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Palladium-catalyzed highly regioselective and stereoselective arylation of electron-rich allylamines with aryl bromides

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ABSTRACT

A palladium-catalyzed, highly efficient Heck arylation of electron-rich *N*,*N*-diprotected allylamine derivatives with a wide range of aryl bromides under ligand-free conditions has been developed. In the presence of $Pd(OAc)_2$ and an appropriate additive, the reaction proceeds with excellent regioselectivity and stereoselectivity, leading exclusively to the γ-arylated (*E*)-allylamine products in good to excellent yields. It was found that the choice of solvent, olefin, additive and temperature has an important influence on the reaction. Worthy of note is that good results were observed only when using *N*,*N*-diprotected allylamines containing carbamate moiety, and the steric properties of allylamines also have important impacts on the regiocontrol. The use of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) or HQ (hydroquinone) as the additive is also crucial for securing a faster reaction rate. This method provides a straightforward approach for the efficient synthesis of various γ-arylated, linear (*E*)-allylamines.

1. Introduction

Allylamines are widespread structural units in a large number of natural and biologically active compounds, and the presence of two highly versatile functional groups renders them valuable substrates for many types of reactions to afford useful products.[1,2] Because of their importance, it is not surprising that much effort has been devoted to the efficient construction of these compounds.[1,3] Consequently, a variety of methods for the synthesis of various functionalized allylamines can now be found in the literature. However, despite the progress made in this area, there is still significant room for improvement of the synthetic efficiency, for example, in terms of reactivity and selectivity.

The Pd-catalyzed Heck reaction has become one of the most powerful tools for the construction of C–C bonds in organic synthesis owing to its simplicity and tolerance of various functional groups.[4] Over the past two decades, improved strategies have been developed to broaden its application, particularly toward highly regioselective arylation of electron-rich olefins, such as vinyl ethers, allylic alcohol derivatives, and enamides.[5–14] In this regard, the application of Pd-catalyzed Heck arylation of electron-rich allylamines to prepare arylated allylamines has recently gained much attention.[2d,2f,2i,15–18] However, this kind of transformation is often complicated by the formation of mixtures of internal and terminal regioisomers (Scheme 1). The efforts of Hallberg and Larhed,[16a,b] Wu[16c] and Baxter[2i] have resulted in useful strategies for highly selective internal β-arylation of allylamine derivatives. However, the γ-regioselective arylation of allylamines has not been well-developed. Ripin[17a] and Wilson[17b] reported that Pd-catalyzed highly regioselective and stereoselective terminal γ-arylation of allylamine derivatives could be accomplished in alcoholic solvents under ligand-free conditions to give exclusively linear (*E*)-allylamine products, but only one aryl iodide substrate was attempted, and the general utility of this chemistry has not been explored. Very recently, Sigman,[18a] Cacchi[18b] and Correia[18c] reported that $Pd_2(dba)_3$ could efficiently catalyze the preferential γ-arylation of allylamines with arenediazonium salts in the absence of ligand. However, the synthetic utility of this chemistry might be restricted by the intrinsic drawbacks of arenediazonium salt, such as instability and explosive potential. Considering the importance of γ-arylated allylamines in chemical synthesis and particularly that leading to biologically active compounds,[19] it is of great interest to

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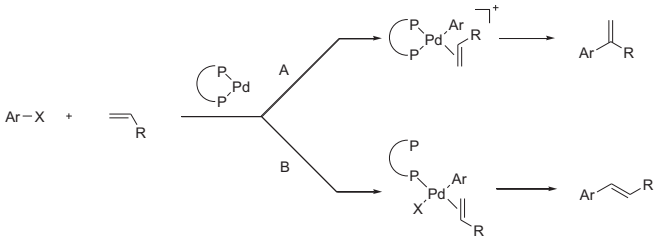


Scheme 1. Formation of regioisomers via two competing pathways in the Heck reaction.

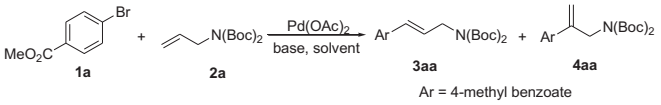
develop practical and highly efficient catalytic synthetic methods to access these compounds from safe and stable aryl halides. In continuing our research in regioselective Heck arylation of electron-rich olefins,[7,9,11] herein we report that, in the presence of $Pd(OAc)_2$ catalyst and appropriate additive, electron-rich *N*,*N*-diprotected allylamines could undergo highly efficient γ-arylation with aryl bromides under ligand-free conditions, affording the desired (*E*)-allylamine products in good to excellent yields in a highly regioselective and stereoselective manner.

2. Results and discussion

We started our investigation with methyl 4-bromobenzoate (**1a**) as the model substrate and *N*,*N*-$(Boc)_2$-allylamine (**2a**) as the model olefin under various reaction conditions (Table 1). Initially, the coupling reaction was carried out in CH_3CN at 85 °C with $Pd(OAc)_2$/PPh_3 as catalyst and K_2CO_3 as the base. Only the linear (*E*)-allylamine product **3aa** was observed, while the internal isomer **4aa** or the *Z* isomer could not be detected after 12 h (Table 1, entry 1). This result indicates that the reaction follows the neutral route (Scheme 1, path B), and the ionic pathway (Scheme 1, path A) is either completely suppressed or its involvement in the arylation is insignificant. Similar experimental observations have been reported in the regioselective Heck coupling reaction of **2a** with aryl iodide and arenediazonium salts under ligand-free conditions.[17a,18] In view of the significant advantage of ligand-free conditions, we then decided to examine the reaction of **1a** and **2a** in the absence of ligand. However, employing Ripin's protocol[17a] resulted in no reaction (Table 2, entry 2). The combination of $Pd_2(dba)_3$, NaOAc and NEt_3, which was reported to work well for the regioselective linear arylation of *N*-allyl-2-methoxyacetamide with aryl iodide,[17b] gave similarly poor result (Table 2, entry 3). Delightfully, the reaction in CH_3CN remained active and regioselectivity was unchanged in the absence of a ligand (Table 2, entry 4). In order to further improve the efficiency, a number of solvents were screened. The use of DMSO, dioxane and toluene afforded the desired product **3aa** in higher yields of 77–81% (Table 1, entries 5–7), and the highest yield of 85% was observed in DMF (Table 1, entry 8). Although ethylene glycol (EG) has been recently identified as a useful solvent for highly regioselective internal arylation of electron-rich olefins,[9] no reaction occurred in this case (Table 1, entry 9). The use of $Pd(OAc)_2$ as a source of palladium was essential for this transformation, with catalysts derived from other Pd precursors being not very efficient (Table 1, entries 10–12). For comparison, the performance of other bases, including Cs_2CO_3, K_3PO_4, KOAc, KO*t*Bu and tetrabutylammonium acetate (TBAA) (Table 1, entries 13–17), was investigated, but none of them could work as effectively as K_2CO_3. The effect of additive was also studied. When 10 mol % HQ was introduced, the reaction could go to completion in 6 h, exclusively giving the desired product **3aa** in 82% yield (Table 1, entry 18). The reaction could proceed more quickly at 100 °C, giving a full conversion in 3 h with a slightly higher yield (Table 1, entry 19). When the temperature was increased to 120 °C, the reaction finished in 1.2 h, but the yield diminished due to the formation of side products (Table 1, entry 20). Interestingly, replacing HQ with TEMPO could enable the reaction to finish in 1.2 h at 100 °C with 89% yield (Table 1, entry 21). It is clear that TEMPO is a better choice. A further increase to 1 equiv TEMPO had negligible effect on the reactivity (Table 1, entry 22). HQ or TEMPO may either inhibit the polymerization of the olefin or function as a ligand or both. The accelerating effect of the free-radical scavenger in Pd-catalyzed cross-coupling reactions has been recently disclosed in the literature.[20] We tried the effect of tetrabutylammonium bromide and tetrabutylammonium chloride, which have been shown to promote the Heck reaction,[21] but none of them led to an increase in yield. The effect of reducing agents, such as hydrazine and sodium formate were also examined, but no acceleration was observed.[22]

