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

Viktoriia Zubar, Jan Sklyaruk, Aleksandra Brzozowska, and Magnus Rueping*

Cite This: https://dx.doi.org/10.1021/acs.orglett.0c01783 Read Online

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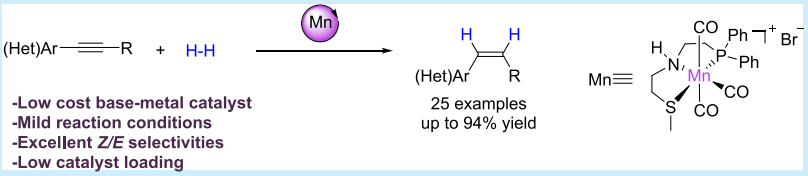


ABSTRACT: A highly selective hydrogenation of alkynes using an air-stable and readily available manganese catalyst has been achieved. The reaction proceeds under mild reaction conditions and tolerates various functional groups, resulting in (*Z*)-alkenes and allylic alcohols in high yields. Mechanistic 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 because 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 and 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 economical 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, rhodium-[5] and palladium-based[6] catalytic systems showed good reactivity and selectivity toward the formation of (*Z*)-alkenes with the application of molecular hydrogen as a reducing source. Thus the replacement of the precious metals by the first-row, earth-abundant catalysts would be a valuable alternative procedure.[7] However, the base-metal-catalyzed homogeneous hydrogenation of alkynes to (*Z*)-alkenes using hydrogen as a 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 coworkers[8b] successfully applied a cobalt complex formed in situ from $Co(OAc)_2(H_2O)_4$, $NaBH_4$, and ethylenediamine in a 1:2:8 ratio for the chemoselective hydrogenation of C−C triple bonds. The 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 [Mn(II)−PNP][Cl_2] complex and ammonia borane as the hydrogen source.[14] Because of 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.

Whereas Mn catalysts have been applied in hydrogenations before,[15−19] to the best of our knowledge, a highly selective manganese-catalyzed reduction of alkynes to (*Z*)-alkenes using molecular hydrogen has only recently been reported,[20] although direct hydrogenations are often superior to transfer hydrogenations because they are 100% atom economical and do not result in byproducts.

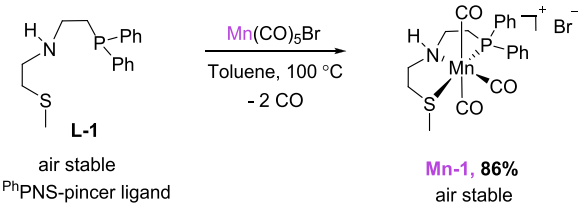
We started our investigation by synthesizing a new air- and moisture-stable ^{Ph}PNS−Mn pincer complex **Mn-1** by using a

Received: May 26, 2020

https://dx.doi.org/10.1021/acs.orglett.0c01783
Org. Lett. XXXX, XXX, XXX−XXX

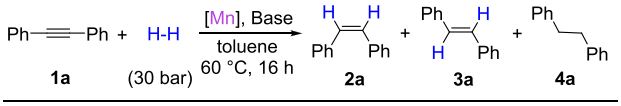
bench-stable ^{Ph}PNS ligand **L-1**. **Mn-1** can be readily synthesized by the treatment of **L-1** with 1 equiv of $Mn(CO)_5Br$ as a metal precursor in toluene at 100 °C for 16 h. The bright-yellow complex was isolated in 86% yield and was characterized by NMR, IR, and mass spectrometry (Scheme 1).

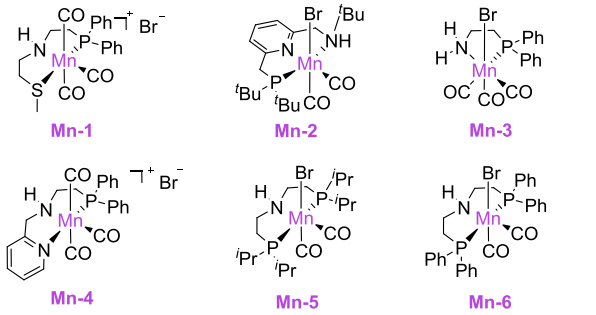
Scheme 1. Synthesis of Mn-1



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^{t}Bu in toluene at 60 °C under 30 bar of H_2 for 16 h. To our delight, diphenylacetylene was fully consumed, producing the desired (*Z*)-stilbene in 88% GC yield as well as 1% of (*E*)-stilbene and 11% of dibenzyl as a result of overhydrogenation (Table 1, entry 1).

