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Recyclable Oxofluorovanadate-Catalyzed Formylation of Amines by Reductive Functionalization of CO_2 with Hydrosilanes

Shanxuan Wu+,[a, b] Zijun Huang+,[b, c] Xiaolin Jiang,[b] Fachao Yan,[b] Yuehui Li,*[b] and Chen-Xia Du*[a]

An efficient method has been developed for the reductive amination of CO_2 by using readily available and recyclable oxofluorovanadates as catalysts. Various amines are transformed into the desired *N*-formylated products in moderate to excellent yields at room temperature in the presence of phenylsilane. Mechanistic studies based on in situ infrared spectroscopy suggest a reaction pathway initiated through F–Si interactions. The activated phenylsilane allows for CO_2 insertion to produce phenylsilyl formate, which undergoes attack by the amine to generate the target product.

Introduction

The intensification of CO_2 greenhouse effects in recent years has attracted considerable research activities to mitigate climate change through CO_2 utilization as inherently nontoxic, abundant, and renewable chemical feedstock.[1–5] Carbon dioxide can be reduced to carbon monoxide, formic acid, formaldehyde, methanol and methane, or can undergo a reduction functionalization process to build C–O, C–C, and C–N bonds; and hence generate a multitude of chemical products.[6–9] Compounds featuring C–N bond are widely present in agrochemicals and pharmaceuticals, and moreover C–N bond assumes an important functionality in the field of organic synthesis.[10] Formamides and amides are representative of C–N bond compounds, and often play the role of solvents and substrates in organic synthesis. Formamides were generally prepared from carbon monoxide as a carbon source requiring high pressures and temperatures and longer reaction times.[10] Recently, with advent of CO_2 utilization technologies, reductive functionalization of carbon dioxide with amines is regarded an effective and a safer synthetic method to access formamides. There are numerous reports on reduction of CO_2 and reductive amination using metal catalysts such as Pt,[11] Ru,[12] Re,[13] Ir,[14] Fe,[15] W,[16] Cu,[17] among others. In addition, the use of some organic catalysts such as TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene),[18] ionic liquids,[19,20] NHCs (*N*-heterocyclic carbene)[21] and betaine[22] have also been reported. Although these catalysts have high efficiency and generate products in shorter reaction times, homogeneous nature of these catalysts are less favored by the industry, and hence new and suitable catalytic systems need to be further explored.

Nonmetallic element fluorine, with a small ionic radius and strong electronegativity, is widely distributed in nature. Organic F-containing compounds and F-containing polymers exhibit excellent physical and chemical properties. The introduction of F atom in drug molecules can fine-tune the molecular structure, easily block metabolized sites, improve the molecular metabolic stability and increase the binding affinity of the compounds.[23,24] Fluorine and silicon are often engaged in strong interaction, which results in silicon-hydrogen bonds activation to achieve phenylsilane hydride transfer accelerating the reductive reaction. The increased nucleophilicity of the hydride ion in the presence of fluoride ions with TBAF (tetrabutylammonium fluoride) or cesium fluoride was reported by the groups of Baba[25] and He[26] using dimethylphenylsilane and triethoxysilane as reducing agents, respectively. However, heterogeneous fluorine-containing materials are rarely used in formamide synthesis reactions involving carbon dioxide, although they are more suitable catalysts for industrial applications.

Vanadate-type compounds have interesting properties (ionic environments with strong polar distortions and Lewis acidity and magnetic properties) that can contribute to small molecule activation and catalysis.[27–30] To our knowledge, the use of oxofluorovanadate materials as catalysts for reductive amination of carbon dioxide has not been reported to date. We investigated K_2VOF_4[31–34] as a heterogeneous catalyst for the formylation of several amines with CO_2 and phenylsilane. We discovered that K_2VOF_4 was able to catalyze formylation

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[a] S. Wu,+ Prof. Dr. C.-X. Du
College of Chemistry
Zhengzhou University
Zhengzhou 450001 (P.R. China)
E-mail: dcx@zzu.edu.cn

[b] S. Wu,+ Z. Huang,+ X. Jiang, F. Yan, Prof. Dr. Y. Li
State Key Laboratory for Oxo Synthesis and Selective Oxidation
Suzhou Research Institute of LICP
Center for Excellence in Molecular Synthesis
Lanzhou Institute of Chemical Physics
Chinese Academy of Sciences
Lanzhou 730000 (P. R. China)
E-mail: yhli@licp.cas.cn

[c] Z. Huang+
College of Chemistry and Chemical Engineering
Hunan Institute of Engineering
Xiangtan, 411104 (P. R. China)

[+] These authors contributed equally to this work.

