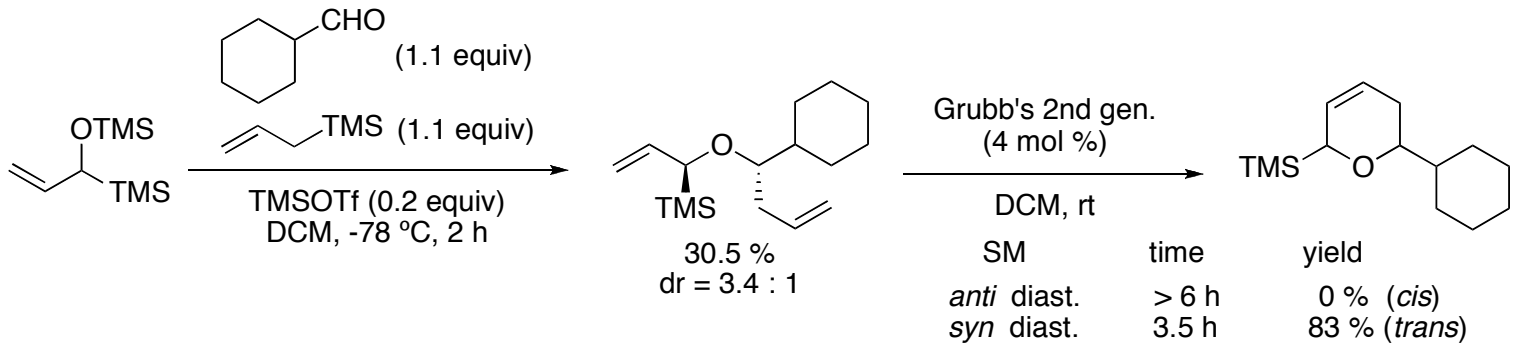
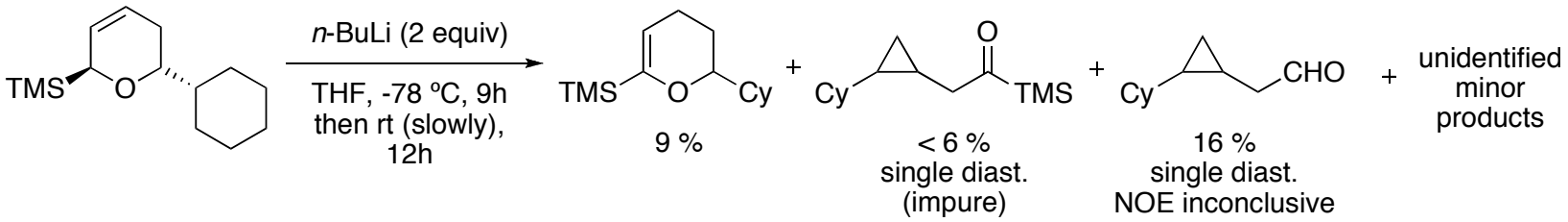
# Research Progress Report

Luis Mori-Quiroz

Maleczka Group Meeting 4-13-9

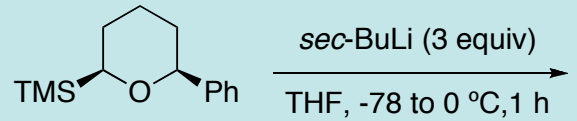
# An alkyl (instead of a benzylic) migrating group?



# Rearrangement of saturated cyclic ethers

## Last report (2/25/9)

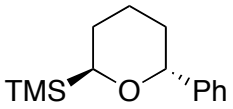



single diastereomer

*sec*-BuLi (3 equiv)

THF, -78 to 0 ºC,1 h
then rt (o.n.)

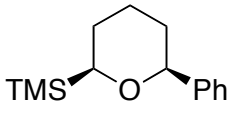
no reaction
ca 100 % SM




single
diast.

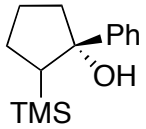
*n*-BuLi (3 equiv)

THF, -78 ºC, 2h
then rt, 45 min.



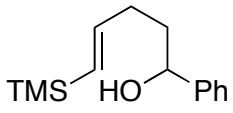

< 2 %

+




34 %
single diastereomer
NOESY inconclusive

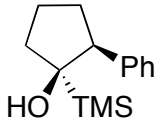
+




*15 %

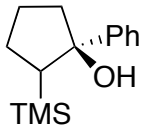
+

One looks like
this (by $^{1}$H NMR)

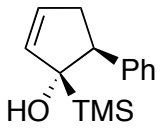



3 %

another
looks like
(by $^{1}$H, $^{13}$C)

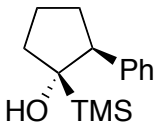



< 17 %
(opposite
diast.)




