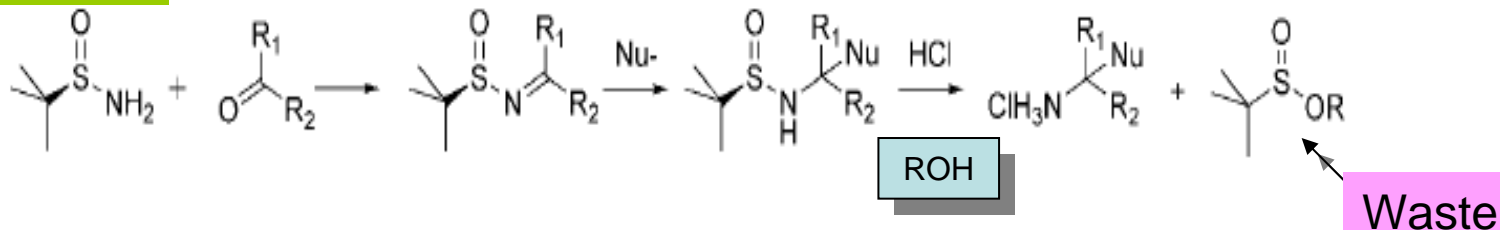


The Latest Information about Cyclopentyl methyl ether (CPME)

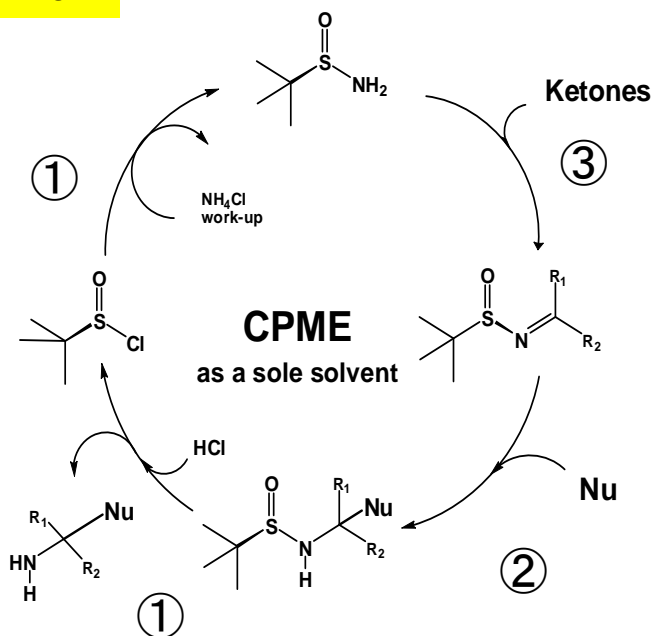


1. Process Innovation (Synthesis of Amine)

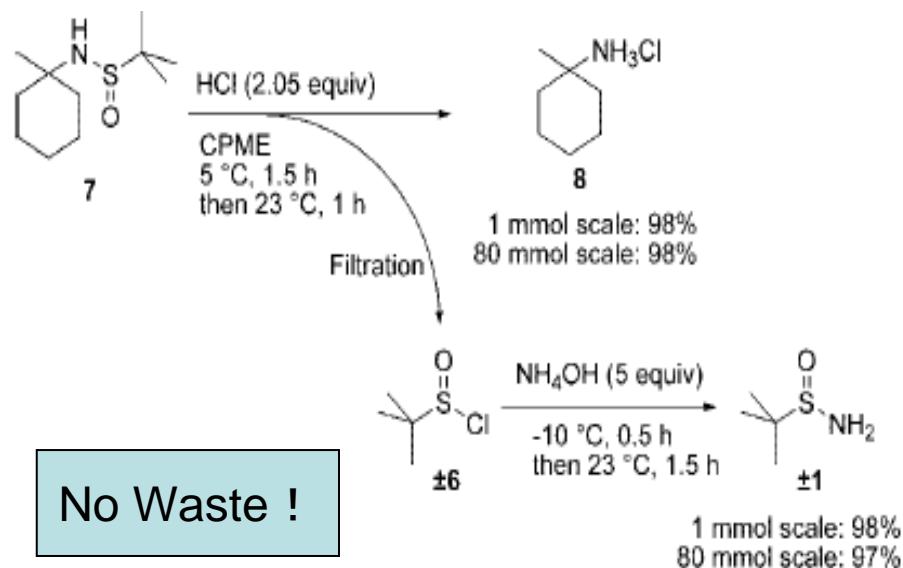
Previous Work



This Work



Example



No Waste !

