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Copper(I)-catalyzed stereoselective hydrogenation of 1,3-diynes and enynes

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ABSTRACT

A stereoselective hydrogenation of 1,3-diynes with an air-stable copper(I)/N-heterocyclic carbene complex, [IPrCuOH], has been developed. The corresponding products, 1,3-dienes, are obtained in a stereoselective manner depending on their substitution pattern: Diaryl-diynes yield *E,E*-1,3-dienes, whereas dialkyl-diynes are converted to the corresponding *Z,Z*-1,3-dienes. Hydrogenation and deuteration experiments with enynes indicate that these are competent reaction intermediates in the hydrogenation of diynes.

1. Introduction

The catalytic hydrogenation of 1,3-diynes can be employed to stereoselectively generate 1,3-dienes, given a suitable hydrogenation catalyst is at hand. Although a plethora of homogeneous hydrogenation catalysts for a wide variety of functional groups is known,[1] surprisingly few reports on the hydrogenation of 1,3-diynes have been disclosed.[2–4] Among these, the use of the Lindlar catalyst (heterogeneous palladium, poisoned with lead additives[5]) has been most prominent, delivering the corresponding *Z,Z*-1,3-dienes.[2,6] However, (semi)hydrogenations with the Lindlar catalyst are frequently plagued by overreduction to the corresponding alkanes and *E/Z*-isomerization of the desired alkenes.[7]

With foresight to the use of more abundant metal catalysts for catalytic hydrogenation,[8] we[9] and others[10] have investigated the use of copper(I) complexes for catalytic semihydrogenation of alkynes. Specifically, the use of copper(I) complexes with oxygen-[9a] and nitrogen-tethered[9c] N-heterocyclic carbene (NHC) ligands have led to chemo- and stereoselective catalysts for the generation of *Z*-alkenes from internal alkynes. In this vein, our group has introduced a copper(I)/NHC hydroxide complex, [IPrCuOH],[11,12] as effective and air-stable catalyst for *Z*-stereoselective alkyne semihydrogenations.[9b,13]

Herein, we disclose our systematic study of copper(I)-catalyzed hydrogenation of 1,3-diynes to 1,3-dienes. We could establish that with the air-stable [IPrCuOH] complex, diaryl-substituted 1,3-diynes are converted to the corresponding *E,E*-1,3-dienes, a stereoselectivity opposite to the one found with isolated alkynes with the same catalyst. Furthermore, this stereoselectivity is contrary to the one generally observed when employing the Lindlar catalyst on 1,3-diynes. On the other hand, dialkyl substituted 1,3-diynes are converted to the *Z,Z*-1,3-dienes (Scheme 1).

2. Results and discussion

Under reaction conditions optimized previously (80 bar H_2, THF, 40 °C, 5 mol-% [IPrCuOH]),[9b] we found that diphenyl-substituted 1,3-diyne **1** was converted stereoselectively to *E,E*-**2** (Scheme 2). This result underscored the particular chemoselectivity of [IPrCuOH] as hydrogenation catalyst, as other copper(I) complexes have failed to give a selective hydrogenation of 1,3-diynes.[10a] Also, our previously reported catalyst system gave a mixture of products with **1** under otherwise identical reaction conditions.[9c]

To probe whether this particular reversal of stereoselectivity towards the *E,E*-diene was general, we prepared a variety of diaryl-1,3-diynes **3** and subjected them to hydrogenation conditions with

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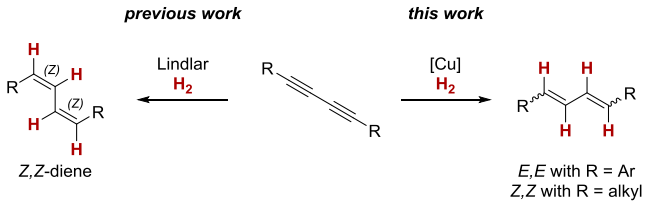
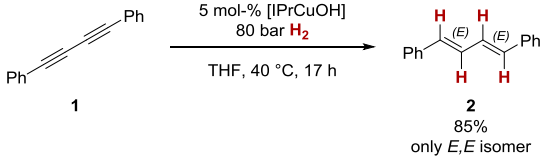
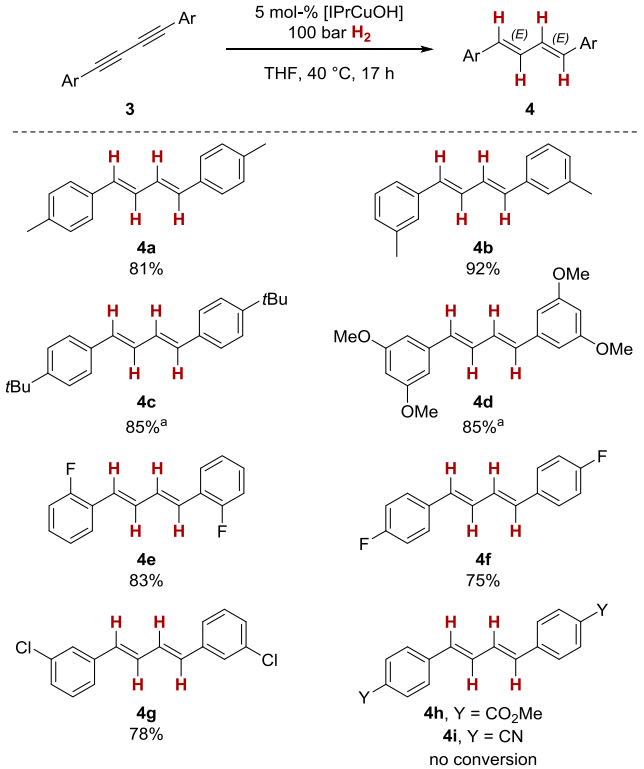


Scheme 1. Catalytic hydrogenation of 1,3-diynes to 1,3-dienes.



