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# Microwave-Assisted *N*-Allylation/Homoallylation-RCM Approach: Access to Pyrrole-, Pyridine-, or Azepine-Appended (Het)aryl Aminoamides

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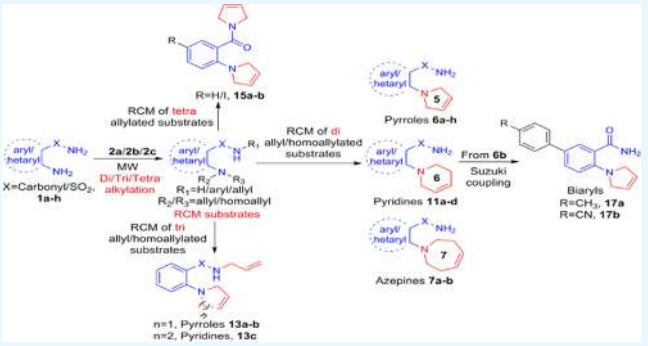
**ABSTRACT:** A facile and diversity-oriented approach has been developed for the synthesis of pyrrole-, pyridine-, or azepine-appended (het)aryl aminoamides via the *N*-allylation/homoallylation-ring-closing metathesis (RCM) strategy. Microwave condition was efficiently utilized for *N*-allylation of (het)aryl aminoamides to synthesize di-, tri-, and tetra-allyl/homoallylated RCM substrates in good yields. All of the RCM substrates were successfully converted to respective pyrroles **6a−h**, **13a,b**, **15a,b**, pyridines **11a−d**, **13c**, and azepines **7a,b** via RCM. All of the five-, six-, and seven-membered *N*-heterocycles were synthesized in shorter reaction times with excellent yields without isomerization products. A one-pot reaction to synthesize compounds **6a** and **6b** without isolating corresponding RCM substrates was achieved successfully. The synthetic utility of the compound **6b** has been demonstrated by synthesizing biaryl derivatives **17a,b** under the microwave Suzuki coupling reaction condition.




## INTRODUCTION

Among the various *N*-heterocycle compounds, pyrroles, pyridines, and azepines are the most predominant constituents in many natural products, pharmaceuticals, and functionalized organic molecules.[1−6]

Particularly, many drug molecules and alkaloids possess dihydro pyrroles, tetrahydro pyridines, and tetrahydroazepines as their core moiety (Figure 1).[7−13]

Thus, various expedient routes have been developed for their synthesis. Individually, dihydro pyrroles have been synthesized from intramolecular hydroamination of homoallylic aminols,[14] cyclization of 4-amino butynols,[15] amines with 1,4-dichloro-2-butene under microwave (MW) condition,[16] reaction of Huisgen zwitter ion with benzoyl chlorides,[17] and Nb-catalyzed ring-closing metathesis (RCM) of *N*,*N*-diallyl-sulfonamides,[18] as well as from allyl alcohols with amines followed by RCM.[19]

On the other hand, tetrahydro pyridines have been synthesized via the reaction of vinyl silanes with iminium/acyl iminium ion,[20] alkyne-aza-Prins cyclization of tosyl amines and aldehydes,[21] radical cyclization of 1,6-enynes,[22] reaction of amine aldehyde and esters via the multicomponent reaction (MCR) approach,[23,24] and chemoenzymatic one-pot cascade approach of diallylamines,[25] as well as from diallyl aniline using additives via RCM.[26]

Tetrahydroazepines have been synthesized from cyclohexanone oxime,[27] Overman rearrangement−RCM pathway of allylic alcohols,[13] vinylation of imine−RCM pathway,[28] and the reaction of methyl acrylate and allyl amine via RCM.[29]

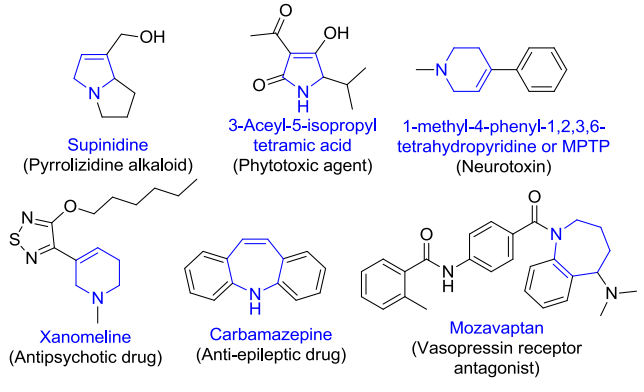



**Figure 1.** Biologically important compounds with pyrrole, pyridine, and azepine heterocycles as cores.

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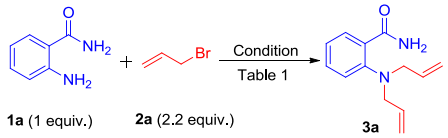
In recent years, the microwave (MW) irradiation method has emerged as a complementary tool to classical synthesis.[30,31] And the ring-closing metathesis (RCM)[32−35] has been proved as a key step in synthesizing five- and six-membered *N*-heterocycles. The methods developed for the synthesis of five-, six-, and seven-membered nitrogen heterocycles[14−29] require longer and harsh reaction conditions, and more importantly, they suffer isomerization of the product, which impacts the yield of the desired product. To overcome these difficulties and also in continuation to our previous efforts,[36] we have developed the microwave-assisted *N*-allylation/homoallylation-RCM approach to synthesize five-, six-, and seven-membered nitrogen heterocycles. The details of the study are presented in this manuscript.

