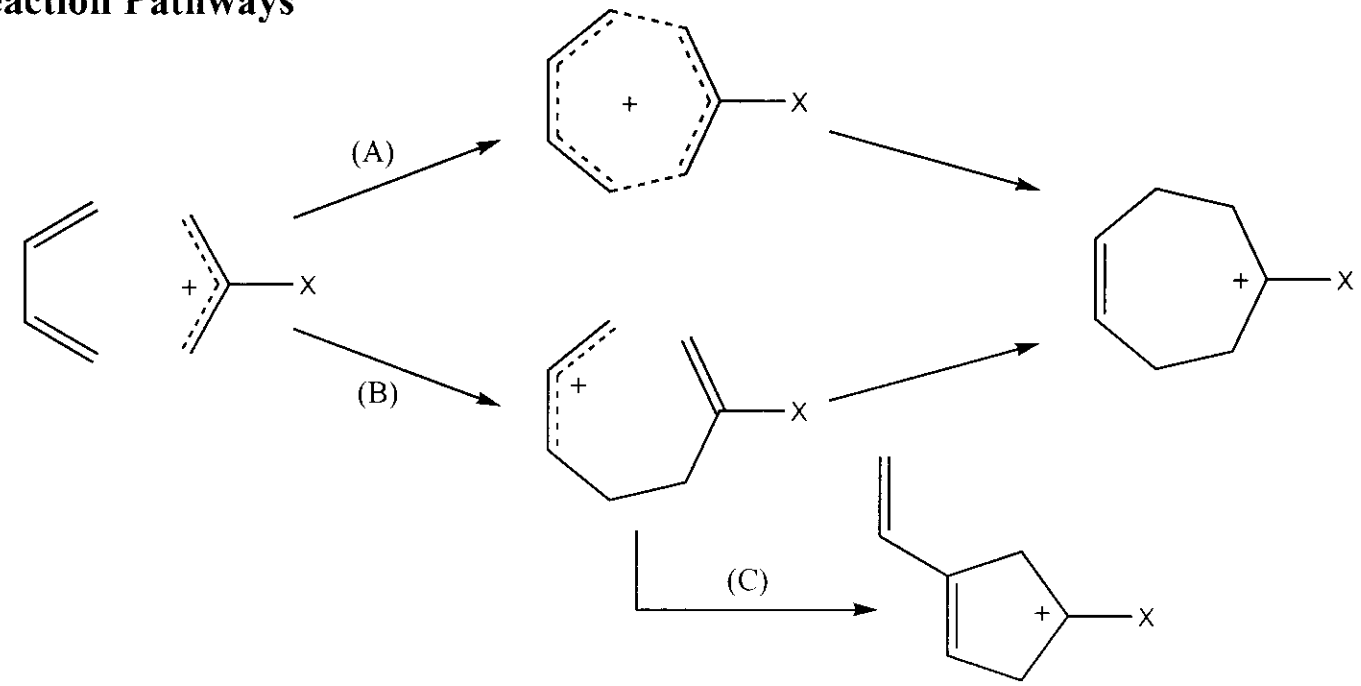
First Reported [4+3] Cycloaddition



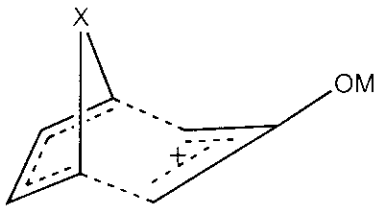
Rigby, J. H.; Pigge, F. C. *Org. React.* **1997**, *51*, 351
Harmata, M.; Rashatasakhon, P. *Tetrahedron*, **2003**, *59*, 2371
Fort, A. W. *J. Am. Chem. Soc.* **1962**, *84*, 4979

Reactivity: Concerted vs. Stepwise

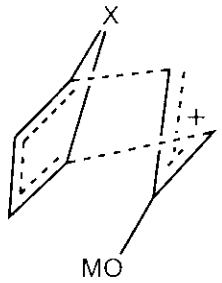
Reaction Pathways



Transition States for [4+3] Cycloadditions



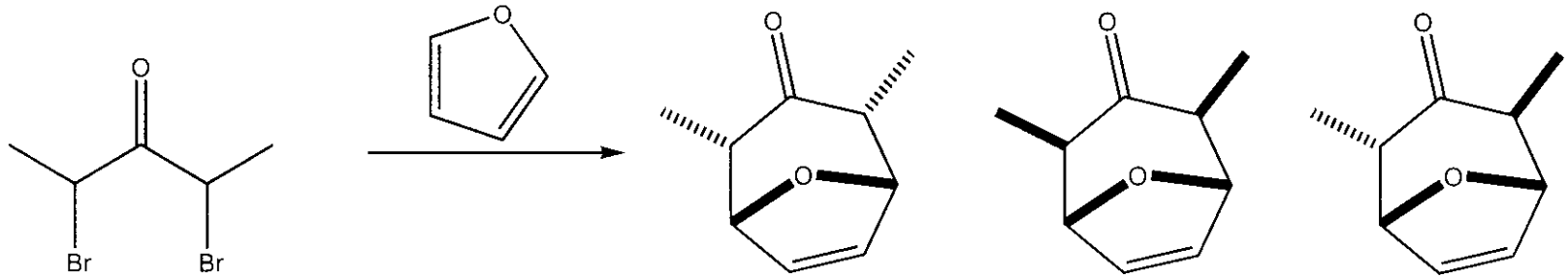
Extended Transition State
(Chair-like)



Compact Transition State
(Boat-like)

