JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Article
pubs.acs.org/JACS

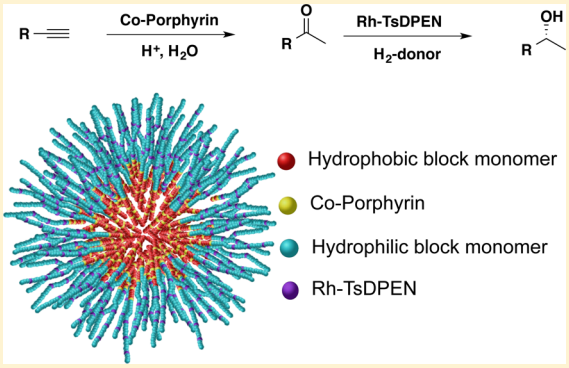
Compartmentalization of Incompatible Catalytic Transformations for Tandem Catalysis

Jie Lu, Jonas Dimroth, and Marcus Weck*

Molecular Design Institute and Department of Chemistry, New York University, New York, New York 10003, United States

Supporting Information

ABSTRACT: In Nature, incompatible catalytic transformations are being carried out simultaneously through compartmentalization that allows for the combination of incompatible catalysts in tandem reactions. Herein, we take the compartmentalization concept to the synthetic realm and present an approach that allows two incompatible transition metal catalyzed transformations to proceed in one pot in tandem. The key is the site isolation of both catalysts through compartmentalization using a core−shell micellar support in an aqueous environment. The support is based on amphiphilic triblock copolymers of poly(2-oxazoline)s with orthogonal functional groups on the side chain that can be used to cross-link covalently the micelle and to conjugate two metal catalysts in different domains of the micelle. The micelle core and shell provide different microenvironments for the transformations: Co-catalyzed hydration of an alkyne proceeds in the hydrophobic core, while the Rh-catalyzed asymmetric transfer hydrogenation of the intermediate ketone into a chiral alcohol occurs in the hydrophilic shell.



INTRODUCTION

At any given moment, the cell is carrying out a large number of incompatible (and competing) catalytic transformations simultaneously.[1−3] This is possible by compartmentalizing these transformations and catalysts thereby shielding them from each other, which not only prevents them from interference but also allows them to run in a variety of microenvironments with differing pH values, salt concentrations, hydrophobic or hydrophilic environments, etc.[4−6] Additionally, Nature is able to shuttle reactants and products through individual compartments allowing for cascade or tandem reaction pathways combining (incompatible) transformations for complex molecule synthesis. To date, synthetic analogues to such chemical reaction diversity do not exist, though there is significant interest in one-pot multistep strategies to supersede intermediate workup procedures.[7−11] Synthetic multicompartment systems are in their infancy[12] and reports of combining incompatible transformations in one pot have been limited to a few examples,[13−28] none of them allowing for multiple incompatible and enantioselective transformations. This contribution closes this gap and describes the compartmentalization of two different transition metal catalysts and their use in asymmetric tandem catalysis. The term one-pot reaction includes domino, cascade and tandem reactions as subsets. We focus on *orthogonal tandem catalysis* that is defined as a one-pot sequence of reactions involving two or more functionally distinct catalytic mechanism using two or more different catalysts that are present from the outset.[12,29]

Compartmentalization spatially isolates incompatible or opposing reagents. Approaches to bypass incompatibility issues were pioneered by Patchornik and co-workers who used two insoluble polymer-immobilized reagents in order to prevent them from reacting with each other, thus enabling so-called "wolf and lamb" reactions.[30] Synthetic non-natural compartmentalization systems have been achieved by immobilization or encapsulation of reagents on polymers,[14−23,25,31] sol−gel materials,[26−28] or Pickering emulsions.[13] Advanced polymerization techniques have led to multiple approaches to integrate site-isolation within polymer systems. In 2005, Frechét and coworkers encapsulated acid and base catalysts within the cores of different star polymers. The highly branched materials enable the performance of a sequence of acid and base reactions in tandem by isolating the acid and base sites effectively while the reactants can penetrate each core.[25] In 2009, the van Hest group demonstrated spatial site-isolation by carrying out a biocatalytic three-step tandem reaction with enzymes immobilized in the lumen, in the bilayer membrane, and on the surface of a polymersome.[32] More recently, the authors presented a polymersomes-in-polymersomes approach for the confinement of enzymes. This system was used to perform three-step tandem reactions employing either compatible or incompatible enzymes.[17] These reports are fascinating examples for multicompartmentalized microreactor architectures for biocatalytic cascade reactions. The combination of different metal complex

Received: July 16, 2015

DOI: 10.1021/jacs.5b07257
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

catalyzed transformations within a single particle, however, has not yet been achieved.

