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A Titanium Dioxide-supported Gold Nanoparticle Catalyst for the Selective *N*-Formylation of Functionalized Amines with CO_2 and H_2

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Keywords: amine, formylation, gold, heterogeneous catalyst, titanium dioxide

Abstract: A TiO_2-supported gold nanoparticle catalyst was found to allow the *N*-formylation of various amines, including normally unreactive anilines, using CO_2 as the carbonyl source under a H_2 atmosphere. A series of reducible functional groups, such as olefins, halogens, carbonyls, carbamates and cyano moieties, were completely retained during the formylation, demonstrating the highly selective formylation of functional amines. The catalyst was also found to be reusable without any loss of activity or selectivity.

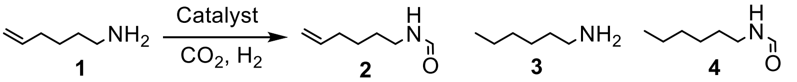
Main text: The chemical utilization of carbon dioxide (CO_2) has attracted considerable attention owing to the potential for reducing this greenhouse gas in the atmosphere and because of the abundance of readily available carbon.[1] In this context, the replacement of harmful C1 building blocks, such as phosgene and carbon monoxide, that are currently used in the chemical industry with low-cost, non-toxic CO_2 could allow the sustainable production of valuable chemicals. To date, CO_2 has been used as a carbonyl source for the catalytic synthesis of a number of compounds, including formamides,[2] formic acid,[3] carbonates,[4] urea[5] and carbamates.[6] Among these, formamides are important intermediates for the production of pharmaceuticals, insecticidal agents and fine chemicals.[7] Formamides are currently synthesized by low-atom-efficient reactions using hydrosilanes as reducing reagents.[8] Therefore, the catalytic *N*-formylation of amines using CO_2 together with hydrogen (H_2) represents a desirable, atom-economical route because it generates only water as a byproduct. Recently, the formylation of amines using CO_2 with H_2 has been studied employing both homogeneous and heterogeneous catalysts.[2] However, these catalysts are only applicable to simple amines, and the *N*-formylation of functionalized amines has been rarely examined.[9] The selective *N*-formylation of functionalized amines bearing reducible groups, such as olefins, halogens, ketones and carbamates, is challenging because the *N*-formylation of amines generally requires the application of high H_2 pressures and elevated temperatures, which can deteriorate these reducible groups. Therefore, there is a strong incentive to develop selective catalysts for the *N*-formylation of functionalized amines.

Heterogeneous metal nanoparticle (NP) catalysts have been recently demonstrated to be quite effective for the chemoselective hydrogenation of various functional groups in the presence of other reducible moieties.[10] This chemoselectivity for specific functional groups is obtained by precisely controlling the size and shape of the NPs as well as by selecting the appropriate supports and tuning the NP composition. Especially, small Au NPs on the appropriate supports have exhibited high activity and selectivity compared to other supported metal NPs.[11] As an example, atomically precise $Au_{25}(SR)_{18}$ NPs catalyze the selective hydrogenation of unsaturated carbonyl compounds to allylic alcohols.[10c] In addition, Au/TiO_2 has been shown to selectively hydrogenate substituted nitroaromatics to the corresponding anilines.[10a] Our own group has also reported that Au NPs supported on hydrotalcite (Au/HT) and CeO_2-encapsulated Au NPs ($Au@CeO_2$) promote the highly chemoselective hydrogenation of epoxides and alkynes to the corresponding alkenes.[11d, g, h]

Herein, we report a TiO_2-supported Au NP catalyst that enables the selective *N*-formylation of a diverse range of functionalized amines using CO_2 as a carbonyl source under a H_2 atmosphere. A number of reducible functional groups, such as olefins, halogens, ketones, carbamates, aryl, and cyano moieties were completely retained during these formylation reactions, thus achieving highly selective synthesis of functionalized formamides. In addition to this high selectivity, the TiO_2-supported Au NP catalyst showed high reusability without any loss of catalytic performance.

