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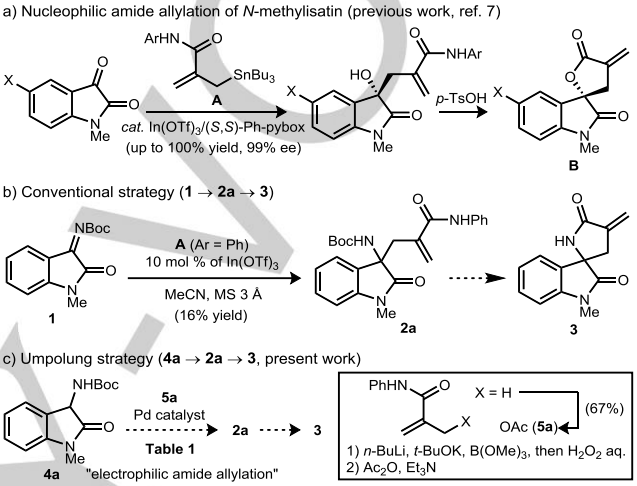
Electrophilic amide allylation of 3-heterosubstituted oxindoles: a new route to spirocyclic 2-oxindole containing α-methylene-γ-butyrolactam structure

Tetsuya Sengoku,[a] Daichi Hayashi,[a] Masaki Takahashi[a] and Hidemi Yoda*[a]

Abstract: This article reports a new route to access spirocyclic 2-oxindole containing α-methylene-γ-butyrolactam structure via "electrophilic amide allylation". The key reaction was accomplished by using acetoxy methacrylamides and tetrakis(triphenylphosphine)palladium as a catalyst, affording a variety of the amide allylated products in excellent yields. The successful cyclization of these products has demonstrated the potential utility of this approach to offer practical synthesis of spirocyclic oxindoles.

Introduction

α-Methylene-γ-butyrolactone and lactam structures are important molecular motifs due to the fact that they are often found in potent bioactive compounds and thus useful for developing pharmaceutical products.[1] For the construction of these functional moieties, cyclization of γ-hydroxy/γ-amino functionalized esters or their analogous compounds could be envisioned as one of the most effective ways.[2,3] In this context, we have established an efficient approach based on indium-catalyzed nucleophilic addition of β-amido functionalized allylstannanes **A** (see structure in Scheme 1a) to a range of carbonyl compounds such as isatins[4] to afford γ-hydroxy amides, which undergo acid-promoted cyclization to successfully generate the α-methylene-γ-butyrolactones. Furthermore, we achieved the enantioselective synthesis of these compounds by the use of chiral ligand combined with indium catalyst.[5] The utility of this "amide allylation" approach has been culminated in the enantioselective synthesis of antineoplastic spirocyclic oxindoles **B**[6] to demonstrate the extremely high levels of stereocontrol (Scheme 1a).[7] In the course of our intensive research work on the catalytic "amide allylation", we have also developed a synthetic approach to α-methylene-γ-butyrolactams by employing imine substrates.[8] However, attempts to extend this strategy for preparing **3**, a lactam analog of **B**, met with failure because imino group of the substrate **1** was highly susceptible to the indium catalyst and decomposed during the reaction (Scheme 1b, **1** → **2a**). In light of our previous results for



Scheme 1. Synthetic approaches for spirocyclic oxindoles containing α-methylene-γ-butyrolactone and lactam structures.

obtaining α-methylene-γ-butyrolactams from the corresponding acyclic precursors,[8] the key to successful synthesis of **3** was to explore an alternative approach toward this synthetic intermediate. Thus, our next challenge was to establish a synthetic route on the basis of umpolung strategy, which would be expected to allow for the synthesis of **2a** from 3-Boc-aminooxindole **4a** and 2-acetoxymethyl acrylamide **5a** under the influence of palladium catalysts (Scheme 1c).[9,10] Here, we report our successful efforts for the development of a new strategy, which we named "electrophilic amide allylation", to complement our previous synthetic approach.

Results and Discussion

The requisite reagent **5a** was prepared by allylic oxidation of *N*-phenyl methacrylamide by way of β-amido allylboronate[11] and successive acetylation (67% yield for 2 steps). Then, we examined the palladium-catalyzed reaction between **4a**[12] and **5a** in dichloromethane solution at room temperature. Our initial attempt was made to carry out the reaction in the presence of Pd(0) species in-situ generated from palladium acetate and triethylamine, which afforded only a 16% yield of the amide allylated product **2a** (Table 1, entry 1). Next, we examined the use of 10 mol % of tris(dibenzylideneacetone)dipalladium ($Pd_2(dba)_3$) instead of the Pd(0) species. In this case, however, no reaction occurred and complete recovery of the starting

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Table 1. Screening of palladium reagents and solvents on the reaction of **4a** with **5a**[a].

Entry	Pd catalyst [mol %]	solvent	time [h]	yield [%][b]
1	$Pd(OAc)_2$ (10) Et_3N (20)	CH_2Cl_2	5	16
2	$Pd_2(dba)_3$ (10)	CH_2Cl_2	24	0
3	$Pd_2(dba)_3$ (10) dppb (20)	CH_2Cl_2	2	78
4	$Pd(PPh_3)_4$ (10)	CH_2Cl_2	0.5	>99
5	$Pd(OAc)_2$ (10) PPh_3 (40)	DCE[c]	2	>99
6	$Pd(PPh_3)_4$ (10)	MeCN	0.5	96
7	$Pd(PPh_3)_4$ (10)	THF	1	95
8	$Pd(PPh_3)_4$ (10)	$CHCl_3$	1	>99
9	$Pd(PPh_3)_4$ (10)	toluene	0.5	>99
10	$Pd(PPh_3)_4$ (10)	EtOH	2	93
11[d]	$Pd(PPh_3)_4$ (1)	CH_2Cl_2	3	98

[a] Reactions of **4a** with **5a** (1.2 equiv.) were conducted at room temperature. [b] Isolated yield of **2a**. [c] The reaction was carried out in 1,2-dichloroethane (DCE) at 40 °C. [d] The product could be synthesized on a gram scale (1.57 g of **2a**).

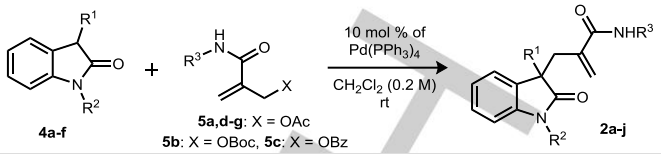

Table 2. Amide allylation of 3-heterosubstituted oxindoles.

entry	**4** (R^1, R^2)	**5** (R^3)	time [h]	**2**	yield [%][a]
1	**4a** (NHBoc, Me)	**5b** (Ph)	1	**2a**	70
2	**4a**	**5c** (Ph)	1	**2a**	91
3	**4a**	**5d** (*p*-anis)	1	**2b**	>99
4	**4a**	**5e** (TBP)[b]	1	**2c**	99
5	**4a**	**5f** (Nap)[c]	1	**2d**	97
6	**4a**	**5g** (Et)	1	**2e**	98
7	**4b** (NHBoc, Ph)	**5a**	1	**2f**	>99
8	**4c** (NHBoc, H)	**5a**	1	**2g**	94
9	**4d** (OH, Me)	**5a**	1	**2h**	80 (91)[d]
10	**4e** (OBoc, Me)	**5a**	2	**2i**	42 (88)[d]
11	**4f** (SPh, Me)	**5a**	1	**2j**	91
12	**4g** (OH, H)	**5a**	2	**2k**	68[e]
13	**4h** (SPh, H)	**5a**	2	**2l**	83

[a] Isolated yield. [b] TBP: *p*-(*tert*-butyl)phenyl. [c] Nap: 1-naphthyl. [d] Yields based on recovery of the starting materials. [e] **2k** was obtained as a mixture with a bisallylated derivative. The yield was calculated from ^{1}H NMR spectrum of the mixture.