Polymeric micelles have been used as catalyst supports, since they feature properties such as concentration effects, shielding, and substrate selectivity, often in conjunction with reusability.[33] Our compartmentalization strategy is based on shell-cross-linked micelles that have been introduced by Wooley and co-workers and used mainly in drug delivery and bioimaging.[34,35] We have reported on the use of this material as support structure in catalysis.[36] The micelle structure contains a hydrophobic core and a hydrophilic shell. This core–shell architecture should provide perfect site-isolation and compartmentalization of incompatible transformations, making it an excellent platform to combine two incompatible catalytic reactions for a multistep sequential reaction.

RESULTS AND DISCUSSION

A requirement for our polymer micelle support strategy is the introduction of orthogonal functional handles located in the core and shell domains to attach the two different metal catalysts. Our target tandem reaction was the synthesis of chiral secondary alcohols that are used as building blocks in the production of pharmaceuticals and fine chemicals. Starting from commercially available alkynes, Co-catalyzed hydration was used to form the corresponding methyl ketones that were then transformed by Rh-catalyzed asymmetric transfer hydrogenation (ATH) into the chiral secondary alcohols. Methyl ketones can be prepared by the catalytic hydration of terminal alkynes using a variety of catalysts including cobalt porphyrin (Co–Por) complexes.[37,38] ATH is a powerful method for the preparation of enantioenriched chiral alcohols from ketones, and transition metal complexes based on N-tosylated 1,2-diphenyl-1,2-ethylenediamine (TsDPEN) derivatives are among the most efficient catalysts for this reaction.[39,40] The overall transformation is shown in Figure 1. One-pot operations

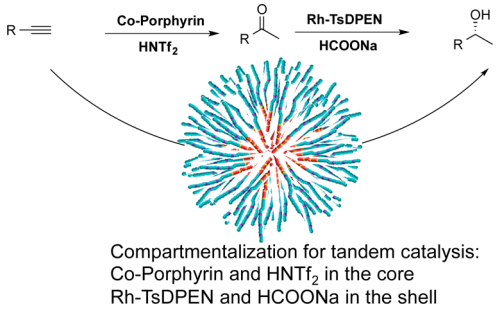


Figure 1. Catalytic tandem reaction: Co-catalyzed hydration of terminal alkynes followed by Rh-catalyzed asymmetric transfer hydrogenation.

of this reaction sequence were reported by Wang et al.[41] and Li et al.[42] In both cases, however, the reactions were carried out stepwise, and successive addition of reactants, as well as intermediate alterations of the reaction conditions, was required.