## RESULTS AND DISCUSSION

Initially, a mixture of 1 equiv of 2-aminobenzamide (**1a**) and 2.2 equiv of allyl bromide (**2a**), with $Et_3N$ as base in $CH_3CN$ was microwave-irradiated (100 W) for 4 min. The reaction afforded 2-(diallylamino)benzamide (**3a**) in 60% yield (Table 1, entry 1).

**Table 1. Optimization of the Synthesis of Compound 3a**[a,b]




**1a** (1 equiv.) **2a** (2.2 equiv.) **3a**

| entry | base | solvent | MW power (W) | irradiation time (min) | % yield **3a**[c] |
|---|---|---|---|---|---|
| 1 | $Et_3N$ | $CH_3CN$ | 100 | 4 | 60 |
| 2 | $Et_3N$ | $CH_3CN$ | 100 | 6 | 75 |
| 3 | $Et_3N$ | $CH_3CN$ | 100 | 8 | 65 |
| 4 | $Et_3N$ | $CH_3CN$ | 200 | 2 | 60 |
| 5 | $Et_3N$ | $CH_3CN$ | 200 | 4 | 85 |
| 6 | $Et_3N$ | $CH_3CN$ | 200 | 6 | 82 |
| 7 | $Et_3N$ | $CH_3CN$ | 300 | 2 | 65 |
| 8 | $Et_3N$ | $CH_3CN$ | 300 | 4 | 80 |
| 9 | $K_2CO_3$ | $CH_3CN$ | 200 | 4 | 92[d] |
| 10 | $Na_2CO_3$ | $CH_3CN$ | 200 | 4 | 87 |
| 11 | $CaH_2$ | $CH_3CN$ | 200 | 4 | 85 |
| 12 | $K_2CO_3$ | DMF | 200 | 4 | 90 |
| 13 | $K_2CO_3$ | toluene | 200 | 4 | 90 |
| 14 | $K_2CO_3$ | $CH_3CN$ | | | 83[e] |

[a]Reaction conditions: All of the reactions were carried out on a CEM Discover-300 microwave synthesizer. [b]Power mode, 50 psi. [c]Isolated yield. [d]Optimized condition. [e]Reflux for 12 h.

The structure of compound **3a** ($N_1$,$N_1$-diallylated product) was confirmed after thorough characterization by the spectroscopic method. It should be noted that the other possible $N_1$,$N_2$-diallylated and $N_1$/$N_2$-monoallylated products were not observed under this condition.

To improve the yield of **3a**, an optimization study was undertaken and the parameters such as microwave power, irradiation time, base, and solvent were considered. Thus, a reaction of compounds **1a** and **2a** in a 1:2.2 ratio was microwave-irradiated at 100 W for 6 min showed a slight improvement of yield of **3a** (75%) (Table 1, entry 2). However, upon prolonging the irradiation time to 8 min, a decreased yield of **3a** was noted (Table 1, entry 3). Further, improved yields of **3a** up to 80% were observed by increasing the microwave power level to 200 and 300 W (Table 1, entries 4−8). Significantly, screening the base afforded compound **3a** in excellent yield of up to 92% (Table 1, entries 9−11). The solvent effect in improving the yield of **3a** was minimal (Table 1, entries 12 and 13). A reaction under conventional heating yielded the desired product **3a** in 83% yield in a longer reaction of 12 h (Table 1, entry 14). Thus, conditions shown in entry 9 of Table 1 were found to be optimum.

Encouraged by the preliminary results, and to expand the scope and diversity of the reaction, various (het)aryl aminoamides **1a−h** and alkyl halides **2a−c** were screened and the reaction afforded respective diallylated/homoallylated products **3a−h**, **4a,b**, and **5a** (Figure 2). Aminoamides **1a−h** with allyl bromide **2a** afforded diallylated products **3a−h** in good to excellent yields, whereas the reaction with **2b** and **2c** afforded products **4a,b** and **5a** in relatively lower yields. This may be due to the reactivity and stability of the corresponding carbocation of allylation/homoallylation reagents **2a−c**. Variable yields were observed for the products **3a**, **3f**, and **3g** as the position of the amine group in the substrate is changed. Thus, the allylation of substrates **1a** (*ortho*-$NH_2$) and **1g** (*para*-$NH_2$) afforded **3a** (92%) and **3g** (91%), respectively. While the allylation of **1f** (*meta*-$NH_2$) afforded product **3f** in a slightly decreased yield of 80% (Figure 2). All of the synthesized compounds were thoroughly characterized by spectroscopic data, including single-crystal X-ray diffraction (XRD) data of representative compound **3d** (Figure 3).[37]

