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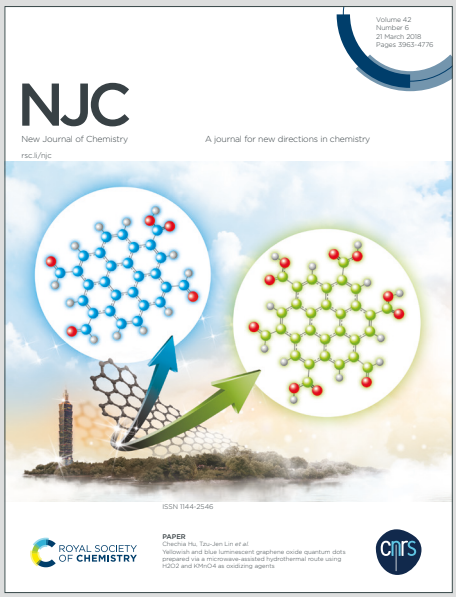

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CaI_2-Catalyzed Direct Transformation of *N*-Alloc-, *N*-Troc-, and *N*-Cbz-Protected Amines to Asymmetrical Ureas

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Abstract

A novel and facile CaI_2-catalyzed direct synthesis of asymmetrical ureas from *N*-Alloc-, *N*-Troc-, and *N*-Cbz-protected amines is developed. In this study, efficient reaction of Alloc-, Troc-, and Cbz-carbamate with amines in the presence of catalytic CaI_2 successfully generated various asymmetrical ureas. This catalytic synthetic procedure provided the desired ureas via reactions of these protected aromatic and aliphatic amines with various amines in high yields without side products. This suggests that novel direct synthesis of ureas from Alloc-, Troc-, and Cbz-carbamates can provide a promising approach for the synthesis of useful ureas.

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Introduction

Urea is an important structure in bioactive natural products, and pharmaceuticals. For examples, many biologically active compounds including antitumor agents, antagonists of natural receptors, allosteric modulators, enzyme inhibitors, anti-Parkinson's agents, and anti-mycobacterial agents, contain urea unit in their chemical structures.[1-9] Various materials have used urea units a large number of organic materials exhibit the urea motif due to its unique properties, including hydrogen bonding and polarity of the urea structure.[10,11] Several types of prepared molecular gels and self-assembled structures, including macrocycles, contain some kind of urea structure.[12-16]

Due to their importance in various fields, several synthetic procedures have been reported for the formation of urea structures.[17,18] Treatment of amines with isocyanate (which are produced from the reaction of phosgene) or carbamoyl chlorides are widely employed protocols in organic synthesis used to produce target ureas.[19] Although many urea structures have been prepared via these methods, they have their weaknesses. Phosgene, for example, is toxic and carbamoyl chloride intermediates are unstable, which limits their use for organic synthesis. Other approaches have employed 1,1'-carbonyldiimidazole (CDI) and *p*-nitrophenyl carbamates to synthesize ureas.[20-23] However, the desired ureas were sometimes prepared with low conversion yield during the treatment of those reagents. In additions, urea derivatives have been prepared from the reaction of amines with CO_2 without utilization of phosgene.[24-27]

Amine is a widely used functional group in organic chemistry. In many multi-step synthetic procedures, amines have been protected by a carbamate protecting group to undergo organic reactions without the production of unwanted side products. In particular, allyl-carbamate (Alloc-carbamate), 2,2,2-Trichloroethyl carbamate (Troc-carbamate), and benzyl-carbamate (Cbz-carbamate) are commonly used as amine protecting groups in many total synthesis works

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and medicinal chemistry[28-34] because easy and simple synthetic methods for the preparation of Alloc-carbamate, Troc-carbamate, and Cbz-carbamate have been developed from primary or secondary amines. However, these protected amines require two separate reactions for urea synthesis: deprotection of amines and the formation of urea via treatment of nucleophilic free amines. Thus, discovery of a new direct conversion of these protected amines to ureas is desirable for efficient multi-step synthesis. Particularly, the catalyst-mediated direct synthetic methods for asymmetrical ureas from *N*-Alloc-, *N*-Troc- and *N*-Cbz-protected amines are not extensively studied. In our previous study, we reported that conversion of Alloc- and Cbz-carbamate compounds to ureas was achieved through the treatment of DABAL-Me_3.[35] However, the previous protocol used 1.2 equiv. of DABAL-Me_3. With an interest in developing efficient transformation, we propose novel catalyst-mediated direct synthesis of ureas. To the best of our knowledge, simple and efficient direct preparation of ureas from protected carbamates using an effective catalyst has not yet been reported. Herein, we report the novel catalytic reagent mediated direct synthesis of various ureas from *N*-Alloc-, *N*-Troc-, and *N*-Cbz-protected amines, which can be readily used to perform multi-step organic syntheses.

Results and Discussion

In the initial study, *N*-Alloc-protected aniline and benzylamine were used as a model substrate and a nucleophilic amine to discover optimal conditions in the preparation of asymmetrical ureas. Urea formation reactions were performed in the presence of 1.0 equiv. of *N*-Alloc-protected aniline, 1.5 equiv. of benzylamine, and 0.15 equiv. of various catalytic reagents at 80 ℃ for 12 h, and the conversion yields from Alloc-protected aniline to the corresponding urea were examined.

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Alkali metals and alkaline earth metals have been widely employed in many useful organic syntheses such as the halogenation of imidazo-fused heterocycles, sulfenylation of 4-anilinocoumarins, synthesis of isatins and isoindigoes, and synthesis of 1,2-dihydroquinolines.[36-41] Therefore, in this study, we tried to employ alkali metals and alkaline earth metals for a highly effective catalytic method for the synthesis of ureas. First, a series of commercially available alkali metal salts such as NaI, KI, RbCl, and CsBr were investigated, as shown in Table 1. However, the catalytic reaction between *N*-Alloc-protected aniline and benzylamine provided the desired product with low yield or did not produce the urea product: the synthetic yield of reactions using alkali metal salts to yield the urea is less than 15%. Some alkaline earth metal salts showed better catalytic ability to prepare the urea structure than alkali metal salts. The reaction experiment with $CaBr_2$ and BaI_2 afforded the target urea with increased yield (77% for $CaBr_2$, and 74% for BaI_2). Using CaI_2 for the catalyst-mediated reaction yielded the desired urea in 93% yield under the same conditions (Figures S1). The screening of catalytic reagents therefore suggested CaI_2 as a highly effective catalyst for the direct conversion of *N*-Alloc-protected amine to urea .