Table 1. Optimization of the Reaction Condition[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_2CO_3	nr	nd
9	Mn-1	Cs_2CO_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

[a]Reaction conditions: **1a** (1 mmol), [**Mn**] (1 mol %), and base (2.5 mol %) in 2 mL of toluene at 60 °C under 30 bar of H_2 for 16 h. [b]Determined by the GC analysis using *m*-xylene as an internal standard. [c]Reaction in THF. [d]Reaction in methanol. [e]20 bar of H_2. [f]50 °C. [g]One drop of mercury was added.

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, whereas dibenzyl was not detected (Table 1, entry 5). The application of **Mn-6** resulted in a lower reactivity albeit a similar selectivity when compared with **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 K_2CO_3 or Cs_2CO_3 for the activation of the catalyst was not successful (Table 1, entries 8 and 9). The use of polar-aprotic THF as a solvent resulted in 11% conversion of **1a** (Table 1, entry 10), whereas 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 products (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]

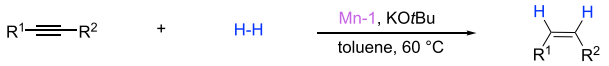
With the optimized reaction conditions in hand, we started to explore the substrate scope for the selective semi-hydrogenation of alkynes using our new ^{Ph}PNS−Mn catalyst (Table 2). A range of substrates bearing different electronic and steric properties were well tolerated and provided the corresponding (*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 toward alkyne hydrogenation, and the ester group remained intact. Importantly, alkynes that contain heterocycles (**1o−q**, **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-(phenylethy-nyl)benzene (**1n**) were applied as substrates.

Moreover, our protocol was suitable for the application of triisopropyl(phenylethynyl)silane **1r** in the hydrogenation reaction. Because of the higher steric hindrance of the substrate, the reaction required 5 mol % of **Mn-1**, a slightly higher hydrogen pressure of 30 bar, and 24 h of the reaction time, resulting in a 76% yield of (*Z*)-triisopropyl-(styryl)silane as a single isomer. Furthermore, the reduction of aryl-alkyl alkynes, including protected propargylic alcohols **1s−y**, 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 a 99% yield of the desired product (Scheme 2), implying that the described protocol could be suitable for the industrial production of (*Z*)-alkenes.

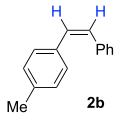
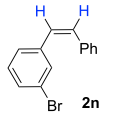
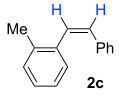
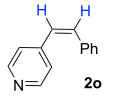
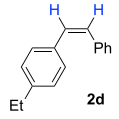
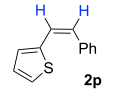
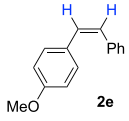
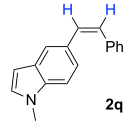
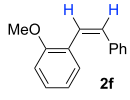
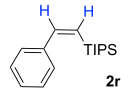
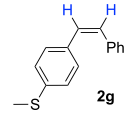
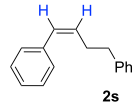
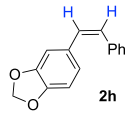
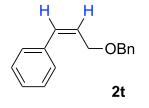
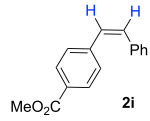
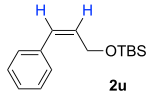
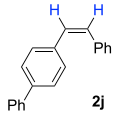
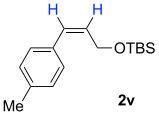
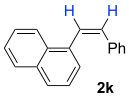
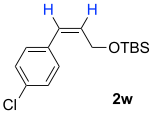
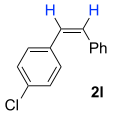
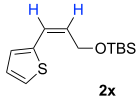
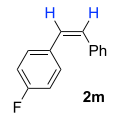
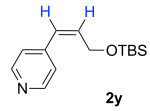
To prove whether the described reaction proceeds *via* metal−ligand cooperativity, we attempted to synthesize the corresponding manganese **N-Me** derivative of **Mn-1** because it would establish whether the proton transfer from the ligand N-atom would occur. Because the formation of the **Mn-1(N-Me)** 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

https://dx.doi.org/10.1021/acs.orglett.0c01783
Org. Lett. XXXX, XXX, XXX−XXX

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



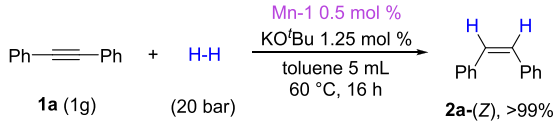
1 (20 bar) 2

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

[a]Reaction conditions: alkyne (0.5 mmol), **Mn-1** (*x* mol %), KO[t]Bu 2.5 equiv to the **Mn-1** in 1 mL of toluene at 60 °C under 20 bar of H_2; yields after purification. [b]Determined by the NMR analysis using CH_2Br_2 as an internal standard. [c]30 bar of H_2. [d]50 °C.

