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Reaction of organozinc halides with aryl isocyanates

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ABSTRACT

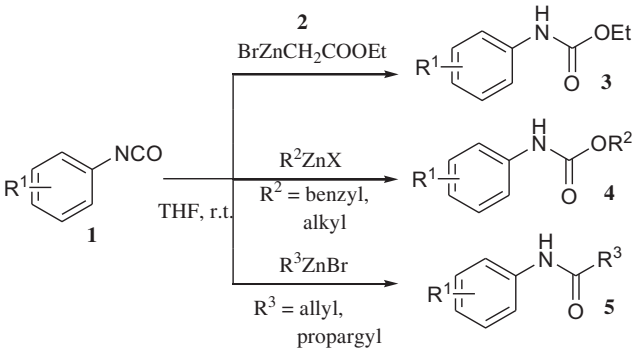
Reformatsky reagent, benzylzinc bromide or alkylzinc iodides react with aryl isocyanates directly to give corresponding *N*-substituted carbamates under mild reaction conditions. However, the reaction of allylzinc bromide or propargylzinc bromide with aryl isocyanates produces the corresponding *N*-substituted amides. The reactions provide alternative methods for the synthesis of *N*-substituted carbamates or amides.

1. Introduction

Organozinc halides have been developed into very useful organometallic reagents for organic synthesis during last decades.[1] They are usually compatible with numerous functional groups because of their low reactivity toward many electrophiles.[2] However, they can reacted with many electrophiles to give multi-functional molecular in the presence of transition metal catalysts such as Pd,[3] Ni,[1f,4] Cu,[5] Fe,[6] Co,[7] Al,[8] and other catalysts.[9] They have also been successfully used in total synthesis of natural products.[10] Although isocyanates are very important in organic synthesis, there are no reports on the direct reactions of aryl isocyanates with organozinc halides. As our on-going research works on organozincs,[11] we investigated the reaction of organozinc halides with aryl isocyanates. Herein we wish to report our results on the reactions of organozinc halides with aryl isocyanates. We firstly found that Reformatsky reagent, alkylzinc iodides and benzylzinc bromide react with aryl isocyanates to give *N*-substituted carbamates. However, when the allyl or propargylzinc bromides were used, the corresponding *N*-substituted amides were obtained (Scheme 1).

2. Results and discussion

As a beginning of our investigation, the reaction of Reformatsky reagent with aryl isocyanates were investigated, and the *N*-substituted carbamates were obtained as products. For example, when isocyanatobenzene **1a** reacted with Reformatsky reagent, the ethyl *N*-phenylcarbamate **3a** was obtained in the yield of 65%. The structure of **3a** was confirmed by the X-ray crystal structure (Fig. 1), ^{1}H NMR and ^{13}C NMR.



Scheme 1. Reaction of organozinc halides with aryl isocyanates.

In order to check the generality of substrates, a variety of aryl isocyanates were used in the reaction. As showed in Table 1, other aryl isocyanates could also react with Reformatsky reagent **2** to give the corresponding *N*-substituted carbamates in reasonable yields.

We next check the reactions of benzylzinc bromide or alkylzinc iodides with aryl isocyanates and *N*-substituted carbamates were obtained (Table 2). The structure of product **4c** was confirmed by the X-ray crystal structure (Fig. 2).

As shown in Table 2, benzylzinc bromide or primary alkylzinc iodides can react with aryl isocyanates directly to generate corresponding *N*-substituted carbamates under mild reaction conditions in moderate yields. However, tertiary alkylzinc halide such as *tert*-butyl zinc bromide reacting with isocyanatobenzene yielded compound **6** in 83% yield and no corresponding *N*-substituted carbamates was obtained.

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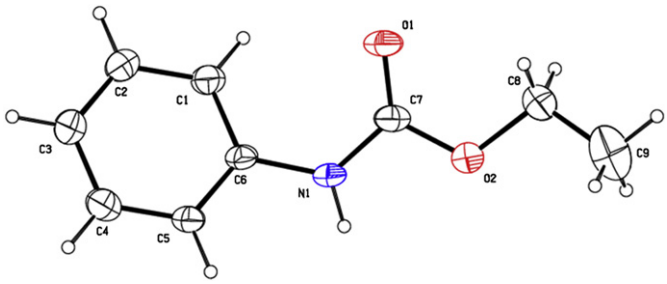
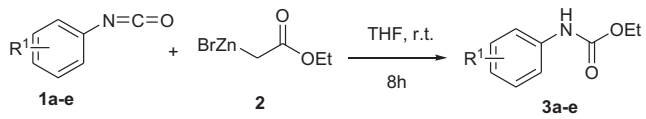
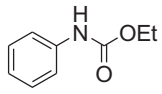
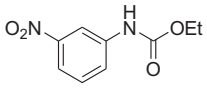
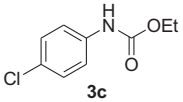
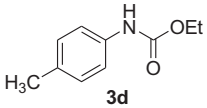
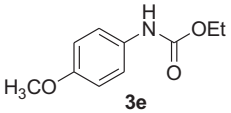


Fig. 1. X-ray crystal structure of **3a**.