Catalyst activity of alkaline earth metal salts on the synthesis of urea can be affected by several factors.[42] The first factor is Lewis acidity of the alkaline earth metal due to the interaction of the metal with oxygen of carbamate. The Lewis acidity increases from Rb^{2+} to $Be^{2+,}$ Therefore, $MgBr_2$ can be better choice. Another factor is the basicity of the catalyst. BaI_2 has the higher basicity than $MgBr_2$. Based on the consideration of two factors, neither Mg salts or Ba salts are not the best choice. Calcium is the alkaline earth metal in the middle of periodic table, and has both the factors. In additions, the basic character of halides follows the order I<Br<Cl<F. In this study, iodide ion, which is known as a weak base, exhibited efficient catalytic properties for the

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urea formation. Iodide ion has larger size, and do not strongly attract electron density from Ca^{2+} like chlorine ion. It means that the negative charge on the iodide ion can be properly dispersed to provide right interaction of Ca^{2+} with amine, not strong interaction with amine. Therefore, our result suggested that CaI_2 is the suitable catalyst to yield the desired urea. Interaction of amine with catalyst can be influenced by counter-anions. Counter-anions can keep and abstract proton from amine. In this reaction, -C(=O)-O- of carbamate can be acting as counter-anions to accelerate the reaction.

Next, the solvent effect was investigated to find the optimized reaction conditions. As shown in Table 2, reactions in 1,4-dioxane and 1,2-dichloroethane (DCE) produced the target urea with low yield. Utilization of tetrahydrofuran (THF) as a reaction solvent allowed us to prepare urea with moderate synthetic yield (75%). When acetonitrile (CH_3CN) and toluene were used for the reaction, desired urea was obtained with highly increased yield (89% for reaction in CH_3CN, and 93% for reaction in toluene), indicating that toluene was a more suitable solvent for CaI_2-catalyzed direct conversion from *N*-Alloc-protected amine to urea than the other solvents. It was interesting note that the reaction using CaI_2 was homogeneous: CaI_2 was completely soluble under reaction conditions, and there was no solid in the reaction mixture. Besides toluene does not contain oxygen and nitrogen which can reduce interaction of Ca^{2+} with carbamate and amine.

Several temperatures for the reaction were also examined. As shown in Table 2, reactions at higher temperature usually resulted in enhanced synthetic yields for the synthesis of target urea (93% for reaction at 80^{o}C and 90^{o}C, and 37% for reaction at 60^{o}C). Thus, a reaction temperature at 80^{o}C was selected for the further study of urea synthesis.

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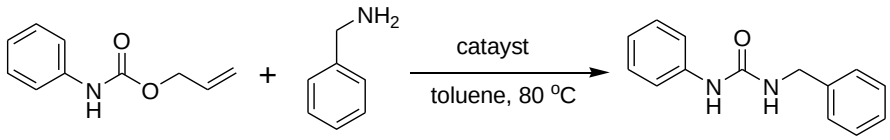
Table 1. Screening of reagents for the preparation of urea structure [a]



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

Entry	Catalyst	time	Temp.	Yield[b] (%)
1	NaI	12 h	80 °C	11
2	KI	12 h	80 °C	5
3	RbCl	12 h	80 °C	NR
4	CsBr	12 h	80 °C	NR
5	$MgBr_2$	12 h	80 °C	9
6	$CaCl_2$	12 h	80 °C	5
7	$CaBr_2$	12 h	80 °C	77
8	CaI_2	12 h	80 °C	93
9	BaI_2	12 h	80 °C	74
10	None	12 h	80 °C	NR

[a] Reaction conditions: 1**a** Alloc-protected amine (1.0 mmol), amine (1.5 mmol), catalyst (0.15 mmol), toluene (2 mL), 12 h.
[b] Isolated yield after column purification.
[c] No reaction

In addition, different amounts of CaI_2 (0.05 equiv., 0.1 equiv., 0.15 equiv., 0.3 equiv., and 1.0 equiv.) were added into the catalyzed reaction and evaluated. The results suggested that the synthetic yield was influenced by the amount of CaI_2. Enhanced amounts of CaI_2 in the reaction resulted in increased conversion yield to give the corresponding urea: The reaction with 0.3 equiv. of CaI_2 for 8 h produced the corresponding urea with 94% yield, and the reaction with 1.0 equiv. of CaI_2 for 6 h afforded the desired urea with 94% yield (Figures S2). A reduced amount of CaI_2 was also tested for the catalyzed reaction, and 0.05 equiv. of CaI_2 were found to yield the target urea product with 61% yield. Besides, different molar ratio (1:1.2 and 1:1) between *N*-

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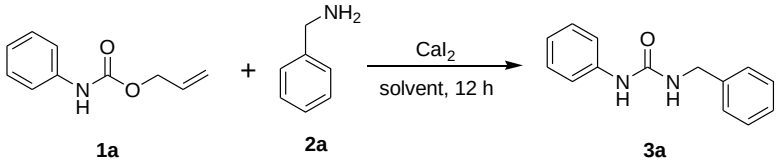
Alloc-protected aniline and benzylamine for CaI_2-catalyzed urea formation reaction were tested. The 1:1.2 ratio reaction and the 1:1 ratio reaction produced the corresponding urea with reduced yield (87% for 1:1.2 ratio reaction, and 80% for 1:1 ratio reaction, respectively). From these primary optimization studies, reaction conditions including 15 mol% CaI_2, toluene solvent, and 80 ^oC were selected for the next studies.

Table 2. Screening of reaction conditions for the preparation of urea structure [a]



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

Entry	CaI_2 (equiv)	Solvent	Temp.	Yield[b] (%)
1	0.15	1,4-dioxane	80 ^oC	3
2	0.15	DCE	80 ^oC	10
3	0.15	THF	reflux	75
4	0.15	CH_3CN	80 ^oC	89
5	0.15	toluene	80 ^oC	93
6	0.15	toluene	90 ^oC	93
7	0.15	toluene	60 ^oC	37
8	0.15	toluene	40 ^oC	14
9[c]	1	toluene	80 ^oC	94
10[d]	0.3	toluene	80 ^oC	94
11	0.1	toluene	80 ^oC	87
12	0.05	toluene	80 ^oC	61

[a] Reaction conditions: 1**a** Alloc-protected amine (1.0 mmol), amine (1.5 mmol), CaI_2 (0.15 mmol), solvent (2 mL), 12 h.
[b] Isolated yield after column purification.
[c] Reaction for 6 h.
[d] Reaction for 8 h.

