

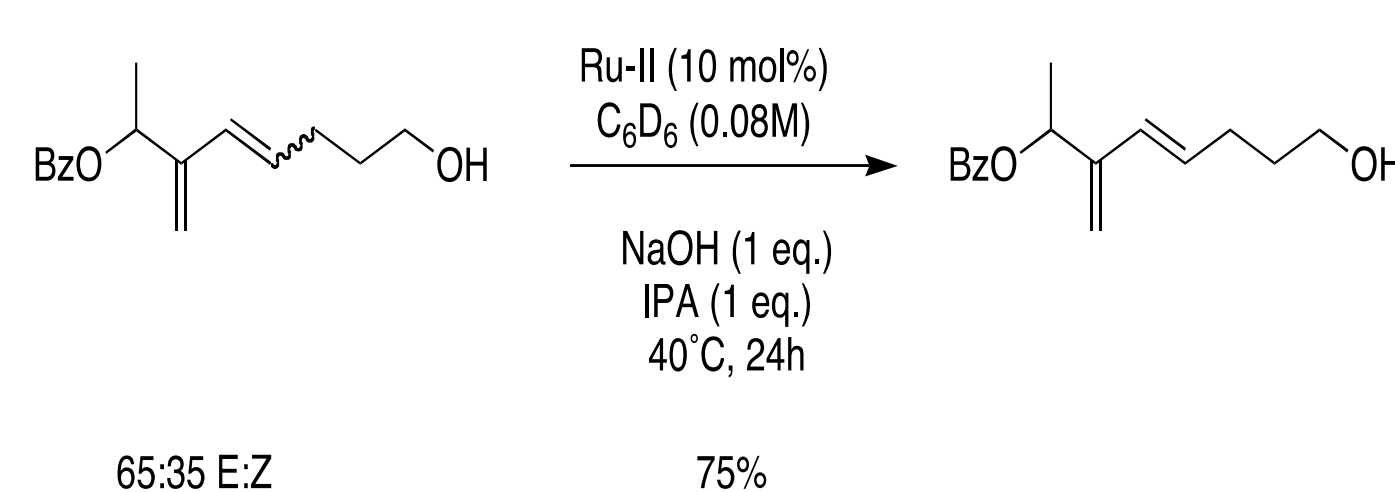
New Diene Isomerization Catalysts

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ABSTRACT

A major problem in organic synthesis is the separation of isomeric mixtures. In ene-yne metathesis, it is common to obtain *EZ* mixtures of products. The purpose of this project is to start with an *EZ* mixture of a conjugated diene and have the *Z* isomer convert fully to the *E* isomer. This would allow chemists using metathesis to obtain a single isomeric product, avoiding tedious separation methods and loss of their final product. An isomeric mixture of a 1,3-diene was converted to the single *E*-isomer using Grubbs second generation catalyst in the presence of isopropanol and trace sodium hydroxide. Reactions were heated at 45 °C in toluene for 24 hours.