Initially, we assessed the catalytic activity of various metal NPs on TiO_2 in the formylation of 5-hexen-1-amine (**1**) as a model functionalized amine under 20 atm of CO_2 and 30 atm of H_2 at 100 °C for 2 h. It was found that Au NPs with a mean diameter of 4.2 nm on TiO_2 (Au/TiO_2) gave the highest activity and afforded the desired product (**2**), while leaving the olefinic moiety of **1** intact (Table 1, entry 1). Upon prolonging the reaction time to 10 h, **2** was obtained as the sole product in >99% yield (Table 1, entry 2) without hydrogenation or migration of the olefinic moiety. In sharp contrast, all the other metal NPs tested, including Pd, Ru, Pt, Rh, Ag and Cu, did not afford **2** at all and, resulted in hydrogenation of the olefinic moiety of **1** (Table 1, entries 3-8). These data demonstrated the highly unique catalytic properties of Au NPs for the selective production of **2**. Subsequently, the effect of the support used in conjunction with the Au NPs was investigated in the *N*-formylation of **1** (Table 1, entries 1 and 9-15). Interestingly, the catalytic activity of the Au NPs varied significantly with the type of support. TiO_2 was found to be especially effective, giving **2** in high yield (Table 1, entry 1), while the other supports showed minimal activity for the *N*-formylation of **1** (Table 1, entries 9-15). It is evident from the above results that a combination of Au NPs and TiO_2 is able to efficiently promote the selective formylation of **1** to **2**.

Table 1. *N*-Formylation of **1** using various metal catalysts[a]



1 **2** **3** **4**

Entry	Catalyst	Time [h]	Yield [%][b]		
			2	**3**	**4**
1	Au/TiO_2	2	30	0	0
2	Au/TiO_2	10	>99	0	0
3	Pd/TiO_2	2	0	49	34
4	Ru/TiO_2	2	0	39	17
5	Pt/TiO_2	2	0	75	0
6	Rh/TiO_2	2	0	69	0
7	Cu/TiO_2	2	0	52	0
8	Ag/TiO_2	2	0	trace	0
9	Au/ZnO	2	trace	0	0
10	Au/CeO_2	2	trace	0	0
11	Au/Al_2O_3	2	0	0	0
12	Au/Nb_2O_5	2	0	0	0
13	Au/ZSM-5	2	0	0	0
14	Au/hydroxyapatite	2	0	0	0
15	Au/hydrotalcite	2	0	0	0

[a]Reaction conditions: Catalyst (0.2 g, Metal: 4.5 mol%), **1** (0.5 mmol), DMA (3 mL), CO_2 (20 atm), H_2 (30 atm), 100 °C. [b]Determined by GC using internal standard technique.

With Au/TiO_2 in hand, the *N*-formylation of the functionalized amines shown in Table 2 with a combination of CO_2 and H_2 was investigated. These amines contained a wide range of reducible functional groups, including olefin (Table 2, entries 1, 5 and 6), carbonyl (Table 2, entry 8), amide (Table 2, entry 9), carbamate (Table 2, entry 10), halogen (Table 2, entries 11 and 12), aryl (Table 2, entries 4,8,11,12,14-16), and cyano (Table 2, entry 13) moieties. All were found to remain intact during the formylation, thereby achieving the highly selective synthesis of functionalized formamides in over 99% yields without any formation of by-products. To the best of our knowledge, this is the first example of the highly selective *N*-formylation of amines with reducible functional groups being retained completely intact. The Au/TiO_2 catalyst was also found to be active for normally unreactive aniline derivatives, giving the corresponding anilides in quantitative yields (Table 2, entries 14 and 15). To our knowledge, there has been only one report of a homogeneous Ru catalyst achieving aniline formylation using H_2, and this reaction requires the use of the strong base DBU.[2e] In contrast, the present Au/TiO_2 allowed aniline formylation without any additives. Moreover, Au/TiO_2 was also found to be applicable to the formylation of *o*-phenylenediamine. The intermediate formanilide evidently underwent a subsequent intramolecular cyclization to afford benzimidazole, which is a key compound in various functional materials, pesticides, and pharmaceuticals (Table 2, entry 16).

