N,N-Dimethylformamide-Protected Single-Sized Metal Nanoparticles and Their Use as Catalysts for Organic Transformations
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ABSTRACT: In this mini-review, we summarize the solution syntheses of N,N-dimethylformamide (DMF)-protected metal nanoparticles (NPs) and nanoclusters (NCs) and their use in catalytic reactions. Representative examples are given of external-stabilizer/protectant-free metal NP and NC syntheses by reduction with DMF. In this method, DMF has three roles, i.e., a solvent, reductant, and protectant. Recent applications of DMF-stabilized metal NPs are summarized. These applications have enabled a versatile organic transformation such as cross-coupling reactions, hydrosilylation, and methylation to be achieved. These reactions proceed under low catalyst loadings and ligandless conditions.

1. INTRODUCTION
Metal nanoparticles (>100 nm) and nanoclusters (<2 nm) (M NPs and NCs) have attracted significant interest as catalysts. The pioneering work conducted by Haruta, which enabled low-temperature Au NP-catalyzed CO oxidations, has had a significant impact on nanocatalysis.1 Because of their high surface to volume ratios, nanocatalysts have high catalytic activities. The use of M NPs as catalysts in organic transformations has greatly expanded because of their activity, selectivity, and recyclability. In recent studies by Jin and our group, atomically precise thiolate-ligand-protected Au NCs [Au(n(SR))m] were used to catalyze reactions such as CO oxidation, alkyne semihydrogenation, and C–C coupling reactions2 and to synthesize propargylamines from amines, aldehydes, and alkynes; these are referred to as A3 coupling reactions3 and hydroaminations.4 Tsukuda’s group5 used poly(N-vinylpyrrolidone) (PVP)-stabilized Au NCs to catalyze hydroaminations and alcohol oxidations.

In general, M NPs and M NCs are synthesized from metal precursors by reduction in the presence of stabilizers in the liquid phase, i.e., the bottom-up method (Scheme 1a). The bottom-up approach has been used to access a variety of M NPs with a size-controlled NP core in the presence of surface stabilizers. However, stabilizers such as thiolate and phosphine surfactants and polymers are needed to avoid undesired aggregation, which hampers access to catalytically active surface sites.6 Surfactant-free synthesis provides a simple way to provide maximum access to catalytically active sites. Surfactant-free synthesis provides a simple way to provide maximum access to catalytically active sites. Surfactant-free synthesis provides a simple way to provide maximum access to catalytically active sites. Surfactant-free synthesis provides a simple way to provide maximum access to catalytically active sites. Surfactant-free synthesis provides a simple way to provide maximum access to catalytically active sites. Surfactant-free synthesis provides a simple way to provide maximum access to catalytically active sites. Surfactant-free synthesis provides a simple way to provide maximum access to catalytically active sites. Surfactant-free synthesis provides a simple way to provide maximum access to catalytically active sites.
of metal precursors and nanocrystal synthesis, Liz-Marzán and co-workers used PVP as a capping agent. To date, surfactant-free metal nanoparticles have been reported by using ethylene glycol and methyl isobutyl ketone as reductant. In contrast, the DMF-reduction method generated thermally stable M NPs/NCs with narrow size distribution (<7 nm). The proposed reduction mechanism is shown in eq 1; carbamic acid is readily oxidized to CO₂ and (CH₃)₂NH. In other reduction pathways, formic acid generated from DMF decomposition serves as a reductant for the metal precursor, and CO or H₂ reduces metal ions (eq 1).

DMF also acts as a protectant in surfactant-free synthesis. Surfactant-free Au NPs were first synthesized by Li and co-workers as fluorescent quantum dots. Since 2011, Kawasaki and our group have reported external-surfactant- and stabilizer-free syntheses of various M NPs and their use as organic transformation catalysts. These metal NPs are stable in moisture and air, and the catalytic reactions under rigorous inert atmosphere conditions are not a prerequisite. Previously reported data are summarized in Table 1.

