

its linear value of 0.42 to a value of  $0.27 \pm 0.015$  at this intensity. Both the real and the imaginary parts of the refractive index saturate for even higher input power. We found that these measurements are highly repeatable and that the material does not exhibit a permanent change of its optical properties.

The magnitude of the optically induced ultrafast change of the real part of the refractive index ( $\Delta n = 0.72 \pm 0.025$ ) and the relative change of 170% in comparison to the linear value are unprecedented. The change in the refractive index corresponds to a change of the permittivity from  $\epsilon = 0 + 0.352i$  to  $\epsilon = 1.22 + 0.61i$  where  $i$  is the square root of  $-1$ . This result shows that ITO can exhibit a reversible transition from metallic to a lossy dielectric state with a subpicosecond time response at wavelengths slightly longer than the bulk plasmon wavelength. Moreover, the usual perturbation expansion description of nonlinear optical effects is not applicable for this material at high intensities.

We have shown that a thin ITO film exhibits an extremely large ultrafast third-order nonlinearity at ENZ wavelengths. Moreover, it can acquire an optically induced change in the refractive index that is unprecedentedly large. Our results challenge the notion that the nonlinear optical response is only a perturbation to the linear response. Materials with such a large nonlinear response are expected to enable exotic nonlinear dynamics (22) and allow all-optical control of metasurface and active plasmonics devices. Thus, our results introduce a completely new paradigm in nonlinear optics and open new avenues for developing optical nanostructures with large nonlinearity for applications in nanophotonics, plasmonics, and nonlinear nano-optics.

#### REFERENCES AND NOTES

- M. Kauranen, A. V. Zayats, *Nat. Photonics* **6**, 737–748 (2012).
- M. Abb, P. Albella, J. Aizpurua, O. L. Muskens, *Nano Lett.* **11**, 2457–2463 (2011).
- M. Silveirinha, N. Engheta, *Phys. Rev. Lett.* **97**, 157403 (2006).
- A. Altu, M. Silveirinha, A. Salandrino, N. Engheta, *Phys. Rev. B* **75**, 155410 (2007).
- A. R. Davoyan, A. M. Mahmoud, N. Engheta, *Opt. Express* **21**, 3279–3286 (2013).
- A. D. Neira et al., *Nat. Commun.* **6**, 7757 (2015).
- H. Suchowski et al., *Science* **342**, 1223–1226 (2013).
- A. Capretti, Y. Wang, N. Engheta, L. Dal Negro, *Opt. Lett.* **40**, 1500–1503 (2015).
- T. S. Luk et al., *Appl. Phys. Lett.* **106**, 151103 (2015).
- N. Kinsey et al., *Optica* **2**, 616 (2015).
- G. V. Naik, V. M. Shalaev, A. Boltasseva, *Adv. Mater.* **25**, 3264–3294 (2013).
- E. Feigenbaum, K. Diest, H. A. Atwater, *Nano Lett.* **10**, 2111–2116 (2010).
- M. Sheik-Bahae, A. A. Said, T.-H. Wei, D. J. Hagan, E. W. Van Stryland, *IEEE J. Quantum Electron.* **26**, 760–769 (1990).
- B. K. Rhee, J. S. Byun, E. W. Van Stryland, *J. Opt. Soc. Am. B* **13**, 2720 (1996).
- H. I. Elim, W. Ji, F. Zhu, *Appl. Phys. B* **82**, 439–442 (2006).
- See supplementary materials on Science Online.
- R. W. Boyd, *Nonlinear Optics* (Elsevier, 2008).
- C. Sun, F. Vallée, L. Aciofi, E. P. Ippen, J. G. Fujimoto, *Phys. Rev. B Condens. Matter* **48**, 12365–12368 (1993).
- S. D. Brorson, J. G. Fujimoto, E. P. Ippen, *Phys. Rev. Lett.* **59**, 1962–1965 (1987).
- E. Carpene, *Phys. Rev. B* **74**, 024301 (2006).
- B. Rethfeld, A. Kaiser, M. Vicanek, G. Simon, *Phys. Rev. B* **65**, 214303 (2002).
- D. de Ceglia, S. Campione, M. A. Vincenti, F. Capolino, M. Scalora, *Phys. Rev. B* **87**, 155140 (2013).

#### ACKNOWLEDGMENTS

The authors gratefully acknowledge the support of the Canada Excellence Research Chairs Program. R.W.B. is the cofounder and Chief Technology Officer of KBN Optics, Pittsford, NY.

#### SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/352/6287/795/suppl/DC1  
Materials and Methods  
Supplementary Text  
Figs. S1 to S4  
References (23–32)

7 December 2015; accepted 12 April 2016  
Published online 28 April 2016  
10.1126/science.aae0330

#### CATALYSIS

## Photochemical route for synthesizing atomically dispersed palladium catalysts

Pengxin Liu,<sup>1</sup> Yun Zhao,<sup>1</sup> Ruixuan Qin,<sup>1</sup> Shiguang Mo,<sup>1</sup> Guangxu Chen,<sup>1</sup> Lin Gu,<sup>2</sup> Daniel M. Chevrier,<sup>3</sup> Peng Zhang,<sup>3</sup> Qing Guo,<sup>1</sup> Dandan Zang,<sup>1</sup> Binghui Wu,<sup>1</sup> Gang Fu,<sup>1\*</sup> Nanfeng Zheng<sup>1\*</sup>

Atomically dispersed noble metal catalysts often exhibit high catalytic performances, but the metal loading density must be kept low (usually below 0.5%) to avoid the formation of metal nanoparticles through sintering. We report a photochemical strategy to fabricate a stable atomically dispersed palladium–titanium oxide catalyst ( $\text{Pd}_1/\text{TiO}_2$ ) on ethylene glycolate (EG)–stabilized ultrathin  $\text{TiO}_2$  nanosheets containing Pd up to 1.5%. The  $\text{Pd}_1/\text{TiO}_2$  catalyst exhibited high catalytic activity in hydrogenation of C=C bonds, exceeding that of surface Pd atoms on commercial Pd catalysts by a factor of 9. No decay in the activity was observed for 20 cycles. More important, the  $\text{Pd}_1/\text{TiO}_2$ -EG system could activate  $\text{H}_2$  in a heterolytic pathway, leading to a catalytic enhancement in hydrogenation of aldehydes by a factor of more than 55.

