Chemoselective Hydrogenation of Alkynes to (Z)-Alkenes using an Air Stable Base Metal Catalyst

Viktoriia Zubar,^{†‡} Jan Sklyaruk,[†] Aleksandra Brzozowska[†] and Magnus Rueping^{*‡}

[†]Institute of Organic Chemistry, RWTH Aachen University, Landoltweg 1, 52074, Aachen, Germany

[‡]KAUST Catalysis Center (KCC), KAUST, Thuwal 23955-6900, Saudi Arabia

Supporting Information Placeholder

ABSTRACT: A highly selective hydrogenation of alkynes using an air stable and readily available manganese catalyst has been achieved. The reaction proceeds under mild reaction conditions and tolerates various functional groups resulting in (Z)-alkenes and allylic alcohols in high yields. Mechanistic experiments suggest that the reaction proceeds *via* a bifunctional activation involving metal-ligand cooperativity.

The selective semihydrogenation of alkynes to alkenes is a valuable catalytic process.¹ It is particularly important as it leads to building blocks relevant for the synthesis of pharmaceuticals, agrochemicals and natural products, which encompass a double bond in defined (*E*) or (*Z*) configuration.² Different approaches have been developed to prepare (*Z*)-alkenes.³ The application of Lindlar's catalyst is the most popular and widely used hydrogenation to form (*Z*)-alkenes from alkynes.⁴ However, the reaction has disadvantages, such as the toxicity of lead additives or the isomerization of the achieved (*Z*) to (*E*)-isomer as well as a possible shift of the double bond. Thus, the development of cost-effective, well-defined, efficient and environmentally friendly catalytic systems for the selective conversion of internal alkynes to (*Z*)-alkenes is desirable. However, the semireduction of alkynes to alkenes using hydrogen as a reducing agent is the most efficient and atom economic approach. Concerning homogeneous catalysis most of the known procedures rely on the use of alternative hydrogen donors, such as formic acid, water, silanes, ammonia borane, isopropanol and others. Apart from that, rhodium⁵ and palladium⁶ based catalytic systems showed good reactivity and selectivity towards the formation of (*Z*)-alkenes with the application of molecular hydrogen as a reducing source. Thus, replacement of the precious metals by the first-row, earth-abundant catalysts would be a valuable alternative procedure.⁷ However, base metal-catalyzed homogeneous hydrogenation of alkynes to (*Z*)-alkenes using hydrogen as reducing agent has hardly been investigated. To the best of our knowledge, the earliest example of a base-metal catalyzed semireduction of alkynes to (*Z*)-alkenes was reported by Ugo's group.^{8a} Phosphine cobalt carbonyl complexes were used for the selective reduction of 2-pentyne resulting in (*Z*)-2-pentene in good yield. In 2017 Zhang and co-workers^{8b} successfully applied a cobalt complex formed in-situ from $\text{Co}(\text{OAc})_2(\text{H}_2\text{O})_4$,

NaBH_4 and ethylenediamine in a 1:2:8 ratio, for the chemoselective hydrogenation of C-C bonds. Iron catalyzed hydrogenation of diphenylacetylene was mentioned in a work of Chirik et al.⁹, where the application of an iron(0) dinitrogen complex initially resulted in the formation of (*Z*)-stilbene which was simultaneously converted to dibenzyl. Furthermore, Cr ¹⁰, V ¹¹, and Cu ¹² salts were also applied.

The availability of manganese as the third most abundant metal in the earth's crust attracted its application in base-metal catalysis.¹³ Recently, we reported the highly selective transfer semihydrogenation of alkynes to (*Z*)-alkenes using a $[\text{Mn}(\text{II})\text{-PNP}][\text{Cl}_2]$ complex and ammonia borane as the hydrogen source.¹⁴ Due to the fact that ammonia borane is a rather expensive and waste producing reducing agent we decided to evaluate Mn-catalysts which are able to activate molecular hydrogen and to apply them in the reduction of alkynes.

While Mn-catalysts have been applied in hydrogenations before¹⁵⁻¹⁹ to the best of our knowledge a highly selective manganese catalyzed reduction of alkynes to (*Z*)-alkenes using molecular hydrogen are only recently reported,²⁰ although direct hydrogenations are often superior to transfer hydrogenations as they are 100% atom economic and do not result in by-products. We started our investigation by synthesizing a new, air and moisture stable ^{Ph}PNS-Mn pincer complex **Mn-1** by using a bench stable ^{Ph}PNS ligand **L-1**. **Mn-1** can be readily synthesized by treatment of **L-1** with 1 equiv. of $\text{Mn}(\text{CO})_5\text{Br}$ as metal precursor in toluene at 100 °C for 16 h. The bright yellow complex was isolated in 86% yield and was characterized by NMR, IR, and mass spectrometry (Scheme 1).

Scheme 1. Synthesis of Mn-1.

