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Selective iron-catalyzed transfer hydrogenation of terminal alkynes†

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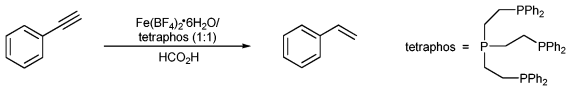
A novel iron-catalyzed transfer hydrogenation of alkynes to the corresponding alkenes applying formic acid as a hydrogen donor is reported. An *in situ* combination of $Fe(BF_4)_2{\cdot}6H_2O$ and tetraphos allows for highly selective hydrogenation of a broad range of aromatic and aliphatic alkynes tolerating different functional groups.

Terminal alkenes constitute important intermediates for organic synthesis. They are widely used in the chemical industry for large-scale polymerisations,[1] but also in more special reactions such as metathesis, epoxidations, hydroformylations, hydroaminations, and others.[2] While simple bulk styrenes are produced *via* dehydrogenation of ethylbenzenes,[3] functionalized styrenes are synthesized *via* dehydrohalogenations and dehydrations.[4] Notably, in the last decades new protocols have been developed for the preparation of functionalized aromatic olefins under mild conditions using cross-coupling reactions.[5] In addition, a common route for styrene synthesis constitutes the selective hydrogenation of alkynes. This reaction is well established using heterogeneous Lindlar catalysts.[6] Here, selectivity is a critical issue and overreduction has to be avoided. Potential improvements of the current Lindlar technology involve the avoidance of the expensive precious metal and the toxic additives, which poison the catalyst. Furthermore, on a smaller scale the replacement of hydrogen gas by low cost liquid hydrogen donors (transfer hydrogenation) is attractive with regard to safety issues and equipment.[7] In this respect, homogeneous catalysis offers the possibility to cope with these challenges, *e.g.*, tuning the defined structure of the catalyst allows us to increase the degree of selectivity control.

Clearly, in the last years remarkable progress has been made in the semihydrogenation of alkynes. Different V-,[8] Pd-,[9] Rh-,[10] Ir-,[11] and Ru[12]-based catalysts have been described for the hydrogenation and transfer hydrogenation of alkynes to give alkenes. Although the replacement of precious metals with iron is a major goal in current research,[13] to the best of our knowledge only one example of an iron-catalyzed hydrogenation of alkynes is reported,[14] focussing on the mechanistic aspects of the selective reduction.[15] Based on our background in iron-catalyzed reductions,[16] we became interested in the development of a more general protocol for the selective transfer hydrogenation of alkynes to alkenes.

Recently, we have shown that the combination of $Fe(BF_4)_2{\cdot}6H_2O$/tris[(2-diphenyl-phosphino)-ethyl]-phosphine [$P(CH_2CH_2PPh_2)_3$; (PP_3)] catalyzes the transfer hydrogenation of nitroarenes to their corresponding anilines.[17] Here, formic acid is applied as the reducing agent, generating only carbon dioxide as the by-product. Notably, no base was required for the process, making it a rare example of a base-free transfer hydrogenation.[18] At the start of our investigations, we employed similar conditions for the reduction of phenylacetylene. To our delight full conversion of the substrate was observed. As shown in Table 1 (entries 1–6) the reaction is highly solvent dependent. High yields were only obtained in tetrahydrofuran, while in other protic or non-polar solvents no reactivity was observed. Next, the reaction temperature was optimized (Table 1, entries 7–9). The desired reaction takes place at 20 °C, albeit 18 hours were required to obtain 77% yield. Increasing the temperature to 40 °C led to faster conversion, while at 65 °C only a slight further rise in the reaction rate was observed.

Table 1 Iron-catalyzed semihydrogenation of phenylacetylene: variation of reaction conditions[a]



Entry	Solvent	Catalyst [mol%]	Time [h]	Yield[b] [%]
1	THF	0.25	48	61
2	EtOH	0.25	48	<1
3	Toluene	0.25	48	17
4	Et_2O	0.25	48	5
5	Acetone	0.25	48	16
6	DCM	0.25	48	6
7[c]	THF	0.5	2	14
			18	77
8	THF	0.5	2	67
9[d]	THF	0.5	2	73
10[e]	THF	0.5	2	10
11[f]	THF	0.5	2	61
12	THF	0.6	2	>99
13	THF	2	10 min	>99

[a] Reaction conditions: 0.5 mmol phenylacetylene, catalyst (ratio 1 : 1): $Fe(BF_4)_2{\cdot}6H_2O/PP_3$, 1 mL dry THF, 2 equiv. formic acid, 40 °C. [b] Determined by GC using *n*-hexadecane as an internal standard. [c] 20 °C. [d] 65 °C. [e] 1 equiv. formic acid. [f] 3 equiv. formic acid.