materials was observed (Table 1, entry 2). Remarkably, we found that addition of 1,4-bis(diphenylphosphino)butane (dppb), which would serve as a common phosphine ligand, led to a dramatic improvement of the reactivity; the reaction yield of **2a** was increased to as high as 78% (Table 1, entry 3). Furthermore, other phosphine-based catalyst such as tetrakis(triphenylphosphine)palladium ($Pd(PPh_3)_4$) was shown to facilitate this conversion, markedly shortening the reaction time to 30 min to provide **2a** in quantitative yield (Table 1, entry 4). Evidently, this reaction was well reproduced, as demonstrated by the replacement with palladium acetate and triphenylphosphine (Table 1, entry 5).[13] With these results in hand, we turned our efforts to screening of solvents with the use of $Pd(PPh_3)_4$ (Table 1, entries 6–10). To our delight, all the solvents tested were well tolerated under the reaction conditions to offer comparably high yields of **2a** even in ethanol (Table 1, entry 10). At this point, dichloromethane was identified as the most effective solvent that solubilizes appreciable amount of the substrates. This solubilization property makes the method adaptable to gram-scale synthesis. Indeed, the reaction performed at a high concentration (1.0 M) proceeded smoothly to give a very high yield (98%) of the product only with a catalyst loading as low as 1 mol % (Table 1, entry 11).

Encouraged by the success of this approach, we next explored the substrate scope by following the optimized procedure as given in entry 4 of Table 1. Under the reaction conditions, *O*-Boc and Bz-substituted reagents **5b**,**c** were shown to undergo the "electrophilic amide allylation" successfully to give **2a** with sufficiently high yields (Table 2, entries 1 and 2). Likewise, other allylic reagents such as *N*-aryl and alkyl-substituted reagents **5d**-**g** also reacted with **4a** to generate the respective products **2b**-**e** in excellent yields (>97%, see Table 2, entries 3-6). At the same time, for other substrates such as *N*-phenyl and unsubstituted variants **4b** and **4c**, the reactions still occurred efficiently to produce **2f** and **2g** in very high yields of >99 and 94%, respectively (Table 2, entries 7 and 8). Furthermore, it is interesting to note that the catalysis showed adequate levels of reactivity toward a broad range of 3-heterosubstituted oxindoles,[14-17] even when catalyst-poisonous 3-phenylthio derivative **4f,h**[18] were used, thereby affording **2h-l** with high catalyst productivity (Table 2, entries 9–13).

At the final stage of the work, we undertook further efforts on constructing the spirocyclic 2-oxindole structure by employing the amide allylated products. As shown in Table 3, we attempted to use all the homoallylic amines **2a-g** for the cyclization. Subjecting these materials to our previous synthetic conditions[7] that involved reaction with Boc anhydride, spontaneous cyclization induced by selective protection at the secondary amide group occurred efficiently to yield *N*-Boc protected spirocyclic lactams **6a**-**c** in 93-99% yields.[19] The Boc group of these compounds could be removed with no significant loss of the structural integrity by exposure to trifluoroacetic acid, which gave rise to deprotected product **3a**-**c** in almost quantitative yields (86-97% overall yields from **4**).

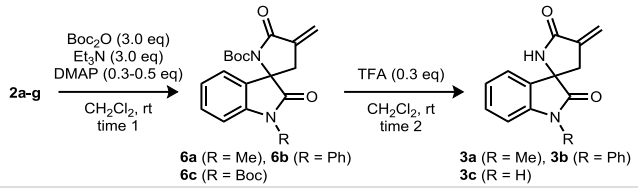

Table 3. Transformation of allyl adducts **2a**-**g** to spirocyclic oxindoles **3a**-**c**.

Entry	**2**	time 1 [h]	**6** [%][a]	time 2 [h]	**3** [%][a]
1	**2a**	24	**6a** (97)	24	**3a** (99)
2	**2b**	12	**6a** (99)	-	**-**
3	**2c**	12	**6a** (95)	-	**-**
4	**2d**	24	**6a** (99)	-	**-**
5	**2e**	24	**6a** (98)	-	**-**
6	**2f**	12	**6b** (96)	24	**3b** (99)
7	**2g**	12[b]	**6c** (93)	24[c]	**3c** (98)

[a] Isolated yield. [b] Reaction was carried out with Boc_2O (6.0 eq), Et_3N (6.0 eq) and DMAP (0.5 eq). [c] Reaction was carried out with TFA (0.5 eq).

Conclusions

In conclusion, we have established a new synthetic route, based on umpolung strategy using "electrophilic amide allylation", to achieve efficient synthesis of spirocyclic 2-oxindole containing α-methylene-γ-butyrolactam structure.[20] The key reaction is highlighted by the toleration of a wide range of functionalities such as oxygen and sulfur substituents at the C3 position of 2-oxindole. The success of transformation of the product into spirocyclic oxindole has shown its potential utility to offer significant advantages compared to our previous strategy for constructing variously 3-heterosubstituted spirooxindole systems. Further investigations on the enantioselective construction of such functionalized heterocycles is underway in our laboratory.

Experimental Section

General methods: All solvents and reagents were of reagent grade quality, and used without further purification unless otherwise stated. Chloroform, acetonitrile, ethanol, toluene, dichloromethane and 1,2-dichloroethane were dried over MS 4 Å or MS 3 Å prior to use, respectively. Tetrahydrofuran was dried over Na wire under a nitrogen atmosphere. The ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra operating at the frequencies of 300 and 75 MHz, respectively, on a JEOL JNM-AL300 spectrometer were recorded in chloroform–*d* ($CDCl_3$) unless otherwise noted. Chemical shifts are reported in parts per million (ppm) relative to TMS and the solvent used as internal standards, and the coupling constants are reported in hertz (Hz). Reactions were monitored by thin layer chromatography (TLC) using Merck TLC silica gel $60F_{254}$, visualized by irradiation with UV light and/or by treatment with phosphomolybdic acid or *p*-anisaldehyde stain followed by heating. Column chromatography was performed using silica gel 60N (spherical neutral) from Kanto Chemical Co. and eluting with the indicated solvent system. Fourier transform infrared (FTIR) spectra were recorded on a JASCO FT/IR-550 spectrometer. Elemental analyses were performed by JSL Model JM 10 instruments. 3-Heterosubstituted oxindoles **4a,d,e,g** and **4h**, were prepared according to the literature procedure.[11-15]

Synthesis and characterization of 4b: To a solution of *N*-phenylisatin[21] (407 mg, 1.82 mmol) in ethanol (3.6 mL) were added hydroxylamine hydrochloride (143 mg, 2.06 mmol) and water (2 drops) at room temperature. After stirring the solution at the same temperature for 3 hours, the reaction mixture was diluted with water (2.0 mL). The resulting mixture was extracted with ethyl acetate (10 mL×2). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to provide a crude material (437 mg) which was used in the next step without further purification. R_f = 0.51 (silica gel, hexane/EtOAc = 1/1).

To a solution of the crude material (437 mg) in methanol (3.6 mL) was added 10% Pd/C (34.2 mg), and the heterogeneous mixture was stirred under a hydrogen atmosphere at room temperature for 4 hours. The reaction mixture was filtered with Celite and concentrated in vacuo to provide a crude material (412 mg) which was used in the next step without further purification. R_f = 0.16 (silica gel, hexane/EtOAc = 1/1).

