

Bimetallic Cooperative Dual Catalysis

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INTRODUCTION

Within the broad field of catalysis, the phenomenon of cooperative dual catalysis, whereby two substrates are coupled together through *separate activation by two distinct catalysts* (Figure 1), has

recently shown great promise as a synthetic method. Such systems have attained useful reactivity unattainable

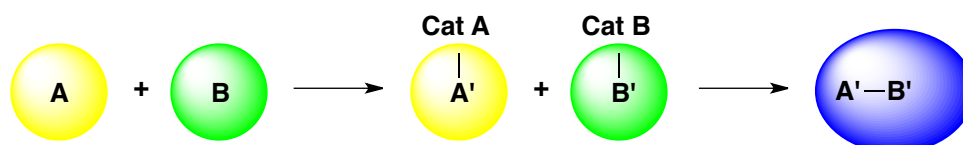


Figure 1: Cooperative Dual Catalysis

with a single catalyst. This Seminar will focus on recent examples involving two distinct metal catalysts. It will highlight advantages to using such systems as well as distinct challenges that were overcome in their development.

CONJUGATE ADDITION OF CYANIDE

Jacobsen has shown that the aluminum(salen)-catalyzed conjugate cyanation of α,β -unsaturated imides can be accomplished more efficiently using a combination of aluminum(salen) and erbium(pybox) complexes than with simply aluminum(salen) alone.¹ Investigation into the source of stereoselectivity for the reaction revealed that both complexes contribute to the reaction's overall enantioselective nature.

CROSS-COUPLING

A classic example of cooperative dual catalysis is the Sonagashira cross-coupling, in which an aryl halide is connected to a terminal alkyne, first activated by a copper catalyst, via a palladium-catalyzed cross-coupling mechanism.² Recent advances by Gooßen and coworkers have shown the utility of a Pd- and Cu-catalyzed coupling of aryl halides and benzoic acids.³ Additionally, bimetallic catalysis has expanded the scope of cross-coupling reactions to include bifunctionalization of arenes and the direct arylation of heteroarenes.^{4,5} These reactions all adopt the strategy of generating an appropriate transmetalation partner for the palladium catalyst.

ALLYLATION

Bimetallic cooperative dual catalysis has shown great promise in the field of selective allylation by harnessing the power of the versatile palladium π -allyl intermediate, which can be generated *in situ* in a reliable, catalytic fashion and captured by an activated nucleophile. Ito and coworkers reported an enantioselective allylic alkylation of rhodium-activated nitriles, where only the rhodium catalyst is

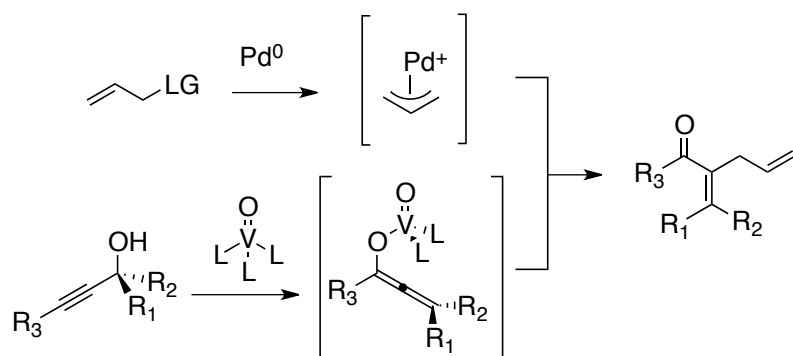


Figure 2: α -allylated- α,β -unsaturated ketones via two catalytic intermediates

vanadium-catalyzed rearrangement of propargylic alcohols followed by allylic substitution (Figure 2); this transformation successfully outcompetes the side reactions for both catalytically-generated intermediates.⁸

SUMMARY

Cooperative dual catalysis involving two metal catalysts is a powerful synthetic strategy capable of offering improvements to existing reactions and, in some cases, novel reactivity. Such methods overcome inherent challenges like catalyst compatibility and key intermediate concentrations. More examples of this exciting strategy can be expected in the future.

REFERENCES

- ¹ Sammis, G.M.; Danjo, H.; Jacobsen, E.N. *J. Am. Chem. Soc.* **2004**, *126*, 9928-9929.
- ² Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467-4470.
- ³ Gooßen, L.J.; Deng, G.; Levy, L.M. *Science*, **2006**, *313*, 662-664.
- ⁴ Jeganmohan, M.; Bhuvaneshwari, S.; Cheng, C-H. *Angew. Chem. Int. Ed.* **2009**, *48*, 391-394.
- ⁵ a.) Huang, J.; Chan, J.; Chen, Y.; Borths, C.J.; Baucom, K.D.; Larson, R.D.; Faul, M.M. *J. Am. Chem. Soc.* **2010**, *132*, 3674-3675. b.) Tan, Y.; Barrios-Landeros, F.; Hartwig, J.F. *J. Am. Chem. Soc.* **2012**, *134*, 3683-3686.
- ⁶ Sawamura, M.; Sudoh, M.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 3309-3310.
- ⁷ Shi, Y.; Roth, K.E.; Ramgren, S.D.; Blum, S.A. *J. Am. Chem. Soc.* **2009**, *131*, 18022-18023.
- ⁸ a.) Trost, B.M.; Luan, X. *J. Am. Chem. Soc.* **2011**, *133*, 1706-1709. b.) Trost, B.M.; Luan, X.; Miller, L. *J. Am. Chem. Soc.* **2011**, *133*, 12824-12833.

responsible for determining the product's enantioselectivity.⁶ Blum and coworkers demonstrated an impressive synthesis of butenolides and isocumarins via gold-catalyzed rearrangement and attack of a palladium π -allyl electrophile.⁷

Additionally, Trost and coworkers reported an especially clever