Preparation of Oxyallyl Cations

Reductive Conditions

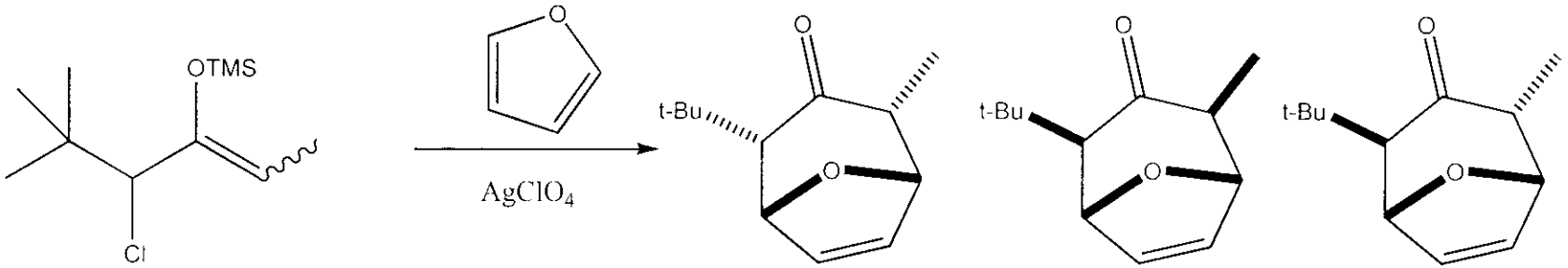


Cu, NaI (48:5:0)
Zn, Cu (69:8:7)
$Fe_2(CO)_9$ (40:0:50)

Increasing electrophilicity of allyl cation

Hoffman, H. M. R.; Clemens, H. E.; Smithers, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 3940

Solvolysis Conditions

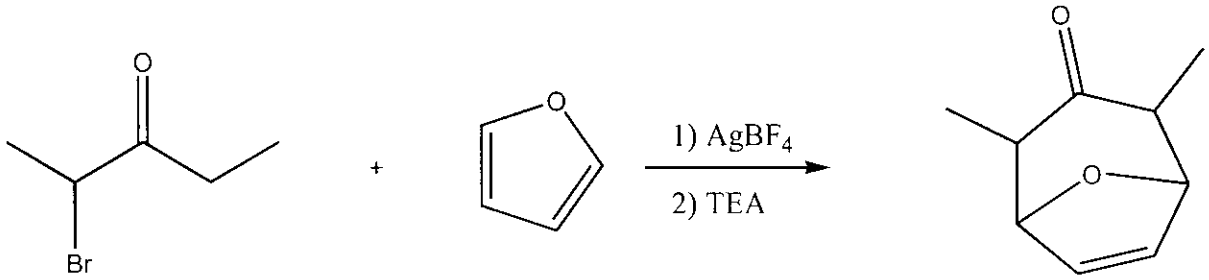


THF-Et_2O (16:22:10)
$MeNO_2$ (63:37:0)

Shimizu, N.; Tanaka, M.; Tsuno, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1330

Preparation of Oxyallyl Cations

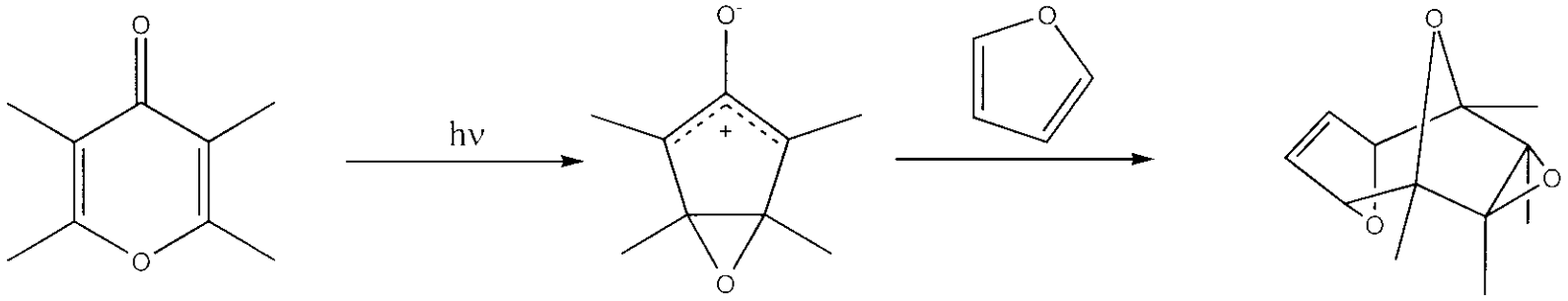
Base-Mediated Conditions



80%

Mann, J.; Wilde, P. D.; Finch, M. W. *J. Chem. Soc., Chem. Commun.* **1985**, 1543

