SAN DIEGO STATE UNIVERSITY Research Foundation | TECHNOLOGY TRANSFER OFFICE

INFO SHEET

Catalysts for control of monoisomerization of terminal alkenes

Generate alkenes vital to fine chemical synthesis while controlling the regiochemistry and stereochemistry

Market Opportunity and The Problem

Alkenes are fundamental chemical feedstocks used on massive industrial scales. The alkene functional group is crucial to fine chemical synthesis, including multistep natural product synthesis. While the existing alkene isomerization catalysts selectively make and react with trans-alkenes from terminal alkenes, they struggle to kinetically control the positional as well as geometric E/Z isomerism. Catalysts that can exhibit regio- and/or stereoselectivity for substrates and control the formation and chemistry of alkenes will be useful for the making of pharmaceuticals or other high value compounds.

SDSU Solution

Prof. Douglas Grotjahn and his research team have designed catalysts that control the monoisomerization of terminal alkenes in a way to control double bond position and molecular shape. The catalysts avoid thermodynamic equilibration of alkene isomers better than any other known catalysts and generate the trans-2-alkenes of both non-functionalized and functionalized alkenes. The catalytic action controls the reaction without the use of substrate control **(Figure 1).**

The team's novel, coordinatively unsaturated, formally 16-electron Cp*Ru catalyst 5 [$Ru^{II}(\eta^5\text{-}C_5H_5)$ (κ^2-PN) (CH_3CN)]$^+$[PF_6]$^-$; PN = (1-methyl-4-tertbutylimidazol-2-yl)-di-iso-propylphosphine)] catalyst 5 has unique capabilities. It facilitates simultaneous regio- and stereoselective isomerization of linear 1-alkenes to their internal analogues, providing consistent yields of (E)-2-alkenes greater than 95%. In addition, it displays a dramatic increase in reaction efficiency (>400 times faster) compared to previously published nitrile-containing analogues 2 + 2a **(Figure 2).**

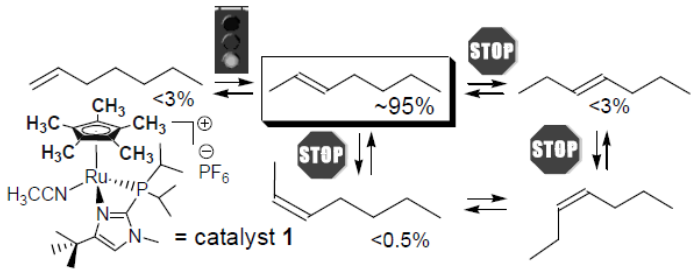

Figure 1. Catalytic control of monoisomerization of terminal alkenes

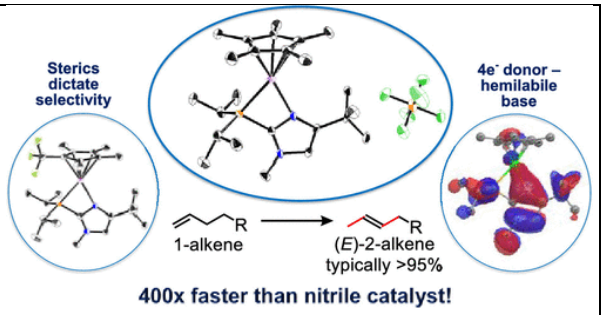

Figure 2. Cp*Ru catalyst 5

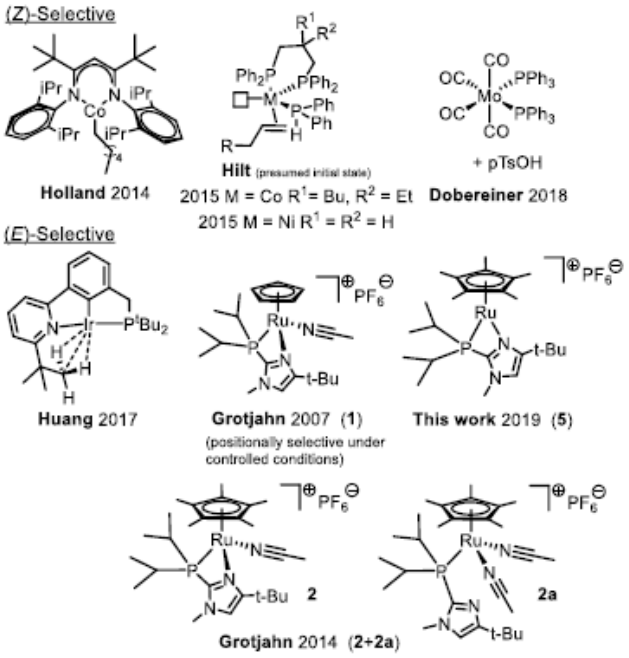

Chart 1. Geometric and Positionally Selective Alkene Isomerization Catalysts. Grotjahn 2007 (1), Grotjahn 2014 (2+2a), and "This work 2019 (5)" refer to the Catalysts 1, 2+2a, and Cp*Ru catalyst 5, respectively.