To a solution of the crude material (412 mg) in dichloromethane (6.1 mL) was added di-*tert*-butyl dicarbonate (411 mg, 1.88 mmmol) under a nitrogen atmosphere at room temperature. The mixture was stirred for 15 hours and concentrated in vacuo to provide a crude material. This material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1) and recrystallization (hexane/EtOAc) to give **4b** (246 mg, 0.758 mmol, 42%) as a white solid. R_f = 0.42 (silica gel, hexane/EtOAc = 2/1); m.p. 180–182 °C; IR (KBr) 3349 (N-H), 2978 (C–H), 1745 (C=O), 1685 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55-7.38 (m, 6H, Ar*H*), 7.28-7.21 (m, 1H, Ar*H*), 7.11 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.81 (d, *J* = 7.5 Hz, 1H, Ar*H*), 5.25 (s, 2H, C*H*, N*H*), 1.47 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9 (*C*), 155.6 (*C*), 143.6 (*C*), 134.2 (*C*), 129.6 (*C*H), 129.0 (*C*H), 128.1 (*C*H), 126.7 (*C*), 126.4 (*C*H), 124.7 (*C*), 123.3 (*C*H), 109.5 (*C*H), 80.6 (*C*), 53.8 (*C*H), 28.2 (*C*H_3). Anal. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.64. Found: C, 70.31; H, 6.06; N, 8.69.

Synthesis and characterization of 4c: To a solution of isatin (515 mg, 3.50 mmol) in ethanol (7.0 mL) were added hydroxylamine hydrochloride (298 mg, 4.29 mmol) and water (2 drops) at room temperature. After stirring the solution at the same temperature for 16 hours, the reaction mixture was diluted with water (5.0 mL). The resulting mixture was extracted with ethyl acetate (30 mL×2). The combined organic extracts

were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to provide a crude material (553 mg) which was used in the next step without further purification. R_f = 0.16 (silica gel, hexane/EtOAc = 1/1).

To a solution of the crude material (553 mg) in methanol (7.0 mL) was added 10% Pd/C (61.2 mg), and the heterogeneous mixture was stirred under a hydrogen atmosphere at room temperature for 18 hours. The reaction mixture was filtered with Celite and concentrated in vacuo to provide a crude material (524 mg) which was used in the next step without further purification. R_f = 0.06 (silica gel, hexane/EtOAc = 1/2).

To a solution of the crude material (524 mg) in dichloromethane (18 mL) was added di-*tert*-butyl dicarbonate (817 mg, 3.74 mmol) under a nitrogen atmosphere at room temperature. The mixture was stirred for 5 hours and concentrated in vacuo to provide a crude material. This material was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to 1/1) and recrystallization (hexane/EtOAc) to give **4c** (277 mg, 1.12 mmol, 32%) as a white solid. R_f = 0.23 (silica gel, hexane/EtOAc = 1/1); m.p. 187–189 °C; IR (KBr) 3443 (N–H), 3276 (N–H), 2986 (C–H), 2928 (C–H), 1748 (C=O), 1673 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (brs, 1H, N*H*), 7.35 (d, *J* = 6.6 Hz, 1H, Ar*H*), 7.27-7.22 (m, 1H, Ar*H*), 7.05 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.86 (d, *J* = 7.5 Hz, 1H, Ar*H*), 5.19 (brs, 1H, C*H*), 5.10 (brs, 1H, N*H*), 1.46 (s, 9H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6, 50 °C) δ 175.7 (*C*), 155.2 (*C*), 142.2 (*C*), 129.1 (*C*), 128.1 (*C*H), 123.3 (*C*H), 121.2 (*C*H), 109.2 (*C*H), 78.3 (*C*), 53.2 (*C*H), 27.9 (*C*H_3). Anal. Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.82; H, 6.28; N, 11.16.

Synthesis and characterization of 4f: To a solution of **4d** (295 mg, 1.81 mmol) in dichloromethane (3.6 mL) were added triethylamine (294 mg, 2.91 mmol) and methanesulfonyl chloride (280 mg, 2.44 mmol) at -20 °C under a nitrogen atmosphere. After stirring the solution at the same temperature for 3 hours, the reaction was quenched by addition of 3% hydrochloric acid (10 mL), and the mixture was then warmed to room temperature. The resulting solution was extracted with ethyl acetate (100 mL). The combined organic extracts were washed with 3% hydrochloric acid (30 mL) and brine (30 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to provide a crude material (461 mg) which was used in the next step without further purification. R_f = 0.26 (silica gel, hexane/EtOAc = 2/1).

To a suspension of sodium hydride (60% oil suspension, 84.3 mg, 2.11 mmol) in tetrahydrofuran (3.8 mL) was added thiophenol (320 mg, 2.90 mmol) at 0 °C under a nitrogen atmosphere. After stirring the solution at the same temperature for 10 minutes, the resulting solution was added to a solution of the crude material (461 mg) in tetrahydrofuran (6.4 mL) at 0 °C and stirred for 30 minutes at the same temperature. The reaction was quenched by addition of water (20 mL), and the mixture was then warmed to room temperature. The solvent was removed under reduced pressure, and the resulting residue was extracted with ethyl acetate (30 mL). The combined organic extracts were washed with saturated aqueous sodium sulfite (10 mL×2) and brine (10 mL×2), dried over Na_2SO_4, filtered, and concentrated in vacuo to provide a crude material. This material was purified by column chromatography (silica gel, hexane/EtOAc = 7/1 to 4/1) and recrystallization (hexane/EtOAc) to give **4f** (262 mg, 1.03 mmol, 57%) as a yellow solid. R_f = 0.28 (silica gel, hexane/EtOAc = 3/1); m.p. 54–56 °C; IR (KBr) 2891 (C–H), 1705 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39-7.35 (m, 3H, Ar*H*), 7.26-7.15 (m, 4H, Ar*H*), 7.07 (dt, *J* = 0.9, 7.5 Hz, 1H, Ar*H*), 6.64 (d, *J* = 7.5 Hz, 1H, Ar*H*), 4.57 (s, 1H, C*H*), 3.03 (s, 1H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2 (*C*), 143.8 (*C*), 136.7 (*C*H), 134.1 (*C*H), 130.9 (*C*), 128.9 (*C*H), 128.5 (*C*H), 126.1 (*C*), 125.2 (*C*H), 122.7 (*C*H), 108.0 (*C*H), 49.1 (*C*H), 26.2 (*C*H_3). Anal. Calcd for $C_{15}H_{13}NOS$: C, 70.56; H, 5.13; N, 5.49. Found: C, 70.64; H, 5.25; N, 5.65.

Synthesis and characterization of 5a: To a solution of *N*-phenylmethacrylamide (2.42 g, 15.0 mmol) and potassium *tert*-butoxide (4.21 g, 37.5 mmol) in THF (150 mL) was added dropwise *n*-butyl lithium (1.55 M in hexane, 22 mL, 34 mmol) at -78 °C under a nitrogen atmosphere. After stirring the solution at the same temperature for 10 min, trimethyl borate (2.5 mL, 22 mmol) was added. After stirring the solution at -78 °C for additional 10 min, 35% aqueous hydrogen peroxide (6.0 mL) and 3.0 M aqueous sodium hydroxide (30 mL) were added. The mixture was then warmed to room temperature and stirred for 9 hours. The reaction was quenched by addition of saturated aqueous sodium thiosulfate (50 mL), and the solvent was removed under reduced pressure. The residue was extracted with ethyl acetate (80 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to provide a crude material. This material was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to 1/1) and recrystallization (hexane/EtOAc) to give allylic alcohol **l** (1.91 g, 10.8 mmol, 72%) as a white solid. R_f = 0.23 (silica gel, hexane/EtOAc = 1/1); m.p. 73–75 °C; IR (KBr) 3412 (N–H), 3304 (O–H), 3058 (C–H), 1653 (C=O), 1624 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.88 (brs, 1H, N*H*), 7.53 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.31 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.11 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.08 (s, 1H, CH_2), 5.55 (s, 1H, CH_2), 4.40 (d, *J* = 2.4 Hz, 2H, CH_2), 3.42 (brs, 1H, O*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5 (*C*), 141.7 (*C*), 137.5 (*C*), 128.9 (*C*H), 124.6 (*C*H), 123.6 (*C*H_2), 120.4 (*C*H), 63.4 (*C*H_2). Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.61; H, 6.12; N, 8.03.