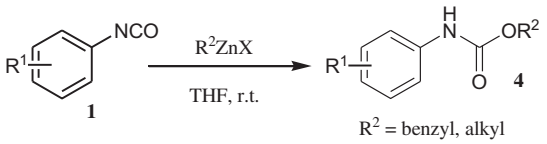
Table 1
Reactions of aryl isocyanates with Reformatsky reagent[a]



Entry	R^1	Products[b]	Yield (%)[c]
1	H	 **3a**	65
2	3-NO_2	 **3b**	67
3	4-Cl	 **3c**	57
4	4-CH_3	 **3d**	60
5	4-OCH_3	 **3e**	62

[a] Reaction conditions: aryl isocyanates (2.0 mmol), Reformatsky reagent (6.0 mmol), THF, at room temperature for 8 h.
[b] All products were characterized by ^{1}H NMR and ^{13}C NMR.
[c] Isolated yield.

Table 2
Reactions of aryl isocyanates with benzylzinc bromide or alkylzinc iodides[a]



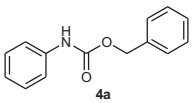
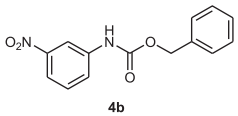
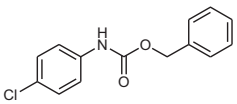
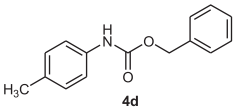
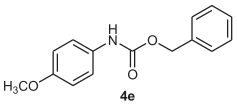
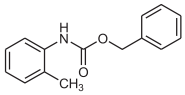
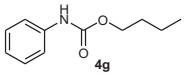
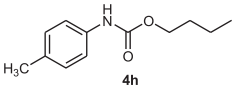
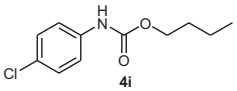
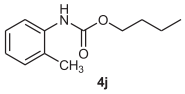
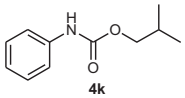
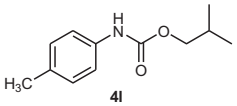
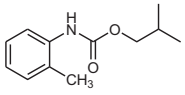
Entry	R^1	Products[b]	Yield (%)[c]
1	H	 **4a**	68
2	3-NO_2	 **4b**	59

Table 2 (*continued*)

Entry	R^1	Products[b]	Yield (%)[c]
3	4-Cl	 **4c**	64
4	4-CH_3	 **4d**	62
5	4-OCH_3	 **4e**	63
6	2-CH_3	 **4f**	70
7	H	 **4g**	65
8	4-CH_3	 **4h**	65
9	4-Cl	 **4i**	60
10	2-CH_3	 **4j**	63
11	H	 **4k**	65
12	4-CH_3	 **4l**	62
13	2-CH_3	 **4m**	61

[a] Reaction conditions: aryl isocyanates (2.0 mmol), organozinc bromides or alkylzinc iodides (4.0 mmol), THF, at 55 °C for 8 h.
[b] All products were characterized by ^{1}H NMR and ^{13}C NMR.
[c] Isolated yield.

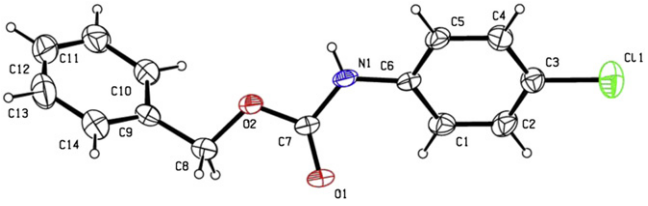
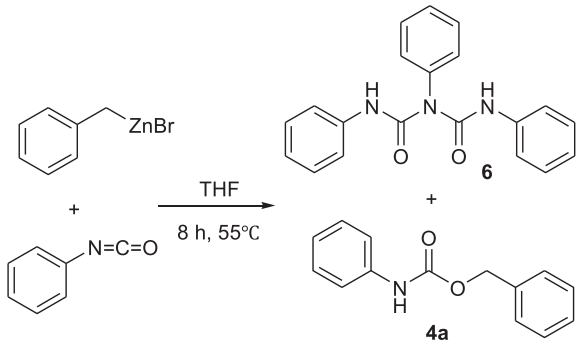


Fig. 2. X-ray crystal structure of **4c**.

