

Asymmetric Intermolecular Cobalt-Catalyzed Pauson–Khand Reaction Using a P-Stereogenic Bis-phosphane

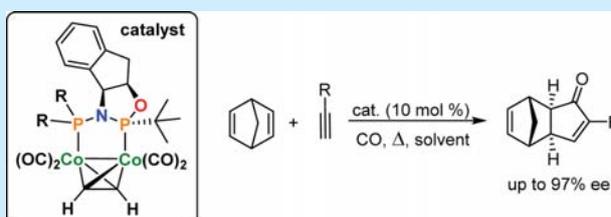
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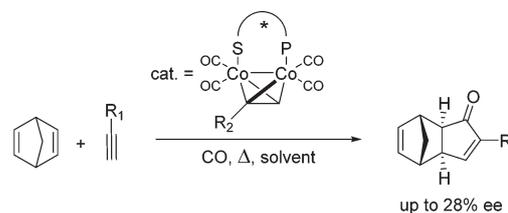
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Supporting Information

ABSTRACT: The asymmetric intermolecular and catalytic Pauson–Khand reaction has remained an elusive goal since Khand and Pauson discovered this transformation. Using a novel family of P-stereogenic phosphanes, we developed the first catalytic system with useful levels of enantioselection for the reaction of norbornadiene and trimethylsilylacetylene. The results demonstrate that Co–bisphosphane systems are sufficiently reactive and that they lead to high selectivity in the intermolecular process.



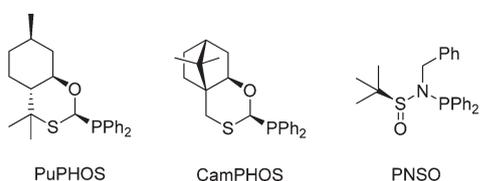
Scheme 2. PKR Reaction between Norbornadiene and Terminal Alkynes Catalyzed by P,S-Co₂-Alkyne Complexes



The Pauson–Khand reaction (PKR), disclosed in 1973, has become a textbook method for the synthesis cyclopentanic compounds.¹ The intramolecular PKR has been widely used in the syntheses of highly complex polycyclic compounds.² Although the intermolecular process has the great advantage of being able to rapidly assemble simple building blocks (alkyne, alkene, and CO) into valuable cyclopentenones, it has been less exploited in synthesis. Nevertheless, our group and others have reported several total syntheses of biologically active compounds using the intermolecular PKR as a key step, thus showing its value in synthesis.³ While several effective catalytic systems have been developed for the asymmetric intramolecular PKR, this goal remains elusive for the intermolecular process.^{4,5}

Over the past two decades, we have developed several Co₂-ligand systems (e.g., PuPHOS, CamPHOS, and PNSO) that provide excellent selectivity (up to 99% ee) in the enantioselective stoichiometric intermolecular PKR (Scheme 1).⁶

Scheme 1. Hemilabile P,S-Ligands Used in the Asymmetric Intermolecular Pauson–Khand Reaction



However, when these ligands are applied to the catalytic reaction, the selectivity drops dramatically. The Co-catalyzed PKR between norbornadiene (NBD) and a bulky propiolamide using CamPHOS ligand provides the corresponding PKR product in only 28% ee (Scheme 2).⁷ We attributed this lack of selectivity to the hemilabile nature of these ligands, which were

unable to maintain the original bridged disposition on the Co₂-alkyne core under the required CO atmosphere.

Chiral bis-phosphanes do not have this limitation; however, they have barely been explored in this process because double-phosphane substitution in Co₂ complexes usually results in impaired reactivity.⁸ One of the few exceptions is the report of Gimbert and co-workers in which the stoichiometric PKR of a binol-derived bisamidophosphinite–Co₂-alkyne complex with norbornene proceeded in excellent yield, although with poor selectivity (17% ee) (Scheme 2).⁹

Inspired by this report, we envisaged the feasibility of an asymmetric catalytic system bearing an aminodiphosphane ligand. The challenge was to improve the stereocontrol without reducing the reactivity. In this respect, a ligand system with a large steric bias was required. We considered oxazaphospholidine **1** (Scheme 3), which we had previously developed in the context of P-stereogenic phosphane synthesis,¹⁰ was ideally suited for this purpose since it could be further derivatized to yield a novel family of C₁-symmetric bis-phosphane ligands with a bulky *tert*-butyl group on one of the phosphorus atoms. Here, we report on the synthesis of the ThaxPHOS family of ligands and how the use

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