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Oxovanadium(V)-Catalyzed Synthesis of Ureas from Disilylamines and Carbon Dioxide under Ambient Pressure

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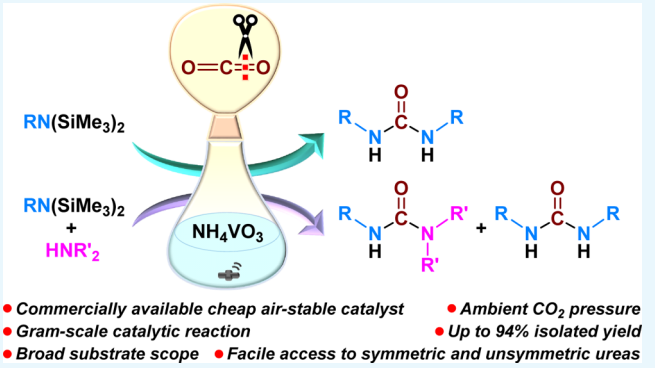
ABSTRACT: Here, a commercially available easy-to-handle oxovanadium(V) compound is demonstrated to serve as an efficient catalyst for the synthesis of ureas from disilylamines and carbon dioxide under ambient pressure. The catalytic activation of carbon dioxide proceeds without any additives, demonstrating a broad substrate scope and easy scalability to validate this catalytic activation of carbon dioxide. This catalytic system can be applied to the synthesis of unsymmetric ureas and chiral urea with retention of chirality.



INTRODUCTION

Carbon dioxide is a non-toxic, abundant, and green carbon resource. The development of methodologies for the transformation of carbon dioxide as a C1 building block into valuable compounds is of fundamental importance for the future sustainable society.[1] Catalytic activation of carbon dioxide under ambient pressure is considered to be essential for developing sustainable chemical transformations. Ureas are among the most important carbonyl compounds widely used as pesticides, herbicides, and raw materials for resins. Catalytic systems for the synthesis of ureas from amines and carbon dioxide under ambient pressure have been limited to the CsOH/ionic liquid,[2] $TBA_2[WO_4]$,[3] and DMAP (4-dimethylaminopyridine)[4] systems, which use an expensive ionic liquid as a solvent or lack substrate versatility. We have recently developed the catalytic carbon dioxide activation system under ambient pressure for the synthesis of ureas from amines (Scheme 1a).[5] This catalytic system, which was not so effective for aniline derivatives, required the use of an air-sensitive oxovanadium(V) catalyst, 3A MS as a dehydrating reagent, and *N*,*N*-diisopropylethylamine as a base, necessitating the development of more practical alternatives. The utilization of disilylamine as a substrate is envisioned to prevent the generation of water, which might cause catalyst deactivation, and the need for the addition of a base. Despite these advantages, no method has been reported to date for the catalytic synthesis of ureas using disilylamines as substrates and carbon dioxide under ambient pressure, although the reaction of silylamide complexes with carbon dioxide has been performed.[6] A few systems for the synthesis of ureas from silylamines and carbon dioxide have been reported, but they generally require high carbon dioxide pressure or supercritical carbon dioxide.[7] From these points of view, we set out to develop a practical catalytic process for the synthesis of ureas from disilylamines and carbon dioxide under ambient pressure by using a commercially available easy-to-handle oxovanadium(V) compound (Scheme 1b).

RESULTS AND DISCUSSION

We initially conducted a study to check whether oxovanadium(V) compounds could act as catalysts for activation of carbon dioxide (supplied by CO_2 balloon) in the synthesis of ureas from disilylamines. 2-Phenylethyl-*N*,*N*-bis(trimethylsilyl)amine (**1a**) was chosen as the disilylamine for product identification. The oxovanadium(V) compound, $VO(O^iPr)_3$, which was effective in the catalytic transformation of various primary amines into the ureas with carbon dioxide,[5] facilitates the catalytic transformation of **1a** with carbon dioxide into the corresponding urea **2a** in 68% yield in the absence of 3A MS (Table 1, entry 1). In the previous report,[5] 3A MS was required to remove the generated water. In the present system, the catalytic reaction proceeded even without the presence of 3A MS because hexamethyldisiloxane might be generated as a byproduct. Encouraged by this result, the efficiency of oxovanadium(V) compounds was screened. A commercially

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Scheme 1. Oxovanadium(V)-Catalyzed Synthesis of Ureas from Carbon Dioxide

