Published in final edited form as:

Small. 2018 February ; 14(7): . doi:10.1002/sml.201702198.

Solubilization of Hydrophobic Catalysts Using Nanoparticle Hosts

Youngdo Jeong[†],

Department of Chemistry, University of Massachusetts Amherst, 710 North Pleasant Street, Amherst, MA 01003, USA

Gulen Yesilbag Tonga[†],

Department of Chemistry, University of Massachusetts Amherst, 710 North Pleasant Street, Amherst, MA 01003, USA

Bradley Duncan,

Department of Chemistry, University of Massachusetts Amherst, 710 North Pleasant Street, Amherst, MA 01003, USA

Bo Yan,

Department of Chemistry, University of Massachusetts Amherst, 710 North Pleasant Street, Amherst, MA 01003, USA

Riddha Das,

Department of Chemistry, University of Massachusetts Amherst, 710 North Pleasant Street, Amherst, MA 01003, USA

Chonticha Sahub, and

Department of Chemistry, University of Massachusetts Amherst, 710 North Pleasant Street, Amherst, MA 01003, USA. Supramolecular Chemistry Research Unit, Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok, 10330, Thailand

Prof. Vincent M. Rotello^{*}

Department of Chemistry, University of Massachusetts Amherst, 710 North Pleasant Street, Amherst, MA 01003, USA

Abstract

We report a modular strategy for the solubilization and protection of hydrophobic transition metal catalysts using the hydrophobic pockets of water soluble gold nanoparticles. Beside preserving original catalyst activity, this encapsulation strategy provides a protective environment for the hydrophobic catalyst and brings reusability. This system provides a versatile platform for the encapsulation of different hydrophobic transition metal catalysts, allowing a wide range of catalysis in water while uniting the advantages of homogeneous and heterogeneous catalysis in the same system.

Tel: (+1) 413-545-2058, Fax: (+1) 413-545-2058, rotello@chem.umass.edu.

[†]These authors contributed equally to this work

Supporting Information Supporting Information is available from the Wiley Online Library or from the author.

Graphical Abstract

Encapsulation of transition metal catalysts into the monolayers of gold nanoparticles generates nanoreactors that provide water solubility and provide a protective environment for the catalysts.

Keywords

catalysis in water; gold nanoparticles; host-guest chemistry; solubilization of hydrophobic catalyst; stability of catalyst

Transition metal-mediated catalysis (TMC) in aqueous media^[1] diminishes the dependence on expensive and environmentally unfriendly organic solvents.^[2,3] However, most TMC reactions are performed in organic solvents due to limited solubility,^[4] activity,^[5] and stability^[6] of the catalysts in water. Therefore, designing a general platform that solubilizes hydrophobic catalysts in water while preserving their activity and stability remains critical for environmental and economical benefits.

Covalent and non-covalent modifications to transition metal (TM) catalysts have been used to improve catalyst solubility in aqueous environments. Widely investigated approaches include covalent conjugation of the catalysts with hydrophilic ligands^[7] or anchoring charged substituents to the coordinating hydrophobic ligands.^[8] These covalent modifications demand specific ligand designs for each catalyst, which can affect the stability and reactivity of the native catalyst.^[9] Meanwhile, improving the solubility of TM catalysts does not inherently protect the catalysts from aqueous degradation. Covalent modification can change the steric and electronic environment of metal center, weakening the bond between the ligand and metal, resulting in poor initiation efficiency,^[6a] decomposition of catalyst,^[10] and loss of activity.^[11] Non-covalent approaches such as host-guest assembly of catalysts with cyclodextrins,^[12] calixarenes,^[13] and cucurbiturils^[14] have been shown as effective methods to solubilize catalysts without the need to alter the structure of the catalysts.^[15] These supramolecular approaches, however, require the catalysts to possess suitable guest sites.^[16]

Another emerging approach to address the challenges associated with catalyst solubility and stability is encapsulating catalysts into platforms such as micelles,^[17] dendrimers,^[18] polymeric capsules,^[19] and hollow polymer shells.^[20] These constructs provide solubility to the catalyst and result in high yield under ambient conditions due to the ability of confined nanocatalysis.^[21] However, issues such as the use of stabilizing agent and additives^[22]/surfactants^[23] and their removal, multistep preparation procedures,^[24] lack of robustness due to the dynamic nature of these systems,^[25] and lack of complete template removal^[26] impede the effective use of the aforementioned platforms. Furthermore, these scaffolds are more suitable for the entrapment of catalyst made up from metal nanoparticles with size of larger than 10 nm.^[27] However, majority of homogeneous catalysts including TM catalysts are in the size range of 1–2 nm.