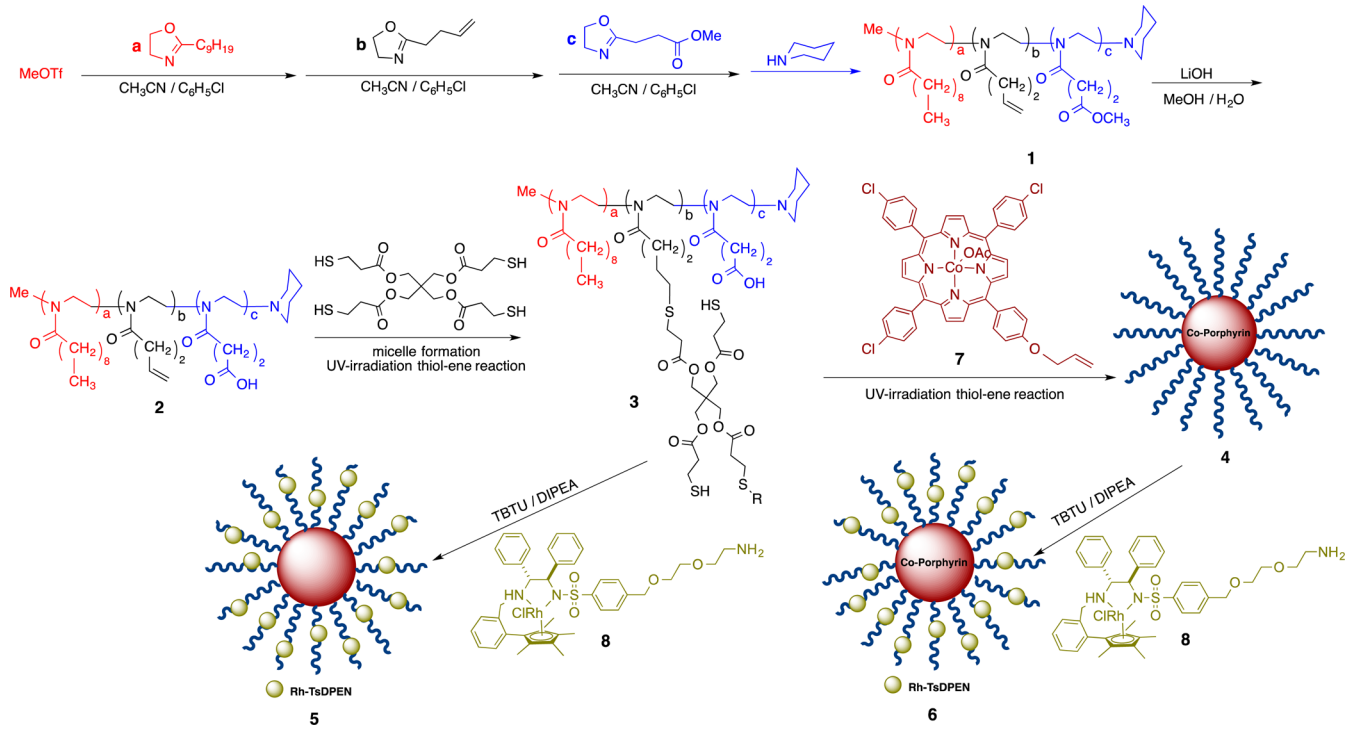
The cross-linked micelle support was formed from amphiphilic ABC-triblock copolymers using poly(2-oxazoline) derivatives. To carry out the tandem reaction in an aqueous environment, the polymer was designed to have a hydrophobic block (a) containing a nine carbon alkyl tail and a carboxylic acid–based hydrophilic block (c) (Scheme 1). To stabilize the micelle, a hydrophobic cross-linking block (b) was introduced as the middle block that can be covalently cross-linked via thiol–ene chemistry.[43,44] We synthesized the poly(2-oxazoline) triblock copolymers via cationic ring-opening polymerization using methyl triflate as the initiator.[45] The polymerization process was monitored by ^{1}H NMR spectroscopy and gel-permeation chromatography (GPC) (see Supporting Information). The disappearance of the monomer backbone ethylene signals at 4.20 and 3.82 ppm in the ^{1}H NMR spectrum and clear shifts of the GPC traces after each block formation proved the stepwise growth of the block copolymer. The dispersity ($Đ$) and apparent molecular weight (M_n^{app}) of the triblock copolymer **1** were 1.23 and 5500 g mol^{-1}, respectively, as determined by GPC (Figure 2).