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Considering the optimized reaction conditions, the scope of the CaI_2-catalyzed direct synthesis of ureas was investigated (Table 3). First, *N*-Alloc-protected aniline, which comes from an aromatic compound, was tested to prepare asymmetrical ureas. *N*-Alloc-protected aniline successfully reacted with benzylamine and butylamine, primary amines, to produce the corresponding asymmetrical ureas (**3a-3b**) in high yield. In the same conditions, reactions of *N*-Alloc-protected anilines with secondary amines such as piperidine **2c**, dipropylamine **2d** and pyrrolidine **2e** readily afforded the desired trisubstituted ureas (**3c-3e**) with 92%, 94% and 90% yield, respectively (Table 3, entries 3-5).

Syntheses of ureas from N-Alloc-protected 4-methylaniline containing the electron-donating group and 4-chloroaniline containing the electron-withdrawing group were also examined. The directional synthesis of ureas proceeded well. The reaction of *N*-Alloc-protected 4-methylaniline with benzylamine, cyclohexylamine and piperidine provided the target ureas in high yield (Table 3, entries 6-8), and the reaction of *N*-Alloc-protected 4-chloroaniline with benzylamine, cyclohexylamine and piperidine yielded the corresponding urea in 80%-85% yield (Table 3, entries 9-11).

N-Alloc-protected benzyl amine, which comes from an aliphatic amine, was used to produce an asymmetric urea to assess this reaction procedure, and the desired asymmetrical benzylureas were successfully obtained in the range of 62%-85% yield via the CaI_2-catalyzed reaction with benzylamine, butylamine, aniline, piperidine and dipropylamine (Table 3, entries 12-16). The reactions of *N*-Alloc-protected *N*-methylaniline with benzylamine and piperidine were also carried out, which produced the corresponding ureas (**3q-3r**).

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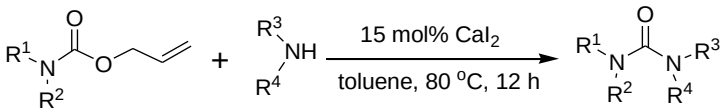
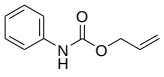
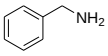
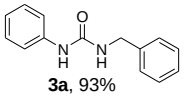
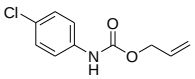
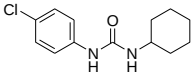
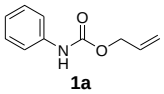
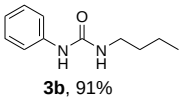
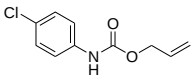
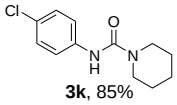
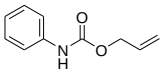
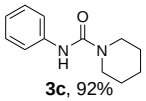
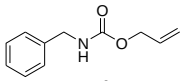
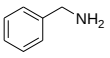
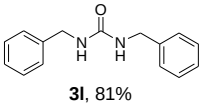
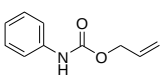
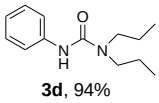
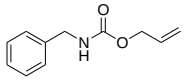
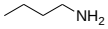
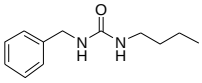
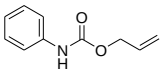
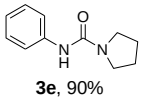
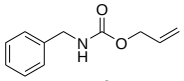
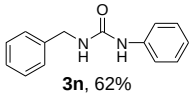
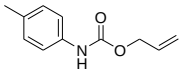
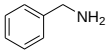
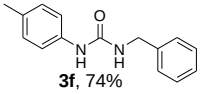
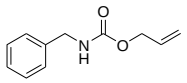
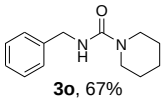
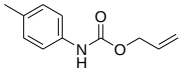
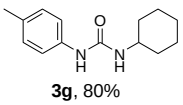
Table 3. Scope of urea formation from *N*-Alloc-protected amines [a]



1 2 3

Entry	Alloc-carbamate	Amine	Product[b]	Entry	Alloc-carbamate	Amine	Product[b]
1	 **1a**	 **2a**	 **3a**, 93%	10	 **1c**	 **2f**	 **3j**, 84%
2	 **1a**	**2b**	 **3b**, 91%	11	 **1c**	 **2c**	 **3k**, 85%
3	 **1a**	 **2c**	 **3c**, 92%	12	 **1d**	 **2a**	 **3l**, 81%
4	 **1a**	 **2d**	 **3d**, 94%	13	 **1d**	 **2b**	 **3m**, 85%
5	 **1a**	 **2e**	 **3e**, 90%	14	 **1d**	 **2g**	 **3n**, 62%
6	 **1b**	 **2a**	 **3f**, 74%	15[c]	 **1d**	 **2c**	 **3o**, 67%
7	 **1b**	 **2f**	 **3g**, 80%	16	**1d**	**2d**	**3p**, 75%
8	**1b**	**2c**	**3h**, 81%	17	**1e**	**2a**	**3q**, 80%
9	**1b**	**2a**	**3i**, 80%	18[c]	**1e**	**2c**	**3r**, 52%

[a] Reaction conditions: Alloc-carbamate (1.0 mmol), amine (1.5 mmol), CaI_2 (0.15 mmol), toluene (2 mL), 80 °C for 12 h,
[b] Isolated yields after column purification.
[c] Reaction at 110 °C for 24 h.

Troc protection groups have been commonly used to protect amines in various organic syntheses.

CaI_2-catalyzed urea formation was also applied for the direct transformation of *N*-Troc-protected

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amines to asymmetrical ureas. The reaction of *N*-Troc-protected aniline with primary amines and secondary amines in the presence of catalytic CaI_2 led to the successful production of corresponding ureas in high yields (Table 4, entries 1-3). In addition, *N*-Troc-protected amines from benzylamine and piperidine readily reacted with several amines to yield the desired ureas (Table 4, entries 4-9).

Next, the scope of CaI_2-catalyzed reaction was extended to the synthesis of ureas from *N*-Cbz-protected amines because many multi-step syntheses have employed *N*-Cbz-protected amines. The CaI_2-catalyzed reaction of *N*-Cbz-protected aniline or *N*-Cbz-protected benzylamine proceeds effectively with primary and secondary amines. CaI_2-catalyzed reactions with benzylamine, butylamine, piperidine, pyrrolidine, and morpholine yielded the corresponding ureas in the range of 62–91% (Table 4, entries 10-18). These results confirmed that catalytic CaI_2-mediated reactions of protected amines with several free amines as an efficient synthesis technique of ureas with high conversion yields.