In our investigation of the reaction of benzylzinc bromide or alkylzinc iodides with aryl isocyanates, we found all the yields of the corresponding products were moderate and cannot be improved effectively. So the by-products were checked to understand

the reason. Finally, a by-product **6** was separated from the reaction of benzylzinc bromide and 1-isocyanatobenzene (Scheme 2). The structure of **6** was confirmed by the X-ray crystal structure (Fig. 3). It was now clear that part of the aryl isocyanates would condense themselves during reaction. In order to check if the by-product was only formed from isocyanate in the presence of zinc Lewis acid, the 1-isocyanatobenzene was reacted with anhydrous $ZnCl_2$ under the same reaction conditions. However, there was no reaction occurred at all. So the by-product should be formed from the intermediates during the reaction of isocyanate with organozinc halide. The reaction mechanism is not clear for us at the moment.



Scheme 2. The reaction of 1-isocyanatobenzene with benzylzinc bromide.

We also found that the reaction temperature greatly affects the ratio of **4a** and **6**. The yield of **6** increased from 12% to 53% when the reaction temperature decreased from 55 °C to −45 °C. On the other hand, the yield of **4a** decreased to 25% at −45 °C. Higher reaction temperature favors the generation of the desired products **4a**–**m**.

Finally, the allylzinc bromide or propargylzinc bromide were used in the reaction. It was found that the allylzinc bromide or propargylzinc bromide could also react with aryl isocyanates in THF at room temperature without any metal catalyst. However, the products were *N*-substituted amides instead of carbamates. The results were summarized in Table 3. As showed in Table 3, entries 1–7, the allylzinc bromide react with aryl isocyanates smoothly to give the corresponding *N*-substituted acryl amides in good to excellent yields. However, the yields of propargyl amides were relatively lower when propargylzinc bromide was reacted with aryl isocyanates. It was found that the reason of low yields was the self-coupling of propargylzinc bromide and 1,5-hexadiyne was obtained as by-product in the reaction. Both electron-donating and electron-withdrawing groups on phenyl ring have little effect on the products yields (Table 3). The reaction mechanism was suggested as

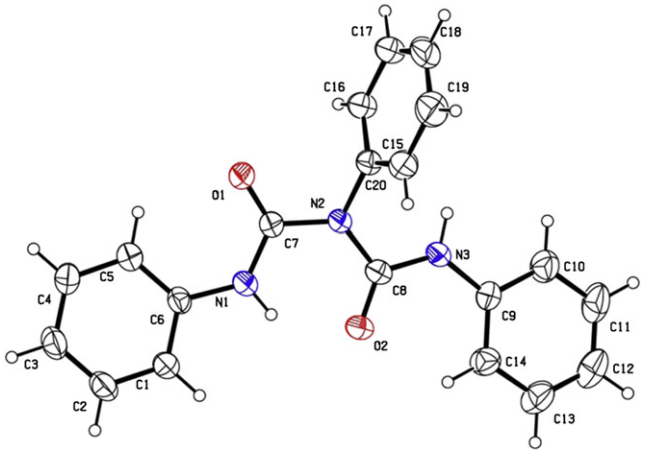
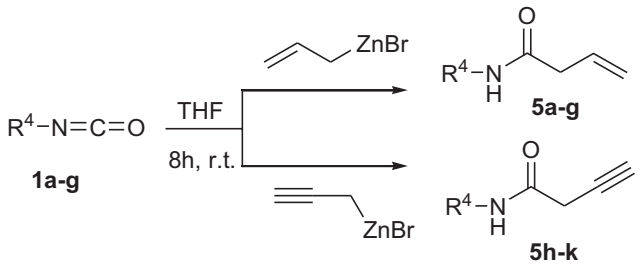
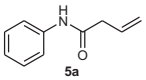
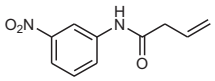
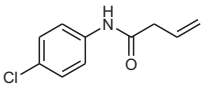
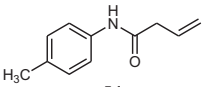
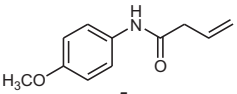
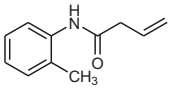
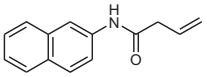
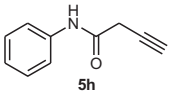
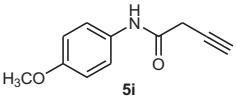
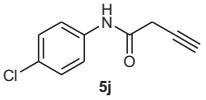
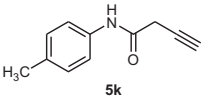


Fig. 3. X-ray crystal structure of **6**.

