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Copper(I)-catalysed transfer hydrogenations with ammonia borane[†]

Eva Korytiaková, Niklas O. Thiel, Felix Pape and Johannes F. Teichert*

Highly Z-selective alkyne transfer semihydrogenations and conjugate transfer hydrogenations of enoates can be effected by employing a readily available and air-stable copper(I)/N-heterocyclic carbene (NHC) complex, [IPrCuOH]. As an easy to handle and potentially recyclable H₂ source, ammonia borane (H₃NBH₃) is used.

Ammonia borane (H₃NBH₃), an easy to prepare and manipulate solid, has attracted interest as a potential dihydrogen (H₂) storage material.¹⁻⁶ Based on the fact that ammonia borane dehydrogenation products (*e.g.*, borazines and polyiminoboranes) can potentially be recycled,⁷ and its exceptionally high H₂ content, many studies have been directed toward controlled catalytic release of H₂ (dehydrocoupling) from ammonia borane.^{1-6,8} Notably, to a much lesser extent has H₃NBH₃ been employed as a reagent for synthesis, for example in the reduction of functional groups or transfer hydrogenations.⁹⁻¹¹

Copper(1) hydride complexes have emerged as powerful catalysts for a wide variety of reductive transformations, generally relying on silanes^{12–15} or, to a much lesser extent, on tin hydrides¹⁶ or dihydrogen^{17,18} (Scheme 1). These terminal reducing agents differ conceptually: Si- and Sn-based compounds will deliver a hydride equivalent and the reaction products remain silylated or stannylated until hydrolysis or protonation. On the other hand, reactions with H₂ can directly deliver the hydride and proton equivalent, circumventing the need for an additional proton source and reducing the waste generated in these processes. As an example, copper(1)-catalysed alkyne semihydrogenations have recently demonstrated the potential replacement of silanes with H₂.^{18–20} However, most of these procedures require elevated H₂ pressure and/or have a limited substrate scope.

On the other hand, homogeneous transfer hydrogenations with copper catalysts are scarce,^{21,22} but circumvent the need



Scheme 1 Hydride and dihydrogen sources employed for copper(i) hydride catalysis.

for high pressure equipment. Given the synthetic utility of copper hydride complexes, we decided to investigate ammonia borane as a reagent for copper-catalysed transfer hydrogenations.

We decided to optimise the copper(1)-catalysed transfer hydrogenation with H₃NBH₃ employing alkyne transfer semihydrogenation of pentynol-derived alkyne 1 as a test reaction (Table 1).²³ Due to the reported reactivity with H_{21}^{18-20} we chose well-defined copper(I)/NHC complexes bearing a copper-oxygen bond as the starting point for our studies. With a copper(1) tertbutanolate complex, generated in situ from [IMesCuCl] and NaOtBu, we observed no turnover to the corresponding alkene Z-2 at room temperature, but full conversion at 50 °C (Table 1, entries 1 and 2). A similar trend was observed with a copper(1) hydroxide/NHC complex, [IPrCuOH],18b,24,25 which also underwent full conversion to Z-2 at 50 °C (Table 1, entries 3-5). Increasing the temperature further to 60 °C led to diminished conversion of 60% (Table 1, entry 6). The use of [IPrCuOH] is particularly attractive, as it does not require the generally common in situ preactivation (to give activated copper(1) alkoxide complexes) and is air-stable for months. It should be noted that in all cases excellent Z-selectivity and negligible overreduction to the corresponding alkane 3 were maintained. This is synthetically

Institut für Chemie, Technische Universität Berlin, Strasse des 17. Juni 115, 10623 Berlin, Germany. E-mail: johannes.teichert@chem.tu-berlin.de; Fax: +49 30 314 28829; Tel: +49 30 314 22791

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ntry	Conditions	Conv. ^{<i>a</i>} [%]	$Z-2/E-2/3^{a}$
	[IMesCuCl], 7.5 mol% NaOtBu, 3 equiv. of H ₃ NBH ₃ , THF, rt, 16 h	_	_
	[IMesCuCl], 7.5 mol% NaOtBu, 3 equiv. of H ₃ NBH ₃ , THF, 50 °C, 16 h	>99	>99:0:0
	[IPrCuOH], 3 equiv. of H ₃ NBH ₃ , THF, rt, 16 h	9	>99:0:0
	As entry 3, 40 °C	68	>99:0:0
	As entry 3, 50 °C	>99	>99:0:0
	As entry 3, 60 °C	60	>99:0:0
	As entry 5, in C_6H_6	18	>99:0:0
	As entry 5, in CH_2Cl_2	6	n.d.
	[IPrCuOH], 3 equiv. of H ₃ NBH ₃ , THF, 50 °C, 4 h	$> 99^{c}$	>99:0:0
b	[IPrCuOH], 2 equiv. of H ₃ NBH ₃ , THF, 50 °C, 4 h	88	>99:0:0
	[IPrCuOH], 20 mol% H ₃ NBH ₃ , 1 bar H ₂ , THF, 50 °C, 16 h	20	>99:0:0
Determined	by ¹ H NMR and GC analysis. ^b Slow addition of H ₃ NBH ₃ in THF solution over 3 h. ^c	Isolated yield: 96%.	