Having established the optimal reaction conditions, we then explored the reaction of **2a** with a range of aryl bromides. As summarized in Table 2, all the reactions proceeded rapidly, with reaction times of as short as less than 2 h observed in some cases (Table 2, entries 1–5). It is notable that all reactions exhibited excellent regioselectivivites (terminal/internal>99:1) and no *Z* isomers could be observed in these transformations. The reaction afforded good to excellent yields of the expected γ-arylated linear (*E*)-allylamines, tolerating electronically different substituents on the aromatic ring. No significant electronic effect on the isolated yield of the desired products was observed, but the reaction proceeded slightly faster in the olefination of electron-deficient aryl bromides (Table 2, entries 1–10), and slightly longer reaction times were needed for the electron-rich ones (Table 2, entries 12–15). The

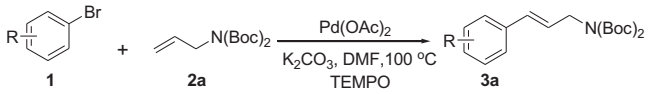
Table 1
Screening conditions for Heck arylation of methyl 4-bromobenzoate (**1a**) with allylamine **2a**[a]



Entry	Solvent	Base	Time (h)	Yield (%)[b]	**3aa**/**4aa**[c]
1[d]	CH_3CN	K_2CO_3	12	30	>99/1
2[e]	*i*PrOH	NEt_3	12	nd	nd
3[e]	EtOH	NaOAc	12	nd	nd
4	CH_3CN	K_2CO_3	12	30	>99/1
5	DMSO	K_2CO_3	12	81	>99/1
6	dioxane	K_2CO_3	12	77	>99/1
7	toluene	K_2CO_3	12	80	>99/1
8	DMF	K_2CO_3	12	85	>99/1
9	EG	K_2CO_3	12	nd	nd
10[e]	DMF	K_2CO_3	12	80	>99/1
11[f]	DMF	K_2CO_3	12	82	>99/1
12[g]	DMF	K_2CO_3	12	44	>99/1
13	DMF	Cs_2CO_3	12	nd	nd
14	DMF	K_3PO_4	12	83	>99/1
15	DMF	KOAc	12	55	>99/1
16	DMF	KO*t*Bu	12	nd	nd
17	DMF	TBAA	12	76	>99/1
18[h]	DMF	K_2CO_3	6	82	>99/1
19[h,i]	DMF	K_2CO_3	3	86	>99/1
20[h,j]	DMF	K_2CO_3	1.2	75	>99/1
21[i,k]	DMF	K_2CO_3	1.2	89	>99/1
22[i,l]	DMF	K_2CO_3	1.2	89	>99/1

[a] Unless otherwise noted, all reactions were carried out with **1a** (1.0 mmol), **2a** (1.2 mmol), $Pd(OAc)_2$ (1 mol %), base (2.0 mmol), solvent (3.0 ml), 85 °C.
[b] Isolated yield.
[c] Determined by ^1H NMR analysis. When no β-arylated product was detected, a value of >99/1 was assigned.
[d] 2 mol % PPh_3 was added.
[e] $Pd_2(dba)_3$ was used to replace $Pd(OAc)_2$.
[f] $PdCl_2$ was used to replace $Pd(OAc)_2$.
[g] $Pd(COCF_3)_2$ was used to replace $Pd(OAc)_2$.
[h] 10 mmol% HQ was added.
[i] Reaction temperature 100 °C.
[j] Reaction temperature 120 °C.
[k] 10 mmol% TEMPO was added.
[l] 1.0 equiv TEMPO was added.

Table 2
Regioselective and stereoselective Heck arylation of **2a** with aryl bromides[a]



1 2a 3a

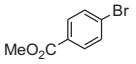
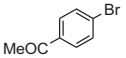
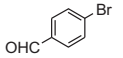
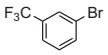
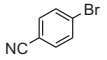
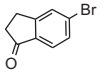
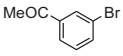
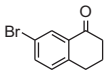
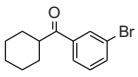
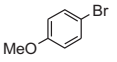
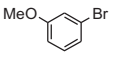
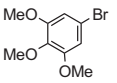
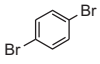
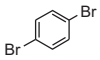
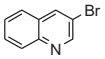
Entry	Substrate		Time (h)	Yield (%)[b]
1		**1a**	1.2	89
2		**1b**	1.5	90
3		**1c**	1.5	83
4		**1d**	1.2	88
5		**1e**	1.5	87
6		**1f**	3	85
7		**1g**	2	81
8		**1h**	2	80
9		**1i**	2	83
10		**1j**	2	85
11		**1k**	3	82
12		**1l**	3	79
13		**1m**	3	81
14		**1n**	3	86
15		**1o**	4	78
16		**1p**	2	79
17[c]		**1p**	4	83
18		**1q**	3	75

Table 2 (*continued*)

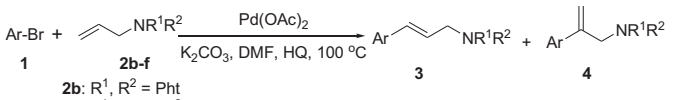
Entry	Substrate		Time (h)	Yield (%)[b]
19		**1r**	3	82
20		**1s**	3	79

