

Alkyne Metathesis based on Molybdenum and

Tungsten Alkylidyne Complexes

Speaker:Gengmu Li (李耕牧)Supervisors:Prof. Zhangjie Shi

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1. Introduction

Development of Molybdenum and Tungsten Alkylidyne Catalysts
 2.1. Monodentate Ligand (First and Second Generation)
 2.2. Multidentate Ligand (Third and Fourth Generation)

3. Application

4. Summary and Outlook





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Shape-persistent molecular architectures







Alkene metathesis? or Alkyne metathesis!



(c) Furstner, A., et al. Angew. Chem. Int. Ed. 2013, 52, 355; (d) Furstner, A., et al. Chem. Commun. 2002, 18, 2182.

Introduction

Representative Homogeneous Alkyne Metathesis Catalysts



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復旦大學





Reactions of alkylidynes with alkynes









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Initial Exploration and Limitation



Schrock 1981



The remarkable Lewis acidity of W made this complex incompatible with substrates containing heteroatoms such as nitrogen heterocycles, divalent sulfur, and carbonyl-containing substrates, like ketones and aldehydes

(a) Mortreux, A., et al. Chem. Commun. 1974, 4, 786; (b) Brizius, G., et al. J. Am. Chem. Soc. 2000, 122, 12435; (c) Wengrovius, J.H., et al. J. Am. Chem. Soc. 1981, 103, 3932.

First Generation Catalyst with Amido Ligand



Fürstner 1999



An important modification by Moore in 2004



(a) Fürstner, A., et al. J. Am. Chem. Soc. 1999, 121, 9453; (b) Moore, J. S., et al. J. Am. Chem. Soc. 2004, 126, 329.

First Generation Catalyst with Amido Ligand





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(a) Fürstner, A., et al. J. Am. Chem. Soc. 1999, 121, 9453; (b) Fürstner, A., et al. Chem.-Eur. J. 2001, 7, 5299; (c) Fürstner, A., et al. Org. Lett. 2001, 3, 221.

First Generation Catalyst with Amido Ligand





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(a) Moore, J. S., et al. J. Am. Chem. Soc. 2004, 126, 329; (b) Moore, J. S., et al. Chem. Commun. 2003, 7, 832; (c) Moore, J. S., et al. J. Am. Chem. Soc. 2018, 140, 5825.

Catalyst with Alkoxy Ligand







7 will form stable metallacyclobutadiene (MCBD)

Tamm, M., et al. Angew. Chem. Int. Ed. 2012, 51, 13019.

Catalyst with Alkoxy Ligand





Catalyst with Alkoxy Ligand





(a) Tamm, M., et al. Angew. Chem. Int. Ed. 2007, 46, 8890; (b) Tamm, M., et al. Chem. Eur. J. 2010, 16, 8868;
(c) Schrock, R. R., et al. Angew. Chem. Int. Ed. 2003, 42, 4555; (d) Tamm, M., et al, Org. Biomol. Chem. 2007, 5, 523.

Second Generation Catalyst with Silanol Ligand 領部 復史大學



Commercially available

(a) Fürstner, A., et al. J. Am. Chem. Soc. 2009, 131, 27, 9468; (b) Fürstner, A., et al. J. Am. Chem. Soc. 2010, 132, 11045.

Beneficial Effect of 5Å Molecular Sieves





Fürstner, A., et al. J. Am. Chem. Soc. 2010, 132, 11045.

Second Generation Catalyst with Silanol Ligand (復興) 復興大學



Fürstner, A., et al. J. Am. Chem. Soc. 2010, 132, 11045.







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Drawbacks of the Monodentate Ligand ——Small Alkyne Polymerization





Zhang, W., et al. Angew. Chem. Int. Ed. 2011, 50, 8478.





Multidentate Catalyst System:

- (1) stronger complexation;
- (2) spatial blocking of binding site inhibits the undesired alkyne polymerization.









The N-Mo coordination would lower the catalyst activity by increasing the electron density on the Mo center

(a) Zhang, W., et al. Adv. Synth. Catal. 2012, 354, 2073; (b) Zhang, W., et al. Adv. Synth. Catal. 2013, 355, 885; (c) Schrock, R. R., Chem. Rev. 2002, 102, 145.







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(a) Zhang, W., et al. Adv. Synth. Catal. 2012, 354, 2073; (b) Zhang, W., et al. Adv. Synth. Catal. 2013, 355, 885.





