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Silver Salt-Mediated Allylation Reactions Using Allyl Bromides

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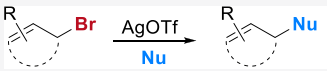
ABSTRACT: A facile, efficient, and chemoselective synthesis of allylic amides has been developed. Allyl bromides were used as the precursors activated by silver triflate. A Ritter-type reaction readily proceeded to give various allyl amides under mild conditions. The reaction protocol was also applicable to different nucleophilic partners to give a wide range of allyl-substituted products in the absence of a base.

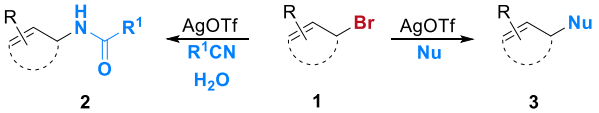


- High selectivity
- Mild reaction conditions
- Wide substrate scope

Allylic substituted molecules are fundamentally important building blocks in organic synthesis.[1] In addition, derivatization of the olefinic moiety allows for access to a wide range of functionalities.[2] Allylic amine represents one of the most frequently used functionalities in the synthesis of bioactive compounds.[3] Therefore, development of novel allylation reactions has become a continuously growing area of research.[4]

Direct substitution of allyl halides by nitrogen nucleophiles in the presence of base promoters is a straightforward way to prepare allylic amines. However, they often suffer from over allylation, and excess amounts of amine are required to alleviate the problem.[5] The situation can be further complicated by a competing elimination pathway when a strong base is present in the reaction. While KF-Celite was found to be useful in the monoallylation of anilines, a high temperature is required to drive the reaction to completion.[6] Silver salts have been used to activate alkyl halides in alkylation reactions.[7] For example, alkyl halides readily react with silver nitrite to give nitroalkanes. However, application of such protocol to the allylation of various nucleophilic partners remains uncommon. Herein, we report a facile and efficient synthesis of allylic amides via a silver salt-mediated Ritter-type reaction of readily available allyl bromides (Scheme 1). This

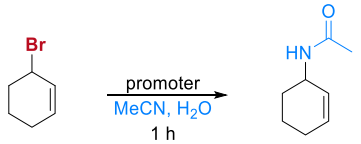
Scheme 1. Silver Salt Mediated Allylation Reactions



protocol can also be applied to various nucleophilic partners to give a wide range of allylated molecules. The present method provides an alternative approach for the allylation reactions using allyl bromides under mild conditions, which proceeds well at 0 °C in the absence of a strong base or acid.

At the outset of this study, 3-bromocyclohexene (**1a**) was reacted with acetonitrile and water (Table 1). No reaction was observed in the absence of silver salt (entry 1). Various silver salts including silver carbonate, nitrate, acetate, and triflate

Table 1. Conditions Optimization[a]



1a 2a

entry	promoter	temp (°C)	yield (%)
1	none	25	0
2	Ag_2CO_3	25	7
3	$AgNO_3$	25	8
4	AgOAc	25	11
5	AgOTf	25	73
6	AgOTf	0	98
7[b]	AgOTf	0	99
8[c]	AgOTf	0	98
9	$SnCl_4$	25	0
10	$AlCl_3$	25	0
11	BBr_3	25	0

[a]Reactions were carried out with 3-bromocyclohexene (**1a**) (0.3 mmol), promoter (0.3 mmol), and water (0.3 mmol) in MeCN (0.3 M) for 1 h. [b]The reaction was performed on a 10 mmol scale. [c]3-Chlorocyclohexene was used instead of 3-bromocyclohexene.

were then examined (entries 2−5). The performance of silver triflate was superior to others and the desired allyl amide **2a** was obtained in 73% yield at 25 °C (entry 5). The product yield was significantly improved to 98% when the reaction was performed at 0 °C (entry 6). The reaction was readily scalable without deterioration of the efficiency (entry 7). A similar yield was observed when 3-chlorocyclohexene was used (entry 8). Other Lewis acids including $SnCl_4$, $AlCl_3$, and BBr_3 were

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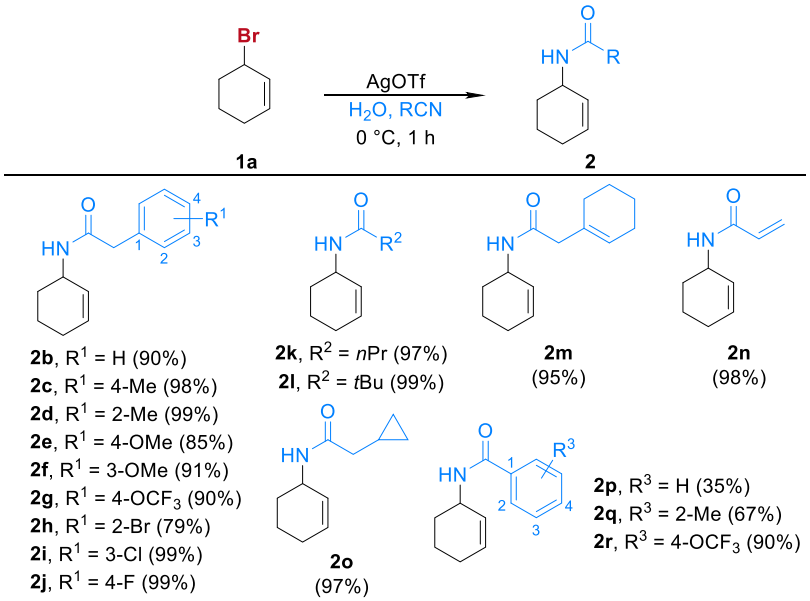
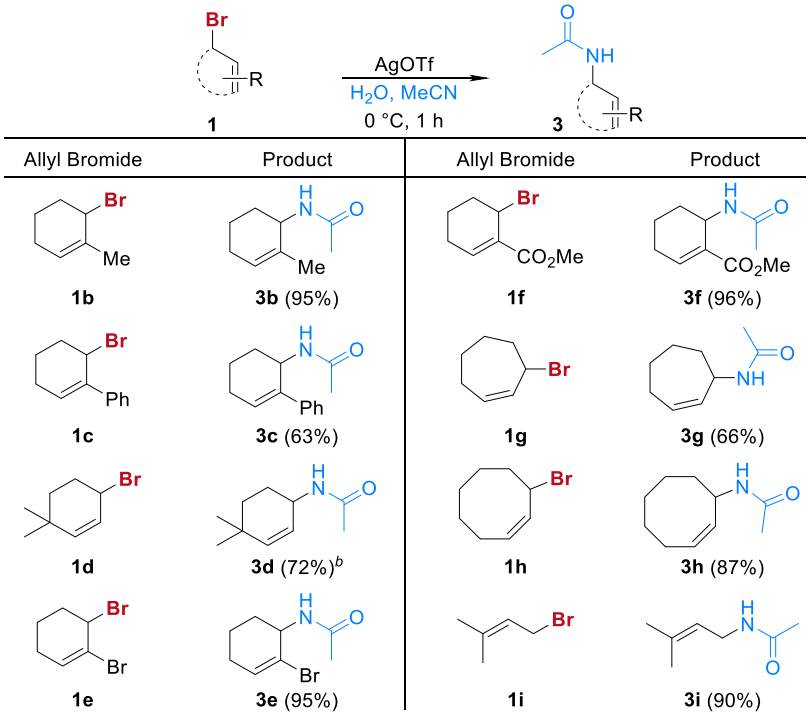
Scheme 2. Substrate Scope with Different Nitriles[a]



[a]Reactions were carried out with 3-bromocyclohexene (**1a**) (0.3 mmol), AgOTf (0.3 mmol) and H_2O (0.3 mmol) in nitrile (0.3 M) at 0 °C for 1 h. The yields are isolated yields.

Scheme 3. Substrate Scope with Different Allyl Bromides[a]



[a]Reactions were carried out with allyl bromide (**1**) (0.3 mmol), AgOTf (0.3 mmol), and H_2O (0.3 mmol) in acetonitrile (0.3 M) at 0 °C for 1 h. The yields are isolated yields. [b]17% of the isomer was detected.

examined, but no desired product was detected, indicating the unique role of silver salt in this type of transformation.