Atomically dispersed catalysts with mononuclear metal complexes or single metal atoms anchored on supports have recently attracted increasing research attention (1–15). With 100% metal dispersity, atomically dispersed catalysts offer the maximum atom efficiency, providing the most ideal strategy to create cost-effective catalysts, particularly those based on Earth-scarce metals such as Pt (1–5), Au (5–8), Pd (9–12), and Ir (13, 14). Moreover, the uniform active sites of atomically dispersed catalysts make them a model system to understand heterogeneous catalysis at the molecular level (4, 6, 10, 12–14, 16–21), bridging the gap between heterogeneous and homogeneous catalysis.

During the past decade, several strategies for atomically dispersing metal sites on catalyst supports have emerged; these include lower-

ing the loading amount of metal components (1, 8–10, 12, 20), enhancing the metal-support interactions (4, 6, 9, 19), and using voids in supports or vacancy defects on supports (3, 11, 14, 22). In most cases, the supports for atomically dispersed catalysts are deliberately chosen. Zeolites provide effective voids to anchor individual metal atoms therein and prevent them from sintering during catalysis (23, 24). Defects on reducible oxides (e.g.,  $\text{TiO}_2$  and  $\text{CeO}_2$ ) (25, 26) and on graphene or  $\text{C}_3\text{N}_4$  (9, 11, 22) help to stabilize atomically dispersed metal atoms on supports. Coordinatively unsaturated  $\text{Al}^{3+}$  ions on  $\gamma\text{-Al}_2\text{O}_3$  act as binding centers to maintain the high dispersion of Pt atoms, but Pt rafts form as the loading amount of Pt increases (3). Currently, two major challenges remain in the field of atomically dispersed catalysts: (i) to ensure a loading content high enough for practical applications while maintaining the metal centers as individual sites under catalytic conditions (27, 28), and (ii) to address whether atomically dispersed catalysts offer distinct active sites and/or undergo catalytic pathways different from those of conventional metal catalysts (1, 4–6, 8–10, 12, 16–21).

We report a room-temperature photochemical strategy to fabricate a highly stable, atomically dispersed Pd catalyst ( $\text{Pd}_1/\text{TiO}_2$ ) on ultrathin  $\text{TiO}_2$  nanosheets with Pd loading up to 1.5%.

<sup>1</sup>State Key Laboratory for Physical Chemistry of Solid Surfaces, Collaborative Innovation Center of Chemistry for Energy Materials, Engineering Research Center for Nano-Preparation Technology of Fujian Province, National Engineering Laboratory for Green Chemical Productions of Alcohols, Ethers, and Esters, and Department of Chemistry, College of Chemistry and Chemical Engineering, Xiamen University, Xiamen 361005, China. <sup>2</sup>Institute of Physics, Chinese Academy of Sciences, Beijing 100190, China. <sup>3</sup>Department of Chemistry, Dalhousie University, Halifax, Nova Scotia B3H 4R2, Canada.

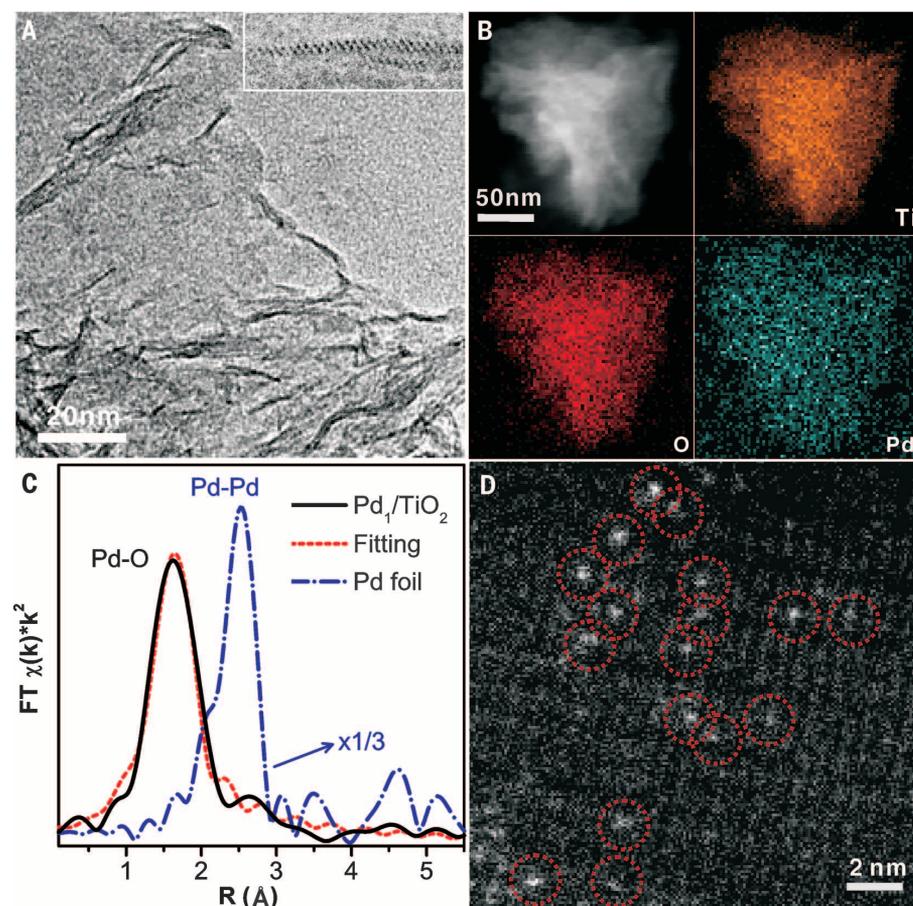
\*Corresponding author. Email: nfhzheng@xmu.edu.cn (N.Z.);

Ultraviolet (UV) light-induced formation of ethylene glycolate (EG) radicals on TiO<sub>2</sub> nanosheets was shown to be critical for preparing Pd<sub>1</sub>/TiO<sub>2</sub>. With abundant Pd-O interfaces, Pd<sub>1</sub>/TiO<sub>2</sub> activates H<sub>2</sub> in a heterolytic pathway distinct from the homolytic pathway on conventional Pd heterogeneous catalysts. The Pd<sub>1</sub>/TiO<sub>2</sub> catalyst exhibits extremely high catalytic activities and stabilities in hydrogenation of C=C and C=O. A turnover frequency (TOF) greater than that of surface Pd atoms on commercial Pd catalysts by a factor of >55 was demonstrated on Pd<sub>1</sub>/TiO<sub>2</sub> in the hydrogenation of aldehyde at room temperature, and no decay in the catalytic activity was observed during catalysis.