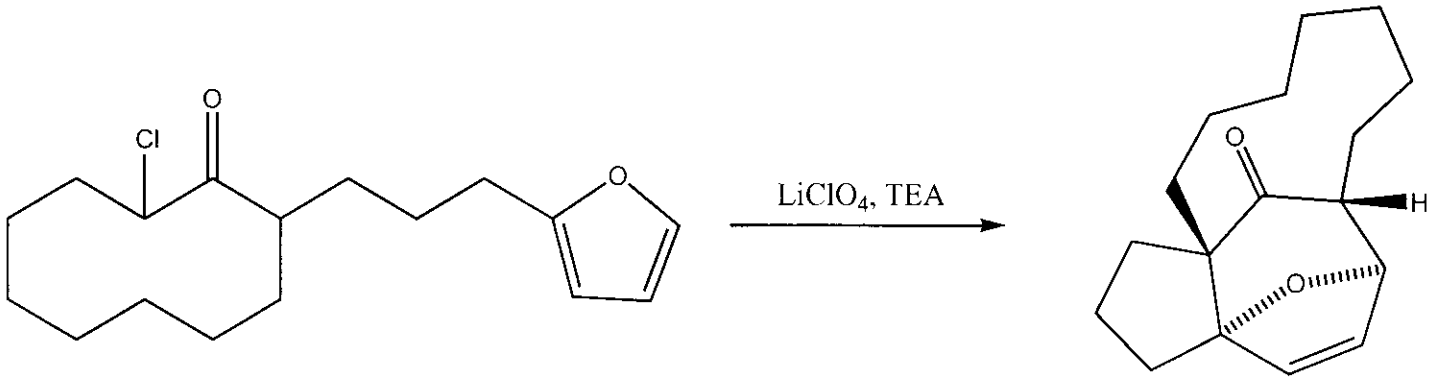
Photochemical Conditions



50%

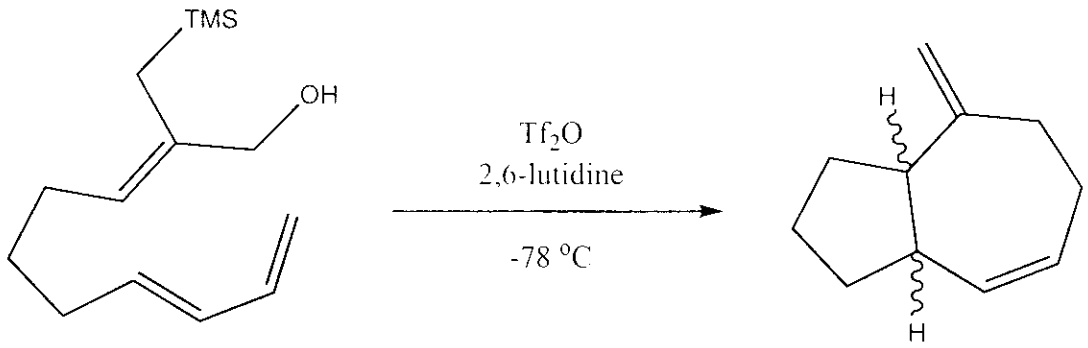
Baltrop, J. A.; Day, A. C.; Samuel, C. *J. Am. Chem. Soc.* **1979**, *101*, 7521

Intramolecular [4+3] Cycloadditions



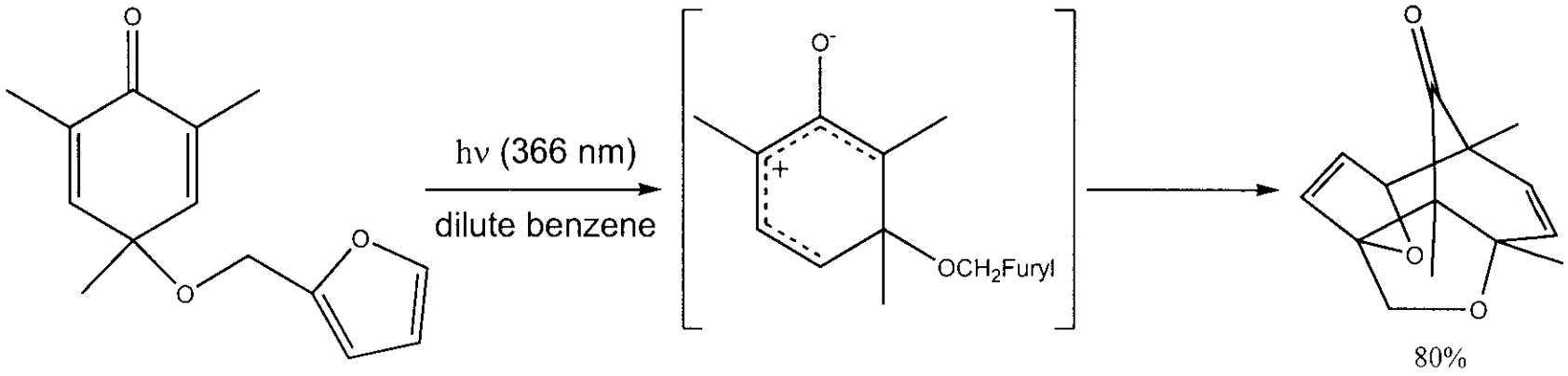
67%

Harmata, M.; Elomari, S.; Barnes, C. L. *J. Am. Chem. Soc.* **1996**, *118*, 2860



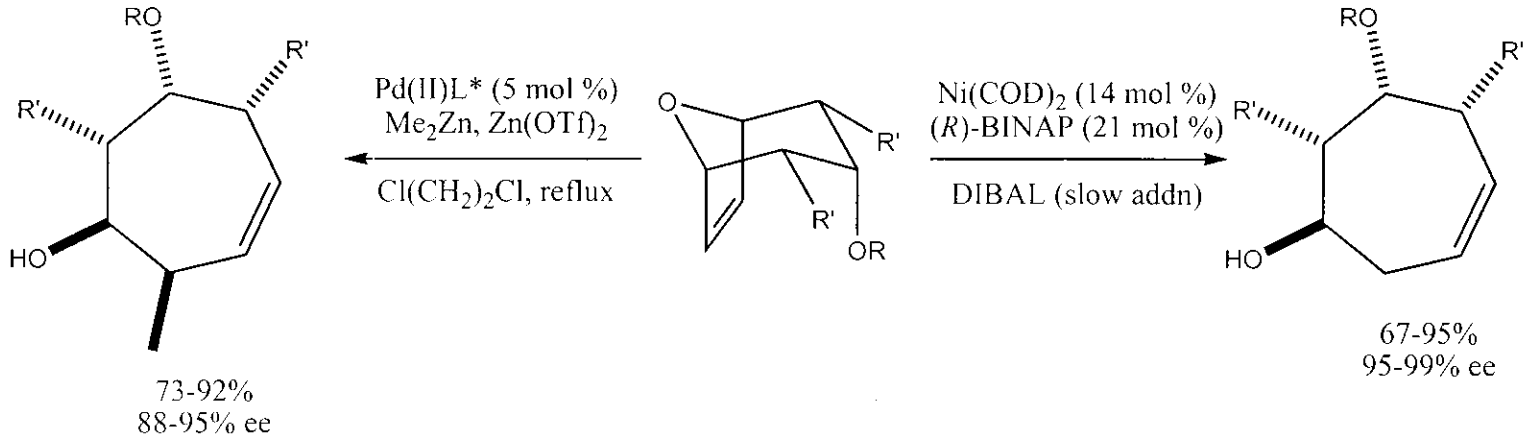
Giguere, R. J.; Duncan, S. M.; Bean, J. M.; Purvis, L. *Tetrahedron Lett.* **1988**, *29*, 6071

Tandem Di-π-Methane Rearrangement/[4+3] Cycloaddition



Schultz, A. G.; Puig, S.; Wang, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 785

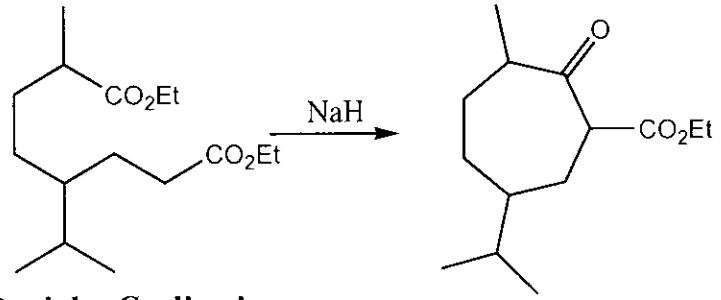
Ring-Opening Reactions of Oxabicylco[3.2.1]octanes