3. DMF-STABILIZED METAL NANOPARTICLES AND NANOCLUSTERS FOR ORGANIC TRANSFORMATIONS

3.1. Gold. Kawasaki and co-workers investigated the catalytic activities and specific properties of Au NPs. The DMF-stabilized Au NCs consisted on average of 13 Au atom clusters. FT-IR and ¹H NMR spectroscopic investigations showed a strongly coordinated DMF layer around the Au NCs. These DMF-stabilized Au NCs catalyzed reduction of 4-nitrophenol to 4-aminophenol by NaBH₄ (eq 3). An induction time (~3000 s) was observed, which indicates that the DMF layer hindered access to the catalytically active site. Thermally aged Au NCs had a shorter induction time (~100 s at 80 °C for 8 h).

Lang et al. reported DMF-stabilized Au NPs of three different sizes (1.0, 2.5, and 5.5 nm). The solution temperature and nucleation time were used to control the particle size. The catalytic activities of these three Au NPs in the Ullmann homocoupling reaction were evaluated (eq 4). The order of the catalytic activities was Au (2.5 nm) > Au (<1 nm) > Au (5.5 nm). These Au NPs were stable. They were recycled fewer than three times, and their catalytic activity gradually decreased.

3.2. Palladium. DMF-stabilized Pd NCs were synthesized from PdCl₂. We reported the synthesis and cross-coupling catalytic activities of DMF-protected Pd NCs. The Pd NCs showed high catalytic activities in the Suzuki–Miyaura cross-coupling and Mizoroki–Heck reactions (eqs 5 and 6). High turnover numbers (TONs) were achieved, i.e., 4.5 × 10⁵ and 6.0 × 10⁸. The DMF-stabilized Pd NCs showed higher TONs than the precedent polymer micelles stabilized by Pd NPs up to 2.8 × 10⁷. The DMF-stabilized Pd NCs were recyclable. The Pd NCs were separated from the substrates and products by simple extraction with hexane/DMF (Scheme 2). The Pd NCs were recycled at least five times without significant loss of activity.

In 2013, DMF-stabilized Pd NCs were used to catalyze the Mignata–Kosugi–Stille coupling reaction (eq 7). Reactions of

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Table 1. Reported Metal Nanoparticle Sizes and Precursors

| metal | precursor | size | characterization methods |
|-------|-----------|------|--------------------------|
| Au    | HAuCl₄    | 1–1.5 nm, 2.5, 5.5 nm | MALDI-MS, TEM, XPS, FT-IR, TGA, NMR, UV/vis, PL |
| Pd    | PdCl₂     | 2 nm | TEM, XPS, FT-IR, TGA, NMR, UV/vis, PL, DLS |
| Cu    | CuCl₂     | 2–7 nm | TEM, XPS, FT-IR, TGA, UV/vis, PL, DLS |
| Fe    | Fe(acac)₃ | 2–5 nm | EGA-MS, TEM, XPS, XANES, FT-IR, TGA, NMR, UV/vis, PL, DLS |
| Ir    | IrCl₃     | 1–1.5 nm | TEM, XPS, FT-IR, TGA, NMR, UV/vis, PL, DLS |

Scheme 2. Procedure for Recycling Pd NCs

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aryl halides with tributylphenyl-/tributyl-vinylstannane gave the corresponding cross-coupling products. The Pd NCs were stable in air and gave high TONs (up to $3.5 \times 10^4$).

Recently, we reported cross-coupling of aryl halides with hydrosilanes/disilanes (eqs 8 and 9). Generally, silylations require relatively high catalyst loadings. The coupling reaction proceeded under phosphorus-ligand- and external-additive-free conditions. The DMF-stabilized Pd NCs can be recycled five times under hydrosilane/disilane reaction conditions. The catalyst recycling procedure is similar to that for Suzuki–Miyaura cross-couplings. XPS analysis showed displacement of DMF molecules surrounding the metal center to $N,N$-dimethylacetamide. DMF dissociation improved the catalytic performance.