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In addition, the amount of the reducing agent was examined (Table 1, entries 8, 10 and 11) and it was found that two equivalents of formic acid give the best results. This slight excess of the reductant is necessary due to some unproductive decomposition of the formic acid into carbon dioxide and hydrogen, which has been recently shown by us.[19] Finally, at higher catalyst concentration an excellent product yield (>99%) was achieved and the reaction is completed in 10 min (Table 1, entry 13).

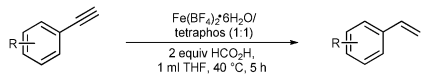
After optimization of the reaction conditions, we investigated the substrate scope of this procedure (Tables 2 and 3). Initially, different alkyl-substituted phenylacetylenes were tested (Table 2, entries 1–4). In each case up to 99% yield was obtained, showing that the nature of the alkyl group and its position on the aryl ring have no influence on the reactivity. Then, different halogenated phenylacetylenes were subjected to the reaction conditions (Table 2, entries 5–8). Electron-withdrawing substituents such as the fluoro-, chloro-, and trifluoromethyl group required a slightly higher catalyst loading to reach full conversion. This finding can be explained by the reduced electron density on the triple bond which hampers the coordination to the catalyst. Interestingly, selective hydrogenation was also achieved in the presence of ketones, esters, and hydroxy groups (Table 2, entries 9–15). Furthermore, *p*-diethynyl-benzene was reduced to the *p*-divinylbenzene in quantitative yield (Table 2, entry 14). It should be noted that internal phenylacetylenes did not react under the optimized conditions probably because of steric problems. Although this limits the scope it should allow for interesting selectivity when terminal and internal alkynes are present in one molecule.

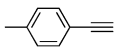
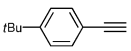
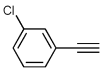
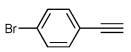
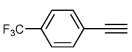
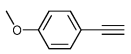
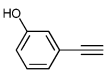
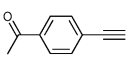
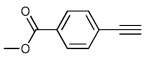
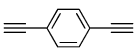
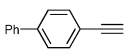
Besides, we tested terminal aliphatic and heteroaromatic alkynes (Table 3). 2-Ethynyl-6-methoxynaphthalene was fully converted to the corresponding vinyl compound (Table 3, entry 1), which serves as a possible intermediate in the asymmetric synthesis of (*S*)-naproxene. Heteroaromatic substrates showed varying reactivity (Table 3, entries 2 and 3): while 3-ethynylthiophene was fully reduced to the corresponding alkene, 3-ethynylpyridine yielded only traces of the vinyl compound. Several aliphatic terminal alkynes were tested, too (Table 3, entries 4–7). To our delight in every case full conversion and excellent selectivity were achieved. As a challenging example 1-ethynylcyclohexene with its conjugated double and triple bonds was selectively transformed into its diene product. In none of the reactions any overreduction or other side-reactions were observed.

The proposed catalytic cycle is shown in Scheme 1. The catalytically active species **1** is formed *in situ* by adding the ligand PP_3 to the iron precursor. Complex **1** splits the formic acid and releases carbon dioxide to form $[FeF(H_2)(PP_3)]^+$ (**2**). Then, phenylacetylene coordinates to the iron centre and is reduced stepwise. Finally, styrene is released to regenerate **1**. To get further insight into the proposed catalytic cycle, we performed experiments with different deuterated formic acids (HCO_2D, DCO_2D, DCO_2H). To our surprise, only the formic acid bearing the deuterium attached to the carbon atom showed reactivity. Applying formic acids with the deuterium at the acidic OH-position, no conversion to the product occurred at all! This clearly demonstrates that coordination and activation of the carboxylic acid group by the active $[FeF(PP_3)]^+$ species constitutes the essential step.[17] Bearing deuterium in the OH-position, the activation is completely hampered and the catalytic cycle is interrupted.

Using D-CO_2H, we analyzed the distribution of the deuterium incorporation. The ratio between *cis*- and *trans*-deuterated styrene is 1 : 1, which indicates that the reduction of the triple bond does not proceed in a concerted way. More likely, the substrate is reduced in a stepwise manner having the intermediates coordinated to the catalyst. This is a clear hint of

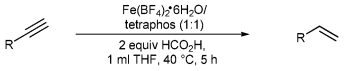
Table 2 Selective iron-catalyzed hydrogenation of phenylacetylene derivatives[a]

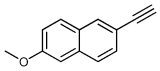
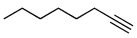
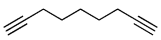