To a solution of **l** (460 mg, 2.60 mmol) in dichloromethane (5.2 mL) were added acetic anhydride (331 mg, 3.24 mmol) and triethylamine (383 mg, 3.78 mmol) at room temperature under a nitrogen atmosphere. The mixture was stirred at the same temperature for 18 hours and concentrated in vacuo to provide a crude material. This material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 2/1) and recrystallization (hexane/EtOAc) to give **5a** (528 mg, 2.41 mmol, 93%) as a white solid. R_f = 0.32 (silica gel, hexane/EtOAc = 2/1); m.p. 97–99 °C; IR (KBr) 3387 (N–H), 1721 (C=O), 1673 (C=O), 1634 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (brs, 1H, N*H*), 7.58 (d, *J* = 7.6 Hz, 2H, Ar*H*), 7.35 (t, *J* = 7.6 Hz, 2H, Ar*H*), 7.14 (m, 1H, Ar*H*), 6.16 (s, 1H, CH_2), 5.77 (s, 1H, CH_2), 4.93 (d, *J* = 0.9 Hz, 2H, CH_2), 2.14 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (*C*), 164.1 (*C*), 139.8 (*C*), 137.6 (*C*), 129.0 (*C*H), 124.6 (*C*H), 124.3 (*C*H_2), 120.1 (*C*H), 63.3 (*C*H_2), 20.9 (*C*H_3). Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.69; H, 6.08; N, 6.29.

Synthesis and characterization of 5b: To a solution of **l** (596 mg, 3.36 mmol) in dichloromethane (17 mL) were added di-*tert*-butyl dicarbonate (733 mg, 3.36 mmol) and *N*,*N*-dimethyl-4-aminopyridine (15.0 mg, 0.122 mmol) under a nitrogen atmosphere at room temperature. The mixture was stirred at the same temperature for 1 hour and concentrated in vacuo to provide a crude material. This material was purified by column chromatography (silica gel, hexane/EtOAc = 4/1) and recrystallization (hexane/EtOAc) to give **5b** (787 mg, 2.84 mmol, 85%) as a white solid. R_f = 0.53 (silica gel, hexane/EtOAc = 2/1); m.p. 93–95 °C; IR (KBr) 3340 (N–H), 2984 (C–H), 1742 (C=O), 1667 (C=O), 1631 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (brs, 1H, N*H*), 7.59 (d, *J* = 7.8 Hz, 2H, Ar*H*), 7.35 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.13 (t, *J* = 7.8 Hz, 1H, Ar*H*), 6.20 (s, 1H, CH_2), 5.80 (s, 1H, CH_2), 4.91 (d, *J* = 0.9 Hz, 2H, CH_2), 1.51 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9 (*C*), 153.4 (*C*), 139.4 (*C*), 137.7 (*C*), 129.0 (*C*H), 125.0 (*C*H), 124.5 (*C*H_2), 120.1 (*C*H), 83.2 (*C*), 65.7 (*C*H_2), 27.7 (*C*H_3). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.85; H, 6.75; N, 4.95.

Synthesis and characterization of 5c: To a solution of **I** (355 mg, 2.00 mmol) in dichloromethane (10 mL) were added benzoyl chloride (350 mg, 2.49 mmol) and triethylamine (309 mg, 3.05 mmol) under a nitrogen atmosphere at room temperature. The mixture was stirred at the same temperature for 13 hours. The reaction was quenched by addition of water (10 mL), and the resulting mixture was extracted with ethyl acetate (30 mL). The combined organic extracts were washed with 1.0 M aqueous sodium hydroxide (10 mL) and brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to provide a crude material. This material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1) and recrystallization (hexane/EtOAc) to give **5c** (276 mg, 0.960 mmol, 48%) as a white solid. R_f = 0.51 (silica gel, hexane/EtOAc = 2/1); m.p. 84–86 °C; IR (KBr) 3317 (N–H), 1721 (C=O), 1663 (C=O), 1629 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.19 (brs, 1H, N*H*), 8.10-8.07 (m, 2H, Ar*H*), 7.63-7.57 (m, 3H, Ar*H*), 7.46 (t, *J* = 7.2 Hz, 2H, Ar*H*), 7.35 (t, *J* = 7.2 Hz, 2H, Ar*H*), 7.14 (t, *J* = 7.2 Hz, 1H, Ar*H*), 6.22 (s, 1H, CH_2), 5.87 (s, 1H, CH_2), 5.20 (d, *J* = 0.6 Hz, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5 (*C*), 164.1 (*C*), 139.8 (*C*), 137.6 (*C*), 133.4 (*C*H), 129.7 (*C*H), 129.4 (*C*), 129.0 (*C*H), 128.5 (*C*H), 124.6 (*C*H), 124.5 (*C*H_2), 120.1 (*C*H), 63.7 (*C*H_2). Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.36; H, 5.57; N, 5.06.

Synthesis and characterization of 5d: According to the synthetic procedure of **5a**, **5d** was prepared from *N*-(*p*-anis)methacrylamide (1.43 g, 7.48 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 3/1) to give **5d** (0.445 g, 1.79 mmol, 24%) as a white solid. R_f = 0.20 (silica gel, hexane/EtOAc = 2/1); m.p. 95–97 °C; IR (KBr) 3292 (N–H), 2960 (C–H), 1743 (C=O), 1661 (C=O), 1624 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.01 (brs, 1H, N*H*), 7.49 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.88 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.13 (s, 1H, CH_2), 5.74 (s, 1H, CH_2), 4.92 (s, 2H, CH_2), 3.80 (s, 3H, CH_3), 2.13 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (*C*), 163.8 (*C*), 156.6 (*C*), 139.7 (*C*), 130.7 (*C*), 124.3 (CH_2), 121.8 (*C*H), 114.2 (*C*H), 63.4 (*C* H_2), 55.5 (*C*H_3), 20.9 (*C*H_3). Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.69; H, 6.18; N, 5.72.

Synthesis and characterization of 5e: According to the synthetic procedure of **5a**, **5e** was prepared from *N*-(*p*-*tert*-butylphenyl)methacrylamide (687 mg, 3.16 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 3/1) to give **5e** (512 mg, 1.86 mmol, 59%) as a white solid. R_f = 0.37 (silica gel, hexane/EtOAc = 2/1); m.p. 90–92 °C; IR (KBr) 3384 (N–H), 2962 (C–H), 1730 (C=O), 1671 (C=O), 1631 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.03 (brs, 1H, N*H*), 7.50 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.36 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.12 (s, 1H, CH_2), 5.74 (s, 1H, CH_2), 4.92 (s, 2H, CH_2), 2.12 (s, 3H, CH_3), 1.31 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (*C*), 164.0 (*C*), 147.6 (*C*), 139.9 (*C*), 135.0 (*C*), 125.8 (*C*H), 124.2 (CH_2), 119.8 (*C*H), 63.4 (CH_2), 34.4 (*C*), 31.3 (CH_3), 20.9 (CH_3). Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.86; H, 7.53; N, 5.33.