This heterogeneous Au/TiO_2 catalyst also has the significant advantages of separation and reuse compared to homogeneous catalysts. Following its use in a reaction, the Au/TiO_2 was easily removed from the reaction mixture by filtration and could then be reused for a subsequent reaction without any pre-treatment. The Au/TiO_2 retained its high catalytic activity and selectivity for the formylation of **1** even after the fifth recycling (Table 2, entry 2). Inductively coupled plasma atomic emission spectrometry (ICP-AES) analysis of the resulting filtrate revealed the absence of Au species (at a detection limit of 0.1 ppm), demonstrating no leaching of Au species during the reaction. The transmission electron microscopy (TEM) images of the reused Au/TiO_2 catalyst (Fig. S1) showed that the average diameter of the Au NPs was 4.2 nm, similar to that of the fresh catalyst, thus confirming the high durability of the Au/TiO_2.

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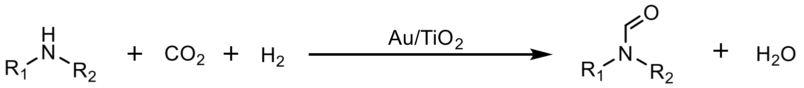
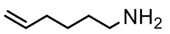
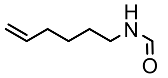
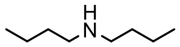
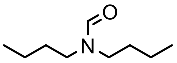
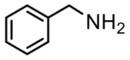
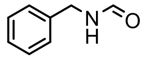
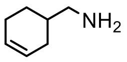
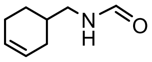
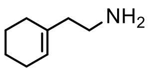
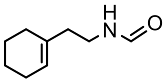
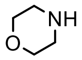
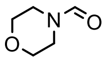
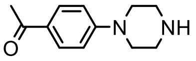
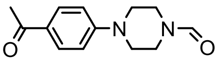
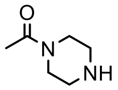
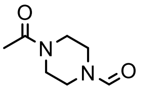
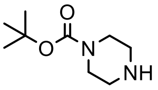
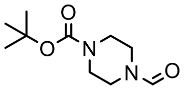
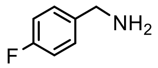
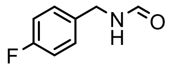
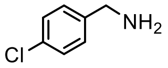
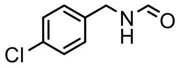
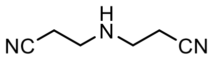
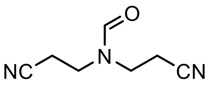
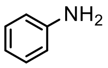
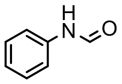
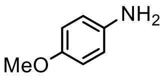
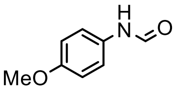
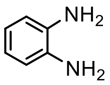
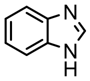
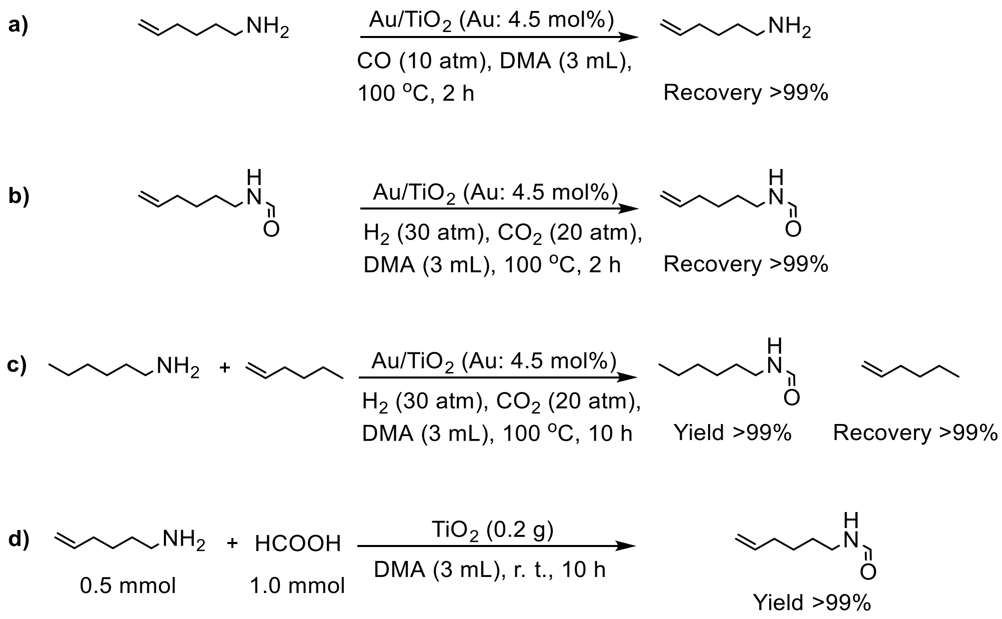
Table 2. *N*-Formylation of various amines catalyzed by Au/TiO_2[a]