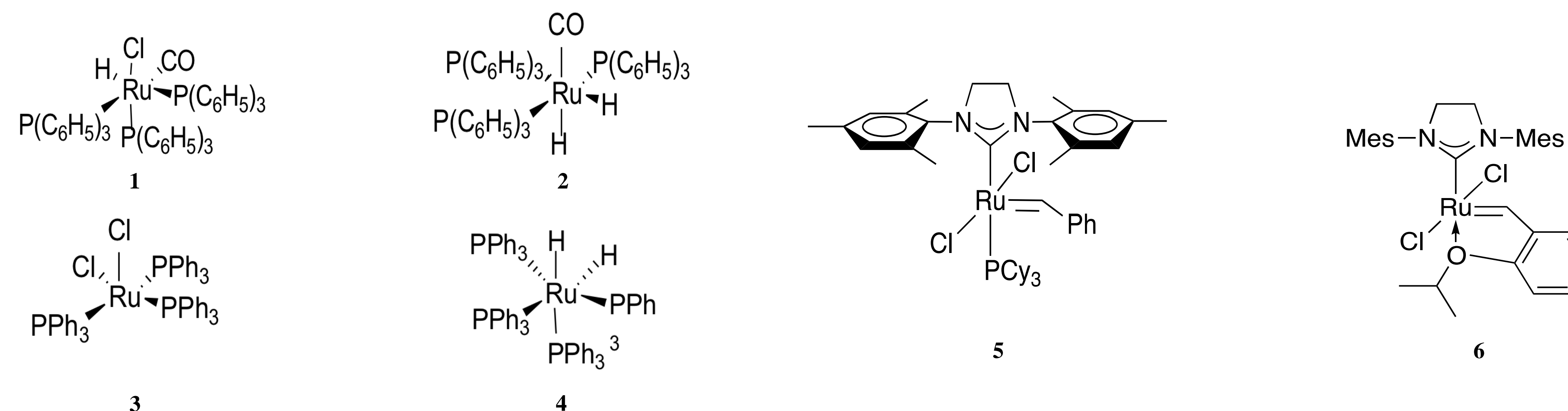
INTRODUCTION

A major problem in organic synthesis is the separation of isomeric mixtures. Chemists attempt to isolate mixtures by using chromatographic techniques, such as medium pressure liquid chromatography (MPLC). However, in risk of using such an instrument, the isolated product yield may be low. In ene-yne metathesis reactions, it is common to obtain *EZ* mixtures of products. Clark et al, applied 10 mol% I_2 to their *EZ* product. This addition gave a 99% crude yield of the *E*-isomer as their final product. However, this procedure is not always effective and the outcome primarily depends on the type of functional groups in the molecule. This method does not generally work with molecules that contain complex substrates such as carbonyl groups. Grubbs' second generation catalyst is commonly used in olefin metathesis reactions. The problem with using this catalyst is it causes unwanted isomerization in ene-yne metathesis reactions. In a paper written by Schmidt et al, they generated a ruthenium hydride species *in situ* by treating Grubbs' first generation catalyst with trace NaOH and isopropanol (IPA) in order to induce alkene isomerization. We wondered if these conditions were general and could be applied to the *Z* to *E* isomerization of dienes.

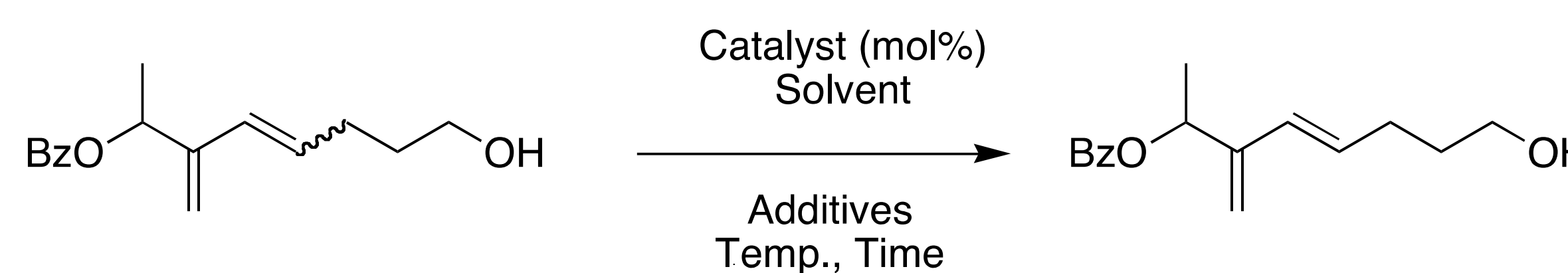
METHODS

- Based on Schmidt's observations of ruthenium hydrides on alkenes, we screened several ruthenium hydride species on a diene.
- In a glove box, a purified *EZ* mixture of a conjugated diene was dissolved in benzene- D_6 and placed in a nuclear magnetic resonance tube (NMR).
- Trace powdered NaOH and 1-equivalence of isopropanol (IPA) were added to the NMR tube along with ruthenium generation II catalyst (Ru-Gen II)
- Percent conversion was determined relative to an internal standard of 1,3,5-trimethylbenzene.
- This method was repeated under different experimental conditions