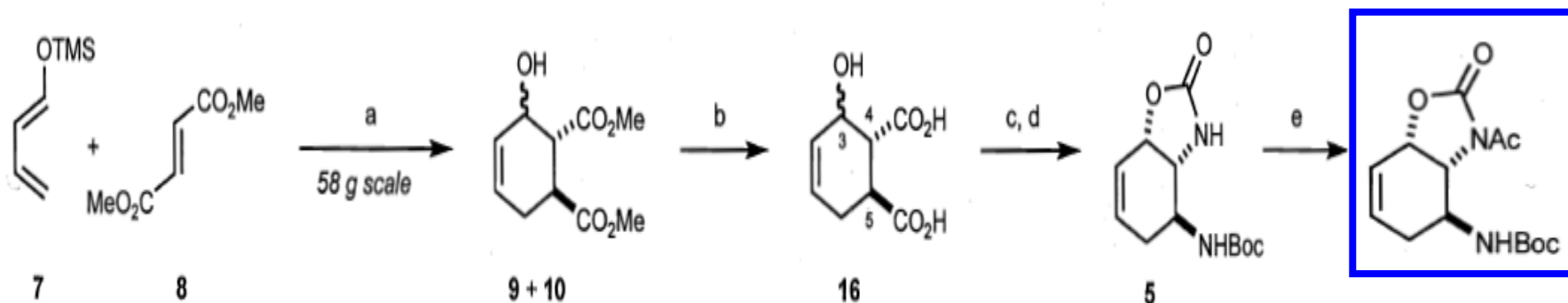
① Masakazu Wakayama, Jonathan A. Ellman, *J. Org. Chem.*, **74**, 2646 (2009).

② Zhongbo Fei, Quanbing Wu, Fei Zhang, Yudong Cao, Chuanqin Liu, Wen-Chung Shieh, Song Xue, Joe McKenna, Kapa Prasad, Mahavir Prashad, Daniel Baeschlin, Kenji Namoto, *J. Org. Chem.*, **73**, 9016 (2009).

③ Goppat K. Datta and Jonathan A. Ellman, *J. Org. Chem.*, **75**, 6283 (2010).

2.Synthetic Applications-1

Tamiflu : M.Shibasaki, *Angew. Chem. Int. Ed.*, 2009, 48, 1070



Recrystallization

Step f: $\text{CH}_2\text{Cl}_2 - \text{CPME}$ (1 : 2) (Y.80%)

ee: 95% \Rightarrow >99%

2.Synthetic Applications-2

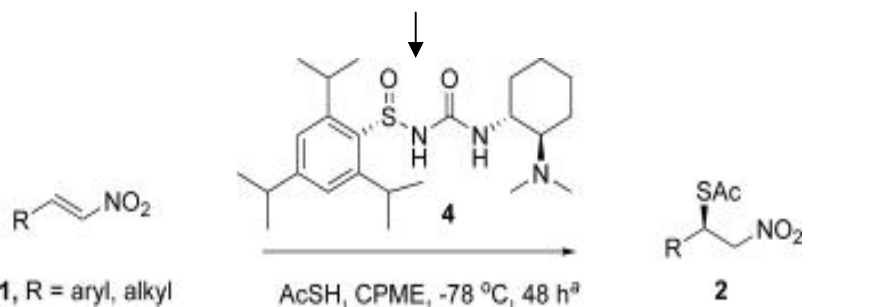
Enantioselective Addition of Thioacetic Acid to Nitroalkenes via *N*-Sulfinyl Urea Organocatalysis

Kyle L. Kimmel, MaryAnn T. Robak, and Jonathan A. Ellman*

Department of Chemistry, University of California, Berkeley, California 94720

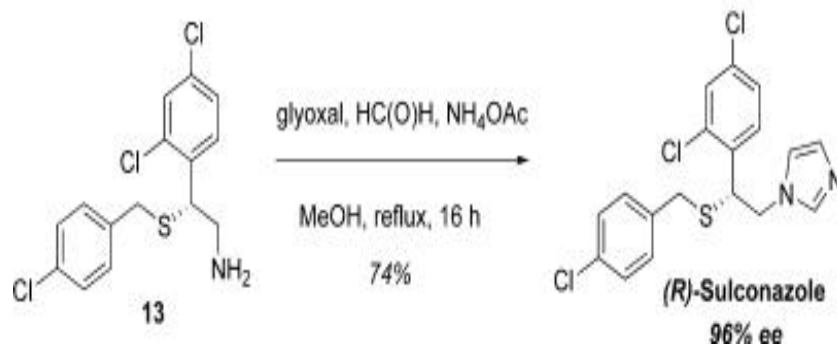
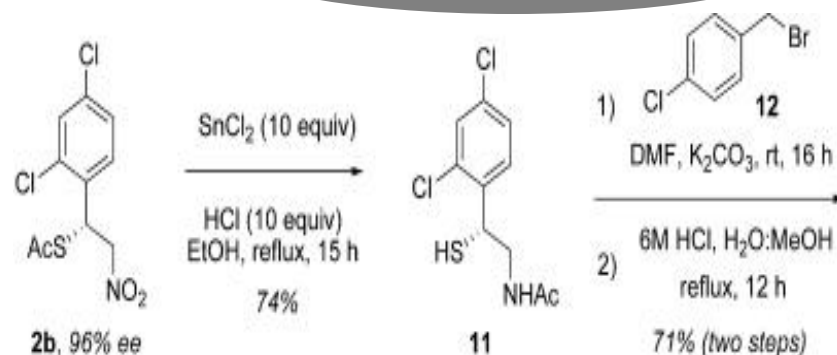
Received April 25, 2009; E-mail: jellman@uclink.berkeley.edu