Two-atom-thick TiO<sub>2</sub>(B) nanosheets [figs. S1 to S4 (29)] were prepared by reacting TiCl<sub>4</sub> with EG and were used as the support (30). H<sub>2</sub>PdCl<sub>4</sub> was introduced into a water dispersion of TiO<sub>2</sub>(B) to allow the adsorption of Pd species (figs. S5 and S6). The mixture was then irradiated by low-density UV provided by a Xe lamp (fig. S7). After 10 min of irradiation, the Pd<sub>1</sub>/TiO<sub>2</sub> catalyst was collected and washed thoroughly with water. No formation of Pd nanoparticles (NPs) was observed in transmission electron microscopy (TEM) images (Fig. 1A and fig. S8) or in the x-ray diffraction pattern (fig. S9) of the obtained Pd<sub>1</sub>/TiO<sub>2</sub> catalyst, even with the loading content of Pd as high as 1.5 weight percent (wt %) as analyzed by inductively coupled plasma mass spectrometry (ICP-MS). **Energy-dispersive x-ray spectroscopy (EDS) analysis in a scanning transmission electron microscope (STEM) revealed that atomic Pd was evenly dispersed in Pd<sub>1</sub>/TiO<sub>2</sub> (Fig. 1B), unlike in supported Pd NPs prepared by a conventional impregnation method followed by calcination in air at 350°C (fig. S10). To verify that Pd atoms were dispersed in Pd<sub>1</sub>/TiO<sub>2</sub>, we performed x-ray absorption near-edge structure (XANES) and extended x-ray absorption fine structure (EXAFS) spectrometry (Fig. 1C and figs. S11 and S12). There was only one notable peak in the region 1 to 2 Å from the Pd-O contribution, and no peak in the region 2 to 3 Å from the Pd-Pd contribution, confirming the sole presence of dispersed Pd atoms in Pd<sub>1</sub>/TiO<sub>2</sub> (table S1). The calcination of the as-prepared Pd<sub>1</sub>/TiO<sub>2</sub> in air at 350°C removed the organic residues on the surface of Pd<sub>1</sub>/TiO<sub>2</sub> and thus allowed direct observation of the atomic dispersion of Pd by aberration-corrected STEM (Fig. 1D and fig. S13).**

After calcination, there were still a large number of dispersed Pd atoms on the TiO<sub>2</sub> support, even with the Pd loading up to 1.5 wt%. We also investigated the CO adsorption behavior of Pd<sub>1</sub>/TiO<sub>2</sub> (fig. S14) to confirm the atomic dispersion of Pd on the catalyst. There was only a weak band at 2100 cm<sup>-1</sup> ascribed to CO adsorbed on Pd<sup>2+</sup> in a top configuration (31). No signals attributed to CO adsorbed on bridge or hollow sites were observed, quite unlike supported Pd nanoparticulate catalysts (fig. S15).

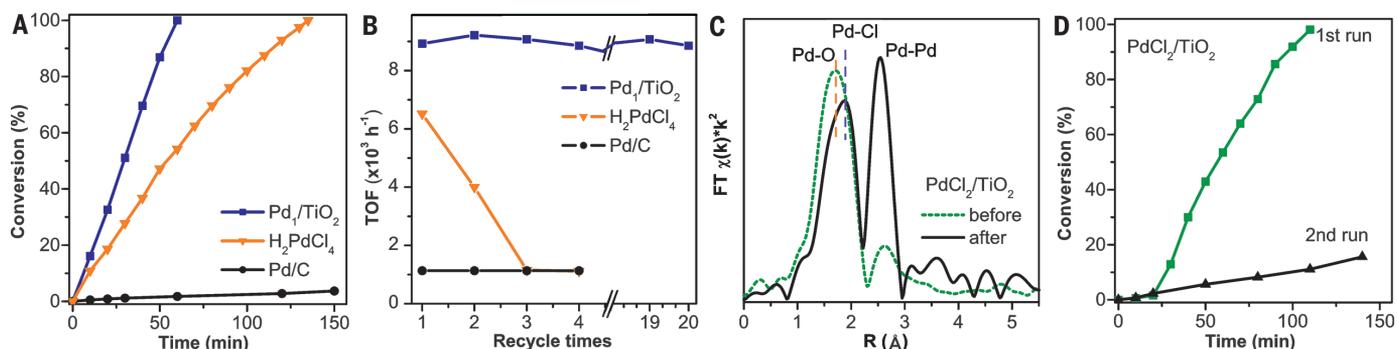
Styrene hydrogenation was chosen as a model reaction to evaluate the catalytic activity of Pd<sub>1</sub>/TiO<sub>2</sub>. The Pd<sub>1</sub>/TiO<sub>2</sub> catalyst displayed an



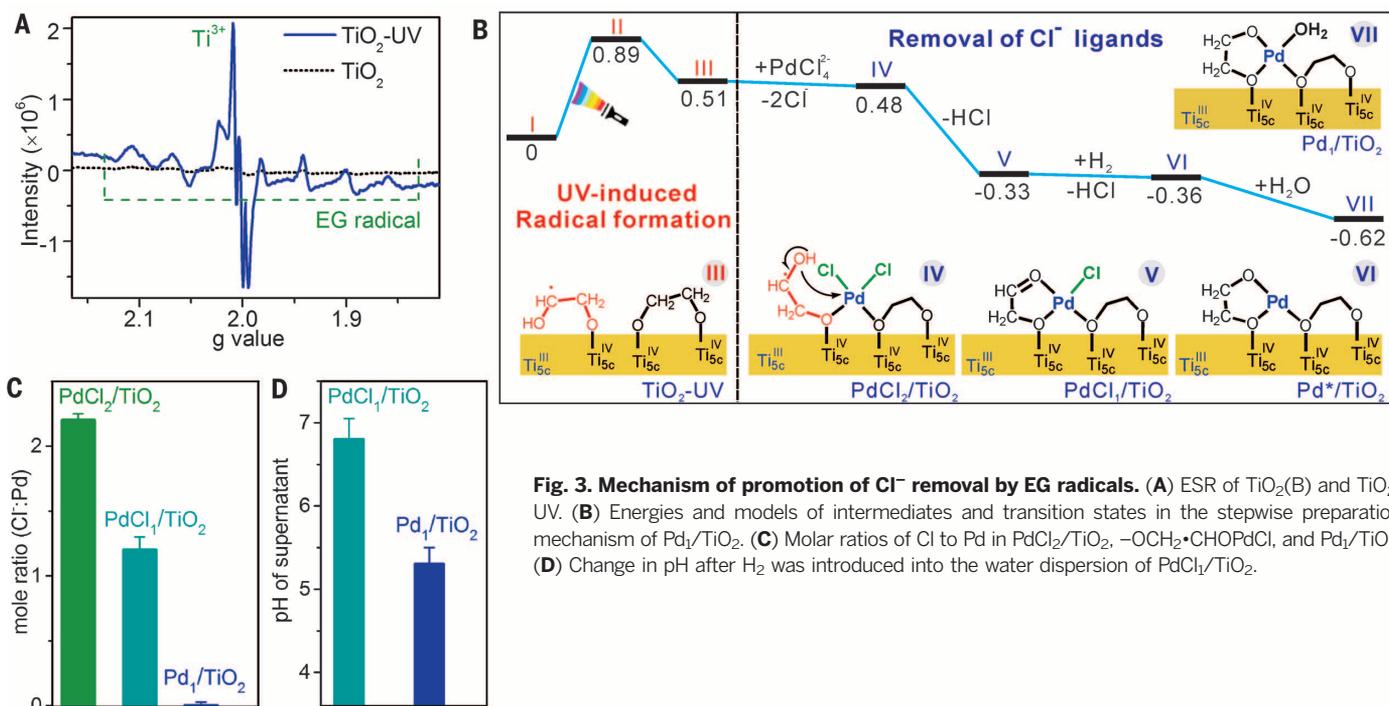
**Fig. 1. Structural characterizations of Pd<sub>1</sub>/TiO<sub>2</sub>.** (A) Representative TEM image of Pd<sub>1</sub>/TiO<sub>2</sub>. The inset is an aberration-corrected STEM image for cross sections of ultrathin TiO<sub>2</sub>(B), showing that it is composed of only two layers of Ti atoms. (B) STEM-EDS elemental mapping of a single Pd<sub>1</sub>/TiO<sub>2</sub> nanosheet. (C) FT-EXAFS spectra of Pd<sub>1</sub>/TiO<sub>2</sub> and bulk palladium foil at the Pd K-edge, showing the surrounding atoms adjacent to Pd atoms. (D) High-resolution high-angle annular dark-field (HAADF) STEM image of Pd<sub>1</sub>/TiO<sub>2</sub>. The sample was calcined in air at 350°C for better contrast.