The ester groups in the side chains of block C were hydrolyzed to yield the free carboxylic acids increasing hydrophilicity and providing a functional handle for the attachment of the amine-functionalized Rh-TsDPEN catalysts. We induced micelle formation by dissolving polymer **2** in water at 1 mg/mL (higher than its CMC) and characterized the resulting micelles using dynamic light scattering (DLS) analysis (see Supporting Information). To cross-link the micelle a multivalent tetrathiol linker was reacted with the terminal vinyl groups in block B. The free thiol groups remaining after the cross-linking step were used to attach the alkene-functionalized Co-porphyrin catalysts (Scheme 1). To covalently attach the Co-catalyst for the alkyne hydration step and the Rh-catalyst for the ATH of the resulting ketone to the micellar support, we introduced functional handles to the metal-complex ligands. The alkene-functionalized Co-porphyrin catalyst **7** was synthesized in three steps.[37,46] First, we obtained the unsymmetrical hydroxyl-functionalized porphyrin ligand via Lindsey's method, followed by the introduction of the terminal alkene via etherification of the hydroxyl-porphyrin and vinyl bromine. Cobalt metalation was carried out in the glovebox and the resulting complex was oxidized in air to form the desired Co(III)–porphyrin catalyst (a reaction scheme can be found in the Supporting Information). The amine-functionalized Rh-TsDPEN catalyst **8** was synthesized in four steps. The original version of this complex, introduced by Wills and co-workers, does not possess a linker.[47] Though a carboxyl-functionalized and immobilized version has been reported,[48] we used a modified synthetic route since an amine linker was required for covalent attachment to our micelle support. In the first step, *R,R*-DPEN was monosubstituted with a cyclopentadienyl moiety via reductive amination. The remaining free amine was then coupled with 4-bromomethylbenzenesulfonyl chloride. The introduced bromine was used for etherification with 2-(2-aminoethoxy)ethanol to yield the amine-functionalized multidentate ligand that was finally metalated with $RhCl_3$ (a reaction scheme can be found in the Supporting Information). We attached the alkene-functionalized Co–porphyrin to the core of **3** obtaining the micelle-supported Co–porphyrin catalyst **4**, while the amine-functionalized Rh-TsDPEN was immobilized in the shell of **3** via peptide coupling to obtain the micelle supported Rh-catalyst **5**. The dual catalyst micelle **6** was obtained by coupling the amine-functionalized Rh-TsDPEN to **4**. The hydrodynamic radius of **6**, determined by DLS, was 36 ± 4 nm, consistent with the radius of 30 ± 6 nm obtained by SEM.

Before using the micelle supported catalytic system, we tested the nonsupported homogeneous small molecule catalysts for each reaction. The Brønsted acid triflimide ($HNTf_2$) was used as cocatalyst for the hydration reaction, while aqueous

DOI: 10.1021/jacs.5b07257
J. Am. Chem. Soc. XXXX, XXX, XXX–XXX

Scheme 1. Synthetic Scheme of the Micelle Supported Metal Catalyst



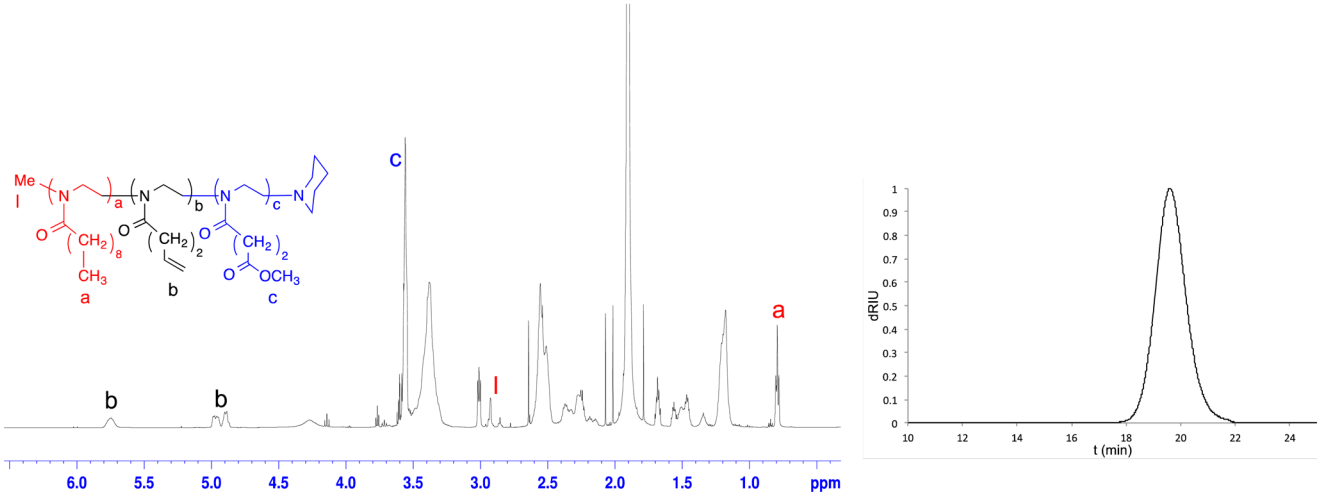


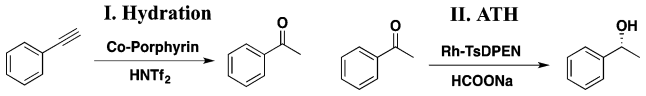
Figure 2. ^{1}H NMR spectrum in $CDCl_3$ and normalized gel-permeation chromatogram of triblock copolymer **1**.