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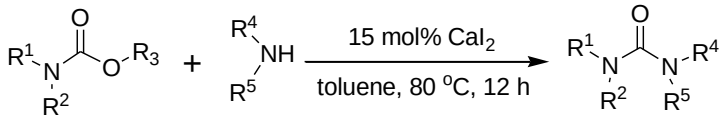
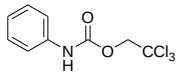
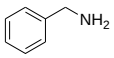
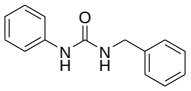
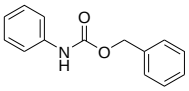
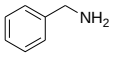
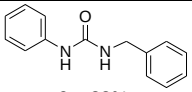
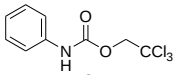
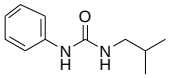
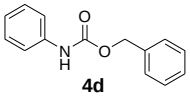
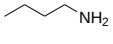
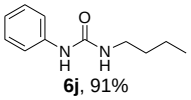
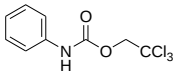
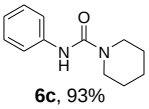
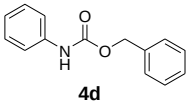
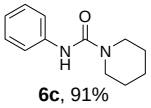
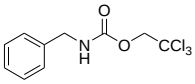
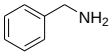
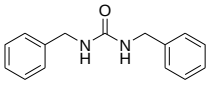
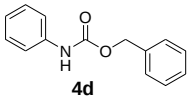
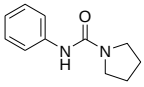
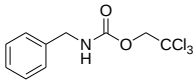
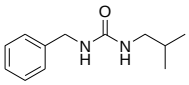
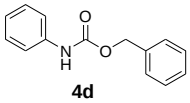
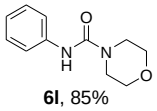
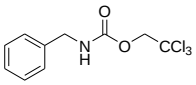
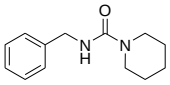
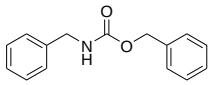
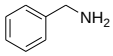
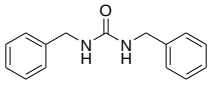
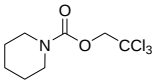
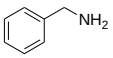
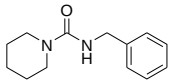
Table 4. Scope of urea formation from *N*-Troc-/ *N*-Cbz-protected amines [a]



4 5 6

Entry	Troc-carbamate	Amine	Product[b]	Entry	Cbz-carbamate	Amine	Product[b]
1	 **4a**	 **5a**	 **6a**, 96%	10	 **4d**	 **5a**	 **6a**, 82%
2	 **4a**	 **5b**	 **6b**, 96%	11	 **4d**	 **5d**	 **6j**, 91%
3	 **4a**	 **5c**	 **6c**, 93%	12	 **4d**	 **5c**	 **6c**, 91%
4	 **4b**	 **5a**	 **6d**, 95%	13	 **4d**	 **5e**	 **6k**, 90%
5	 **4b**	 **5b**	 **6e**, 94%	14	 **4d**	 **5f**	 **6l**, 85%
6	 **4b**	 **5c**	 **6f**, 91%	15	 **4e**	 **5a**	 **6d**, 72%
7[c]	 **4c**	 **5a**	 **6g**, 65%	16	**4e**	**5d**	**6m**, 81%
8	**4c**	**5d**	**6h**, 72%	17	**4e**	**5c**	**6f**, 62%
9[c]	**4c**	**5c**	**6i**, 53%	18	**4e**	**5e**	**6n**, 71%

[a] Reaction conditions: Troc-/Cbz-carbamate (1.0 mmol), amine (1.5 mmol), CaI_2 (0.15 mmol), toluene (2 mL), 80 °C for 12 h
[b] Isolated yields after column purification.
[c] Reaction at 110 °C for 24 h.

Next, a scaled-up CaI_2-catalyzed conversion of *N*-Alloc-protected amines to ureas was performed (Scheme 1). The gram-scale reaction using 0.15 equiv. of CaI_2 successfully gave the

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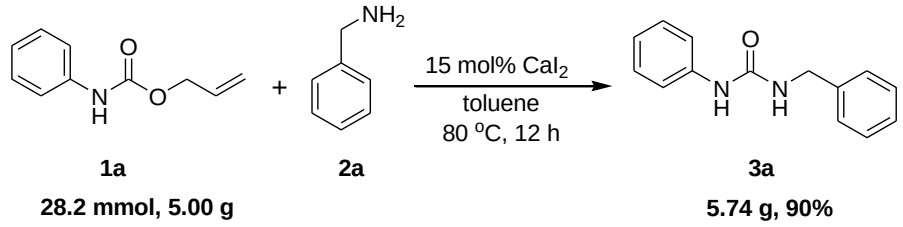
target product. The reaction of *N*-Alloc-protected aniline **1a** (5.00 g, 28.2 mmol) with benzylamine **2a** in toluene (100 mL) within 250 mL round-bottom flask afforded the corresponding product **3a** in 90% yield under the optimized reaction conditions. It showed that the CaI_2-catalyzed reaction procedure was scalable and practical.



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

28.2 mmol, 5.00 g **5.74 g, 90%**

Scheme 1. The gram-scale reaction of *N*-Alloc-protected aniline with benzylamine

A proposed reaction mechanism for CaI_2-catalyzed direct synthesis of ureas is shown in Scheme 2. Carbamate is coordinated with CaI_2 to generate a stable CaI_2-carbamate complex intermediate. Then nucleophilic attacking by amine affords urea unit and releases alcohol. After urea product was produced, CaI_2 was regenerated and given back to the synthetic reaction of urea.