Having diallylated products in hand, we then performed a preliminary RCM reaction of the diallylated product **3a** in dichloromethane (DCM) with 5 mol % Grubbs I catalyst. The reaction afforded the cyclized product **6a** in 87% yield in 5 min (Table 2, entry 1). Further, an optimization study was undertaken by varying the parameters such as catalyst, catalyst loading, temperature, and solvent. Thus, repeating the reaction by increasing the reaction time did not alter the yield (Table 2, entries 2 and 3). Further, the RCM of compound **3a** was carried out using Grubbs II catalyst and a slight improvement in the yield was observed (Table 2, entry 4). Subsequent reactions with increased reaction time did not improve the yield of **6a** (Table 2, entries 5 and 6). The RCM of **3a** was carried out in different solvents such as DCM, toluene, and tetrahydrofuran (THF). The results revealed that toluene was found to be a suitable solvent with an optimum yield of 98% (Table 2, entry 7). The reactions at elevated temperature did not alter the yield, and a slight decrease in the yield was observed after 30 min at 120 °C (Table 2, entry 11). To optimize the catalyst load, RCM reactions with 3 and 10 mol % Grubbs II catalyst were carried out and it was found that 3 mol % catalyst would be sufficient to produce optimum yield (Table 2, entries 12 and 13). Thus, the condition shown in entry 12 of Table 2 was found to be optimum.

To demonstrate the scope of the reaction, under optimized condition, diallylated products **3b−h** and **4a,b** afforded the corresponding dihydro pyrrole derivatives **6b−h** and tetrahydroazepine derivatives **7a,b** in excellent yield (Figure 4). The RCM reaction of 2-(di(pent-4-en-1-yl)amino)benzamide **5a** was unsuccessful to yield the cyclic product, which might be due to free −NH groups in the substrate.[38]

After the successful synthesis of five- and seven-membered *N*-heterocycles via a two-step procedure, we then explored the possibility of one-pot procedure to synthesize **6a,b** directly from **1a,b**. Thus, the reaction of **1a**/**1b** with **2a** under optimized condition (Table 1, entry 9) and the crude reaction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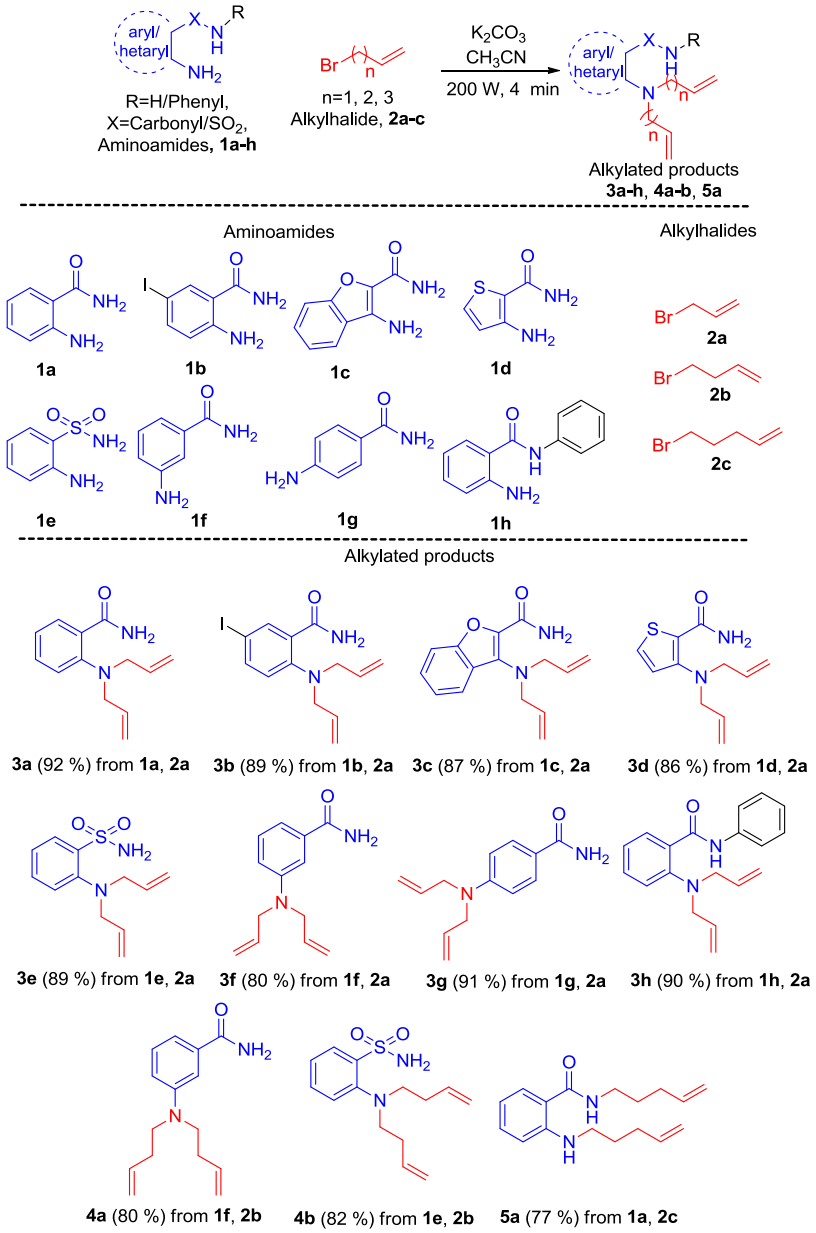


**Figure 2.** Screened aminoamides **1a**−**1h** and alkylbromides **2a**−**c** and $N_1$,$N_1$-dialkylated products **3a**−**3h, 4a**,**b**, and **5a**.