Zhang, W., et al. Nat Commun. 2021, 12, 1136.

а



Fourth Generation— "Canopy Catalysts"



🛇 C1

01

Si1

02

03



Only sp²-hybridized C atoms reduces the degrees of conformational freedom.

Ar

Ph

Ph

Ph

Preorganized structure shows a cyclic array of hydrogen bonds between -Si-OH units.

(a) Furstner, A., et al. Angew. Chem. Int. Ed. 2019, 58, 15690; (b) Furstner, A., et al. J. Am. Chem. Soc. 2020, 142, 11279.

Fourth Generation— "Canopy Catalysts"





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(a) Furstner, A., et al. Angew. Chem. Int. Ed. 2019, 58, 15690; (b) Furstner, A., et al. J. Am. Chem. Soc. 2020, 142, 11279.

New Air-Stable Alkylidyne Catalysts





Furstner, A., et al. J. Am. Chem. Soc. 2023, 145, 26993.

New Air-Stable Alkylidyne Catalysts









Only trace impurities caused by hydrolysis



(a) Furstner, A., et al. J. Am. Chem. Soc. 2023, 145, 26993; (b) Buchmeiser, M. R., et al. Eur. J. Inorg. Chem. 2023, 26, 649

Rational Design of the Catalysts





Appropriate ligands can regulate the Lewis acidity of the metal center, allowing both processes to proceed smoothly



pKa values (in DMSO) of selected ROH and amines, and general reactivity of $M(\equiv CR)X_3$ (M = Mo, W) with the alkyne EtC \equiv CEt at ambient temperature.

(a) Furstner, A., et al. J. Am. Chem. Soc. 2022, 143, 15538; (b) Jia, G., et al. J. Am. Chem. Soc. 2022, 144, 12546; (c) Neese, F., et al. ACS Catal. 2021, 11, 9086.

Intermediate of Alkyne Metathesis Catalysts





Surprising Metallatetrahedrane Complex







Furstner, A., et al. J. Am. Chem. Soc. 2021, 143, 5643.

Tautomerization Between A and B







Tautomerization Between C and D





Furstner, A., et al. J. Am. Chem. Soc. 2021, 143, 5643.





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Total Synthesis of Neurymenolide A





Furstner, A., et al. Angew. Chem., Int. Ed. 2012, 51, 6929.

Total Synthesis of Casbane Diterpenes





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(a) Furstner, A., et al. Angew. Chem., Int. Ed. 2015, 54, 6241; (b) Furstner, A., et al. Angew. Chem., Int. Ed. 2021, 60, 5316.

Total Synthesis of Amphidinolide F





Polysubstituted diyne 40 have three free hydroxyl-group. "Canopy Catalyst" 22 successfully gave the ring closure product 41, while catalyst 12 fail to accomplish this process.

(a) Furstner, A., et al. Angew. Chem., Int. Ed. 2013, 52, 9534; (b) Furstner, A., et al. Chem.-Eur. J. 2015, 21, 2398.

Total Synthesis of Njaoamine C



Grubbs catalyst only Grubbs cat, CH₂Cl₂, reflux gave 10-20% of the monocyclized compound \mathbf{O} 50 and 1-2% of 51 49 **50** (10 - 20%) **51** (1 - 2%) **22** (20 mol%), 5 steps MS 5Å, toluene, 60 °C 29% Mes 91% OBoc 0-1 Ph **BocHN** Ph Ph H_2N^{-1} 52 ·ОН 54 53 22 **NHBoc** (-) Njaoamine C `^{OBoc} 42

Furstner, A., et al. J. Am. Chem. Soc. 2023, 145, 21197.

Mobius Tris((ethynyl)[5]helicene) Macrocycle







Synthesis of Cycloparaphenyleneacetylene





Moore, J. S., et al. J. Am. Chem. Soc. 2016, 138, 13814.

Rectangular Prism





Zhang, W., et al. J. Am. Chem. Soc. 2011, 133, 51, 20995.





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• The current inability to perform reactions in water or other protic media and the still largely missing compatibility with strongly acidic groups.

• Compared with alkyne metathesis, metathesis reactions of alkylidynes with heterotriple bonded species are less known and worth more exploration.











Thanks

Supporting Information





Supporting Information