extremely high activity and stability (Fig. 2, A and B) relative to commercial Pd/C (fig. S16), TiO<sub>2</sub>(B)-supported Pd NPs (fig. S17), and unsupported homogeneous H<sub>2</sub>PdCl<sub>4</sub> catalysts. We achieved 100% styrene conversion in 1 hour at a molar ratio of 1:10<sup>4</sup> (Pd:styrene). The calculated TOF value of Pd<sub>1</sub>/TiO<sub>2</sub>, 8973 hours<sup>-1</sup>, was greater than that of surface Pd atoms on the Pd/C catalyst (972 hours<sup>-1</sup>) by a factor of 9. The reaction rate of Pd<sub>1</sub>/TiO<sub>2</sub> was maintained even after 20 cycles with the same catalyst (fig. S18), which suggests that the atomically dispersed structure of Pd<sub>1</sub>/TiO<sub>2</sub> was robust under the catalytic conditions. There was no detectable change in the EXAFS fitting profiles after 20 catalytic cycles (fig. S19 and table S2). In contrast, an obvious decreased activity was observed on unsupported H<sub>2</sub>PdCl<sub>4</sub> in the second cycle and even at the end of the first run (fig. S20). Because styrene hydrogenation is a zero-order reaction whose reaction rate is independent of the styrene's concentration (32, 33), the decline in the reaction rate of H<sub>2</sub>PdCl<sub>4</sub> (Fig. 2B) was caused by the changing status of the catalyst. After reaction, small Pd NPs were detected in the reaction mixture (figs. S21 and S22).

To better understand why the Pd<sub>1</sub>/TiO<sub>2</sub> catalyst possessed such a high catalytic activity and stability, we prepared a catalyst (denoted PdCl<sub>2</sub>/TiO<sub>2</sub>) by the same method as for Pd<sub>1</sub>/TiO<sub>2</sub> but without the UV treatment (fig. S23). No Pd-Pd bonds in PdCl<sub>2</sub>/TiO<sub>2</sub> were detected by EXAFS (Fig. 2C and fig. S24), similar to Pd<sub>1</sub>/TiO<sub>2</sub>. The coordination numbers of Pd-O and Pd-Cl in the obtained PdCl<sub>2</sub>/TiO<sub>2</sub> were 2.2 and 1.7, respectively (table S3). The Pd:Cl molar ratio of ~1:2 in the catalyst was confirmed by the elemental analysis (fig. S25). All of these data indicated that Pd atoms in PdCl<sub>2</sub>/TiO<sub>2</sub> were in the form of individual PdCl<sub>2</sub> species bound on TiO<sub>2</sub>(B). The presence of two Cl<sup>-</sup> ligands on each Pd atom made the catalytic performance of PdCl<sub>2</sub>/TiO<sub>2</sub> much poorer than that of Pd<sub>1</sub>/TiO<sub>2</sub> (Fig. 2D). The reaction rate already declined during the first run and kept decreasing after every recycle, suggesting a deleterious effect of Pd-Cl bonds on the catalysis. Similar to H<sub>2</sub>PdCl<sub>4</sub>, the decreased activity of PdCl<sub>2</sub>/TiO<sub>2</sub> was attributed to the sintering of Pd atoms into NPs during catalysis. EXAFS studies revealed that a peak in the region 2 to 3 Å from the Pd-Pd contribution emerged for the PdCl<sub>2</sub>/TiO<sub>2</sub> catalyst after catalysis (Fig. 2C and table S4).



**Fig. 2. Catalytic performances of Pd<sub>1</sub>/TiO<sub>2</sub> and reference materials in styrene hydrogenation.** (A and B) Catalytic performances for the first run (A) and TOF (B) of several recycles of repeated reactions for Pd<sub>1</sub>/TiO<sub>2</sub>, H<sub>2</sub>PdCl<sub>4</sub>, and commercial Pd/C. The same portion of Pd<sub>1</sub>/TiO<sub>2</sub> catalyst was recycled and used for 20 runs without loss of activity. (C) FT-EXAFS spectra at the Pd K-edge of PdCl<sub>2</sub>/TiO<sub>2</sub> before and after catalysis reaction. (D) First- and second-run catalytic performances of PdCl<sub>2</sub>/TiO<sub>2</sub>. Reaction conditions: ethanol, 10 ml; Pd, 0.005 μmol; styrene, 50 μmol; T = 303 K; pressure = 0.1 MPa.



**Fig. 3. Mechanism of promotion of Cl<sup>-</sup> removal by EG radicals.** (A) ESR of TiO<sub>2</sub>(B) and TiO<sub>2</sub>-UV. (B) Energies and models of intermediates and transition states in the stepwise preparation mechanism of Pd<sub>1</sub>/TiO<sub>2</sub>. (C) Molar ratios of Cl to Pd in PdCl<sub>2</sub>/TiO<sub>2</sub>, -OCH<sub>2</sub>•CHOPdCl, and Pd<sub>1</sub>/TiO<sub>2</sub>. (D) Change in pH after H<sub>2</sub> was introduced into the water dispersion of PdCl<sub>1</sub>/TiO<sub>2</sub>.