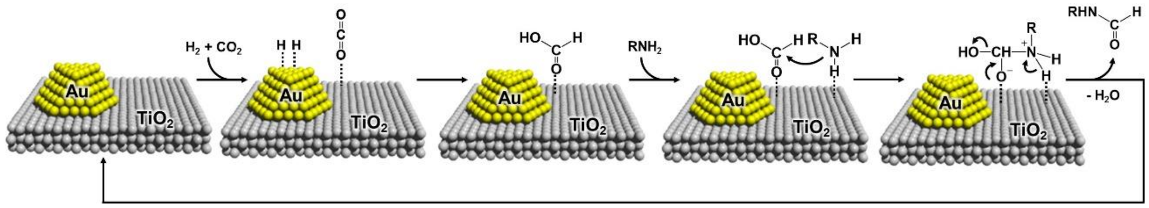
Entry	Substrate	Product	Temp. [°C]	Time [h]	Yield [%][b]
1			100	10	>99 (91[c])
2[d]			100	10	>99
3			140	20	>99
4			120	5	>99 (97[c])
5			100	10	>99
6			120	10	>99
7			120	5	>99
8			140	10	98[c]
9			140	5	>99 (98[c])
10			140	5	>99
11			120	5	>99 (96[c])
12			120	5	>99 (94[c])
13			140	10	>99
14			100	10	>99 (97[c])
15			100	10	>99
16			100	10	>99

[a]Reaction conditions: Au/TiO_2 (0.2 g, Au: 4.5 mol%), amine (0.5 mmol), DMA (3 mL), CO_2 (20 atm), H_2 (30 atm). [b]Determined by GC using internal standard technique. [c]Isolated yield. [d]5th reuse.

To elucidate the origin of the high selectivity of Au/TiO_2 during the *N*-formylation of functionalized amines, several control experiments were carried out. The *N*-formylation of **1** using Au/TiO_2 was found not to proceed under a CO atmosphere (Scheme 1a). In addition, the product **2** was not consumed when employed as the starting material under the same reaction conditions as in Table 1 (Scheme 1b). The *N*-formylation of *n*-hexylamine using Au/TiO_2 in the presence of 1-hexene gave *n*-hexylformamide in 99% yield, while 1-hexene was not hydrogenated and was quantitatively recovered (Scheme 1c). These results show that Au/TiO_2 is effective for the hydrogenation of CO_2, but completely inactive for the hydrogenation of the olefinic moiety. *In situ* Fourier transform infrared (FTIR) analysis of the Au/TiO_2 after treatment with a mixture of H_2 (120 mmHg) and CO_2 (30 mmHg) found new peaks attributed to the formation of formic acid (Figure S3). Moreover, subjecting formic acid to a dimethylacetamide (DMA) solution of **1** in the presence of TiO_2 under an Ar atmosphere at room temperature selectively generated **2** (Scheme 1d). From these results, it is evident that the Au NPs hydrogenate CO_2 to formic acid while not attacking various functional groups on the amine.[12] Subsequently, the formic acid generated *in situ* is activated by the Lewis acid sites of the TiO_2[13] and the nucleophilic attack of the adsorbed amine on the formic acid gives the corresponding formamide (Scheme 2).[14] This cooperative bifunctional catalysis, in which the Au NPs hydrogenate CO_2 to formic acid and the TiO_2 promotes the *N*-formylation of the amine with formic acid, enables the selective *N*-formylation of functionalized amines.