To investigate the substrate scope of the Ritter-type reaction, 3-bromocyclohexene (**1a**) was used in combination with various nitrile derivatives (Scheme 2). Benzyl cyanide afforded the allylic amide **2b** in 90% yield. The electronic effects of the nitrile partner on the reaction were investigated using benzyl cyanides with various substituents. Both electron-rich and electron-deficient benzyl cyanides reacted smoothly with good-to-excellent yields. The electron-rich benzyl cyanides gave the corresponding amides **2c–f** in high yields (85–99%), and the relatively electron-deficient benzyl cyanides also reacted efficiently to give amides **2g–j** in 79–99% yields. The aliphatic *n*-butyronitrile and sterically bulky pivalonitrile both reacted cleanly to give the desired allylic amides **2k** and **2l** in 97% and 99%, respectively. Nitrile

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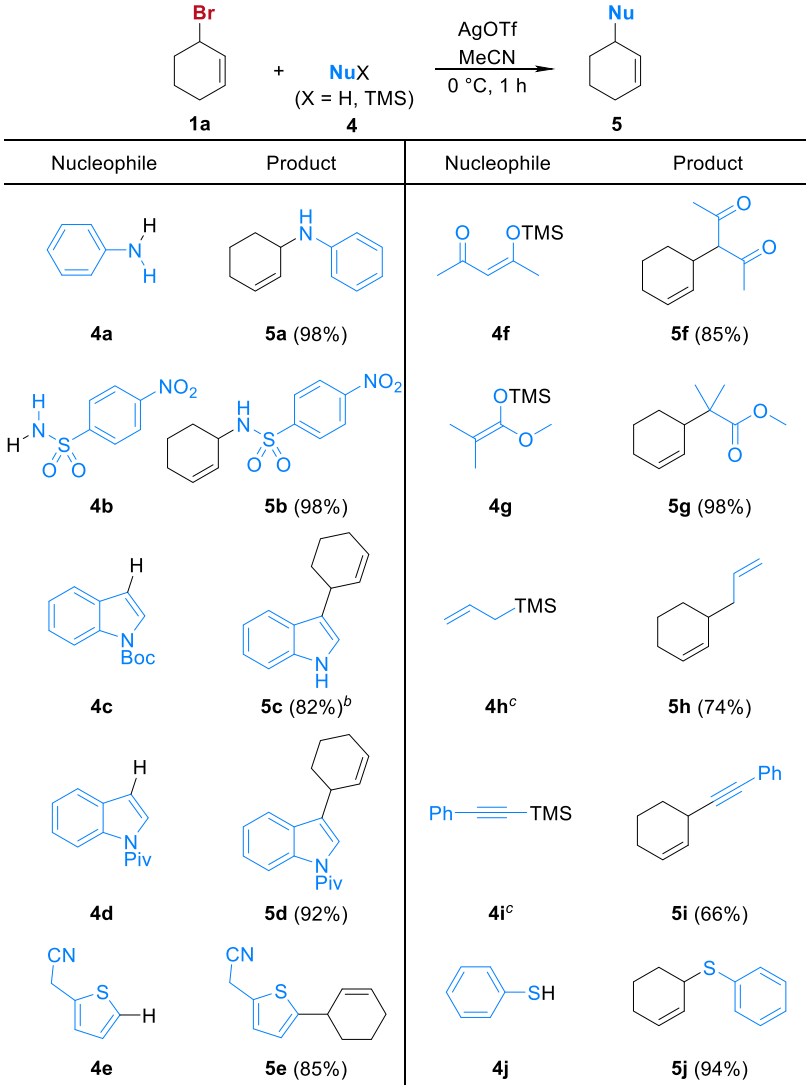
Scheme 4. Substrate Scope with Different Nucleophiles[a]



[a]Reactions were carried out with 3-bromocyclohexene (**1a**) (0.3 mmol), AgOTf (0.3 mmol), and nucleophile (**4**) (0.3 mmol) in acetonitrile (0.3 M) at 0 °C for 1 h. The yields are isolated yields. [b]The *N*-Boc was deprotected during the purification process. [c]Three equiv of the nucleophile was used.

compounds bearing other substituents such as olefinic and cyclopropyl groups were also well tolerated; 1-cyclohexenylacetonitrile, acrylonitrile, and cyclopropylacetonitrile gave the respective amides **2m** (95%), **2n** (98%), and **2o** (97%). Allyl benzamides **2p**−**2r** were synthesized from the corresponding benzonitriles.

Next, various allylic bromide substrates were examined (Scheme 3). 2-Methyl-3-bromocyclohexene (**1b**), 2-phenyl-3-bromocyclohexene (**1c**), and 6-bromo-3,3-dimethylcyclohexene (**1d**) reacted to give amides **3b**−**3d** in good yields. The relatively electron-deficient bromocyclohexene derivatives **1e** and **1f** also gave excellent yields of the corresponding amides **3e** (95%) and **3f** (96%). Medium rings such as 3-bromocycloheptene (**1g**) and 3-bromocyclooctene (**1h**) were compatible with the reaction protocol, yielding amides **3g** (66%) and **3h** (87%). The aliphatic allyl bromide **1i** gave amide **3i** as the sole product in 90% yield. The structures of **3c** and **3h** were confirmed unambiguously by X-ray crystallographic analysis.

Substitution of allylic bromide with other nucleophilic partners **4** was also studied (Scheme 4). Aniline (**4a**) and 4-nitrobenzenesulfonamide (**4b**) both reacted cleanly to give allylic amines **5a** and **5b** in excellent yields, and no over allylation was observed. Indoles **4c** and **4d** also reacted smoothly under these conditions yielding exclusively 3-allylindoles **5c** (82%) and **5d** (92%).[8,9] 2-Thienylacetonitrile **4e** reacted exclusively at the C-4 position to give **5e** in 85% yield. Silyl enol ethers **4f** and **4g** were also well tolerated under the mild conditions, forming **5f** and **5g** smoothly. Using allyltrimethylsilane (**4h**) and trimethylsilylacetylene **4i** as the nucleophilic partners was also applicable to the reaction system, giving 1,5-diene **5h** and 1-en-4-yne **5i** in 74% and 66% yields, respectively. Thioether **5j** was synthesized successfully using thiophenol **4j** as the nucleophilic partner. It is noteworthy that these reactions proceeded smoothly without any basic additives.

The synthetic utilities of the allylic amides were demonstrated by a number of transformations (Scheme 5). The bromocyclization of **2r** proceeded efficiently to give oxazoline

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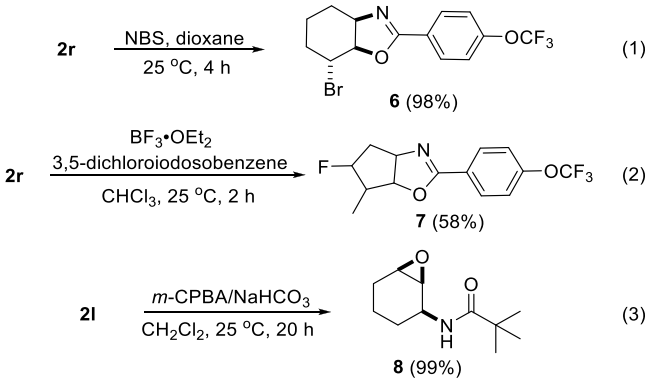
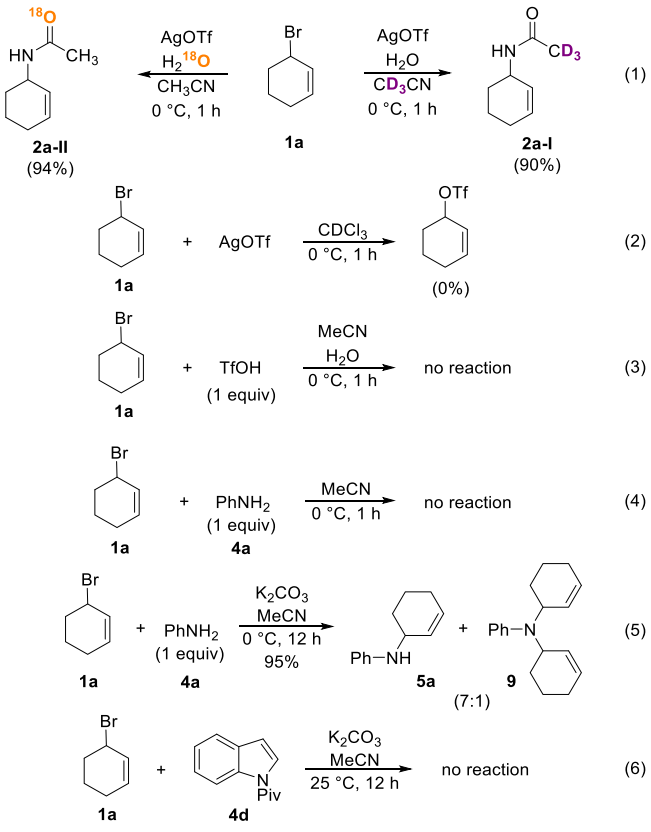
Scheme 5. Synthetic Transformation of the Allylic Amides