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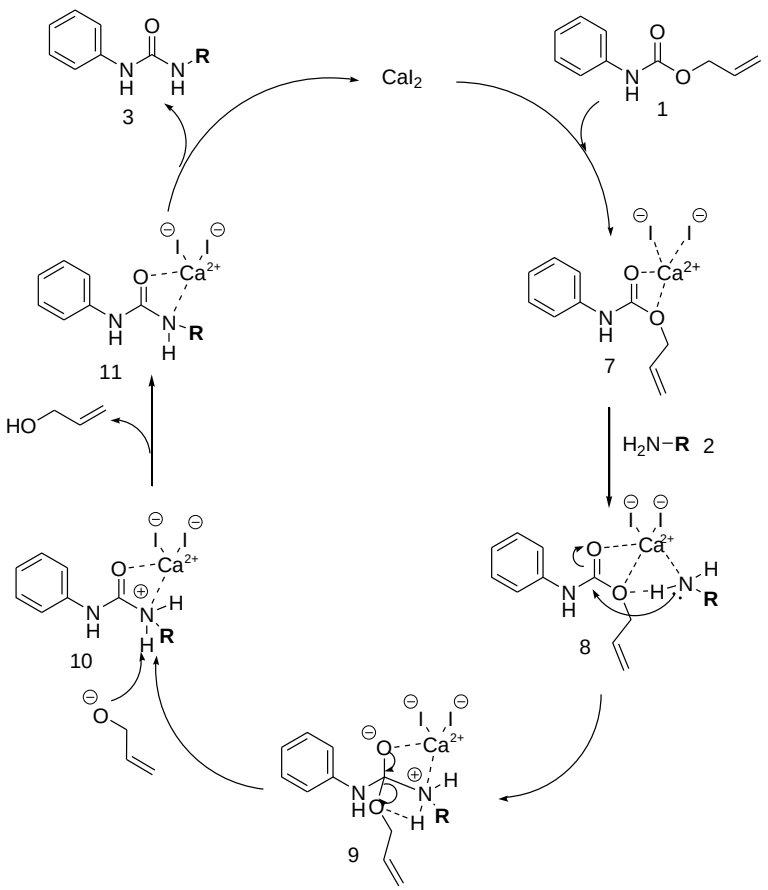

Scheme 2. Proposed etherification mechanism for the preparation of ureas using CaI_2.

Conclusions

Novel and practical CaI_2-catalyzed direct preparation of asymmetrical ureas from *N*-Alloc-, *N*-Troc-, and *N*-Cbz-protected amines has been described. Several reagents such as alkali metals and alkaline earth metals were examined to discover an efficient catalyst to yield ureas, and CaI_2 was demonstrated as an effective catalyst for the direct reaction of *N*-Alloc-, *N*-Troc-, and *N*-Cbz-protected amines to produce target asymmetrical ureas in high yields. Our results show that the novel CaI_2-catalyzed direct conversion of *N*-Alloc-, *N*-Troc- and *N*-Cbz-protected amines into asymmetrical ureas is efficient and applicable for the preparation of many useful ureas.

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Experimental

General information

All chemicals were purchased from Sigma-Aldrich and used without further purification. Reaction progress was monitored by thin-layer chromatography (TLC) analysis. TLC analysis was performed using an aluminum plate with silica gel 60 F_{254}, and TLC spots were visualized by UV light (254nm) exposure. Flash chromatography was performed using 230–400 mesh silica gel and analytical grade solvent. Melting points were recorded using a Stuart SMP10 Melting Point Apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a 600 MHz & 150 MHz respectively JEOL JNM-ECA600 spectrometer or a 400 MHz & 100 MHz respectively Bruker Avance 400 spectrometer. The chemical shifts were reported in δ units (ppm) relative to the residual protonated solvent resonance, and the coupling constants (*J*) quoted in Hz.

General procedure for the preparation of allyl phenylcarbamate compounds (1a-1f)

To a solution of aniline (2.0 g, 21.47 mmol) and $NaHCO_3$ (2.16 g, 25.76 mmol) in tetrahydrofuran, ally chloroformate (3.104 g, 25.76 mmol) was added. The reaction mixture was stirred for 2 h at room temperature. The reaction mixture was quenched by the addition of H_2O (5 mL) and extracted with EtOAc (3 x 20 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The resulting residue was then purified by flash column chromatography on silica gel with hexane-EtOAc 20/1 as eluent to afford the desired product 1a (3.6 g, 95%).

Allyl phenylcarbamate (1a). Yield 95%; white solid. m.p 65-66°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 – 5.89 (m, 1H), 5.32 -5.26 (dq, J = 17.2 Hz, J = 1.6 Hz, 1H), 5.21 -5.17 (dq, J = 10.4 Hz, J = 1.2 Hz, 1H), 4.59 – 4.57 (dt, J = 5.6 Hz, J = 1.2 Hz, 2H), 3.43 (t, J = 5.6 Hz, 4H), 1.62 – 1.52

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(m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.14, 133.31, 116.98, 65.75, 44.78 (2C), 25.66, 24.36 (2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{10}H_{12}NO_2$ = 178.0868; found 178.0863.

Allyl *p*-tolylcarbamate (1b). Yield 96%; m.p 48-50°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 – 7.28 (m, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.81 (s, 1H), 6.03 – 5.95 (m, 1H), 5.14 -5.35 (dq, *J* = 17.2 Hz, *J* = 1.6 Hz, 1H), 5.29 -5.26 (dq, *J* = 10.4 Hz, *J* = 1.2 Hz, 1H), 4.69 (d, *J* = 5.6 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.45, 135.24, 133.05, 132.56, 129.53 (2C), 118.87, 118.13 (2C), 65.78, 20.77; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{11}H_{14}NO_2$ = 192.1025; found 192.1022.

Allyl 4-chlorophenylcarbamate (1c). Yield 96%; white solid. m.p 68-70°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.35 (m, 2H), 7.29 – 7.26 (m, 2H), 6.73 (s, 1H), 6.03 – 5.93 (m, 1H), 5.15 -5.36 (dq, *J* = 17.2 Hz, *J* = 1.6 Hz, 1H), 5.31 -5.28 (dq, *J* = 10.4 Hz, *J* = 1.2 Hz, 1H), 4.69 (d, *J* = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.08, 136.39, 132.23, 129.06 (2C), 128.52, 119.89, 118.46 (2C), 66.04; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{10}H_{11}ClNO_2$ = 212.0478; found 212.0473.

Allyl benzylcarbamate (1d). Yield 95%; colorless; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 6.00 – 5.91 (m, 1H), 5.35 (d, *J* = 17.2 Hz, 1H), 5.25 -5.22 (dd, *J* = 10.8 Hz, *J* = 1.2 Hz, 1H), 5.15 (s, 1H), 4.62 (d, *J* = 5.6 Hz, 2H), 4.41 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.31, 138.47, 132.87, 128.66 (2C), 127.49 (2C), 117.71, 65.69, 45.10; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{11}H_{14}NO_2$ = 192.1025; found 192.1020.