Our newly synthesized catalyst **Mn-1** was subsequently investigated in the hydrogenation of diphenylacetylene. Our initial attempts proceeded by applying 1 mol % of **Mn-1** and 2.5 mol % of KO^tBu in toluene at 60 °C under 30 bar of H₂ for 16 h. To our delight, diphenylacetylene was fully consumed producing the desired (*Z*)-stilbene in 88% GC yield, 1% of (*E*)-stilbene and 11% of dibenzyl as a result of over-hydrogenation (Table 1, entry 1).

The use of manganese complexes, **Mn-2**, **Mn-3** and **Mn-4** provided less satisfactory results (Table 1, entries 2-4). To our delight, catalyst **Mn-5** showed better reactivity, resulting in 60% conversion and a selectivity of 98:2 while dibenzyl was not detected (Table 1, entry 5). The application of **Mn-6** resulted in lower reactivity albeit similar selectivity when compared to **Mn-1** (Table 1, entry 6). A control experiment showed that the reaction does not take place without the catalyst (Table 1, entry 7). Interestingly, the use of K₂CO₃ or Cs₂CO₃ for the activation of the catalyst was not successful (Table 1, entries 8 and 9). Use of polar aprotic-THF as a solvent resulted in 11% conversion of **1a** (Table 1, entry 10) while no reaction occurred if polar protic MeOH was used (Table 1, entry 11). Decreasing the hydrogen pressure to 20 bar helped to reduce the formation of undesired over hydrogenation product (Table 1, entry 12). Performing the reaction at 50 °C led to the same result (Table 1, entry 13), nevertheless, 60 °C appeared to be more suitable for a substrate scope preparation. Additionally, no impact was observed when a drop of mercury was added to the reaction mixture, which suggests the homogeneous nature of the catalyst under these reaction conditions (Table 1, entry 14)²¹

With the optimized reaction conditions in hand we started to explore the substrate scope for the selective semihydrogenation of alkynes using our new Mn-PNS catalyst. A range of substrates bearing different electronic and steric properties were well tolerated and provided the corresponding (*Z*)-alkenes in good yields with excellent chemoselectivity. It should be noted that the substrates bearing electron withdrawing substituents were significantly more reactive than the ones bearing electron donating groups. Additionally, the hydrogenation of **1i**, bearing ester functionality, proceeded chemoselectively towards alkyne hydrogenation and the ester group remained intact. Importantly, alkynes which contain heterocycles (**1o-1q**, **1x**, **1y**) could also be applied and provided excellent reactivity and selectivity. Remarkably, no proto-dehalogenation of C-Cl and C-Br bond took place when 1-chloro-4-(phenylethynyl)benzene (**1l**) and 1-bromo-3-(phenylethynyl)benzene (**1n**) were applied as substrates.

Table 1. Optimization of the Reaction Conditions ^a

entry	[Mn]	base	conv. (%) ^b	ratio 2a:3a:4a ^b
1	Mn-1	KO ^t Bu	>99	88:01:11
2	Mn-2	KO ^t Bu	nr	nd
3	Mn-3	KO ^t Bu	nr	nd
4	Mn-4	KO ^t Bu	05	82:18:00
5	Mn-5	KO ^t Bu	60	98:02:00
6	Mn-6	KO ^t Bu	48	95:05:00
7	-	KO ^t Bu	nr	nd
8	Mn-1	K ₂ CO ₃	nr	nd
9	Mn-1	Cs ₂ CO ₃	17	90:10:00
10 ^c	Mn-1	KO ^t Bu	11	51:49:00
11 ^d	Mn-1	KO ^t Bu	nr	nd
12 ^e	Mn-1	KO ^t Bu	>99	96:01:03
13 ^{e,f}	Mn-1	KO ^t Bu	>99	96:01:03
14 ^{e,g}	Mn-1+Hg	KO ^t Bu	>99	93:01:06

^aReaction conditions: **1a** (1 mmol), [Mn] (1 mol %), base (2.5 mol %) in 2 mL of toluene at 60 °C under 30 bar of H₂ for 16 h. ^bDetermined by the GC analysis using m-xylene as internal standard. ^cReaction in THF. ^dReaction in methanol. ^e20 bar of H₂. ^f50 °C. ^gOne drop of mercury was added.

Moreover, our protocol was suitable for the application of triisopropyl(phenylethynyl)silane **1r** in the hydrogenation reaction. Due to higher steric hindrance of the substrate the reaction required 5 mol % of the **Mn-1**, a slightly higher hydrogen pressure of 30 bar and 24 hours of the reaction time, resulting in 76% yield of (*Z*)-triisopropyl-(styryl)silane as a single isomer. Furthermore, the reduction of aryl-alkyl alkynes, including protected propargylic alcohols **1s-1y** led to the formation of the corresponding (*Z*)-allylic alcohols demonstrating the wide scope of substrates. Additionally, a gram-scale synthesis of (*Z*)-stilbene could also be achieved using only 0.5 mol % of **Mn-1**, leading to the formation of 99% yield of the desired product (Scheme 2) implying that the described protocol could be suitable for industrial production of (*Z*)-alkenes.