Scheme 1. Control experiments for *N*-formylation using Au/TiO_2 or TiO_2.



Scheme 2. Proposed reaction path for the Au/TiO_2-catalized *N*-formylation of amines with CO_2 and H_2.

In conclusion, the highly selective *N*-formylation of functionalized amines using CO_2 with H_2 was achieved with a Au/TiO_2 catalyst. The Au/TiO_2 efficiently promoted the selective *N*-formylation of a number of different amines to formamides in excellent yields without hydrogenation of reducible functional groups. This catalytic system allows simple work-up procedures and exhibits excellent reusability while demonstrating a broad substrate range. The cooperative bifunctional catalysis of the Au NPs, which provide CO_2 hydrogenation, and the TiO_2, which promotes amine formylation with formic acid, plays a crucial role in the selective *N*-formylation.

References

[1] a) M. Cokoja, D.-C. C. Bruckmeier, B. Rieger, W. A. Herrmann, F. E. Kühn, *Angew. Chem. Int. Ed.* **2011**, *50*, 8510-8537; *Angew. Chem.* **2011**, *123*, 8662-8690. b) Q. Liu, L. Wu, R. Jackstell, M. Beller, *Nature Commun*. **2015**, *6*, 5933. c) J. Klankermayer, S. Wesselbaum, K. Beydoun, W. Leitner, *Angew. Chem. Int. Ed.* **2016**, *55*, 7296-7343; *Angew. Chem.* **2016**, *128*, 7416-7467. d) M. D. Porosoff, B. Yan, J. G. Chen, *Energy Environ. Sci*. **2016**, *9*, 62-73.

[2] a) M. W. Farlow, H. Adkins, *J. Am. Chem. Soc*. **1935**, *57*, 2222-2223. b) P. G. Jessop, Y. Hsiao, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1994**, *116*, 8851-8852. c) O. Kröcher, R. A. Köppel, A. Baiker, *Chem. Commun*. **1997**, 453-454. d) O. Kröcher, R. A. Köppel, M. Fröba, A. Baiker, *J. Catal*. **1998**, *178*, 284-298. e) P. Munshi, D. J. Heldebrant, E. P. McKoon, P. A. Kelly, C.-C. Tai, P. G. Jessop, *Tetrahedron Lett.* **2003**, *44*, 2725-2727. f) L. Schmid, A. Canonica, A. Baiker, *Appl. Catal. A: Gen.* **2003**, *255*, 23-33. g) L. Schmid, M. S. Schneider, D. Engel, A. Baiker, *Catal. Lett*. **2003**, *88*, 105-113. h) M. Rohr, J.-D. Grunwaldt, A. Baiker, *J. Mol. Catal. A: Chem.* **2005**, *226*, 253-257. i) M. Rohr, J.-D. Grunwaldt, A. Baiker, *J. Catal.* **2005**, *229*, 144-153. j) C. Federsel, A. Boddien, R. Jackstell, R. Jennerjahn, P. J. Dyson, R. Scopelliti, G. Laurenczy, M. Beller, *Angew. Chem. Int. Ed*. **2010**, *49*, 9777-9780; *Angew. Chem*. **2010**, *122*, 9771-9774. k) C. Ziebart, C. Federsel, P. Anbarasan, R. Jacksell, W. Baumann, A. Spannerberg, M. Beller, *J. Am. Chem. Soc.* **2012**, *134*, 20701-20704. l) C. Federsel, C. Ziebart, R. Jacksell, W. Baumann, M. Beller, *Chem. Eur. J.* **2012**, *18*, 72-75. m) T. Schaub, R. Paciello, M. Pazicky, G. Fachinetti, D. Preti, BASF SE, Germany, US20130102807A1, **2013**. n) S. Kumar, S. L. Jain, *RSC Adv*. **2014**, *4*, 64277-64279. o) L. Zhang, Z. Han, X. Zhao, Z. Wang, K. Ding, *Angew. Chem. Int. Ed.* **2015**, *54*, 6186-6189; *Angew. Chem*. **2015**, *127*, 6284-6287. p) H. Liu, Q. Mei, Q. Xu, J. Song, H. Liu, B. Han, *Green Chem*. **2017**, *19*, 196-201. q) P. Ju, J. Chen, A. Chen, L. Chen, Y. Yu,