sodium formate (HCOONa) was the hydrogen source for the ATH reaction. The reaction conditions were based on literature procedures (Table 1, entries 1 and 2).[37,48] The hydration reaction of phenylacetylene reached 95% conversion over 24 h, while the ATH reaction of acetophenone reached 99% conversion over 12 hours. When we attempted a tandem reaction by combining the two catalysts, neither ketone nor alcohol was observed, demonstrating the incompatibility of the two transformations (Table 1, entry 3). We then investigated which part(s) of the reaction conditions are interfering and found that the hydration reaction using Co-porphyrin did not proceed in the presence of sodium formate (Table 1, entry 4), whereas the ATH reaction did operate in the presence of trifilimde (Table 1, entry 5). The observation that sodium formate was the source of the incompatibility was supported by an additional experiment. When both reactions were set up in a sequential fashion in one pot, in which the hydration was run to completion before water, HCOONa, and Rh-TsDPEN were added, the chiral alcohol was observed (Table 1, entry 6). We reasoned that this tandem reaction presents a good testbed to investigate whether our compartmentalization strategy can suppress the interference of the identified components.

We investigated the catalytic activity of **4** for the hydration of phenylacetylene to the corresponding acetophenone. The reaction was set up with 2 mol % $HNTf_2$ as the cocatalyst and 1 mg of **4** in pure water at 40 °C. Over 36 h, the corresponding methyl ketone was obtained in 75% yield (Table 2, entry 1). To analyze the compatibility of the hydration and ATH reactants, we added five equivalents of HCOONa (Table 2, entry 2) to the micellar solution. In contrast to the reaction under homogeneous conditions, the alkyne hydration proceeded in the presence of the salt, and a slightly improved yield

DOI: 10.1021/jacs.5b07257
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

Table 1. Catalytic Tests of Nonsupported Co- and Rh-Catalysts



entry	reaction[a]	catalyst[b]	$HNTf_2$ (mol %)	HCOONa (eq)	T (h)	conv. (%)[c]
1	I	Co	2	0	24	95
2	II	Rh	0	5	12	99
3	Tandem	Co + Rh	2	5	24	0
4	I	Co	2	5	24	0
5	II	Rh	2	5	24	99
6	I + II	Co	2	0	24	99
	sequential test[d]	Rh	0	5	12	99

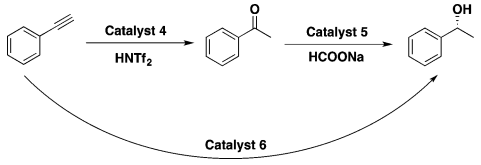
[a]Reactions were carried out with 0.25 mmol substrate in 1 mL MeOH at 40 °C. [b]Catalyst loading is 1 mol %. [c]Determined by GC analyses. [d]Started with the hydration reaction, after it was completed, added 0.5 mL of H_2O, HCOONa, and Rh-catalyst.