Nanoparticles (NPs) with their unique tunable physical and chemical properties are promising platforms to encapsulate/immobilize a variety of catalysts including small-sized TM catalysts.^[28] Performing catalysis using NP systems brings the advantages of both homogenous and heterogeneous catalysis into the same system.^[29] While efficient and diverse reactions are catalyzed within these NPs, reaction products are easily separated using simple separation methods such as filtration.^[30] Recently we have shown that gold nanoparticles (AuNPs) can solubilize hydrophobic TM catalysts for drug activation.^[31] We present here the extension of this methodology to important synthetic transformations, providing a general method to solubilize and stabilize hydrophobic TM catalysts while preserving catalytic activity using a water soluble AuNP platform (Figure 1). This water soluble NP host was designed bearing two crucial features: an aliphatic interior to create hydrophobic pockets for catalyst encapsulation and a water soluble exterior for aqueous solubility.^[32] In our method, there is no need for covalent modification of the catalyst, and the supramolecular template supplies a protective niche for hydrophobic catalysts. Using this platform we demonstrate the efficiency of two commercially important reactions.

Our initial catalysis studies focused on commercially available Hoveyda-Grubbs 2nd generation (HG2), widely used for ring opening metathesis polymerization (ROMP). Hydrophobic (HG2) catalysts were encapsulated using a solvent displacement method.^[32] Water soluble NP hosts and hydrophobic HG2 catalysts molecules were dissolved in acetone/water mixtures and then the organic solvents were allowed to evaporate slowly. During the evaporation process, HG2 catalysts were encapsulated into the hydrophobic pockets in the monolayer of AuNP, providing HG2 catalyst-encapsulated nanoreactors (AuNP-HG2), while excess hydrophobic catalyst precipitated out. Then filtrations using molecular weight cutoff filters were performed to unbound catalysts followed by dialysis against water (Figure 1a) (Supporting Information). Other catalyst encapsulations were prepared in analogous fashion to obtain AuNP-cat nanoreactors.

To determine parameters for effective catalyst design, two different sized gold cores (2 and 7 nm), each with two different ligand structures (TTMA and TMA, Figure 2a) were investigated. Both TTMA and TMA ligands possess a hydrophobic chain, crucial for hydrophobic pocket formation and a charged ammonium head group for water solubility (Figure 2a). Qualitative confirmation of catalyst presence in the monolayer of nanoreactor was monitored by ¹H-NMR in D₂O after encapsulation. Peaks observed at ~6.8–7.8 ppm

demonstrate that 2nd generation Hoveyda-Grubbs catalysts (HG2) were entrapped inside the nanoreactor (Figure S1). The size of the nanoreactor was monitored before and after encapsulation of HG2 as well as after the purification process by transmission electron microscopy (TEM), showing no size change or aggregation (Figure S2).

Catalyst loading in the NP was calculated by tracking TM ions using KCN-induced decomposition experiments^[32] followed by inductively coupled plasma mass spectrometry (ICP-MS) measurements. The results indicate that 7 nm core NP holds more catalysts, however the 2 nm core NPs has higher encapsulation yield according to the weight ratio between catalyst and NP core (Figure 2b and Figure S3). When same core size but different ligand structure was considered, NP bearing TEG groups showed a higher catalyst loading efficiency. The surface ligand coverage was obtained using the laser desorption/ionization mass spectrometry^[33] to probe the effect of ligand coverage on encapsulation yield. The results revealed that the TTMA AuNPs possess more remaining pentanethiols after place exchange reaction than TMA AuNPs, suggesting that the pentanethiols provide a larger space to encapsulate the catalysts (Figure S4). Overall, the 2nm core TTMA NP host is the most efficient and catalytic reactions were performed using these NPs (Figure 2b).