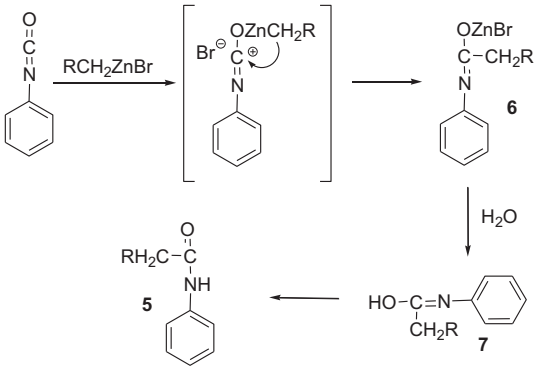
Table 3
Reactions of aryl isocyanates with allylzinc bromide or propargylzinc bromide[a]



Entry	R^4	Products[b]	Yield (%)[c]
1	Ph	 5a	92
2	3-NO_2	 5b	77
3	4-ClC_6H_4	 5c	82
4	4-$CH_3C_6H_4$	 5d	81
5	4-$CH_3OC_6H_4$	 5e	80
6	2-$CH_3C_6H_4$	 5f	96
7	β-Naphthyl	 5g	86
8	Ph	 5h	55
9	4-$CH_3OC_6H_4$	 5i	43
10	4-ClC_6H_4	 5j	34
11	4-$CH_3C_6H_4$	 5k	42

[a] Reaction conditions: aryl isocyanates (2.0 mmol), allylzinc bromide or propargylzinc bromide (6.0 mmol), THF, at room temperature for 8 h.
[b] All products were characterized by ^1H NMR and ^{13}C NMR.
[c] Isolated yields.

following (Scheme 3). Firstly, aryl isocyanates react with allylzinc bromide or propargylzinc bromide giving products 6, which generate 7 by hydrolyzation. Then, hydrogen atom migrates from oxygen atom to carbon atom yielding *N*-substituted amides 5.



Scheme 3. Proposed mechanism for the formation of **5**.

3. Conclusions

In conclusion, we firstly disclosed that Reformatsky reagent, benzylzinc bromide or alkylzinc iodides could react with aryl isocyanates directly to give corresponding *N*-substituted carbamates under mild reaction conditions. On the other hand, the reaction of allylzinc bromide or propargylzinc bromide with aryl isocyanates produces the corresponding *N*-substituted amides. The reaction provides an alternative method for the synthesis of *N*-substituted carbamates or amides.

4. Experimental section

4.1. General methods

Column chromatography was performed using silica gel. Tetrahydrofuran (THF) was dried and distilled, and zinc powder was activated prior to use. Other organic chemical, 1,2-dibromoethane, trimethylchlorosilane, diethyl ether, magnesium sulfate, and ammonium chloride were commercially available, and were used without further purification. All reactions were carried out under nitrogen atmosphere, unless otherwise noted. ^{1}H NMR spectra were measured at 400 MHz using tetramethylsilane (TMS) as internal standard. ^{13}C NMR spectra were measured at 100 MHz using TMS or the center peak of chloroform (δ=77.0 ppm) as internal standard. High resolution mass spectra were obtained on Bruker ESQ6K spectrometer. X-ray crystal data were obtained on SMART APEX II BRUKER. Isocyanates and halides were commercially available and used without a further purification.

4.2. General procedure for the synthesis of 3a–e

Under nitrogen atmosphere, two drops of 1,2-dibromoethane was added to a solution of zinc powder (6.0 mmol) in dry THF (5.0 mL). The reaction mixture was warmed for a while, cooled naturally to room temperature and then trimethylchlorosilane (0.01 mL) was added. After stirring for 15 min at room temperature, ethyl 2-bromoacetate (6.0 mmol) was added. The mixture was stirred until the zinc powder disappeared to get the Reformatsky reagent. Isocyanate (2.0 mmol) was added to the above solution, and then the mixture was stirred for 8 h at room temperature. The reaction was quenched with saturated ammonium chloride solution (4 mL). The organic phase was separated and the aqueous phase was extracted with diethyl ether (3×10 mL), and the combined organic layer was dried over anhydrous $MgSO_4$. The solvent was evaporated off under reduced pressure. The crude product was purified by column on silica gel using mixture of petroleum ether and ethyl acetate as eluent.

*4.2.1. Ethyl phenylcarbamate (**3a**).* 0.27 g (65%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38 (d, *J*=8.0 Hz, 2H), 7.30 (t, *J*=8.0 Hz, 2H), 7.06 (t, *J*=7.2 Hz, 1H), 6.59 (br, 1H), 4.23 (q, *J*=7.2 Hz, 2H), 1.31 (t, *J*=7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.6, 137.9, 129.0, 123.3, 118.6, 61.2, 14.5 ppm. HRMS (ES+) calcd for $C_9H_{11}NO_2$ (M+H) 166.0863, found 166.0866.

