E-Selective Semi-Hydrogenation of Alkynes by Heterobimetallic Catalysis

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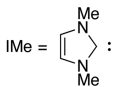
S *Supporting Information*

ABSTRACT: A unique cooperative H_2 activation reaction by heterobimetallic (NHC)M′-MCp(CO)$_2$ complexes (NHC = N-heterocyclic carbene, M′ = Cu or Ag, M = Fe or Ru) has been leveraged to develop a catalytic alkyne semi-hydrogenation transformation. The optimal Ag–Ru catalyst gives high selectivity for converting alkynes to E-alkenes, a rare selectivity mode for reduction reactions with H_2. The transformation is tolerant of many reducible functional groups. Computational analysis of H_2 activation thermodynamics guided rational catalyst development. Bimetallic alkyne hydrogenation and alkene isomerization mechanisms are proposed.

Catalytic hydrogenation of unsaturated organic substrates remains a crucial application of homogeneous catalysis, in part due to the exquisite control of selectivity that is possible through catalyst design. The classical approach to catalytic hydrogenation involves single-site oxidative addition/reductive elimination mechanisms. This approach is exemplified by well-known examples such as Wilkinson's catalyst,[1] the Schrock–Osborn catalyst,[2] and Crabtree's catalyst[3] that all operate by Rh^I/Rh^{III} or Ir^I/Ir^{III} cycles initiated through single-site oxidative addition of H_2. Exciting developments have emerged through exploring non-classical approaches to H_2 activation. Representative examples include catalysts that activate H_2 using metal–ligand cooperativity[4−8] or non-metal frustrated Lewis acid–base cooperativity.[9−11]

Another cooperative effect to potentially exploit is bimetallic cooperativity, wherein two metal sites within a catalyst cooperate to activate H_2 and initiate catalytic reduction of a substrate. Although bimetallic H_2 cleavage reactions have been long known,[12] their use in catalytic transformations is underdeveloped.[13−15] Previous examples of bimetallic hydrogenation catalysts often suffer from poor activity,[16] and in some cases faster rates can actually be achieved by using monometallic analogues that omit one of the two metal sites.[17] In this Communication, we report a semi-hydrogenation reaction of alkynes that *requires* bimetallic cooperativity to proceed. Through optimizing the nature of the bimetallic pairing within a tunable catalyst design, we have achieved unusual E-selectivity in the alkyne reduction, a rare selectivity mode in hydrogenation catalysis[18,19] that complements the famously Z-selective Lindlar catalyst[20] and more modern updates. Other methods for converting alkynes to E-alkenes, including stoichiometric Birch reduction or various catalytic methods,[21,22] do not use H_2 as the terminal reductant.

Our interest in bimetallic H_2 activation began through the study of a heterobimetallic catalyst for the dehydrogenative borylation of arenes.[24] The proposed mechanism for this transformation includes a key turnover step involving bimetallic reductive elimination from (NHC)CuH + FpH (NHC = N-heterocyclic carbene; Fp = FeCp(CO)$_2$) to regenerate the (NHC)Cu-Fp catalyst through loss of H_2. The calculated pathway[25] for this dehydrogenation event has a low-energy transition state that could reasonably be approached from the reverse direction, i.e., in a hypothetical H_2 cleaving reaction. We thus reasoned that a (NHC)Cu-Fp complex or one of its (NHC)Cu-[M] analogues[26] ([M] = metal carbonyl anion) might be active for bimetallic H_2 addition. To explore this possibility, we calculated the thermodynamics of this hypothetical H_2 activation, as a function of [M], using DFT methods with a truncated NHC model (IMe = N,N'-dimethylimidazol-2-ylidene, Table 1). The relative trends that emerged (Table 1)

Table 1. Thermodynamics for H_2 Activation by (NHC)Cu-[M]

(IMe)Cu—[M] $\xrightarrow[- H_2]{+ H_2}$ (IMe)Cu—H + H—[M]

IMe =

entry	[M]	relative nucleophilicity of [M]$^{-a}$	$\Delta G_{298\ K}$ (kcal/mol)^b
1	FeCp(CO)$_2$	70,000,000	21.9
2	RuCp(CO)$_2$	7,500,000	20.1/14.5^c
3	Re(CO)$_5$	25,000	26.4
4	WCp(CO)$_3$	500	24.8
5	Mn(CO)$_5$	77	33.0
6	MoCp(CO)$_3$	67	34.0
7	CrCp(CO)$_3$	4	34.5
8	Co(CO)$_4$	1	49.0

^{a}From ref 23. ^{b}Calculated by DFT for H_2 cleavage. ^{c}For (IMes)Ag in place of (IMe)Cu.

guided our experimental catalyst development, although the energies would be more accurate by including NHC sterics, solvation, and (NHC)CuH dimerization[27] energies.