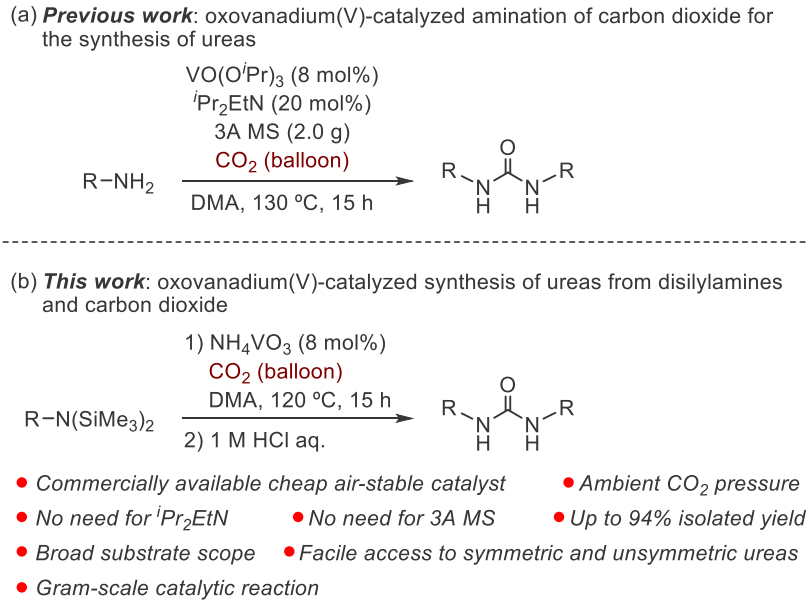
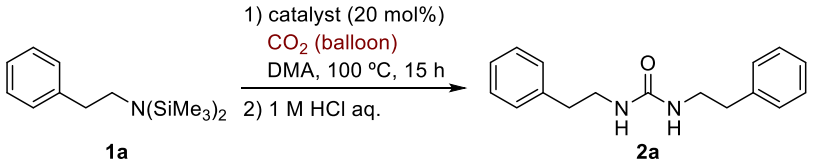
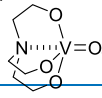


Table 1. Metal-Catalyzed Urea Synthesis from 1a and CO_2[a]



entry	catalyst	NMR yield[b] (%)
1	$VO(O^iPr)_3$	68
2	NH_4VO_3	95
3	——	N.D.
4	VO(TEA)[c]	70
5	V_2O_5	47
6	$VOSO_4{\cdot}nH_2O$	56
7	$VO(acac)_2$	48
8	TiO_2	9
9	NbO_2	2
10	Nb_2O_5	N.D.
11	WO_3	8
12	FeO	23
13	Fe_2O_3	3

[a]Reaction conditions: **1a** (0.3 mmol) and catalyst (20 mol %) in DMA (1.0 mL) under CO_2 (balloon) at 100 °C for 15 h. [b]NMR (%) = [**2a** (mmol) × 2/**1a** (mmol)] × 100. [c]VO(TEA) =  .

available easy-to-handle NH_4VO_3 was found to perform excellent catalytic activity, affording **2a** in 95% yield (entry 2). The control experiment showed that the oxovanadium(V) catalyst is indispensable for this catalytic transformation of carbon dioxide (entry 3). The catalytic reaction with VO(TEA)[8] instead of NH_4VO_3 proceeded well to give **2a** in a good yield (entry 4). Using V_2O_5, the corresponding urea **2a** was also obtained, albeit in a lower yield (entry 5). Tetravalent oxovanadium(IV) compounds such as $VOSO_4{\cdot}nH_2O$ and $VO(acac)_2$ exhibited moderate catalytic activities (entries 6 and 7). Catalytic activities of transition-metal oxides other than oxovanadium compounds were also examined. In this paper, TiO_2, NbO_2, Nb_2O_5, WO_3, FeO, and Fe_2O_3 were selected, but no promising results were observed (entries 8−13).

As NH_4VO_3 was found to have a high catalytic activity, the reaction was optimized using this catalyst to improve the reaction further. First, the solvent was changed from DMA (*N*,*N*-dimethylacetamide) to other polar solvents such as DMF (*N*,*N*-dimethylformamide), DMSO (dimethyl sulfoxide), and NMP (*N*-methylpyrrolidone), in which carbon dioxide can be dissolved efficiently. In all cases, the yields of the desired product **2a** were good but not better than that using DMA as a solvent (Table 2, entries 1−4). 1,4-Dioxane was found to be not effective in this catalytic system (entry 5). When non-polar solvents such as toluene and mesitylene were used, **2a** was not obtained at all (entries 6 and 7). The desired urea **2a** was not produced under neat conditions (entry 8). Next, the optimal amount of DMA was examined (entries 1 and 9−11), and 0.3