RUTHENIUM CATALYSTS



OPTIMIZATION TABLE



Entry	E:Z	Catalyst	Mol%	Temp., Time	Additives	Solvent	Results	NMR Yield (%)	Isolated Yield (%)
1*	90:10	1	10	60° C, 2.5 h	None	PhCH ₃	No Change		
2*	90:10	2	10	60° C, 2h,	None	PhCH ₃	No Change		
3*	90:10	2	10	60° C, 24h	None	PhCH ₃	Decomposition of Z-isomer		
4*	57:43	3	10	110° C, 3h	None	PhCH ₃	No Change		
5	57:43	4	10	40° C, 72h,	None	C ₆ D ₆	No Change		
6	57:43	4	100	60° C, 48h	None	C ₆ D ₆	Decomposition		
7	57:43	4	40	60° C, 48h,	None	C ₆ D ₆	Decomposition		
8	0:100	5	10	80° C, 1h	None	C ₆ D ₆	Z to E isomerization		
9	0:100	5	10	80° C, 1h	None	C ₆ D ₆	Z to E isomerization	E=22% Z=28%	
10	0:100	5	10	80° C, 2h	None	C ₆ D ₆	Z to E isomerization	E=20% Z=19%	
11	65:35	5	10	80° C, 1h	Benzoquinone, NaOH, IPA	C ₆ D ₆	Z to E isomerization	E=81% Z=10%	
12	65:35	5	10	80° C, 2h	Benzoquinone, NaOH, IPA	C ₆ D ₆	Z to E isomerization	E=81% Z=14%	
13	65:35	5	10	80° C, 3h	Benzoquinone, NaOH, IPA	C ₆ D ₆	Z to E isomerization	E=60% Z=6%	
14	65:35	5	10	45° C, 24h	Benzoquinone, NaOH, IPA	C ₆ D ₆	Z to E isomerization	E=100% Z=0%	75%
15	65:35	5	10	40° C, 24h	NaOH, IPA	C ₆ D ₆	Z to E isomerization	E=100% Z=0%	75%
16	65:35	6	10	80° C, 1.5h	Benzoquinone, NaOH, IPA	C ₆ D ₆	Z to E isomerization	E=47% Z=5%	
17	65:35	6	10	40° C, 16h	Benzoquinone, NaOH, IPA	C ₆ D ₆	Z to E isomerization	E=70% Z=30%	
18	65:35	6	10	60° C, 3h	Benzoquinone, NaOH, IPA	C ₆ D ₆	Z to E isomerization	E=60% Z=10%	