Synthesis and characterization of 5f: According to the synthetic procedure of **5a**, **5f** was prepared from *N*-(1-naphthyl)methacrylamide (635 mg, 3.01 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 3/1) to give **5f** (327 mg, 1.21 mmol, 40%) as a white solid. R_f = 0.25 (silica gel, hexane/EtOAc = 2/1); m.p. 63–65 °C; IR (KBr) 3299 (N–H), 3055 (C–H), 1736 (C=O), 1660 (C=O), 1626 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.37 (brs, 1H, N*H*), 8.01 (d, *J* = 7.2 Hz, 1H, Ar*H*), 7.88 (m, 2H, Ar*H*), 7.73 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.57-7.47 (m, 3H, Ar*H*), 6.26 (s, 1H, CH_2), 5.83 (s, 1H, CH_2), 5.01 (s, 2H, CH_2), 2.18 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (*C*), 164.7 (*C*), 139.6 (*C*), 134.1 (*C*), 132.0 (*C*), 128.9 (*C*H), 127.0 (*C*), 126.4 (*C*H), 126.0 (*C*H), 125.7 (*C*H), 124.7 (CH_2), 120.8 (*C*H), 120.4 (*C*H), 63.7 (*C* H_2), 21.0 (CH_3). Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.51; H, 5.64; N, 5.26.

Synthesis and characterization of 5g: According to the synthetic procedure of **5a**, **5g** was prepared from *N*-ethylmethacrylamide (1.72 g, 15.2 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 1/1) to give **5g** (0.646 g, 3.77 mmol, 25%) as a colorless oil. R_f = 0.23 (silica gel, hexane/EtOAc = 1/1); IR (KBr) 3290 (N–H), 1739 (C=O), 1664 (C=O), 1620 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.08 (brs, 1H, N*H*), 5.95 (s, 1H, CH_2), 5.61 (s, 1H, CH_2), 4.84 (d, *J* = 0.9 Hz, 2H, CH_2), 3.37 (dq, *J* = 5.7, 7.2 Hz, 2H, CH_2), 2.11 (s, 3H, CH_3), 1.19 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (*C*), 165.9 (*C*), 139.3 (*C*), 121.9 (CH_2), 63.3 (CH_2), 34.4 (CH_2), 20.8 (CH_3), 14.5 (CH_3). Anal. Calcd for $C_8H_{13}NO_3$: C, 56.13; H, 7.65; N, 8.18. Found: C, 55.88; H, 7.57; N, 7.90.

General procedure for the synthesis of 2a-i: All the experiments for the synthesis of **2a-i** were carried out as described in the following typical procedure. The reaction of **4a** with **5a** for the synthesis of **2a** was exemplified as follows.

Synthesis and characterization of 2a: To a stirred solution of **4a** (52.5 mg, 0.200 mmol) and **5a** (51.8 mg, 0.236 mmol) in dichloromethane (0.20 M) was added $Pd(PPh_3)_4$ (10 mol%). The resulting yellow solution was stirred for 30 min at room temperature and concentrated under reduced pressure to give a crude material. This material was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to $CHCl_3$/MeOH = 50/1) to give **2a** (83.7 mg, 0.199 mmol, >99%) as a white solid. R_f = 0.23 (silica gel, hexane/EtOAc = 1/1); m.p. 238–240 °C; IR (KBr) 3345 (N–H), 3288 (N–H), 2981 (C–H), 2925 (C–H), 1713 (C=O), 1686 (C=O), 1626 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (brs, 1H, N*H*), 7.49 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.33 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.28-7.20 (m, 2H, Ar*H*), 7.14 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.98 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.82 (d, *J* = 7.5 Hz, 1H, Ar*H*), 6.54 (brs, 1H, N*H*), 5.76 (s, 1H, CH_2), 5.24 (s, 1H, CH_2), 3.23 (s, 3H, CH_3), 2.89 (d, *J* = 13.5 Hz, 1H, CH_2), 2.75 (d, *J* = 13.5 Hz, 1H, CH_2), 1.21 (s, 9H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6, 50 °C) δ 175.5 (*C*), 166.4 (*C*), 153.2 (*C*), 143.2 (*C*), 138.5 (*C*), 138.1 (*C*), 129.6 (C), 128.0 (*C*H), 123.4 (CH_2), 123.3 (*C*H), 122.6 (*C*H), 121.3 (*C*H), 120.4 (*C*H), 107.7 (*C*H), 78.3 (*C*), 61.3 (*C*), 38.2 (CH_2), 27.6 (CH_3), 25.7 (CH_3). Anal. Calcd for $C_{24}H_{27}N_3O_4$: C, 68.39; H, 6.46; N, 9.97. Found: C, 68.23; H, 6.45; N, 9.73.

Synthesis and characterization of 2b: According to the synthetic procedure of **2a**, **2b** was synthesized from **4a** (52.4 mg, 0.200 mmol) and **5d** (59.1 mg, 0.237 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to $CHCl_3$/MeOH = 50/1) to give **2b** (89.8 mg, 0.199 mmol, >99%) as a white solid. R_f = 0.29 (silica gel, hexane/EtOAc = 1/2); m.p. 178–180 °C; IR (KBr) 3347 (N–H), 3294 (N–H), 2979 (C–H), 2931 (C–H), 1715 (C=O), 1686 (C=O), 1617 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54 (brs, 1H, N*H*), 7.39 (d, *J* = 9.0 Hz, 2H, Ar*H*), 7.28-7.19 (m, 2H, Ar*H*), 6.99 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.89-6.81 (m, 3H, Ar*H*), 6.68 (brs, 1H, N*H*), 5.75 (s, 1H, CH_2), 5.21 (s, 1H, CH_2), 3.80 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 2.89 (d, *J* = 13.5 Hz, 1H, CH_2), 2.71 (d, *J* = 13.5 Hz, 1H, CH_2), 1.22 (brs, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6 (*C*), 167.5 (*C*), 156.5 (*C*), 153.9 (*C*), 142.8 (*C*), 138.8 (*C*), 130.6 (*C*), 130.1 (*C*), 128.7 (*C*H), 123.8 (CH_2), 123.4 (*C*H), 122.3 (*C*H), 122.2 (*C*H), 121.9 (*C*H), 113.9 (*C*H), 108.0 (*C*H), 79.8 (*C*), 61.5 (*C*), 55.4 (CH_3), 39.7 (CH_2), 28.0 (CH_3), 26.4 (CH_3). Anal. Calcd for $C_{25}H_{29}N_3O_5$: C, 66.50; H, 6.47; N, 9.31. Found: C, 66.40; H, 6.55; N, 9.07.

Synthesis and characterization of 2c: According to the synthetic procedure of **2a**, **2c** was synthesized from **4a** (52.3 mg, 0.199 mmol) and **5e** (64.6 mg, 0.235 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to $CHCl_3$/MeOH = 50/1) to give **2c** (94.2 mg, 0.197 mmol, 99%) as a white solid. R_f = 0.28 (silica gel, hexane/EtOAc = 1/1); m.p. 215–217 °C; IR (KBr) 3330 (N–H), 3276 (N–H), 2967 (C–H), 1715 (C=O), 1685 (C=O), 1618 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (brs, 1H, N*H*), 7.42 (d, *J* = 8.4 Hz, 2H, Ar*H*),

7.34 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.26 (dt, *J* = 1.5, 8.1 Hz, 1H, Ar*H*), 7.18 (d, *J* = 7.5 Hz, 1H, Ar*H*), 6.98 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.86 (brs, 1H, N*H*), 6.81 (d, *J* = 7.5 Hz, 1H, Ar*H*), 5.76 (s, 1H, CH_2), 5.19 (s, 1H, CH_2), 3.21 (s, 3H, CH_3), 2.88 (d, *J* = 13.5 Hz, 1H, CH_2), 2.66 (d, *J* = 13.5 Hz, 1H, CH_2), 1.31 (s, 9H, CH_3), 1.21 (brs, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.5 (*C*), 167.6 (*C*), 153.9 (*C*), 147.6 (*C*), 142.9 (*C*), 139.3 (*C*), 134.8 (*C*), 130.1 (*C*), 128.8 (*C*H), 125.7 (*C*H), 123.5 (*C*H$_2$), 123.3 (*C*H), 122.3 (*C*H), 120.2 (*C*H), 108.0 (*C*H), 79.9 (*C*), 61.5(*C*), 39.7 (*C*H$_2$), 34.4 (*C*), 31.3 (*C*H$_3$), 28.0 (*C*H$_3$), 26.4 (*C*H$_3$). Anal. Calcd for $C_{28}H_{35}N_3O_4$: C, 70.42; H, 7.39; N, 8.80. Found: C, 70.32; H, 7.07; N, 8.77.