appealing, as alkyne semihydrogenations are commonly carried out with heterogeneous palladium catalysts which generally suffer from these particular limitations.²⁶ Furthermore, another report of alkyne transfer semihydrogenation with copper catalysts does not give turnover with internal alkynes,^{21c} which underscores the orthogonal reactivity of the present catalyst.²⁷

The use of THF as a solvent proved to be optimal, as the reactions in benzene and dichloromethane under otherwise similar reaction conditions gave lower conversion of 1 (Table 1, entries 7 and 8). At the onset of the described reactions in THF, gas evolution (most likely H₂) was observed, accompanied by a relatively slow reaction rate (>99% conversion was reached after \sim 12 h reaction time). This hinted at the loss of H2 equivalents for the desired transfer semihydrogenation through concomitant dehydrocoupling. Consequently, when an H₃NBH₃ solution in THF was added slowly (3 h) to the reaction mixture, a generally faster conversion and higher yield of Z-2 were observed (Table 1, entry 9, 96%). Nevertheless, a total of three equivalents of H₃NBH₃ were required for >99% conversion since slow addition of two equivalents of ammonia borane did not lead to complete consumption of 1 (Table 1, entry 10).²⁸ Based on these results, we decided to probe whether a direct transfer of a hydride equivalent to copper or H₂ activation after dehydrocoupling of ammonia borane was present. Therefore, we carried out the alkyne transfer semihydrogenation with a catalytic amount of H₃NBH₃ under a H₂ atmosphere. These reactions gave only 20% conversion of 1 (Table 1, entry 11); hence, we conclude that a direct hydride transfer mechanism is present.

With the optimised reaction conditions in hand, we explored the substrate scope of the copper-catalysed alkyne transfer semihydrogenation. A variety of phenylacetylene derivatives with both electron-donating and electron-withdrawing functional groups 4a-4g could successfully be transformed into alkenes 5a-5g with good yields and consistently high Z-selectivity (Table 2, entries 1-7). Of note is the low conversion achieved with 3-anisole derivative 4d (30%, Table 2, entry 4); we suspect substrate coordination detrimental to the catalyst, which is absent with the other two regioisomers 4c and 4e (Table 2, entries 3 and 5). With strongly electron-withdrawing substituents (as in 5h-5j, Table 2, entries 8-10), we observed partial overreduction to the corresponding alkanes, although the Z/E-ratios remained high. The same is true for the acetophenone derivative 4k, where overreduction to the benzyl alcohol 5k was detected (Table 2, entry 11).²⁹ A variety of Z-stilbenes 51-50 can be synthesised from the corresponding tolane derivatives 41-40 with good yields (Table 2, entries 12-15). Here, a similarly detrimental influence of the electron-withdrawing trifluoromethyl substituent in 50 was observed as 8% alkane was detected (Table 2, entry 15). The alkyne transfer semihydrogenation can also be applied to dialkylalkynes, as demonstrated by the formation of Z-alkenes 5p and 5q (Table 2, entries 16 and 17). For full consumption of the former, one more equivalent of H₃NBH₃ was added. Finally, protected allyl alcohols 5r and 5s can be obtained with high Z-selectivity from the corresponding propargylic silvl ethers 4r and 4s (Table 2, entries 18 and 19). Generally, the obtained yields are good; in some cases we observed undesired hydroboration/ oxidation of the alkene products.²³ We attribute the somewhat diminished yields to this side reaction.

Finally, we investigated the transfer semihydrogenation of alkyl and aryl propiolates 6 (Scheme 2). In both cases the desired

ChemComm Table 2 Cu-catalysed transfer semihydrogenation of alkynes with ammonia borane: substrate scope 5 mol% [IPrCuOH] \mathbf{R}^2 R^2 3 equiv. H₃NBH₃ $R^{1'}$ THF. 50 °C Ĥ. 5 4 Entry Product Yield [%] Z/E/alkane^a **5a:** R = 4-Me 1 63 >99:0:0 BnO >99:0:0 2 **5b:** R = 4-*t*Bu 50 3 5c: R = 4-OMe 69 95:5:0 5d: R = 3-OMe >99:0:0 4 30 conv. 5 **5e:** R = 2-OMe 71 >99:0:0 6 5f: R = Br 80 >99:0:07 5g: R = Cl 63 >99:0:08 **5h**: $R = CO_2Me$ 65 80:0:20 5i: R = CN 89:4:7 9 51 10 5j: R = CF₃ 71 81:0:19 5k: 11 55 84:1:15 BnO 51: R = H12 57 >99:0:0 13 5m: R = 4-OMe 66 >99:0:0 5n: R = 4-Cl >99:0:0 14 77 92:0:8 15 50: R = 4-CF 50 5p: 16^b 74 >99:0:0 BnC 5q: 17 >99:0:080 conv. 5r: OTIPS 74 18 >99:0:0BnC 5s:



Z-acrylates 7**a** and 7**b** were found, however, in the presence of overreduced esters 8**a** and 8**b**. This indicated the viability of a conjugate transfer hydrogenation of the initially formed acrylates 7. We therefore decided to investigate the conjugate transfer hydrogenation of α , β -unsaturated esters with ammonia borane next.