[a] Unless otherwise noted, all reactions were carried out with aryl bromide (1.0 mmol), allylamine **2a** (1.2 mmol), $Pd(OAc)_2$ (1 mol %), TEMPO (10 mmol%), K_2CO_3 (2.0 mmol), DMF (3.0 ml), 100 °C.
[b] Isolated yield.
[c] 2.4 mmol allylamine **2a** was added.

catalytic system also worked effectively for the olefination of a polyhaloarene, furnishing mono- or poly-olefinated products in good yields (Table 2, entries 16–17). Thus, in the presence of 1.2 equiv **2a**, compound **1p** (1,4-dibromobenzene) was mono-olefinated to provide the product **3pa1** as the main product, leaving another position for further functionalization (Table 2, entry 16). Indeed, using 2.4 equiv **2a** led to the di-olefinated product **3pa2** (Table 2, entry 17). The reaction is not only limited to aryl bromides, and heteroaryl bromides participated equally well to afford the corresponding allylamines in good yields (Table 2, entries 18–20). Noteworthy is that all the substrates underwent clean conversions without any allylic migration, diarylation or partial deprotection.

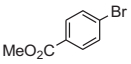
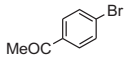
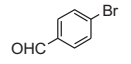
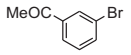
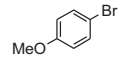
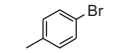
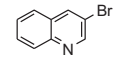
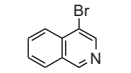
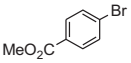
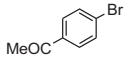
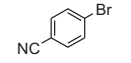
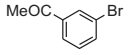
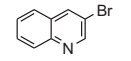
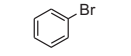
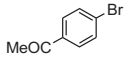
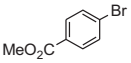
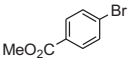
With the success in allylamine **2a**, we then turned our attention to the Heck arylation of other allylamine derivatives. However, under the conditions established for **2a** the arylation of *N*,*N*-diprotected allylamines 2**b**-**d** proved to be problematic. For example, the coupling reaction of **1a** with allylamine **2b** (2-allylisoindoline-1,3-dione) provided the desired (*E*)-allylamine **3ab** in only 30% yield along with a number of unknown side products after 6 h. Gratifyingly, replacing TEMPO with HQ could result in a clean reaction, furnishing an improved yield of 90% (Table 3, entry 1). As can be seen from the results shown in Table 3, the combination of $Pd(OAc)_2$ with HQ could efficiently catalyze the regioselective and stereoselective coupling reactions of aryl bromides with **2b** regardless of the nature of the substituents on the aryl ring, exclusively delivering the linear (*E*)-allylamine products in good to excellent yields. It should be noted, however, that the reaction of aryl bromide bearing electron-rich group required a longer reaction time of 10 h (Table 3, entries 6–7). In the arylation of allylamine **2c** (*N*-Boc-*N*-Cbz-allylamine), it was found that the main reaction product was the γ-arylated *N*-Boc-allylamine product, most probably as a result of the deprotection of Cbz group during the reaction. This problem could be easily resolved simply by decreasing the reaction temperature from 100 °C to 85 °C, which allowed the smooth olefination of electron-deficient aryl bromides to exclusively afford γ-arylated (*E*)-*N*-Boc-*N*-Cbz-allylamines in high yields (Table 3, entries 9–13), albeit with longer reaction times. Likewise, due to the occurrence of deprotection at 100 °C, the more electron-rich allylamine **2d** (ethyl allyl(naphthalen-1-ylmethyl)carbamate) was also arylated at a low temperature of 85 °C, which afforded the (*E*)-allylamine products in high yields with excellent regioselectivities (Table 3, entries 14–15). However, the reaction of electron-rich aryl bromides with either **2c** or **2d** did not proceed under the present conditions. No reaction was observed in the arylation of *N*,*N*-diethyl allylamine (**2e**) (Table 3, entry 16). It is believed that the strong coordination of the nitrogen atom of allylamine **2e** to Pd could result in catalyst poisoning, thereby

Table 3
Regioselective and stereoselective Heck arylation of **2b**–**f** with aryl bromides[a]



1 2b-f 3 4

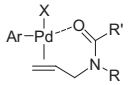
2b: R^1, R^2 = Pht
2c: R^1 = Boc, R^2 = Cbz
2d: R^1 = NaphCH$_2$, R^2 = CO_2Et
2e: R^1 = R^2 = Et
2f: R^1 = Boc, R^2 = H

Entry	Substrate		Olefin	**3**/**4**[b]	Time (h)	Yield (%)[c]
1		**1a**	**2b**	>99/1	6	90
2		**1b**	**2b**	>99/1	6	91
3		**1c**	**2b**	>99/1	6	88
4		**1h**	**2b**	>99/1	6	89
5		**1l**	**2b**	>99/1	10	83
6		**1o**	**2b**	>99/1	10	79
7		**1r**	**2b**	>99/1	6	80
8		**1s**	**2b**	>99/1	6	75
9[d]		**1a**	**2c**	98/2	12	87
10[d]		**1b**	**2c**	98/2	12	89
11[d]		**1e**	**2c**	97/3	12	83
12[d]		**1h**	**2c**	98/2	12	88
13[d]		**1r**	**2c**	98/2	12	81
14[d]		**1k**	**2d**	99/1	12	79
15[d]		**1b**	**2d**	99/1	12	82
16		**1a**	**2e**	nd	12	0
17		**1a**	**2f**	43/57	12	30

[a] Unless otherwise noted, all reactions were carried out with aryl bromide (1.0 mmol), allylamine (1.2 mmol), $Pd(OAc)_2$ (3 mol %), HQ (10 mmol%), K_2CO_3 (2.0 mmol), DMF (3.0 ml), 100 °C; Pht=phthalimidoyl.
[b] Determined by ^{1}H NMR analysis. When no β-arylated product was detected, a value of >99/1 was assigned.
[c] Isolated yield after column chromatography.
[d] The reaction temperature was 85 °C.

inhibiting the arylation. Similar poor performance of *N*,*N*-dialkyl allylamine has been reported recently.[16b,18b] We also tried the arylation of monosubstituted allylamide **2f** (*N*-Boc-allylamine) (Table 3, entry 17), but a mixture of γ- and β-arylated products were obtained with a γ/β ratio of 43/57. It should be pointed out that no product from a potentially competing allylic migration reaction could be detected in all these reactions.

The results presented in Tables 2and 3 indicate that high regioselectivities and stereoselectivities could be obtained only in the arylation of *N*,*N*-diprotected allylamines bearing carbamate protecting groups. In recent studies by Jiao and co-workers,[14a] the high regioselectivities and stereoselectivities observed in the arylation of allyl esters and allylamides was attributed to the chelation between the carbonyl O atom and the Pd atom. In our current investigation, this chelation effect, as shown in **5**, may contribute similarly to the stereoselectivity, as the γ carbon is ideally positioned to accept the migrating aryl group. The necessity for diprotection may partly stem from the steric effect; with decreased steric demanding from the amino moiety, β arylation may become easier, leading to regioisomers in the case of **2f**.