As expected on the basis of facile dehydrogenation reactivity observed previously,[24,25] the H_2 activation is thermodynamically unfavorable for all systems calculated. Two key observations guided our experimental trials. First, the general trend is for H_2 activation to be less favorable with decreasing

$[M]^-$ nucleophilicity.[23] Second, among the most promising candidates, the (NHC)Cu-Rp system (Rp = RuCp(CO)$_2$) has an unusually low ΔG value for H$_2$ addition (Table 1, entry 2) considering the relative nucleophilicity of [Rp]$^-$. Based on these observations, we began experimental studies with (NHC)Cu-Fp and (NHC)Cu-Rp complexes. In a related study, Meyer recently observed stoichiometric H$_2$ activation based on cooperation between [Rp]$^-$ and a carbon Lewis acid.[28]

As expected, no evidence for any reaction occurring was obtained by NMR spectroscopy when different (NHC)Cu-Fp and (NHC)Cu-Rp complexes were exposed to H$_2$. However, when the reactions were done in the presence of alkynes at elevated temperatures, alkene products were observed, indicating that H$_2$ was indeed being activated by the catalyst. Preliminary experimentation indicated that appropriate conditions for catalytic hydrogenation would include 150 °C reaction temperature in xylenes solvent at 1 atm of H$_2$ pressure. Rapid catalyst decomposition was observed when polar solvents were used in place of xylenes or when higher H$_2$ pressures were employed. Catalysis was observed at lower temperatures, but multiple days were required for reaction progress to reach completion.

When comparing diphenylacetylene hydrogenation results for (NHC)Cu-Fp catalysts (Table 2, entries 1 and 2) with

Table 2. Alkyne Semi-Hydrogenation Catalyst Optimization
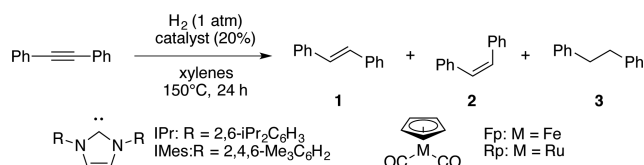
entry	catalyst	conversion (%)^a	1:2:3^a
1	(IPr)Cu-Fp	32	8:23:1
2	(IMes)Cu-Fp	64	12:50:2
3	(IPr)Cu-Rp	60	40:18:3
4	(IMes)Cu-Rp	61	42:17:2
5	(IPr)Ag-Fp	29	17:12:1
6	(IMes)Ag-Fp	32	21:11:0
7	(IPr)Ag-Rp	84	54:24:5
8	**(IMes)Ag-Rp**	**95.7^b**	**90.2:4.2:1.2^b**
9	(IPr)AgOAc	0	N/A
10	Rp$_2$^{c}	7	4:3:0
11	(IMes)Ag-Rp + Hg drop	89	67:18:4

^{a}From ^{1}H NMR integration against an internal standard. ^{b}Averaged over two independent runs ($\pm$0.2 error bars). ^{c}Catalyst loading was 10%, i.e., 20% Ru.

those for (NHC)Cu-Rp catalysts (entries 3 and 4), we found that selectivity for *trans*-stilbene increased significantly when substituting Fe for Ru. In all cases, the total conversions of diphenylacetylene were low to modest, and so we proceeded to test (NHC)Ag-Fp (entries 5 and 6) and (NHC)Ag-Rp analogues (entries 7 and 8), which were predicted by DFT to activate H$_2$ more readily (Table 1, entry 2). Only for the (NHC)Ag-Rp catalysts were high conversions realized. The optimal catalyst was (IMes)Ag-Rp (IMes = *N,N′*-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene), which gave 96% conversion of diphenylacetylene and yielded *trans*-stilbene as 95% of the product mixture (Table 2, entry 8). The *cis*-stilbene was the main side product, while 1,2-diphenylethane was formed only

in trace amounts. To confirm that both metal sites are required for catalysis, we note that neither (IPr)AgOAc nor Rp$_2$ catalyze hydrogenation of diphenylacetylene (entries 9 and 10). Preliminary indications are that the reaction does involve homogeneous catalysis: a drop of Hg did not significantly poison catalysis (entry 11), and we believe that the modest lowering of conversion and erosion of selectivity is due to a slow background reaction between (IMes)Ag-Rp and Hg, evident from a visible color change even prior to heating (IMes)Ag-Rp + Hg with H$_2$ and alkyne.