Pd NPs were observed in TEM images for the used PdCl<sub>2</sub>/TiO<sub>2</sub> catalyst (fig. S26), indicating that the presence of Pd-Cl bonds would destabilize atomically dispersed Pd on TiO<sub>2</sub> and induce their sintering into NP during catalysis.

The removal of Cl<sup>-</sup> ligands on Pd under mild UV conditions appears vital for preparing highly stable and active Pd catalysts. To confirm this, we thoroughly washed PdCl<sub>2</sub>/TiO<sub>2</sub> with water until no Cl<sup>-</sup> was detected in the supernatant. The water dispersion of PdCl<sub>2</sub>/TiO<sub>2</sub> was then exposed to UV for 10 min. As expected, all Cl<sup>-</sup> ligands on PdCl<sub>2</sub>/TiO<sub>2</sub> were released into the supernatant (figs. S25 and S27). The molar ratio of the released Cl<sup>-</sup> to the anchored Pd was measured to be ~2, confirming the formation of the Cl<sup>-</sup>-free Pd<sub>1</sub>/TiO<sub>2</sub> catalyst after the UV treatment.

The UV-induced elimination of Cl<sup>-</sup> from PdCl<sub>2</sub>/TiO<sub>2</sub> was attributed to the photoreactivity of TiO<sub>2</sub>(B) nanosheets. As shown in Fig. 3A, TiO<sub>2</sub>(B)

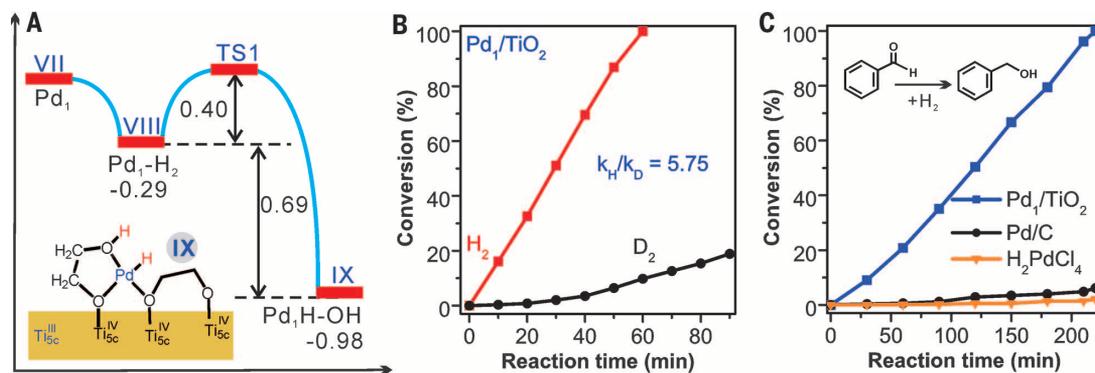
nanosheets treated by UV alone (denoted as TiO<sub>2</sub>-UV) already displayed an electron spin resonance (ESR) spectrum with an intense peak corresponding to a Ti<sup>3+</sup> species and a set of six peaks that matched perfectly with EG radicals (HOCH<sub>2</sub>•CHOH) (34). Similar signals were observed for the as-prepared Pd<sub>1</sub>/TiO<sub>2</sub> catalyst (fig. S28). However, no obvious ESR peaks were found on the original TiO<sub>2</sub>(B) nanosheets without UV treatment (Fig. 3A).

Together with selected-area electron diffraction (SAED) (fig. S1) and the aberration-corrected STEM (fig. S2), thermogravimetric analysis (fig. S29) and infrared (IR) spectroscopy (fig. S30) suggested that two-atom-thick TiO<sub>2</sub> nanosheets used in this work had TiO<sub>2</sub>(B)(010) as their major exposed facets, and these exposed facets were highly covered by deprotonated EG (~19 wt %) (fig. S31). Once exposed to UV, electron-hole pairs were generated on TiO<sub>2</sub>(B) nanosheets. Electrons

were trapped in Ti-3d orbitals to form Ti<sup>3+</sup> sites (35), and holes broke Ti-O bonds between glycolate and TiO<sub>2</sub>, leading to the formation of -OCH<sub>2</sub>CH<sub>2</sub>O• radicals (from I to II in Fig. 3B) (figs. S32 and S33). Because of the presence of α-H, -OCH<sub>2</sub>CH<sub>2</sub>O• was not stable and would thus undergo hydrogen transfer to give -OCH<sub>2</sub>•CHOH. According to density functional theory (DFT) calculations, such a process (from II to III in Fig. 3B) was predicted to be exothermic by 0.38 eV. Such UV-generated surface organic radicals are not unusual, as the oxidation potentials of most organic compounds lie below that of the holes in the valence band of TiO<sub>2</sub> (36–38). The ESR signals from the samples after washing and drying processes suggest that, once formed upon UV irradiation, the EG radicals on the surface of TiO<sub>2</sub> nanosheets were quite stable.

To understand how EG radicals promoted the release of Cl<sup>-</sup> from Pd sites, we also designed a

**Fig. 4. Catalytic mechanism of Pd<sub>1</sub>/TiO<sub>2</sub> in hydrogenation reactions. (A)** Energies and model of intermediates and transition states in the heterolytic H<sub>2</sub> activation process for Pd<sub>1</sub>/TiO<sub>2</sub>. **(B)** Primary isotope effect observed for Pd<sub>1</sub>/TiO<sub>2</sub> in styrene hydrogenation. **(C)** First-run reaction performances for Pd<sub>1</sub>/TiO<sub>2</sub>, Pd/C, and H<sub>2</sub>PdCl<sub>4</sub> in benzaldehyde hydrogenation.



