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Mechanistic insight into cobalt-catalyzed stereodivergent semihydrogenation of alkynes: The story of selectivity control ☆

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ABSTRACT

Selectivity control is a challenging and important subject in semihydrogenation of alkynes. Here, a combined theoretical and experimental study was performed to reveal the origin of the chemo- and stereoselectivity in cobalt-catalyzed stereodivergent semihydrogenation of alkynes. Three NNP and PNP type pincer ligands were considered in calculation. The computational results show that over-reduction of the alkene is forbidden in this catalytic system because the alkylcobalt(I) intermediate formed by alkene insertion prefers to undergo *β*-H elimination rather than protonation of the Co—C bond. Distortion–interaction analysis along the reaction coordinate suggests that the higher distortion energy during methanol-mediated protonation of the alkylcobalt(I) species suppresses formation of the side product, thereby determined the chemoselectivity. Mechanistic investigation reveals that the active cobalt(I) hydride species formed by pre-catalyst [**C**] has strong catalytic activity for alkene isomerization. Subsequent control experiments combined with free energy comparison confirms this conclusion and reveals that fast deactivation of catalyst and the weaker reactivity of the cis-alkene intermediate in the presence of the alkyne substrate prevents *Z*/*E* alkene isomerization using pre-catalyst [**C**]. This results in the divergent stereoselectivity in the presence of different cobalt pincer complexes.

1. Introduction

Semihydrogenation of alkynes is a practical strategy for synthesis of alkenes [1]. This transformation has been widely used to construct various natural products and medicinal molecules that require specific *Z* or *E* configurations of the carbon–carbon double bonds [2]. A significant amount of effort has been devoted to investigating semihydrogenation of alkynes [3]. For example, using the Lindlar catalyst [4] with H_2 gas can give (*Z*)-alkenes in good regioselectivity [5]. Furthermore, more challenging (*E*)- selective hydrogenation of alkynes has also been realized [6]. Several environmentally benign catalytic approaches have been reported as alternatives to the classical Birch-type reduction [7] of alkynes using alkali metals (Li, Na) in liquid ammonia. The pioneering work of Fürstner's group achieved *in situ* generation of active catalytic species from [Cp * RuCl(cod)] and AgOTf under hydrogen pressure [8]. Milstein and co-workers also prepared an imino borohydride iron pincer complex for the (*E*)-selective semihydrogenation of alkynes [9]. In addition, Mankad and co-workers reported innovative bimetallic cooperativity of an (NHC)Ag-RuCp$(CO)_2$ complex [10] that exhibits good activity for this transformation. We recently report cobalt-catalyzed stereodivergent transfer hydrogenation of alkynes to (*Z*)- and (*E*)-alkenes with good chemo- and stereoselectivity [11]. Fout's group subsequently developed an (*E*)-selective alkyne semihydrogenation reaction using a well-defined nonclassical Co—H_2 catalyst and H_2 gas as the hydrogen donor [12].

With the impressive progress from an experimental viewpoint, theoretical investigation of alkyne semihydrogenation has emerged as an important research area [13]. Semihydrogenation of alkynes always encounters two problems: control of the *E*/*Z* selectivity of the alkenes [14] and undesired over-reduction of the alkenes to alkanes [15]. Clarifying the rationale behind these phenomena by theoretical investigation would help to resolve the above two problems and also provide practical guidance for rational design of alkyne hydrogenation catalysts. In a mechanistic study of [Cp * Ru] complex catalyzed trans-hydrogenation of internal alkynes by a combination of density functional theory (DFT) calculations and para-hydrogen induced polarization transfer NMR spectroscopy, Fürstner [16] revealed that olefin isomerization

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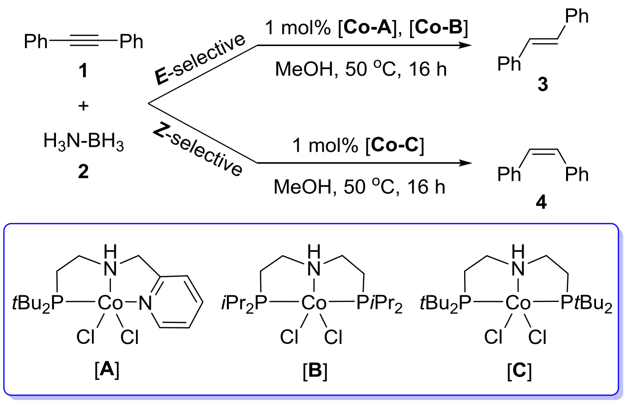
and over-reduction are derived from a ruthenium carbenoid. This special metal carbenoid intermediate was determined to be the key factor for understanding the chemoselectivity and side reaction. The computational results provided mechanistic insight and paved the way for subsequent experimental optimization [17], which is important for alkyne semihydrogenation.