Quantitative conversions of both an electron-rich and an electron-poor diarylalkyne were achieved under these catalytic conditions, still with high *E*:*Z* selectivity (Table 3, entries 2 and

Table 3. Alkyne Semi-Hydrogenation by (IMes)Ag-Rp

entry	R	R′	conversion (%)^a	1:2:3^a
1	Ph	Ph	95.7^b	90.2:4.2:1.1^b
2	4-MeOC$_6$H$_4$	4-MeOC$_6$H$_4$	>99	71:24:5
3	4-F$_3$CC$_6$H$_4$	4-F$_3$CC$_6$H$_4$	>99	72:20:8
4	4-(n-H$_{11}$C$_5$)C$_6$H$_4$	H	91	91^c:n.d.^{d}
5	Ph	nBu	>99	n.d.^{d}

^{a}From ^{1}H NMR integration against an internal standard. ^{b}Averaged over two independent runs ($\pm$0.2 error bars). ^{c}Terminal alkene. ^{d}Not determined.

3). A terminal alkyne also underwent quantitative reduction (entry 4). 1-phenyl-1-hexyne underwent efficient reduction, but we were unable to identify the product(s) formed (entry 5).

A hypothetical hydrogenation mechanism is shown in Figure 1a. Reversible H$_2$ activation by the (NHC)M′-[M] catalyst
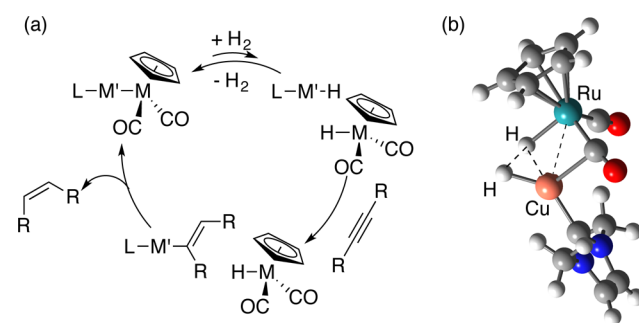

Figure 1. (a) Hypothetical mechanism for alkyne semi-hydrogenation by (NHC)M′-[M] catalysts (M = Fe or Ru, M′ = Cu or Ag, L = IPr or IMes). (b) Transition state for H$_2$ activation by (IMe)Cu-Rp calculated by DFT.

produces (NHC)M′-H + [M]-H. This H$_2$ activation can be viewed as a heterolysis, producing an equilibrium mixture of a protic species and a hyridic species. The calculated transition state for H$_2$ activation by (IMe)Cu-Rp is shown in Figure 1b ($\Delta H^{\ddagger}$ = 20.1 kcal/mol, $\Delta S^{\ddagger}$ = −29.8 eu, $\Delta G^{\ddagger}_{298K}$ = 29.0 kcal/mol). As expected for a late transition state, the Cu−Ru and H−H bonds are almost completely broken (2.74 and 1.28 Å, respectively, vs 2.44 and 0.75 Å in reactants). As we have noted previously for a related reaction,[29] one of the CO ligands bridges the two metals in the transition state (Cu···CO = 2.64

Å) to provide stability as the metals separate. As evidence for this step occurring, we note that ^{1}H NMR peaks (e.g., in toluene-d_8: δ = 4.52 and −12.04, 5:1 integration) assigned to RpH were observed in typical product mixtures, along with precipitation of the coinage metal consistent with known decomposition of (NHC)M′-H complexes.[27,30,31] Following H$_2$ activation, alkyne insertion into (NHC)M′-H produces a σ-alkenyl intermediate. This hydrometalation step is expected to proceed with *syn* stereochemistry, based on the known reactivity of the (IPr)CuH dimer.[27] Less is known about the insertion chemistry of analogous (NHC)Ag-H species.[30,31] Finally, protonolysis of the σ-alkenyl ligand by [M]-H regenerates the (NHC)M′-[M] catalyst through bimetallic elimination of the *Z*-alkene.

According to this proposal, the alkyne substrate is initially reduced to the *Z*-alkene, which must then be isomerized under the reaction conditions. To probe the validity of this proposal, we exposed *cis*-stilbene to the catalytic conditions and, indeed, observed isomerization to the *trans* isomer (Table 4, entry 1).