ACS Sus. Chem. Eng. **2017**, DOI: 10.1021/acssuschemeng.6b02865.

[3] a) P. G. Jessop, T. Ikariya, R. Noyori, *Nature* **1994**, *368*, 231-233. b) R. Tanaka, M. Yamashita, K. Nozaki, *J. Am. Chem. Soc*. **2009**, *131*, 14168-14169. c) C. Federsel, A. Boddien, R. Jackstell, R. Jennerjahn, P. J. Dyson, R. Scopelliti, G. Laurenczy, M. Beller, *Angew. Chem. Int. Ed*. **2010**, *49*, 9777-9780; *Angew. Chem*. **2010**, *122*, 9971-9974. d) D. Preti, C. Resta, S. Squarcialupi, G. Fachinetti, *Angew. Chem. Int. Ed*. **2011**, *50*, 12551-12554; *Angew. Chem.* **2011**, *123*, 12759-12762.

[4] a) K. Yamaguchi, K. Ebitani, T. Yoshida, H. Yoshida, K. Kaneda, *J. Am. Chem. Soc*. **1999**, *121*, 4526-4527. b) K. Mori, Y. Mitani, T. Hara, T. Mizugaki, K. Ebitani, K. Kaneda, *Chem. Commun*. **2005**, 3331-3333. c) G. W. Coates, D. R. Moore, *Angew. Chem. Int. Ed.* **2004**, *43*, 6618-6639; *Angew. Chem*. **2004**, *116*, 6784-6806. d) G. Martín, G. Fiorani, A. W. Kleij, *ACS Catal*. **2015**, *5*, 1353-1370.

[5] a) F. Shi, Y. Deng, T. SiMa, J. Peng, Y. Gu, B. Qiao, *Angew. Chem. Int. Ed*. **2003**, *42*, 3257-3260; *Angew. Chem*. **2003**, *115*, 3379-3382. b) D. Diaz, A. K. Darko, L. McElwee-White, *Eur. J. Org. Chem*. **2007**, 4453-4465. c) M. Tamaru, K. Ito, Y. Nakagawa, K. Tomishige, *J. Catal.* **2016**, *343*, 75-85.

[6] a) R. N. Salvatore, S. I. Shin, A. S. Nagle, K. W. Jung, *J. Org. Chem*. **2001**, *66*, 1035-1037. b) R. Srivastava, D. Srinivas, P. Ratnasamy, *J. Catal.* **2005**, *233*, 1-15. c) A. Ion, C. V. Dooeslaer, V. Parvulescu, P. Jacobs, D. De Vos, *Green. Chem.* **2008**, *10*, 111-116. d) J. Shang, X. Guo, Z. Li, Y. Deng, *Green. Chem*. **2016**, *18*, 3082-3088.