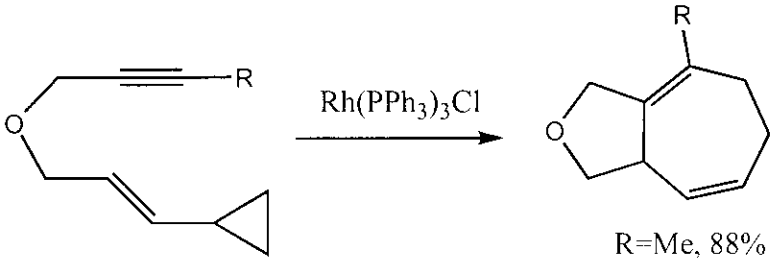


Lautens, M.; Fagnou, K.; Hiebert, S. *Acc. Chem. Res.* **2003**, *36*, 48
Lautens, M.; Hiebert, S.; Renaud, J. -L. *J. Am. Chem. Soc.* **2001**, *123*, 6834
Lautens, M.; Rovis, T. *J. Am. Chem. Soc.* **1997**, *119*, 11090

Preparation of 7-Membered Rings

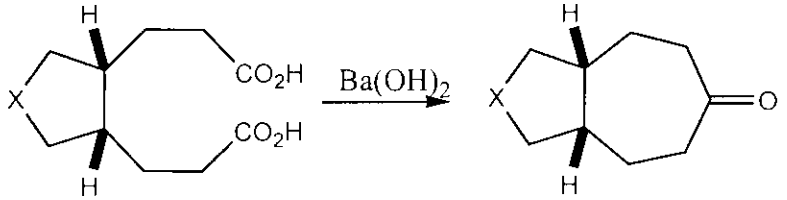
Dieckmann Condensation





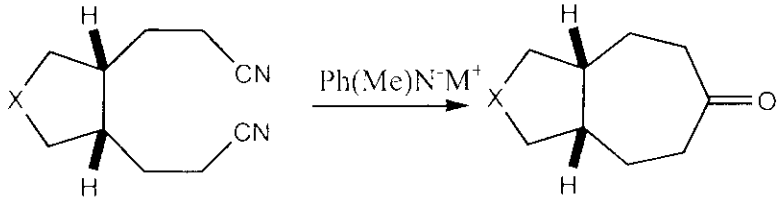
R=Me, 88%

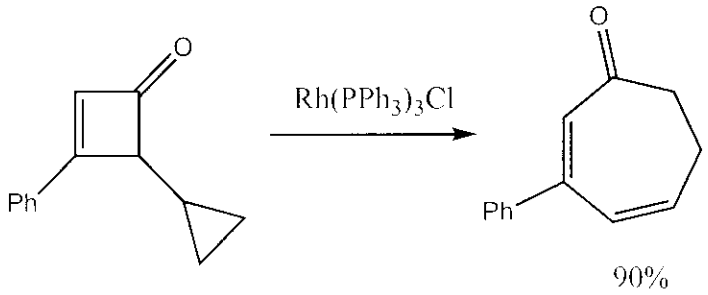
Ruzicka Cyclization



Wender, P. A.; Takahashi, H.; Witulski, B.; *J. Am. Chem. Soc.* **1995**, *117*, 4720