$H_2$ (1 atm)
10 % Pd/C

EtOAc, rt, < 1 h



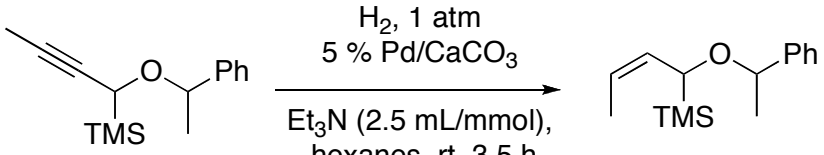

~ 100 %

doesn't match with any
of the compounds above

*JACS **2000**, 122, 11348-11357..

# Preparation of starting material

Last report:




The same conditions were applied to diastereomerically enriched samples but reproducibility is poor. The catalyst tends to precipitate and several extra loadings are required to consume the SM. Initial cat loading was doubled and half $Et_3N$ was used with no improvement. SM is very unstable, so it seems decomposition products 'kill' the catalyst.

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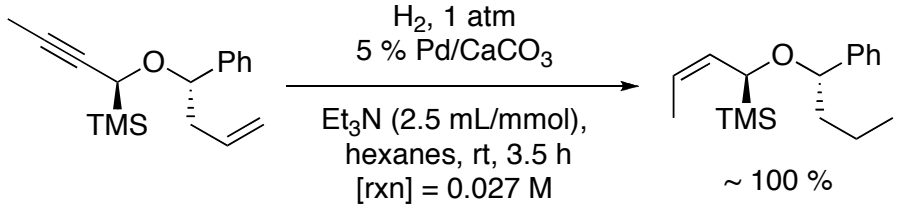
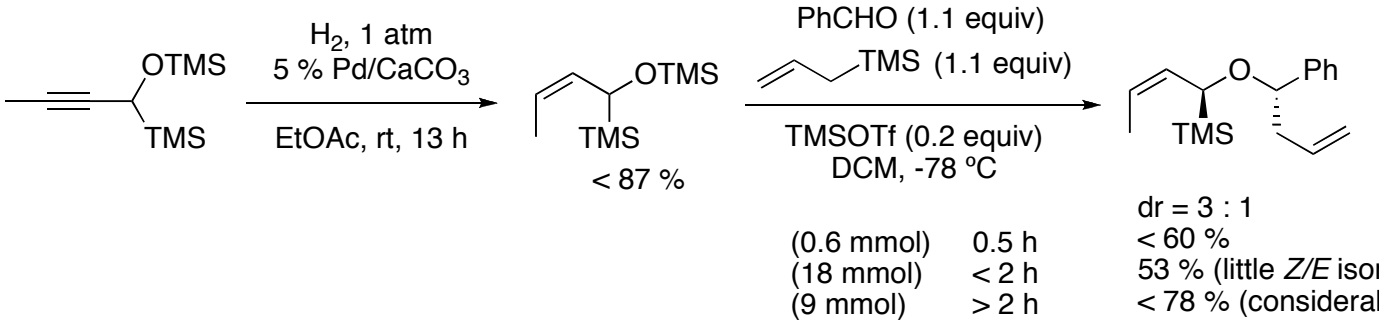
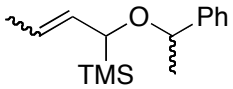


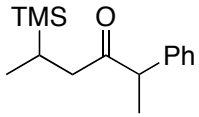

| | | |
|---|---|---|
| (0.6 mmol) | 0.5 h | dr = 3 : 1 |
| (18 mmol) | < 2 h | < 60 % |
| (9 mmol) | > 2 h | 53 % (little *Z/E* isom. took place) ~100:1 |
| | | < 78 % (considerable *Z/E* isom.) ~5:1 |

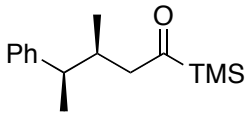
note: *Z/E* isomerization was detected only for the *anti* diastereomer

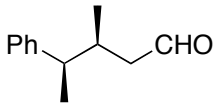
# Rearrangement of *E/Z* substrates (1)