Indole derivatives are key motifs in many bioactive compounds. The reaction of 2-haloanilines with alkynes, namely, the Larock indole synthesis, is a useful method for accessing indole motifs. DMF-stabilized Pd NCs successfully catalyzed the synthesis of 2,3-disubstituted indoles from 2-iodoanilines and internal alkynes under external-ligand-free conditions at low catalyst loadings (0.3 mol %) (eq 10). The Pd NC catalyst can be reused at least three times.

Sanda and our group achieved Sonagashira–Hagihara (eq 11) and Mizoroki–Heck coupling (eq 12) polymerization by using DMF-stabilized Pd NCs as the catalyst. The catalytic reaction provided poly(phenylethynylene) and poly(phenylenevinylene) of moderate molecular weights ($M_n$ 6700 and 5900). These results are similar to those achieved with conventional PdCl$_2$(PPh$_3$)$_2$ and Pd(PPh$_3$)$_4$ complex catalysts. The ligand-free Pd NC polymerization system avoids contamination of the growing polymer by ligand-derived phosphorus impurities.

3.3. Copper. DMF-stabilized Cu NPs were prepared from CuCl$_2$. The particle size was determined by HRTEM and DLS (2–7 nm). The catalytic activity in Ullmann-type cross-coupling of aryl halides with phenol derivatives under ligand-free conditions was evaluated (eq 13); the reaction of iodobenzene (1.5 mmol) with 3,5-dimethylphenol (1.0 mmol) was used as a model reaction. When this reaction was performed in the presence of DMF-protected Cu NPs (0.2 mol %) and Cs$_2$CO$_3$ (2.0 mmol) in DMF at 110 °C for 24 h under Ar, the corresponding product was obtained in 92% yield. The DMF-stabilized Cu NPs showed high catalytic activity (TONs up to $2.2 \times 10^5$). The Cu NPs can be reused three times.

The Sonogashira–Hagihara coupling reaction is a powerful tool for obtaining acetylenes. The DMF-stabilized Cu NPs showed high catalytic activity in this reaction (eq 14). In a typical procedure, a mixture of iodobenzene (0.5 mmol), phenylacetylene (0.75 mmol), and PPh$_3$ (10 mol %) in DMF (1 mL) was heated at 135 °C for 24 h in the presence of DMF-stabilized Cu NPs (0.2 mol %). The corresponding product was obtained in 92% yield. The presence of PPh$_3$ or bipyridine (bpy) was necessary for this reaction. TEM observations showed that the Cu NPs retained their single-nanosized structure after the catalytic reaction. The DMF-stabilized Cu NPs are themselves inactive, but they act as a catalyst precursor when PPh$_3$ and bpy are used as additives. Some of the DMF dissociates from the Cu NPs and in situ generated PPh$_3$-stabilized Cu NPs catalyze the Sonogashira cross-coupling.
3.4. Iron. Iron oxide NPs were prepared from Fe(acac)₃ under open-air conditions. The DMF-stabilized Fe NPs were characterized by XANES and XPS. The Fe NPs were identified as α-Fe₂O₃. The Fe₂O₃ NPs were efficient catalysts in hydrosilylation of alkenes (eq 15).²² In a typical reaction, 1-decene and phenylsilane were reacted in the presence of DMF-stabilized Fe₂O₃ NPs at 70 °C for 24 h to give the corresponding hydrosilylation products in 84% yield. Various alkenes and primary/secondary hydrosilanes were used under these conditions, and the corresponding hydrosilylation products were obtained in moderate to good yields. Alkenes with various functional groups were tolerated in this reaction (Scheme 3). The Fe₂O₃ NPs were recycled multiple times. Catalyst preactivation was not needed prior to their reuse. The catalyst particle size and photoluminescence characteristics were retained before and after the reaction. Therefore, the Fe₂O₃ NPs can be recycled at least five times without loss of considerable catalytic activity.