Supporting information for this article is available on the WWW under https://doi.org/10.1002/cssc.202100117 reactions at room temperature and at atmospheric pressure of CO_2 (1 bar) producing formamides in excellent yields.

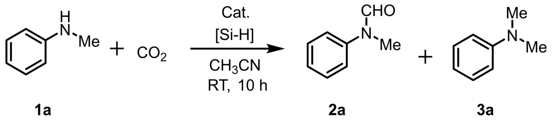
Results and Discussion

Based on our recent work in developing fluoride-type catalysts for aminocarbonylation[35] and arylborate catalysts for CO_2 reductive amination,[36] we commenced by investigating inorganic fluorides as catalysts for *N*-formylation reactions. Initially, various fluoride salts were tested with *N*-methylaniline (**1 a**) as a model substrate for the optimization of the reaction conditions (Table 1). A blank experiment without catalyst resulted in unsuccessful formamide formation (Table 1, entry 1). Various common fluoride salts such as FeF_2, FeF_3, K_2TiF_6 have been tested and also resulted in no product formation (Table 1, entries 2–4). In contrast, when K_2NbF_7 catalyst was used, *N*-methylformanilide was afforded in 64 % yield at room temperature (Table 1, entry 5). To our delight, an excellent yield of 90 % was obtained when K_2VOF_4 was used as catalyst with phenylsilane (Table 1, entry 6). Encouraged by this result we turned to optimize the reducing agents through simple silane screening. Unfortunately, most silanes were ineffective in the formation of the product (Table 1, entries 8–11), with the exception of diphenylsilane, which gave a reduced yield of 22 % (Table 1, entry 7).

With the optimal reaction conditions in hand, we then started to explore the scope and limitations of K_2VOF_4-catalyzed *N*-formylation reaction as shown in Table 2. *p*-Substituted anilines were transformed smoothly to give the corresponding products in excellent yields (**2 b**–**2 d**), with the exception of *p*-iodo-aniline substrate providing *N*-formylated product in only 35 % yield (**2 e**). *N*-methylaniline compounds with various aryl substituents were also investigated and provided the *N*-formylated in good yields (**2 f**–**2 j**). Both electron withdrawing or donating substituents have little effect on the reaction yield with chloride, methyl, methoxy and acetyl *para*-substituents gave excellent yields of 83 % (**2 f**), 95 % (**2 g**, **2 h**), 87 % (**2 i**) and 77 % (**2 j**), respectively. Under optimized conditions, *N*-butylaniline can also be *N*-formylated in 92 % yield (**2 k**). Furthermore, benzylamine compounds (**2 l**–**2 r**), heterocyclic amines (**2 s**, **2 t**), and aliphatic amines (**2 u**, **2 v**) were also investigated with moderate to excellent yields obtained (Table 2). *N*-methylbenzylamine with different substituents provided the *N*-formylated products with comparable yields, 78∼83 % (**2 m**–**2 o**). *N*-ethylbenzylamine provided an excellent yield of 97 % (**2 q**). *N*-*t*Bu-benzylamine with bulky tertiary butyl group gave in lower yield of 76 % (**2 p**) while GC determined yield for dibenzylamine was up to 87 % (**2 r**). Indoline and 1,2,3,4-tetrahydroquinoline were formylated in 87 % (**2 s**) and 94 % (**2 t**) yield (isolated products), respectively. The yields of aliphatic hexylamine (**2 u**) and *N*-[2-(dimethylamino)ethyl]-*N*-methylformamide (**2 v**) were determined by GC, and the results were satisfactory.

To gain more information about the mechanism for this transformation, we studied the interactions between K_2VOF_4, phenylsilane and CO_2 by NMR and in situ infrared spectroscopy.

Table 1. Optimization of the reaction conditions.[a]