*4.2.2. Ethyl 3-nitrophenylcarbamate (**3b**).* 0.35 g (67%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.31 (t, *J*=2.0 Hz, 1H), 7.91 (d, *J*=8.4 Hz, 1H), 7.76 (d, *J*=8.0 Hz, 1H), 7.47 (t, *J*=8.0 Hz, 1H), 6.99 (br, 1H), 4.27 (q, *J*=7.2 Hz, 2H), 1.33 (ddd, *J*=7.2, 1.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.3, 148.6, 139.2, 129.8, 124.1, 117.9, 113.2, 61.8, 14.4 ppm. HRMS (ES+) calcd for $C_9H_{10}N_2O_4$ (M+NH_4) 228.0979, found 228.0982.

*4.2.3. Ethyl 4-chlorophenylcarbamate (**3c**).* 0.28 g (57%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.34–7.25 (m, 4H), 6.65 (br, 1H), 4.22 (q, *J*=7.2 Hz, 2H), 1.31 (t, *J*=7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.4, 136.5, 129.0, 128.3, 119.8, 61.4, 14.5 ppm. HRMS (ES+) calcd for $C_9H_{10}ClNO$ (M+H) 200.0473, found 200.0475.

*4.2.4. Ethyl p-tolylcarbamate (**3d**).* 0.27 g (60%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26 (d, *J*=8.8 Hz, 2H), 7.10 (d, *J*=8.8 Hz, 2H), 6.62 (br, 1H), 4.21 (q, *J*=7.2 Hz, 2H), 2.30 (s, 3H), 1.30 (t, *J*=7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.7, 135.3, 132.8, 129.5, 118.7, 61.1, 20.7, 14.5 ppm. HRMS (ES+) calcd for $C_{10}H_{13}NO_2$ (M+H) 180.1019, found 180.1015.

*4.2.5. Ethyl 4-methoxyphenylcarbamate (**3e**).* 0.30 g (62%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.28 (t, *J*=8.0 Hz, 2H), 6.84 (d, *J*=8.0 Hz, 2H), 6.57 (br, 1H), 4.21 (q, *J*=7.2 Hz, 2H), 3.78 (s, 3H), 1.29 (t, *J*=7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=155.8, 154.0, 131.0, 120.6, 114.2, 61.0, 55.4, 14.5 ppm. HRMS (ES+) calcd for $C_{10}H_{13}NO_3$ (M+H) 196.0968, found 196.0972.

4.3. General procedure for the synthesis of 4a–m

Under nitrogen atmosphere, two drops of 1,2-dibromoethane was added to a solution of zinc powder (4.0 mmol) in dry THF (5.0 mL). The reaction mixture was warmed for a while, cooled naturally to room temperature and then trimethylchlorosilane (0.01 mL) was added. After stirring for 15 min at room temperature, benzyl bromine or alkyl iodides (4.0 mmol) was added. The mixture was stirred until the zinc powder disappeared to get benzylzinc bromine or alkylzinc iodides. Isocyanate (2.0 mmol) reacted with organozinc halide (4.0 mmol) for 8 h at 55 °C. The reaction was quenched with saturated ammonium chloride solution (4 mL), the reaction mixture was extracted with diethyl ether (3×10 mL), and the organic layer was dried with anhydrous $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by preparative TLC on silica gel (petroleum ether and ethyl acetate as eluent). *N*-substituted carbamates were isolated.

*4.3.1. Benzyl phenylcarbamate (**4a**).* 0.31 g (68%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38–7.31 (m, 9H), 7.07–7.04 (m, 1H), 6.77 (br, 1H), 5.19 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.3, 137.7, 136.0, 129.0, 128.6, 128.3, 128.2, 123.5, 118.7, 67.0 ppm. HRMS (ES+) calcd for $C_{14}H_{13}NO_2$ (M+H) 228.1019, found 228.1014.

*4.3.2. Benzyl 3-nitrophenylcarbamate (**4b**).* 0.32 g (59%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.30 (t, *J*=2.0 Hz, 1H), 7.92–7.90 (m, 1H), 7.74 (d, *J*=7.6 Hz, 1H), 7.48–7.44 (m, 1H), 7.42–7.34 (m, 5H),

6.95 (br, 1H), 5.23 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=152.9, 148.7, 139.0, 135.5, 129.8, 128.7, 128.6, 128.4, 124.1, 118.1, 113.3, 67.6 ppm. HRMS (ES+) calcd for $C_{14}H_{12}N_2O_4$ (M+NH_4) 290.1135, found 290.1127.

*4.3.3. Benzyl 4-chlorophenylcarbamate (**4c**).* 0.34 g (64%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.33–7.29 (m, 6H), 7.27–7.18 (m, 2H), 7.04–7.00 (m, 1H), 6.91 (br, 1H), 5.15 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.2, 136.3, 135.8, 129.0, 128.6, 128.5, 128.4, 128.3, 119.8, 67.1 ppm. HRMS (ES+) calcd for $C_{14}H_{12}ClNO_2$ (M+H) 262.0629, found 262.0625.