6 as a single stereoisomer in 98% yield (Scheme 5, eq 1).[10] In addition, a hypervalent iodine-mediated ring-contraction reaction of **2r** yielded monofluorinated oxazoline **7** smoothly (Scheme 5, eq 2).[11] Treatment of **2l** with *m*-CPBA furnished epoxide **8** stereospecifically in a quantitative yield (Scheme 5, eq 3).[12]

When **1a** was subjected to the reaction conditions using acetonitrile-d_3, deuterium-labeled product **2a-I** was isolated in 90% yield (Scheme 6, eq 1). When $H_2{}^{18}O$ was used in place of

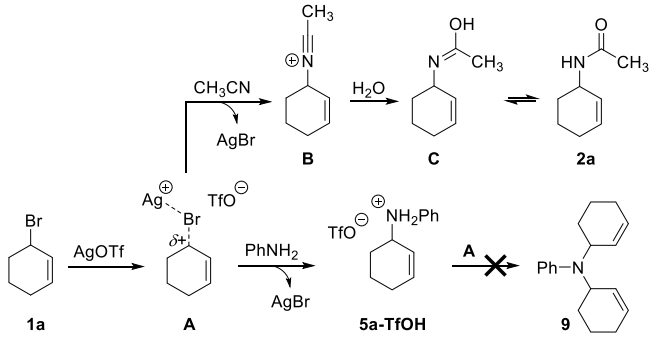
Scheme 6. Mechanistic Studies



$H_2{}^{16}O$, the ^{18}O-labeled product **2a-II** was isolated in 94% yield. The two products were verified by NMR and HRMS. These isotopic labeling experiments validated the Ritter-type reaction mechanism.[13] Some control experiments were also conducted in order to shed light on the mechanistic picture. An NMR experiment on a 1:1 mixture of **1a** and AgOTf was carried out, and there was no observable change nor precipitation of AgBr, suggesting that the reaction is unlikely to go through the putative cyclohexenyl triflate species (Scheme 6, eq 2). We had suspected that TfOH, which was generated in the reaction, might catalyze the allylation. However, this possibility is ruled out because no reaction was observed when AgOTf was replaced by TfOH as the promoter (Scheme 6, eq 3). For the relatively strong nucleophiles such as aniline, no reaction was observed in the absence of AgOTf (Scheme 6, eq 4). Although substitution proceeded when potassium carbonate was used, a significant amount of diallylation side product **9** was detected (Scheme 6, eq 5). For the case with *N*-protected indole as the nucleophile, no reaction was observed even in the presence of K_2CO_3 (Scheme 6, eq 6). These results suggest that the mechanism with AgOTf may differ from the classical base-mediated substitution.

A plausible mechanism is depicted in Scheme 7. We believe that the silver cation might act as a Lewis acid to activate the

Scheme 7. A Plausible Mechanism



bromide in the substrate **1** (e.g. **1a**) to give species **A**.[14] Subsequently, substitution of the bromide by a nucleophile (e.g., nitrile) could afford species **B** together with the elimination of AgBr. Finally, the addition of water to species **B** followed by tautomerization of species **C** could yield product **2** (e.g. **2a**). Under a similar mechanism, we believe that other nucleophilic partners such as aniline (**4a**) could also react with species **A** to give the substitution products **5a**. Since TfOH is generated as a byproduct, we suspect that it might protonate the basic nitrogen in amines and indoles so that over alkylation (e.g., **5a-TfOH** → **9**) could be suppressed.

In summary, we have developed an efficient allylation protocol mediated by silver salt, which allows for the formation of various allylic amides from allylic bromides under mild conditions. Furthermore, this protocol can be modified to achieve allylic substitution of various nucleophiles without the need of any basic additive.

EXPERIMENTAL SECTION

General Information. Unless otherwise specified, commercially available reagents were used directly without further purification. All reactions requiring anhydrous conditions were conducted by standard procedures under a nitrogen atmosphere. The solvents were dried over a solvent purification system from Innovative Technology. Melting points were determined on a Buchi B-540b melting point apparatus. ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were recorded on a Bruker AMX500 (500 MHz) spectrometer or a Bruker AMX400 (400 MHz) spectrometer. Proton and carbon chemical shifts are reported in parts per million (ppm) values downfield from TMS (δ 0.00) and referenced to residual protons in NMR solvents ($CDCl_3$ at δ 7.26, CD_2Cl_2 at δ 5.36) or carbon signals in NMR solvent ($CDCl_3$ at δ 77.16, CD_2Cl_2 at δ 55.42). ^{1}H NMR data were reported as follows:

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chemical shift, multiplicity, coupling constants (Hz), and integration. High-resolution mass spectra were obtained on a Thermo Finnigan MAT95XL Magnetic Sector mass spectrometer (ionization mode: EI) or a Thermo Q Exactive Hybrid Quadrupole-Orbitrap mass spectrometer (ESI). Crystallographic data of crystals **3c** and **3h** were collected on a Bruker D8 VENTURE diffractometer at 296 K with Mo K_α radiation (λ = 0.71073 Å). Analytical thin layer chromatography (TLC) was performed with Merck precoated TLC plates, silica gel 60F-254, with a layer thickness of 0.25 mm. Flash chromatography separations were performed on Merck 60 (0.040−0.063 mm) mesh silica gel.

General Procedure for the Silver Salt Mediated Ritter-Type Reactions. Allyl bromide **1** (0.3 mmol, 1 equiv) was added to a stirred mixture of silver trifluoromethanesulfonate (77.1 mg, 0.3 mmol, 1 equiv) and water (5.4 μL, 0.3 mmol, 1 equiv) in nitrile solvent (1.0 mL, 0.5 mL of CH_2Cl_2 was added if the nitrile is a solid) at 0 °C. The resultant mixture was stirred at 0 °C for 1 h. The crude product mixture was then filtered through a thin plug of Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel to afford product **2**.

*N-(Cyclohex-2-en-1-yl)acetamide (**2a**).* Yield: 98%, 40.9 mg (at 0.3 mmol scale); 99%, 1.37 g (at 10 mmol scale). Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.79−5.83 (m, 1H), 5.72 (br. s, 1H), 5.51−5.56 (m, 1H), 4.40−4.47 (m, 1H), 1.95−1.99 (m, 2H), 1.94 (s, 3H), 1.83−1.90 (m, 1H), 1.58−1.64 (m, 2H), 1.44−1.51 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.4, 130.9, 127.8, 44.8, 29.5, 24.8, 23.5, 19.8. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_8H_{13}NNaO$, 162.0889; found, 162.0889.

*N-(Cyclohex-2-en-1-yl)-2-phenylacetamide (**2b**).* Yield: 90%, 58.1 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.36 (m, 2H), 7.27−7.29 (m, 1H), 7.24−7.27 (m, 2H), (m, *J* = Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.3, 135.1, 131.1, 129.4, 129.0, 127.6, 127.3, 44.9, 44.0, 29.4, 24.8, 19.8. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{14}H_{17}NNaO$, 238.1202; found, 238.1202.

*N-(Cyclohex-2-en-1-yl)-2-(p-tolyl)acetamide (**2c**).* Yield: 98%, 67.4 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.11−7.14 (m, 4H), 5.75−5.79 (m, 1H), 5.45−5.48 (m, 1H), 4.42−4.49 (m, 1H), 3.50 (s, 2H), 2.33 (s, 3H), 1.91−1.95 (m, 2H), 1.82−1.88 (m, 1H), 1.49−1.61 (m, 2H), 1.36−1.43 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 170.6, 136.9, 132.0, 130.9, 129.7, 129.3, 127.6, 44.9, 43.5, 29.4, 24.8, 21.1, 19.8. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{15}H_{19}NNaO$, 252.1359; found, 252.1358.