(82%) was achieved as compared to the use of the supported catalyst without sodium formate. We hypothesize that these results are based on the creation of micellar microenvironments that differ significantly in the concentration of sodium formate. While the hydrophobic micelle core is assumed to be largely free of the formate and sodium ions, the hydrophilic environment in the shell displays a high concentration thereof. We then examined the catalytic activity of **5** for the asymmetric transfer hydrogenation of acetophenone to the corresponding chiral alcohol, considering the effect of the presence of $HNTf_2$. First, we set up the reaction with 5 equiv of sodium formate as the H-donor and 1 mg of **5** in pure water at 40 °C. Over 12 h, the corresponding chiral alcohol was obtained in 99% yield and 97% ee (Table 2, entry 3). When adding 2 mol % $HNTf_2$, the reaction was not affected, and equally high values of conversion and ee were observed (Table 2, entry 4). After demonstrating that the two catalytic transformations using the individually supported catalysts worked separately, we tested whether the micelle-supported catalysts could carry out both catalytic transformations in a one-pot fashion. We first set up the test reaction in a stepwise manner. The hydration reaction was carried out using **4**, $HNTf_2$, HCOONa and the alkyne substrate. After 24 h, we added **5** to initiate the ATH reaction. After additional 24 h, we observed the final product, the chiral alcohol, in 60% yield and 96% ee (Table 2, entry 5). This result proved that the micelle support enables the one-pot performance of the originally incompatible hydration and ATH reactions. We then combined catalysts **4** and **5** with $HNTf_2$, HCOONa, and the alkyne substrate in one pot from the outset to test whether the tandem reaction proceeds (Table 2, entry 6). After 36 h, we found the desired chiral alcohol in 74% yield with 96% ee. Within the reaction time, the intermediate methyl ketone did not fully convert to the final alcohol. We hypothesize that the intermediate might be trapped in the micellar support of **4** preventing the reaction from reaching completion. Micelle support **6**, the Co–Rh dual catalyst micelle, should overcome this limitation, since the intramicellar diffusion of the substrates is assumed to be faster than the intermicellar diffusion. We combined **6** with $HNTf_2$, HCOONa and the alkyne substrate (Table 2, entry 7). The reaction reached 95% conversion with 96% ee over 36 h. The only product observed was the chiral alcohol, indicating that the intermediate methyl ketone was entirely reacted to the desired product. The dual catalyst system provides significantly higher yields than both the stepwise reaction and the two micelle catalyst system. Compared to the homogeneous nonsupported catalytic system, the dual catalyst micelle system not only enables two incompatible reactions to occur simultaneously in one pot, but also allows the tandem reaction to run to completion using lower catalyst loadings for both transformations than those employed under homogeneous conditions.[41,42]

A basic substrate screen revealed that, using the dual catalyst system (**6**), aliphatic substrates can be converted with high efficiency (Table 3, entries 3 and 4), whereas aromatic substrates substituted with electron-withdrawing groups yielded poor results and nonterminal alkynes were not converted at all. These observations are in agreement with previous reports on Co–porphyrin catalyzed alkyne hydrations.[37]

In summary, we translated the concept of multicompartmentalization from Nature to asymmetric transition metal complex catalysis. Using the domains of a core–shell cross-linked micelle to immobilize two transition metal catalysts in site-isolated microenvironments, we demonstrate that a non-orthogonal two-step catalytic tandem reaction proceeds in

Table 2. Catalytic Tests of Micelle Supported Co- and Rh-Catalysts

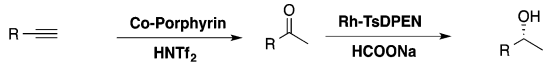


entry[a]	starting material	catalyst[b]	$HNTf_2$ (mol %)	HCOONa (eq)	time (h)	conv. (%)[c]	ee (%)[d]
1	Phenylacetylene	**4**	2	0	36	75	-
2	Phenylacetylene	**4**	2	5	36	82	-
3	Acetophenone	**5**	0	5	12	99	97
4	Acetophenone	**5**	2	5	12	99	97
5	Phenylacetylene	**4**; **5**[e]	2	5	48	60	96
6	Phenylacetylene	**4** + **5**[e]	2	5	36	74	96
7	Phenylacetylene	**6**	2	5	36	95	96

[a]Reactions were carried out with 0.25 mmol substrate in 1 mL of H_2O at 40 °C. [b]Catalyst loading of Co in **4** is 0.17 mol %, Rh in **5** is 0.07 mol %, Co in **6** is 0.13 mol % and Rh in **6** is 0.07 mol %. [c]Determined by GC analyses. [d]Determined by HPLC analyses. [e]Semicolon (;) means two catalysts were added stepwise while plus symbol (+) means two catalysts were added at the same time.