Table 4. Alkene Isomerization Studies

entry	alkene	variation on conditions	1:2:3[a]
1	*cis*-stilbene	none	92:4:5
2	*trans*-stilbene	none	98:0:2
3	*cis*-stilbene	catalyst omitted	<1:99:0
4	*cis*-stilbene	H$_2$ omitted	22:78:0

[a]From ^{1}H NMR integration against an internal standard.

On the other hand, exposing the *trans*-stilbene to the catalytic conditions resulted in no isomerization (entry 2). The *Z*-to-*E* isomerization was stopped when the catalyst was omitted (entry 3) and slowed when H$_2$ was omitted (entry 4). These observations indicate that *cis*-stilbene is a viable reaction intermediate that isomerizes to *trans*-stilbene under the reaction conditions, and that the isomerization is catalyzed by a H$_2$-derived metal−hydride species.

A proposed mechanism for isomerization is shown in Figure 2. The mechanism involves *Z*-alkene insertion into the (NHC)M′-H intermediate to generate a metal−alkyl species. This metal−alkyl subsequently undergoes β-hydride elimination to extrude either the *E* or *Z* alkene, the former of which is favored thermodynamically. The metal−alkyl intermediate

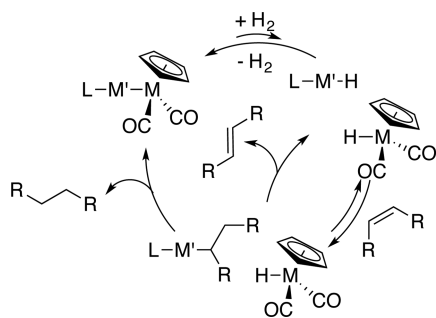**Figure 2.** Hypothetical mechanism for alkene isomerization under hydrogenation conditions by (NHC)M′-[M] catalysts (M = Fe or Ru, M′ = Cu or Ag, L = IPr or IMes).

species should also be susceptible to protonolysis by [M]-H, consistent with our observation of trace alkanes in most product mixtures. According to our catalyst optimization results (Table 2), the general trends are for the cycle in Figure 2 to be faster for M′ = Ag, M = Ru, and NHC = IMes.

Finally, we sought to explore the functional group tolerance of the transformation using a modified version of Glorius's robustness screening method.[32] The reduction of diphenylacetylene was conducted in the presence of various additives containing potentially reactive functional groups. Product mixtures were analyzed at both partial (6 h) and full (24 h) conversion (Table 5). It is clear from the partial conversion

Table 5. Time-Dependent Robustness Screening Data

entry	additive	conversion (%)[a,b]	1:2:3[a,b]
1	none	55/96	49:4:1/90:4:1
2	heptaldehyde	36/96	8:22:5/15:81:1
3	6-undecanone	74/90	61:12:1/71:16:2
4	acetonitrile	55/94	37:17:2/78:16:2
5	ethyl acetate	58/>99	43:13:2/92:0:8
6	1-butanol	79/99	69:8:2/84:11:4
7	pyridine	68/79	62:5:1/66:11:2
8	1-dodecene	65/>99	48:15:2/96:1:3
9	neopentyl chloride	54/99	39:13:2/94:2:3

[a]From ^{1}H NMR integration against an internal standard. [b]Listed as 6 h/24 h.

data that the rate of catalysis is not slowed by any of the functional group tested, other than by aldehydes (entry 2). From the full conversion data, it is evident that the alkyne reduction is tolerant of many reactive functional groups. The *E*:*Z* selectivity was eroded slightly by the presence of a pyridine or a ketone (entries 3 and 7), and was actually inverted by the presence of an aldehyde (entry 2). As an illustrative example, the aldehyde additive was detected at the end of the reaction, indicating that (IMes)Ag-Rp is capable of catalyzing alkyne hydrogenation but *not* aldehyde reduction. The selective reduction of alkynes in the presence of other reducible functional groups (e.g., aldehydes, ketones, alkenes, nitriles) is quite remarkable.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b10357.

> Experimental procedures and spectral data (PDF)
> Computational output (ZIP)
> Crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) Osborn, J. A.; Jardine, F. H.; Young, J. F.; Wilkinson, G. *J. Chem. Soc. A* **1966**, 1711.

(2) Schrock, R. R.; Osborn, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 4450.

(3) Crabtree, R. H.; Felkin, H.; Morris, G. E. *J. Organomet. Chem.* **1977**, *141*, 205.