catalyst	mol %[a]	time (min)	temp (°C)	conv (%)	% 2-alkene	E/Z ratio	TOF (min^{-1})[b]
Holland 2014[7]	0.5	720	80	not listed	88[c]	1:5.3	>0.24
limited functional group tolerance							
Hilt 2015 (Co)[8a]	10	90	rt	95	92[d]	1:5.6	0.11
Hilt 2015 (Ni)[8b]	10	360	-60	90	72[e]	1:2.6	0.025
catalysts made from Ph_2PH, Zn, ZnI_2, and MX_2(dppb); Ni catalyst selectivity erodes at higher temperatures							
Dobereiner 2018[9]	0.5	30	66	94	92[c]	1:4.0	6.3
fast, good functional group tolerance, but slower in their presence and with longer alkenes							
Grotjahn 2007 (1)	0.1	15	rt	98	86[c]	>99:1	65
fast, excellent (E)-selectivity; lower positional selectivity							
Grotjahn 2014 (2+2a)	1	2880	40	98	96[c]	>99:1	0.034
excellent (E)- and monoselectivity, but slow							
Huang 2017[11]	0.1	480	rt	96	95[c]	25:1	2.0
fast, very (E)- and monoselective; alkenes distilled from $LiAlH_4$ in many cases							
this work (5)	0.1	180	rt	98	97[c]	>400:1	5.4
fast, very (E)- and monoselective, good functional group tolerance							

[a]All reactions were run between 0.5–1.0 M in substrate. [b]Calculated with conversions at indicated time point without factoring temperature. [c]2-Hexene. [d]2-Hexadecene. [e]2-Decene.

Table 1. Summary of Isomerization of Terminal Linear Alkenes with Selected Catalysts in Chart 1. Grotjahn 2007 (1), Grotjahn 2014 (2+2a), and "this work 2019 (5)" refer to the team's Catalysts 1, 2+2a, and Cp*Ru catalyst 5, respectively. UV−vis, NMR, and computational studies depict the imidazolyl fragment on the phosphine as a hemilabile, four-electron donor in κ2-P,N coordination.

Value Proposition

- This is the first direct experimental evidence that the PN ligand has accepted a proton from the substrate by characterizing the intermediate Cp*Ru[η3-allyl][κ1-P)P−N+H]. This emphasizes the vital role of the bifunctional ligand in promoting rapid and selective alkene isomerizations. Kinetic studies and computations reveal the role of alkene binding in selectivity of unsaturated catalyst 5.
- Direct evidence for reversible and highly positionally specific binding of alkenes as well as the first direct spectroscopic evidence of the pendent imidazole involved in proton transfer through an allyl intermediate.
- The ruthenium-bound imidazole ring engages in π-bonding, thus stabilizing the formally 16-electron Ru center of 5. The steric bulk of the Cp* ligand (and not its greater electron donation) is responsible for ***slowing the further positional isomerization.***

Advantages

- Control of the formation and chemistry of non-functionalized and functionalized alkenes
- Minimal thermodynamic equilibration of alkene isomers
- Effective control of the double-bond position and the molecular shape
- Faster and more efficient synthesis than existing catalysts
- No need for substrate control

Applications

- Fine chemical synthesis such as multistep natural product synthesis
- Manufacture of pharmaceuticals
- Creation of other high value compounds for use in industry and academia

Stage of Development

Catalyst engineering, characterization, and optimization completed

Intellectual Property

Issued U.S. Patent Number 9,708,236 – "Terminal alkene monoisomerization catalysts and methods"

Key publication

Paulson ER, Moore CE, Rheingold AL, Pullman DP, Sindewald RW, Cooksy AL and Grotjahn DB, "Dynamic π-Bonding of Imidazolyl Substituent in a Formally 16-electron Cp*Ru(κ2-P,N)+ Catalyst Allows Dramatic Rate Increases in (E)-Selective Monoisomerization of Alkenes," *ACS Catal*, 2019, 9, 7217−7231.

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