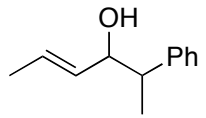


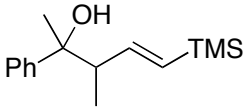

see procedure below

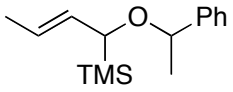
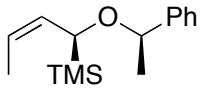
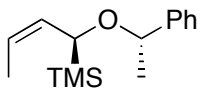


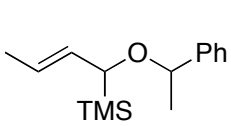




| Substrate | Time (days) | **SM** | **via [1,2]** | **[1,4]** | **Si/Li [1,4]** | **Si/Li [1,2]** | **[2,3]** |
|---|---|---|---|---|---|---|---|
|  dr = 1 : 1 | 4 | 25 % (*anti*)<br>dr = 13 : 1 | *22 %<br>dr = 1.35 : 1.0 | *26 %<br>dr = 1.2 : 1.0 | < 3.5 %<br>dr = 1 : 1 | < 2 %<br>dr = 1 : 1 | < 1 %<br>dr = 9 : 1 |
|  dr = 18.5 : 1.0 | 2 | 56 %<br>dr = 18 : 1 | *2.3 %<br>dr = 1.6 : 1.0 | *2.5 %<br>dr = 1.37 : 1.0 | < 3 %<br>dr = 1.3 : 1 | < 7.2 %<br>dr = n.d. | 6.3 %<br>dr ~ 1 : 10 |
|  dr = 39 : 1 | 2.7 | 77 %<br>dr = 26 : 1 | < *1 %<br>dr = n.d. | < *1 %<br>dr = 1.25 : 1.0 | < 3.4 %<br>dr = 1 : 1 | < 4 %<br>dr = n.d. | < 1 %<br>dr = 10 : 1 |

***** calculated from NMR (mixture of SM + [1,2] + [1,4]) **n.d.** not determined. **Si/Li** products formed probably via silicon/lithium exchange. Procedure: *n* -BuLi (1.6 M, 4 equiv) was added to a cold (-78 ºC) solution of the substrate (1-2 mmol) in THF (0.1 M solution). After ~ 5 minutes, the cold bath was removed. After the indicated time the reaction was cooled down at -78 ºC and quenched with $NH_4Cl_{(sat)}$.

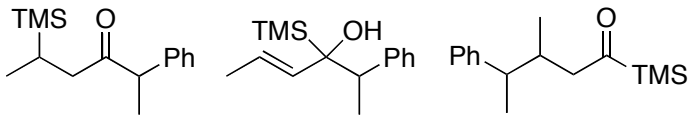
## Report by Edith (Thesis):



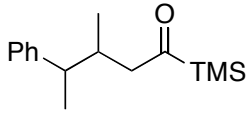

11 mmol
no dr reported

*n*-BuLi (4 equiv)
THF, -78 ºC

then -30 ºC, 4 days

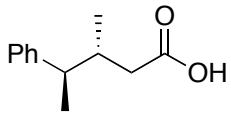



37 % (combined yield, ratios couldn't be obtained)



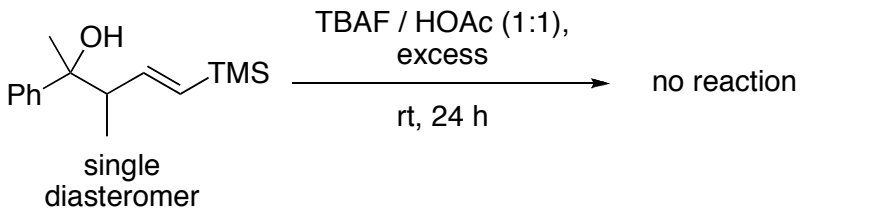

3M NaOH
30 % $H_2O_2$

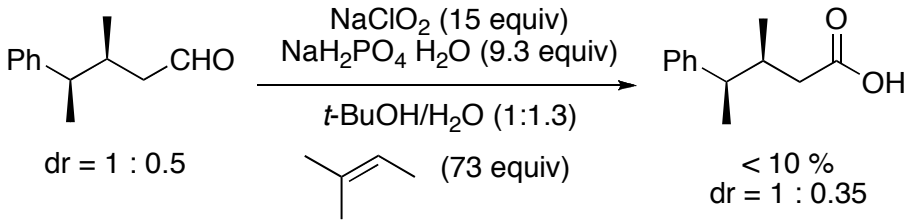
THF, 40 ºC, 2 h



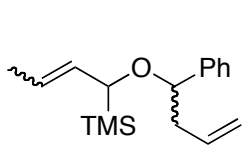

*anti/syn* (2.8 : 1)