Allyl methyl(phenyl)carbamate (1e). Yield 94%; white solid. m.p 42-44°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.22 (m, 5H), 5.96 - 5.89 (m, 1H), 5.31 - 5.18 (m, 2H), 4.64 (d, *J* = 5.2 Hz, 2H), 3.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.36, 143.22, 132.77, 128.86 (2C), 126.13,

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125.79, 117.25 (2C), 66.24, 37.77; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{11}H_{14}NO_2$ = 192.1025; found 192.1020.

General procedure for the preparation of urea compounds (3a-3t)

To a solution of **1a** (0.177 g, 1.00 mmol) in toluene (2 mL), benzylamine (0.160 g, 1.5 mmol) and CaI_2 (0.044 g, 0.15 mmol) was added. The mixture was stirred for 12 h at 80 ℃. The reaction mixture was extracted with CH_2Cl_2 (2 x 20 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The resulting residue was then purified by flash column chromatography on silica gel with hexane-EtOAc as eluent to afford the desired product **3a** (0.21 g, 93%).

1-Benzyl-3-phenylurea (3a). Yield 93%; white solid; m.p. 210 - 212°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.56 (s,1H), 7.42 – 7.22 (m, 9H), 6.89 (t, J = 7.2 Hz, 1H), 6.61 (t, J = 5.6 Hz, 1H), 4.31 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.67, 140.91, 140.81, 129.11 (2C), 128.76 (2C), 127.56 (2C), 127.17, 121.53, 118.12 (2C), 43.18; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{14}H_{15}N_2O$ = 227.1184; found 227.1179.

1-Butyl-3-phenylurea (3b). Yield 91%; white solid; m.p. 129 - 130°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.35 (s,1H), 7.39 – 7.36 (m, 2H), 7.22 – 7.18 (m, 2H), 6.89 (t, J = 7.2 Hz, 1H), 6.08 (t, J = 5.2 Hz, 1H), 3.08 (q, J = 6.0 Hz, 2H), 1.45 – 1.38 (m, 2H), 1.34 – 1.24 (m, 2H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.64, 141.06, 129.05 (2C), 112.31, 111.7 (2C), 39.13, 32.35, 19.99, 14.16; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{11}H_{17}N_2O$ = 193.1341; found 193.1336.

***N*-Phenylpiperidine-1-carboxamide (3c).** Yield 92%; white solid; m.p. 131 - 132°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.41 (s, 1H), 7.46 (d, J = 7.6 Hz, 2H), 7.21 (t, J = 8.4 Hz, 2H), 6.91 (t, J

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= 7.2 Hz, 1H), 3.41 (t, *J* = 5.6 Hz, 4H), 1.61 -1.55 (m, 2H), 1.51 – 1.46 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.33, 141.23, 128.66 (2C), 121.91, 120.00 (2C), 45.13 (2C), 25.98 (2C), 24.58; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{12}H_{17}N_2O$ = 205.1341; found 205.1356.

3-Phenyl-1,1-dipropylurea (3d). Yield 94%; white solid; m.p. 68 - 70°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 - 7.36 (m, 2H), 7.30 - 7.25 (m, 2H), 7.03 – 6.99 (m, 1H), 6.32 (s, 1H), 3.27 (t, *J* = 7.6 Hz, 4H), 1.71- 1.61 (m, 4H), 0.96 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.98, 139.29, 128.81 (2C), 122.74, 119.75 (2C), 49.46 (2C), 21.88(2C), 11.44 (2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{13}H_{21}N_2O$ = 211.1654; found 211.1677.

***N*-Phenylpyrrolidine-1-carboxamide (3e)**. Yield 90%; white solid; m.p. 132 - 134°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.40 (m, 2H), 7.30 – 7.25 (m, 2H), 7.04 – 6.99 (m, 1H), 6.23 (s, 1H), 3.48 -3.45 (m, 4H), 2.01 – 1.93 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.91, 139.16, 128.85 (2C), 122.75, 119.47 (2C), 45.86 (2C), 25.62 (2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{11}H_{15}N_2O$ = 191.1184; found 191.1196.

1-Benzyl-3-*p*-tolylurea (3f). Yield 74%; white solid; m.p. 182 - 184°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.43 (s, 1H), 7.34 – 7.24 (m, 7H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.55 (t, *J* = 6.0 Hz, 1H), 4.29 (d, *J* = 6.0 Hz, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.73, 140.87, 138.35, 130.23, 129.52 (2C) 128.80 (2C), 127.56 (2C), 127.14, 118.30 (2C), 43.19, 20.76; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{15}H_{17}N_2O$ = 241.1341; found 241.1337.

1-Cyclohexyl-3-*p*-tolylurea (3g). Yield 80%; white solid; m.p. 199 - 201°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.16 (d, *J* = 5.2 Hz, 1H), 7.25 – 7.22 (m, 2H), 7.02 – 7.98 (m, 2H), 6.02 (d, *J* = 7.2 Hz, 1H), 3.48 – 3.43 (m, 1H), 2.21 (s, 3H), 1.81 – 1.76 (m, 2H), 1.67 -1.65 (m, 2H), 1.53-1.52 (m, 1H), 1.35 – 1.26 (m, 2H), 1.22 – 1.09 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ

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154.92, 138.46, 129.97, 129.96 (2C), 117.99 (2C), 47.98, 33.48 (2C), 24.83 (2C), 20.75; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{14}H_{21}N_2O$ = 233.1654; found 233.1660.

***N*-*p*-Tolylpiperidine-1-carboxamide (3h).** Yield 81%; white solid. m.p. 155 – 157°C; ^{1}H NMR (400 MHz, DMSO-d6) δ 8.30 (s, 1H), 7.34 (d, J = 9.2 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 3.39 (t, J = 4.8 Hz, 4H), 2.22 (s, 3H), 1.57- 1.54 (m, 2H), 1.49 – 1.45 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d6) δ 155.43, 138.62, 130.66 (), 128.58 (2C), 120.19 (2C), 45.09 (2C), 25.98 (2C), 24.60, 20.79; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{13}H_{19}N_2O$ = 219.1497; found 219.1495.

1-Benzyl-3-(4-chlorophenyl)urea (3i). Yield 80%%; white solid. m.p 206 – 208°C; ^{1}H NMR (400 MHz, DMSO-d6) δ 8.72 (s, 1H), 7.45 – 7.42 (dt, J = 8.8 Hz, J = 1.6 Hz, 2H), 7.36 – 7.23 (m, 7H), 6.67 (t, J = 6.0 Hz, 1H), 4.31 (t, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d6) δ 155.52, 140.67, 139.94, 128.91 (2C), 128.76 (2C), 127.57 (2C), 127.19, 124.98, 119.63 (2C), 43.21; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{14}H_{14}ClN_2O$ = 261.0795; found 261.0798.