5

3. Conclusions

In summary, we have developed efficient Pd-catalyzed Heck cross-coupling conditions that allow a wide range of aryl bromides to couple, highly regioselectively and stereoselectively, with electron-rich allylamine derivatives, furnishing γ-arylated (*E*)-allylamines in good to excellent yields. The reaction proceeds under ligand-free conditions, and tolerates a diverse range of functionalities. The catalytic efficacy was influenced by a number of factors, such as solvent, protection group, reaction temperature and additives. It is noteworthy that the choice of allylamine derivatives was found to be essential for securing high regioselectivity and stereoselectivity. Further investigation focusing on the arylation of aryl chlorides with allylamines is underway in our laboratory, and will be reported in due course.

4. Experimental section

4.1. General

Unless otherwise noted, all experiments were carried out under an atmosphere of nitrogen using standard Schlenk techniques. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Model Avance DMX 400 Spectrometer (^{1}H 400 MHz and ^{13}C 106.6 MHz, respectively). Chemical shifts (δ) are given in parts per million and are referenced to residual solvent peaks. All organic solvents were dried using standard, published methods and were distilled before use. *N*,*N*-(Boc)$_2$-allylamine (**2a**),[17a] 2-allylisoindoline-1,3-dione (**2b**),[23] *N*-Boc-*N*-Cbz-allylamine (**2c**),[2l] ethyl allyl(naphthalen-1-ylmethyl)carbamate (**2d**),[18c] *N*,*N*-diethyl-allylamine (**2e**)[2n] and *N*-Boc-allylamine (**2f**)[2e] were prepared according to the previous reports. All other chemicals were used as received from Aldrich or Acros without further purification.

4.2. General procedure for the Heck arylation of *N*,*N*-(Boc)$_2$-allylamine (2a)

An oven-dried, two-necked round-bottom flask containing a stir bar was charged with an aryl bromide **1** (1.0 mmol), $Pd(OAc)_2$ (6.8 mg, 0.03 mmol), K_2CO_3 (165.9 mg, 1.2 mmol), TEMPO (15.6 mg, 0.1 mmol), *N*,*N*-(Boc)$_2$-allylamine (308.8 mg, 1.2 mmol) and DMF (3.0 ml) under nitrogen at room temperature. Following degassing

three times, the flask was placed in an oil bath, and the mixture was stirred and heated at 100 °C. After an appropriate reaction time (Tables 2 and 3), the flask was removed from the oil bath and cooled to room temperature. Water (20 ml) was added, and the mixture was extracted with CH_2Cl_2 (3×20 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated in vacuo. The linear arylated allylamine was isolated out of the crude product by flash chromatography on silica gel using a mixture of ethyl acetate and hexane.

*4.2.1. (E)-Methyl 4-(3-(bis(tert-butoxycarbonyl)amino)prop-1-enyl) benzoate (**3aa**).*[18b] White solid, mp 82–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J*=8.24 Hz, 2H), 7.38 (d, *J*=8.28 Hz, 2H), 6.53 (d, *J*=15.92 Hz, 1H), 6.32 (dt, *J*=15.94, 6.04 Hz, 1H), 4.33 (d, *J*=6.04 Hz, 2H), 3.86 (s, 3H), 1.49 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.6, 152.2, 141.2, 131.1, 129.8, 129.0, 128.0, 126.2, 82.4, 51.8, 47.9, 28.0; HRMS (ESI) calcd for $C_{21}H_{29}NNaO_6$ $[M+Na]^+$: 414.1887, found: 414.1896.

*4.2.2. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(4-acetylphenyl)prop-2-en-1-amine (**3ba**).*[18b] Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J*=8.16 Hz, 2H), 7.33 (d, *J*=8.08 Hz, 2H), 6,46 (d, *J*=15.88 Hz, 1H), 6.26 (dt, *J*=15.88, 5.92 Hz, 1H), 4.26 (d, *J*=5.76 Hz, 2H), 2.45 (s, 3H), 1.41 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.6, 152.2, 141.3, 135.9, 130.9, 128.6, 128.2, 126.3, 82.4, 47.6, 28.0, 26.4; HRMS (ESI) calcd for $C_{21}H_{29}NNaO_5$ $[M+Na]^+$: 398.1938, found: 398.1939.

*4.2.3. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(4-formylphenyl)prop-2-en-1-amine (**3ca**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.82 (d, *J*=8.20 Hz, 2H), 7.50 (d, *J*=8.20 Hz, 2H), 6.57 (d, *J*=15.92 Hz, 1H), 6.39 (dt, *J*=15.92, 6.00 Hz, 1H), 4.37 (d, *J*=6.00 Hz, 2H), 1.52 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.3, 142.8, 135.4, 130.9, 130.1, 129.1, 126.9, 82.7, 47.9, 28.1; HRMS (ESI) calcd for $C_{20}H_{27}NNaO_5$ $[M+Na]^+$: 384.1781, found: 384.1789.

*4.2.4. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(3-(trifluoromethyl)phenyl)prop-2-en-1-amine (**3da**).*[18b] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.51 (d, *J*=7.56 Hz, 1H), 7.45 (d, *J*=7.68 Hz, 1H), 7.40 (t, *J*=7.64 Hz, 1H), 6.54 (d, *J*=15.92 Hz, 1H), 6.29 (dt, *J*=15.88, 6.08 Hz, 1H), 4.35 (d, *J*=6.08 Hz, 2H), 1.51(s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.4, 137.6, 130.7, 129.5, 129.0, 127.3, 124.0, 123.0, 122.9, 116.1, 82.5, 47.9, 28.0; HRMS (ESI) calcd for $C_{20}H_{26}NNaF_3O_4$ $[M+Na]^+$: 424.1706, found: 424.1708.

*4.2.5. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(4-cyanophenyl)prop-2-en-1-amine (**3ea**).*[18b] Yellow solid, mp 79–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J*=8.16 Hz, 2H), 7.43 (d, *J*=8.24 Hz, 2H), 6.53 (d, *J*=15.96 Hz, 1H), 6.35 (dt, *J*=15.88, 5.96 Hz, 1H), 4.36 (d, *J*=7.72 Hz, 2H), 1.51 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.3, 141.3, 132.4, 130.3, 129.4, 126.9, 118.9, 110.8, 82.7, 47.8, 28.1; HRMS (ESI) calcd for $C_{20}H_{26}N_2NaO_4$ $[M+Na]^+$: 381.1785, found: 381.1789.