[7] a) M. Gall, J. M. McCall, R. E. TenBrink, P. F. VonVoigtlander, J. S. Mohrland, *J. Med. Chem*. **1988**, *31*, 1816-1820. b) K. Kobayashi, S. Nagato, M. Kawakita, O. Morikawa, H. Konishi, *Chem. Lett.* **1995**, *24*, 575-576. c) B.-C. Chen, M. S. Bednarz, R. Zhao, J. E. Sundeen, P. Chen, Z. Shen, A. P. Skoumbourdis, J. C. Barrish, *Tetrahederon Lett.* **2000**, *41*, 5453-5456. d) A. Dömling, *Chem. Rev*. **2006**, *106*, 17-89. e) J. Pouessel, O. Jacquet, T. Cantat, *ChemCatChem* **2013**, *5*, 3552-3556.

[8] a) C. D. N. Gomes, O. Jacquet, C. Villiers, P. Thuëry, M. Ephritikhine, T. Cantat, *Angew. Chem. Int. Ed.* **2012**, *51*, 187-190; *Angew. Chem.* **2012**, *124*, 191-194. b) O. Jacquet, C. D. N. Gomes, M.

Ephritikhine, T. Cantat, *J. Am. Chem. Soc*. **2012**, *134*, 2934-2937. c) K. Motokura, N. Takahashi, D. Kashiwame, S. Yamaguchi, A. Miyaji, T. Baba, *Catal. Sci. Technol.* **2013**, *3*, 2392-2396. d) X. Frogneux, O. Jacquet, T. Cantat, *Catal. Sci. Technol.* **2014**, *4*, 1529-1533. e) K. Motokura, N. Takahashi, A. Miyaji, Y. Sakamoto, S. Yamaguchi, T. Baba, *Tetrahedron*, **2014**, *70*, 6951-6956. f) L. Hao, Y. Zhao, B. Yu, Z. Yang, H. Zhang, B. Han, X. Gao, Z. Liu, *ACS Catal*. **2015**, *5*, 4989-4993. g) T. V. Q. Nguyen, W. J. Yoo, S. Kobayashi, *Angew. Chem. Int. Ed.* **2015**, *54*, 9209-9212; *Angew. Chem.* **2015**, *127*, 9341-9344. h) C. C. Chong, R. Kinjo, *Angew. Chem. Int. Ed.* **2015**, *54*, 12116-12120; *Angew. Chem.* **2015**, *127*, 12284-12288. i) S. Zhang, Q. Mei, H. Liu, H. Liu, Z. Zhang, B. Han, *RSC Adv*. **2016**, *6*, 322370-32373. j) X.-F. Liu, R. Ma, C. Qiao, H. Cao, L.-N. He, *Chem. Eur. J.* **2016**, *46*, 16489-16493. k) J. Song, B. Zhou, H. Liu, C. Xie, Q. Meng, Z. Zhang, B. Han, *Green Chem.* **2016**, *18*, 3956-3961. l) H. Lv, Q. Xing, C. Yue, Z. Lei, F. Li, *Chem. Commun*. **2016**, *52*, 6545-6548. m) C. Fang, C. Lu, M. Liu, Y. Zhu, Y. Fu, B.-L. Lin, *ACS Catal.* **2016**, *6*, 7876-7881. n) R. Luo, X. Lin, Y. Chen. W. Zhang, X. Zhou, H. Ji, *ChemSusChem* **2017**, *10*, 1224-1232. o) R. Luo, Y. Chen, Q. Han, X. Lin, Q. Xu, X. He, W. Zhang, X. Zhou, H. Ji, *ChemSusChem* **2017**, doi: 10.1002/cssc.201601846. p) X.-F. Liu, C. Qiao, X.-Y. Li, L.-N. He, *Green Chem*. **2017**, doi: 10.1039/C7GC00484B.

[9] During our study on this work, a homogeneous catalyst for the *N*-formylation of amines bearing olefinic moiety has been reported. See: Ref. 2p.