In our HG2 kinetic studies, ROMP was performed in water using a positively charged norbornene monomer^[34] (Figure 3a–b). After 24 hours, a white suspension was observed indicative of polymer formation. Without catalyst encapsulation, however, polymer generation was not detected (Figure S5). The effect of reaction time on polymerization was monitored by using gel permeation chromatography (GPC). Polymers collected at different time points were characterized for molecular weight and PDI (polydispersity index) (Figure 3c–d and Figure S6), showing a typical linear trend of living polymerization. Narrow PDI values were obtained as expected from a living ROMP reaction (Figure 3c–d).

Catalysts containing ruthenium carbene complexes generally decompose quickly in aqueous solvents^[35] due to water coordination at ruthenium in the methylenide-propagating species.^[36] We have checked the stability of free HG2 catalyst and found that in the presence of monomer and free HG2 catalyst in 1:1 acetone/water mixture, the reaction failed to produce any polymer. (Figure 3d, 3f and Figure S7). However, HG2 catalyst embedded into the monolayer of AuNPs successfully catalyzed the ROMP reaction under same conditions (Figure 3d–e and Figure S6) indicating that our NP host provides a protective environment blocking water mediated catalyst decomposition.

Hydrogenation of alkenes is a particularly important class of reaction. The RhCl(PPh₃)₃ complex (Wilkinson's catalyst) is a hydrophobic, highly active catalyst for hydrogenation reactions (Figure 4a–b). We encapsulated Wilkinson catalyst into the nanoreactor and ICP-MS detected 29.7 ± 6.9 catalysts per AuNP (Figure S3). NP-Wilkinson catalyst (0.7 mole percent) were reacted with sodium 4-vinylbenzenesulfonate in water under hydrogen (3 atm) at room temperature and monitored by NMR. After hydrogenation, the alkene peaks (5.2–6.8 ppm) disappear while triplet and quartet peaks appear. The integration of those peaks show ~100% conversion after 24 hours of reaction (Figure 4c and Figure S8). These hydrogenation experimental conditions prove the AuNP-cat system can effectively catalyze

not only monophasic water solvent systems (ROMP reaction) but also gas-water biphasic systems (hydrogenation reaction).

Catalytic reusability is an important for industrial applications. We examined the reusability of AuNP host-catalyst system for hydrogenation reaction. After the first reaction, a molecular weight cutoff filter (10 K) was used to separate AuNP-Wilkinson catalyst and the product, 4-ethylbenzenesulfonate. AuNP-Wilkinson catalyst was recovered after three times washing and reacted again with substrate sodium 4-vinylbenzenesulfonate under the same conditions (room temperature, 3 atm). This cycle repeated up to five times and 100% conversion was obtained as a proof of the recyclability of NP-catalyst template (Figure 4d and Figure S9).

In summary, we have developed a versatile AuNP-based platform for the encapsulation of hydrophobic transition metal catalysts through host-guest interactions. This supramolecular system eliminates the dependence on organic solvents and provides cost-effective and environmentally safe catalysis. Our NP platform is amenable to encapsulate a variety of catalysts without the need to specifically tailor the host structure for each hydrophobic catalyst. The functionalized monolayer of the NP host serves as a phase transfer agent for the catalyst while concurrently preventing catalyst 'drowning' through supramolecular stabilization. Future studies will explore the use of this platform in biological systems and as multifunctional catalytic reactors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by grants from the NIH (EB EB022641)