DOI: 10.1021/jacs.5b07257
J. Am. Chem. Soc. XXXX, XXX, XXX–XXX

Table 3. Substrate Scope for the Tandem Reactions Using 6



Entry	Substrate[a]	Time (h)	Conv. (%)[b]	*ee* (%)[c]
1		36	95	97
2		36	12	-[d]
3		24	88	94[e]
4		24	67	96[e]
5		48	0	-

[a]Reactions are carried out with 0.251 mmol substrate in 1 mL of MeOH H_2O at 40 °C and catalyst loading of Co of 0.13 mol % and of Rh of 0.07 mmol %. [b]Determined by GC analyses. [c]Determined by chiral HPLC (column, OD-H). [d]ee not determined due to low conversion [e]Determined by HPLC using OD-H after converting the product into phenyl carbamate (phenyl isocyanate).

one pot with outstanding yields and enantioselectivities. While the tandem reaction works in principle even when the two catalysts are immobilized on different micelles, the multicompartmentalized micelle containing both catalysts gave significantly better results. We assume that the reason for the high efficiency of the dual catalyst micelle is that it provides optimal microenvironments for each reaction and fast intramicellar diffusion of the intermediate. Our strategy should be generalizable and paves the way for unforeseen tandem reactions that involve incompatible catalytic transformations. The number of catalytic steps that can be combined using this strategy is currently limited by the number of functionalized domains within a micelle. Future research in our group will therefore address the preparation of multicompartment micelles with more than two domains to compartmentalize more sophisticated sequential catalytic reactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b07257.

Chrystallographic data (CIF)

Syntheses and characterizations of the triblock copolymer **1**, functionalized metal catalysts, synthetic procedures and characterization of micelle supported catalysts **4**−**6**, and experimental procedures for tandem catalysis tests (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*marcus.weck@nyu.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Funding provided by the U.S. Department of Energy, Office of Basic Energy Sciences, through Catalysis Science Contract DE-FG02-03ER15459, is gratefully acknowledged. J.D. is thankful to the *Thomas-und-Ulla-Kolbeck-Stiftung* for financial support. We thank the NYU Molecular Design Institute for the purchase of the Bruker SMART APEXII Diffractometer, and Dr. Chunhua Hu for his assistance with the single crystal data collection and structure determination.