*4.3.4. Benzyl p-tolylcarbamate (**4d**).* 0.30 g (62%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.36–7.29 (m, 5H), 7.25–7.21 (m, 2H), 7.07 (d, J=8.0 Hz, 2H), 6.72 (br, 1H), 5.16 (s, 2H), 2.28 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=149.2, 147.4, 129.9, 120.6, 113.2, 109.0, 70.6, 29.7, 26.5, 26.3, 26.2 ppm. HRMS (ES+) calcd for $C_{15}H_{15}NO_2$ (M+H) 242.1176, found 242.1170.

*4.3.5. Benzyl 4-methoxyphenylcarbamate (**4e**).* 0.32 g (63%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38–7.32 (m, 5H), 7.29–7.25 (m, 2H), 6.86–6.83 (m, 2H), 6.60 (br, 1H), 5.18 (s, 2H), 3.77 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=155.9, 153.7, 136.1, 130.8, 128.6, 128.3, 120.6, 114.2, 66.9, 55.4 ppm. HRMS (ES+) calcd for $C_{15}H_{15}NO_3$ (M+H) 258.1125, found 258.1121.

*4.3.6. Benzyl o-tolylcarbamate (**4f**).* 0.34 g (70%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.82 (s, 1H), 7.40–7.34 (m, 4H), 7.24–7.14 (m, 2H), 7.02 (t, J=7.6 Hz, 1H), 6.47 (br, 1H), 5.21 (s, 2H), 2.23 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.6, 136.1, 135.8, 130.4, 128.6, 128.4, 128.3, 126.9, 124.2, 121.1, 67.1, 17.6 ppm. HRMS (ES+) calcd for $C_{15}H_{15}NO_2$ (M+H) 242.1176, found 242.1172.

*4.3.7. Butyl phenylcarbamate (**4g**).* 0.25 g (65%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38 (d, J=8.0 Hz, 2H), 7.29 (t, J=8.4 Hz, 2H), 7.05 (t, J=7.6 Hz, 1H), 6.68 (br, 1H), 4.16 (t, J=7.2 Hz, 2H), 1.69–1.62 (m, 2H), 1.46–1.37 (m, 2H), 0.95 (t, J=7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.7, 138.0, 129.0, 123.3, 118.6, 65.1, 30.9, 19.0, 13.7 ppm. HRMS (ES+) calcd for $C_{11}H_{15}NO_2$ (M+H) 194.1176, found 194.1180.

*4.3.8. Butyl p-tolylcarbamate (**4h**).* 0.27 g (68%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.25 (t, J=7.6 Hz, 2H), 7.10 (d, J=8.4 Hz, 2H), 6.56 (br, 1H), 4.15 (t, J=6.8 Hz, 2H), 2.30 (s, 3H), 1.68–1.61 (m, 2H), 1.46–1.37 (m, 2H), 0.95 (t, J=7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.8, 135.4, 132.8, 129.5, 118.7, 65.0, 31.0, 20.7, 19.1, 13.7 ppm. HRMS (ES+) calcd for $C_{12}H_{17}NO_2$ (M+H) 208.1332, found 208.1333.

*4.3.9. Butyl 4-chlorophenylcarbamate (**4i**).* 0.27 g (60%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.33 (d, J=8.0 Hz, 2H), 7.26 (d, J=8.8 Hz, 2H), 6.61 (br, 1H), 4.16 (t, J=6.8 Hz, 2H), 1.69–1.61 (m, 2H), 1.46–1.36 (m, 2H), 0.95 (t, J=7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.6, 136.6, 129.0, 128.3, 119.8, 65.3, 30.9, 19.0, 13.7 ppm. HRMS (ES+) calcd for $C_{11}H_{14}ClNO_2$ (M+H) 228.0786, found 228.0783.

*4.3.10. Butyl o-tolylcarbamate (**4j**).* 0.26 g (63%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.78 (s, 1H), 7.25–7.18 (m, 1H), 7.15 (d, J=7.6 Hz, 1H), 7.03–7.00 (m, 1H), 6.38 (br, 1H), 4.17 (t, J=6.8 Hz, 2H), 2.25 (s, 3H), 1.70–1.63 (m, 2H), 1.47–1.37 (m, 2H), 0.96 (t, J=7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=154.1, 135.9, 133.5, 130.4, 126.9, 124.0, 121.0, 65.2, 31.0, 19.1, 17.7, 13.8 ppm. HRMS (ES+) calcd for $C_{12}H_{17}NO_2$ (M+H) 208.1332, found 208.1338.