*4.2.6. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(2-cyanophenyl)prop-2-en-1-amine (**3fa**).* Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (m, 3H), 7.22 (m, 1H), 6.77 (d, *J*=15.88 Hz, 1H), 6.35 (dt, *J*=15.88, 5.94 Hz, 1H), 4.31 (d, *J*=6.00 Hz, 2H), 1.44 (s, 18H), ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.1, 139.7, 132.8, 132.7, 130.6, 127.7, 127.5, 125.6, 117.6, 110.9, 82.6, 47.8, 28.0; HRMS (ESI) calcd for $C_{20}H_{26}N_2NaO_4$ $[M+Na]^+$: 381.1785, found: 381.1792.

*4.2.7. (E)-Di-tert-butyl 3-(1-oxo-2,3-dihydro-1H-inden-5-yl)allyliminodicarbonate (**3ga**).* Yellow solid, mp 55–57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J*=7.96 Hz, 1H), 7.27 (s, 1H), 7.20 (d, *J*=8.08 Hz, 1H), 6.42 (d, *J*=15.92 Hz, 1H), 6.24 (dt, *J*=15.92, 5.96 Hz, 1H), 4.22 (d, *J*=5.76 Hz, 2H), 2.93 (m, 2H), 2.47 (m, 2H), 1.37 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 205.8, 155.6, 152.1, 142.9, 136.1, 131.2, 128.6, 125.5, 124.1, 123.6, 82.3, 47.9, 36.2, 27.9, 25.5; HRMS (ESI) calcd for $C_{22}H_{29}NNaO_5$ $[M+Na]^+$: 410.1938, found: 410.1941.

*4.2.8. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(3-acetylphenyl)prop-2-en-1-amine (**3ha**).* Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.81 (d, *J*=7.72 Hz, 1H), 7.56 (d, *J*=7.76 Hz, 1H), 7.41 (t, *J*=7.72 Hz, 1H), 6.57 (d, *J*=15.92 Hz, 1H), 6.31 (dt, *J*=6.12, 15.88 Hz, 1H), 4.36 (d, *J*=6.12 Hz, 2H), 2.61 (s, 3H), 1.52 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.0, 152.4, 137.4, 137.3, 131.2, 130.8, 128.8, 127.5, 126.7, 126.1, 82.5, 48.0, 28.1, 26.7; HRMS (ESI) calcd for $C_{21}H_{29}NNaO_5$ $[M+Na]^+$: 398.1938, found: 398.1943.

*4.2.9. (E)-Di-tert-butyl-3-(8-oxo-5,6,7,8-tetrahydronaphthalen-2-yl) allyliminodicarbonate (**3ia**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.45 (m, 1H), 7.18 (d, *J*=7.92 Hz, 1H), 6.51 (d, *J*=15.88 Hz, 1H), 6.25 (dt, *J*=15.88, 6.08 Hz, 1H), 4.32 (d, *J*=6.08 Hz, 2H), 2.89 (m, 2H), 2.60 (m, 2H), 2.08 (m, 2H), 1.50 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.3, 152.3, 143.7, 135.3, 132.6, 131.1, 131.0, 129.1, 125.9, 124.8, 82.4, 48.0, 39.1, 29.4, 28.1, 23.2; HRMS (ESI) calcd for $C_{23}H_{31}NNaO_5$ $[M+Na]^+$: 424.2094, found: 424.2099.

*4.2.10. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(3-(cyclohexanecarbonyl) phenyl)prop-2-en-1-amine (**3ja**).* White solid, mp: 76–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.75 (d, *J*=7.72 Hz, 1H), 7.50 (d, *J*=7.72 Hz, 1H), 7.35 (m, 1H), 6.54 (d, *J*=15.92 Hz, 1H), 6.28 (dt, *J*=15.92, 6.08 Hz, 1H), 4.32 (d, *J*=6.08 Hz, 2H), 3.20 (m, 1H), 1.78 (m, 4H), 1.38 (m, 24H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 203.5, 152.3, 137.3, 136.6, 131.3, 130.3, 128.7, 127.3, 126.5, 126.1, 82.4, 47.9, 45.6, 29.3, 28.0, 25.9, 25.7; HRMS (ESI) calcd for $C_{26}H_{37}NNaO_5$ $[M+Na]^+$: 466.2564, found: 466.2568.

*4.2.11. (E)-N,N-Bis(tert-butoxycarbonyl)-3-phenyl prop-2-en-1-amine (**3ka**).*[18b] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 2H), 7.31 (t, *J*=7.76, 2H), 7.24 (t, *J*=7.16 Hz, 1H), 6.54 (d, *J*=15.88 Hz, 1H), 6.23 (dt, *J*=15.88, 6.24 Hz, 1H), 4.34 (d, *J*=6.08 Hz, 2H), 1.52 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.4, 136.8, 133.8, 128.5, 127.6, 126.4, 125.1, 82.4, 48.5, 28.1; HRMS (ESI) calcd for $C_{19}H_{27}NNaO_4$ $[M+Na]^+$: 356.1832, found: 356.1836.

*4.2.12. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(4-methoxyphenyl)prop-2-en-1-amine (**3la**).*[18b,c] Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J*=8.68 Hz, 2H), 7.30 (d, *J*=8.64 Hz, 2H), 6.49 (d, *J*=15.84 Hz, 1H), 6.26 (dt, *J*=15.84, 6.00 Hz, 1H), 4.26 (d, *J*=8.00 Hz, 2H), 2.45 (s, 3H), 1.41 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 159.2, 152.4, 131.9, 129.5, 127.5, 122.7, 113.9, 82.2, 55.1, 48.2, 28.1; HRMS (ESI) calcd for $C_{20}H_{29}NNaO_5$ $[M+Na]^+$: 386.1938, found: 386.1941.

*4.2.13. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(3-methoxyphenyl)prop-2-en-1-amine (**3ma**).* Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (m, 1H), 6.95 (d, *J*=7.68 Hz, 1H), 6.90 (s, 1H), 6.78 (m, 1H), 6.51 (d, *J*=15.84 Hz, 1H), 6.22 (dt, *J*=15.84, 5.90 Hz, 1H), 4.34 (m, 2H), 3.79 (s, 3H), 1.51 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 159.8, 152.3, 138.2, 132.2, 129.5, 125.4, 119.0, 113.2, 111.7, 82.4, 55.1, 48.1, 28.1; HRMS (ESI) calcd for $C_{20}H_{29}NNaO_5$ $[M+Na]^+$: 386.1938, found: 386.1943.