Thorpe-Ziegler Cyclization

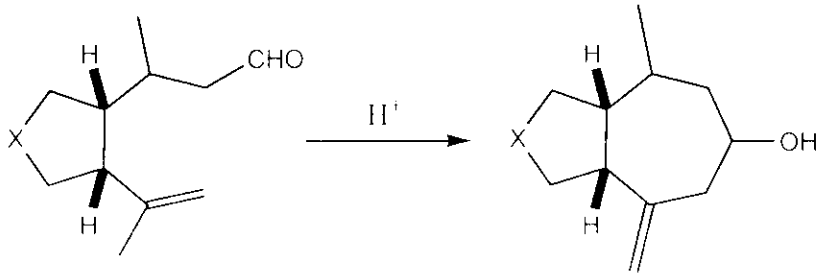




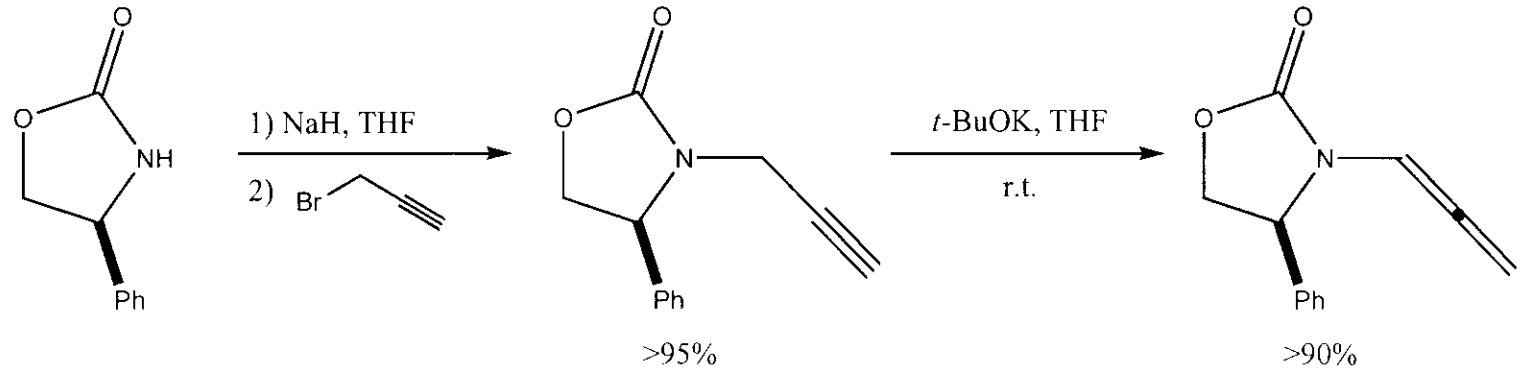
90%

Prins Cyclization

Huffman, M. A.; Liebeskind, L. S.; *J. Am. Chem. Soc.* **1993**, *115*, 4895

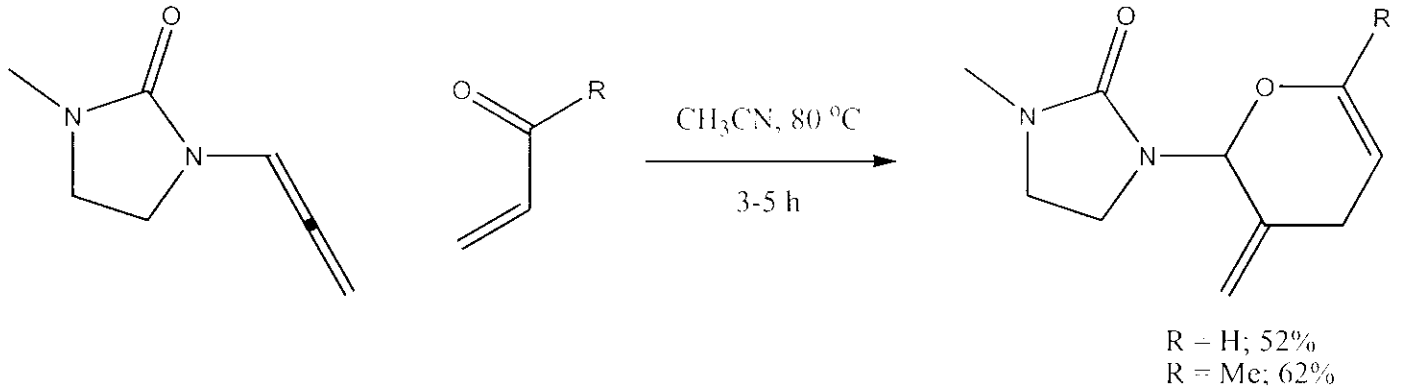


Preparation of Allenamides



Wei, L. -L.; Hsung, R. P.; Xiong, H.; Mulder, J. A.; Nkansah, N. T. *Org. Lett.* **1999**, *1*, 2145

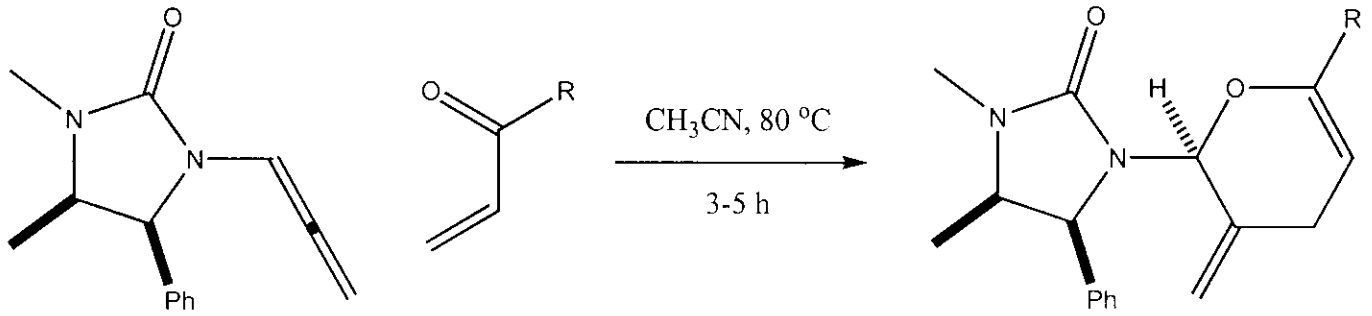
Inverse Electron Demand Diels-Alder Reactions



Wei, L. -L.; Xiong, H.; Douglas, C. J.; Hsung, R. P. *Tetrahedron Lett.* **1999**, *40*, 6903

Reactions of Allenamides

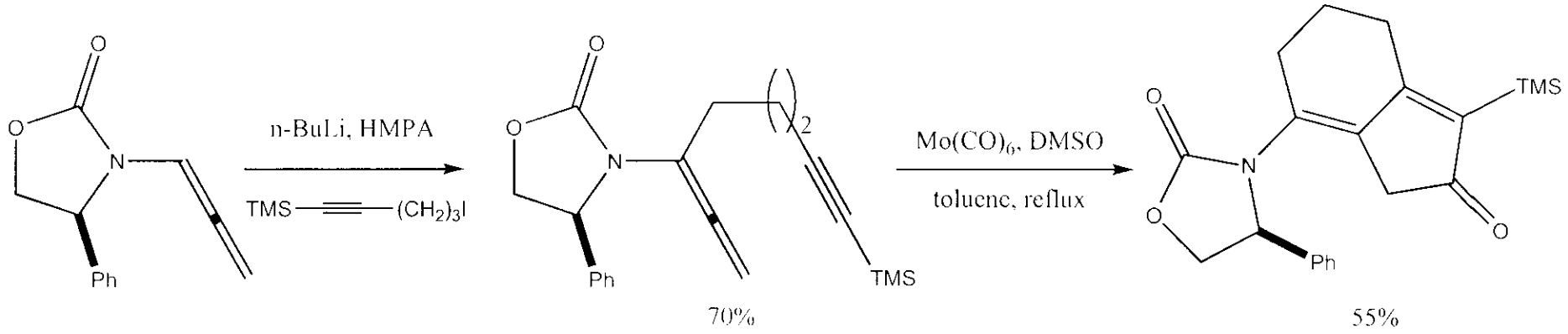
Auxilliary-Controlled Inverse Electron Demand Diels-Alder Reactions