*4.3.11. Isobutyl phenylcarbamate (**4k**).* 0.25 g (65%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.39 (d, J=7.6 Hz, 2H), 7.32–7.26 (m, 2H), 7.06 (t, J=7.2 Hz, 1H), 6.65 (br, 1H), 3.95 (d, J=6.8 Hz, 2H), 2.02–1.92 (m, 1H), 0.97 (d, J=6.8 Hz, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.7, 137.9, 129.0, 123.3, 118.6, 71.3, 27.9, 19.0 ppm. HRMS (ES+) calcd for $C_{11}H_{15}NO_2$ (M+H) 194.1176, found 194.1178.

*4.3.12. Isobutyl p-tolylcarbamate (**4l**).* 0.26 g (62%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.27 (d, J=6.4 Hz, 2H), 7.11 (d, J=8.0 Hz, 2H), 6.54 (br, 1H), 3.94 (d, J=6.8 Hz, 2H), 2.30 (s, 3H), 2.02–1.92 (m, 1H), 0.96 (d, J=6.8 Hz, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=153.8, 135.3, 132.9, 129.5, 118.6, 71.3, 33.4, 28.0, 20.0 ppm. HRMS (ES+) calcd for $C_{12}H_{17}NO_2$ (M+H) 208.1332, found 208.1336.

*4.3.13. Isobutyl o-tolylcarbamate (**4m**).* 0.25 g (61%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.78 (s, 1H), 7.25–7.14 (m, 2H), 7.02 (t, J=7.2 Hz, 1H), 6.41 (br, 1H), 3.95 (d, J=7.2 Hz, 2H), 2.26 (s, 3H), 2.01–1.95 (m, 1H), 0.96 (d, J=6.8 Hz, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=154.1, 135.9, 130.4, 126.8, 124.1, 121.1, 71.4, 28.0, 19.1, 17.7 ppm. HRMS (ES+) calcd for $C_{12}H_{17}NO_2$ (M+H) 228.1332, found 228.1338.

4.4. General procedure for the synthesis of 5a–k

Under nitrogen atmosphere, two drops of 1,2-dibromoethane was added to a solution of zinc powder (6.0 mmol) in dry THF (5.0 mL). The reaction mixture was warmed for a while, cooled naturally to room temperature and then trimethylchlorosilane (0.01 mL) was added. After stirring for 15 min at room temperature, allyl bromide or propargyl bromide (6.0 mmol) was added. The mixture was stirred until the zinc powder disappeared to get allylzinc bromide or propargylzinc bromide. Isocyanate (2.0 mmol) reacted with allylzinc bromide or propargylzinc bromide for 8 h at room temperature. The reaction was quenched with saturated ammonium chloride solution (4 mL), the reaction mixture was extracted with diethyl ether (3×10 mL), and the organic layer was dried with anhydrous $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by preparative TLC on silica gel (petroleum ether and ethyl acetate as eluent). *N*-substituted amides were isolated.

*4.4.1. N-phenylbut-3-enamide (**5a**).* 0.30 g (92%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.63 (br, 1H), 7.51 (d, J=7.6 Hz, 2H), 7.30 (t, J=8.0 Hz, 2H), 7.10 (t, J=7.2 Hz, 1H), 6.07–5.97 (m, 1H), 5.32–5.27 (m, 2H), 3.16 (d, J=8.0 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=169.1, 137.7, 131.0, 128.8, 124.3, 120.0, 119.9, 42.4 ppm. HRMS (ES+) calcd for $C_{10}H_{11}NO$ (M+H) 162.0913, found 162.0917.

*4.4.2. N-(3-Nitrophenyl)but-3-enamide (**5b**).* 0.32 g (77%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.34 (s, 1H), 7.32–7.25 (m, 3H), 6.79 (br, 1H), 6.00–5.91 (m, 1H), 5.36 (dd, J=17.2, 1.6 Hz, 1H), 5.26 (dd, J=10.4, 1.2 Hz, 1H), 4.66 (d, J=6.0 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=169.2, 148.5, 138.8, 130.4, 129.9, 125.5, 121.2, 119.0, 114.5, 42.5 ppm. HRMS (ES+) calcd for $C_{10}H_{10}N_2O_3$ (M+H) 207.0764, found 207.0767.

*4.4.3. N-(4-Chlorophenyl)but-3-enamide (**5c**).* 0.32 g (82%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.46 (d, J=8.8 Hz, 2H), 7.42 (br, 1H), 7.27 (d, J=8.8 Hz, 2H), 6.07–5.97 (m, 1H), 5.35 (d, J=4.8 Hz, 1H), 5.33 (d, J=13.6 Hz, 1H), 3.18 (d, J=7.2 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=168.6, 136.2, 130.8, 129.4, 129.0, 121.0, 120.9, 42.6 ppm. HRMS (ES+) calcd for $C_{10}H_{10}ClNO$ (M+H) 196.0524, found 196.0528.