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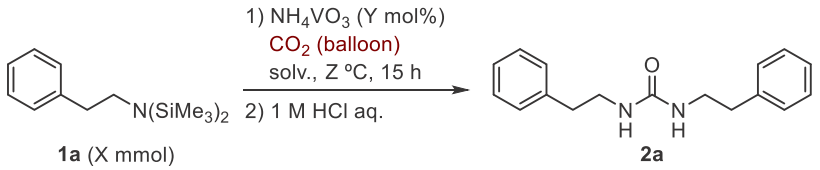
Table 2. NH_4VO_3-Catalyzed Urea Synthesis from 1a and CO_2[a]



entry	1a (X mmol)	NH_4VO_3 (Y mol %)	temperature (Z °C)	solvent	NMR yield[b] (%)
1	0.3 mmol	20	100	DMA	95
2	0.3 mmol	20	100	DMF	80
3	0.3 mmol	20	100	DMSO	87
4	0.3 mmol	20	100	NMP	89
5	0.3 mmol	20	100	1,4-dioxane	N.D.
6	0.3 mmol	20	100	toluene	N.D.
7	0.3 mmol	20	100	mesitylene	N.D.
8	0.3 mmol	20	100	neat	N.D.
9	0.3 mmol	20	100	DMA (0.5 mL)	81
10	0.3 mmol	20	100	DMA (2.0 mL)	77
11	0.3 mmol	20	100	DMA (4.0 mL)	73
12	0.6 mmol	8	100	DMA	79
13	0.6 mmol	8	100	DMA	78[c]
14	0.6 mmol	8	120	DMA	94[d]

[a]Reaction conditions: **1a** (*X* mmol) and NH_4VO_3 (*Y* mol %) in solvent (1.0 mL) under carbon dioxide (balloon) at *Z* °C for 15 h. [b]NMR (%) = [**2a** (mmol) × 2/**1a** (mmol)] × 100. [c]For 24 h. [d]Isolated yield.

M was found to be the appropriate reaction concentration under the conditions. When the amount of catalyst loading was reduced from 20 to 8 mol %, a 16% drop in the yield was observed (entry 12). The reaction time was extended from 15 to 24 h, but no improvement of the reaction efficiency was observed (entry 13). When the reaction temperature was increased from 100 to 120 °C, the yield was improved from 79% (entry 12) to 94% isolated yield (entry 14). From the above, we concluded that the reaction conditions at entry 14 were optimal.

With the optimized reaction conditions established, the substrate scope of disilylamines was explored (Table 3). The catalytic reaction of alkyl-substituted disilylamines proceeded smoothly to afford the corresponding ureas **2a**−**g** in good yields (entries 1−7). In the case of 2-(4-bromophenyl)ethyl-*N*,*N*-bis(trimethylsilyl)amine (**1b**), the corresponding urea **2b** was obtained in 76% isolated yield, in which the obtained product can be utilized for further transformation using the Br group (entry 2). This catalytic system could be applied to chiral disilylamine **1g** derived from (*R*)-(+)-1-phenylethylamine, converting into the corresponding chiral urea **2g** without loss of chirality as determined by chiral HPLC analysis (entry 7).[9] When phenyldisilylamine (entry 8) and *para*-substituted phenyldisilylamines (entries 9 and 10) were used, the yields slightly decreased compared with those of alkyl-substituted disilylamines (entries 1−7). The reason for the decrease in yield is probably that the bulky and electron-withdrawing phenyl group compared with the alkyl group is bonded to the nitrogen atom which coordinates to the vanadium center in the catalytic cycle. The catalytic reaction of the disilylamine consisting of a linear or cyclic alkyl group took place well to provide the corresponding ureas in good yields (entries 11−13). An ether group could be incorporated in disilylamine and did not interfere with this reaction (entry 14).

To demonstrate the practical utility of this catalytic system, a gram-scale catalytic reaction of **1a** was performed (Scheme 2). Using 15 mol % of NH_4VO_3, 1.2 mL (4.0 mmol) of **1a** reacted smoothly with carbon dioxide to yield 385 mg (72% isolated yield) of the desired urea **2a**.