After initial optimisation we also found that conjugate transfer hydrogenation of enoates 9 with ammonia borane was feasible under similar reaction conditions (Table 3). Conjugate transfer hydrogenation of disubstituted ethyl esters 9a-9i could be realised with generally good isolated yields when the reaction was carried out under previously optimised conditions (Table 3, entries 1-9). Isolated yields for esters 10 generally are higher than in the alkyne transfer semihydrogenation. This is possibly due to the absence of a reactive double bond in the products, which could lead to further reactions. Only thiophene derivative 10f was obtained in a somewhat lower yield (Table 3, entry 6). Of note is the different reactivity of the catalyst toward double bond isomers: while the E-enoate 9d underwent smooth conversion to the desired saturated product 10d (Table 3, entry 4), the reaction with Z-enoate 9e proceeded sluggishly (46% conversion to 10e after 16 h) under otherwise similar conditions (Table 3, entry 5). Higher substituted acrylates 10j-10l proved to be more difficult to obtain, most probably due to steric hindrance (Table 3, entries 10-12). However, by addition of 6 equivalents of H₃NBH₃, esters 10j-10l could be isolated in good yields.30

 Table 3
 Cu-catalysed conjugate transfer hydrogenation: substrate scope

R ² R ¹ 9	OEt	5 mol% [IPrCuOH] 3 equiv. H ₃ NBH ₃ THF, 50 °C	$R^2 H$ R^1 10 H	O OEt
Entry	Prod	uct		Yield [%]
$ \frac{1^{a}}{2^{a}} $ $ \frac{3^{a}}{4} $ $ \frac{4}{5^{b}} $ $ \frac{6}{7^{a}} $ $ 9 $ $ 9 $	10a: 10b: 10c: 10d: 10c: 10f: 10g: 10h: 10i: 10i:	$R^{1} = Ph, R^{2} = H$ $R^{1} = 2$ -naphthyl, $R^{2} = H$ $R^{1} = 4$ -OMe-C ₆ H ₄ , $R^{2} = H$ $R^{1} = 4$ -OBn-C ₆ H ₄ , $R^{2} = H$ $R^{1} = H, R^{2} = 4$ -OBn-C ₆ H ₄ $R^{1} = 2$ -thiophenyl, $R^{2} = H$ $R^{1} = 4$ -OFa-C ₆ H ₄ , $R^{2} = H$ $R^{1} = 4$ -OFa-C ₆ H ₄ , $R^{2} = H$ $R^{1} = 4$ -OFa-C ₆ H ₄ , $R^{2} = H$ $R^{1} = 4$ -OFa-C ₆ H ₄ , $R^{2} = H$ $R^{1} = 4$ -OFa-C ₆ H ₄ , $R^{2} = H$ $R^{1} = 4$ -OFa-C ₆ H ₄ , $R^{2} = H$ $R^{1} = 4$ -OFa-C ₆ H ₄ , $R^{2} = H$		82 83 83 87 46 conv. 66 88 82 89 92
11^c 12^c	10j. 1 10k: 10l: 1	$R^1 = Ph, R^2 = Me$ $R^1 = Ph, R^2 = Ph$		76 73 ^d

^{*a*} These reactions reached >99% conversion with 2 equiv. of H_3NBH_3 . ^{*b*} The methyl ester of **9e** was employed. ^{*c*} 6 equiv. of H_3NBH_3 was used. ^{*d*} Contains 14% of the starting material.



63

>99:0:0

OTIPS

TIPSC

19

In summary, we have developed copper(1) hydride-mediated transfer hydrogenation reactions employing ammonia borane (H_3NBH_3) as a H_2 equivalent. Alkynes can be converted into the corresponding alkenes with high *Z*-selectivities in transfer semihydrogenations. Also, the protocol enables a conjugate transfer hydrogenation of enoates. An air-stable and preactivated copper(1) hydroxide/NHC complex is used, circumventing the need for generally common *in situ* activation of the copper catalyst. We think that these results could be of importance with foresight to the use of readily available transition metal catalysts (such as copper) for transfer hydrogenations.

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- 28 Reaction analysis by ¹¹B NMR shows the formation of polyaminoboranes (see the ESI^{\dagger} for details), which indicates the transfer of 1 equiv. of H₂ per molecule of ammonia borane. This could account for the high loadings of ammonia borane required.
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