We recently designed a series of NNP and PNP pincer cobalt catalysts that are effective for stereodivergent semihydrogenation of alkynes to (*E*)- and (*Z*)-alkenes (Scheme 1) [11]. This catalytic system exhibits excellent stereoselectivity when a specific dichloride cobalt pincer complex is used with no over-reduction products of the alkenes. From a mechanistic point of view, the (*E*)-alkene is generated by alkyne insertion, protonation of the Co—C(sp^2) bond, and isomerization of the (*Z*)-alkene (Scheme 2). It is noteworthy that protonation of the Co—C(sp^3) bond might occur during the *Z*/*E* isomerization process, which would lead to formation of an alkane and interfere with the expected isomerization step. Although our catalytic system avoids this side reaction, the cause of this chemoselectivity deserves further investigation. Moreover, both pre-catalysts [**A**] and [**B**] give the (*E*)-alkene as the main product, while replacing the isopropyl group in [**B**] by the tertiary butyl group changes the stereoselectivity to the (*Z*)-alkene. The steric effect of the ligands plays a significant role in the selectivity control, although the origin of the stereoselectivity remains unclear (Scheme 2). In this study, DFT calculations were performed to investigate cobalt-catalyzed stereodivergent semihydrogenation of alkynes to reveal the complete story of selectivity control by combining theoretical calculations with experiments.



Scheme 1. Stereodivergent transfer semihydrogenation of alkynes using cobalt pincer complexes.

2. Computational methods

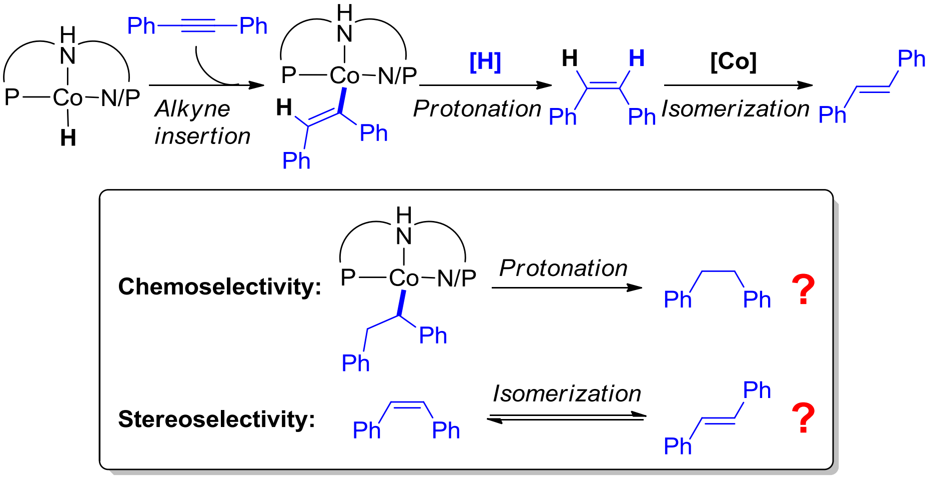
All the DFT calculations were performed with the Gaussian 09 series of programs [18]. The B3LYP functional [19] with the standard 6-31G(d) basis set (SDD [20] basis set for Co) was used for geometry optimization in the gas phase. Harmonic vibrational frequency calculations were performed for all of the stationary points to determine whether the points are local minima or transition structures and to derive the thermochemical corrections for the enthalpies and free energies. The solvent effect was considered by single point calculations of the gas-phase stationary points using the SMD continuum solvation model [21]. The M06 functional [22] with the 6-311 + G(d,p) basis set (SDD basis set for Co) was used to calculate the solvation single point energies in methanol solvent to provide more accurate energy information. The Gibbs free energies of the stationary points calculated using the M06 functional are used to discuss the energies.

3. Results and discussion

3.1. Stability of ammonia borane in methanol

Ammonia borane was used as the hydrogen source. This complex is a potential hydrogen storage material because of its high gravimetric hydrogen capacity (19.6 wt%) [23]. Despite its interesting properties, research into the use of ammonia borane [24] in transfer hydrogenation of alkynes is rare compared with other widely used hydrogen donors, such as isopropanol and formic acid [25]. Thus, the reactivity and protonation mechanism of ammonia borane in alkyne hydrogenation reactions require in-depth investigation. Deuterium labeling experiments have found that one hydrogen atom of the alkene product comes from methanol [11]. In this study, the reaction of ammonia borane with methanol was investigated by DFT.

The computational results (Fig. 1a) show that S_N2 attack of ammonia borane by methanol could occur via transition state **6-ts**, leading to formation of $MeOH–BH_3$ **8** with concomitant release of ammonia. However, the activation free energy of this process is 28.2 kcal/mol and formation of **8** is endergonic by 15.9 kcal/mol, so this process is both kinetically and thermodynamically unfavorable. Thus, $MeOH–BH_3$ most likely does not form. The stability of ammonia borane was also considered. As



Scheme 2. Questions about the selectivity control in pincer cobalt-catalyzed alkyne semi-hydrogenation.