To further evaluate the synthetic utility of the current methodology, we turned our attention toward the synthesis of unsymmetric ureas, which are important compounds for pharmaceuticals, agricultural chemicals, and materials. The reaction of **1a** with carbon dioxide in the presence of 2 equiv of morpholine (**3a**) under the catalytic reaction conditions was found to lead to the formation of the corresponding unsymmetric urea **4aa** in 60% yield with the concomitant formation of the symmetric urea **2a** in 19% yield (Table 4). When 4 equiv of **3a** was used, the unsymmetric urea **4aa** was obtained in 71% yield. By the addition of piperidine (**3b**) or dibutylamine (**3c**), the corresponding unsymmetric ureas **4ab** or **4ac** were produced in good yields (60 and 67% yields, respectively). It is worth mentioning that these unsymmetric ureas were main products, although a small amount of symmetric urea was produced. To the best of our knowledge, this is the first example of the catalytic synthesis of unsymmetric ureas derived from disilylamines and carbon dioxide under ambient pressure.

CONCLUSIONS

In conclusion, a commercially available easy-to-handle NH_4VO_3 was demonstrated to serve as an efficient catalyst in the catalytic utilization of carbon dioxide as a C1 building block under ambient pressure for the synthesis of ureas from disilylamines. This is the first example of the catalytic synthesis of ureas from disilylamine and carbon dioxide under ambient pressure. This catalytic system, which is convenient and easily handleable, displayed a wide range of substrate applicability without the use of any dehydrating reagent or base, including a gram-scale catalytic reaction. Another interesting feature is that this transformation can be applied to the synthesis of unsymmetric ureas and chiral urea without loss of chirality. Studies on the reaction mechanism and synthetic versatility

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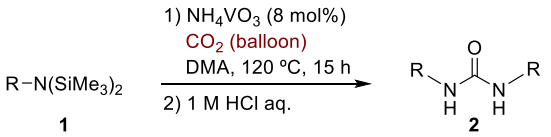
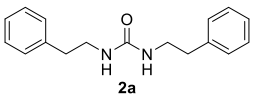
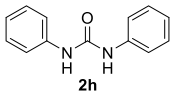
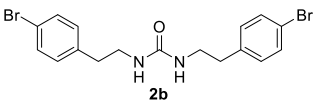
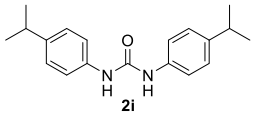
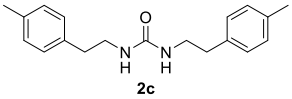
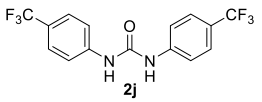
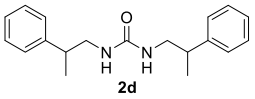
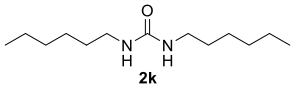
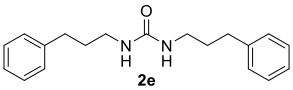
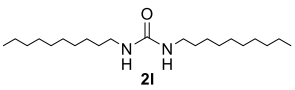
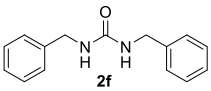
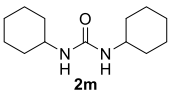
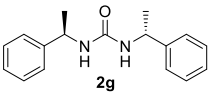
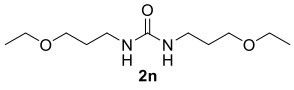
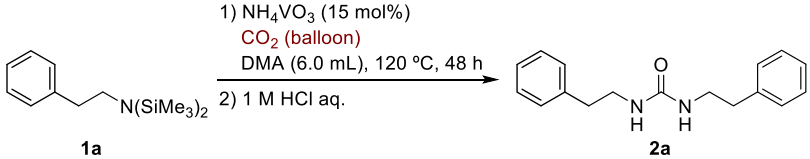
Table 3. Substrate Scope of Disilylamines in the Catalytic Synthesis of Ureas[a]



entry	product	isolated yield (%)[b]	entry	product	isolated yield (%)[b]
1	 **2a**	94	8	 **2h**	58
2	 **2b**	76	9	 **2i**	46
3	 **2c**	76	10	 **2j**	54
4	 **2d**	79	11	 **2k**	70
5	 **2e**	85	12	 **2l**	63
6	 **2f**	89	13	 **2m**	72
7	 **2g**	77	14	 **2n**	68

[a]Reaction conditions: substrate **1** (0.60 mmol) and NH_4VO_3 (8 mol %) in DMA (1.0 mL) under CO_2 (balloon) at 120 °C for 15 h. [b]Isolated yield (%) = [**2** (mmol) × 2/**1** (mmol)] × 100.