Synthesis and characterization of 2d: According to the synthetic procedure of **2a**, **2d** was synthesized from **4a** (52.6 mg, 0.201 mmol) and **5f** (64.8 mg, 0.241 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to $CHCl_3$/MeOH = 50/1) to give **2d** (91.3 mg, 0.194 mmol, 97%) as a white solid. R_f = 0.21 (silica gel, hexane/EtOAc = 1/1); m.p. 210–212 °C; IR (KBr) 3329 (N–H), 2977 (C–H), 2926 (C–H), 1712 (C=O), 1656 (C=O), 1617 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (brs, 1H, N*H*), 7.89-7.81 (m, 3H, Ar*H*), 7.73 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.54-7.46 (m, 3H, Ar*H*), 7.28-7.21 (m, 2H, Ar*H*), 7.00 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.83 (d, *J* = 7.5 Hz, 1H, Ar*H*), 6.53 (brs, 1H, N*H*), 5.92 (s, 1H, CH_2), 5.34 (s, 1H, CH_2), 3.26 (s, 3H, CH_3), 2.91 (d, *J* = 13.5 Hz, 1H, CH_2), 2.84 (d, *J* = 13.5 Hz, 1H, CH_2), 1.18 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3 (*C*), 168.5 (*C*), 153.8 (*C*), 142.9 (*C*), 139.7 (*C*), 134.0 (*C*), 131.9 (*C*), 130.2 (*C*), 128.8 (*C*H), 128.6 (*C*H), 127.5 (*C*), 126.4 (*C*H), 126.3 (*C*H), 126.0 (*C*H), 125.6 (*C*H), 123.3 (*C*H), 123.2 (*C*H$_2$), 122.4 (*C*H), 121.5 (*C*H), 121.0 (*C*H), 108.0 (*C*H), 79.9 (*C*), 61.6 (*C*), 39.8 (*C*H$_2$), 28.0 (*C*H$_3$), 26.4 (*C*H$_3$). Anal. Calcd for $C_{28}H_{29}N_3O_4$: C, 71.32; H, 6.20; N, 8.91. Found: C, 71.15; H, 6.13; N, 8.67.

Synthesis and characterization of 2e: According to the synthetic procedure of **2a**, **2e** was synthesized from **4a** (52.5 mg, 0.200 mmol) and **5g** (40.0 mg, 0.234 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to $CHCl_3$/MeOH = 50/1) to give **2e** (73.3 mg, 0.196 mmol, 98%) as a white solid. R_f = 0.28 (silica gel, hexane/EtOAc = 1/2); m.p. 178–180 °C; IR (KBr) 3367 (N–H), 3290 (N–H), 2983 (C–H), 2929 (C–H), 1709 (C=O), 1690 (C=O), 1657 (C=O), 1617 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.24 (m, 1H, Ar*H*), 7.15 (d, *J* = 6.9 Hz, 1H, Ar*H*), 7.00 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.81 (d, *J* = 7.5 Hz, 1H, Ar*H*), 5.92 (brs, 1H, N*H*), 5.61 (s, 1H, CH_2), 5.08 (s, 1H, CH_2), 3.37-3.25 (m, 2H, CH_2), 3.23 (s, 3H, CH_3), 2.82 (d, *J* = 13.5 Hz, 1H, CH_2), 2.55 (d, *J* = 13.5 Hz, 1H, CH_2), 1.26 (brs, 9H, CH_3), 1.16 (t, *J* = 7.5 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.5 (*C*), 169.5 (*C*), 153.9 (*C*), 142.9 (*C*), 139.0 (*C*), 130.2 (*C*), 128.6 (*C*H), 123.4 (*C*H), 122.7 (*C*H$_2$), 122.1 (*C*H), 107.9 (*C*H), 79.6 (*C*), 61.4 (*C*), 39.8 (*C*H$_2$), 34.9 (*C*H$_2$), 28.1 (*C*H$_3$), 26.4 (*C*H$_3$), 14.6 (*C*H$_3$). Anal. Calcd for $C_{20}H_{27}N_3O_4$: C, 64.32; H, 7.29; N, 11.25. Found: C, 64.03; H, 7.26; N, 10.90.

Synthesis and characterization of 2f: According to the synthetic procedure of **2a**, **2f** was synthesized from **4b** (64.9 mg, 0.200 mmol) and **5a** (51.4 mg, 0.234 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to $CHCl_3$/MeOH = 50/1) to give **2f** (96.2 mg, 0.199 mmol, >99%) as a white solid. R_f = 0.25 (silica gel, hexane/EtOAc = 1/1); m.p. 204–206 °C; IR (KBr) 3342 (N–H), 2978 (C–H), 2924 (C–H), 1716 (C=O), 1697 (C=O), 1657 (C=O), 1611 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (brs, 1H, N*H*), 7.54-7.28 (m, 10H, Ar*H*), 7.20-7.11 (m, 2H, Ar*H*), 7.02 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.82 (brd, *J* = 7.4 Hz, 1H, Ar*H*), 6.54 (brs, 1H, N*H*), 5.79 (s, 1H, CH_2), 5.34 (s, 1H, CH_2), 2.99 (d, *J* = 13.8 Hz, 1H, CH_2), 2.93 (d, *J* = 13.8 Hz, 1H, CH_2), 1.25 (s, 9H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6, 50 °C) δ 175.0 (*C*), 166.2 (*C*), 153.5 (*C*), 142.8 (*C*), 138.4 (*C*), 138.0 (*C*), 134.5 (*C*), 129.5 (*C*), 129.0 (*C*H), 128.0 (*C*H), 127.4 (*C*H), 126.3 (*C*H), 123.6 (*C*H$_2$), 123.3 (*C*H), 123.2 (*C*H), 122.0 (*C*H), 120.6 (*C*H), 108.3 (*C*H), 78.6 (*C*), 61.3 (*C*), 38.3 (*C*H$_2$), 27.8 (*C*H$_3$). Anal. Calcd for $C_{29}H_{29}N_3O_4$: C, 72.03; H, 6.05; N, 8.69. Found: C, 71.84; H, 6.10; N, 8.44.

Synthesis and characterization of 2g: According to the synthetic procedure of **2a**, **2g** was synthesized from **4c** (49.5 mg, 0.200 mmol) and **5a** (51.1 mg, 0.233 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to $CHCl_3$/MeOH = 50/1) to give **2g** (76.1 mg, 0.187 mmol, 94%) as a white solid. R_f = 0.13 (silica gel, hexane/EtOAc = 1/1); m.p. 160–162 °C; IR (KBr) 3332 (N–H), 2979 (C–H), 2928 (C–H), 1732 (C=O), 1699 (C=O), 1666 (C=O), 1621 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 7.36 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.25 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.14-7.04 (m, 3H, Ar*H*), 6.90-6.82 (m, 2H, Ar*H*), 5.80 (s, 1H, CH_2), 5.36 (s, 1H, CH_2), 3.17 (d, *J* = 13.2 Hz, 1H, CH_2), 2.63 (d, *J* = 13.2 Hz, 1H, CH_2), 1.28 (s, 9H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6, 50 °C) δ 177.3 (*C*), 166.7 (*C*), 153.4 (*C*), 141.7 (*C*), 138.5 (*C*), 138.0 (C), 130.4 (*C*), 128.0 (*C*H), 127.8 (*C*H), 123.8 (*C*H$_2$), 123.3 (*C*H), 123.1 (*C*H), 120.6 (*C*H), 120.4 (*C*H), 109.1 (*C*H), 78.4 (*C*), 61.4 (*C*), 38.1 (*C*H$_2$), 27.6 (*C*H$_3$). Anal. Calcd for $C_{23}H_{25}N_3O_4$: C, 67.80; H, 6.18; N, 10.31. Found: C, 67.52; H, 6.19; N, 10.58.