*N-(Cyclohex-2-en-1-yl)-2-(o-tolyl)acetamide (**2d**).* Yield: 99%, 68.1 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14- 7.20 (m, 4H), 5.72−5.77 (m, 1H), 5.41−5.45 (m, 2.4 Hz, 1H), 5.37 (br. d, *J* = 7 Hz, 1H), 4.43−4.50 (m, 1H), 3.55 (s, 2H), 2.27 (s, 3H), 1.89−1.93 (m, 2H), 1.80−1.87 (m, 1H), 1.52−1.60 (m, 1H), 1.44−1.51 (m, 1H), 1.33−1.40 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 170.0, 137.1, 133.5, 131.0, 130.7, 130.4, 127.8, 127.5, 126.6, 44.7, 42.0, 29.4, 24.7, 19.8, 19.5. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{15}H_{19}NNaO$, 252.1359; found, 252.1358.

*N-(Cyclohex-2-en-1-yl)-2-(4-methoxyphenyl)acetamide (**2e**).* Yield: 85%, 62.6 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 20:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.75−5.80 (m, 1H), 5.44−5.48 (m, 1H), 5.41 (br. d, *J* = 7.4 Hz, 1H), 4.42−4.48 (m, 1H), 3.79 (s, 3H), 3.48 (s, 2H), 1.91−1.95 (m, 2H), 1.81−1.87 (m, 1H), 1.47−1.62 (m, 2H), 1.36−1.43 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 170.7, 158.8, 131.0, 130.5, 127.6, 127.1, 114.5, 55.3, 44.8, 43.1, 29.4, 24.8, 19.8. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{15}H_{19}NNaO_2$, 268.1308; found, 268.1308.

*N-(Cyclohex-2-en-1-yl)-2-(3-methoxyphenyl)acetamide (**2f**).* Yield: 91%, 67.0 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 20:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (t, *J* = 7.8 Hz, 1H), 6.78−6.82 (m, 3H), 5.74−5.79 (m, 1H), 5.55 (br. d, *J* = 6.7 Hz, 1H), 5.44−5.49 (m, 1H), 4.40−4.48 (m, 1H), 3.77 (s, 3H), 3.50 (s, 2H), 1.90−1.95 (m, 2H), 1.80−1.88 (m, 1H), 1.48−1.62 (m, 2H), 1.36−1.44 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 170.1, 160.0, 136.6, 131.0, 130.0, 127.5, 121.6, 114.9, 112.8, 55.2, 44.9, 44.0, 29.3, 24.7, 19.8. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{15}H_{19}NNaO_2$, 268.1308; found, 268.1307.

*N-(Cyclohex-2-en-1-yl)-2-[4-(trifluoromethoxy)phenyl]-acetamide (**2g**).* Yield: 90%, 80.8 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.26 (br. d, *J* = 7.4 Hz, 1H), 5.87−5.91 (m, 1H), 5.63−5.67 (m, 1H), 4.63−4.69 (m, 1H), 1.95−2.05 (m, 3H), 1.59−1.70 (m, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 165.6, 151.5, 151.4, 133.4, 131.6, 128.9, 127.4, 121.5, 120.7, 119.4, 45.4, 29.5, 24.9, 19.9. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{14}H_{14}F_3NNaO_2$, 308.0869; found, 308.0867.

*2-(2-Bromophenyl)-N-(cyclohex-2-en-1-yl)acetamide (**2h**).* Yield: 79%, 69.7 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.33 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.28 (td, *J* = 7.5, 1.1 Hz, 1H), 7.14 (td, *J* = 7.9, 1.8 Hz, 1H), 5.77−5.81 (m, 1H), 5.48−5.52 (m, 1H), 4.44−4.50 (m, 1H), 3.66 (s, 2H), 1.92−1.96 (m, 2H), 1.82−1.88 (m, 1H), 1.51−1.63 (m, 2H), 1.42−1.48 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.7, 135.0, 133.1, 131.8, 131.1, 129.1, 128.0, 127.5, 125.0, 44.9, 44.3, 29.3, 24.8, 19.8. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{14}H_{16}BrNNaO$, 316.0308; found, 316.0307.

*2-(3-Chlorophenyl)-N-(cyclohex-2-en-1-yl)acetamide (**2i**).* Yield: 99%, 74.2 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22−7.33 (m, 1H), 7.20−7.21 (m, 2H), 7.10−7.13 (m, 1H), 6.04 (br. d, *J* = 7.3 Hz, 1H), 5.76−5.80 (m, 1H), 5.46−5.50 (m, 1H), 4.40−4.45 (m, 1H), 3.45 (s, 2H), 1.91−1.95 (m, 2H), 1.80−1.86 (m, 1H), 1.53−1.59 (m, 2H), 1.39−1.45 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.5, 137.2, 134.4, 130.9, 129.9, 129.3, 127.5, 127.4, 127.2, 45.0, 43.2, 29.3, 24.7, 19.8. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{14}H_{16}ClNNaO$, 272.0813; found, 272.0812.

*N-(Cyclohex-2-en-1-yl)-2-(4-fluorophenyl)acetamide (**2j**).* Yield: 99%, 69.3 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (dd, *J* = 8.5, 5.4 Hz, 2H), 7.03 (t, *J* = 8.6 Hz, 2H), 5.78−5.83 (m, 1H), 5.46−5.50 (m, 1H), 5.34 (br. s, 1H), 4.43−4.50 (m, 1H), 3.51 (s, 2H), 1.93−1.98 (m, 2H), 1.83−1.90 (m, 1H), 1.48−1.64 (m, 2H), 1.38−1.46 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 170.0, 163.1, 161.2, 131.3, 131.1, 131.0, 127.5, 116.0, 115.9, 44.9, 43.1, 29.4, 24.8, 19.8. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{14}H_{16}FNNaO$, 256.1114; found, 256.1121.

*N-(Cyclohex-2-en-1-yl)butyramide (**2k**).* Yield: 97%, 48.7 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.81−5.85 (m, 1H), 5.54−5.57 (m, 1H), 5.46 (br. s, 1H), 4.45−4.51 (m, 1H), 2.12 (t, *J* = 7.3, 2H), 1.96−2.01 (m, 2H), 1.86−1.92 (m, 1H), 1.60−1.69 (m, 4H), 1.46−1.53 (m, 1H), 0.93 (t, *J* = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 172.3, 131.0, 127.9, 44.6, 39.0, 29.6, 24.9, 19.8, 19.4, 13.8. HRMS (ESI-Q-orbitrap) *m/z*: [M + Na]$^+$ calcd for $C_{10}H_{17}NNaO$, 190.1202; found, 190.1201.

*N-(Cyclohex-2-en-1-yl)pivalamide (**2l**).* Yield: 99%, 53.8 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.77−5.82 (m, 1H), 5.55 (br. s, 1H), 5.50−5.53 (m, 1H), 4.37−4.43 (m, 1H), 1.93−1.98 (m, 2H), 1.80−1.86 (m, 1H), 1.55−1.62 (m, 2H), 1.40−1.47 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 177.6, 130.8, 128.0, 44.4, 38.6, 29.4, 27.6, 24.9, 19.8. HRMS (ESI-Q-

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orbitrap) m/z: $[M + Na]^+$ calcd for $C_{11}H_{19}NNaO$, 204.1359; found, 204.1360.

*2-(Cyclohex-1-en-1-yl)-N-(cyclohex-2-en-1-yl)acetamide (**2m**).* Yield: 95%, 62.5 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^1H NMR (500 MHz, $CDCl_3$): δ 5.78−5.83 (m, 1H), 5.71 (br. d, J = 7.7 Hz, 1H), 5.55−5.59 (m, 1H), 5.48−5.53 (m, 1H), 4.39−4.46 (m, 1H), 2.81 (s, 2H), 1.89−2.04 (m, 6H), 1.81−1.88 (m, 1H), 1.49−1.63 (m, 6H), 1.40−1.49 (m, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.3, 133.0, 130.9, 127.8, 126.7, 46.5, 44.5, 29.5, 28.3, 25.4, 24.8, 22.8, 22.1, 19.8. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_{14}H_{21}NNaO$, 242.1515; found, 242.1515.