Scheme 2. Gram-Scale NH_4VO_3-Catalyzed Urea Synthesis of 2a



and applications of this practical catalytic system to other reactions are now in progress.

EXPERIMENTAL SECTION

General Information. Disilylamines (**1a**−**1g**,[10] **1h**−**1j**,[11] and **1k**−**1n**[10]) and VO(TEA)[8] were prepared according to the literature method. The other catalysts and solvents were purchased from commercial sources and further purified by the standard methods if necessary. ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and ^{29}Si NMR spectra were recorded in $CDCl_3$, DMSO-d_6, CD_3OD, or CD_3CN on a JEOL JNM-ECS 400 MHz spectrometer. Chemical shifts of ^{1}H NMR and ^{13}C NMR spectra were given in δ (ppm) relative to the residual solvent signal as an internal standard. Chemical shifts of ^{29}Si{^{1}H} NMR spectra were reported relative to the external reference Me_4Si (δ = 0 ppm). Chemical shifts of ^{19}F{^{1}H} NMR spectra were referenced to an external $PhCF_3$ (δ = −63.7 ppm). High-resolution mass spectroscopy (HRMS) was performed on a JEOL JMS-700 spectrometer. The analysis of the chiral urea product **2g** was carried out using HPLC (Chiralpak IA, hexane/$CHCl_3$/EtOH = 8:2:1, flow 0.5 mL/min, 254 nm).

*Disilylamine **1b**.* ^{1}H NMR (400 MHz, C_6D_6): δ 7.19−7.16 (m, 2H), 6.78−6.75 (m, 2H), 2.81−2.77 (m, 2H), 2.43−2.39 (m, 2H), 0.09 (s, 18H); ^{13}C NMR (100 MHz, C_6D_6): δ 139.1,

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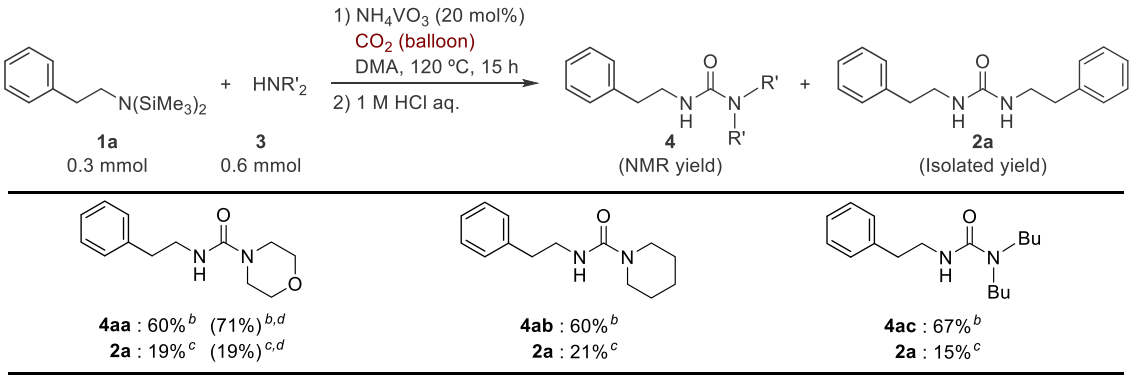
Table 4. NH_4VO_3-Catalyzed Unsymmetric Urea Synthesis[a]



[a]Reaction conditions: substrate **1a** (0.30 mmol), **3** (0.60 mmol), and NH_4VO_3 (20 mol %) in DMA (1.0 mL) under CO_2 (balloon) at 120 °C for 15 h. [b]NMR yield (%) = [**4** (mmol)/**1a** (mmol)] × 100. [c]Isolated yield (%) = [**2a** (mmol) × 2/**1a** (mmol)] × 100. [d]1.2 mmol of **3a** was used.

131.9, 130.5, 120.2, 48.1, 42.0, 2.5; ^{29}Si NMR (79 MHz, C_6D_6): δ 5.19; HRMS (ESI) *m/z* calcd for $C_{14}H_{27}BrNSi_2$ ([M + H]$^+$), 344.0865; found, 344.0875.

Disilylamine ***1c***. ^{1}H NMR (400 MHz, C_6D_6): δ 7.21−7.15 (m, 4H), 3.16−3.08 (m, 2H), 2.81−2.73 (m, 2H), 2.36 (s, 3H), 0.35 (s, 18H); ^{13}C NMR (100 MHz, C_6D_6): δ 137.3, 135.4, 129.5, 128.8, 48.6, 42.4, 21.2, 2.4; ^{29}Si NMR (79 MHz, C_6D_6): δ 4.96; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}NSi_2$ ([M + H]$^+$), 280.1917; found, 280.1917.