Molecular cat.



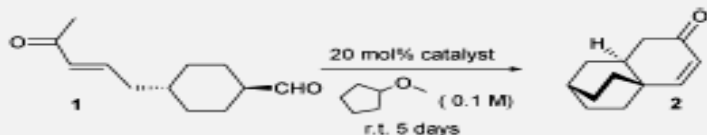
entry	R	product	yield ^b (%)	ee ^c (%)
1	C ₆ H ₅	2a	73	90
2	<i>o,p</i> -Cl ₂ C ₆ H ₃	2b	84	96
3	<i>p</i> -CF ₃ C ₆ H ₄	2c	88	85
4	<i>p</i> -MeC ₆ H ₄	2d	65	91
5	<i>p</i> -MeOC ₆ H ₄	2e	65	93
6	<i>o</i> -MeC ₆ H ₄	2f	63	94
7	Me	2g	64	78
8	<i>n</i> -Pr	2h	82	80
9	<i>c</i> -Hex ^d	2i	95	84

Michael Addition



2.Synthetic Applications-3

Table 1 Amino acid salt catalyzed intramolecular Robinson annulation



Entry	Catalyst	Yield ^a (%)	ee ^b (%)
1 ^c		NR ^d	—
2	M — H	23	91
	— Li	54 ^e	96 ^f
3	— Na	38	91
4	— K	14	70
5	— Rb	17	92
6	— Cs	50	94
	— Cs	29 ^g	96 ^g
7	— N ^t Bu ₄	31	97
	— N ^t Bu ₄	84 ^h	97 ^h
	— N ^t Bu ₄	71 ⁱ	96 ⁱ
	— N ^t Bu ₄	80 ^k	96 ^k
8 ^c		25	90
9 ^c		36	94
10 ^c		56	88
11 ^c		36	64
12 ^c		NR ^d	—
13 ^c		NR ^d	—

^a Isolated yield. ^b Determined by HPLC on OJ-H column. ^c CH₂Cl₂ is used as solvent. ^d NR = no reaction. ^e Et₂O is used as solvent. ^f 1st run, 50 mol% silica gel absorbed catalyst is used. ^g 2nd run, using 50 mol% recovered silica gel absorbed catalyst from 1st run. ^h 3rd run, using 50 mol% recovered silica gel absorbed catalyst from 2nd run.

Michael Addition

Molecular cat.

H.Yamamoto:

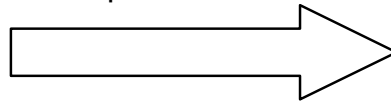
Chem.Comm.,2009,5412

3. To improve the solubility of CPME, the mixture of THF and CPME (1 : 1 by weight) may be useful

Homogeneous

Mixed solvent
THF : 50g
CPME : 50g

1. Addition of 20g-Water
2. Stirr
3. Separation



Heterogeneous

Organic Layer
THF : 47.5g
CPME : 47.5g
Aqueous Layer

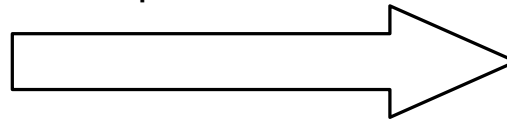
95% of THF was transferred to CPME Layer
CPME/THF... Separated by Distillation

4. THF in water can be recovered with CPME (In P7, CPME \leftrightarrow Water)

Homogeneous

Wet Solvent
THF : 50g
Water : 20g

1. Addition of 50g-CPME
2. Stirr
3. Separation



Heterogeneous

Organic Layer
THF : 47.5g
CPME : 47.5g
Aqueous Layer

95% of THF was transferred to CPME Layer
CPME/THF... Separated by Distillation