3.5. Iridium. DMF-stabilized Ir NCs were prepared from IrCl₆. The particle diameter was determined to be 1–1.5 nm from HR-TEM images. Ir complexes are generally efficient catalysts in alkylation with alcohols, which involve a hydrogen-borrowing reaction.²³ In particular, methylation is a widely used modification in medicinal chemistry. Methylation uses hazardous reagents, e.g., (CH₃O₂)₂SO₄ and MeI. Methylation using methanol as the C1 source is a challenging transformation. However, methanol oxidation requires harsh conditions. DMF-stabilized Ir NCs showed high catalytic activity in promoter-free methylation of anilines by alcohols.²⁴ In a typical procedure, the reaction of 1-phenyl-1-ethanol with methanol (2 mL) in the presence of Ir NCs (0.1 mol %) and Cs₂CO₃ gave the desired dimethylated product in 94% yield with high alcohol selectivity (eq 16). Iridium complexes, [Cp*IrCl₂]₂ and [IrCl(cod)]₂, known to be efficient catalysts for α-methylation resulted in the product in low yields under...
these conditions (25% and 21%, respectively). Monomethylation at the β-carbon (eq 17) and N-alkylation of anilines (eq 18) were achieved under modified conditions. The DMF-stabilized Ir NCs have high catalytic activity in N-methylation. A high TON was achieved for N-methylation of anilines (up to 310 000).

4. CONCLUSIONS AND OUTLOOK

We have reported the solution syntheses of a series of DMF-stabilized M NPs/NCs and their use as catalysts in various organic transformations. In these syntheses, DMF served as a stabilizer, reductant, and solvent. In the DMF-stabilized M NPs and NCs, the DMF molecules surrounded the surface of the metal center. A possible mechanism of high catalytic performance of metal NPs is attributed to the generation of open sites by heat-assisted liberation of the DMF molecules that may act as an active catalyst in the organic reactions. The DMF-stabilized M NPs/NCs are as thermally stable (>100 °C) as thiolate-stabilized M NCs. Stabilizers such as thiolas and phosphines strongly covered the active site on the metal clusters, which led to a decrease in their catalytic activity. In contrast, the DMF-stabilized M NPs/NCs generate partially catalytically active open sites by liberation of DMF molecules. The resulting M NPs were stable for a long time, which hampered aggregation during catalytic reactions.

The DMF-stabilized M NPs showed high catalytic activities (TONs and selectivities). Partial liberation of DMF molecules from the surfaces of the M NPs opened active sites to serve as the active catalyst in various organic transformations such as cross-coupling reactions, hydrogen borrowing reactions, and alkene hydrosilylation reactions. In addition, the use of M NPs enabled catalyst recycling in various reaction systems by using liquid–liquid extraction. Finally, control of the M NP properties (shape, size, and capping state) will provide new and specific reactivities. Innovative transformations could be achieved by alloying NPs (e.g., Pd–Cu) to modify the catalytic properties of M NPs. Heteroatom doping can control and improve catalytic activities, as has been shown by photoluminescence properties. Further advances in combining M NPs and NCs will play a key role in future progress in organic chemistry. We hope that this mini-review will inspire readers to explore further applications of stable, practical, and highly active catalytic DMF-stabilized M NPs in organic chemistry.

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Yasushi Obora received his Ph.D. degree in 1995 (Gifu University). After working as a postdoctoral fellow at Northwestern University under a supervision of Prof. Tobin J. Marks, he moved to the National Institute of Materials and Chemical Research, AIST, in 1997. He moved to Hokkaido University as a Research Associate in 1999 (Prof. Yasushi Tsuji). He was appointed Associate Professor at Kansai University in 2006, and he has been a full Professor at Kansai University since 2013. His current research interests include the development of innovative catalysis including nanosized colloidal catalyst and homogeneous transition-metal-complex catalysts and their application to new organic transformations.

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