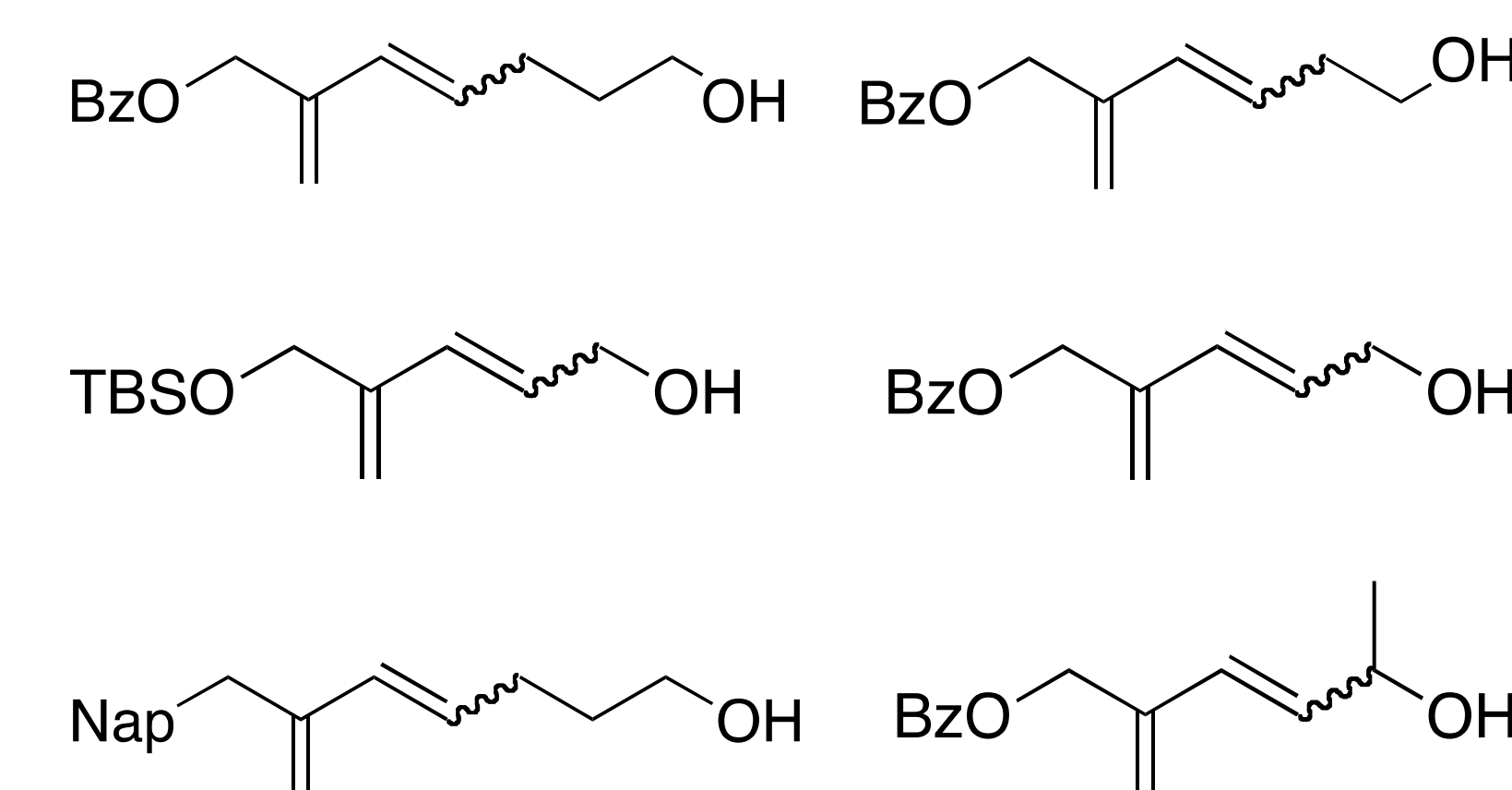
*Note: * indicates that the reaction was done in a Schlenk tube under argon instead of a glove box

DISCUSSION

- Catalysts 1, 2 and 3 did not change the *E* to *Z* ratio of our original conjugate diene.
- Catalyst 4 is air sensitive. Initially, it was thought that the catalyst was promoting *Z* to *E* isomerization. However, even though the NMR spectra showed that there was no *Z*-isomer remaining in the reaction, there was no additional *E*-isomer. Therefore, we conclude that the *Z*-isomer is decomposing first followed by the *E*-isomer.
- Catalyst 5 gave the best results. We initially used an all *Z*-isomeric solution of our conjugated diene and saw some conversion to the *E*-isomer. If this catalyst did not work, we would not see any *E*-isomer peaks in our NMR spectra. However, peaks correlating to the *E*-isomer were present. Benzoquinone was taken out as an additive because it was not needed. Benzoquinone is used to prevent 1,5-hydride shifts and under our experimental conditions, we were not getting a 1,5-hydride shift as one of our side products. Quantitative *Z* to *E* isomerization of a diene was successful using RuGen-II (10 mol%), trace NaOH and IPA at 40° C for 24 hours.
- Catalyst 6 is similar in structure to catalyst 5. However, there was poor *Z* to *E* isomerization. One explanation for this is the Hoveyda-II catalyst does not have a phosphine group so the hydride species may be too unstable to form.

FUTURE WORK

- Apply these optimal conditions to other substrate and expand the substrate scope.



ACKNOWLEDGEMENTS

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References:
1.Clark DA, Clark JR, Diver ST (2008). "Alkenol-Alkyne Cross Metathesis". *Org. Lett.*, **10** (10): 2055–2058.
2.Schmidt B, (February 2004). "In situ conversion of a Ru catalyst to an isomerization catalyst". *Chem. Commun.* (6): 742-743.