Disilylamine ***1d***. ^{1}H NMR (400 MHz, C_6D_6): δ 7.20−7.06 (m, 5H), 2.99−2.93 (m, 1H), 2.88−2.82 (m, 1H), 2.76−2.67 (m, 1H), 1.19 (d, *J* = 7.1 Hz, 3H), 0.13 (s, 18H); ^{13}C NMR (100 MHz, C_6D_6): δ 146.0, 128.7, 127.8, 126.6, 53.9, 43.9, 18.5, 2.7; ^{29}Si NMR (79 MHz, C_6D_6): δ 5.44; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}NSi_2$ ([M + H]$^+$), 280.1917; found, 280.1922.

Disilylamine ***1e***. ^{1}H NMR (400 MHz, C_6D_6): δ 7.28−7.14 (m, 5H), 2.88−2.83 (m, 2H), 2.50 (t, *J* = 7.6 Hz, 2H), 1.82−1.73 (m, 2H), 0.21 (s, 18H); ^{13}C NMR (100 MHz, C_6D_6): δ 142.2, 128.7, 128.6, 126.1, 45.6, 37.6, 34.0, 2.4; ^{29}Si NMR (79 MHz, C_6D_6): δ 4.76; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}NSi_2$ ([M + H]$^+$), 280.1917; found, 280.1917.

Disilylamine ***1g***. ^{1}H NMR (400 MHz, C_6D_6): δ 7.39−7.08 (m, 5H), 4.30 (q, *J* = 7.1 Hz, 1H), 1.50 (d, *J* = 7.1 Hz, 3H), 0.11 (s, 18H); ^{13}C NMR (100 MHz, C_6D_6): δ 147.7, 128.2, 127.1, 126.3, 53.2, 23.3, 3.6; ^{29}Si NMR (79 MHz, C_6D_6): δ 4.13; elemental analysis (%) calcd for $C_{14}H_{27}NSi_2$: C, 10.25; H, 63.32; N, 5.27; found: C, 10.32; H, 63.14; N, 5.33%.

Disilylamine ***1i***. ^{1}H NMR (400 MHz, C_6D_6): δ 7.02−6.98 (m, 2H), 6.88−6.83 (m, 2H), 2.73 (sept., *J* = 7.1 Hz, 1H), 1.15 (d, *J* = 7.1 Hz, 6H), 0.11 (s, 18H); ^{13}C NMR (100 MHz, C_6D_6): δ 145.7, 144.3, 130.3, 126.8, 33.9, 24.4, 2.4; ^{29}Si NMR (79 MHz, C_6D_6): δ 3.55; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}NSi_2$ ([M + H]$^+$) 280.1917; found, 280.1917.

General Procedure for Oxovanadium(V)-Catalyzed Urea Synthesis. In a 10 mL two-necked flask, disilylamine **1** (0.60 mmol), NH_4VO_3 (5.6 mg, 0.048 mmol), and DMA (1.0 mL) were placed in a glovebox filled with nitrogen. Next, nitrogen in the flask was replaced with CO_2. The mixture was stirred at 120 °C for 15 h, followed by treatment with 1 M HCl aq. and extraction with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtrated, and removed under reduced pressure. Urea **2** was isolated by reprecipitation from CH_2Cl_2 and hexane or preparative TLC (ethyl acetate/CH_2Cl_2 = 1:2). 1,3,5-Trimethoxybenzene was used as an internal standard, and ^{1}H NMR analysis was performed to determine the NMR yield. Spectral data of the products were identical with those of authentic samples.

N,N′-Bis(2-phenylethyl)urea ***(2a)***.[12] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.16 (m, 10H), 4.17 (br, 2H), 3.44−3.39 (m, 4H), 2.79 (t, *J* = 6.8 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 139.3, 129.0, 128.7, 126.5, 41.8, 36.5; HRMS (ESI) *m/z* calcd for $C_{17}H_{20}N_2ONa$ ([M + Na]$^+$), 291.1473; found, 291.1478.

N,N′-Bis[2-(4-bromophenyl)ethyl]urea ***(2b)***.[5] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.2 Hz, 4H), 7.05 (d, *J* = 8.2 Hz, 4H), 4.13 (br, 2H), 3.41−3.37 (m, 4H), 2.75 (t, *J* = 6.6 Hz, 4H); ^{13}C NMR (100 MHz, CD_3OD): δ 160.9, 140.1, 132.5, 131.9, 120.9, 42.2, 36.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{19}Br_2N_2ONa$ ([M + Na]$^+$), 446.9684; found, 446.9687.