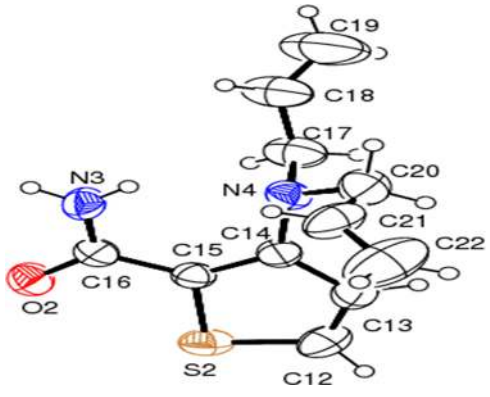


**Figure 3.** ORTEP diagram of compound **3d** (CCDC 1838002).

mixture further subjected to RCM (Table 2, entry 12) afforded compounds **6a** and **6b** in 55 and 63% yields, respectively (Scheme 1).

The fruitful results shown in Scheme 1 prompted us to explore the synthesis of six-membered *N*-heterocycle from the sequential reaction of **1a** with allyl bromide **2a**, followed by homoallyl bromide **2b** and finally RCM cyclization. To achieve the synthesis of six-membered *N*-heterocycles, as shown in Scheme 2, we have proposed two synthetic routes for the synthesis of 2-(allyl(but-3-en-1-yl)amino)-benzamide **10a**. According to route 1, the first $N_1$-allylated product **8a** was synthesized from **1a** and allyl bromide **2a**, and then, $N_1$-allyl,$N_1$-homoallylated product **10a** was synthesized in 90% yield from the reaction of **8a** and homoallyl bromide **2b** under basic condition. In route 2, $N_1$-homoallylated product **9a** was synthesized from **1a** and homoallyl bromide **2b** and compound **10a** was synthesized in 95% yield from **9a** and **2a**. In both routes 1 and 2, 1 equiv of alkyl halide **2a**/**2b** was used (Table 1, entry 9). It has been observed that $N_1$-allyl,$N_1$-homoallylated product **10a** synthesized via route 2 has a slight edge over route 1 in terms of yield. Further, the scope of the reaction was


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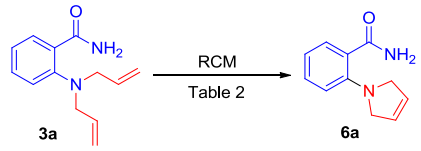
**Table 2. Optimization of the Synthesis of Compound 6a**




| entry | solvent | catalyst (mol %) | time (min) | temp (°C) | % yield 6a[a] |
|---|---|---|---|---|---|
| 1 | DCM | Grubbs I (5) | 5 | RT | 87 |
| 2 | DCM | Grubbs I (5) | 10 | RT | 89 |
| 3 | DCM | Grubbs I (5) | 15 | RT | 89 |
| 4 | DCM | Grubbs II (5) | 3 | RT | 90 |
| 5 | DCM | Grubbs II (5) | 5 | RT | 92 |
| 6 | DCM | Grubbs II (5) | 10 | RT | 92 |
| 7 | toluene | Grubbs II (5) | 3 | RT | 98 |
| 8 | THF | Grubbs II (5) | 3 | RT | 93 |
| 9 | toluene | Grubbs II (5) | 5 | 50 | 98 |
| 10 | toluene | Grubbs II (5) | 5 | 100 | 98 |
| 11 | toluene | Grubbs II (5) | 30 | 120 | 92 |
| 12 | toluene | Grubbs II (3) | 3 | RT | 98[b] |
| 13 | toluene | Grubbs II (10) | 3 | RT | 98 |

[a]Isolated yield. [b]Optimized condition.

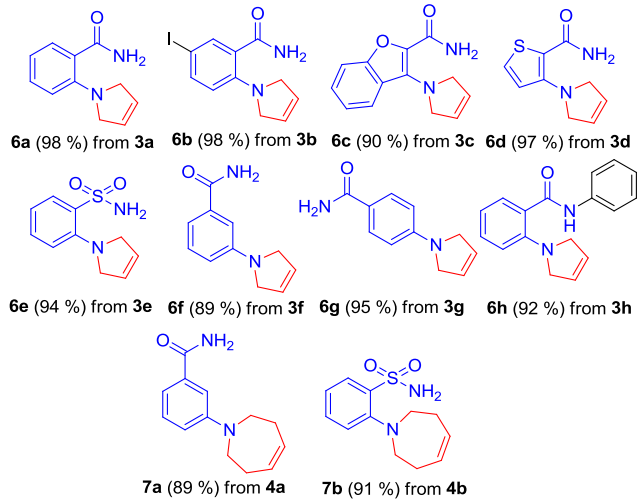
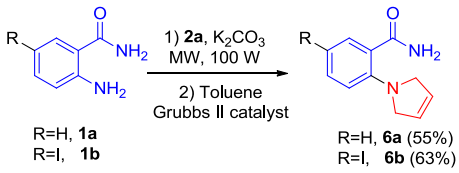



**Figure 4.** Synthesized 2,5-dihydro-1*H*-pyrrol-1-yl and 2,3,6,7-tetrahydro-1*H*-azepin-1-yl-substituted aminoamides **6a−h** and **7a,b**.