*N-(Cyclohex-2-en-1-yl)acrylamide (**2n**).* Yield: 98%, 44.5 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^1H NMR (500 MHz, $CDCl_3$): δ 6.23 (dd, J = 17.0, 1.6 Hz, 1H), 6.11 (dd, J = 16.8, 10.1 Hz, 2H), 5.79−5.84 (m, 1H), 5.57 (dd, J = 10.1, 1.7 Hz, 1H), 5.53−5.58 (m, 1H), 4.47−4.55 (m, 1H), 1.93−2.00 (m, 2H), 1.84−1.92 (m, 1H), 1.57−1.68 (m, 2H), 1.47−1.57 (m, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 164.9, 131.2, 130.9, 127.6, 126.1, 44.8, 29.4, 24.8, 19.8. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_7H_{13}NNaO$, 174.0889; found, 174.0890.

*N-(Cyclohex-2-en-1-yl)-2-cyclopropylacetamide (**2o**).* Yield: 97%, 52.2 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^1H NMR (500 MHz, $CDCl_3$): δ 6.05 (br. s, 1H), 5.75−5.79 (m, 1H), 5.49−5.53 (m, 1H), 4.39−4.45 (m, 1H), 2.06 (d, J = 7.2 Hz, 2H), 1.90−1.96 (m, 2H), 1.80−1.86 (m, 1H), 1.55−1.60 (m, 2H), 1.42−1.48 (m, 1H), 0.86−0.94 (m, 1H), 0.49−0.53 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 171.7, 130.7, 127.9, 44.4, 41.5, 29.4, 24.8, 19.8, 7.2, 4.5. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_{11}H_{17}NNaO$, 202.1208; found, 202.1215.

*N-(cyclohex-2-en-1-yl)benzamide (**2p**).* Yield: 35%, 21.1 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.75−7.79 (m, 2H), 7.47−7.51 (m, 1H), 7.40−7.45 (m, 2H), 6.10 (br. s, 1H), 5.89−5.95 (m, 1H), 5.66−5.72 (m, 1H), 4.68−4.74 (m, 1H), 1.98−2.10 (m, 3H), 1.62−1.75 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 135.0, 131.5, 128.7, 127.7, 127.0, 45.2, 29.6, 25.0, 19.9. HRMS (APCI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_{13}H_{15}NO$, 202.1225; found, 202.1226.

*N-(cyclohex-2-en-1-yl)-2-methylbenzamide (**2q**).* Yield: 67%, 43.3 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.75−7.79 (m, 2H), 7.47−7.51 (m, 1H), 7.40−7.45 (m, 2H), 6.10 (br. s, 1H), 5.89−5.95 (m, 1H), 5.66−5.72 (m, 1H), 4.68−4.74 (m, 1H), 1.98−2.10 (m, 3H), 1.62−1.75 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.8, 135.0, 131.5, 128.7, 127.7, 127.0, 45.2, 29.6, 25.0, 19.9. HRMS (APCI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_{13}H_{15}NO$, 238.1202; found, 238.1209.

*N-(cyclohex-2-en-1-yl)-4-(trifluoromethoxy)benzamide (**2r**).* Yield: 90%, 77.0 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.32−7.35 (m, 1H), 7.27−7.31 (m, 1H), 7.16−7.21 (m, 2H), 5.87−5.91 (m, 1H), 5.76 (br. d, J = 6.2 Hz, 1H), 4.64−4.70 (m, 1H), 2.44 (s, 3H), 1.97−2.06 (m, 3H), 1.61−1.73 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.5, 136.8, 135.9, 131.4, 131.0, 129.8, 127.5, 126.8, 125.8, 45.0, 29.6, 24.9, 19.8. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_{14}H_{17}NNaO$, 238.1202; found, 238.1209.

*N-(2-Methylcyclohex-2-en-1-yl)acetamide (**3b**).* Yield: 95%, 43.7 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^1H NMR (400 MHz, $CDCl_3$): δ 5.80 (br. d, J = 7.25 Hz, 1H), 5.50−5.54 (m, 1H), 4.27−4.33 (m, 1H), 1.88−1.96 (m, 5H), 1.51−1.73 (m, 6H), 1.40−1.50 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.7, 133.2, 126.1, 47.5, 29.8, 25.1, 23.4, 21.0, 18.7. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_9H_{15}NNaO$, 176.1046; found, 176.1046.

*N-(2,3,4,5-tetrahydro-[1,1′-biphenyl]-2-yl)acetamide (**3c**).* Yield: 63%, 40.7 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.34−7.38 (m, 2H), 7.26−7.32 (m, 2H), 7.19−7.26 (m, 1H), 6.30 (t, J = 3.8 Hz, 1H), 5.54 (br. d, J = 7.9 Hz, 1H), 5.06−5.12 (m, 1H), 2.18−2.26 (m, 2H), 1.85−1.96 (m, 2H), 1.83 (s, 3H), 1.68−1.78 (m, 1H), 1.54−1.66 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.4, 139.3, 136.6, 129.6, 128.5, 127.3, 125.6, 44.7, 29.8, 26.0, 23.5, 18.2. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_{14}H_{17}NNaO$, 238.1202; found, 238.1202.

*N-(4,4-Dimethylcyclohex-2-en-1-yl)acetamide (**3d**).*[11] Yield: 72%, 36.1 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^1H NMR (400 MHz, $CDCl_3$): δ 5.55 (dd, J = 10.0, 1.7 Hz, 1H), 5.41 (dd, J = 10.0, 3.2 Hz, 2H), 4.36−4.38 (m, 1H), 1.97 (s, 3H), 1.88−1.95 (m, 1H), 1.45−1.56 (m, 3H), 0.99 (s, 3 H), 0.97 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.5, 141.3, 125.3, 45.1, 34.5, 31.8, 29.4, 29.3, 26.7, 23.7.

*N-(6,6-Dimethylcyclohex-2-en-1-yl)acetamide (**3d′**).* Yield: 17%, 8.5 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^1H NMR (400 MHz, $CDCl_3$): δ 5.71−5.77 (m, 1H), 5.37−5.44 (m, 2H), 4.25−4.32 (m, 1H), 1.97−2.04 (m, 5H), 1.34−1.48 (m, 2H), 0.94 (s, 3H), 0.85 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.8, 129.2, 127.7, 52.8, 33.8, 32.9, 26.9, 23.7, 22.8, 22.5. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_{10}H_{17}NNaO$, 190.1202; found, 190.1203.

*N-(2-Bromocyclohex-2-en-1-yl)acetamide (**3e**).* Yield: 95%, 62.2 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^1H NMR (400 MHz, $CDCl_3$): δ 6.27 (br. d, J = 7.7 Hz, 1H), 6.20 (t, J = 4.0 Hz), 4.55−4.62 (m, 1H), 2.00−2.08 (m, 2H), 1.98 (s, 3H), 1.83−1.92 (m, 1H), 1.73−1.82 (m, 1H), 1.50−1.68 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.8, 133.8, 122.4, 50.6, 30.9, 27.6, 23.3, 18.0. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_8H_{12}BrNNaO$, 239.9995; found, 239.9995.

*Methyl 6-Acetamidocyclohex-1-enecarboxylate (**3f**).* Yield: 96%, 56.8 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.09 (t, J = 3.7 Hz, 1H), 5.90 (d, J = 7.4 Hz, 1H), 4.79−4.84 (m, 1H), 4.02−4.18 (m, 2H), 2.17−2.28 (m, 1H), 2.03−2.15 (m, 1H), 1.84−1.92 (m, 4H), 1.59−1.67 (m, 1H), 1.43−1.57 (m, 2H), 1.19 (t, J = 7.2, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.0, 166.2, 144.1, 130.3, 60.5, 42.4, 28.5, 25.7, 23.3, 16.8, 14.2. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_{10}H_{15}NNaO_3$, 220.0944; found, 220.0940.