References

1. a) Leenders SHAM, Gramage-Doria R, de Bruin B, Reek JNH. Chem Soc Rev. 2015; 44:433. [PubMed: 25340992] b) Butler RN, Coyne AG. Chem Rev. 2010; 110:6302. [PubMed: 20815348] c) Yin Q, Tan JM, Besson C, Geletii YV, Musaev DG. Science. 2010; 328:342. [PubMed: 20223949] d) Cornils, B., Hermann, WA. Aqueous-Phase Organometallic Catalysis. Wiley-VCH: Weinheim; Germany: 2004.
2. a) Rios-Lombardia N, Vidal C, Liardo E, Moris F, Garcia-Alvarez J, Gonzalez-Sabin J. Angew Chem Int Ed. 2016; 55:8691. b) Blackmond DG, Armstrong A, Coombe V, Wells A. Angew Chem Int Ed. 2007; 46:3798. c) Lindstrom UM. Chem Rev. 2002; 102:2751. [PubMed: 12175267] d) Li, CJ., Chan, TH. Comprehensive Organic Reactions in Aqueous Media. 2. Wiley; New York: 2007.
3. Lancaster, M., editor. M Lancaster in Green Chemistry: An Introductory Text. The Royal Society of Chemistry; London: 2002.
4. Hong SH, Grubbs RH. J Am Chem Soc. 2006; 128:3508. [PubMed: 16536510]
5. a) Himeda Y, Onozawa-Komatsuzaki N, Sugihara H, Kasuga K. Organometallics. 2007; 26:702. b) Cole-Hamilton DJ. Science. 2003; 299:1702. [PubMed: 12637737]
6. a) Lynn DM, Mohr B, Grubbs RH, Henling LM, Day MW. J Am Chem Soc. 2000; 122:6601. b) Gallivan JP, Jordan JP, Grubbs RH. Tetrahedron Lett. 2005; 46:2577.
7. a) Tomás-Gamasa M, Martínez-Calvo M, Couceiro JR, Mascareñas JL. Nat Commun. 2016; 7:125381. b) Schaper LA, Hock SJ, Herrmann WA, Kühn FE. Angew Chem Int Ed. 2013; 52:270. c)