# Attempts to derivatize / identify products or assign stereochemistry

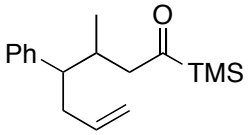


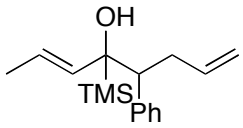



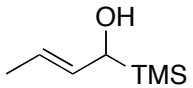
# Rearrangement of *E/Z* substrates (2)

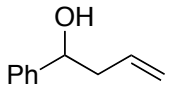


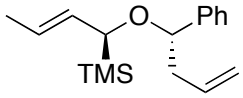
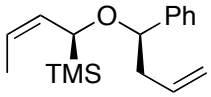
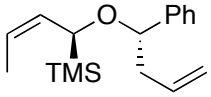

see procedure below



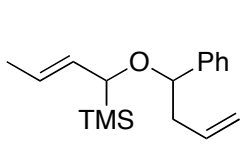




| Entry | Substrate[a] | Time (days) | **SM** | **[1,4]** | **[1,2]** | | |
|---|---|---|---|---|---|---|---|
| 1[a] |  dr = 8.2 : 1 | 4 | 46 % (*anti*) dr = 4.2 : 1 | 14 % dr > 20 : 1 | < *2 % dr = 7 : 1 | 20 % | 12 % |
| 2[b] |  dr = 27 : 1 | 3.5 | 41 % | - | - | 13 % | < 6 % |
| 3[b] |  *E/Z* = 100 : 3 | 3.8 | 72 % dr = 26 : 1 | - dr | - | < 3.4 % | < 4 % |

Procedure: *n* -BuLi (1.6 M, 4 equiv) was added to a cold (-78 ºC) solution of the substrate (0.6 - 1.8 mmol) in THF (0.1 M solution). After ~ 5 minutes the temperature was raised [see a,b]. After the indicated time the reaction was cooled down again at -78 ºC and quenched with $NH_4Cl_{(sat)}$. [a] -35 ºC. [b] room temp. * estimated from NMR.

## Report by Edith (Thesis):




24 mmol
no dr reported

*n*-BuLi (4 equiv)
THF, -78 ºC

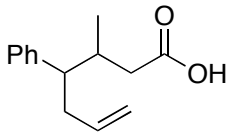
then -30 ºC, 4 days

all possible Wittig products

37 %
0.6 g of the mixture
was oxidized

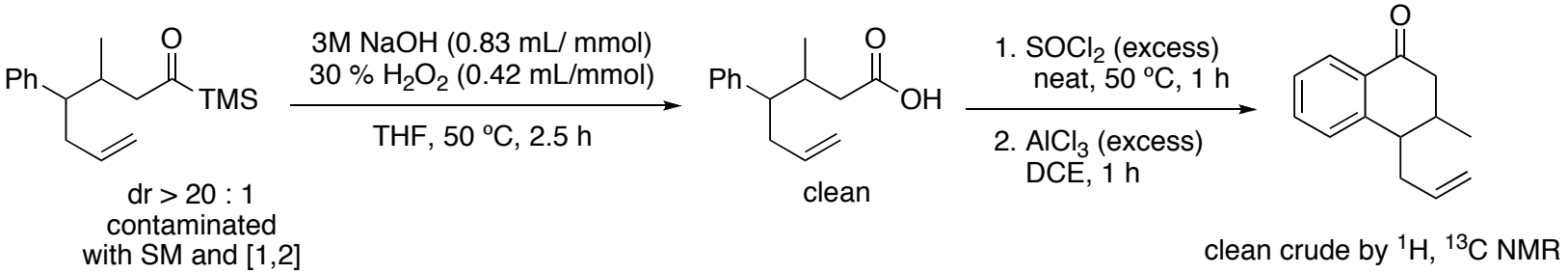
3M NaOH
30 % $H_2O_2$

THF, 40 ºC, 2 h




30 %
dr = 1 : 1
(5 % calculated
from experimental part)

# Attempts to derivatize / identify products or assign stereochemistry




dr > 20 : 1
contaminated
with SM and [1,2]

clean

clean crude by $^{1}H$, $^{13}C$ NMR
GC/MS = 200.1
(2 peaks on chromat)
Exact Mass: 200.1201