Entry	Substrate	Catalyst [mol%]	Conv. [%]	Yield[b] [%]
1		0.75	>99	>99
2		0.75	>99	>99
3		0.75	>99	>99
4		0.75	>99	>99
5		1	>99	>99
6		1	>99	>99
7		0.75	>99	>99
8		1.25	>99	98
9		0.75	>99	>99
10		0.75	>99	>99 (99)[c]
11		0.75	>99	>99 (99)[c]
12		1	>99	>99 (99)[c]
13		2.5	>99	>99 (96)[c]
14[d]		2	>99	>99
15		0.75	>99	>99

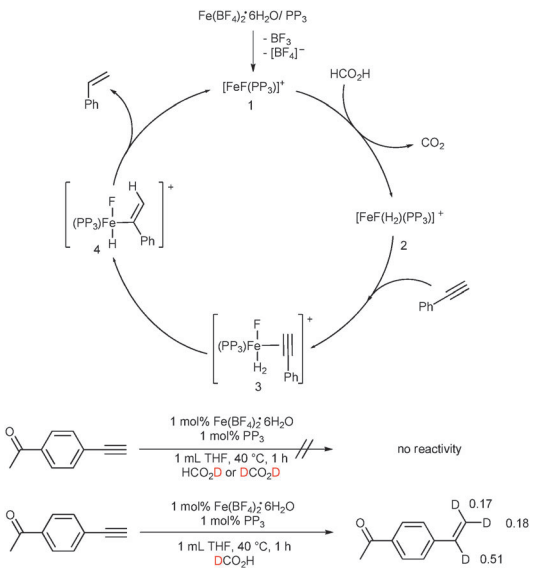
[a] Reaction conditions: 0.5 mmol substrate, catalyst (ratio 1 : 1): $Fe(BF_4)_2 \cdot 6H_2O/PP_3$, 1 mL dry THF, 2 equiv. formic acid, 40 °C, 5 h. [b] Determined by GC using *n*-hexadecane as an internal standard. [c] Upscaling by factor of 2 and isolated yield given in brackets. [d] 3 equiv. formic acid; product is the *p*-divinylbenzene.

Table 3 Semihydrogenation of other (hetero)aromatic and aliphatic alkynes[a]



Entry	Substrate	Catalyst [mol%]	Conv. [%]	Yield[b] [%]
1		0.75	>99	96
2		1	>99	>99
3		0.75	2	2
4		0.75	>99	97
5		1	>99	96
6[c]		3	>99	96
7		3	>99	97

[a] Reaction conditions: 0.5 mmol substrate, catalyst (ratio 1 : 1): $Fe(BF_4)_2{\cdot}6H_2O/PP_3$, 1 mL dry THF, 2 equiv. formic acid, 40 °C, 5 h. [b] Determined by GC using *n*-hexadecane as an internal standard. [c] 3 equiv. formic acid.



Scheme 1 Proposed catalytic cycle and experiments using deuterated formic acid as reducing agent.

an inner-sphere hydrogenation mechanism. Additionally, the deuterium is non-selectively distributed between the α- and β-positions of the styrene. This result is in agreement with the formation of an active iron dihydrido species $[(HD)FeF(PP_3)]^+$ from the corresponding formate complex by elimination of carbon dioxide.[17]

In summary, we have developed the first iron-based catalytic system for the selective transfer hydrogenation of alkynes. Applying formic acid as a hydrogen donor a broad range of aromatic and aliphatic terminal alkynes is selectively reduced under mild and base-free conditions tolerating several functional groups.