- Samanta D, Kratz K, Zhang X, Emrick T. *Macromolecules*. 2008; 41:530.d) Nishioka T, Shibata T, Kinoshita I. *Organometallics*. 2007; 26:1126.e) Shi, J-c, Lei, N., Tong, Q., Peng, Y., Wei, J., Jia, L. *Eur J Inorg Chem*. 2007:2221.f) Zhang X, Qiu Y, Rao B, Luo M. *Organometallics*. 2009; 28:3093.
8. a) Bellini R, Chikkali SH, Berthon-Gelloz G, Reek JNH. *Angew Chem, Int Ed*. 2011; 50:7342.b) Bellini R, Reek JNH. *Chem – Eur J*. 2012; 18:7091. [PubMed: 22532382] c) Mesnager J, Lammel P, Jeanneau E, Pinel C. *Appl Catal A*. 2009; 368:22.d) Syska H, Herrmann WA, Kahn FE. *J Organomet Chem*. 2012; 703:56.e) Almasy A, Nagy CE, Banyei AC, Joa F. *Organometallics*. 2010; 29:2484.f) Godoy F, Segarra C, Poyatos M, Peris E. *Organometallics*. 2011; 30:684.
9. a) Elemans JAAW, Bijsterveld EJA, Rowan AE, Nolte RJM. *Chem Commun*. 2000:2443.b) Mohr B, Lynn DM, Grubbs RH. *Organometallics*. 1996; 15:4317.c) Kirkland TA, Lynn DM, Grubbs RH. *J Org Chem*. 1998; 63:9904.d) Lynn DM, Mohr B, Grubbs RH, Henling LM, Day MW. *J Am Chem Soc*. 2000; 122:6601.e) Lynn DM, Grubbs RH. *J Am Chem Soc*. 2001; 123:3187. [PubMed: 11457052] f) Kamer PC, van Leeuwen PW, Reek JN. *Acc Chem Res*. 2001; 34:895. [PubMed: 11714261] g) Linker T. *Angew Chem, Int Ed Engl*. 1997; 36:2060.
10. Burtscher D, Grela K. *Angew Chem Int Ed*. 2009; 48:442.
11. Grubbs, RH. *Aqueous Organometallic Chemistry and Catalysis*. Horvath, IT., Joo, F., editors. Kluwer Academic Publishers; The Netherlands: 1995. p. 15
12. a) Jouffroy M, Gramage-Doria R, Armspach D, Sémeril D, Oberhauser W, Matt D, Toupet L. *Angew Chem, Int Ed*. 2014; 53:3937.b) Guitet M, Zhang P, Marcelo F, Tugny C, Jiménez-Barbero J, Buriez O, Amatore C, Mouriès-Mansuy V, Goddard JP, Fensterbank L, Zhang Y, Roland S, Ménand M, Sollogoub M. *Angew Chem, Int Ed*. 2013; 52:7213.c) Hapiot F, Tilloy S, Monflier E. *Chem Rev*. 2006; 106:767. [PubMed: 16522008] d) Breslow R. *Acc Chem Res*. 1995; 28:146.
13. Ikeda A, Shinkai S. *Chem Rev*. 1997; 97:1713. [PubMed: 11851464]
14. a) Ong W, Kaifer MG, Kaifer AE. *Org Lett*. 2002; 4:1791. [PubMed: 12000300] b) Jeon WS, Moon K, Park SH, Chun H, Ko YH, Lee JY, Lee ES, Samal S, Selvapalam N, Rekharsky MV, Sindelar V, Sobransingh D, Inoue Y, Kaifer AE, Kim K. *J Am Chem Soc*. 2005; 127:12984. [PubMed: 16159293] c) Lagona J, Mukhopadhyay P, Chakrabarti S, Isaacs L. *Angew Chem Int Ed*. 2005; 44:4844.
15. Brown CJ, Miller GM, Johnson MW, Bergman RG, Raymond KN. *J Am Chem Soc*. 2011; 133:11964. [PubMed: 21736357]
16. Fiedler D, Leung DH, Bergman RG, Raymond KN. *Acc Chem Res*. 2005; 38:351.
17. a) Dwars T, Haberland J, Grassert I, Oehme G, Kragl U. *J Mol Catal A-Chem*. 2001; 168:81–86.b) Liu S, Weaver JVM, Save M, Armes SP. *Langmuir*. 2002; 18:8350.c) Liu Y, Wang Y, Wang Y, Lu J, Piñón V III, Weck M. *J Am Chem Soc*. 2011; 133:14260. [PubMed: 21846087] d) Newkome GR, Shreiner C. *Chem Rev*. 2010; 110:6338. [PubMed: 20666373]
18. a) Liu CP, Wu TH, Lin YL, Liu CY, Wang S, Lin SY. *Small*. 2016; 12:4127. [PubMed: 27346719] b) Deraedt C, Pinaud N, Astruc D. *J Am Chem Soc*. 2014; 136:12092. [PubMed: 25093967] c) Ooe M, Murata M, Mizugaki T, Ebitani K, Kaneda K. *Nano Lett*. 2002; 2:999.d) Ooe M, Murata M, Mizugaki T, Ebitani K, Kaneda K. *J Am Chem Soc*. 2004; 126:604.
19. Che H, van Hest JCM. *J Mater Chem B*. 2016; 4:4632.
20. a) Jia Y, Shmakov SN, Register P, Pinkhassik E. *Chem - Eur J*. 2015; 21:12709. [PubMed: 26223572] b) Dergunov SA, Durbin J, Pattanaik S, Pinkhassik E. *J Am Chem Soc*. 2014; 136:2212. [PubMed: 24369096]
21. a) Gao Z, Dong M, Wang G, Sheng P, Wu Z, Yang H, Zhang B, Wang G, Wang J, Qin Y. *Angew Chem Int Ed*. 2015; 54:9006.b) Chen Z, Guan Z, Li M, Yang Q, Li C. *Angew Chem Int Ed*. 2011; 50:4913.c) Mahmoud MA, Saira F, El-Sayed MA. *Nano Lett*. 2010; 10:3764. [PubMed: 20701250]
22. Zhang S, Zhao Y. *Chem Commun*. 2012; 48:9998.
23. Wang F, Liu H, Cun L, Zhu J, Deng J, Jiang Y. *J Org Chem*. 2005; 70:9424. [PubMed: 16268617]
24. a) McQuade DT, Seeberger PH. *J Org Chem*. 2013; 78:6384. [PubMed: 23750988] b) Kamata K, Lu Y, Xia Y. *J Am Chem Soc*. 2003; 125:2384. [PubMed: 12603113]
25. a) Bae YH, Yin H. *J Control Release*. 2008; 131:2–4. [PubMed: 18625275] b) Chen H, Kim S, Li L, Wang S, Park K, Cheng JX. *Proc Natl Acad Sci USA*. 2008; 105:6596–6601. [PubMed: 18445654]