*N-(Cyclohept-2-en-1-yl)acetamide (**3g**).* Yield: 66%, 30.3 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^1H NMR (400 MHz, $CDCl_3$): δ 5.90 (br. s, 1H), 5.73−5.81 (m, 1H), 5.46−5.52 (m, 1H), 4.52−4.60 (m, 1H), 2.03−2.20 (m, 2H), 1.95 (s, 3H), 1.75−1.90 (m, 2H), 1.59−1.72 (m, 2H), 1.45−1.56 (m, 1H), 1.28−1.39 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.1, 134.9, 132.3, 50.6, 34.1, 28.6, 27.8, 26.8, 23.5. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_9H_{15}NNaO$, 176.10460; found, 176.1045.

*(Z)-N-(Cyclooct-2-en-1-yl)acetamide (**3h**).* Yield: 87%, 43.7 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^1H NMR (400 MHz, $CDCl_3$): δ 6.05 (t, J = 7.9 Hz, 1H), 5.88 (t, J = 7.9 Hz, 1H), 5.47−5.68 (m, 1H), 5.35 (br. d, J = 7.6 Hz, 1H), 3.68 (q, J = 9.9 Hz, 1H), 2.24−2.35 (m, 2H), 2.06−2.22 (m, 1H), 1.68−1.93 (m, 5H), 1.54−1.68 (m, 5H), 1.30−1.54 (m, 8H), 1.14−1.29 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.3, 131.6, 130.2, 47.8, 36.6, 29.0, 26.5, 26.1, 24.4, 23.6. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_{10}H_{17}NNaO$, 190.1202; found, 190.1202.

*N-(3-Methylbut-2-en-1-yl)acetamide (**3i**).* Yield: 90%, 34.3 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^1H NMR (400 MHz, $CDCl_3$): δ 6.00 (br. s, 1H), 5.10−5.16 (m, 1H), 3.75 (t, J = 6.2 Hz, 2H), 1.91 (s, 3H), 1.65 (s, 3H), 1.60 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.1, 136.1, 120.2, 37.6, 25.6, 23.1, 17.8. HRMS (ESI-Q-orbitrap) m/z: $[M + Na]^+$ calcd for $C_7H_{13}NNaO$, 150.0889; found, 150.0889.

General Procedure for the Silver Salt Mediated Allylation Reactions. 3-Bromocyclohexene (**1a**) (0.3 mmol, 1 equiv) was

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added to a stirred mixture of silver trifluoromethanesulfonate (77.1 mg, 0.3 mmol, 1 equiv) and nucleophile **4** (0.3 mmol, 1 equiv) in acetonitrile (1.0 mL) at 0 °C. The resultant mixture was stirred at 0 °C for 1 h. The crude product mixture was then filtered through a thin plug of Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel to afford product **5**.

*N-(Cyclohex-2-en-1-yl)aniline (**5a**).*[15] Yield: 98%, 50.9 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.20 (dd, J = 8.6, 7.3 Hz, 2H), 6.72 (tt, J = 7.3, 1.0 Hz, 1H), 6.65 (dd, J = 8.5, 1.0 Hz, 2H), 5.86−5.90 (m, 1H), 5.77−5.81 (m, 1H), 4.00−4.05 (m, 1H), 3.65 (br. s, 1H), 2.00−2.14 (m, 2H), 1.91−1.97 (m, 1H), 1.71−1.79 (m, 1H), 1.62−1.71 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 147.3, 130.2, 129.4, 128.7, 117.2, 113.3, 48.0, 29.0, 25.3, 19.8.

*N-(Cyclohex-2-en-1-yl)-4-nitrobenzenesulfonamide (**5b**).* Yield: 98%, 83.0 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 20:1). ^{1}H NMR (400 MHz, Acetone): δ 8.44 (dt, J = 8.9, 1.9 Hz, 2H), 8.17 (td, J = 8.9, 1.9 Hz, 2H), 6.96 (d, J = 7.9 Hz, 1H), 5.71−5.77 (m, 1H), 5.36−5.41 (m, 1H), 3.85−3.92 (m, 1H), 1.88−1.96 (m, 2H), 1.70−1.78 (m, 1H), 1.61−1.69 (m, 1H), 1.46−1.57 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, Acetone): δ 206.3, 150.7, 149.0, 131.5, 129.0, 128.1, 125.2, 50.2, 30.8, 25.0, 20.2. HRMS (ESI-Q-orbitrap) m/z: [M + Na]$^+$ calcd for $C_{12}H_{14}N_2NaO_4S$, 281.0602; found, 281.0602.

*3-(Cyclohex-2-en-1-yl)-1H-indole (**5c**).*[16] Yield: 82%, 48.5 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 25:1). ^{1}H NMR (500 MHz, $CHCl_3$): δ 7.87 (br. s, 1H), 7.71 (d, J = 7.6 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 7.3 Hz, 1H), 7.15 (t, J = 7.3 Hz, 1H), 5.91 (s, 2H), 3.77 (s, 1H), 2.07−2.19 (m, 3H), 1.81−1.89 (m, 1H), 1.74−1.81 (m, 1H), 1.64−1.74 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CHCl_3$): δ 136.7, 130.5, 127.7, 126.8, 122.0, 121.5, 121.0, 119.3, 119.2, 111.3, 32.8, 30.3, 25.4, 21.0.

*1-[3-(Cyclohex-2-en-1-yl)-1H-indol-1-yl]-2,2-dimethylpropan-1-one (**5d**).* Yield: 92%, 77.7 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, J = 8.2 Hz, 1H), 7.58 (d, J = 7.7, 1H), 7.44 (s, 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.27 (t, J = 7.2 Hz, 1H), 5.92−5.98 (m, 1H), 5.81−5.86 (m, 1H), 3.64−3.71 (m, 1H), 2.03−2.17 (m, 3H), 1.63−1.85 (m, 3H), 1.51 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 177.0, 137.7, 128.9, 128.8, 126.0, 125.2, 123.3, 122.7, 122.0, 118.9, 117.7, 41.2, 32.4, 29.3, 28.8, 25.2, 20.6. HRMS (ESI-Q-orbitrap) m/z: [M + Na]$^+$ calcd for $C_{19}H_{23}NNaO$, 304.1672; found, 304.1670.

*2-[5-(Cyclohex-2-en-1-yl)thiophen-2-yl]acetonitrile (**5e**).* Yield: 85%, 51.8 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.86 (d, J = 3.5 Hz, 1H), 6.68 (d, J = 3.5 Hz, 1H), 5.83−5.89 (m, 1H), 5.72−5.77 (m, 1H), 3.84 (s, 2H), 3.60−3.67 (m, 1H), 2.01−2.10 (m, 3H), 1.57−1.79 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.5, 129.1, 128.9, 128.3, 126.8, 123.6, 117.2, 36.8, 32.4, 24.9, 20.5, 18.9. HRMS (ESI-Q-orbitrap) m/z: [M + Na]$^+$ calcd for $C_{12}H_{13}NNaS$, 226.0661; found, 226.0661.

*3-(Cyclohex-2-en-1-yl)pentane-2,4-dione (**5f**).* Yield: 85%, 46.0 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 40:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.71−5.76 (m, 1H), 5.32−5.37 (m, 1H), 3.57 (d, J = 10.7 Hz, 1H), 2.94−3.02 (m, 1H), 2.15 (s, 3H), 2.14 (s, 3H), 1.92−1.98 (m, 2H), 1.62−1.73 (m, 2H), 1.48−1.59 (m, 1H), 1.12−1.22 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 204.1, 203.8, 130.1, 127.1, 74.9, 35.7, 30.1, 29.7, 26.7, 25.0, 20.7. HRMS (ESI-Q-orbitrap) m/z: [M + Na]$^+$ calcd for $C_{11}H_{16}NaO_2$, 203.1043; found, 203.1042.

*Methyl 2-(Cyclohex-2-en-1-yl)-2-methylpropanoate (**5g**).* Yield: 98%, 53.6 mg. Purified by flash column chromatography through silica gel (dichloromethane/methanol, 30:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.70−5.77 (m, 1H), 5.41−5.47 (m, 1H), 3.65 (s, 3H), 2.43−2.51 (m, 1H), 1.90−1.97 (m, 2H), 1.73−1.81 (m, 1H), 1.58−1.66 (m, 1H), 1.43−1.55 (m, 1H), 1.18−1.29 (m, 1H), 1.12 (s, 3H), 1.08 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 178.5, 129.2, 127.7, 51.7, 45.4, 43.1, 25.2, 24.3, 22.5, 22.0, 21.7. HRMS (ESI-Q-orbitrap) m/z: [M + Na]$^+$ calcd for $C_{11}H_{18}NaO_2$, 183.1380; found, 183.1380.