stepwise route (fig. S34) to prepare the Pd<sub>1</sub>/TiO<sub>2</sub> catalyst. UV treatment was first used to obtain TiO<sub>2</sub>-UV nanosheets containing EG radicals on their surfaces. H<sub>2</sub>PdCl<sub>4</sub> was then introduced into the water dispersion of TiO<sub>2</sub>-UV. Our calculations showed that once adsorbed onto TiO<sub>2</sub>, each PdCl<sub>4</sub><sup>2-</sup> liberated two Cl<sup>-</sup> ligands, yielding an intermediate with individual PdCl<sub>2</sub> units adsorbed on TiO<sub>2</sub> (IV in Fig. 3B) (fig. S35). Such a process was predicted to be slightly exothermic by 0.03 eV. Subsequently, the OH group in -OCH<sub>2</sub>•CHOH attacked its nearby Pd site by replacing one Cl<sup>-</sup>, leading to the formation of PdCl<sub>1</sub>/TiO<sub>2</sub> intermediate (V in Fig. 3B) with an exothermicity of 0.81 eV. As shown in fig. S35, PdCl<sub>1</sub>/TiO<sub>2</sub> has three Ti-O bonds and one Pd-Cl bond. Experimentally, both EXAFS data and elemental analysis showed a Cl: Pd molar ratio of ~1:1 for PdCl<sub>1</sub>/TiO<sub>2</sub> (Fig. 3C, figs. S36 and S37, and table S4), lower than the 2:1 molar ratio in PdCl<sub>2</sub>/TiO<sub>2</sub> made from untreated TiO<sub>2</sub>. Moreover, mixing TiO<sub>2</sub>(B)-UV with H<sub>2</sub>PdCl<sub>4</sub> solution decreased the amount of EG radicals, as evidenced by the reduced intensity of each ESR peak (fig. S38).

All of these results strongly confirmed that the UV-generated EG radicals facilitated the removal of Cl<sup>-</sup> on Pd and stabilized individual Pd atoms by forming more Pd-O bonds. The remaining Cl<sup>-</sup> on PdCl<sub>1</sub>/TiO<sub>2</sub> could be easily removed by using H<sub>2</sub> treatment, giving rise to H<sup>+</sup> and Cl<sup>-</sup> (from V to VII in Fig. 3B) (table S5). This result explained why treating the water dispersion of PdCl<sub>1</sub>/TiO<sub>2</sub> resulted in a pH drop from 6.8 to 5.3 (Fig. 3D). Alternatively, further UV treatment completely removed Cl<sup>-</sup> from PdCl<sub>1</sub>/TiO<sub>2</sub> (fig. S39), also leading to the formation of Pd<sub>1</sub>/TiO<sub>2</sub>. The catalyst prepared in the stepwise procedure showed the same catalytic properties as that prepared by the one-pot method in which the aqueous mixture of TiO<sub>2</sub> and H<sub>2</sub>PdCl<sub>4</sub> was directly treated with UV (fig. S40). More important, the insight into the formation mechanism of Pd<sub>1</sub>/TiO<sub>2</sub> allowed us to prepare the catalyst in large scale by using a continuous UV-flow reactor (fig. S41).

To evaluate the importance of EG radicals in the preparation of the atomically dispersed Pd<sub>1</sub>/TiO<sub>2</sub> catalyst, we also synthesized EG-free TiO<sub>2</sub> by calcination of TiO<sub>2</sub>(B) nanosheets at 350°C in air and used it as the support for the

catalyst preparation. A photochemical strategy similar to that used in the one-step preparation of Pd<sub>1</sub>/TiO<sub>2</sub> was applied to load Pd onto EG-free TiO<sub>2</sub>, but Pd NPs were formed (fig. S42); this result shows that surface EG helps to stabilize atomically dispersed Pd catalysts during their preparation. When surface EG was removed by calcination, the obtained Pd<sub>1</sub>/TiO<sub>2</sub>-cal catalyst displayed a substantially decreased activity with a TOF of only 1930 hours<sup>-1</sup> (fig. S43).

It is generally accepted that H<sub>2</sub> would undergo homolytic dissociation on conventional Pd particulate catalysts into H atoms with partially negative charge (H<sup>δ-</sup>) (39). In this case, the presence of more than two Pd atoms in the vicinity is required. However, all Pd atoms in Pd<sub>1</sub>/TiO<sub>2</sub> are individually dispersed, with no Pd-Pd pairs available for homolytic dissociation of H<sub>2</sub>, so the dissociation of H<sub>2</sub> must go via an alternative pathway on Pd<sub>1</sub>/TiO<sub>2</sub>. According to our DFT calculations (Fig. 4A and figs. S44 to S46), H<sub>2</sub> adsorbed on Pd was readily split into two H atoms. One of the H atoms moved to a nearby oxygen on EG to yield O-H<sup>δ+</sup>, leaving the other H atom on Pd as H<sup>δ-</sup> (Fig. 4A). This step was calculated to be exothermic by 0.69 eV and exhibited a barrier of 0.40 eV. We expected that both Pd-H<sup>δ-</sup> and O-H<sup>δ+</sup> should then be involved in the hydrogenation catalysis. DFT calculations revealed that the hydrogenation of styrene using Pd<sub>1</sub>/TiO<sub>2</sub> followed a stepwise process. Computationally, we considered two possible pathways (figs. S44 to S46), one beginning with H<sup>δ-</sup> transfer from Pd to C=C and the other beginning with H<sup>δ+</sup> transfer. The first of these is energetically favorable, with a barrier of only 0.47 eV required for the H<sup>δ-</sup> transfer from Pd to the terminal CH<sub>2</sub> to make the half-hydrogenated intermediate, which in turn adds H<sup>δ+</sup> from a nearby O-H group by overcoming a barrier of 0.73 eV. This pathway leads to the formation of ethylbenzene and simultaneously recovers the Pd-EG interfaces.

To test the proposed mechanism, we explored the kinetic isotope effect (KIE) with the use of D<sub>2</sub> in styrene hydrogenation. For Pd/C, the reaction was slowed down by a factor of 1.43 (fig. S47) as a result of the zero-point energy difference between isotopic isomers. However, on Pd<sub>1</sub>/TiO<sub>2</sub>, a larger KIE was observed (ratio of

reaction rates using H<sub>2</sub> and D<sub>2</sub>, k<sub>H</sub>/k<sub>D</sub> = 5.75) (Fig. 4B) because the bond cleavage was O-D rather than Pd-D in the rate-determining step. Both our IR spectroscopy and nuclear magnetic resonance measurements, which were performed with deuterium-labeled reagents, confirmed the proposed mechanism (figs. S48 and S49). Such a large KIE in hydrogenation caused by the participation of both H<sup>δ-</sup> and H<sup>δ+</sup> has usually been observed on homogeneous catalysts (e.g., Au, Pd, and Ru complexes) (7, 40, 41) but has not been reported on heterogeneous Pd catalysts. In this regard, atomically dispersed metal catalysts can share the same hydrogenation mechanism as homogeneous catalysts.