Synthesis and characterization of 2h: According to the synthetic procedure of **2a**, **2h** was synthesized from **4d** (32.6 mg, 0.200 mmol) and **5a** (51.3 mg, 0.234 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to $CHCl_3$/MeOH = 50/1) to give **2h** (51.3 mg, 0.159 mmol, 80%) as a white solid. R_f = 0.28 (silica gel, hexane/EtOAc = 1/2); m.p. 184–186 °C; IR (KBr) 3380 (N–H), 3304 (O–H), 1719 (C=O), 1655 (C=O), 1618 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (brs, 1H, N*H*), 7.52 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.36-7.28 (m, 4H, Ar*H*), 7.14 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.04 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.82 (d, *J* = 7.5 Hz, 1H, Ar*H*), 5.91 (s, 1H, CH_2), 5.37 (s, 1H, CH_2), 5.32 (s, 1H, O*H*), 3.17 (s, 3H, CH_3), 3.08 (d, *J* = 14.1 Hz, 1H, CH_2), 2.77 (d, *J* = 14.1 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 176.8 (*C*), 166.5 (*C*), 143.1 (*C*), 139.3 (*C*), 138.9 (*C*), 130.0 (C), 129.0 (*C*H), 128.3 (*C*H), 124.4 (*C*H), 123.3 (*C*H), 122.6 (*C*H$_2$), 121.8 (*C*H), 120.3 (*C*H), 108.3 (*C*H), 75.4 (*C*), 25.8 (*C*H$_3$). Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.75; H, 5.88; N, 8.54.

Synthesis and characterization of 2i: According to the synthetic procedure of **2a**, **2i** was synthesized from **4e** (53.9 mg, 0.205 mmol) and **5a** (53.0 mg, 0.242 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to $CHCl_3$/MeOH = 50/1) to give **2i** (36.2 mg, 0.0857 mmol, 42%) as a white solid. R_f = 0.18 (silica gel, hexane/EtOAc = 2/1); m.p. 126–128 °C; IR (NaCl) 3583 (N–H), 3496 (O–H), 3012 (C–H), 2982 (C–H), 2934 (C–H), 1750 (C=O), 1725 (C=O), 1669 (C=O), 1618 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (brs, 1H, N*H*), 7.51 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.33-7.24 (m, 4H, Ar*H*), 7.10 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.01 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.85 (d, *J* = 7.5 Hz, 1H, Ar*H*), 5.88 (s, 1H, CH_2), 5.24 (s, 1H, CH_2), 3.24 (s, 3H, CH_3), 3.13 (d, *J* = 14.1 Hz, 1H, CH_2), 3.02 (d, *J* = 14.1 Hz, 1H, CH_2), 1.30 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1 (*C*), 166.4 (*C*), 150.3 (*C*), 143.4 (*C*), 138.3 (*C*), 137.9 (*C*), 130.2 (*C*H), 128.7 (*C*H), 126.4 (*C*), 124.9 (*C*H$_2$), 124.2 (*C*H), 123.7 (*C*H), 122.9 (*C*H), 120.1 (*C*H), 108.4 (*C*H), 83.7 (*C*), 80.3 (*C*), 39.0 (*C*H$_2$), 27.4 (*C*H$_3$), 26.5 (*C*H$_3$). Anal. Calcd for $C_{24}H_{26}N_2O_5$: C, 68.23; H, 6.20; N, 6.63. Found: C, 67.93; H, 6.40; N, 6.84.

Synthesis and characterization of 2j: According to the synthetic procedure of **2a**, **2j** was synthesized from **4f** (50.8 mg, 0.199 mmol) and **5a** (52.1 mg, 0.238 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 2/1) to give **2j** (75.5 mg, 0.182 mmol, 91%) as a white solid. R_f = 0.18 (silica gel, hexane/EtOAc = 2/1); m.p. 46–48 °C; IR (NaCl) 3312 (N-H), 3006 (C-H), 1713 (C=O), 1669 (C=O), 1612 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (brs, 1H, N*H*), 7.39-7.36 (m, 3H, Ar*H*), 7.30-7.22 (m, 3H, Ar*H*), 7.20-7.05 (m, 6H, Ar*H*), 7.00 (dt, *J* = 0.9, 7.5 Hz, 1H, Ar*H*), 6.49 (d, *J* = 7.5 Hz,

1H, Ar*H*), 5.69 (s, 1H, C*H*$_2$), 5.26 (s, 1H, C*H*$_2$), 3.42 (dd, *J* = 0.9, 14.1 Hz, 1H, C*H*$_2$), 3.21 (d, *J* = 14.1 Hz, 1H, C*H*$_2$), 2.87 (s, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0 (*C*), 166.3 (*C*), 143.0 (*C*), 140.4 (*C*), 137.7 (*C*), 136.7 (*C*H), 129.7 (*C*H), 129.0 (*C*H), 128.9 (*C*), 128.7 (*C*H), 128.2 (*C*, *C*H), 125.3 (*C*H), 124.2 (*C*H), 123.7 (CH_2), 122.9 (*C*H), 120.2 (*C*H), 107.8 (*C*H), 59.0 (*C*), 35.6 (CH_2), 26.1 (CH_3). Anal. Calcd for $C_{25}H_{22}N_2O_2S$: C, 72.44; H, 5.35; N, 6.76. Found: C, 72.32; H, 5.39; N, 6.51.

Synthesis and characterization of 2k: According to the synthetic procedure of **2a**, **2k** was synthesized from **4g** (29.9 mg, 0.200 mmol) and **5a** (51.4 mg, 0.234 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 1/4) to give **2k** (51.2 mg) as a mixture with a bisallylated derivative (68% NMR yield). R_f = 0.32 (silica gel, hexane/EtOAc = 1/3); m.p. 91–93 °C; IR (KBr) 3252 (N-H), 3061 (C-H), 2962 (C-H), 1732 (C=O), 1642 (C=O), 1621 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 7.35-7.21 (m, 5H, Ar*H*), 7.13 (dt, *J* = 1.2, 7.5 Hz, 1H, Ar*H*), 7.06 (tt, *J* = 1.2, 7.5 Hz, 1H, Ar*H*), 6.88 (dt, *J* = 0.9, 7.5 Hz, 1H, Ar*H*), 6.83 (d, *J* = 7.8 Hz, 1H, Ar*H*), 5.77 (s, 1H, C*H*$_2$), 5.39 (s, 1H, C*H*$_2$), 3.25 (d, *J* = 13.2 Hz, 1H, C*H*$_2$), 2.84 (d, *J* = 13.2 Hz, 1H, C*H*$_2$); ^{13}C NMR (75 MHz, CD_3OD) δ 181.3 (*C*), 169.5 (*C*), 142.6 (*C*), 140.9 (*C*), 139.4 (*C*), 131.4 (*C*), 130.7 (*C*H), 129.5 (*C*H), 126.4 (*C*H), 125.4 (*C*H), 124.1 (CH_2), 123.4 (*C*H), 122.3 (*C*H), 111.2 (*C*H), 77.7 (*C*), 40.7 (CH_2). Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 69.76; H, 5.17; N, 8.92.