Scheme 2. Cu(I)-catalyzed hydrogenation of 1,4-diphenyl-1,3-butadiyne.

5 mol-% [IPrCuOH] as catalyst (Scheme 3). We found that to generally ensure full conversion of the starting materials **3**, the dihydrogen (H_2) pressure had to be raised to 100 bar. In all cases, high *E,E*-selectivity for the corresponding products **4** was detected. Electron-rich diynes bearing alkyl or methoxy substituents **3a**-**3d** were converted to the corresponding *E,E*-1,3-dienes **4a**-**4d** with generally high yields (81%–92%). To achieve full conversion of the latter (**3c** and **3d**), the catalyst loading had to be raised to 10 mol-%. Electronic factors seem to be non-interfering for the catalytic hydrogenation protocol, as electron-poor 1,3-dienes **4e**-**4g** were also obtained with similarly high yields and stereoselectivity. No conversion was observed with benzoic ester derivative **3h** and bis-nitrile **3i**, this is most probably due to their insolubility in THF.



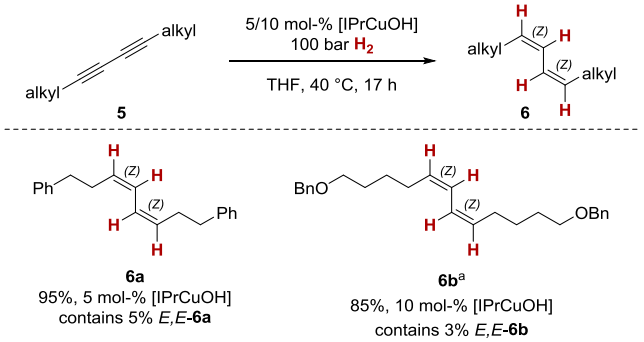
Scheme 3. Cu(I)-catalyzed hydrogenation of diaryl-1,3-butadiynes, substrate scope. [a]10 mol-% [IPrCuOH] were used.

When dialkyl-substituted 1,3-butadiynes **5** were used as substrates for the copper(I)-catalyzed hydrogenation, we observed that in the absence of an aryl substituent on the alkyne a reversal of stereoselectivity towards the *Z,Z*-1,3-dienes **6** took place. This high *Z*-selectivity now resembles the case of copper(I)-catalyzed semi-hydrogenation of simple internal alkynes[9] and that of hydrogenation of 1,3-diynes with the Lindlar catalyst:[2] With 5 mol-% [IPrCuOH] at 100 bar H_2, *Z,Z*-**6a** was isolated in excellent yield of 95%. Similarly, *Z,Z*-**6b** could be furnished in 85%, albeit with a higher catalyst loading to ensure full conversion. In both cases, the amount of *E,E*-isomers was negligible (5% and 3%, respectively).

Configurations of the products **4** and **6** (Schemes 3 and 4) were determined by the three bond indirect coupling constants between the hydrogen atoms. Because the products **4a-4g** possess AA'MM′ spin systems in the center of the molecules due to their symmetry, analysis through spin simulations were necessary to extract these three bond coupling constants.[14] In the case of **6a** and **6b** the even more complex spin systems were simplified by homonuclear decoupling experiments with irradiation on the aliphatic positions next to the double bonds. In such a way, AA'MM′ spin systems could be observed in these experiments as well and subsequently analyzed with spin simulations instead of the original ^{1}H NMR spectra.[14]

The marked difference in stereoselectivity of diaryl vs. dialkyl substituted diynes lead us to the hypothesis that the aryl substituents on the diyne starting materials **1** and **3** facilitates an isomerization process ultimately furnishing the thermodynamically more stable *E,E*-1,3-dienes.

To shed light on a possible isomerization mechanism, a series of experiments with enynes **7** to **9**, putative reaction intermediates in the hydrogenation of 1,3-diynes, were carried out (Scheme 5). We observed that the alkene geometry of the enyne (as in **7** or **8**) has a marked effect on the stereoselectivity for the following step towards the 1,3-dienes. Whereas *Z*-enyne **7** selectively gave *E,E*-diene **2**, the corresponding *E*-enyne **8** produced the *E,Z*-enyne **2** under standard hydrogenation conditions.[9b] However, in the latter reaction, the stereoselectivity showed a dependence on the H_2 pressure: Raising the pressure to 100 bar H_2 led to the formation of a mixture of *E,Z*-**2** and *E,E*-**2** (62: 38, full conversion of **8**). This indicated that under the reaction conditions and elevated H_2 pressure, an isomerization process of *E,Z*-**2** to *E,E*-**2** can occur. Viewing the abovementioned reactions of the enyne isomers as a whole, we propose that *Z*-enynes such as **7** are viable intermediates in the diyne hydrogenation towards *E,E*-dienes such as **2**. In this case, the conversion/putative isomerization towards the *E,E*-diene is fast. On the contrary, emanating from the *E*-enyne **8**, a mixture of 1,3-diene stereoisomers was found, which does not correspond to the high *E,E*-selectivity observed in the abovementioned cases of diaryl-1,3-



Scheme 4. Cu(I)-catalyzed hydrogenation of dialkyl-1,3-butadiynes. [a]Reaction was carried out at 90 bar H_2.