■ REFERENCES

(1) Hopwood, D. A. *Annu. Rev. Genet.* **1990**, *24*, 37.
(2) Arigoni, D.; Sagner, S.; Latzel, C.; Eisenreich, W.; Bacher, A.; Zenk, M. H. *Proc. Natl. Acad. Sci. U. S. A.* **1997**, *94*, 10600.
(3) Agapakis, C. M.; Boyle, P. M.; Silver, P. A. *Nat. Chem. Biol.* **2012**, *8*, 527.
(4) Longstreet, A. R.; McQuade, D. T. *Acc. Chem. Res.* **2013**, *46*, 327.
(5) Marguet, M.; Bonduelle, C.; Lecommandoux, S. *Chem. Soc. Rev.* **2013**, *42*, 512.
(6) Fischlechner, M.; Schaerli, Y.; Mohamed, M. F.; Patil, S.; Abell, C.; Hollfelder, F. *Nat. Chem.* **2014**, *6*, 791.
(7) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115.
(8) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134.
(9) Zhou, J. *Chem. - Asian J.* **2010**, *5*, 422.
(10) Lu, L.-Q.; Chen, J.-R.; Xiao, W.-J. *Acc. Chem. Res.* **2012**, *45*, 1278.
(11) Pellissier, H. *Chem. Rev.* **2013**, *113*, 442.
(12) Lohr, T. L.; Marks, T. J. *Nat. Chem.* **2015**, *7*, 477.
(13) Yang, H.; Fu, L.; Wei, L.; Liang, J.; Binks, B. P. *J. Am. Chem. Soc.* **2015**, *137*, 1362.
(14) Huang, H.; Denard, C. A.; Alamillo, R.; Crisci, A. J.; Miao, Y.; Dumesic, J. A.; Scott, S. L.; Zhao, H. *ACS Catal.* **2014**, *4*, 2165.
(15) Wang, Z. J.; Clary, K. N.; Bergman, R. G.; Raymond, K. N.; Toste, F. D. *Nat. Chem.* **2013**, *5*, 100.
(16) Yang, Y.; Liu, X.; Li, X.; Zhao, J.; Bai, S.; Liu, J.; Yang, Q. *Angew. Chem., Int. Ed.* **2012**, *51*, 9164.
(17) Peters, R. J. R. W.; Louzao, I.; van Hest, J. C. M. *Chem. Sci.* **2012**, *3*, 335.
(18) Shi, J.; Zhang, L.; Jiang, Z. *ACS Appl. Mater. Interfaces* **2011**, *3*, 881.
(19) Runge, M. B.; Mwangi, M. T.; Miller, A. L., II; Perring, M.; Bowden, N. B. *Angew. Chem., Int. Ed.* **2008**, *47*, 935.
(20) Miller, A. L., II; Bowden, N. B. *Adv. Mater.* **2008**, *20*, 4195.
(21) Pilling, A. W.; Boehmer, J.; Dixon, D. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 5428.
(22) Poe, S. L.; Kobašlija, M.; McQuade, D. T. *J. Am. Chem. Soc.* **2006**, *128*, 15586.
(23) Phan, N. T. S.; Gill, C. S.; Nguyen, J. V.; Zhang, Z. J.; Jones, C. W. *Angew. Chem., Int. Ed.* **2006**, *45*, 2209.
(24) Motokura, K.; Fujita, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2005**, *127*, 9674.
(25) Helms, B.; Guillaudeu, S. J.; Xie, Y.; McMurdo, M.; Hawker, C. J.; Fréchet, J. M. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 6384.
(26) Gelman, F.; Blum, J.; Avnir, D. *J. Am. Chem. Soc.* **2002**, *124*, 14460.
(27) Gelman, F.; Blum, J.; Avnir, D. *Angew. Chem., Int. Ed.* **2001**, *40*, 3647.
(28) Gelman, F.; Blum, J.; Avnir, D. *J. Am. Chem. Soc.* **2000**, *122*, 11999.
(29) Fogg, D. E.; dos Santos, E. N. *Coord. Chem. Rev.* **2004**, *248*, 2365.
(30) Cohen, B. J.; Kraus, M. A.; Patchornik, A. *J. Am. Chem. Soc.* **1981**, *103*, 7620.
(31) Chi, Y.; Scroggins, S. T.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2008**, *130*, 6322.
(32) van Dongen, S. F. M.; Nallani, M.; Cornelissen, J. J. L. M.; Nolte, R. J. M.; van Hest, J. C. M. *Chem. - Eur. J.* **2009**, *15*, 1107.
(33) Cotanda, P.; Petzetakis, N.; O'Reilly, R. K. *MRS Commun.* **2012**, *2*, 119.
(34) Elsabahy, M.; Wooley, K. L. *Chem. Soc. Rev.* **2012**, *41*, 2545.
(35) O'Reilly, R. K.; Hawker, C. J.; Wooley, K. L. *Chem. Soc. Rev.* **2006**, *35*, 1068.
(36) Liu, Y.; Wang, Y.; Wang, Y.; Lu, J.; Pinon, I.; Victor; Weck, M. *J. Am. Chem. Soc.* **2011**, *133*, 14260.

DOI: 10.1021/jacs.5b07257
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

(37) Tachinami, T.; Nishimura, T.; Ushimaru, R.; Noyori, R.; Naka, H. *J. Am. Chem. Soc.* **2013**, *135*, 50.
(38) Beller, M.; Seayad, J.; Tillack, A.; Jiao, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 3368.
(39) Ikariya, T.; Blacker, A. J. *Acc. Chem. Res.* **2007**, *40*, 1300.
(40) Gladiali, S.; Alberico, E. *Chem. Soc. Rev.* **2006**, *35*, 226.
(41) Wang, S.; Miao, C.; Wang, W.; Lei, Z.; Sun, W. *ChemCatChem* **2014**, *6*, 1612.
(42) Li, F.; Wang, N.; Lu, L.; Zhu, G. *J. Org. Chem.* **2015**, *80*, 3538.
(43) Lowe, A. B. *Polym. Chem.* **2010**, *1*, 17.
(44) Gress, A.; Volkel, A.; Schlaad, H. *Macromolecules* **2007**, *40*, 7928.
(45) Hoogenboom, R. *Macromol. Chem. Phys.* **2007**, *208*, 18.
(46) Lindsey, J. S.; Schreiman, I. C.; Hsu, H. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827.
(47) Matharu, D. S.; Morris, D. J.; Kawamoto, A. M.; Clarkson, G. J.; Wills, M. *Org. Lett.* **2005**, *7*, 5489.
(48) Dimroth, J.; Keilitz, J.; Schedler, U.; Schomacker, R.; Haag, R. *Adv. Synth. Catal.* **2010**, *352*, 2497.

DOI: 10.1021/jacs.5b07257
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX