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Palladium-Catalyzed C-N Bond Cleavage of *2H*-Azirines for the Synthesis of Functionalized α-Amidoketones

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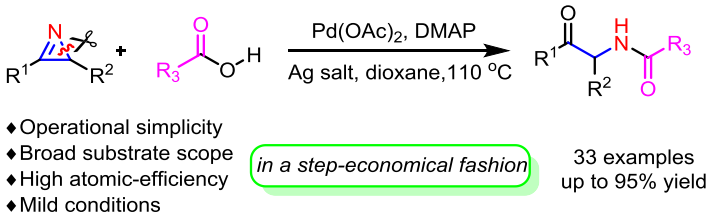


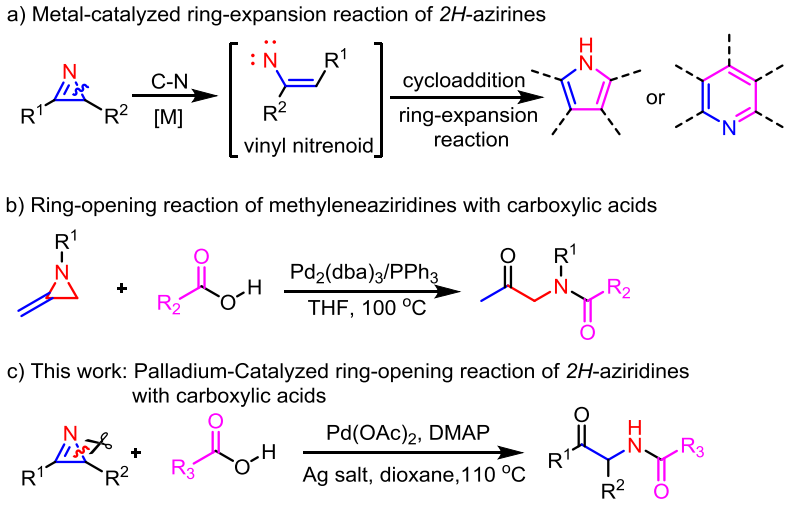
ABSTRACT: A Pd-catalyzed ring-opening reaction of *2H*-azirines with carboxylic acids was developed. This reaction undergoes nucleophilic addition between 2,3-diaryl-2*H*-azirines and carboxylic acids followed by C-N single bond cleavage and a subsequent thermal rearrangement. This method enables the rapid construction of valuable α-amidoketone derivatives with high atomic efficiency and superb functional-group tolerance.

INTRODUCTION

The metal-catalyzed conversion of 2*H*-azirines has attracted considerable attention in modern organic synthesis to build up highly complex molecular skeletons.[1-6] Based on their inherently high ring-strain energy,[7-10] *2H*-azirines undergo various ring expansion reactions, such as [3+2],[11-17] [3+3],[18-22] [3+2+2][23] cycloaddition with unsaturated molecules, aza-Diels-Alder reactions,[24] intramolecular rearrangement[25]

and various nucleophilic addition reactions.[26-30] Among these events, three general models for the chemical bond cleavage of 2*H*-azirines have been well-established: i) heterolytic C−N single-bond-cleavage mode to generate vinyl nitrenoid intermediates,[31,32] ii) transition-metal-assisted or visible light-induced C−C cleavage mode to generate nitrile ylides,[33] and iii) simultaneous cleavage of both C−C and C−N mode to form carbenoid species[34] (Scheme 1, a). Compared with the prevalence of ring expansion *via* cycloaddition reactions, the exploration of new applications of *2H*-azirines is highly desirable.

Scheme 1. Representative applications of *2H*-azirines.



The α-amidoketones are very important structural motifs that are widely found in pharmaceuticals and several natural active molecules, such as herbicides, fungicides, and enzyme inhibitors.[35-37] They are also important synthetic intermediates, for instance in the synthesis of *N*-heterocycles such as oxazoles,[38] imidazoles[39], thiazoles[40], and others. Therefore, considerable efforts have been devoted to their synthesis.[41-50] Nevertheless, some of these synthetic methods suffer from the following drawbacks: the difficulties of preparing starting substrates, rigorous

conditions, and/or limitations of the substrate scope. Therefore, new synthetic methods featuring high atomic-efficiency and operational simplicity are still under great demand. In this regard, method based on direct Pd-catalyzed ring-opening reaction of methyleneaziridine with carboxylic acid has been applied to access α-amidoketones[51] (Scheme 1, b). However, this transformation was limited to the synthesis of tertiary amide, and was also restricted by strict inert conditions and lack of substrate variation. In view of high ring strain and the easy ring-opening nature of *2H*-azirines, reaction of *2H*-azirines with carboxylic acids was also developed. However, the substrates were limited to amino-azirines[52,53], 2-phenylazirine[54,55] and phosphorus substituted azirines.[56,57] Very recently, Nakamura's group described an oxidative ring-opening reaction of aziridines with α-nitroesters using a cinchona alkaloid amide/$NiBr_2$ catalyst to construct α-amidoketones,[58] whereas this process is confined to low atomic-efficiency, and limited substrate scope. Nevertheless, despite the potential interest of *2H*-azirines, three-membered heterocycles directly substituted with two aryl functional group, easily accessed from 1,2-diarylethan-1-one and hydroxylamine,[14] have received scarce attention. In this context, the development of ring-opening reaction of 2,3-diaryl-*2H*-azirines with carboxylic acids is highly demand. Key challenges in developing the proposed transformation include: (1) poorer nucleophilicity of carboxyl group compared to nitrogen atom[27,59] and Grignard reagent,[60] and (2) difficulty in controlling the desired thermal rearrangement. Herein, we describe the discovery of the first Pd-catalyzed ring-opening reaction of 2,3-diaryl-2*H*-azirines with carboxylic acids in a step-economical fashion, affording

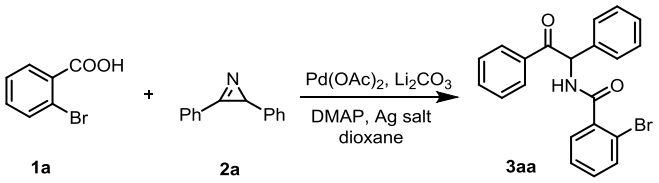
α-amidoketones involving a C-N single bond cleavage and a subsequent thermal rearrangement (Scheme 1, c).

RESULTS AND DISCUSSION

Initially, the reaction of 2-bromobenzoic acid **1a** and 2,3-diphenyl-*2H*-azirine **2a** was investigated (Table 1). The desired product **3aa** was obtained in 38% yield when the reaction was proceeded using AgOAc and DMAP (4-dimethylaminopyridine) as additives in the presence of $Pd(OAc)_2$ in dioxane at 110 ^oC. Based on this preliminary result, we first investigated the impact of Ag salts and discovered that the yield of **3aa** could be improved when $AgPF_6$, AgOTf, and Ag_2CO_3 were employed (entries 2-4). In contrast, low yields were obtained when $AgOSO_2CF_3$, AgOBz (Silver benzoate) and AgCl were used (entries 5-7). It should be noted that the expected product **3aa** was obtained in 92% yield by using Ag-1 as the additive (entry 8). Furthermore, we screened different solvents such as THF, CH_3CN, toluene, EtOH, and tert-amyl alcohol. However, none of these solvents gave better result than dioxane (entries 9-14). The yield was marginally decreased upon increasing the loading of Ag-1 from 10 mol% to 50 mol% (entry 15). To our disappointment, decreasing the reaction temperature to 80 ℃ led to the expected product **3aa** in 38% yield, while the reaction afforded **3aa** in trace at room temperature (entries 16-17). The control experiments revealed that reaction efficiency was significantly decreased in absence of DMAP or Ag-1 (entries 18-19). Therefore, the use of 10 mol% Pd(OAc), 10 mol% Ag salt, 100 mol% DMAP in the presence of Li_2CO_3 in dioxane at 110 ℃ for 18 h was found to be

the best reaction conditions for the ring-opening reaction of *2H*-aziridines with carboxylic acids (entry 8).

Table 1. Optimization of the reaction conditions.[a]

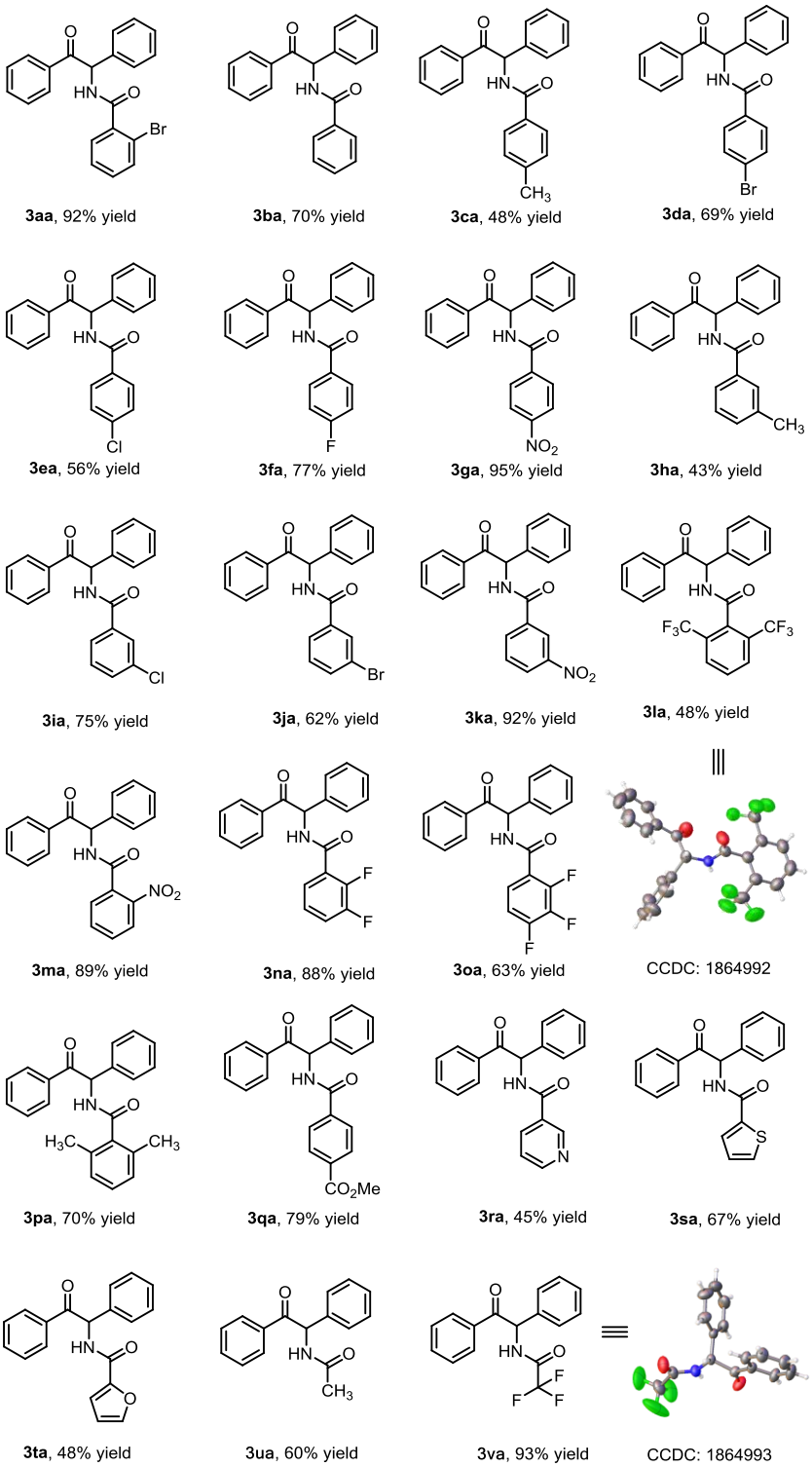


Entry	Solvent	Ag salt	Yield[b]
1	dioxane	AgOAc	38
2	dioxane	$AgPF_6$	49
3	dioxane	AgOTf	65
4	dioxane	Ag_2CO_3	60
5	dioxane	$AgOSO_2CF_3$	38
6	dioxane	AgOBz	41
7	dioxane	AgCl	45
8	dioxane	Ag-1	92
9[c]	THF	Ag-1	N.D
10[d]	CH_3CN	Ag-1	49
11	Toluene	Ag-1	75
12	DMF	Ag-1	17
13[d]	EtOH	Ag-1	26
14	tert-amyl alcohol	Ag-1	73
15[e]	dioxane	Ag-1	78
16[d]	dioxane	Ag-1	38
17[c]	dioxane	Ag-1	N.D
18[f]	dioxane	Ag-1	58
19[g]	dioxane	No	55

[a] Reaction conditions: **1a** (0.125 mmol), **2a** (0.125 mmol), $Pd(OAc)_2$ (10 mol%), DMAP (1 equiv), Ag-1 (Chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]silver) (10 mol%), and Li_2CO_3 (1 equiv) in dioxane (2 mL) at 110 °C for 18 h. [b] Isolated yields. [c] 40 °C. [d] 80 °C. [e] Ag-1 (50 mol%). [f] Without DMAP. [g] Without Ag salt.

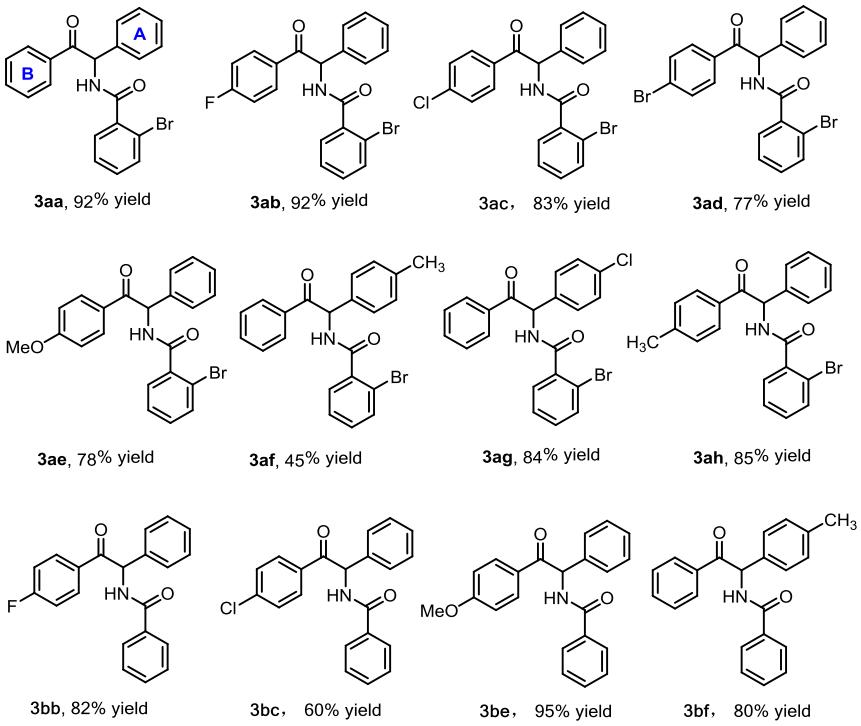
With the optimized reaction conditions, the scope of the carboxylic acids for Pd-catalyzed ring-opening reaction was investigated, as illustrated in Scheme 2. Generally, various carboxylic acids furnished the expected products **3aa-3va** with moderate-to-good yields in this protocol. We observed that the electronic properties of the substituents on the aromatic ring of benzoic acid have a decisive effect on the reaction efficiency, as the substrates bearing electron-withdrawing groups (56-95%) gave better yields than the one bearing electron-donating groups (43-70% yield). In addition, substituents such as halides, nitro, alkyl, CF_3, and ester, at different positions of benzoic acid were well-tolerated, providing new opportunities for potential further derivatization. In addition, the reaction efficiency was not very sensitive to the steric hindrance of the substituents, wherein the substrates with two *ortho*-CF_3 or *ortho*-methyl substituents worked smoothly, affording the desired products **3la** and **3pa** in 48% and 70% yields, respectively. The structure of **3la** was unambiguously determined by single crystal X-ray crystallography and NMR (see Pages S5-S6 of the Supporting Information). To our delight, the introduction of two or three electron-withdrawing groups such as fluoro on the aromatic ring furnished the expected products **3na** and **3oa** in 88% and 63% yields. Remarkably, thiophene-2-carboxylic acid, furan-2-carboxylic acid, and nicotinic acid were also amenable for the reactions (**3ra-3ta**). Most importantly, aliphatic carboxylic acids **1u** and **1v** also performed well with good yields (**3ua** and **3va**, 60% and 93%).

Scheme 2. Pd-catalyzed ring-opening cascade of *2H*-azirines with various carboxylic acids. [a]



[a] Reaction Conditions: **1a-1v** (0.125 mmol), **2a** (0.125 mmol), $Pd(OAc)_2$ (10 mol%), DMAP (1 equiv), and Li_2CO_3 (1 equiv) in dioxane (2 mL) at 110 ^oC for 18 h. Yields are those of isolated products.

Scheme 3. Substrate scope of *2H*-azirines.[a]

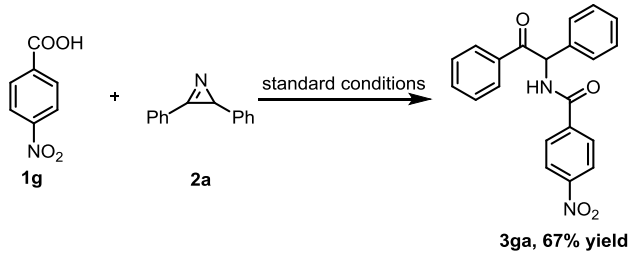


[a] Reaction Conditions: **1a** (0.125 mmol), **2a**-**2g** (0.125 mmol), $Pd(OAc)_2$ (10 mol%), DMAP (1 equiv), and Li_2CO_3 (1 equiv) in dioxane (2 mL) at 110 ^oC for 18 h. Yields are those of isolated products.

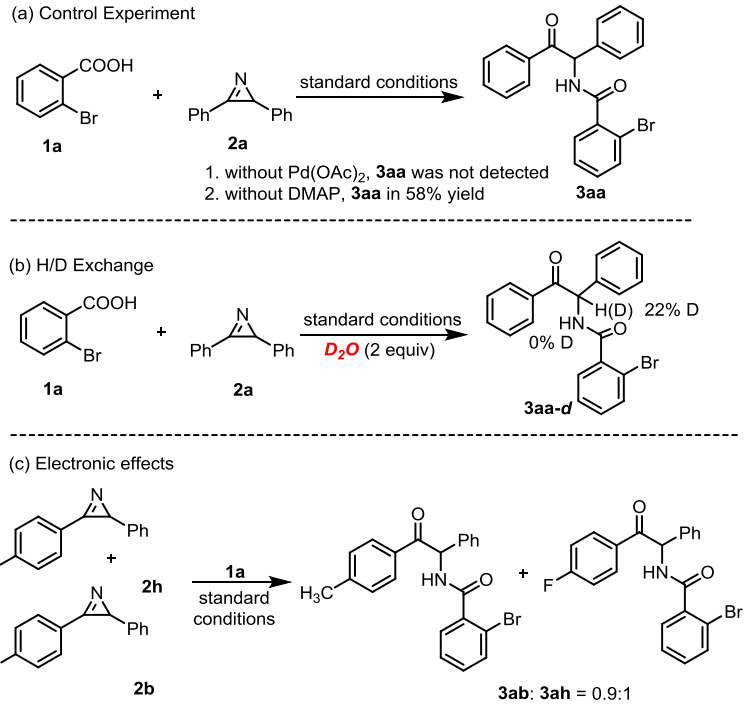
To assess the reaction generality, we next explored the scope of the reaction by variation of the substitution patterns of *2H*-azirines under the optimized conditions, and the results are summarized in Scheme 3. We first sought to investigate the effect of different substituents on the phenyl ring **B** of *2H*-azirines. Substrates bearing various electron-withdrawing groups, such as F, Cl, and Br, along with electron-donating methoxy group, all generated the targeted α-aminoketones in satisfying yields (**3ab**-**3ae**). The reaction of 3-phenyl-2-(p-tolyl)-*2H*-azirine **2f** with **1a** delivered the α-aminoketone **3af** in lower yield than that observed with **2a**-**2e**. As for 2-(4-chlorophenyl)-3-phenyl-*2H*-azirine **2g** and 2-phenyl-3-(p-tolyl)- *2H*-azirine **2h**, a chlorine atom and Me- group on the phenyl ring of *2H*-azirines were well tolerated, and the desired product **3ag** and **3ah** were obtained in 84% and 85% yields.

We also carried out the reactions between various *2H*-azirines and benzoic acid **1b** under optimal reaction conditions, in which moderate to good yields and high efficiency were observed for substrates **2b**, **2c**, **2e**, and **2f** (Scheme 3, **3bb**, **3bc**, **3be**, and **3bf**). To our delight, when 1 mmol scale of **1g** and **2a** were used in the reaction under the optimized reaction conditions, **3ga** was isolated in 67% yield (Scheme 4).

Scheme 4. Scale-up reaction



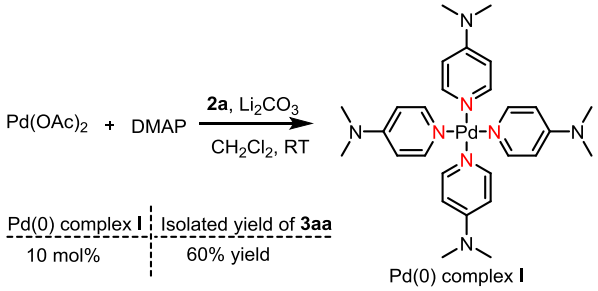
Scheme 5. Mechanistic experiments.



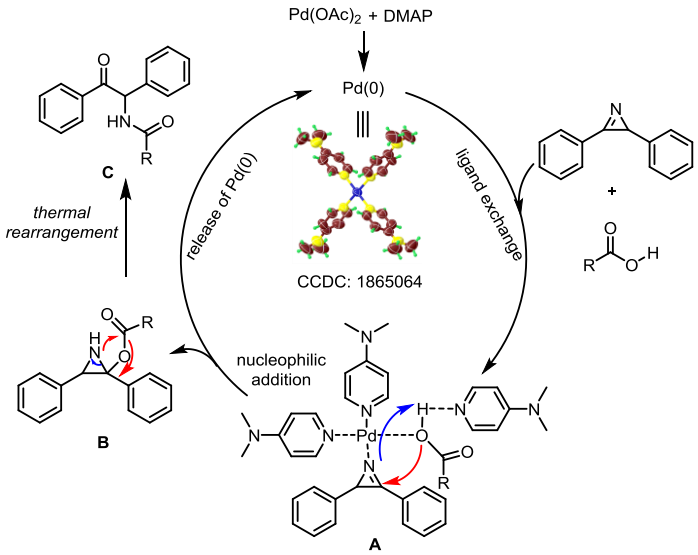
To gain insights into the reaction mechanism, several control experiments were performed (Scheme 5, and see Scheme S1-S4 in SI). First, control experiments were conducted to investigate the transformation of **1a** and **2a** to **3aa**. It was found that

DMAP could promote the reaction, while no product was detected without $Pd(OAc)_2$ (Scheme 5, eq. a). Second, the reaction of **1a** and **2a** in the presence of 2 equiv of D_2O at 110 ^oC for 18 h furnished **3aa** in 76% yield and ^{1}HNMR analysis of the isolated product revealed H/D exchange (22%) was observed at α-H of **3aa**-*d* (Scheme 5, eq. b, and see Figure S1 in SI). After that, we probed the electronic preference of this cascade reaction *via 2H*-azirines competition experiments. The reaction between **2h** and **2b** differing in electronic effects was conducted with **1a**. The small difference is perhaps due to the substrate structure (Scheme 5, eq. c).

Scheme 6. Comparative trial experiment.



Scheme 7. Proposed mechanism.



The reaction of $Pd(OAc)_2$ with 1 equiv of DMAP in the presence of 2,3-diphenyl-*2H*-azirine **2a** at room temperature led to the formation of a stable Pd (0)

complex **I**, which was determined by a single crystal X-ray analysis (Scheme 6, and see Scheme S5 in SI). In the comparative trial using Pd (0) complex **I** as the catalyst under the standard conditions, **3aa** was isolated in 60% yield, suggesting that the transformation is probably initiated by reducing of Pd (II) to Pd (0) species (see Scheme S6 in SI). Based on the previous work[23,51] and the above results, a proposed catalytic cycle for Pd-catalyzed cascade nucleophilic addition/ring-opening reaction is depicted in Scheme 7. Initially, Pd(II) salt is reduced to Pd(0) species. Coordination and ligand exchange of Pd(0) complex with 2*H*-azirines and carboxylic acids are followed by the nucleophilic addition of carboxylic acids to reactive unsaturated C-N double bonds to generate intermediate **B**. The intermediate **B** subsequently undergoes C-N single bond cleavage and a thermal rearrangement to generate the ring-opening product **C** and releases the Pd(0) species. Key to the success of this catalytic cycle is reduction of Pd(II) salt by DMAP, which probably facilitate ligand exchange and nucleophilic addition.

CONCLUSION

In summary, we have established the Pd-catalyzed cascade nucleophilic addition/ring-opening reaction between 2,3-diaryl-*2H*-azirines and carboxylic acid derivatives in a step-economical fashion. The reaction exhibited outstanding functional-group compatibility with respect to both *2H*-azirines and carboxylic acids, allowing for the formation of functionalized α-amidoketones in good to excellent yields (up to 95%). The notable features of this protocol comprise operational simplicity, broad substrate scope, high atomic-efficiency, and mild conditions. From a

mechanistic point of view, the Pd(II) complex is reduced to Pd(0) species and then coordinated to the DMAP. This process probably facilitates ligand exchange and nucleophilic addition. Further applications of this promising strategy are in progress in our laboratory.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all the reactions were carried out in a glassware under air condition. The commercially available chemicals and solvents were used as received without further purification. *2H*-Azirines were prepared according to the published procedure.[10,11,61,62] The reactions were monitored by TLC using UV-light or by staining with iodine. Column chromatography was performed on silica gel (200-300 mesh). Single-crystal X-ray data in this work were collected on an Agilent Technologies SuperNova Single Crystal Diffractometer at different temperatures equipped with graphite-monochromatic Mo Kα or Cu Kα radiation (λ = 0.71073 Å or 1.54184 Å). The structures were solved by SHELXS (direct methods) and refined by SHELXL (full matrix least-squares techniques) in the Olex2 package. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms attached to carbon were placed in geometrically idealized positions and refined using a riding model. ^{1}H, ^{13}C, and ^{19}F NMR were recorded on a 600 or 400 MHz Bruker NMR spectrometer in $CDCl_3$ (7.26 ppm for ^{1}H and 77.16 ppm for ^{13}C) using tetramethylsilane (TMS) as the internal standard (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet). High-resolution mass

spectra HRMS data were obtained with Micromass HPLC–Q–TOF mass spectrometer.

Procedure for Cascade C-N Bond Cleavage of *2H*-Azirines. A mixture of $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), Ag-1 (Chloro[1,3-bis(2,6-diisopropylphenyl) imidazole-2-ylidene]silver) (6.6 mg, 10 mol%), Li_2CO_3 (1 equiv), 2*H*-azirines (0.125 mmol), carboxylic acids (0.125 mmol), DMAP (1 equiv), and dioxane (2 mL) was stirred at 110 °C for 18 h. After cooling the reaction to room temperature, the solvent was removed under vacuum and the residue was purified by silica gel chromatography using ethyl acetate/petroleum ether (10:1~4:1) to afford desired products.

Scale-up Synthesis. A mixture of $Pd(OAc)_2$ (22.4 mg, 0.1 mmol), Ag-1 (52.8 mg, 10 mol%), Li_2CO_3 (1 equiv), *2H*-azirines **2a** (1 mmol, 193.3 mg), carboxylic acid **1g** (1 mmol, 167.1 mg), DMAP (1 equiv), and dioxane (16 mL) was stirred at 110 °C for 18 h. After cooling the reaction to room temperature, the solvent was removed under vacuum and the residue was purified by silica gel chromatography using ethyl acetate/petroleum ether (10:1~4:1) to afford desired product **3ga** (241.5 mg, 67% yield).

3-(4-fluorophenyl)-2-phenyl-2H-azirine (2b).[14] White solid. Petroleum ether/ethyl acetate = 10:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.03 – 7.86 (m, 2H), 7.40 – 7.20 (m, 5H), 7.20 – 7.08 (m, 2H), 3.32 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ = 165.6 (d, *J* = 255.5 Hz), 162.5, 140.6, 132.2 (d, *J* = 9.3 Hz), 128.4, 127.2, 126.1, 120.5, 116.8 (d, *J* = 22.4 Hz), 34.6.

3-(4-bromophenyl)-2-phenyl-2H-azirine (2d).[62] White solid. Petroleum ether/ethyl acetate = 10:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.80 (d, *J*=8.5, 2H), 7.73 (d, *J*=8.5,

2H), 7.31 (m, 3H), 7.21 – 7.10 (m, 2H), 3.37 (s, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 163.1, 140.4, 132.7, 131.1, 128.4, 128.2, 127.3, 126.1, 123.0, 34.7.

2-bromo-N-(2-oxo-1,2-diphenylethyl)benzamide (3aa). White solid (45.3 mg, isolated yield 92%). m.p 144.6-146.5. Petroleum ether/ethyl acetate = 4:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 (dd, *J*=5.2, 3.4, 2H), 7.62 (d, *J*=7.0, 1H), 7.58 (dd, *J*=7.9, 1.1, 1H), 7.56 – 7.51 (m, 2H), 7.51 – 7.46 (m, 2H), 7.42 (dd, *J*=10.6, 4.8, 2H), 7.37 – 7.30 (m, 3H), 7.30 – 7.24 (m, 2H), 6.76 (d, *J*=7.2, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 195.2, 166.5, 137.0, 136.8, 134.2, 133.9, 133.5, 131.5, 129.9, 129.2, 128.8, 128.5, 128.4, 127.5, 124.4, 119.6, 59.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{17}BrNO_2^+$, 394.0443, found 394.0420.

N-(2-oxo-1,2-diphenylethyl)benzamide (3ba). White solid (27.6 mg, isolated yield 70%). m.p 144.5-146.3. Petroleum ether/ethyl acetate = 10:1. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 – 7.99 (m, 2H), 7.91 – 7.81 (m, 2H), 7.74 (d, *J* = 6.7 Hz, 1H), 7.57 – 7.47 (m, 4H), 7.43 (m, 3H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.23 (m, 1H), 6.76 (d, *J* = 7.0 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ = 195.8, 166.3, 137.3, 134.2, 133.9, 133.9, 131.8, 129.3, 129.2, 128.8, 128.6, 128.4, 128.3, 127.2, 58.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{18}NO_2^+$, 316.1338, found 316.1330.

4-methyl-N-(2-oxo-1,2-diphenylethyl)benzamide (3ca). White solid (19.7 mg, isolated yield 48%). m.p 141.6-143.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 – 7.99 (m, 2H), 7.75 (d, *J*=8.2, 2H), 7.69 (d, *J*=6.9, 1H), 7.57 – 7.51 (m, 1H), 7.50 – 7.45 (m, 2H), 7.42 (t, *J*=7.7, 2H), 7.35 – 7.29 (m, 2H), 7.28 – 7.20 (m, 3H), 6.75 (d, *J*=7.0, 1H), 2.39 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 195.9, 166.3, 149.8, 142.2, 137.4,

134.4, 133.9, 131.0, 129.2, 129.2, 128.8, 128.39, 128.35, 127.2, 58.9, 21.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}NO_2^+$, 330.1494, found 330.1499.

4-bromo-N-(2-oxo-1,2-diphenylethyl)benzamide (3da). White solid (34.0 mg, isolated yield 69%). m.p 149.3-150.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05 – 7.96 (m, 2H), 7.78 – 7.67 (m, 3H), 7.61 – 7.51 (m, 3H), 7.45 (dt, *J*=15.4, 4.5, 4H), 7.37 – 7.29 (m, 2H), 7.29 – 7.24 (m, 1H), 6.72 (d, *J*=7.0, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.7, 171.1, 165.4, 137.1, 134.2, 134.0, 132.8, 131.8, 129.3, 129.2, 128.8, 128.6, 128.4, 126.5, 59.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{17}BrNO_2^+$, 394.0443, found 394.0446.

4-chloro-N-(2-oxo-1,2-diphenylethyl)benzamide (3ea). White solid (24.5 mg, isolated yield 56%). m.p 131.8-133.5. Petroleum ether/ethyl acetate = 4:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.09 – 7.97 (m, 2H), 7.78 (t, *J*=5.4, 2H), 7.71 (d, *J*=6.8, 1H), 7.54 (t, *J*=7.4, 1H), 7.50 – 7.38 (m, 6H), 7.33 (t, *J*=7.4, 2H), 7.30 – 7.23 (m, 1H), 6.72 (d, *J*=7.0, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.7, 165.3, 138.0, 137.1, 134.1, 134.0, 132.3, 129.3, 129.2, 128.9, 128.8, 128.6, 128.6, 128.4, 59.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{17}ClNO_2$+, 350.0948, found 350.0943.

4-fluoro-N-(2-oxo-1,2-diphenylethyl)benzamide (3fa). White solid (32.1 mg, isolated yield 77%). m.p 139.1-140.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 7.98 (m, 2H), 7.91 – 7.81 (m, 2H), 7.68 (d, *J*=6.7, 1H), 7.58 – 7.52 (m, 1H), 7.50 – 7.39 (m, 4H), 7.38 – 7.29 (m, 2H), 7.29 – 7.24 (m, 1H), 7.17 – 7.06 (m, 2H), 6.73 (d, *J*=7.0, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.8, 186.2, 181.1 (d, *J* = 282.1 Hz) , 165.3, 138.1, 137.2, 134.0, 129.6 (d, *J* = 9.0 Hz), 129.3, 129.2, 128.8, 128.5, 128.4, 115.6 (d,

J = 21.9 Hz), 59.0. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ = -108.07. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{17}FNO_2^+$, 334.1243, found 334.1236.

4-nitro-N-(2-oxo-1,2-diphenylethyl)benzamide (3ga). Yellow solid (42.8 mg, isolated yield 95%). m.p 186.4-187.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.34 – 8.25 (m, 2H), 8.06 – 7.95 (m, 4H), 7.83 (d, *J*=6.7, 1H), 7.59 – 7.52 (m, 1H), 7.51 – 7.39 (m, 4H), 7.39 – 7.31 (m, 2H), 7.31 – 7.24 (m, 1H), 6.72 (d, *J*=6.9, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 195.4, 164.3, 149.8, 139.5, 136.7, 134.2, 134.0, 129.4, 129.2, 128.9, 128.8, 128.4, 128.4, 123.8, 59.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{17}N_2O_4^+$, 361.1188, found 361.1192.

3-methyl-N-(2-oxo-1,2-diphenylethyl)benzamide (3ha). White solid (17.7 mg, isolated yield 43%). m.p 120.1-121.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05 – 8.00 (m, 2H), 7.71 (d, *J*=6.9, 1H), 7.68 – 7.61 (m, 2H), 7.56 –7.50 (m, 1H), 7.51 – 7.46 (m, 2H), 7.42 (dd, *J*=10.6, 4.7, 2H), 7.32 (m, 4H), 7.28 – 7.23 (m, 1H), 6.75 (d, *J*=7.1, 1H), 2.40 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 195.9, 166.5, 138.4, 137.3, 134.3, 133.9, 133.9, 132.5, 129.2, 129.2, 128.8, 128.5, 128.4, 128.4, 127.8, 124.2, 58.9, 21.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}NO_2^+$, 330.1494, found 330.1485.

3-chloro-N-(2-oxo-1,2-diphenylethyl)benzamide (3ia). White solid (32.8 mg, isolated yield 75%). m.p 135.3-137.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 – 7.98 (m, 2H), 7.83 (t, *J*=1.8, 1H), 7.77 – 7.67 (m, 2H), 7.52 (dd, *J*=4.9, 3.7, 1H), 7.50 – 7.36 (m, 6H), 7.36 – 7.30 (m, 2H), 7.29 – 7.23 (m, 1H), 6.72 (d, *J*=7.0, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 195.6, 165.0, 137.0, 135.8, 134.8, 134.2, 134.0, 131.8, 130.0,

129.3, 129.2, 128.8, 128.6, 128.4, 127.6, 125.2, 59.0. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{17}ClNO_2^+$, 350.0948, found 350.0963.

3-bromo-N-(2-oxo-1,2-diphenylethyl)benzamide (3ja). White solid (30.6 mg, isolated yield 62%). m.p 181.3-183.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 – 7.95 (m, 3H), 7.76 (d, *J*=7.7, 1H), 7.71 (d, *J*=6.6, 1H), 7.63 (d, *J*=7.9, 1H), 7.54 (t, *J*=7.3, 1H), 7.51 – 7.39 (m, 4H), 7.38 – 7.23 (m, 4H), 6.72 (d, *J*=7.0, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.6, 164.9, 137.0, 135.9, 134.7, 134.1, 134.0, 130.5, 130.2, 129.3, 129.2, 128.8, 128.6, 128.4, 125.7, 122.8, 59.0. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{17}BrNO_2^+$, 394.0443, found 394.0442.

3-nitro-N-(2-oxo-1,2-diphenylethyl)benzamide (3ka). Yellow solid (41.4 mg, isolated yield 92%). m.p 168.8-170.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.68 (t, *J*=1.9, 1H), 8.36 (m, 1H), 8.23 – 8.14 (m, 1H), 8.06 – 7.99 (m, 2H), 7.85 (d, *J*=6.8, 1H), 7.65 (t, *J*=8.0, 1H), 7.59 – 7.52 (m, 1H), 7.52 – 7.47 (m, 2H), 7.43 (dd, *J*=10.6, 4.8, 2H), 7.39 – 7.32 (m, 2H), 7.32 – 7.24 (m, 1H), 6.74 (d, *J*=6.9, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.3, 164.0, 148.3, 136.7, 135.7, 134.1, 134.0, 133.1, 129.8, 129.4, 129.2, 128.9, 128.8, 128.4, 126.3, 122.3, 59.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{17}N_2O_4^+$, 361.1188, found 361.1189.

N-(2-oxo-1,2-diphenylethyl)-2,6-bis(trifluoromethyl)benzamide (3la). White solid (27.1 mg, isolated yield 48%). m.p 135.9-137.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 8.00 (m, 2H), 7.93 (d, *J*=8.0, 2H), 7.72 (t, *J*=8.0, 1H), 7.61 – 7.50 (m, 3H), 7.45 (t, *J*=7.7, 2H), 7.42 – 7.36 (m, 3H), 7.25 (d, *J*=1.4, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 191.9, 164.2, 134.6, 133.6, 132.8, 130.4, 129.88 (dd, J = 8.4, 4.2 Hz),

129.6, 129.3, 129.1, 128.9 (d, J = 5.6 Hz), 128.7, 126.8, 122.66 (dd, J = 277.6, 7.9 Hz), 118.6, 79.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{16}F_6O_2^+$, 452.1085, found 452.1082.

2-nitro-N-(2-oxo-1,2-diphenylethyl)benzamide (3ma). Yellow solid (40.1 mg, isolated yield 89%). m.p 154.2-156.0. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.09 – 7.97 (m, 3H), 7.67 (t, *J*=7.5, 1H), 7.62 – 7.50 (m, 3H), 7.50 – 7.40 (m, 4H), 7.32 (m, 4H), 6.76 (d, *J*=7.1, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.2, 165.4, 163.7, 146.6, 136.5, 134.1, 134.0, 133.6, 132.4, 130.7, 129.3, 129.3, 128.8, 128.7, 128.4, 124.6, 59.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{17}N_2O_4^+$, 361.1188, found 361.1183.

2,3-difluoro-N-(2-oxo-1,2-diphenylethyl)benzamide (3na). White solid (38.7 mg, isolated yield 88%). m.p 121.1-122.9. Petroleum ether/ethyl acetate = 4:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (dd, *J*=9.9, 7.1, 1H), 8.02 (dd, *J*=5.2, 3.3, 2H), 7.78 (ddt, *J*=8.1, 6.4, 1.7, 1H), 7.58 – 7.46 (m, 3H), 7.42 (dd, *J*=10.6, 4.8, 2H), 7.38 – 7.22 (m, 4H), 7.16 (tdd, *J*=8.1, 4.7, 1.4, 1H), 6.74 (dd, *J*=6.7, 1.7, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.0, 161.4, 150.63 (d, *J* = 249.3 Hz), 150.49 (d, *J* = 249.7 Hz), 136.8, 134.2, 133.9, 129.3, 128.98 (d, *J* = 40.5 Hz), 128.6, 128.4, 127.1, 126.35 (d, *J* = 3.2 Hz), 124.43 (dd, *J* = 6.7, 4.5 Hz), 123.04 (d, *J* = 8.8 Hz), 120.47 (d, *J* = 17.2 Hz), 59.4. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -137.8 (d, *J* = 21.7 Hz), -138.9 (d, *J* = 21.7 Hz). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}F_2NO_2^+$, 352.1149, found 352.1147.

2,3,4-trifluoro-N-(2-oxo-1,2-diphenylethyl)benzamide (3oa). White solid (29.1 mg, isolated yield 63%). m.p 128.3-129.7. Petroleum ether/ethyl acetate = 4:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.31 – 8.17 (m, 1H), 8.10 – 7.98 (m, 2H), 7.85 (m, 1H), 7.60 – 7.54 (m, 1H), 7.51 (dd, *J*=5.2, 3.3, 2H), 7.45 (dd, *J*=10.6, 4.8, 2H), 7.39 – 7.33 (m, 2H), 7.33 – 7.26 (m, 1H), 7.09 (m, 1H), 6.74 (dd, *J*=6.7, 1.7, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.0, 160.6, 153.31 (ddd, *J* = 256.6, 10.0, 3.5 Hz), 150.28 (ddd, *J* = 252.4, 11.2, 3.7 Hz), 139.79 (ddd, *J* = 253.3, 17.0, 15.6 Hz), 136.7, 134.0, 134.0, 129.3, 129.2, 128.8, 128.6, 128.4, δ125.74 (ddd, *J* = 8.3, 4.1, 2.5 Hz), 118.44 (ddd, *J* = 9.1, 3.6, 2.1 Hz), 112.74 (dd, *J* = 17.5, 3.5 Hz), 59.4. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ -127.93 (dd, *J* = 20.1, 11.3 Hz), -134.19 (dd, *J* = 21.8, 11.3 Hz), -159.45 (t, *J* = 21.0 Hz). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}F_3NO_2^+$, 370.1055, found 370.1070.

2,6-dimethyl-N-(2-oxo-1,2-diphenylethyl)benzamide (3pa). White solid (30.0 mg, isolated yield 70%). m.p 162.7-164.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05 (dd, *J*=5.2, 3.3, 2H), 7.59 – 7.53 (m, 1H), 7.51 – 7.42 (m, 4H), 7.39 – 7.33 (m, 2H), 7.31 (dt, *J*=5.3, 2.1, 1H), 7.20 – 7.15 (m, 1H), 7.12 (d, *J*=7.5, 1H), 7.02 (d, *J*=7.6, 2H), 6.84 (d, *J*=7.7, 1H), 2.22 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.4, 169.3, 137.1, 136.9, 134.5, 134.2, 133.9, 129.3, 129.2, 128.9, 128.8, 128.5, 128.3, 127.5, 58.5, 19.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{22}NO_2^+$, 344.1651, found 344.1630.

Methyl 4-((2-oxo-1,2-diphenylethyl)carbamoyl)benzoate (3qa). White solid (36.9 mg, isolated yield 79%). m.p 151.6-153.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.14 – 8.06 (m,

2H), 8.06 – 7.97 (m, 2H), 7.94 – 7.88 (m, 2H), 7.79 (d, *J*=6.9, 1H), 7.57 – 7.51 (m, 1H), 7.51 – 7.46 (m, 2H), 7.42 (dd, *J*=10.6, 4.8, 2H), 7.37 – 7.30 (m, 2H), 7.30 – 7.24 (m, 1H), 6.74 (d, *J*=7.0, 1H), 3.95 (d, *J*=7.9, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 195.6, 166.3, 165.5, 137.8, 137.0, 134.2, 134.0, 133.0, 129.8, 129.3, 129.2, 128.8, 128.6, 128.4, 127.3, 59.1, 52.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{20}NO_4^+$, 374.1392, found 374.1388.

N-(2-oxo-1,2-diphenylethyl)nicotinamide (3ra). White solid (17.8 mg, isolated yield 45%). m.p 122.1-123.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.09 (d, *J*=1.7, 1H), 8.74 (dd, *J*=4.9, 1.6, 1H), 8.18 (dt, *J*=8.0, 1.9, 1H), 8.01 (dd, *J*=5.2, 3.3, 2H), 7.82 (d, *J*=6.8, 1H), 7.58 – 7.51 (m, 1H), 7.49 (dd, *J*=5.3, 3.3, 2H), 7.43 (ddd, *J*=10.9, 5.9, 2.5, 3H), 7.38 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 6.73 (d, *J*=6.9, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 195.4, 164.3, 152.0, 148.0, 136.8, 135.5, 134.1, 134.0, 129.8, 129.4, 129.2, 128.8, 128.7, 128.4, 123.6, 59.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{17}N_2O_2^+$, 317.1290, found 317.1272.

N-(2-oxo-1,2-diphenylethyl)thiophene-2-carboxamide (3sa). White solid (26.9 mg, isolated yield 67%). m.p 139.1-140.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 – 7.97 (m, 2H), 7.63 – 7.51 (m, 3H), 7.51 – 7.38 (m, 5H), 7.36 – 7.29 (m, 2H), 7.29 – 7.22 (m, 2H), 7.08 (dd, *J*=4.9, 3.8, 1H), 6.71 (d, *J*=7.0, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 195.6, 160.9, 144.5, 138.5, 137.1, 134.2, 133.9, 130.4, 129.3, 129.2, 128.8, 128.5, 128.4, 127.6, 58.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{16}NO_2S^+$, 322.0902, found 322.0882.

N-(2-oxo-1,2-diphenylethyl)furan-2-carboxamide (3ta). White solid (18.3 mg, isolated yield 48%). m.p 149.2-150.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05 – 7.98 (m, 2H), 7.85 (d, *J*=7.3, 1H), 7.58 – 7.51 (m, 1H), 7.51 – 7.38 (m, 5H), 7.37 – 7.29 (m, 2H), 7.29 – 7.22 (m, 1H), 7.11 (dd, *J*=3.5, 0.7, 1H), 6.71 (d, *J*=7.4, 1H), 6.49 (dd, *J*=3.5, 1.8, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.4, 157.4, 147.7, 144.2, 137.1, 134.3, 133.9, 129.3, 129.2, 128.8, 128.5, 128.4, 114.7, 112.1, 58.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{16}NO_3^+$, 306.1130, found 306.1123.

N-(2-oxo-1,2-diphenylethyl)acetamide (3ua). White solid (19.0 mg, isolated yield 60%). m.p 143.1-144.8. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 – 7.93 (m, 2H), 7.55 – 7.48 (m, 1H), 7.44 – 7.36 (m, 4H), 7.34 – 7.24 (m, 3H), 6.97 (d, *J*=6.7, 1H), 6.58 (d, *J*=7.4, 1H), 2.05 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.9, 169.2, 137.3, 134.3, 133.8, 129.2, 129.1, 128.7, 128.4, 128.2, 58.5, 23.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}NO_2^+$, 254.1181, found 254.1180.

2,2,2-trifluoro-N-(2-oxo-1,2-diphenylethyl)acetamide (3va). White solid (35.7 mg, isolated yield 93%). m.p 167.2-168.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.04 – 7.88 (m, 3H), 7.55 (t, *J*=7.4, 1H), 7.46 – 7.38 (m, 4H), 7.38 – 7.27 (m, 3H), 6.49 (d, *J*=7.0, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 193.7, 156.27 (q, J = 37.8 Hz), 147.1, 135.3, 134.4, 133.4, 129.5, 129.08 (d, J = 33.0 Hz), 129.2, 128.3, 115.65 (dd, J = 284.9, 15.0 Hz), 58.9. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ = -75.73. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{13}F_3NO_2^+$, 308.0898, found 308.0896.

2-bromo-N-(2-(4-fluorophenyl)-2-oxo-1-phenylethyl)benzamide (3ab). White solid (47.4 mg, isolated yield 92%). m.p 152.1-153.8. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06

– 8.00 (m, 2H), 7.70 (d, *J*=6.8, 1H), 7.64 – 7.54 (m, 3H), 7.54 – 7.43 (m, 4H), 7.38 (td, *J*=7.5, 1.2, 1H), 7.32 (dd, *J*=7.7, 1.8, 1H), 7.09 – 7.01 (m, 2H), 6.79 – 6.73 (m, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 195.1, 166.5, 162.62 (d, *J* = 248.1 Hz), 136.9, 134.1, 134.0, 134.0, 133.6, 132.75 (d, *J* = 3.1 Hz), 131.5, 130.24 (d, *J* = 8.4 Hz), 129.8, 129.03 (d, *J* = 32.8 Hz), 127.5, 119.6, 116.21 (d, *J* = 21.8 Hz), 58.4. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ = -112.85. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}BrFNO_2^+$, 412.0348, found 412.0356.

2-bromo-N-(2-(4-chlorophenyl)-2-oxo-1-phenylethyl)benzamide (3ac). White solid (44.5 mg, isolated yield 83%). m.p 169.5-171.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 (d, *J*=7.9, 2H), 7.73 (d, *J*=6.7, 1H), 7.64 – 7.52 (m, 3H), 7.46 (dd, *J*=7.6, 4.2, 4H), 7.40 – 7.26 (m, 4H), 6.74 (d, *J*=6.9, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 194.9, 166.5, 136.8, 135.4, 134.5, 134.2, 133.9, 133.6, 131.6, 129.9, 129.8, 129.4, 129.2, 128.9, 127.5, 119.6, 58.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}BrClNO_2^+$, 430.0032, found 430.0034.

2-bromo-N-(2-(4-bromophenyl)-2-oxo-1-phenylethyl)benzamide (3ad). White solid (45.5 mg, isolated yield 77%). m.p 185.9-187.7. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.04 – 7.94 (m, 2H), 7.69 (d, *J*=6.7, 1H), 7.62 – 7.50 (m, 3H), 7.49 – 7.41 (m, 4H), 7.41 – 7.32 (m, 3H), 7.29 (dd, *J*=7.8, 1.8, 1H), 6.70 (d, *J*=6.9, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ = 194.8, 166.5, 136.8, 135.9, 134.2, 133.9, 133.6, 132.4, 131.6, 130.1, 129.9, 129.2, 128.9, 127.5, 122.7, 119.6, 58.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}Br_2NO_2^+$, 473.9527, found 473.9526.

2-bromo-N-(2-(4-methoxyphenyl)-2-oxo-1-phenylethyl)benzamide (3ae). White solid (41.4 mg, isolated yield 78%). m.p 137.9-139.8. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 (dd, *J*=5.2, 3.4, 2H), 7.63 – 7.49 (m, 4H), 7.46 – 7.38 (m, 4H), 7.34 (td, *J*=7.5, 1.2, 1H), 7.30 – 7.24 (m, 2H), 6.88 – 6.82 (m, 1H), 6.70 (d, *J*=7.1, 1H), 3.76 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.3, 166.4, 159.6, 137.1, 134.3, 133.8, 133.5, 131.4, 129.9, 129.7, 129.2, 128.9, 128.8, 127.5, 119.6, 114.6, 58.6, 55.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{19}BrNO_3^+$, 424.0548, found 424.0544.

2-bromo-N-(2-oxo-2-phenyl-1-(p-tolyl)ethyl)benzamide (3af). White solid (23.0 mg, isolated yield 45%). m.p 151.3-153.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, *J*=8.3, 2H), 7.64 (d, *J*=6.9, 1H), 7.58 (dd, *J*=7.9, 1.0, 1H), 7.54 (dd, *J*=7.6, 1.7, 1H), 7.51 – 7.45 (m, 2H), 7.37 – 7.29 (m, 3H), 7.29 – 7.24 (m, 2H), 7.22 (d, *J*=8.0, 2H), 6.73 (d, *J*=7.2, 1H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 194.8, 166.4, 159.8, 145.0, 137.1, 133.5, 131.7, 131.4, 129.8, 129.5, 129.4, 129.2, 128.40, 128.38, 127.5, 119.6, 59.0, 21.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{19}BrNO_2^+$, 408.0599, found 408.0593.

2-bromo-N-(1-(4-chlorophenyl)-2-oxo-2-phenylethyl)benzamide (3ag). White solid (45.0 mg, isolated yield 84%). m.p 129.7-131.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 (d, *J*=8.5, 2H), 7.57 (dd, *J*=15.2, 7.7, 3H), 7.46 (d, *J*=7.2, 2H), 7.39 (d, *J*=8.5, 2H), 7.34 (t, *J*=7.4, 3H), 7.31 – 7.26 (m, 2H), 6.70 (d, *J*=7.0, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 194.1, 166.5, 140.5, 136.9, 136.4, 133.6, 132.5, 131.6, 130.6, 129.9, 129.4, 129.2, 128.7, 128.4, 127.5, 119.6, 59.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{15}BrClNO_2^+$, 430.0032, found 430.0018.

2-bromo-N-(2-oxo-1-phenyl-2-(p-tolyl)ethyl)benzamide (3ah). White solid (43.4 mg, isolated yield 85%). m.p 116.9-118.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 (d, *J*=7.5, 2H), 7.64 – 7.49 (m, 4H), 7.37 (ddd, *J*=16.6, 11.4, 7.3, 5H), 7.29 – 7.23 (1H), 7.13 (d, *J*=7.9, 2H), 6.72 (d, *J*=7.2, 1H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.3, 166.4, 138.4, 137.1, 134.3, 133.8, 133.8, 133.5, 131.4, 129.9, 129.9, 129.2, 128.8, 128.3, 127.5, 119.6, 58.9, 21.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{19}BrNO_2$+, 408.0599, found 408.0584.

N-(2-(4-fluorophenyl)-2-oxo-1-phenylethyl)benzamide (3bb). White solid (34.2 mg, isolated yield 82%). m.p 158.1-159.7. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 (d, *J*=7.7, 2H), 7.85 (d, *J*=7.6, 2H), 7.79 (d, *J*=5.9, 1H), 7.60 – 7.38 (m, 8H), 7.00 (t, *J*=8.2, 2H), 6.73 (d, *J*=6.4, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.7, 166.4, 162.6 (d, *J* = 247.9 Hz), 134.1, 133.8, 133.24, 133.21, 131.9, 130.2 (d, *J* = 8.4 Hz), 129.2, 128.7, 128.6, 127.2, 116.2 (d, *J* = 21.7 Hz), 58.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{17}FNO_2^+$, 334.1243, found 334.1237.

N-(2-(4-chlorophenyl)-2-oxo-1-phenylethyl)benzamide (3bc). White solid (26.2 mg, isolated yield 60%). m.p 177.6-179.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 (d, *J*=7.8, 2H), 7.84 (d, *J*=7.5, 2H), 7.79 (d, *J*=6.4, 1H), 7.60 – 7.49 (m, 2H), 7.44 (m, 6H), 7.29 (d, *J*=8.4, 2H), 6.71 (d, *J*=6.7, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 212.2, 195.5, 166.4, 157.6, 135.7, 134.5, 134.2, 133.9, 133.7, 131.9, 129.7, 129.5, 129.2, 128.9, 128.6, 127.2, 58.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{17}ClNO_2^+$, 350.0948, found 350.0955.

N-(2-(4-methoxyphenyl)-2-oxo-1-phenylethyl)benzamide (3be). White solid (41.1 mg, isolated yield 95%). m.p 176.3-177.7. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 7.96 (m, 2H), 7.84 (dd, *J*=5.2, 3.3, 2H), 7.71 (d, *J*=6.8, 1H), 7.58 – 7.48 (m, 2H), 7.47 – 7.36 (m, 6H), 6.90 – 6.81 (m, 2H), 6.70 (d, *J*=7.0, 1H), 3.74 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.9, 166.3, 159.6, 134.3, 134.0, 133.8, 131.7, 129.6, 129.3, 129.2, 128.8, 128.6, 127.2, 114.7, 58.4, 55.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}NO_3^+$, 346.1443, found 346.1433.

N-(2-oxo-2-phenyl-1-(p-tolyl)ethyl)benzamide (3bf). White solid (32.9 mg, isolated yield 80%). m.p 213.3-214.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 (d, *J*=8.1, 2H), 7.88 (d, *J*=7.7, 2H), 7.81 (d, *J*=6.8, 1H), 7.49 (tt, *J*=15.0, 7.3, 5H), 7.34 (t, *J*=7.5, 2H), 7.25 (t, *J*=7.4, 3H), 6.76 (d, *J*=7.0, 1H), 2.39 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 195.4, 166.3, 145.0, 137.6, 134.0, 131.7, 131.7, 129.5, 129.4, 129.2, 128.6, 128.34, 128.31, 127.2, 58.7, 21.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}NO_2^+$, 330.1494, found 330.1494.

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SUPPORTING INFORMATION STATEMENT

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Copies of ^{1}H, ^{13}C, and ^{19}F spectra for all products (PDF)

X-ray crystallographic data for product **3la** (CIF)

X-ray crystallographic data for product **3va** (CIF)

X-ray crystallographic data for product **3ah** (CIF)

X-ray crystallographic data for product Pd (0) complex **I** (CIF)

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NOTES

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REFERENCES

(1) Wang, L.; Li, H.; Wang, L. Iron-Catalyzed C(sp^3)–H Acyloxylation of Aryl-2H Azirines with Hypervalent Iodine(III) Reagents. *Org. Lett.* **2018**, *20*, 1663-1666.

(2) Chen, L.; Li, H.; Li, P.; Wang, L. Visible-Light Photoredox Catalyzed Three-Component Cyclization of 2H-Azirines, Alkynyl Bromides, and Molecular Oxygen to Oxazole Skeleton. *Org. Lett.* **2016**, *18*, 3646-3649.

(3) Zhou, W.; Zhang, M.; Li, H.; Chen, W. One-Pot Three-Component Synthesis of Enamine-Functionalized 1,2,3-Triazoles via Cu-Catalytic Azide-Alkyne Click (CuAAC) and Cu-Catalyzed Vinyl Nitrene Transfer Sequence. *Org. Lett.* **2017**, *19*, 10-13.

(4) Novikov, M. S.; Khlebnikov, A. F.; Rostovskii, N. V.; Tcyrulnikov, S.; Suhanova, A. A.; Zavyalov, K. V.; Yufit, D. S. Pseudopericyclic 1,5- versus Pericyclic 1,4- and 1,6-Electrocyclization in Electron-Poor 4-Aryl-2-azabuta-1,3-dienes: Indole Synthesis from 2H-Azirines and Diazo Compounds. *J. Org. Chem.*

2015, *80*, 18-29.

(5) Jiang, Y.; Park, C. M.; Loh, T. P. Transition-metal-free synthesis of substituted pyridines via ring expansion of 2-allyl-2H-azirines. *Org. Lett.* **2014**, *16*, 3432-3435.

(6) Wang, F.; Zhu, N.; Chen, P.; Ye, J.; Liu, G. Copper-Catalyzed Trifluoromethylazidation of Alkynes: Efficient Access to CF3-Substituted Azirines and Aziridines. *Angew. Chem. Int. Ed.* **2015**, *54*, 9356-9360.

(7) Novikov, M. S.; Rostovskii, N. V.; Koronatov, A. N.; Zavyalov, K. V.; Zubakin, G. V.; Khlebnikov, A. F.; Starova, G. L. Synthesis of 1,2-Dihydropyrimidine-2-carboxylates via Regioselective Addition of Rhodium(II) Carbenoids to 2H-Azirine-2-carbaldimines. *J. Org. Chem.* **2017**, *82*, 13396-13404.

(8) Duan, X.; Yang, K.; Lu, J.; Kong, X.; Liu, N.; Ma, J. Base-Mediated Cascade Substitution-Cyclization of 2H-Azirines: Access to Highly Substituted Oxazoles. *Org. Lett.* **2017**, *19*, 3370-3373.

(9) Sujatha, C.; Bhatt, C. S.; Ravva, M. K.; Suresh, A. K.; Namitharan, K. Copper-Catalyzed Ring-Expansion Cascade of Azirines with Alkynes: Synthesis of Multisubstituted Pyridines at Room Temperature. *Org. Lett.* **2018**, *20*, 3241-3244.

(10) Li, T.; Xin, X.; Wang, C.; Wang, D.; Wu, F.; Li, X.; Wan, B. Cu-catalyzed ring opening reaction of 2H-azirines with terminal alkynes: an easy access to 3-alkynylated pyrroles. *Org. Lett.* **2014**, *16*, 4806-4809.

(11) Li, T.; Yan, H.; Li, X.; Wang, C.; Wan, B. Ruthenium-Catalyzed [3 + 2] Cycloaddition of 2H-Azirines with Alkynes: Access to Polysubstituted Pyrroles. *J. Org. Chem.* **2016**, *81*, 12031-12037.

(12) Thangaraj, M.; Bhojgude, S. S.; Jain, S.; Gonnade, R. G.; Biju, A. T. Selective Synthesis of N-Unsubstituted and N-Arylindoles by the Reaction of Arynes with Azirines. *J. Org. Chem.* **2016**, *81*, 8604-8611.

(13) Rostovskii, N. V.; Sakharov, P. A.; Novikov, M. S.; Khlebnikov, A. F.; Starova, G. L. Cu(I)-NHC-Catalyzed (2 + 3)-Annulation of Tetramic Acids with 2H-Azirines: Stereoselective Synthesis of Functionalized Hexahydropyrrolo[3,4-b]pyrroles. *Org. Lett.* **2015**, *17*, 4148-4151.

(14) Zeng, T. T.; Xuan, J.; Ding, W.; Wang, K.; Lu, L. Q.; Xiao, W. J. [3 + 2] Cycloaddition/Oxidative Aromatization Sequence via Photoredox Catalysis: One-Pot Synthesis of Oxazoles from 2H-Azirines and Aldehydes. *Org. Lett.* **2015**, *17*, 4070-4073.

(15) Wang, H.; Ren, Y.; Wang, K.; Man, Y.; Xiang, Y.; Li, N.; Tang, B. Visible light-induced cyclization reactions for the synthesis of 1,2,4-triazolines and 1,2,4-triazoles. *Chem. Commun.* **2017**, *53*, 9644-9647.

(16) Zhu, L.; Yu, Y.; Mao, Z.; Huang, X. Gold-Catalyzed Intermolecular Nitrene Transfer from 2H-Azirines to Ynamides: A Direct Approach to Polysubstituted Pyrroles. *Org. Lett.* **2014**, *17*, 30-33.

(17) Pawar, S. K.; Sahani, R. L.; Liu, R. S. Diversity in Gold-Catalyzed Formal Cycloadditions of Ynamides with Azidoalkenes or 2H-Azirines: [3+2] versus [4+3] Cycloadditions. *Chem. - Eur. J.* **2015**, *21*, 10843-10850.

(18) Wang, Y.; Lei, X.; Tang, Y. Rh(II)-catalyzed cycloadditions of 1-tosyl 1,2,3-triazoles with 2H-azirines: switchable reactivity of Rh-azavinylcarbene as [2C]- or aza-[3C]-synthon. *Chem. Commun.* **2015**, *51*, 4507-4510.

(19) Ryu, T.; Baek, Y.; Lee, P. H. Synthesis of pyrazines from rhodium-catalyzed reaction of 2H-Azirines with N-sulfonyl 1,2,3-triazoles. *J. Org. Chem.* **2015**, *80*, 2376-2383.

(20) Baek, Y.; Maeng, C.; Kim, H.; Lee, P. H. Regioselective Synthesis of Indolopyrazines through a Sequential Rhodium-Catalyzed Formal [3+3] Cycloaddition and Aromatization Reaction of Diazoindolinimines with Azirines. *J. Org. Chem.* **2018**, *83*, 2349-2360.

(21) Ding, H.; Wang, Z.; Bai, S.; Lu, P.; Wang, Y. Rh-Catalyzed Conversion of 3-Diazoindolin-2-imines to

5H-Pyrazino[2,3-b]indoles with Photoluminescent Properties. *Org. Lett.* **2017**, *19*, 6514-6517.

(22) Ding, H.; Hong, S.; Zhang, N. Rhodium(II)-catalyzed transannulation of 1-sulfonyl-1,2,3-triazoles with 2 H -azirines: a new method to dihydropyrazines. *Tetrahedron Lett.* **2015**, *56*, 507-510.

(23) Li, T.; Xu, F.; Li, X.; Wang, C.; Wan, B. Ruthenium-Catalyzed C-C Bond Cleavage of 2H-Azirines: A Formal [3+2+2] Cycloaddition to Fused Azepine Skeletons. *Angew. Chem. Int. Ed.* **2016**, *55*, 2861-2865.

(24) Xu, H.-D.; Zhou, H.; Pan, Y.-P.; Ren, X.-T.; Wu, H.; Han, M.; Han, R.-Z.; Shen, M.-H. Stereoselective Synthesis of Polycycles Containing an Aziridine Group: Intramolecular aza-Diels-Alder Reactions of Unactivated 2H-Azirines with Unactivated Dienes. *Angew. Chem. Int. Ed.* **2016**, *55*, 2540-2544.

(25) Jin, L.; Wu, Y.; Zhao, X. Theoretical Insight into the Mechanism of Gold(I)-Catalyzed Rearrangement of 2-Propargyl 2H-Azirines to Pyridines. *J. Org. Chem.* **2015**, *80*, 3547-3555.

(26) Nakamura, S.; Hayama, D. Enantioselective Reaction of 2H-Azirines with Phosphite Using Chiral Bis(imidazoline)/Zinc(II) Catalysts. *Angew. Chem. Int. Ed.* **2017**, *56*, 8785-8789.

(27) An, D.; Guan, X.; Guan, R.; Jin, L.; Zhang, G.; Zhang, S. Organocatalyzed nucleophilic addition of pyrazoles to 2H-azirines: asymmetric synthesis of 3,3-disubstituted aziridines and kinetic resolution of racemic 2H-azirines. *Chem. Commun.* **2016**, *52*, 11211-11214.

(28) Nakamura, S.; Hayama, D. Enantioselective Reaction of 2H-Azirines with Phosphite Using Chiral Bis(imidazoline)/Zinc(II) Catalysts. *Angew. Chem. Int. Ed.* **2017**, *56*, 8785-8789.

(29) Risberg, E.; Fischer, A.; Somfai, P. Asymmetric radical additions of trialkylboranes to 2H-azirine-3-carboxylates. *Chem. Commun.* **2004**, 2088-2089.

(30) José Alves, M.; L. Gilchrist, T.; H. Sousa, J. Reactions of methyl 2-aryl-2H-azirine-3-carboxylates with nucleophiles. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1305-1310.

(31) Zhao, M. N.; Ren, Z. H.; Yang, D. S.; Guan, Z. H. Iron-Catalyzed Radical Cycloaddition of 2H-Azirines and Enamides for the Synthesis of Pyrroles. *Org. Lett.* **2018**, *20*, 1287-1290.

(32) Prechter, A.; Henrion, G.; Faudot dit Bel, P.; Gagosz, F. Gold-catalyzed synthesis of functionalized pyridines by using 2H-azirines as synthetic equivalents of alkenyl nitrenes. *Angew. Chem. Int. Ed.* **2014**, *53*, 4959-4963.

(33) Xuan, J.; Xia, X. D.; Zeng, T. T.; Feng, Z. J.; Chen, J. R.; Lu, L. Q.; Xiao, W. J. Visible-light-induced formal [3+2] cycloaddition for pyrrole synthesis under metal-free conditions. *Angew. Chem. Int. Ed.* **2014**, *53*, 5653-5656.

(34) Okamoto, K.; Mashida, A.; Watanabe, M.; Ohe, K. An unexpected disproportional reaction of 2H-azirines giving (1E,3Z)-2-aza-1,3-dienes and aromatic nitriles in the presence of nickel catalysts. *Chem. Commun.* **2012**, *48*, 3554-3556.

(35) Lee, A.; Huang, L.; Ellman, J. A. General Solid-Phase Method for the Preparation of Mechanism-Based Cysteine Protease Inhibitors. *J. Am. Chem. Soc.* **1999**, *121*, 9907-9914.

(36) Bunce Richard, A.; Herron Derrick, M.; Hale Lu, Y. Dihydrobenzoxazines and tetrahydroquinoxalines by a tandem reduction-reductive amination reaction. *J. Heterocycl. Chem.* **2009**, *40*, 1031-1039.

(37) El-Dahshan, A.; Al-Gharabli, S. I.; Radetzki, S.; Al-Tel, T. H.; Kumar, P.; Rademann, J. Flexible, polymer-supported synthesis of sphingosine derivatives provides ceramides with enhanced biological activity. *Biorg. Med. Chem.* **2014**, *22*, 5506-5512.

(38) Zhou, R.-R.; Cai, Q.; Li, D.-K.; Zhuang, S.-Y.; Wu, Y.-D.; Wu, A.-X. Acid-Promoted Multicomponent Tandem Cyclization to Synthesize Fully Substituted Oxazoles via Robinson–Gabriel-Type Reaction. *J. Org. Chem.* **2017**, *82*, 6450-6456.

(39) Frantz, D. E.; Morency, L.; Soheili, A.; Murry, J. A.; Grabowski, E. J. J.; Tillyer, R. D. Synthesis of

Substituted Imidazoles via Organocatalysis. *Org. Lett.* **2004**, *6*, 843-846.

(40) Biron, E.; Chatterjee, J.; Kessler, H. Solid-Phase Synthesis of 1,3-Azole-Based Peptides and Peptidomimetics. *Org. Lett.* **2006**, *8*, 2417-2420.

(41) Lantos, I.; Zhang, w.-Y. Synthesis of α-amidoketones. An application of the multi-hetero cope rearrangement. *Tetrahedron Lett.* **1994**, *35*, 5977-5980.

(42) Ooi, T.; Takahashi, M.; Doda, K.; Maruoka, K. Asymmetric Induction in the Neber Rearrangement of Simple Ketoxime Sulfonates under Phase-Transfer Conditions: Experimental Evidence for the Participation of an Anionic Pathway. *J. Am. Chem. Soc.* **2002**, *124*, 7640-7641.

(43) Mennen, S. M.; Gipson, J. D.; Kim, Y. R.; Miller, S. J. Thiazolylalanine-Derived Catalysts for Enantioselective Intermolecular Aldehyde−Imine Cross-Couplings. *J. Am. Chem. Soc.* **2005**, *127*, 1654-1655.

(44) DiRocco Daniel, A.; Rovis, T. Catalytic Asymmetric Cross-Aza-Benzoin Reactions of Aliphatic Aldehydes with N-Boc-Protected Imines. *Angew. Chem. Int. Ed.* **2012**, *51*, 5904-5906.

(45) Wilde, M. M. D.; Gravel, M. Bis(amino)cyclopropenylidene (BAC) Catalyzed Aza-Benzoin Reaction. *Org. Lett.* **2014**, *16*, 5308-5311.

(46) Wende Raffael, C.; Seitz, A.; Niedek, D.; Schuler Sören, M. M.; Hofmann, C.; Becker, J.; Schreiner Peter, R. The Enantioselective Dakin–West Reaction. *Angew. Chem. Int. Ed.* **2016**, *55*, 2719-2723.

(47) Miura, T.; Biyajima, T.; Fujii, T.; Murakami, M. Synthesis of α-Amino Ketones from Terminal Alkynes via Rhodium-Catalyzed Denitrogenative Hydration of N-Sulfonyl-1,2,3-triazoles. *J. Am. Chem. Soc.* **2011**, *134*, 194-196.

(48) Zheng, G.; Li, Y.; Han, J.; Xiong, T.; Zhang, Q. Radical cascade reaction of alkynes with N-fluoroarylsulfonimides and alcohols. *Nat Commun* **2015**, *6*, 7011.

(49) Holthusen, K.; Leitner, W.; Francio, G. Synthesis of alpha-Amidoketones from Vinyl Esters via a Catalytic/Thermal Cascade Reaction. *J. Org. Chem.* **2016**, *81*, 4823-4828.

(50) Kim, Y.; Pak, H. K.; Rhee, Y. H.; Park, J. Catalytic transformation of esters of 1,2-azido alcohols into alpha-amido ketones. *Chem. Commun.* **2016**, *52*, 6549-6552.

(51) Oh, B. H.; Nakamura, I.; Yamamoto, Y. Palladium-Catalyzed Ring-Opening Reaction of Methyleneaziridines with Carboxylic Acids: Synthesis of α-Amidoketones. *J. Org. Chem.* **2004**, *69*, 2856-2858.

(52) Hyatt, J. A. Neber rearrangement of amidoxime sulfonates. Synthesis of 2-amino-1-azirines. *J. Org. Chem.* **1981**, *46*, 3953-3955.

(53) Lehmann, J.; Linden, A.; Heimgartner, H. Site-selective incorporation of thioamide-linkages into a growing peptide. *Tetrahedron* **1999**, *55*, 5359-5376.

(54) Black, D. S. C.; Doyle, J. E. Direct conversion of α-halo acids into α-halo amides by reaction with 2-phenylazirine. *Aust. J. Chem.* **1978**, *31*, 2313-2315.

(55) Sato, S.; Kato, H.; Ohta, M. Azirines. II. The Reaction of 2-Phenylazirine with Acylating Agents. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2938-2942.

(56) Palacios, F.; Aparicio, D.; Ochoa de Retana, A. M.; de los Santos, J. M.; Gil, J. I.; Alonso, J. M. Asymmetric Synthesis of 2H-Azirines Derived from Phosphine Oxides Using Solid-Supported Amines. Ring Opening of Azirines with Carboxylic Acids. *J. Org. Chem.* **2002**, *67*, 7283-7288.

(57) Palacios, F.; Ochoa de Retana, A. M. a.; Gil, J. I.; Alonso, J. M. a. Synthesis of optically active oxazoles from phosphorylated 2H-azirines and N-protected amino acids or peptides. *Tetrahedron: Asymmetry* **2002**, *13*, 2541-2552.

(58) Shiomi, N.; Yamamoto, K.; Nagasaki, K.; Hatanaka, T.; Funahashi, Y.; Nakamura, S.

Enantioselective Oxidative Ring-Opening Reaction of Aziridines with α-Nitroesters Using Cinchona Alkaloid Amide/Nickel(II) Catalysts. *Org. Lett.* **2017**, *19*, 74-77.

(59) Hu, H.; Liu, Y.; Lin, L.; Zhang, Y.; Liu, X.; Feng, X. Kinetic Resolution of 2H-Azirines by Asymmetric Imine Amidation. *Angew. Chem. Int. Ed.* **2016**, *55*, 10098-10101.

(60) Palacios, F.; Ochoa de Retana, A. M.; Alonso, J. M. Reaction of 2H-Azirine Phosphine Oxide and -Phosphonates with Nucleophiles. Stereoselective Synthesis of Functionalized Aziridines and α- and β-Aminophosphorus Derivatives. *J. Org. Chem.* **2005**, *70*, 8895-8901.

(61) Xuan, J.; Xia, X.-D.; Zeng, T.-T.; Feng, Z.-J.; Chen, J.-R.; Lu, L.-Q.; Xiao, W.-J. Visible-Light-Induced Formal [3+2] Cycloaddition for Pyrrole Synthesis under Metal-Free Conditions. *Angew. Chem. Int. Ed.* **2014**, *53*, 5653-5656.

(62) Hu, H.; Xu, J.; Liu, W.; Dong, S.; Lin, L.; Feng, X. Copper-Catalyzed Asymmetric Addition of Tertiary Carbon Nucleophiles to 2H-Azirines: Access to Chiral Aziridines with Vicinal Tetrasubstituted Stereocenters. *Org. Lett.* **2018**, *20*, 5601-5605.