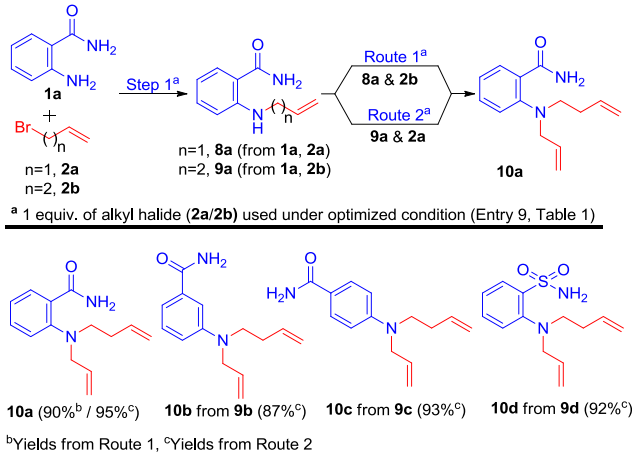
**Scheme 1. One-Pot Synthesis of Compounds 6a,b from 1a,b**



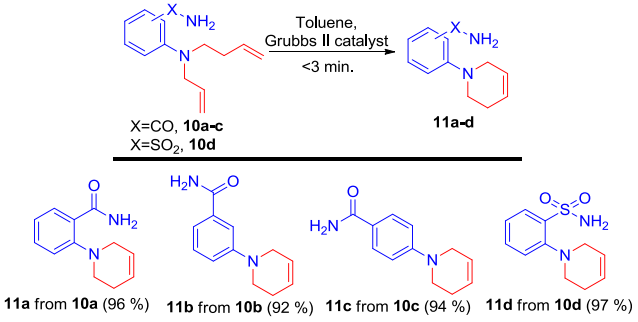

extended by synthesizing $N_1$-allyl,$N_1$-homoallylated products **10b,c** from **1f**, **1g**, and **1e** via route 2 (Scheme 2).

To achieve six-membered *N*-heterocycles, the RCM reaction of compounds **10a−d** under optimized condition (Table 2, entry 12) was carried out to synthesize 1,2,3,6-tetrahydropyridine-substituted aminoamides **11a−d** in very good yields (Scheme 3). All of the new compounds were thoroughly characterized by spectroscopic data including single-crystal XRD data of compound **11b** (Figure 5).[37]

**Scheme 2. Synthesis of $N_1$-Allyl, $N_1$-Homoallylated Aminoamides 10a−d**




**Scheme 3. Synthesis of 5,6-Dihydropyridin-1(2*H*)-yl-Substituted Aminoamides 11a−d**



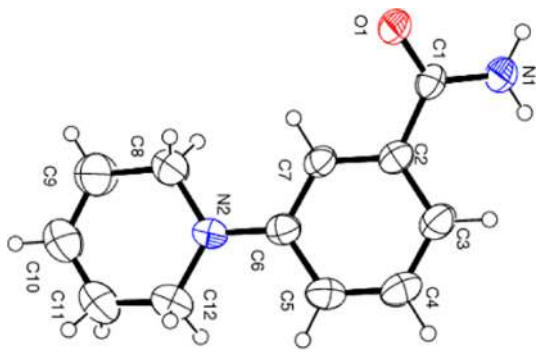




**Figure 5.** ORTEP diagram of compound **11b** (CCDC 1947372).

All of the five-, six-, and seven-membered *N*-heterocycles were synthesized via diallylated/homoallylated RCM substrates. However, we envisaged the possibility of synthesis of tri- and tetra-allylation substrate followed by the RCM cyclization approach to construct the title compounds. Initially, to achieve the synthesis of triallylated RCM substrates, a reaction of **3a** with 1 equiv of compound **2a** was carried out, although the expected triallylated product **12a** was obtained only in 10% yield. The reaction was optimized by varying base, substrate ratio, and solvent. Among the different conditions explored, the reaction of **3a** and **2a** in a 1:1.2 ratio in dimethyl sulfoxide (DMSO) using NaH as base and microwave power level of 200 W and 4 min irradiation was found to be optimum with 85% yield of **12a** (see Table S1, entry 5).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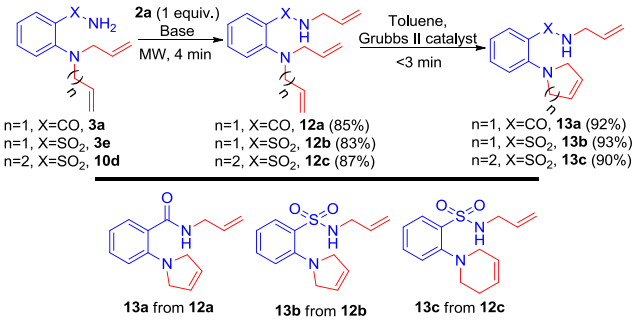
Under similar conditions, triallylated products **12b,c** were obtained from **3e** and **10d**, respectively. All of the trialkylated RCM substrates **12a−c** were converted to $N_2$-allylated 2,5-dihydro-1*H*-pyrrol-1-yl-substituted aminoamides **13a,b** and *N*-allyl-2-(5,6-dihydropyridin-1(2H)-yl)benzenesulfonamide **13c** under optimized RCM cyclization (Scheme 4). We did not observe other possible cyclized products from cyclization of $N_1$ and $N_2$ allyl groups.[21]