*3-Allylcyclohex-1-ene (**5h**).*[17] Yield: 74%, 27.1 mg. Purified by flash column chromatography through silica gel (hexane/ethyl acetate, 30:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.75−5.87 (m, 1H), 5.64−5.72 (m, 1H), 5.55−5.62 (m, 1H), 4.98−5.07 (m, 2H), 2.11−2.20 (m, 1H), 2.01−2.10 (m, 2H), 1.93−2.01 (m, 2H), 1.66−1.81 (m, 2H), 1.46−1.58 (m, 1H), 1.21−1.29 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 137.4, 131.5, 127.4, 115.9, 40.8, 35.2, 29.0, 25.4, 21.6.

*(Cyclohex-2-en-1-ylethynyl)benzene (**5i**).*[18] Yield: 66%, 36.1 mg. Purified by flash column chromatography through silica gel (hexane/ethyl acetate, 30:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.45 (m, 2H), 7.23−7.30 (m, 3H), 5.70−5.82 (m, 2H), 3.30 (s, 1H), 1.93−2.10 (m, 3H), 1.75−1.93 (m, 2H), 1.58−1.69 (m, 1 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 131.7, 128.3, 128.2, 127.7, 127.2, 124.0, 93.0, 80.4, 29.5, 28.1, 24.8, 20.8.

*Cyclohex-2-en-1-yl(phenyl)sulfane (**5j**).* Yield: 94%, 57.1 mg. Purified by flash column chromatography through silica gel (hexane/ethyl acetate, 30:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, J = 7.5 Hz, 2H), 7.29 (t, J = 7.4 Hz, 2H), 7.22 (t, J = 7.4 Hz, 1H), 5.84 (d, J = 10.0 Hz, 1H), 5.77 (d, J = 10.0 Hz, 1H), 3.86 (s, 1H), 2.00−2.11 (m, 2H), 1.85−1.99 (m, 2H), 1.75−1.82 (m, 1H), 1.57−1.65 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 136.1, 131.5, 130.7, 129.1, 127.1, 126.8, 44.1, 29.0, 25.2, 19.7. HRMS (APCI-Q-orbitrap) m/z: [M + H]$^+$ calcd for $C_{12}H_{14}S$, 191.0890; found, 191.0889.

*7-Bromo-2-(4-(trifluoromethoxy)phenyl)-3a,4,5,6,7,7a-hexahydrobenzo[d]oxazole (**6**).* Yield: 98%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (d, J = 8.9 Hz, 2H), 7.25 (d, J = 8.9 Hz, 2H), 4.85 (t, J = 7.7 Hz, 1H), 4.26−4.31 (m, 1H), 4.00−4.06 (m, 1H), 2.06−2.20 (m, 2H), 1.91−2.00 (m, 1H), 1.78−1.87 (m, 1H), 1.69−1.77 (m, 1H), 1.50−1.59 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 178.0, 54.4, 54.2, 45.0, 38.0, 27.6, 26.3, 23.2, 18.5. HRMS (ESI-Q-orbitrap) m/z: [M + Na]$^+$ calcd for $C_{14}H_{13}BF_3NNaO_2$, 385.9980; found, 385.9973.

*5-Fluoro-6-methyl-2-(4-(trifluoromethoxy)phenyl)-4,5,6,6a-tetrahydro-3aH-cyclopenta[d]oxazole (**7**).* Yield: 58%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, J = 9.0 Hz, 2H), 7.23 (d, J = 9.0 Hz, 2H), 4.74−4.87 (m, 3H), 2.70−2.80 (m, 1H), 2.20−2.43 (m, 2H), 0.99 (d, J = 8 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 162.1, 151.5, 151.4, 130.2, 126.6, 123.6, 121.5, 120.6, 119.5, 117.4, 101.1, 99.7, 89.8, 71.0, 47.1, 47.0, 38.5, 38.3, 15.6, 15.5. HRMS (ESI-Q-orbitrap) m/z: [M + H]$^+$ calcd for $C_{14}H_{13}F_4NNaO_2$, 304.0955; found, 304.0955.

*N-[(1R,6S)-7-Oxabicyclo[4.1.0]heptan-2-yl]pivalamide (**8**).*[12] Yield: 99%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.93 (br. d, J = 6.1 Hz, 1H), 4.28−4.34 (m, 1H), 3.22−3.26 (m, 1H), 3.17 (t, J = 3.4 Hz, 1H), 1.78−1.83 (m, 2H), 1.40−1.50 (m, 2H), 1.22−1.32 (m, 2H), 1.16 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 178.0, 54.4, 54.2, 45.0, 38.7, 27.6, 26.3, 23.2, 18.5.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00480.

^{1}H and ^{13}C NMR spectra of all new compounds (PDF)

Accession Codes

CCDC 1978161−1978162 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Trost, B. M.; Crawley, M. L. Asymmetric Transition-Metal-Catalyzed Allylic Alkylations: Applications in Total Synthesis. *Chem. Rev.* **2003**, *103*, 2921−2943. (b) Nugent, T. C. *Chiral Amine Synthesis: Methods, Developments and Applications*; Wiley-VCH, 2010.

(2) (a) Davies, S. G.; Long, M. J. C.; Smith, A. D. Ammonium directed dihydroxylation of *N,N*-dibenzylaminocyclohex-2-ene: metal-free syntheses of the diastereoisomers of 3-dibenzylamino-1,2-dihydroxycyclohexane. *Chem. Commun.* **2005**, 4536−4538. (b) Yamatsugu, K.; Kanai, M.; Shibasaki, M. An alternative synthesis of Tamiflu®: a synthetic challenge and the identification of a ruthenium-catalyzed dihydroxylation route. *Tetrahedron* **2009**, *65*, 6017−6024. (c) Skoda, E. M.; Davis, G. C.; Wipf, P. Allylic Amines as Key Building Blocks in the Synthesis of (*E*)-Alkene Peptide Isosteres. *Org. Process Res. Dev.* **2012**, *16*, 26−34. (d) Brennan, M. B.; Csatayová, K.; Davies, S. G.; Fletcher, A. M.; Green, W. D.; Lee, J. A.; Roberts, P. M.; Russell, A. J.; Thomson, J. E. Syntheses of Dihydroconduramines (±)-B-1, (±)-E-1, and (±)-F-1 via Diastereoselective Epoxidation of N-Protected 4-Aminocyclohex-2-en-1-ols. *J. Org. Chem.* **2015**, *80*, 6609−6618. (e) Sato, S.; Fukuda, Y.; Ogura, Y.; Kwon, E.; Kuwahara, S. Synthesis of the Epimeric Secosteroids Strophasterols A and B. *Angew. Chem., Int. Ed.* **2017**, *56*, 10911−10914.

(3) (a) Knapp, S.; Sebastian, M. J.; Ramanathan, H.; Bharadwaj, P.; Potenza, J. A. Synthesis of (−)-fortamine and (+)-2-deoxyfortamine from resolved 3S,4S-N-carbomethoxy-3-aminocyclohexen-4-ol. *Tetrahedron* **1986**, *42*, 3405−3410. (b) Betancor, C.; León, E. I.; Prange, T.; Salazar, J. A.; Suárez, E. 2-Oxazolines (4,5-dihdro-oxazoles) by organoselenium-induced cyclisation of allylic ureas. *J. Chem. Soc., Chem. Commun.* **1989**, 450−452. (c) Dong, J. J.; Harvey, E. C.; Fañanás-Mastral, M.; Browne, W. R.; Feringa, B. L. Palladium-Catalyzed Anti-Markovnikov Oxidation of Allylic Amides to Protected *β*-Amino Aldehydes. *J. Am. Chem. Soc.* **2014**, *136*, 17302−17307. (d) Calder, E. D. D.; McGonagle, F. I.; Harkiss, A. H.; McGonagle, G. A.; Sutherland, A. Preparation of Amino-Substituted Indenes and 1,4-Dihydronaphthalenes Using a One-Pot Multireaction Approach: Total Synthesis of Oxybenzo[*c*]phenanthridine Alkaloids. *J. Org. Chem.* **2014**, *79*, 7633−7648.