Notes and references

1 J. Scheirs and D. B. Priddy, *Modern Styrenic Polymers: Polystyrenes and Styrenic Copolymers*, John Wiley, Chichester, 2003.
2 J. Seayad, A. Tillack and M. Beller, *Angew. Chem., Int. Ed.*, 2004, **43**, 3368.
3 H.-J. Arpe, *Industrial Organic Chemistry*, Wiley-VCH, Weinheim, 2010.
4 F. Kerins and D. F. O'Shea, *J. Org. Chem.*, 2002, **67**, 4968.
5 (*a*) S. E. Denmark and C. R. Butler, *J. Am. Chem. Soc.*, 2008, **130**, 3690; (*b*) C. Amatore, A. A. Bahsoun, A. Jutand, G. Meyer, A. N. Ntepe and L. Ricard, *J. Am. Chem. Soc.*, 2003, **125**, 6070; (*c*) R. F. Heck, *Org. React.*, 1982, **27**, 345.
6 H. Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.
7 For reviews, see: (*a*) S. Gladiali and E. Alberico, *Chem. Soc. Rev.*, 2006, **35**, 226; (*b*) J. S. M. Samec, J.-E. Bäckvall, P.-G. Andersson and P. Brandt, *Chem. Soc. Rev.*, 2006, **35**, 237.
8 H. S. La Pierre, J. Arnold and F. D. Toste, *Angew. Chem., Int Ed.*, 2011, **50**, 3900.
9 (*a*) P. Hauwert, R. Boerleider, S. Warsink, J. J. Weigand and C. J. Elsevier, *J. Am. Chem. Soc.*, 2010, **132**, 16900; (*b*) P. Hauwert, G. Maestri, J. W. Sprengers, M. Catellani and C. J. Elsevier, *Angew. Chem., Int. Ed.*, 2008, **47**, 3223.
10 (*a*) M. A. Esteruelas, I. González, J. Herrero and L. A. Oro, *J. Organomet. Chem.*, 1998, **551**, 49; (*b*) R. R. Schrock and J. A. Osborn, *J. Am. Chem. Soc.*, 1976, **98**, 4450.
11 M. A. Esteruelas, A. M. Lopez, L. A. Oro, A. Perez, M. Schulz and H. Werner, *Organometallics*, 1993, **12**, 1823.
12 C. Belger, N. M. Neisius and B. Plietker, *Chem.–Eur. J.*, 2010, **16**, 12214.
13 (*a*) K. Junge, K. Schröder and M. Beller, *Chem. Commun.*, 2011, **47**, 4849; (*b*) C.-L. Sun, B.-J. Li and Z.-J. Shi, *Chem. Rev.*, 2011, **111**, 1293; (*c*) R. H. Morris, *Chem. Soc. Rev.*, 2009, **38**, 2282; (*d*) W. M. Czaplik, M. Mayer, J. Cvengroš and A. J. v. Wangelin, *ChemSusChem*, 2009, **2**, 396; (*e*) B. D. Sherry and A. Fürstner, *Acc. Chem. Res.*, 2008, **41**, 1500; (*f*) S. Enthaler, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2008, **47**, 3317; (*g*) B. Plietker, *Iron Catalysis in Organic Chemistry*, Wiley-VCH, Weinheim, 2008.
14 C. Bianchini, A. Meli, M. Peruzzini, P. Frediani, C. Bohanna, M. A. Esteruelas and L. Oro, *Organometallics*, 1992, **11**, 138.
15 For an iron-catalyzed hydrosilylation of internal alkynes, see: (*a*) S. Enthaler, M. Harberberger and E. Irran, *Chem.–Asian J.*, 2011, **6**, 1613; (*b*) S. C. Bart, E. Lobkovsky and P. J. Chirik, *J. Am. Chem. Soc.*, 2004, **126**, 13794.
16 For recent examples, see: (*a*) S. Zhou, S. Fleischer, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2011, **50**, 5120; (*b*) K. M. Driller, S. Prateeptongkum, R. Jackstell and M. Beller, *Angew. Chem., Int. Ed.*, 2011, **50**, 537; (*c*) K. Schröder, B. Join, A. J. Amali, K. Junge, X. Ribas, M. Costas and M. Beller, *Angew. Chem., Int. Ed.*, 2011, **50**, 1425; (*d*) C. Federsel, A. Boddien, R. Jackstell, R. Jennerjahn, P. J. Dyson, R. Scopelitti, G. Laurenczy and M. Beller, *Angew. Chem., Int. Ed.*, 2010, **49**, 9777; (*e*) K. Junge, B. Wendt, N. Shaikh and M. Beller, *Chem. Commun.*, 2010, **46**, 1769; (*f*) A. Boddien, F. Gärtner, R. Jackstell, H. Junge, A. Spannenberg, W. Baumann, R. Ludwig and M. Beller, *Angew. Chem., Int. Ed.*, 2010, **49**, 8993; (*g*) S. Prateeptongkum, K.-M. Driller, R. Jackstell and M. Beller, *Chem.–Asian J.*, 2010, **5**, 2173–2176; (*h*) S. Zhou, S. Fleischer, K. Junge, S. Das, D. Addis and M. Beller, *Angew. Chem., Int. Ed.*, 2010, **49**, 8121; (*i*) N. S. Shaikh, S. Enthaler, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2008, **47**, 2497.
17 G. Wienhöfer, I. Sorribes, A. Boddien, F. Westerhaus, K. Junge, H. Junge, R. Llusar and M. Beller, *J. Am. Chem. Soc.*, 2011, **133**, 12875.
18 (*a*) P. O. Lagaditis, A. J. Lough and R. H. Morris, *J. Am. Chem. Soc.*, 2011, **133**, 9662; (*b*) T. Ohkuma, M. Koizumi, K. Muniz, G. Hilt, C. Kabuto and R. Noyori, *J. Am. Chem. Soc.*, 2002, **124**, 6508.
19 A. Boddien, D. Mellmann, F. Gärtner, R. Jackstell, H. Junge, P. J. Dyson, G. Laurenczy, R. Ludwig and M. Beller, *Science*, 2011, **333**, 1733.