**Scheme 4. Synthesis of $N_2$-Allylated 2,5-Dihydro-1*H*-pyrrol-1-yl and 5,6-Dihydropyridin-1(2*H*)-yl-Substituted Aminoamides 13a−c**



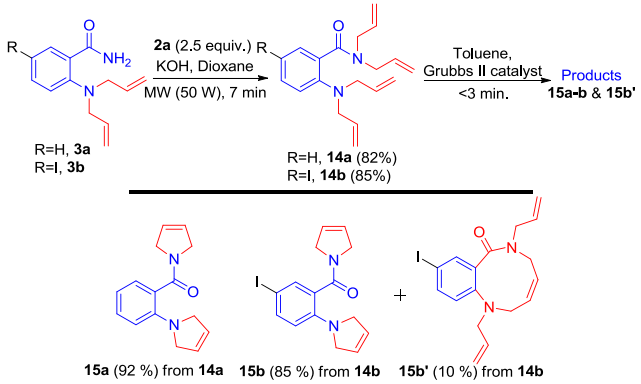

To begin with, the tetra-allylated RCM substrate **14a** was obtained in 20% yield from compounds **3a** and **2a** (2 equiv) using 1,4-dioxane as solvent and NaH as base. The reaction was carried out at 50 W power level and 50 psi pressure under microwave condition over 5 min (see Table S2, entry 1). To improve the yield of compound **14a**, an optimization study was conducted. To begin with, a slight increase in the yield was observed by increasing the irradiation time and equivalence of **2a** (see Table S2, entries 2−5). Interestingly, a sharp increase in the yield of compound **14a** to 82% was observed when the KOH was used as base (see Table S2, entry 6). Repeating the reaction with base NaOH did not improve the yield (see Table S2, entry 7). Thus, the condition shown in entry 6 of Table S2 (see Supporting Information) was found to be optimum. Similarly, compound **14b** was synthesized in 85% yield from substrate **3b**. Under optimized RCM condition, the synthesized tetra-allylated RCM substrates **14a,b** were converted to respective cyclic (2,5-dihydro-1*H*-pyrrol-1-yl)(2-(2,5-dihydro-1*H*-pyrrol-1-yl)aryl)methanones **15a,b** in excellent yield. Notably, the diazoninone derivative **15b′** was isolated in 10% yield along with **15b** from the RCM reaction of **14b**, which might be due to the metathesis of $N_1$ and $N_2$ allyl groups (Scheme 5).

To demonstrate the synthetic utility of the products, the microwave-assisted Suzuki reaction[39] of **6b** with aryl boronic acids **16a,b** was successfully attempted to afford 4-(2,5-dihydro-1H-pyrrol-1-yl)-4′-methyl-[1,1′-biphenyl]-3-carboxamide **17a** and 4′-cyano-4-(2,5-dihydro-1H-pyrrol-1-yl)-[1,1′-biphenyl]-3-carboxamide**17b** in 82 and 78% yields, respectively (Scheme 6).

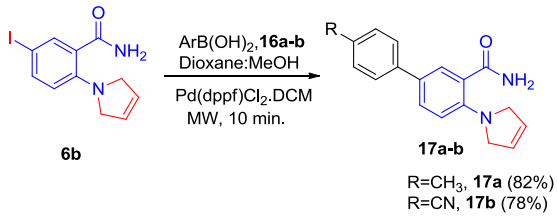
## CONCLUSIONS

In conclusion, we have synthesized five-, six-, and seven-membered *N*-heterocycles via the *N*-allylation-RCM strategy from (het)aryl aminoamides. Di-, tri-, and tetra-allylated products (**3a−h**, **4a,b**, **5a**, **10a−d**, **12a−c**, **14a,b**) were synthesized via *N*-allylation of (het)aryl aminoamides under variable optimized microwave irradiation conditions. Dihydro

**Scheme 5. Synthesis of (2,5-Dihydro-1*H*-pyrrol-1-yl)(2-(2,5-dihydro-1*H*-pyrrol-1-yl)aryl)methanones 15a,b**




**Scheme 6. Synthesis of 2,5-Dihydro-1*H*-pyrrole-Substituted [1,1′-biphenyl]-3-carboxamides 17a,b from 6b via Suzuki Coupling**




pyrrole derivatives **6a−h** and tetrahydroazepine derivatives **7a,b** were synthesized from dialkylated RCM substrates **3a−h** and **4a,b**, respectively. A direct one-pot reaction has been demonstrated for the synthesized compounds **6a,b** without isolating their corresponding diallylated intermediates. Dihydropyridin-1(2*H*)-yl derivatives **11a−d** were synthesized from $N_1$-allyl,$N_1$-homoallylated RCM substrates **10a−d**. Trialkylated RCM substrates **12a−c** were converted to the corresponding $N_2$-allylated pyrroles **13a,b** and $N_2$-allylated pyridine **13c** derivatives. Tetra-allylated RCM substrates **14a,b** were converted to (2,5- dihydro-1*H*-pyrrol-1-yl)(2-(2,5-dihydro-1*H*-pyrrol-1-yl)aryl) methanones **15a,b**. The synthetic utility of compound **6b** has been demonstrated by synthesizing pyrrole-substituted biaryl derivatives **17a,b** via Suzuki coupling.