R = H; 65% *dr* 87:13
R = Me; 57% *dr* 94:6

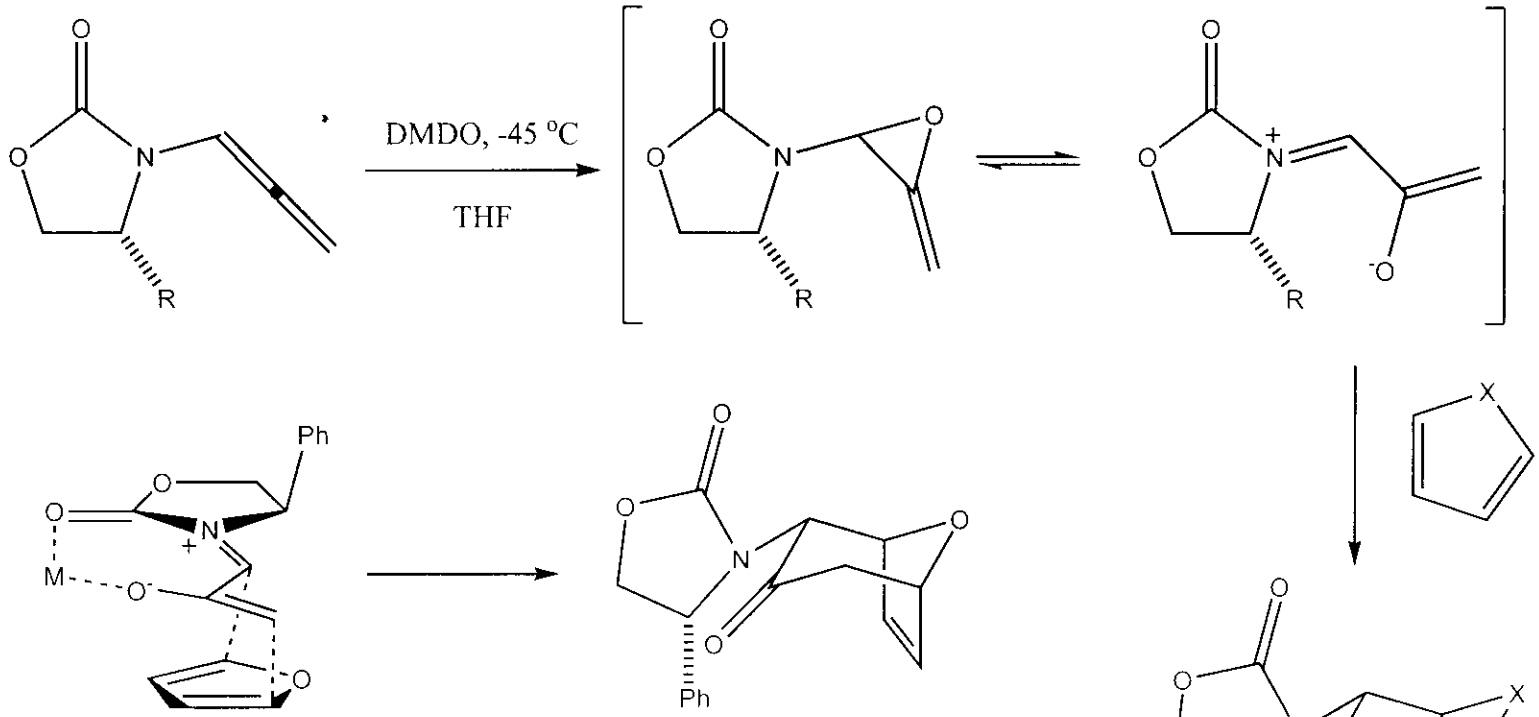
For R = alkyl, aryl, *dr* >92:8

Wei, L. -L.; Hsung, R. P.; Xiong, H.; Mulder, J. A.; Nkansah, N. T. *Org. Lett.* **1999**, *1*, 2145



Xiong, H.; Hsung, R. P.; Wei, L. -L.; Berry, C. R.; Mulder, J. A.; Stockwell, B. *Org. Lett.* **2000**, *2*, 2869