(4) (a) Trowbridge, A.; Walton, S. M.; Gaunt, M. J. New Strategies for the Transition-Metal Catalyzed Synthesis of Aliphatic Amines. *Chem. Rev.* **2020**, *120*, 2613−2692. (b) Qin, H.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. Bismuth-Catalyzed Intermolecular Hydroamination of 1,3-Dienes with Carbamates, Sulfonamides, and Carboxamides. *J. Am. Chem. Soc.* **2006**, *128*, 1611−1614. (c) Qin, H.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. Bismuth-catalyzed direct substitution of the hydroxy group in alcohols with sulfonamides, carbamates, and carboxamides. *Angew. Chem., Int. Ed.* **2007**, *46*, 409−413. (d) Silva, S.; Rodrigues, P.; Bento, I.; Maycock, C. D. The Aza-Wharton Reaction: Syntheses of Cyclic Allylic Amines and Vicinal Hydroxyamines from the Respective Acylaziridines. *J. Org. Chem.* **2015**, *80*, 3067−3074. (e) Guo, W.; Martínez-Rodríguez, L.; Kuniyil, R.; Martin, E.; Escudero-Adán, E. C.; Maseras, F.; Kleij, A. W. Stereoselective and Versatile Preparation of Tri- and Tetrasubstituted Allylic Amine Scaffolds under Mild Conditions. *J. Am. Chem. Soc.* **2016**, *138*, 11970−11978. (f) Lei, H.; Rovis, T. Ir-Catalyzed Intermolecular Branch-Selective Allylic C-H Amidation of Unactivated Terminal Olefins. *J. Am. Chem. Soc.* **2019**, *141*, 2268−2273. (g) Knecht, T.; Mondal, S.; Ye, J.; Das, M.; Glorius, F. Intermolecular, Branch-Selective, and Redox-Neutral Cp^*Ir^{III} -Catalyzed Allylic C-H Amidation. *Angew. Chem., Int. Ed.* **2019**, *58*, 7117−7121. (h) Zhao, X.; Zhang, F.; Liu, K.; Zhang, X.; Lv, H. Nickel-Catalyzed Chemoselective Asymmetric Hydrogenation of *α,β*-Unsaturated Ketoimines: An Efficient Approach to Chiral Allylic Amines. *Org. Lett.* **2019**, *21*, 8966−8969. (i) Cheng, Q.; Chen, J.; Lin, S.; Ritter, T. Allylic Amination of Alkenes with Iminothianthrenes to Afford Alkyl Allylamines. *J. Am. Chem. Soc.* **2020**, *142*, 17287−17293.

(5) (a) March, J. *Advanced Organic Chemistry*, Vol. 4; Wiley: New York, 1992; p 653. (b) Onaka, M.; Umezono, A.; Kawai, M.; Izumi, Y. *N*-alkylation of aniline derivatives by use of potassium cation-exchanged Y-type zeolite. *J. Chem. Soc., Chem. Commun.* **1985**, 1202. (c) Sen, S. E.; Roach, S. L. A Convenient Two-Step Procedure for the Synthesis of Substituted Allylic Amines from Allylic Alcohols. *Synthesis* **1995**, *1995*, 756−758. (d) Johannsen, M.; Jørgensen, K. A. Allylic Amination. *Chem. Rev.* **1998**, *98*, 1689−1708. (e) Salvatore, R. N.; Yoon, C. H.; Jung, K. W. Synthesis of secondary amines. *Tetrahedron* **2001**, *57*, 7785−7811.

(6) Pace, V.; Martínez, F.; Fernández, M.; Sinisterra, J. V.; Alcántara, A. R. Effective Monoallylation of Anilines Catalyzed by Supported KF. *Org. Lett.* **2007**, *9*, 2661−2664.

(7) (a) Kornblum, N.; Smiley, R. A.; Blackwood, R. K.; Iffland, D. C. The Mechanism of the Reaction of Silver Nitrite with Alkyl Halides. The Contrasting Reactions of Silver and Alkali Metal Salts with Alkyl Halides. The Alkylation of Ambident Anions. *J. Am. Chem. Soc.* **1955**, *77*, 6269−6280. (b) Hammond, G. S.; Emmons, W. D.; Parker, C. O.; Graybill, B. M.; Waters, J. H.; Hawthorne, M. F. Silver salt alkylation reactions and the preparation of polynitroalkanes. *Tetrahedron* **1963**, *19*, 177−195. (c) Kagiya, T.; Izu, M.; Maruyama, H.; Fukui, K. Relationship between structures and activities of silver salt-organic halide catalyst systems for styrene polymerization. *J. Polym. Sci., Part A-1: Polym. Chem.* **1969**, *7*, 917−923. (d) Wang, Y.-G.; Barnes, E. C. O-Regioselective Synthesis with the Silver Salt Method. *ACS Omega* **2018**, *3*, 4557−4572.

(8) Westermaier, M.; Mayr, H. Electrophilic Allylations and Benzylations of Indoles in Neutral Aqueous or Alcoholic Solutions. *Org. Lett.* **2006**, *8*, 4791−4794.

(9) Jana, U.; Maiti, S.; Biswas, S. An $FeCl_3$-catalyzed highly C3-selective Friedel-Crafts alkylation of indoles with alcohols. *Tetrahedron Lett.* **2007**, *48*, 7160−7163.

(10) Yeung, Y.-Y.; Gao, X.; Corey, E. J. A General Process for the Haloamidation of Olefins. Scope and Mechanism. *J. Am. Chem. Soc.* **2006**, *128*, 9644−9645.

(11) Han, T.-C.; Zhang, Y.-D.; Jia, Q.; Cui, J.; Zhang, C. Hypervalent-Iodine-Mediated Ring-Contraction Monofluorination Affording Monofluorinated Five-Membered Ring-Fused Oxazolines. *Org. Lett.* **2017**, *19*, 5300−5303.

(12) O'Brien, P.; Childs, A. C.; Ensor, G. J.; Hill, C. L.; Kirby, J. P.; Dearden, M. J.; Oxenford, S. J.; Rosser, C. M. *cis-* and *trans-*

stereoselective epoxidation of *N*-protected 2-cyclohexen-1-ylamines. *Org. Lett.* **2003**, *5*, 4955−4957.
(13) (a) Ritter, J. J.; Minieri, P. P. A New Reaction of Nitriles. I. Amides from Alkenes and Mononitriles. *J. Am. Chem. Soc.* **1948**, *70*, 4045−4048. (b) Korch, K. M.; Watson, D. A. Cross-Coupling of Heteroatomic Electrophiles. *Chem. Rev.* **2019**, *119*, 8192−8228.
(14) Hayat, S.; Rahman, A.; Choudhary, M. I.; Khan, K. M.; Schumann, W.; Bayer, E. N-Alkylation of anilines, carboxamides and several nitrogen heterocycles using CsF-Celite/alkyl halides/CH_3CN combination. *Tetrahedron* **2001**, *57*, 9951−9957.
(15) Wang, D.-Y.; Peng, X.-M.; Wang, G.-Z.; Zhang, Y.-J.; Guo, T.; Zhang, P.-K. Iron-Catalyzed Synthesis of Amines and Thioethers Directly from Allylic Alcohols. *Asian J. Org. Chem.* **2018**, *7*, 875−878.
(16) Dethe, D. H.; Das, S.; Kumar, V. B.; Mir, N. A. Enantiospecific Total Syntheses of (+)-Hapalindole H and (−)-12-epi-Hapalindole U. *Chem. - Eur. J.* **2018**, *24*, 8980−8984.
(17) Di, Y.; Yoshimura, T.; Naito, S.; Kimura, Y.; Kondo, T. Homogeneous $Sc(OTf)_3$-Catalyzed Direct Allylation Reactions of General Alcohols with Allylsilanes. *ACS Omega* **2018**, *3*, 18885−18894.
(18) Almasalma, A. A.; Mejia, E. Allylic C-H Alkynylation via Copper-Photocatalyzed Cross-Dehydrogenative Coupling. *Synthesis* **2020**, *52*, 529−536.

https://doi.org/10.1021/acs.joc.1c00480
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