*4.2.14. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(3,4,5-trimethoxyphenyl) prop-2-en-1-amine (**3na**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 (s, 2H), 6.44 (d, *J*=15.76 Hz, 1H), 6.12 (dt, *J*=15.76, 6.28 Hz, 1H), 4.31(d, *J*=6.26 Hz, 2H), 3.85 (s, 6H), 3.82 (s, 3H), 1.50 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.3, 152.5, 137.8, 132.5, 132.3, 124.6, 103.5, 82.4, 60.9, 56.1, 48.1, 28.1; HRMS (ESI) calcd for $C_{22}H_{33}NNaO_7$ $[M+Na]^+$: 446.2149, found: 446.2157.

*4.2.15. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(4-tolyl)prop-2-en-1-amine (**3oa**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J*=7.04 Hz, 2H), 7.11 (d, *J*=8.0 Hz, 2H), 6.50 (d, *J*=15.88 Hz, 1H), 6.16

(dt, *J*=15.88, 6.12 Hz, 1H), 4.32 (d, *J*=6.28 Hz, 2H), 2.33 (s, 3H), 1.51 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.3, 133.8, 132.3, 129.2, 126.3, 124.0, 116.2, 82.2, 48.5, 28.0; HRMS (ESI) calcd for $C_{20}H_{29}NNaO_4$ $[M+Na]^+$: 370.1989, found: 370.1995.

*4.2.16. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(4-bromophenyl)prop-2-en-1-amine (**3pa1**).*[18b] Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J*=8.45 Hz, 2H), 7.24 (d, *J*=8.44 Hz, 2H), 6.46 (d, *J*=15.88 Hz, 1H), 6.22 (dt, *J*=15.88, 6.12 Hz, 1H), 4.32 (d, *J*=6.28 Hz, 2H), 1.51(s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.3, 135.7, 131.6, 131.0, 127.9, 126.0, 121.3, 82.5, 48.0, 28.1; HRMS (ESI) calcd for $C_{19}H_{26}BrNNaO_4$ $[M+Na]^+$: 434.0937, found: 434.0933.

*4.2.17. (2E,2′E)-N,N,N,N-Tetra(tert-butoxycarbonyl)-3,3′-(1,4-phenylene)diprop-2-en-1-amine (**3pa2**).* White solid, mp 119–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 4H), 6.52 (d, *J*=15.86 Hz, 2H), 6.22 (dt, *J*=6.24, 15.86 Hz, 2H), 4.34 (d, *J*=6.0 Hz, 4H), 1.53 (s, 36H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.4, 136.1, 131.9, 126.6, 125.1, 82.4, 48.2, 28.1; HRMS (ESI) calcd for $C_{32}H_{48}N_2NaO_8$ $[M+Na]^+$: 611.3303, found:611.3308.

*4.2.18. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(3-pyridyl)prop-2-en-1-amine (**3qa**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J*=1.6 Hz, 1H), 8.29 (m, 1H), 7.52 (d, *J*=7.92 Hz, 1H), 7.07 (m, 1H), 6.36 (d, *J*=16.00 Hz, 1H), 6.16 (dt, *J*=16.00, 5.98 Hz, 1H), 4.20 (d, *J*=5.92 Hz, 2H), 1.36 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.1, 148.3, 148.0, 132.6, 132.2, 128.3, 127.5, 123.2, 82.2, 47.7, 27.8; HRMS (ESI) calcd for $C_{18}H_{27}N_2O_4$ $[M+H]^+$: 335.1965, found: 335.1971.

*4.2.19. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(quinolin-3-yl)prop-2-en-1-amine (**3ra**).* White solid, mp 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, *J*=2.04 Hz, 1H), 8.06 (m, 2H), 7.80 (d, *J*=8.08 Hz, 1H), 7.67 (m, 1H), 7.54 (m, 1H), 6.70 (d, *J*=16.00 Hz, 1H), 6.48 (dt, *J*=16.00, 5.98 Hz 1H), 4.42 (m, 2H), 1.54 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.4, 149.3, 147.5, 132.4, 129.7, 128.9, 128.0, 127.8, 126.9, 82.7, 48.1, 28.1; HRMS (ESI) calcd for $C_{22}H_{29}N_2O_4$ $[M+H]^+$: 385.2122, found: 385.2125.

*4.2.20. (E)-N,N-Bis(tert-butoxycarbonyl)-3-(isoquinolin-4-yl)prop-2-en-1-amine (**3sa**).* Yellow solid, mp 90–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.59 (s, 1H), 8.05 (d, *J*=8.44 Hz, 1H), 7.98 (d, *J*=8.08 Hz, 1H), 7.73 (t, *J*=7.26 Hz, 1H), 7.62 (t, *J*=7.28 Hz, 1H), 7.14 (d, *J*=15.72 Hz, 1H), 6.33 (dt, *J*=15.76, 5.92 Hz, 1H), 4.47 (d, *J*=5.88 Hz, 2H), 1.55 (s, 18H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.4, 151.9, 140.6, 133.7, 130.4, 130.2, 128.2, 128.1, 127.3, 127.2, 126.1, 122.9, 82.6, 48.2, 28.1; HRMS (ESI) calcd for $C_{22}H_{29}N_2O_4$ $[M+H]^+$: 385.2122, found: 385.2129.

4.3. General procedure for Heck arylation of allylamines 2b–f

An oven-dried, two-necked round-bottom flask containing a stir bar was charged with an aryl bromide **1** (1.0 mmol), $Pd(OAc)_2$ (6.8 mg, 0.03 mmol), K_2CO_3 (165.9 mg, 1.2 mmol), HQ (15.6 mg, 0.1 mmol), allylamine (1.2 mmol), and DMF (3.0 ml) under nitrogen at room temperature. Following degassing three times, the flask was placed in an oil bath, and the mixture was stirred and heated at the appropriate temperature. After an appropriate reaction time, the flask was removed from the oil bath and cooled to room temperature. Water (20 ml) was added, and the mixture was extracted with CH_2Cl_2 (3×20 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated in vacuo. The product was purified by flash column chromatography on silica gel using ethyl acetate/hexane as an eluent.

*4.3.1. (E)-methyl 4-(3-(1,3-dioxoisoindolin-2-yl)prop-1-enyl)benzoate (**3ab**).* White solid, mp 153–155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J*=8.24 Hz, 2H), 7.91 (m, 2H), 7.77 (m, 2H), 7.44 (d, *J*=8.28 Hz, 2H), 6.71 (d, *J*=15.84, 1H), 6.41 (dt, *J*=15.84, 6.28 Hz, 1H), 4.51 (d, *J*=6.24 Hz, 2H), 3.94 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 168.0, 166.8, 140.8, 134.3, 134.2, 132.7, 132.2, 129.9, 126.5, 125.6, 123.4, 52.1, 39.6; HRMS (ESI) calcd for $C_{19}H_{15}NNaO_4$ $[M+Na]^+$: 344.0893, found: 344.0899.

*4.3.2. (E)-2-(3-(4-acetylphenyl)allyl)isoindoline-1,3-dione (**3bb**).* White solid, mp 145–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (m, 4H), 7.74 (d, *J*=8.44 Hz, 2H), 7.44 (d, *J*=8.28 Hz, 2H), 6.69 (d, *J*=15.84 Hz, 1H), 6.39 (dt, *J*=15.84, 6.28 Hz, 1H), 4.49 (d, *J*=6.28 Hz, 2H), 2.59 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.5, 167.9, 140.9, 136.3, 134.1, 132.5, 132.1, 128.7, 126.6, 125.8, 123.4, 39.5, 26.6; HRMS (ESI) calcd for $C_{19}H_{15}NNaO_3$ $[M+Na]^+$: 328.0944, found: 328.0946.

*4.3.3. (E)-4-(3-(1,3-Dioxoisoindolin-2-yl)prop-1-enyl)benzaldehyde (**3cb**).* White solid, mp 168–170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.90 (m, 2H), 7.82 (d, *J*=8.2 Hz, 2H), 7.76 (m, 2H), 7.52 (d, *J*=8.2 Hz, 2H), 6.71 (d, *J*=15.88 Hz, 1H), 6.44 (dt, *J*=15.88, 6.28 Hz, 1H), 4.50 (d, *J*=6.25 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 191.7, 167.9, 142.2, 135.6, 134.1, 132.4, 132.1, 130.1, 127.0, 126.6, 123.4, 39.5; HRMS (ESI) calcd for $C_{18}H_{13}NNaO_3$ $[M+Na]^+$: 314.0788, found: 314.0794.

*4.3.4. (E)-2-(3-(3-Acetylphenyl)allyl)isoindoline-1,3-dione (**3hb**).* White solid, mp 153–155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.88 (m, 2H), 7.81 (d, *J*=7.68 Hz, 1H), 7.74 (m, 2H), 7.55 (d, *J*=7.72 Hz, 1H), 7.39 (t, *J*=7.72 Hz, 1H), 6.69 (d, *J*=15.84 Hz, 1H), 6.34 (dt, *J*=15.84, 6.28 Hz, 1H), 4.48 (d, *J*=6.24 Hz, 2H), 2.60 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.9, 167.9, 137.4, 136.7, 134.1, 132.6, 132.1, 130.9, 128.8, 127.7, 126.4, 124.3, 123.4, 39.5, 26.7; HRMS (ESI) calcd for $C_{19}H_{15}NNaO_3$ $[M+Na]^+$: 328.0944, found: 328.0949.

*4.3.5. (E)-2-(3-(4-Methoxyphenyl)allyl)isoindoline-1,3-dione (**3lb**).*[18c] White solid, mp 140–142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (m, 2H), 7.73 (m, 2H), 7.31 (d, *J*=8.72 Hz, 2H), 6.83 (d, *J*=8.72 Hz, 2H), 6.63 (d, *J*=15.78 Hz, 1H), 6.13 (dt, *J*=15.76, 6.56 Hz, 1H), 4.44 (dd, *J*=6.62, 1.04 Hz, 2H), 3.81 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 168.0, 159.4, 134.0, 133.4, 132.2, 129.0, 127.8, 123.3, 120.5, 113.9, 55.3, 39.8; HRMS (ESI) calcd for $C_{18}H_{15}NNaO_3$ $[M+Na]^+$: 316.0944, found: 316.0947.

*4.3.6. (E)-2-(3-p-Tolylallyl)isoindoline-1,3-dione (**3ob**).* White solid, mp 164–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (m, 2H), 7.73 (m, 2H), 7.27 (d, *J*=8.08 Hz, 2H), 7.11 (d, *J*=8.08 Hz, 2H), 6.65 (d, *J*=15.84 Hz, 1H), 6.22 (dt, *J*=15.84, 6.56 Hz, 1H), 4.45 (d, *J*=6.52 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 168.0, 127.8, 134.0, 133.8, 133.5, 132.2, 129.2, 126.5, 123.3, 121.7, 39.8, 21.2; HRMS (ESI) calcd for $C_{18}H_{15}NNaO_2$ $[M+Na]^+$: 300.0995, found: 300.0997.

*4.3.7. (E)-2-(3-(Quinolin-3-yl)allyl)isoindoline-1,3-dione (**3rb**).* White solid, mp 178–180 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, *J*=2.12 Hz, 1H), 8.05 (m, 2H), 7.88 (m, 2H), 7.74 (m, 3H), 7.67 (m, 1H), 7.48 (m, 1H), 6.80 (d, *J*=16.32 Hz, 1H), 6.50 (dt, *J*=16.32, 6.28 Hz, 1H), 4.54 (d, *J*=6.28 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.9, 149.2, 147.6, 134.1, 132.8, 132.1, 130.4, 129.4, 129.2, 129.1, 127.9, 127.0, 125.3, 123.4, 122.7, 39.6; HRMS (ESI) calcd for $C_{20}H_{15}N_2O_2$ $[M+H]^+$: 315.1128, found: 315.1135.

*4.3.8. (E)-2-(3-(Isoquinolin-4-yl)allyl)isoindoline-1,3-dione (**3sb**).* White solid, mp 162–164 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.53 (s, 1H), 8.00 (d, *J*=8.36 Hz, 1H), 7.91 (d, *J*=8.12 Hz, 1H), 7.84 (m, 2H), 7.69 (m, 3H), 7.57 (m, 1H),7.23 (d, *J*=15.72 Hz, 1H), 6.31 (dt, *J*=15.68, 6.32 Hz, 1H), 4.54 (d, *J*=6. 32 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.9, 152.1, 140.6, 134.1, 133.9, 133.5, 132.1,

130.6, 128.0, 127.9, 127.8, 127.7, 127.2, 123.4, 122.9, 39.8; HRMS (ESI) calcd for $C_{20}H_{15}N_2O_2$ $[M+H]^+$: 315.1128, found: 315.1132.

*4.3.9. (E)-Methyl4-(3-(N-carbobenzyloxy-N-tert-butoxycarbonyl amino)prop-1-enyl)benzoate (**3ac**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J=8.24 Hz, 2H), 7.36 (m, 7H), 6.53 (d, J=15.92 Hz, 1H), 6.33 (dt, J=15.92, 6.08 Hz, 1H), 5.26 (s, 2H), 4.44 (d, J=5.88 Hz, 2H), 3.91 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.8, 153.6, 151.8, 141.1, 135.4, 131.6, 129.9, 129.1, 128.6, 128.4, 128.3, 127.4, 126.3, 83.2, 68.5, 52.1, 48.1, 28.0; HRMS (ESI) calcd for $C_{24}H_{27}NNaO_6$ $[M+Na]^+$: 448.1731, found: 448.1738.

*4.3.10. (E)-N-Carbobenzyloxy-N-tert-butoxycarbonyl-3-(4-acetylphenyl)prop-2-en-1-amine (**3bc**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J=8.24 Hz, 2H), 7.38 (m, 7H), 6.55 (d, J=15.92 Hz, 1H), 6.36 (dt, J=15.92, 6.08 Hz, 1H), 5.28 (s, 2H), 4.46 (d, J=5.88 Hz, 2H), 2.62 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.5, 153.6, 151.8, 141.3, 136.2, 135.4, 131.6, 128.7, 128.6, 128.4, 128.3, 127.7, 126.5, 83.2, 68.6, 48.2, 28.0, 26.6; HRMS (ESI) calcd for $C_{24}H_{27}NNaO_5$ $[M+Na]^+$: 432.1781, found: 432.1783.

*4.3.11. (E)-N-Carbobenzyloxy-N-tert-butoxycarbonyl-3-(4-cyanophenyl)prop-2-en-1-amine (**3ec**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J=8.28 Hz, 2H), 7.38 (m, 7H), 6.50 (d, J=15.96 Hz, 1H), 6.35 (dt, J=15.92, 5.96 Hz, 1H), 5.26 (s, 2H), 4.45 (d, J=5.96 Hz, 2H), 1.50 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.6, 151.8, 141.1, 135.4, 132.4, 130.8, 128.8, 128.6, 128.5, 128.4, 126.9, 118.9, 110.9, 83.4, 68.6, 48.0, 28.0; HRMS (ESI) calcd for $C_{23}H_{24}N_2NaO_4$ $[M+Na]^+$: 415.1628, found: 415.1635.

*4.3.12. (E)-N-Carbobenzyloxy-N-tert-butoxycarbonyl-3-(3-acetylphenyl)prop-2-en-1-amine (**3hc**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.82 (d, J=7.72 Hz, 1H), 7.62 (d, J=7.76 Hz, 1H), 7.39 (m, 6H), 6.54 (d, J=15.88 Hz, 1H), 6.30 (dt, J=15.88, 6.16 Hz, 1H), 5.25 (s, 2H), 4.43 (d, J=6.12 Hz, 2H), 2.60 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.0, 153.6, 151.9, 137.4, 137.1, 135.4, 131.7, 130.8, 128.8, 128.6, 128.4, 128.3, 127.6, 126.2, 126.1, 83.2, 68.5, 48.1, 28.0, 26.7; HRMS (ESI) calcd for $C_{24}H_{27}NNaO_5$ $[M+Na]^+$: 432.1781, found: 432.1787.

*4.3.13. (E)-N-Carbobenzyloxy-N-tert-butoxycarbonyl-3-(quinolin-3-yl)prop-2-en-1-amine (**3rc**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, J=2.12 Hz, 1H), 8.08 (d, J=8.52 Hz, 1H), 7.97 (s, 1H), 7.78 (d, J=7.68 Hz, 1H), 7.67 (m, 1H), 7.53 (m, 1H), 7.42 (m, 2H), 7.35 (m, 3H), 6.64 (d, J=16.02 Hz, 1H), 6.45 (dt, J=16.04, 6.08 Hz, 1H), 5.28 (s, 2H), 4.49 (d, J=6.08 Hz, 2H), 1.52 (s, 9H) H; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.6, 151.9, 149.2, 147.5, 135.4, 132.6, 129.5, 129.4, 129.3, 129.2, 128.6, 128.4, 128.3, 127.9, 127.8, 127.2, 127.0, 83.3, 68.6, 48.2, 28.0; HRMS (ESI) calcd for $C_{25}H_{27}N_2O_4$ $[M+H]^+$: 419.1965, found: 419.1971.

*4.3.14. (E)-Ethyl 3-(4-acetylphenyl)(naphthalen-1-ylmethyl)allylcarbamate (**3bd**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (m, 1H), 7.76 (d, J=7.36 Hz, 3H), 7.70 (d, J=8.28 Hz, 1H), 7.39 (m, 4H), 7.19 (d, J=8.24 Hz, 2H), 6.16 (m, 2H), 4.97 (d, J=15.44 Hz, 2H), 4.24 (dd, J=7.08, 1.6 Hz, 2H), 3.95 (m, 2H), 2.44 (s, 3H), 1.25 (t, J=7.92 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.2, 156.3, 141.2, 135.9, 133.9, 132.8, 131.8, 131.3, 130.8, 128.6, 128.0, 126.8, 126.3, 125.9, 125.3, 124.9, 123.8, 123.0, 61.7, 48.0, 47.2, 26.4, 14.8; HRMS (ESI) calcd for $C_{25}H_{25}NNaO_3$ $[M+Na]^+$: 410.1727, found: 410.1723.

*4.3.15. Ethyl cinnamyl(naphthalen-1-ylmethyl)carbamate (**3kd**).* White solid, mp 48–50 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (m, 1H), 7.92 (d, J=7.60 Hz, 1H), 7.85 (d, J=8.21 Hz, 1H), 7.56 (m, 2H), 7.51 (m, 1H), 7.41 (s, 1H), 7.34 (m, 4H), 7.27 (m, 1H), 6.41 (d, J=15.88 Hz, 1H), 6.24 (dt, J=15.88, 6.48 Hz, 1H), 5.07 (s, 2H), 4.32 (dd, J=6.49, 1.5 Hz, 2H), 4. 02 (m, 2H), 1.34 (t, J=8.2 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.6, 136.7, 133.9, 132.9, 132.3, 128.8, 128.6, 128.2, 127.7, 126.8, 126.4, 125.9, 125.4, 125.3, 124.8, 124.0, 123.0, 61.8, 47.6, 47.2, 14.9; HRMS (ESI) calcd for $C_{23}H_{23}NNaO_2$ $[M+Na]^+$: 368.1621, found: 368.1629.

*4.3.16. (E)-Methyl 4-(3-((tert-butoxycarbonyl)amino)prop-1-en-1-yl)benzoate (**3af**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J=8.21 Hz, 2H), 7.41 (d, J=8.24 Hz, 2H), 6.55 (d, J=15.92 Hz, 1H), 6.33 (dt, J=15.88, 5.72 Hz, 1H), 4.81 (bs, 1H), 3.95 (s, 2H), 3.92 (s, 3H), 1.49 (s, 9H) zHzHz H; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.9, 155.8, 141.2, 130.2, 129.9, 129.4, 128.6, 126.2, 79.6, 52.1, 42.6, 28.4; HRMS (ESI) calcd for $C_{16}H_{22}NO_4$ $[M+H]^+$: 292.1543, found: 292.1548.

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