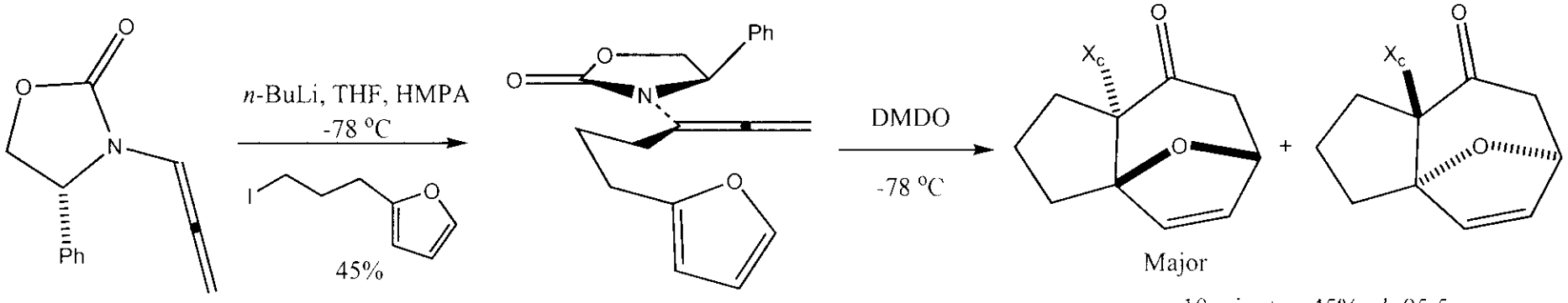
Epoxidation of Amidoallenes

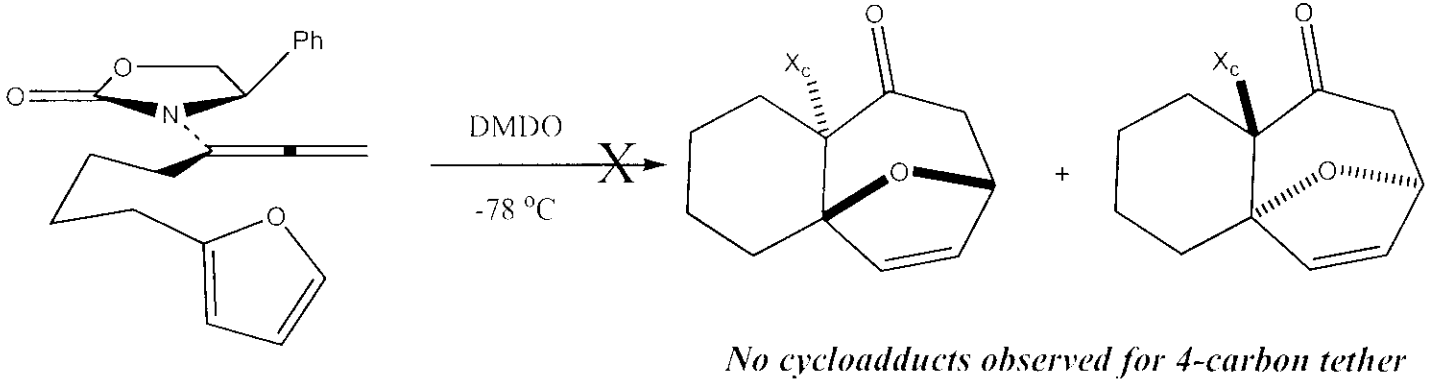


Additive	Temp	Yield (%)	dr
None	-40 °C	80	3:1
$LiClO_4$	-40 °C	81	3:1
$ZnCl_2$	-40 °C	77	94:6
$ZnCl_2$	-78 °C	80	>96:4

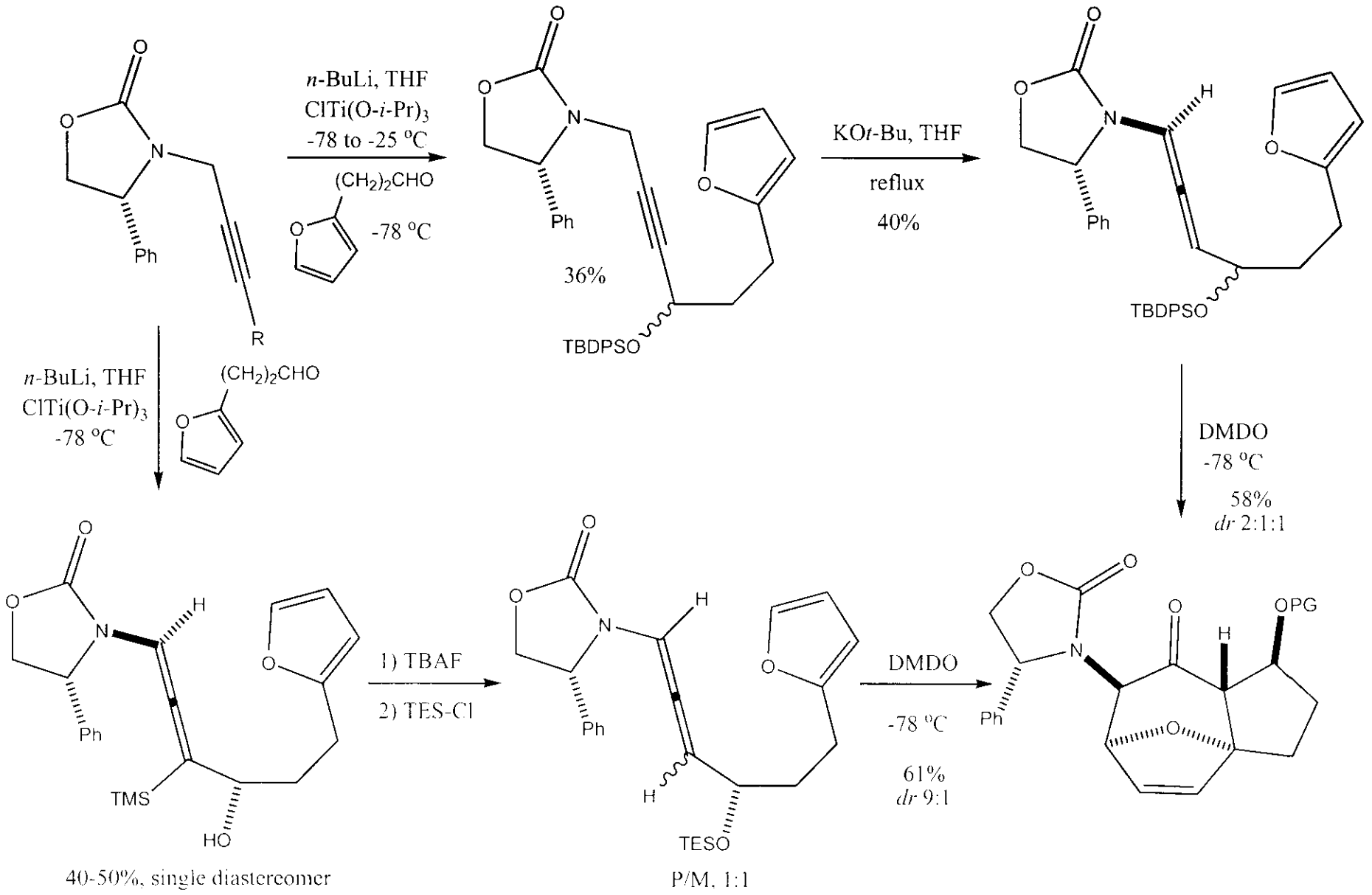
Xiong, H.; Hsung, R. P.; Berry, C. R.; Rameshkumar, C. *J. Am. Chem. Soc.* **2001**, *123*, 7174

A Tandem Epoxidation/Stereoselective Intramolecular [4+3] Cycloaddition Reaction Involving Nitrogen-Stabilized Oxyallyl Cations Derived from Chiral Allenamides



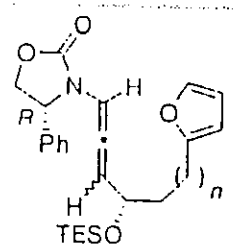
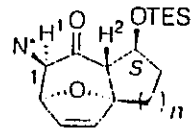
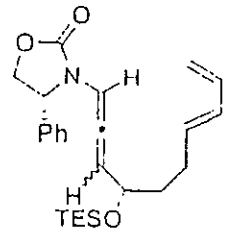
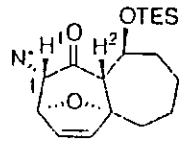
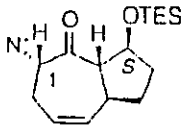
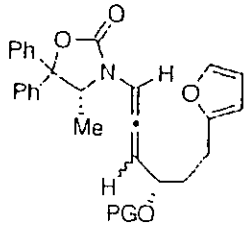
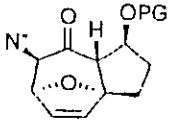
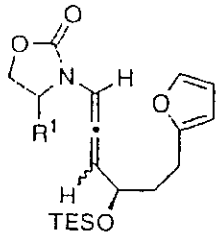
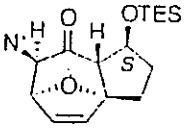
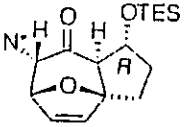