## EXPERIMENTAL SECTION

**Materials and Methods.** All of the reactions were carried out in oven-dried glassware. A CEM Discover-300 microwave synthesizer was used for all of the microwave irradiation reactions. All of the chemicals, including (het)aryl aminoamides (**1a−g**), alkyl halides (**2a−c**), aryl boronic acids (**16a,b**), Grubbs II catalyst, and palladium reagent were purchased from Sigma-Aldrich and used as received. Thin-layer chromatography (TLC) monitored the progress of the reactions, while purification of crude compounds was done by column chromatography using silica gel (mesh size, 100−200). The nuclear magnetic resonance (NMR) spectra were recorded on a Bruker-400 MHz NMR spectrometer (400 MHz for $^1$H NMR and 100 MHz for $^{13}$C NMR) with $CDCl_3$ or $(CD_3)_2SO$ as the solvent and tetramethylsilane (TMS) as an internal reference. Integrals are in accordance with assignments; coupling constant (*J*) was reported in hertz (Hz). All $^{13}$C NMR spectra reported are proton-decoupled. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q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(quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). High resolution mass spectrometry (HRMS) analyses were conducted using Q-T of a Micro mass spectrometer (different mass analyses based on the availability of instruments). Yields refer to quantities obtained after chromatography. All of the commercial solvents were purified before use.

**General Experimental Procedure for the Synthesis of $N_1$,$N_1$-Dialkylated (Het)aryl aminoamides (3a−h, 4a,b) and 5a.** To a solution of (het)aryl aminoamides **1a−h** (1 equiv) and alkyl bromide **2a−c** (2 equiv) in $CH_3CN$ (1 mL) was added $K_2CO_3$ (2.5 equiv), and the reaction mixture was microwave-irradiated (power mode) at 200 W for 4 min. After completion of the reaction (monitored by TLC), the reaction mixture was extracted with ethyl acetate and washed with HCl (0.25 M, 10 mL) followed by brine and distilled water, dried over $Na_2SO_4$, and the solvent was evaporated under reduced pressure. The crude product was purified on a silica gel column to afford the corresponding *N*,*N*-dialkylated (het)aryl aminoamides **3a−h** in excellent yields, and **4a**,**b** and **5a** in good yields (eluent: *n*-hexane/EtOAc).

**Experimental Procedure for the Synthesis of $N_1$-Monoalkylated Aminoamides (8a and 9a−d).** To a solution of (het)aryl aminoamides **1a−h** (1 equiv) and alkyl bromide **2a**/**2b** (1 equiv) in $CH_3CN$ (1 mL) was added $K_2CO_3$ (2.5 equiv), and the reaction mixture was microwave-irradiated (power mode) at 200 W for 4 min. After completion of the reaction (monitored by TLC), the reaction mixture was extracted with ethyl acetate and washed with HCl (0.25 M, 10 mL) followed by brine and distilled water, dried over $Na_2SO_4$, and the crude product was purified on a silica gel column to afford the corresponding $N_1$-monoallylated aminoamides **8a** and $N_1$-mono homoallylated aminoamides **9a−d** in good yields (eluent: *n*-hexane/EtOAc).

**Experimental Procedure for the Synthesis of $N_1$-Allyl,$N_1$-Homoallylated Aminoamides 10a−d.** *Synthesis from (Allylamino)benzene Amides (**8a**).* To a solution of (allylamino)benzene amides **8a** (1 equiv) and 4-bromo-1-butene **2b** (1 equiv) in $CH_3CN$ (1 mL) was added $K_2CO_3$ (1.2 equiv), and the reaction mixture was microwave-irradiated (power mode) at 200 W for 4 min. After completion of the reaction (monitored by TLC), the reaction mixture was extracted with ethyl acetate and washed with HCl (0.25 M, 10 mL) followed by brine and distilled water, dried over $Na_2SO_4$, and the crude product was purified over a column of silica gel to afford the corresponding $N_1$-allyl,$N_1$-homoallylated aminobenzamide **10a** in good yield (eluent: *n*-hexane/EtOAc).

*Synthesis from (Homoallylamino)Benzene Amides (**9a−d**).* To a solution of (homoallylamino)benzene amides **13** (1 equiv) and allyl bromide **2a** (1 equiv) in $CH_3CN$ (1 mL) was added $K_2CO_3$ (1.2 equiv), and the reaction mixture was microwave-irradiated (power mode) at 200 W for 4 min. After completion of the reaction (monitored by TLC), the reaction mixture was extracted with ethyl acetate and washed with HCl (0.25 M, 10 mL) followed by brine and distilled water, dried over $Na_2SO_4$, and the crude product was purified on a silica gel column to afford the corresponding $N_1$-allyl,$N_1$-homoallylated aminobenzamides **10a−d** in excellent yields (eluent: *n*-hexane/EtOAc).