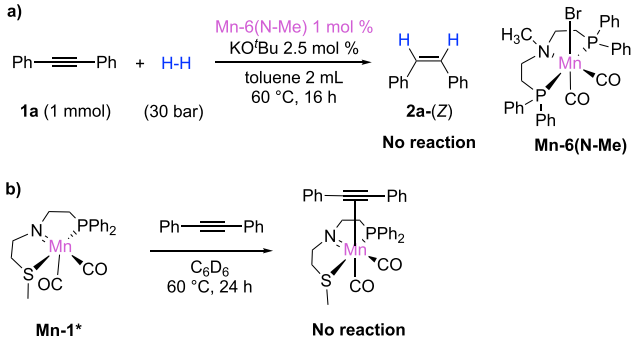
https://dx.doi.org/10.1021/acs.orglett.0c01783
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 2. Gram-Scale Synthesis of (*Z*)-Stilbene



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

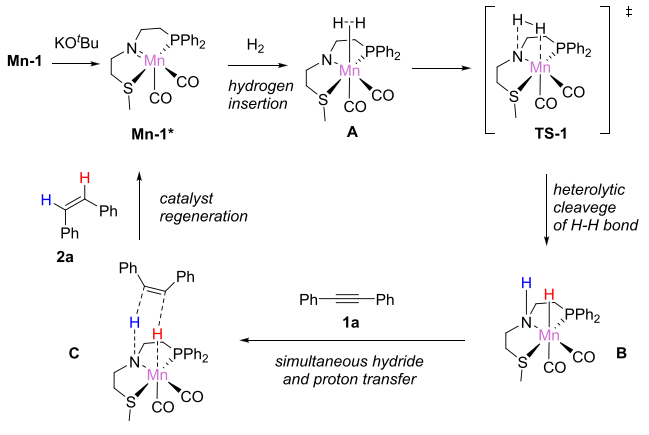
Scheme 3. Mechanistic Studies to Prove Metal−Ligand Cooperativity



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 KO^{t}Bu to the **Mn-1** complex and heated for 24 h in C_6D_6 (Scheme 3b). The chemical shift of the activated **Mn-1*** remained unaffected, indicating that no coordination of the alkyne and potentially inhibition occurs. (See the SI.)

On the basis of 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 the formation of the intermediate **A**. Next, the 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

Scheme 4. Proposed Reaction Mechanism of Alkyne Hydrogenation Using Mn-1 Complex



substrate, giving an intermediate **C**, which later releases the desired product **2a** and the active catalyst **Mn-1***.

In conclusion, a manganese-catalyzed semihydrogenation of alkynes using molecular hydrogen as a 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 ^{Ph}PNS−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 with transfer hydrogenations with the use of different hydride donors, the use of molecular hydrogen is 100% atom economical, as no byproducts are formed. Thus this mild manganese-catalyzed 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 at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01783.

General information, ligand and complex synthesis and characterization, experimental procedure and characterizations of the products, and NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Magnus Rueping − *KAUST Catalysis Center (KCC), KAUST, Thuwal 23955-6900, Saudi Arabia;* orcid.org/0000-0003-4580-5227; Email: magnus.rueping@kaust.edu.sa

Authors

Viktoriia Zubar − *Institute of Organic Chemistry, RWTH Aachen University, 52074 Aachen, Germany; KAUST Catalysis Center (KCC), KAUST, Thuwal 23955-6900, Saudi Arabia*

Jan Sklyaruk − *Institute of Organic Chemistry, RWTH Aachen University, 52074 Aachen, Germany*

Aleksandra Brzozowska − *Institute of Organic Chemistry, RWTH Aachen University, 52074 Aachen, Germany*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c01783

Funding

J.S. is thankful for the 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

The authors declare no competing financial interest.

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