*4.4.4. N-p-Tolylbut-3-enamide (**5d**).* 0.28 g (81%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.42 (br, 1H), 7.38 (d, J=8.0 Hz, 2H), 7.10 (d, J=8.0 Hz, 2H), 6.06–5.97 (m, 1H), 5.33–5.28 (m, 2H), 3.16 (d, J=8.0 Hz, 2H), 2.30 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$):

δ=168.6, 135.1, 134.0, 131.2, 129.4, 120.3, 119.9, 42.6, 20.8 ppm. HRMS (ES+) calcd for $C_{11}H_{13}NO$ (M+H) 176.1070, found 176.1074.

*4.4.5. N-(4-Methoxyphenyl)but-3-enamide (**5e**).* 0.31 g (80%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.29 (d, J=7.6 Hz, 2H), 6.84 (d, J=8.8, 2H), 6.73 (br, 1H), 5.99–5.91 (m, 1H), 5.34 (d, J=16.8 Hz, 1H), 5.24 (d, J=10.4 Hz, 1H), 4.65 (d, J=5.6 Hz, 2H), 3.77 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=155.9, 153.6, 132.5, 130.8, 120.6, 118.1, 114.2, 65.7, 55.4 ppm. HRMS: none.

*4.4.6. N-o-Tolylbut-3-enamide (**5f**).* 0.34 g (96%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.86 (d, J=8.0 Hz, 1H), 7.25–7.16 (m, 2H), 7.07 (t, J=7.6 Hz, 1H), 6.13–6.02 (m, 1H), 5.39–5.35 (m, 2H), 3.22 (d, J=6.8 Hz, 2H), 2.23 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=168.4, 135.5, 131.3, 130.4, 128.6, 126.8, 125.1, 122.6, 120.9, 42.6, 17.6. HRMS (ES+) calcd for $C_{11}H_{13}NO$ (M+H) 176.1070, found 176.1072.

*4.4.7. N-(Naphthalen-2-yl)but-3-enamide (**5g**).* 0.36 g (86%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.19 (d, J=1.6 Hz, 1H), 7.77 (d, J=8.0 Hz, 3H), 7.61 (br, 1H), 7.46–7.38 (m, 3H), 6.12–6.01 (m, 1H), 5.37 (s, 1H), 5.33 (d, J=8.4 Hz, 1H), 3.23 (d, J=7.2 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=168.9, 135.1, 133.8, 131.0, 130.1, 128.7, 127.6, 127.5, 126.5, 125.0, 120.6, 119.7, 116.6, 42.7 ppm. HRMS (ES+) calcd for $C_{14}H_{13}NO$ (M+H) 212.1070, found 212.1067.

*4.4.8. N-Phenylbut-3-ynamide (**5h**).* 0.17 g (55%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.21 (br, 1H), 7.54 (dd, J=8.0, 0.8 Hz, 2H), 7.35 (t, J=7.6 Hz, 2H), 7.15 (t, J=7.6 Hz, 1H), 3.39 (d, J=2.8 Hz, 2H), 2.51 (t, J=2.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=164.0, 137.1, 129.1, 124.9, 119.9, 75.1, 28.4 ppm. HRMS (ES+) calcd for $C_{10}H_9NO$ (M+H) 160.0757, found 160.0762.

*4.4.9. N-(4-Methoxyphenyl)but-3-ynamide (**5i**).* 0.16 g (43%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.14 (br, 1H), 7.43–7.27 (m, 2H), 6.89–6.86 (m, 2H), 3.82 (s, 3H), 3.36 (d, J=2.8 Hz, 2H), 2.48 (t, J=2.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=164.0, 156.8, 130.2, 122.0, 114.2, 74.8, 55.4, 28.1 ppm. HRMS (ES+) calcd for $C_{11}H_{11}NO_2$ (M+H) 190.0863, found 190.0866.

*4.4.10. N-(4-Chlorophenyl)but-3-ynamide (**5j**).* 0.15 g (40%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.21 (br, 1H), 7.50 (d, J=8.8 Hz, 2H), 7.31 (d, J=8.8 Hz, 2H), 3.39 (d, J=2.8 Hz, 2H), 2.51 (t, J=2.8 Hz, 1H). ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=164.0, 135.7, 129.9, 129.7, 129.1, 121.1, 75.3, 28.3 ppm. HRMS (ES+) calcd for $C_{10}H_8ClNO$ (M+H) 194.0367, found 194.0370.

*4.4.11. N-p-Tolylbut-3-ynamide (**5k**).* 0.15 g (42%); white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.17 (br, 1H), 7.41–7.26 (m, 2H), 7.15–7.09 (m, 2H), 3.36 (d, J=2.8 Hz, 2H), 2.48 (t, J=2.8 Hz, 1H), 2.32 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=164.0, 134.6, 129.5, 120.0, 74.9, 28.3, 20.8 ppm. HRMS (ES+) calcd for $C_{11}H_{11}NO$ (M+H) 174.0913, found 174.0917.

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Supplementary data

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References and notes

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