1-(4-Chlorophenyl)-3-cyclohexylurea (3j). Yield 84%; white solid; m.p. 239 - 240°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.43 (s, 1H), 7.40 – 7.37 (m, 2H), 7.26 – 7.22 (m, 2H), 6.11 (d, J = 8.0 Hz, 1H), 3.49 – 3.42 (m, 1H), 1.81 – 1.78 (m, 2H), 1.68 -1.63 (m, 2H), 1.56-1.52 (m, 1H), 1.35 – 1.25 (m, 2H), 1.19 – 1.11 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 154.66, 140.01, 128.96 (2C), 124.73, 119.45 (2C), 48.07, 33.37 (2C), 25.68, 24.80 (2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{13}H_{18}ClN_2O$ = 253.1108; found 253.1104.

***N*-(4-Chlorophenyl)piperidine-1-carboxamide (3k)**. Yield 85%; white solid; m.p. 143 - 145°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.30 (m, 2H), 7.23 – 7.21 (m, 2H), 6.54 (s, 1H), 3.44 (t, J = 4.4 Hz, 4H), 1.68 -1.61 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.70, 137.95, 128.74 (2C),

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127.72, 121.07 (2C), 45.27 (2C), 25.67 (2C), 24.32; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{12}H_{16}ClN_2O$ = 239.0951; found 239.0956.

1,3-Dibenzylurea (3l). Yield 81%; white solid; m.p. 167 – 169°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.20 (m,10H), 4.27 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.34, 139.16 (2C), 128.56 (4C), 127.34 (4C), 127.22 (2C), 44.42 (2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{15}H_{17}N_2O$ = 241.1341; found 241.1338.

1-Benzyl-3-butylurea (3m). Yield 85%; white solid; m.p. 99 - 101°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 5H), 4.33 (s, 2H), 3,13 (t, J = 7.2 Hz, 2H), 1.46 – 1.42 (m, 2H), 1.34 – 1.30 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.44, 139.32, 128.58 (2C), 127.38 (2C), 127.23, 44.46, 40.29, 32.26, 20.00, 13.78; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{12}H_{19}N_2O$ = 207.1497; found 207.1492.

***N*-Benzylpiperidine-1-carboxamide (3o)**. Yield 70%; white solid; m.p. 103 - 105°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H), 4.74 (s, 1H), 4.46 (d, J = 5.2 Hz, 2H), 3.36 (t, J = 4.8 Hz, 4H), 1.66 – 1.5 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.51, 139.64, 128.60 (2C), 127.80 (2C), 127.24, 45.06 (2C), 25.62 (2C), 24.41, 43.35, 29.11, 20.49(2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{13}H_{19}N_2O$ = 219.1497; found 219.1520.

3-Benzyl-1,1-dipropylurea (3p). Yield 75%; white solid; m.p. 42 - 45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.25 (m, 5H), 4.64 (s,1H), 4.46 (d, J = 4.8 Hz, 2H), 3.19 (t, J = 8.0 Hz, 4H), 1.64- 1.55 (m, 4H), 0.91 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.57, 139.93, 128.81 (2C), 127.58 (2C), 127.13, 49.19 (2C), 44.92, 21.80 (2C), 11.38 (2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{14}H_{23}N_2O$ = 235.1810; found 235.1843.

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3-Benzyl-1-methyl-1-phenylurea (3q). Yield 80%; white solid; m.p. 92 - 95°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 2H), 7.32 – 7.23 (m, 8H), 4.68 (s, 1H), 4.42 (t, J = 5.2 Hz, 2H), 3.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.19, 143.29, 139.55, 130.09 (2C), 128.51 (2C), 127.42 (3C), 127.31 (2C), 127.08, 44.74, 37.37; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{15}H_{17}N_2O$ = 241.1341; found 241.1352.

***N*-Methyl-*N*-phenylpiperidine-1-carboxamide (3r).** Yield 52%; colorless liquid; ^{1}H NMR (400 MHz, DMSO-d6) δ 7.36 – 7.31 (m, 2H), 7.10 – 7.06 (m, 3H), 3.09 (t, J = 5.2 Hz, 4H), 3.07 (s, 3H), 1.46- 1.40 (m, 2H), 1.31 – 1.25 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d6) δ 160.58, 147.24, 129.71 (2C), 124.03, 123.02 (2C), 46.46 (2C), 39.28, 25.41 (2C), 24,41; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{13}H_{19}N_2O$ = 219.1497; found 219.1494.

General procedure for the preparation of 2,2,2-trichloroethyl phenylcarbamate compounds (4a-4c)

To a solution of aniline (1.4 g, 15.0 mmol) and pyridine (4,74 g, 60.0 mmol) in dichloromethane, 2,2,2-chloroethyl chloroformate (3.8 g, 18.0 mmol) was added. The reaction mixture was stirred for 10 h at room temperature. The reaction mixture was quenched by the addition of H_2O (20 mL) and extracted with EtOAc (3 x 20 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The resulting residue was then purified by flash column chromatography on silica gel with hexane-EtOAc 20/1 as eluent to afford the desired product **4a** (3.75 g, 94%).

General procedure for the preparation of benzyl phenylcarbamate compound (4d-4e)

To a solution of aniline (2.04 g, 21.9 mmol) and $NaHCO_3$ (2.02 g, 24.0 mmol) in tetrahydrofuran, benzyl chloroformate (3.4 ml, 25.76 mmol) was added. The reaction mixture was stirred for 2 h at room temperature. The reaction mixture was quenched by the addition of

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H_2O (15 mL) and extracted with EtOAc (3 x 20 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The resulting residue was then purified by flash column chromatography on silica gel with hexane-EtOAc 20/1 as eluent to afford the desired product **4d** (4.72 g, 95%).

2,2,2-Trichloroethyl phenylcarbamate (4a). Yield 96%; White solid. m.p 72-74°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.32 (m, 4H), 7.12 (t, J = 7.6 Hz, 1H), 6.86 (s, 1H), 4.83 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.47, 137.00, 129.09 (2C), 124.20, 118.87 (2C), 95.25, 74.52; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_9H_9Cl_3NO_2$ = 267.9699; found 267.9695.

2,2,2-Trichloroethyl benzylcarbamate (4b). Yield 95%; white solid. m.p 66-68°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 5.33 (s, 1H), 4.79 (s, 2H), 4.46 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.62, 137.72, 128.78 (2C), 127.77, 127.57 (2C), 95.56, 74.62, 45.35; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{10}H_{11}Cl_3NO_2$ = 281.9855; found 281.9858.