(4) Shvo, Y.; Czarkie, D.; Rahamim, Y.; Chodosh, D. F. *J. Am. Chem. Soc.* **1986**, *108*, 7400.

(5) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40.

(6) Balaraman, E.; Gunanathan, C.; Zhang, J.; Shimon, L. J. W.; Milstein, D. *Nat. Chem.* **2011**, *3*, 609.

(7) Lin, T.-P.; Peters, J. C. *J. Am. Chem. Soc.* **2014**, *136*, 13672.

(8) Xu, X.; Kehr, G.; Daniliuc, C. G.; Erker, G. *J. Am. Chem. Soc.* **2015**, *137*, 4550.

(9) Welch, G. C.; San Juan, R. R.; Masuda, J. D.; Stephan, D. W. *Science* **2006**, *314*, 1124.

(10) Stephan, D. W.; Greenberg, S.; Graham, T. W.; Chase, P.; Hastie, J. J.; Geier, S. J.; Farrell, J. M.; Brown, C. C.; Heiden, Z. M.; Welch, G. C.; Ullrich, M. *Inorg. Chem.* **2011**, *50*, 12338.

(11) Chernichenko, K.; Madarász, Á.; Pápai, I.; Nieger, M.; Leskelä, M.; Repo, T. *Nat. Chem.* **2013**, *5*, 718.

(12) Baranger, A. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1994**, *116*, 3822 and references therein.

(13) Zhang, Y.; Roberts, S. P.; Bergman, R. G.; Ess, D. H. *ACS Catal.* **2015**, *5*, 1840.

(14) Buchwalter, P.; Rosé, J.; Braunstein, P. *Chem. Rev.* **2015**, *115*, 28.

(15) Cooper, B. G.; Napoline, J. W.; Thomas, C. M. *Catal. Rev.: Sci. Eng.* **2012**, *54*, 1.

(16) Man, M. L.; Zhou, Z.; Ng, S. M.; Lau, C. P. *Dalton Trans.* **2003**, 3727.

(17) Kato, H.; Seino, H.; Mizobe, Y.; Hidai, M. *J. Chem. Soc., Dalton Trans.* **2002**, 1494.

(18) Radkowski, K.; Sundararaju, B.; Fürstner, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 355.

(19) Srimani, D.; Diskin-Posner, Y.; Ben-David, Y.; Milstein, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 14131.

(20) Lindlar, H. *Helv. Chim. Acta* **1952**, *35*, 446.

(21) Trost, B. M.; Ball, Z. T.; Jöge, T. *J. Am. Chem. Soc.* **2002**, *124*, 7922.

(22) Shen, R.; Chen, T.; Zhao, Y.; Qiu, R.; Zhou, Y.; Yin, S.; Wang, X.; Goto, M.; Han, L.-B. *J. Am. Chem. Soc.* **2011**, *133*, 17037.

(23) King, R. B. *Acc. Chem. Res.* **1970**, *3*, 417.

(24) Mazzacano, T. J.; Mankad, N. P. *J. Am. Chem. Soc.* **2013**, *135*, 17258.

(25) Parmelee, S. R.; Mazzacano, T. J.; Zhu, Y.; Mankad, N. P.; Keith, J. A. *ACS Catal.* **2015**, *5*, 3689.

(26) Banerjee, S.; Karunananda, M. K.; Bagherzadeh, S.; Jayarathne, U.; Parmelee, S. R.; Waldhart, G. W.; Mankad, N. P. *Inorg. Chem.* **2014**, *53*, 11307.

(27) Mankad, N. P.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 3369.

(28) Kalz, K. F.; Brinkmeier, A.; Dechert, S.; Mata, R. A.; Meyer, F. *J. Am. Chem. Soc.* **2014**, *136*, 16626.

(29) Karunananda, M. K.; Parmelee, S. R.; Waldhart, G. W.; Mankad, N. P. *Organometallics* **2015**, *34*, 3857.

(30) Tate, B. K.; Wyss, C. M.; Bacsa, J.; Kluge, K.; Gelbaum, L.; Sadighi, J. P. *Chem. Sci.* **2013**, *4*, 3068.

(31) Tate, B. K.; Nguyen, J. T.; Bacsa, J.; Sadighi, J. P. *Chem. - Eur. J.* **2015**, *21*, 10160.

(32) Collins, K. D.; Glorius, F. *Nat. Chem.* **2013**, *5*, 597.