N,N′-Bis[2-(4-methylphenyl)ethyl]urea ***(2c)***.[5] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11−7.05 (m, 8H), 4.34 (br, 2H), 3.40−3.34 (m, 4H), 2.73 (t, *J* = 6.9 Hz, 4H), 2.32 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 136.09, 136.08, 129.4, 128.8, 41.8, 35.9, 21.2; HRMS (ESI) *m/z* calcd for $C_{19}H_{24}N_2ONa$ ([M + Na]$^+$), 319.1786; found, 319.1791.

N,N′-Bis(2-phenylpropyl)urea ***(2d)***.[5] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30−7.14 (m, 10H), 4.24 (br, 2H), 3.43−3.35 (m, 2H), 3.14−3.05 (m, 2H), 2.90−2.80 (m, 2H), 1.21 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 144.5, 128.7, 127.4, 126.6, 47.29, 47.26, 40.3, 19.3; HRMS (ESI) *m/z* calcd for $C_{19}H_{24}N_2ONa$ ([M + Na]$^+$), 319.1786; found, 319.1779.

N,N′-Bis(3-phenylpropyl)urea ***(2e)***.[13] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28−7.14 (m, 10H), 4.92 (br, 2H), 3.18−3.13 (m, 4H), 2.62 (t, *J* = 7.6 Hz, 4H), 1.79 (quint., *J* = 7.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 141.7, 128.5, 128.4, 126.0, 40.2, 33.3, 31.9; HRMS (ESI) *m/z* calcd for $C_{19}H_{24}N_2ONa$ ([M + Na]$^+$), 319.1786; found, 319.1786.

N,N′-Bis(phenylmethyl)urea ***(2f)***.[5,12] ^{1}H NMR (400 MHz, CD_3OD): δ 7.32−7.20 (m, 10H), 4.34 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 138.9, 128.7, 127.48, 127.47, 44.7; HRMS (ESI) *m/z* calcd for $C_{15}H_{16}N_2ONa$ ([M + Na]$^+$), 263.1160; found, 263.1161.

N,N′-Bis[(1R)-1-phenylethyl]urea ***(2g)***.[5,7b] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28−7.11 (m, 10H), 4.78−4.73 (m, 2H), 4.55 (br, 2H), 1.39 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8, 144.1, 128.8, 127.3, 125.8, 50.4, 23.5; HRMS (ESI) *m/z* calcd for $C_{17}H_{20}N_2ONa$ ([M + Na]$^+$), 291.1473; found, 291.1487.

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N,N′-Diphenylurea (**2h**).[14] ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.64 (br, 2H), 7.42−7.39 (m, 2H), 7.26−7.21(m, 2H), 6.95−6.90 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 153.1, 140.2, 129.3, 122.3, 118.7; HRMS (EI) m/z calcd for $C_{13}H_{12}N_2ONa$ ([M + Na]$^+$), 235.0847; found, 235.0831.

N,N′-Bis(4-isopropylphenyl)urea (**2i**).[15] ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.73 (br, 2H), 7.32 (d, J = 8.5 Hz, 4H), 7.10 (d, J = 8.5 Hz, 4H), 2.78 (sept., J = 7.1 Hz, 2H), 1.14 (d, J = 7.1 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.7, 145.5, 135.5, 127.4, 122.0, 33.7, 24.1; HRMS (ESI) m/z calcd for $C_{19}H_{24}N_2ONa$ ([M + Na]$^+$), 319.1786; found, 319.1782.

N,N′-Bis(4-trifluoromethylphenyl)urea (**2j**).[5] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 8.5 Hz, 4H), 7.53 (d, J = 8.5 Hz, 4H), 6.66 (br, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.1, 143.1, 126.2 (q, $^3J_{F-C}$ = 3.8 Hz), 124.6 (q, $^1J_{F-C}$ = 271.3 Hz), 122.1 (q, $^2J_{F-C}$ = 32.0 Hz); ^{19}F NMR (377 Hz, DMSO-d_6): δ −63.0; HRMS (EI) m/z calcd for $C_{15}H_9F_6N_2O$ ([M]$^-$), 347.0619; found, 347.0623.