Table 2. (Z)-Selective Hydrogenation of Alkynes Catalyzed by Mn-1^a

$\text{R}^1\text{—}\text{C}\equiv\text{C—}\text{R}^2 + \text{H—H} \xrightarrow[\text{toluene, 60 } ^\circ\text{C}]{\text{Mn-1, KO}^t\text{Bu}}$						$\text{R}^1\text{—}\text{CH=CH—}\text{R}^2$					
entry	alkene	cat. (mol%)	t (h)	ratio 2:4 ^b	yield (%)	entry	alkene	cat. (mol%)	t (h)	ratio 2:4 ^b	yield (%)
1	2b	2	12	95:05	81	13 ^d	2n	1	16	89:11	75
2 ^c	2c	2	16	94:06	79	14	2o	1	8	92:08	77
3	2d	2	16	96:04	94	15 ^c	2p	1	16	93:07	90
4	2e	2	16	93:07	83	16 ^c	2q	2	16	95:05	79
5 ^c	2f	1	16	94:06	90	17 ^c	2r	5	24	100:0	76
6 ^d	2g	1	16	93:07	80	18 ^c	2s	3	16	90:10	69
7 ^c	2h	2	20	91:09	72	19	2t	2	16	100:0	91
8 ^c	2i	2	16	91:09	82	20	2u	1	16	89:11	81
9	2j	3	16	93:07	86	21	2v	2	16	100:0	94
10 ^c	2k	3	16	92:08	78	22	2w	1	16	90:10	73
11	2l	1	12	92:08	85	23	2x	1	16	95:05	76
12	2m	1	16	90:10	82	24	2y	1	12	94:06	82

^aReaction conditions: alkyne (0.5 mmol), **Mn-1** (x mol %), KO^tBu 2.5 equiv. to the **Mn-1** in 1 mL of toluene at 60 °C under 20 bar of H₂; yields after purification. ^bDetermined by the NMR analysis using CH₂Br₂ as internal standard. ^c30 bar of H₂. ^d50 °C.

Scheme 2. Gram-scale Synthesis of (Z)-Stilbene

To prove whether the described reaction proceeds *via* metal-ligand cooperativity we attempted to synthesize the corresponding manganese **N-Me** derivative of **Mn-1** as it would establish whether the proton transfer from the ligand N-atom would occur. As the formation of the **Mn-1(N-Me)** catalyst was not successful after several attempts, using different solvents and temperatures, we prepared the corresponding **N-Me** manganese complex for **Mn-6**, which also showed reactivity in the hydrogenation. As expected, the methylated complex **Mn-6(N-Me)** appeared to be inactive in the hydrogenation of diphenylacetylene under the optimized reaction conditions, indicating that the formation of the N-H is critical for the activity of the catalyst (Scheme 3a). To exclude the possibility of the interaction between the substrate and the catalyst, diphenylacetylene was stoichiometrically added to the **Mn-1*** (active species), *in-situ* formed by the addition of KOtBu to the **Mn-1** complex and heated for 24 hours in C₆D₆ (Scheme 3b). The chemical shift of the activated **Mn-1*** remained unaffected, indicating that no coordination of the alkyne and potentially inhibition occurs (See SI).

Scheme 3. Mechanistic Studies to Prove Metal-Ligand Cooperativity

Based on the observed experimental results we propose that the reaction proceeds *via* metal-ligand cooperativity following an outer-sphere pathway (Scheme 4).²² Thus, the catalytic cycle begins with the addition of the molecular hydrogen to the metal site of the catalyst and formation of the intermediate **A**. Next, heterolytic cleavage of the H-H bond takes place leading to the hydrogenated catalyst **B** via transition state **TS-1**. A proton and a hydride are transferred simultaneously from the intermediate **B** to the substrate giving an intermediate **C**, which later releases the desired product **2a** and the active catalyst **Mn-1***.

Scheme 4. Proposed reaction mechanism of alkyne hydrogenation using Mn-1 complex

In conclusion, a manganese catalyzed semi-hydrogenation of alkynes using molecular hydrogen as reducing agent has been developed. The reaction proceeds under mild conditions and provides the desired (Z)-alkenes with very high selectivity. The applied catalyst **Mn-1** can be synthesized from a commercially available manganese precursor and an air stable and readily available PhPNS-pincer ligand highlighting the practicability of the developed protocol. The **Mn-1** catalyst shows good reactivity and chemoselectivity and tolerates a variety of functional groups and heterocycles leading to a practical synthesis of (Z)-olefins as well as allylic alcohols. Compared to transfer hydrogenations with the use of different hydride donors, the use of molecular hydrogen is 100% atom economic as no by-products are formed. Thus, this mild manganese catalysed reaction provides a good tool to access (Z)-alkenes in a stereoselective fashion.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website
Experimental data (PDF)

AUTHOR INFORMATION

Corresponding Author

*magnus.rueping@kaust.edu.sa
* @rwth-aachen.de

ORCID

Magnus Rueping: 0000-0003-4580-5227

Notes

The authors declare no competing financial interest

Funding Sources

J.S. is thankful for a financial support provided by the Fonds der Chemischen Industrie. This work was financially supported by the King Abdullah University of Science and Technology (KAUST), Saudi Arabia, Office of Sponsored Research (FCC/1/1974).

Notes

Any additional relevant notes should be placed here.

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