Because the heterolytic activation of H<sub>2</sub> yielded both H<sup>δ-</sup> and H<sup>δ+</sup> at the Pd-O interface, Pd<sub>1</sub>/TiO<sub>2</sub> should allow better hydrogenation of polar unsaturated bonds. As expected, in the hydrogenation of benzaldehyde, we observed a much superior catalytic performance by Pd<sub>1</sub>/TiO<sub>2</sub> (Fig. 4C and fig. S50). Pd<sub>1</sub>/TiO<sub>2</sub> readily converted all of the benzaldehyde into benzyl alcohol in 3.5 hours at room temperature with a TOF of 1002 hours<sup>-1</sup>. No decay in the catalysis was observed after the catalyst was used for five cycles. In comparison, both Pd/C and H<sub>2</sub>PdCl<sub>4</sub> showed negligible activity under the same catalytic condition, with TOF less than 18 hours<sup>-1</sup>. This work demonstrates that upgrading catalytically active components from nanoparticles to single atoms not only boosts the catalytic reaction because of the high atom efficiency, but also endows atomically dispersed catalysts with catalytic capability that conventional nanocatalysts do not possess.

#### REFERENCES AND NOTES

1. B. Qiao et al., *Nat. Chem.* **3**, 634–641 (2011).
2. K. Ding et al., *Science* **350**, 189–192 (2015).
3. J. H. Kwak et al., *Science* **325**, 1670–1673 (2009).
4. Y. Zhai et al., *Science* **329**, 1633–1636 (2010).
5. Q. Fu, H. Saltsburg, M. Flytzani-Stephanopoulos, *Science* **301**, 935–938 (2003).
6. M. Yang et al., *Science* **346**, 1498–1501 (2014).
7. A. Comas-Vives et al., *J. Am. Chem. Soc.* **128**, 4756–4765 (2006).
8. X. Zhang, H. Shi, B. Q. Xu, *Angew. Chem. Int. Ed.* **44**, 7132–7135 (2005).
9. G. Vilé et al., *Angew. Chem. Int. Ed.* **54**, 11265–11269 (2015).
10. S. Abbet et al., *J. Am. Chem. Soc.* **122**, 3453–3457 (2000).
11. H. Yan et al., *J. Am. Chem. Soc.* **137**, 10484–10487 (2015).
12. E. J. Peterson et al., *Nat. Commun.* **5**, 4885 (2014).
13. J. Lin et al., *J. Am. Chem. Soc.* **135**, 15314–15317 (2013).

14. V. Ortalan, A. Uzun, B. C. Gates, N. D. Browning, *Nat. Nanotechnol.* **5**, 506–510 (2010).
15. J. M. Thomas, *Nature* **525**, 325–326 (2015).
16. W. E. Kaden, T. Wu, W. A. Kunkel, S. L. Anderson, *Science* **326**, 826–829 (2009).
17. J. M. Thomas, Z. Saghii, P. L. Gai, *Top. Catal.* **54**, 588–594 (2011).
18. G. Kyriakou et al., *Science* **335**, 1209–1212 (2012).
19. M. Yang, L. F. Allard, M. Flytzani-Stephanopoulos, *J. Am. Chem. Soc.* **135**, 3768–3771 (2013).
20. H. Wei et al., *Nat. Commun.* **5**, 5634 (2014).
21. M. Yang et al., *J. Am. Chem. Soc.* **137**, 3470–3473 (2015).
22. S. Sun et al., *Sci. Rep.* **3**, 1775 (2013).
23. J. O. Ehresmann et al., *Angew. Chem. Int. Ed.* **45**, 574–576 (2006).
24. A. Uzun, B. C. Gates, *J. Am. Chem. Soc.* **131**, 15887–15894 (2009).
25. X.-Q. Gong, A. Selloni, O. Dulub, P. Jacobson, U. Diebold, *J. Am. Chem. Soc.* **130**, 370–381 (2008).
26. D. Matthey et al., *Science* **315**, 1692–1696 (2007).
27. M. Flytzani-Stephanopoulos, B. C. Gates, *Annu. Rev. Chem. Biomol. Eng.* **3**, 545–574 (2012).
28. J. M. Thomas, R. Raja, *Top. Catal.* **40**, 3–17 (2006).
29. See supplementary materials on Science Online.
30. G. Xiang, T. Li, J. Zhuang, X. Wang, *Chem. Commun. (Camb.)* **46**, 6801–6803 (2010).
31. V. V. Kaichev et al., *J. Phys. Chem. B* **107**, 3522–3527 (2003).
32. Z. Király, B. Veisz, Á. Mastalir, *Catal. Lett.* **95**, 57–59 (2004).
33. B. Veisz, Z. Király, L. Tóth, B. Pécz, *Chem. Mater.* **14**, 2882–2888 (2002).
34. T. Shiga, *J. Phys. Chem.* **69**, 3805–3814 (1965).
35. R. F. Howe, M. Gratzel, *J. Phys. Chem.* **89**, 4495–4499 (1985).
36. M. R. Hoffmann, S. T. Martin, W. Choi, D. W. Bahnemann, *Chem. Rev.* **95**, 69–96 (1995).
37. Y. Chen, S. Yang, K. Wang, L. Lou, *J. Photochem. Photobiol. Chem.* **172**, 47–54 (2005).
38. L. Yu et al., *Phys. Chem. Chem. Phys.* **14**, 3589–3595 (2012).
39. S. Syrenova et al., *Nat. Mater.* **14**, 1236–1244 (2015).
40. A. M. Kluwer, T. S. Koblenz, T. Jonischkeit, K. Woelk, C. J. Elsevier, *J. Am. Chem. Soc.* **127**, 15470–15480 (2005).
41. A. Dedieu, S. Humbel, C. Elsevier, C. Grauffel, *Theor. Chem. Acc.* **112**, 305–312 (2004).

## ACKNOWLEDGMENTS

Supported by Ministry of Science and Technology of China grant 2015CB932303; National Natural Science Foundation of China grants 21420102001, 21131005, 21390390, 21133004, 21373167, 21573178, and 21333008; a NSERC CGS Alexander Graham Bell scholarship (D.M.C.); and a NSERC Discovery grant (P.Z.). We thank the XAFS station (BL14W1) of the Shanghai Synchrotron Radiation Facility.

## SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/352/6287/797/suppl/DC1  
Materials and Methods  
Supplementary Text  
Figs. S1 to S50  
Tables S1 to S5  
References (42–55)

22 February 2016; accepted 5 April 2016  
10.1126/science.aaf5251

## ORGANIC CHEMISTRY

# A general alkyl-alkyl cross-coupling enabled by redox-active esters and alkylzinc reagents

Tian Qin,<sup>1\*</sup> Josep Cornella,<sup>1\*</sup> Chao Li,<sup>1\*</sup> Lara R. Malins,<sup>1</sup> Jacob T. Edwards,<sup>1</sup> Shuhei Kawamura,<sup>1</sup> Brad D. Maxwell,<sup>2</sup> Martin D. Eastgate,<sup>3</sup> Phil S. Baran<sup>1†</sup>

Alkyl carboxylic acids are ubiquitous in all facets of chemical science, from natural products to polymers, and represent an ideal starting material with which to forge new connections. This study demonstrates how the same activating principles used for decades to make simple C–N (amide) bonds from carboxylic acids with loss of water can be used to make C–C bonds through coupling with dialkylzinc reagents and loss of carbon dioxide. This disconnection strategy benefits from the use of a simple, inexpensive nickel catalyst and exhibits a remarkably broad scope across a range of substrates (>70 examples).

The heart of chemical synthesis relies on forging new C–C bonds, with the evolution and advancement of the field being easily correlated to new developments on this front. For example, pioneering work on the cross-coupling of halogenated aromatic or vinylic (sp<sup>2</sup>) systems (Heck, Suzuki, Negishi, and Stille) has transformed the practice of organic synthesis (1). Similarly, a general and practical approach to C(sp<sup>3</sup>)–C(sp<sup>3</sup>) variants would have the potential to open up new vistas in retrosynthetic analysis. Indeed, such transformations have been on organic chemists' wish list for well over a century (2, 3). Historically, alkyl-alkyl transition metal-catalyzed cross-coupling reactions have been difficult to accomplish, but exam-

ples can be traced to the early work of Kharasch in the 1950s (4), followed by Noller (5, 6) and Kochi and Tamura (7, 8) in the 1960s to more recent work from the groups of Suzuki (9), Fu (10), Knochel (11), Kambe (12), Oshima (13), and many others (14). Thus far, the vast majority of approaches to this problem have involved the coupling of alkyl halides (or related species) to organometallic reagents (15–18). However, the limited availability, perceived instability, and frequent toxicity of alkyl halides has perhaps prevented the area of alkyl cross-coupling from blossoming. If one only considers convenience, stability, and availability as desired attributes in a functional group for such a coupling, the carboxylic acid reigns supreme (Fig. 1A). Alkyl carboxylic acids are ubiquitous in every aspect of chemistry and can be readily found in medicines, materials, and natural products and in the pages of commercial chemical supplier catalogs. They are a stable functional group, nontoxic, and eminently diversifiable owing to the field of combinatorial chemistry, in which they are the “workhorse” building block. Although

central carboxylic acids have already been demonstrated to engage in cross-coupling reactions (19), the use of alkyl carboxylic acids in alkyl-alkyl cross-coupling remains elusive.

Carboxylic acids can be primed for reaction through a process known as activation (such as formation of an active ester, –OA\*), dating back to the classic work of Sheehan in the synthesis of penicillin (20). Once activated, a gateway opens to access a myriad of related functional groups such as amides, ketones, esters, or alcohols via addition of a nucleophile or alternative oxidation states by the formal addition of hydrogen. In this Report, we present a broadly useful transform that is able to forge C(sp<sup>3</sup>)–C(sp<sup>3</sup>) bonds via this age-old activation process.

We recently reported a Ni-catalyzed decarboxylative cross-coupling of alkyl carboxylic acids with arylzinc reagents to forge C(sp<sup>3</sup>)–C(sp<sup>2</sup>) bonds by repurposing activating methods more typically associated with amide-bond formation (21, 22). Certain active esters [such as HOAt (*N*-hydroxy-7-azabenzotriazole), HOBt (*N*-hydroxybenzotriazole), NHPI (*N*-hydroxyphthalimide), and TCNHPI (*N*-hydroxytetrachlorophthalimide)] can accept an electron to trigger an ensuing cascade of events that liberates CO<sub>2</sub> from the parent alkyl group (Alk<sub>1</sub>); such esters (23) are termed redox-active (21, 22). The application of this chemistry to sp<sup>3</sup>–sp<sup>3</sup> C–C bond formation poses a number of substantial challenges, with potentially unproductive pathways far outnumbering the desired reaction (Fig. 1B) (15–18). For example, β-hydride elimination from the alkyl metal intermediates, dimerization of the organometallic reagent, reduction of the electrophile, and proto-demetalation are problems that also historically plague traditional C(sp<sup>3</sup>)–C(sp<sup>3</sup>) cross-coupling reactions. With a redox-active ester as an electrophile, oxidative addition of low-valent Ni into the activated C–O bond could result in the formation of an acyl-Ni complex, which could reductively eliminate and ultimately result in undesired ketone by-products. These fundamental challenges notwithstanding, we describe a straightforward solution to this problem.

Dialkylzinc reagents were chosen for the organometallic coupling partner because of their

<sup>1</sup>Department of Chemistry, Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA.

<sup>2</sup>Discovery Chemistry Platforms–Radiochemistry, Bristol-Myers Squibb, Post Office Box 4000, Princeton, NJ, USA.

<sup>3</sup>Chemical Development, Bristol-Myers Squibb, One Squibb Drive, New Brunswick, NJ 08903, USA.

\*These authors contributed equally to this work. †Corresponding author. Email: pbaran@scripps.edu



**Photochemical route for synthesizing atomically dispersed palladium catalysts**

Pengxin Liu, Yun Zhao, Ruixuan Qin, Shiguang Mo, Guangxu Chen, Lin Gu, Daniel M. Chevrier, Peng Zhang, Qing Guo, Dandan Zang, Binghui Wu, Gang Fu and Nanfeng Zheng (May 12, 2016) *Science* **352** (6287), 797-800. [doi: 10.1126/science.aaf5251]

Editor's Summary

**Lightly dispersed palladium**

Catalysts made from atomically dispersed metal atoms on oxide supports can exhibit very high per atom activity. However, the low loadings needed to prevent metal particle formation can limit overall performance. Liu *et al.* stably decorated titanium oxide nanosheets with relatively high loadings of single palladium atoms by reducing the ions with ultraviolet light and ethylene glycol. These catalysts cleaved H<sub>2</sub> into atoms and were highly effective for hydrogenating alkenes and aldehydes.

*Science*, this issue p. 797

---

This copy is for your personal, non-commercial use only.

---

- Article Tools** Visit the online version of this article to access the personalization and article tools:  
<http://science.sciencemag.org/content/352/6287/797>
- Permissions** Obtain information about reproducing this article:  
<http://www.sciencemag.org/about/permissions.dtl>

*Science* (print ISSN 0036-8075; online ISSN 1095-9203) is published weekly, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. Copyright 2016 by the American Association for the Advancement of Science; all rights reserved. The title *Science* is a registered trademark of AAAS.