2,2,2-Trichloroethyl piperidine-1-carboxylate (4c). Yield 94%; white solid. m.p 48-50°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.74 (m, 2H), 3.52 (d, J = 20.4 Hz, 2H), 3.37 – 3.32 (q, J = 7.2 Hz, 2H), 1.66 – 1.57 (m, 3H), 1.21 – 1.15 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.94, 95.87, 74.97, 45.25, 45.17, 42.36, 24.27; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_8H_{13}Cl_3NO_2$ = 260.0012; found 260.0005.

Benzyl phenylcarbamate (4d). Yield 95%; white solid. m.p 77-78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.29 (m, 9H), 7.07 (t, J = 7.6 Hz, 1H), 6.76 (s, 1H), 5.21 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.36, 137.78, 136.06, 129.08 (2C), 128.64 (2C), 128.37 (2C), 128.34 (2C), 123.54, 118.72, 67.04; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{14}H_{14}NO_2$ = 228.1025; found 228.1020.

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Benzyl benzylcarbamate (4e). Yield 96%; white solid. m.p 63-65°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 10H), 5.17 (s, 2H), 5.10 (s, 1H), 4.42 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.39, 138.38 (2C), 136.48 (2C), 128.68 (2C), 128.53 (2C), 128.15 (2C) 127.53 (2C), 66.89, 45.18; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{15}H_{16}NO_2$ = 242.1181; found 242.1177.

General procedure for the preparation of urea compounds (6a-6n)

To a solution of **4a** (0.268 g, 1.00 mmol) in toluene (2 mL), benzylamine (0.160 g, 1.50 mmol) and CaI_2 (0.044 g. 0.15 mmol) was added. The mixture was stirred for 12 h at 80 ℃. The reaction mixture was extracted with CH_2Cl_2 (2 x 20 mL). The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The resulting residue was then purified by flash column chromatography on silica gel with hexane-EtOAc as eluent to afford the desired product **6a** (0.216 g, 96%).

1-Isobutyl-3-phenylurea (6b). Yield 96%; white solid; m.p. 156 - 158°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.37 (s,1H), 7.38 – 7.36 (m, 2H), 7.23 – 7.21 (m, 2H), 6.89 (t, J = 7.6 Hz, 1H), 6.16 (t, J = 5. Hz, 1H), 2.92 (d, J = 0.4 Hz, 2H), 1.70 -1.65 (m,1H), 0.88 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.69, 141.05, 129.07 (2C), 112.07, 117.94 (2C), 46.95, 28.94, 20.47(2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{11}H_{17}N_2O$ = 193.1341; found 193.1346.

1-Benzyl-3-isobutylurea (6e). Yield 94%; white solid; m.p. 143 - 145°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.33 – 7.21 (m, 5H), 6.25 (t, J = 6.0 Hz, 1H), 5.95 (t, J = 6.0 Hz, 1H), 4.21 (d, J = 6.0 Hz, 2H), 2.85 (d, J = 6.4 Hz, 2H), 1.66 – 1.59 (m,1H), 0.84 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.59, 141.49, 128.65 (2C), 127.39 (2C), 126.94, 47.35, 43.35, 29.11, 20.49(2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{12}H_{19}N_2O$ = 207.1497; found 207.1505.

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***N*-Butylpiperidine-1-carboxamide (6h).** Yield 72%; white solid; m.p. 43 - 45°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.81 (s, 1H), 3.29 (d, J = 4.8 Hz, 4H), 3.25- 3.15 (m, 2H), 1.60 -1.42 (m, 8H), 1.38 – 1.23 (m, 2H), 0.91 – 0.88 (t, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.79, 44.90 (2C), 40.66, 32.43, 25.58 (2C), 24.42, 20.12, 13.84; HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{10}H_{21}N_2O$ = 185.1654; found 185.1674.

Dipiperidin-1-ylmethanone (**6i**). Yield 53%; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.18 – 3.13 (m, 8H), 1.59 – 1.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.82, 47.91 (4C), 25.78 (4C), 24.78 (2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{11}H_{21}N_2O$ = 197.1654; found 197.1675.

***N*-Phenylmorpholine-4-carboxamide (6l).** Yield 85%; white solid; m.p. 260 - 262°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 4H), 7.09 – 7.05 (m, 1H), 6.45 (s, 1H), 3.75 (t, J = 5.2 Hz, 4H), 3.49 (t, J = 5.2 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.09, 138.65, 128.95 (2C), 123.39, 120.06 (2C), 66.49 (2C), 44.31 (2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{11}H_{15}N_2O_2$ = 207.1134; found 207.1129.

***N*-Benzylpyrrolidine-1-carboxamide (6n).** Yield 71%; light yellow solid; m.p. 120 - 123°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 5H), 4.55 (s, 1H), 4.46 (s, 2H), 3.41 -3.35 (m, 4H), 1.96 – 1.88 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.68, 139.83, 128.52 (2C), 127.72 (2C), 127.17, 45.61 (2C), 45.54, 25.63 (2C); HRMS (ESI) m/z $(M+H)^+$ calcd for $C_{12}H_{17}N_2O$ = 205,1341; found 205.1336.

Electronic supplementary material

Electronic Supplementary Material (ESI) available: ^{1}H and ^{13}C NMR spectra of all compounds.

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Conflicts of interest

There are no conflicts to declare.

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A practical CaI_2-catalyzed direct synthesis of asymmetrical ureas from *N*-Alloc-, *N*-Troc-, and *N*-Cbz-carbamate compounds has been developed.

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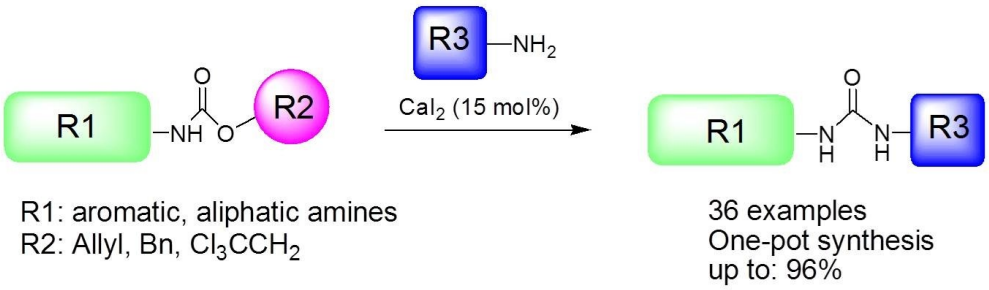

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