N,N′-Dihexylurea (**2k**).[12] ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.50 (br, 2H), 3.16−3.11 (m, 4H), 1.51−1.43 (m, 4H), 1.34−1.25 (m, 12H), 0.87 (t, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 40.7, 31.7, 30.3, 26.7, 22.7, 14.1; HRMS (ESI) m/z calcd for $C_{13}H_{28}N_2ONa$ ([M + Na]$^+$), 251.2099; found, 251.2093.

N,N′-Didecylurea (**2l**).[16] ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.20 (br, 2H), 3.16−3.12 (m, 4H), 1.52−1.45 (m, 4H), 1.29−1.25 (m, 28H), 0.88 (t, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 40.9, 32.0, 30.3, 29.72, 29.70, 29.48, 29.46, 27.0, 22.8, 14.3; HRMS (ESI) m/z calcd for $C_{21}H_{44}N_2ONa$ ([M + Na]$^+$), 363.3351; found, 363.3340.

N,N′-Dicyclohexylurea (**2m**).[12] ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.07 (br, 2H), 3.50−3.43 (m, 2H), 1.95−1.90 (m, 4H), 1.71−1.49 (m, 6H), 1.39−1.29 (m, 4H), 1.19−1.07 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 49.6, 33.8, 25.6, 25.0; HRMS (ESI) m/z calcd for $C_{13}H_{24}N_2ONa$ ([M + Na]$^+$), 247.1786; found, 247.1784.

N,N′-Bis(3-ethoxypropyl)urea (**2n**).[5] ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.86 (br, 2H), 3.52−3.44 (m, 8H), 3.27 (t, J = 6.3 Hz, 4H), 1.79−1.73 (m, 4H), 1.20 (t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 69.2, 66.5, 39.1, 30.0, 15.4; HRMS (ESI) m/z calcd for $C_{11}H_{24}N_2O_3Na$ ([M + Na]$^+$), 255.1685; found, 255.1691.

N-(2-Phenylethyl)-4-morpholinecarboxamide (**4aa**).[17] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.19 (m, 5H), 4.44 (br, 1H), 3.67−3.65 (m, 4H), 3.53−3.49 (m, 2H), 3.29−3.26 (m, 4H), 2.83 (t, J = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8, 139.4, 128.9, 128.7, 126.6, 66.6, 44.0, 42.1, 36.4; HRMS (ESI) m/z calcd for $C_{13}H_{18}N_2O_2Na$ ([M + Na]$^+$), 257.1266; found, 257.1272.

N-(2-Phenylethyl)-1-piperidinecarboxamide (**4ab**).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.18 (m, 5H), 4.47 (br, 1H), 3.50−3.45 (m, 2H), 3.27−3.24 (m, 4H), 2.82 (t, J = 7.0 Hz, 2H), 1.60−1.48 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 139.7, 129.0, 128.6, 126.4, 44.9, 42.2, 36.5, 25.7, 24.5; HRMS (ESI) m/z calcd for $C_{14}H_{20}N_2ONa$ ([M + Na]$^+$), 255.1473; found, 255.1478.

N,N-Dibutyl-N′-(2-phenylethyl)urea (**4ac**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.19 (m, 5H), 4.23 (br, 1H), 3.51−3.47 (m, 2H), 3.10−3.07 (m, 4H), 2.83 (t, J = 6.8 Hz, 2H), 1.45−1.37 (m, 4H), 1.23 (sext., J = 7.3 Hz, 4H), 0.88 (t, J = 7.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 139.7, 129.0, 128.7, 126.5, 47.2, 42.0, 36.4, 30.8, 20.3, 14.0; HRMS (ESI) m/z calcd for $C_{17}H_{28}N_2ONa$ ([M + Na]$^+$), 299.2099; found, 299.2105.

Procedure for Gram-Scale NH_4VO_3-Catalyzed Urea Synthesis of 2a. In a 10 mL two-necked flask, 2-phenylethyl-*N*,*N*-bis(trimethylsilyl)amine (**1a**) (1.2 mL, 4.0 mmol), NH_4VO_3 (70.2 mg, 0.60 mmol), and DMA (6.0 mL) were placed in a glovebox filled with nitrogen. Next, nitrogen in the flask was replaced with CO_2. The mixture was stirred at 120 °C for 48 h, followed by treatment with 1 M HCl aq. and extraction with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtrated, and removed under reduced pressure. The residue was isolated by reprecipitation from CH_2Cl_2 and hexane to give 385 mg (72% yield) of *N*,*N*′-bis(2-phenylethyl)urea (**2a**).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c07367.

^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and ^{29}Si NMR spectral data and HPLC charts (PDF)

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Notes

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