**Typical Experimental Procedure for the Preparation of Trialkylated Aminoamides 12a−c from 3a/3e/10d.** A mixture of $N_1$,$N_1$-diallylated aminoamides **3a**/**3e**/**10d** (1 equiv), allyl bromide **2a** (1 equiv), and sodium hydride (1.5 equiv) in 1,4-dioxane (1 mL) was microwave-irradiated (power mode) at 200 W for 4 min. The reaction was quenched with cold water upon completion (monitored by TLC). The crude was extracted with ethyl acetate and washed with dilute HCl (0.25 M, 10 mL) followed by brine and distilled water. The combined organic layer was dried over $Na_2SO_4$, and the mixture was purified through silica gel column chromatography by gradient elution using EtOAc/hexane as eluent to afford *N*-allyl-2-(diallylamino)benzamide (**12a**)/sulfonamide(**12b**) and *N*-allyl-2-(allyl(but-3-en-1-yl)-amino)benzenesulfonamide (**12c**) in very good yields.

**Experimental Procedure for the Synthesis of *N*,*N*-Diallyl-2-(diallylamino)-Substituted Benzamides 14a,b.** To a mixture of **3a**/**3b** (1 equiv) and allyl bromide **2a** (2 equiv) in 1,4-dioxane (1 mL) was added potassium hydroxide (KOH) (2.5 mmol) and microwave-irradiated (power mode) at 50 W for 7 min. The reaction was quenched with cold water upon completion (monitored by TLC). The crude was extracted with ethyl acetate and washed with dilute HCl and distilled water. The combined organic layer was dried over anhydrous $Na_2SO_4$. The solvent was removed under vacuum, and the crude was purified by silica gel column chromatography to afford pure *N*,*N*-diallyl-2-(diallylamino)-substituted benzamides **14a**,**b** in excellent yields.

**General RCM Procedure for the Preparation of Compounds 2,5-Dihydro-1H-pyrrole-Substituted Aminoamides (6a−h, 13a,b, and 15a,b), 5,6-Dihydropyridin-1(2H)-yl-Substituted Aminoamides (11a−d) and 2,3,6,7-Tetrahydro-1*H*-azepine-Substituted Aminoamides (7a,b).** To a solution of RCM substrates (**3a−h**/**4a**,**b**/**5a**/**10a−d**/**13a−c**/**14a**,**b**) in toluene, 3 mol % of Grubbs II catalyst (6 mol % Grubbs II catalyst was used for the substrates **14a**,**b**) was added and stirred at RT for 3 min. After completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography using EtOAc/hexane as eluent to afford pure 2,5-dihydro-1*H*-pyrrole-substituted aminoamides (**6a−h**, **13a**,**b**, and **15a**,**b**), 5,6-dihydropyridin-1(2H)-yl-substituted aminoamides (**11a−d**), and 2,3,6,7-tetrahydro-1*H*-azepine-substituted aminoamides (**7a**,**b**) in excellent yields.

**General Procedure for the Preparation of 2,5-Dihydro-1*H*-pyrrole-Substituted [1,1′-biphenyl]-3-carboxamides 17a,b by Suzuki Coupling.** A mixture of 2-(2,5-dihydro-1*H*-pyrrol-1-yl)-5-iodo- benzamide **6b** (1 equiv), arylboronic acids **16** (1.5 equiv), Pd(dppf)$Cl_2$·DCM (10 mol %), and 0.5 N $K_2CO_3$ (1 mL) in 4 mL of dioxane−methanol (3:1) was microwave-irradiated (power mode) at 200 W for 10 min. After completion of the reaction (TLC), the solvent was removed in vacuo and the residue was extracted with ethyl acetate and washed with HCl (0.25 M, 20 mL) followed by brine. The combined organic layer was dried over $Na_2SO_4$, and the mixture was purified through silica gel column chromatography by gradient elution using EtOAc/hexane to afford 2,5-dihydro-1*H*-pyrrole-substituted [1,1′-biphenyl]-3-carboxamides **17a**,**b** in very good yields.

**One-Pot Preparation of 2,5-Dihydro-1*H*-pyrrole-Substituted Aminoamides 6a,b from 1a and 1b.** To a solution of (het)aryl aminoamides **1a**/**1b** (1 equiv) and alkyl bromide **2a** (2 equiv) in toluene (1 mL) was added $K_2CO_3$ (2.5 equiv), and the reaction mixture was microwave-irradiated (power mode) at 200 W for 4 min. After 4 min, the reaction mixture was cooled to room temperature and a 3 mol % of Grubbs II catalyst was added and stirred at RT for 3 min. After completion of the reaction (monitored by TLC), the solvent


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was removed under reduced pressure and the residue was purified by silica gel column chromatography using EtOAc/hexane as eluent to afford pure 2,5-dihydro-1*H*-pyrrole-substituted aminoamides **6a,b** in good overall yields.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.9b04038.

Optimization of synthesis of compounds **12a** and **14a**; copies of $^{1}$H NMR,$^{13}$C NMR, DEPT-135, and HRMS data for all of the new compounds; basic crystallographic data of compounds **3d** and **11b** (PDF)

Single-crystal XRD data for compound **3d** (CIF)

Single-crystal XRD data for compound **11b** (CIF)

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