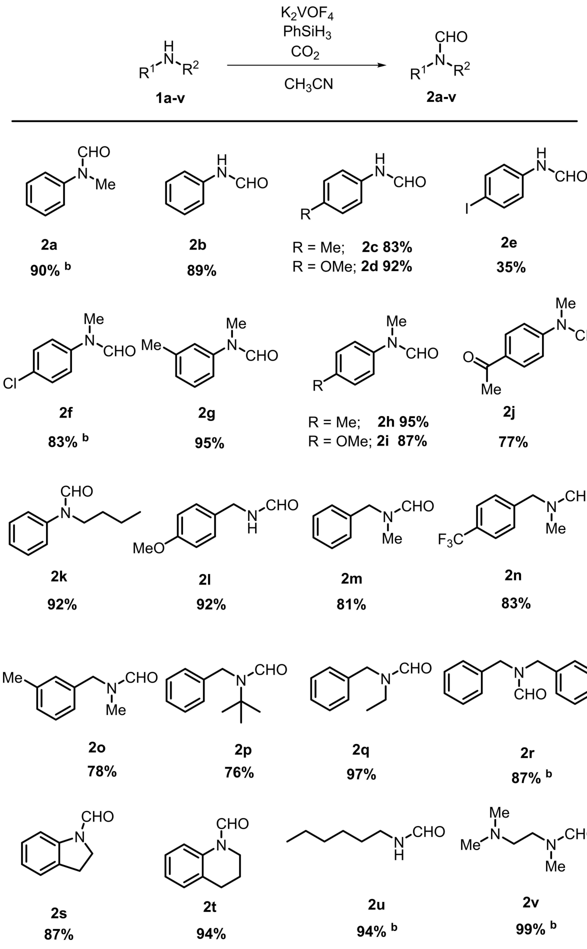


1a **2a** **3a**

Entry	Cat./mol %	Si–H/equiv.	Yield (**2 a**) [%][b]	Yield (**3 a**) [%][b]
1	none	$PhSiH_3$/2	0	0
2	FeF_2/10	$PhSiH_3$/2	0	0
3	FeF_3/10	$PhSiH_3$/2	0	0
4	K_2TiF_6/10	$PhSiH_3$/2	5	0
5	K_2NbF_7/10	$PhSiH_3$/2	64	0
6	K_2VOF_4/10[c]	$PhSiH_3$/2	90	trace
7	K_2VOF_4/10[c]	Ph_2SiH_2/2	22	0
8	K_2VOF_4/10[c]	$(EtO)_3SiH$/2	0	0
9	K_2VOF_4/10[c]	PMHS[d]/2	0	0
10	K_2VOF_4/10[c]	Et_3SiH/2	0	0
11	K_2VOF_4/10[c]	Ph_2MeSiH/2	0	0

[a] Reaction conditions: **1 a** (0.2 mmol); CO_2 pressure: 1 bar; acetonitrile (0.5 mL). [b] GC yield with *n*-dodecane as internal standard. [c] 10 mg. [d] PMHS = polymethylhydrosiloxane.

Table 2. Substrate scope study.



[a] Reaction conditions: **1** (0.2 mmol), CO_2 (1 bar), K_2VOF_4 (10 mg) $PhSiH_3$ (1.2 equiv.) acetonitrile (0.5 mL), room temperature, 10 h; yields refer to isolated products. [b] Yield determined by GC.

A new characteristic peak at 1139 cm^{-1} can be observed, which is red-shifted from the signal of phenylsilane at 1118 cm^{-1}, when adding the catalyst to the acetonitrile solution of phenylsilane under carbon dioxide atmosphere (see the Supporting Information). When the amine was added to the reaction mixture, we observed that the peak continues to increase (Figure 1). We speculate that the alkalinity of the reaction system increases which increases the solubility of carbon dioxide and also increases the interaction between the silane and the catalyst.

Based on NMR and IR spectroscopy results, we have proposed a plausible reaction mechanism (Scheme 1). At first, intermediate **B** was formed through interactions of **A** with phenylsilane, owing to the Lewis acidity of vanadium, which was consistent with previous reports.[37] The activated Si–H bond was easily attacked by carbon dioxide accompanied by hydride transfer, leading to the formation of intermediate **C**. This is followed by C–O bond cleavage[19,38] and amine/formyl condensation giving product **E** with the release of silanol. On the surface of oxofluorovanadate catalysts, V–H interactions might also be involved to activate hydrosilanes, considering the strong Lewis acidity of V^{IV} center.

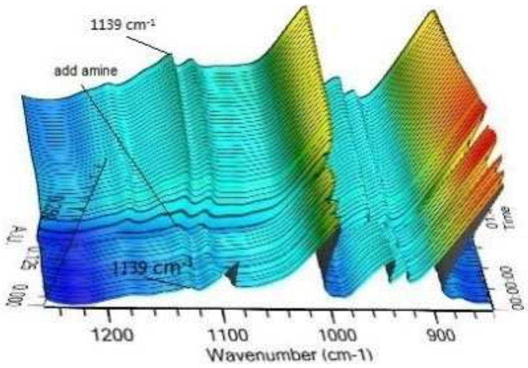
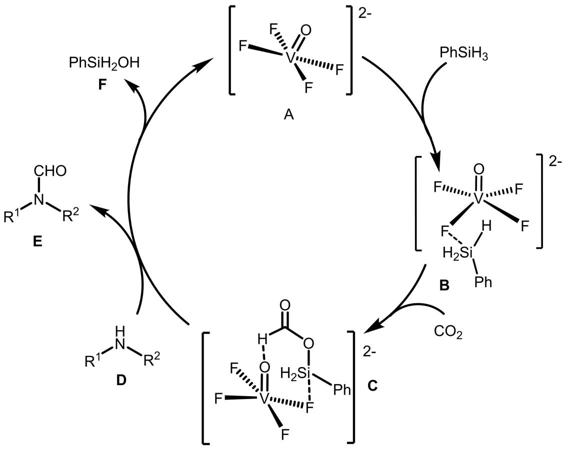


Figure 1. In situ infrared spectrum showing the characteristic peaks of $PhSiH_3$.