No cycloadducts observed for 4-carbon tether

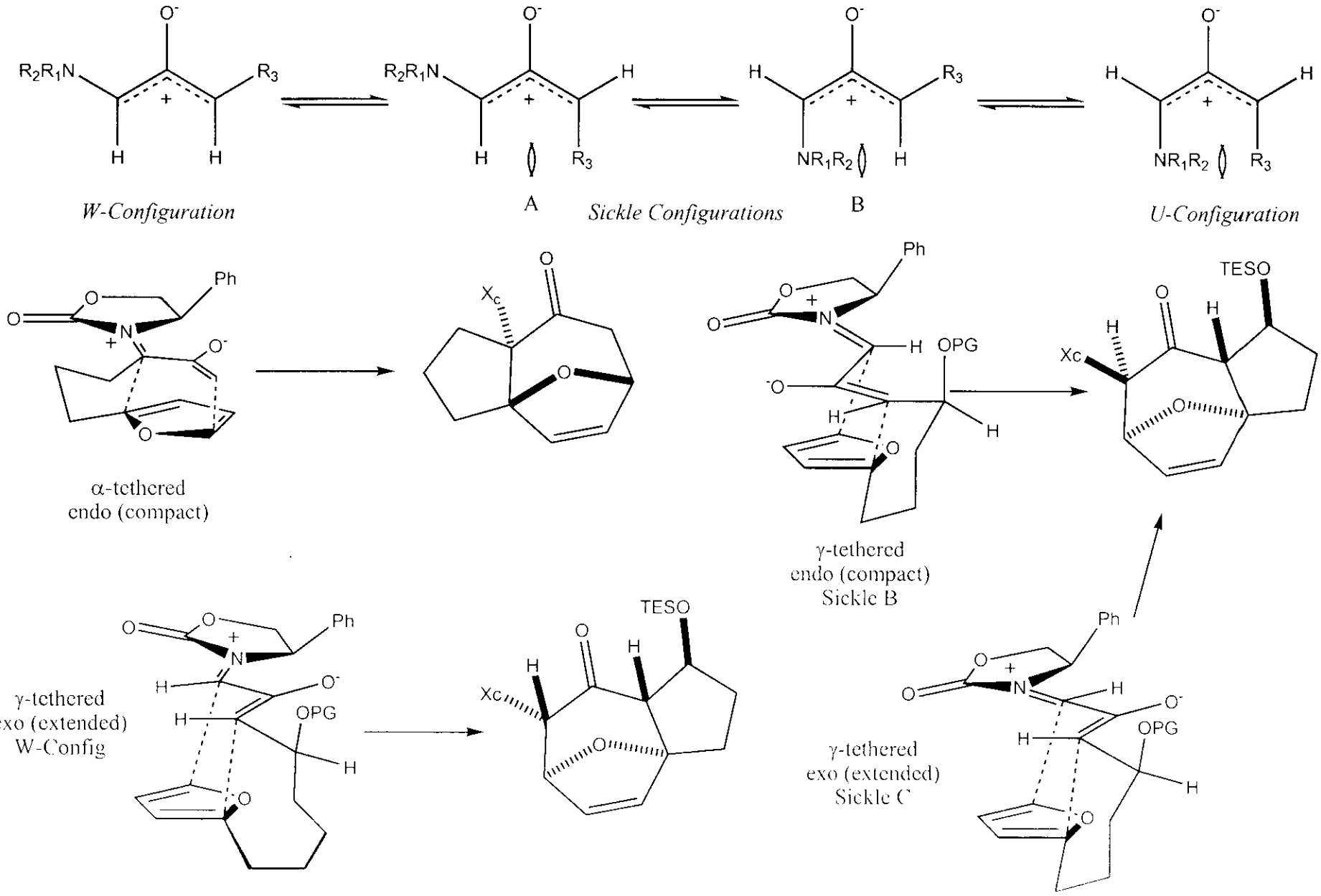


Gaul, C.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 963

Table 1. The scope and stereoselectivity of cycloadditions of γ-tethered allenamides.

Entry	Allenamides[a]	Cycloadducts[b]	Yield [%][c]	Ratio[d]
1		(*P*)-20: $n=1$	18b	60	90:10
2		(*M*)-20: $n=1$	18b	75	90:10
3		23: $n=2$; $P/M=1:1$	 25[e]	65	93:7
4		24: $n=3$; $P/M=1:1$	 26	55	≤5:95
5		(*M*)-27	 28	30	≤5:95
6		(*P*)-27	28	34	≤:95
7		29: PG=TES: *P*/*M*=2.5:1	31	78	86:14
8		30: PG=Ac: $P/M=2.5:1$	 32	83	90:10
9		R^1=*R*-Bn 33: $P/M=3:1$	 34	65	71:29
10		35: R^1=(*S*)-Ph; *P*/*M*=1:1	 *ent*-18b[f]	60	90:10
11		R^1=(*S*)-*i*Pr; $P/M=2:1$ (*P*)-36	37	60	95:5
12		(*M*)-36	37	60	95:5

[a] Details of the syntheses of the allenamides are given in the Supporting Information. All reactions were carried out in CH_2Cl_2 (conc. ca. 0.075 M) at −78 °C; DMDO (2.5 equiv) was added as a solution in acetone and CH_2Cl_2 was added at −78 °C through a cannula. The reaction was complete after 5–15 min. [b] N* denotes the corresponding chiral auxiliary. [c] Yields of isolated products. [d] Ratios of isomers determined by ^1H and/or ^{13}C NMR spectroscopy. [e] The X-ray structure was obtained. [f] Assigned by NOE measurements.


W-Configuration
A
Sickle Configurations
B
U-Configuration
α-tethered
endo (compact)
γ-tethered
endo (compact)
Sickle B
γ-tethered
exo (extended)
W-Config
γ-tethered
exo (extended)
Sickle C