26. Shmakov SN, Pinkhassik E. Chem Commun. 2010; 46:7346.
27. a) Yusop RM, Unciti-Broceta A, Johansson EMV, Sánchez-Martín RM, Bradley M. Nat Chem. 2011; 3:239. [PubMed: 21336331] b) Lou XW, Archer LA, Yang Z. Adv Mater. 2008; 20:3987.c) Shmakov SN, Pinkhassik E. Chem Commun. 2010; 46:7346.
28. a) Hu A, Liu S, Lin W. RSC Adv. 2012; 2:2576.b) Wang D, Salmon L, Ruiz J, Astruc D. Chem Commun. 2013; 49:6956.
29. Dergunov SA, Khabiyev AT, Shmakov SN, Kim MD, Ehterami N, Weiss MC, Birman VB, Pinkhassik E. ACS Nano. 2016; 10:11397. [PubMed: 28024370]
30. Thomas JM, Hernandez-Garrido JC, Raja R, Bell RG. Phys Chem Chem Phys. 2009; 11:2799. [PubMed: 19421495]
31. Tonga GY, Jeong Y, Duncan B, Mizuhara T, Mout R, Das R, Kim ST, Yeh Y-C, Yan B, Hou S, Rotello VM. Nat Chem. 2015; 7:597. [PubMed: 26100809]
32. Kim CK, Ghosh P, Pagliuca C, Zhu Z-J, Menichetti S, Rotello VM. J Am Chem Soc. 2009; 131:1360. [PubMed: 19133720]
33. Yan B, Zhu Z-J, Miranda OR, Chompoosor A, Rotello VM, Vachet RW. Anal Bioanal Chem. 2010; 396:1025. [PubMed: 19911174]
34. Lynn DM, Mohr B, Grubbs RH. J Am Chem Soc. 1998; 120:1627.
35. a) Binder JB, Blank JJ, Raines RT. Org Lett. 2007; 9:4885. [PubMed: 17949009] b) Burtscher D, Grela K. Angew Chem Int Ed. 2009; 48:442.
36. a) Ulman M, Grubbs RH. J Org Chem. 1999; 64:7202.b) Binder JB, Blank JJ, Raines RT. Org Lett. 2007; 9:4885. [PubMed: 17949009]

Figure 1.

a) The encapsulation process of hydrophobic catalysts in water-soluble NP hosts. b) Schematic illustrating catalytic reactions within the NP monolayer.

Figure 2.

a) The structure of NP hosts (core 2 and 7 nm) and the structure of TTMA and TMA ligands. b) The encapsulation efficacy of various NP hosts.

Figure 3.

a) 2nd generation Hoveyda-Grubbs catalyst (HG2). b) ROMP using NP host and water-soluble monomer. c) The molecular weight and PDI values of polymers in terms of reaction time. d) While the free HG2 in acetone/water mixture failed to produce the polymers, polymer formation was detected in the presence of the AuNP-HG2. e) GPC of NP host-HG2-monomer mixture after 24 h. f) GPC result of free catalyst-monomer mixture after 24 h, no polymerization was observed.

Figure 4.

a) Wilkinson catalyst. b) Hydrogenation using NP host and sodium 4-vinylbenzenesulfonate.

c) Hydrogenation conversion profile in terms of reaction time for AuNP-Wilkinson. d)

Reusability of AuNP-Wilkinson system for five consecutive cycles.