Scheme 1. Proposed mechanism for the transformation.

The solubility of the catalyst in the reaction solution was tested by ICP-MS. The test results showed that a very small amount of vanadium was present in the reaction solution (25.942 ppb). The fluorine-containing inorganic salt catalyst was evaluated on a 10 mg catalyst scale in batch mode over several cycles in the *N*-formylation of *N*-methylaniline, affording *N*-methyl-*N*-phenylformamide in $>90\%$ yield (GC yield) over 5 batches recycling (Figure 2). After the initial reaction, the catalyst was retained by centrifugation, then the catalyst was washed twice with a small amount of acetonitrile and reused in the next cycle without drying.

Conclusion

In summary, we have reported oxofluorovanadate K_2VOF_4 as an effective catalyst in the *N*-formylation of primary and secondary amines in the presence of phenylsilane and CO_2. The catalyst is readily available, cost effective, and reusable. Aromatic amines, benzylamines, N–H bond-containing heterocycles, and aliphatic amines were all efficiently converted into the corresponding *N*-formamides under standard conditions. This new approach for *N*-formylation of amines uses CO_2 with inorganic oxofluorovanadate catalysts proceeded at room temperature and at atmospheric pressure of CO_2 with high efficiency and catalyst recyclability. The work also highlighted the reaction pathway initiated through F–Si interactions and the utility of oxofluorovanadate heterogeneous catalysts in *N*-formylation reactions.

Experimental Section

Preparation of K_2VOF_4

K_2VOF_4 was prepared according to a reported method,[31] with slight modifications. V_2O_5 (0.364 g, 2.00 mmol) was weighed into a 50 mL poly(tetrafluoroethylene) (PTFE)-lined stainless steel autoclave and dissolved in 48% HF (1 mL) at room temperature. Then, water (10 mL) and ethylene glycol (10 mL) were mixed and added and the

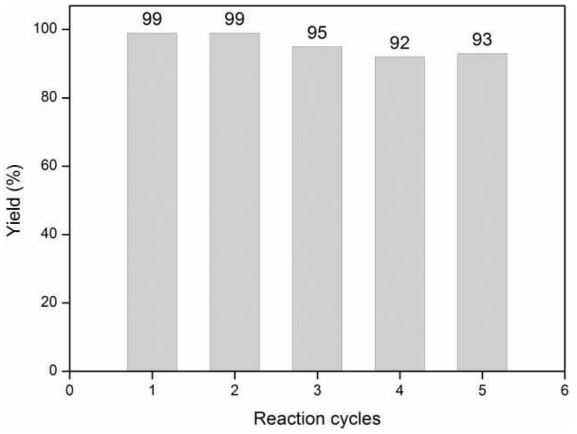


Figure 2. Recycling of the K_2VOF_4 catalyst in the *N*-formylation of *N*-methylaniline to *N*-methyl-*N*-phenylformamide. Yields determined by GC using *n*-dodecane as an internal standard.

color of the solution turned orange. After that, potassium nitrate (0.600 g, 6.00 mmol) was added at once. Sonication for 5 min for absolute dispersion. The kettle was sealed and placed at 100 °C oven for 24 h. After the reaction was completed and cooled down to room temperature, the reaction mixture was collected and washed with a small amount of water and ethanol for several times, following by drying at 150 °C for 6 h to give blue powders.

General procedure for the preparation of formamides

To a dried 5 mL glass vial was added the mixture of K_2VOF_4 (10 mg), amine **1** (0.2 mmol), and phenylsilane (0.24 mmol) in CH_3CN (0.5 mL) successively. Then the sample vial was moved into the autoclave. Once sealed, the autoclave was purged 3 times with carbon dioxide and then the pressure was set to 1 bar. The reaction mixture was stirred at room temperature for 10 h. Upon completion of the reaction, the mixture was concentrated under reduced pressure and the crude residue was purified by column chromatography on a silica gel column using petroleum ether/ethyl acetate as eluent to give the desired product **2**.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: amides · carbon dioxide · fluorides · heterogeneous catalysis · silanes

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