[10] a) M. Sankar, N. Dimitratos, P. J. Miedziak, P. P. Wells, C. J. Kiely, G. J. Hutchings, *Chem. Soc. Rev.* **2012**, *41*, 8099-8139. b) L. L. Chng, N. Erathodiyil, Y. Ying, *Acc. Chem. Res*. **2013**, *46*, 1825-1837. c) I. Lee, F. Zaera, *Top. Catal*. **2013**, *56*, 1284-1298. d) P. Serna, A. Corma, *ACS Catal.* **2015**, *5*, 7114-7121.

[11] a) A. Corma, P. Serna, *Science* **2006**, *313*, 332-334. b) A. Corma, H. Garcia, *Chem. Soc. Rev.* **2008**, *37*, 2096-2126. c) Y. Zhu, H. Qian, B. A. Drake, R. Jin, *Angew. Chem. Int. Ed*. **2010**, *49*, 1295-1298; *Angew. Chem*. **2010**, *122*, 1317-1320. d) A. Noujima, T. Mitsudome, T. Mizugaki, K. Jitsukawa,

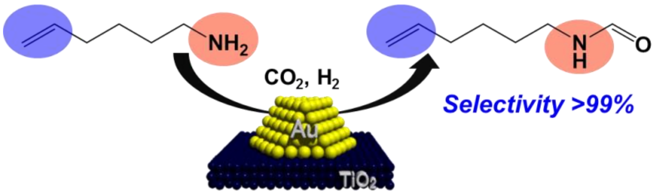
K. Kaneda, *Angew. Chem. Int. Ed*. **2011**, *50*, 2986-2989; *Angew. Chem*. **2011**, *123*, 3042-3045. e) T. Mitsudome, K. Kaneda, *Green Chem*. **2013**, *15*, 2636-2654. f) I. Cano, A. M. Chapman, A. Urakawa, P. W. N. M. van Leeuwen, *J. Am. Chem. Soc*. **2014**, *136*, 2520-2528. g) T. Mitsudome, M. Yamamoto, Z. Maeno, T. Mizugaki, K. Jitsukawa, K. Kaneda, *J. Am. Chem. Soc.* **2015**, *137*, 13452-13455. h) T. Urayama, T. Mitsudome, Z. Maeno, T. Mizugaki, K. Jitsukawa, K. Kaneda, *Chem. Eur. J.* **2016**, *22*, 17962-17966. i) B. S. Takale, X. Feng, Y. Lu, M. Bao, T. Jin, T. Minato, Y. Yamamoto, *J. Am. Chem. Soc*. **2016**, *138*, 10356-10364.

[12] A control experiment involving the *N*-formylation of **1** with formic acid using various metal oxides demonstrated that both CeO_2 and TiO_2 were active (Table S1), although Au/CeO_2 showed minimal activity for the formylation of **1** under CO_2 and H_2 (Table 1, entry 10). The results indicated that the TiO_2 participated in both the formic acid activation step and the CO_2 hydrogenation step through the activation of CO_2 and/or H_2.

[13] The activation of formic acid by the Lewis acid sites of TiO_2 has been previously reported. See B. Krishnakumar, M. Swaminathan, *J. Mol. Catal. A: Chem.* **2011**, *334*, 98-102.

[14] The initial reaction rate (R_0) was proportional to the concentration of the amine and inversely proportional to the formic acid concentration, suggesting that this reaction proceeds through the Langmuir-Hinshelwood mechanism. See: Figures S4 and S5 in Supporting Information.

COMMUNICATION



For the first time, TiO_2-supported Au NPs have been shown to promote the selective *N*-formylation of various amines to formamides in excellent yields without hydrogenation of reducible functional groups. This catalytic system has the significant advantages of simple work-up procedures, high reusability, and applicability to a wide range of substrates.

*Takato Mitsudome, Teppei Urayama, Shu Fujita, Zen Maeno, Tomoo Mizugaki, Koichiro Jitsukawa, Kiyotomi Kaneda**

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