Synthesis and characterization of 2l: According to the synthetic procedure of **2a**, **2l** was synthesized from **4h** (48.2 mg, 0.200 mmol) and **5a** (51.9 mg, 0.237 mmol). The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 2/1) to give **2l** (65.9 mg, 0.165 mmol, 83%) as a white solid. R_f = 0.25 (silica gel, hexane/EtOAc = 1/1); m.p. 66–68 °C; IR (KBr) 3253 (N-H), 3058 (C-H), 2962 (C-H), 1719 (C=O), 1707 C=O), 1656 (C=O), 1620 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (brs, 1H, N*H*), 7.57 (brs, 1H, NH), 7.32-6.91 (m, 13H, Ar*H*), 6.56 (d, *J* = 7.8 Hz, 1H, Ar*H*), 5.59 (s, 1H, C*H*$_2$), 5.28 (s, 1H, C*H*$_2$), 3.44 (d, *J* = 13.8 Hz, 1H, C*H*$_2$), 3.12 (d, *J* = 13.8 Hz, 1H, C*H*$_2$); ^{13}C NMR (75 MHz, CD_3OD) δ 179.5 (*C*), 169.3 (*C*), 142.7 (*C*), 141.9 (*C*), 139.2 (*C*), 137.6 (*C*H), 130.6 (*C*H), 130.1 (*C*H), 129.7 (*C*), 129.5 (*C*H), 129.4 (*C*H), 127.2 (*C*H), 125.4 (*C*H), 123.3 (*C*H), 123.2 (CH_2), 122.4 (*C*H), 110.8 (*C*H), 61.0 (*C*), 37.5 (CH_2). Anal. Calcd for $C_{24}H_{20}N_2O_2S$: C, 71.98; H, 5.03; N, 6.99. Found: C, 71.83; H, 5.33; N, 7.28.

General procedure for the synthesis of 3a-c: All the experiments for the synthesis of **2a-i** were carried out as described in the following typical procedure. The transformation of **2a** to **3a** was exemplified as follows.

Synthesis and characterization of 3a: To a solution of **2a** (143 mg, 0.339 mmol) in dichloromethane (0.34 mL) was added Boc_2O (220 mg, 1.01 mmol), triethylamine (102 mg, 1.01 mmol) and *N*,*N*-dimethyl-4-aminopyridine (12.2 mg, 0.100 mmol) at room temperature under a nitrogen atmosphere. After stirring the solution at the same temperature for 24 hours, the solvent was removed under reduced pressure. The crude residue was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 2/1) to give *N*-Boc protected spirocyclic lactam **6a** (108 mg, 0.329 mmol, 97%) as a white solid. R_f = 0.30 (silica gel, hexane/EtOAc = 1/1); m.p. 149–151 °C; IR (NaCl) 3018 (C-H), 1782 (C=O), 1734 (C=O), 1615 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (dt, *J* = 1.0, 7.5 Hz, 1H, Ar*H*), 7.17 (dd, *J* = 1.0, 7.5 Hz, 1H, Ar*H*), 7.06 (dd, *J* = 1.0, 7.5 Hz, 1H, Ar*H*), 6.87 (d, *J* = 7.5 Hz, 1H, Ar*H*), 6.38 (t, *J* = 2.6 Hz, 1H, C*H*$_2$), 5.59 (t, *J* = 2.6 Hz, 1H, C*H*$_2$), 3.25 (s, 3H, C*H*$_3$), 3.12 (td, *J* = 2.6, 16.8 Hz, 1H, C*H*$_2$), 2.78 (td, *J* = 2.6, 16.8 Hz, 1H, C*H*$_2$), 1.19 (s, 9H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2 (*C*), 166.3 (*C*), 148.3 (*C*), 142.9 (*C*), 135.8 (*C*), 130.1 (*C*), 129.7 (*C*H), 123.2 (*C*H), 121.6 (*C*H), 120.9 (CH_2), 108.5 (*C*H), 83.7 (*C*), 63.9 (*C*), 36.3 (CH_2), 27.4 (CH_3), 26.5 (CH_3). Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.45; H, 6.38; N, 8.60.

To a solution of **6a** (136 mg, 0.414 mmol) in dichloromethane (4.1 mL) was added trifluoroacetic acid (12.7 mg, 0.111 mmol) under a nitrogen atmosphere at room temperature. After stirring the solution at the same temperature for 24 hours, the resulting mixture was concentrated under reduced pressure. The crude residue was purified by column chromatography (silica gel, hexane/EtOAc = 2/1 to 1/2) to give **3a** (93.4 mg, 0.409 mmol, 99%) as a white solid. R_f = 0.15 (silica gel, hexane/EtOAc = 1/2); m.p. 174–176 °C; IR (KBr) 3176 (N-H), 3059 (C-H), 1735 (C=O), 1721 (C=O), 1660 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (dt, *J* = 1.2, 7.5 Hz, 1H, Ar*H*), 7.30 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.12 (dt, *J* = 1.2, 7.5 Hz, 1H, Ar*H*), 6.88 (d, *J* = 7.5 Hz, 1H, Ar*H*), 6.18 (t, *J* = 2.7 Hz, 1H, C*H*$_2$), 5.92 (brs, 1H, N*H*), 5.51 (t, *J* = 2.7 Hz, 1H, C*H*$_2$), 3.22 (td, *J* = 2.6, 17.0 Hz, 1H, C*H*$_2$), 3.23 (s, 3H, C*H*$_3$), 2.94 (td, *J* = 2.6, 17.0 Hz, 1H, C*H*$_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2 (*C*), 170.4 (*C*), 143.0 (*C*), 136.7 (*C*), 130.2 (*C*H), 129.6 (*C*), 123.6 (*C*H), 123.5 (*C*H), 117.5 (CH_2), 108.7 (*C*H), 60.8 (*C*), 38.4 (CH_2), 26.6 (CH_3). Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.63; H, 5.45; N, 12.13.

According to the above synthetic procedure, **6a** was obtained from **2b** (77.2 mg, 0.171 mmol) in 99% yield (55.8 mg, 0.170 mmol).

According to the above synthetic procedure, **6a** was obtained from **2c** (64.8 mg, 0.136 mmol) in 95% yield (42.5 mg, 0.129 mmol).

According to the above synthetic procedure, **6a** was obtained from **2d** (39.5 mg, 0.0838 mmol) in 99% yield (27.2 mg, 0.0828 mmol).

According to the above synthetic procedure, **6a** was obtained from **2e** (70.7 mg, 0.189 mmol) in 98% yield (60.8 mg, 0.185 mmol).

Synthesis and characterization of 3b: According to the above synthetic procedure, **6b** was obtained from **2f** (287 mg, 0.594 mmol) in 96% yield (225 mg, 0.576 mmol) as a white solid. R_f = 0.38 (silica gel, hexane/EtOAc = 2/1); m.p. 50–52 °C; IR (KBr) 3019 (C-H), 2983 (C-H), 1785 (C=O), 1742 (C=O), 1718 (C=O), 1609 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57-7.42 (m, 5H, Ar*H*), 7.31-7.24 (m, 2H, Ar*H*), 7.12 (dt, *J* = 0.9, 7.5 Hz, 1H, Ar*H*), 6.95 (d, *J* = 7.8 Hz, 1H, Ar*H*), 6.39 (t, *J* = 2.7 Hz, 1H, C*H*$_2$), 5.61 (t, *J* = 2.7 Hz, 1H, C*H*$_2$), 3.24 (td, *J* = 2.7, 16.8 Hz, 1H, C*H*$_2$), 2.92 (td, *J* = 2.7, 16.8 Hz, 1H, C*H*$_2$), 1.29 (s, 9H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6 (*C*), 166.0 (*C*), 148.8 (*C*), 142.9 (*C*), 135.9 (*C*), 134.1 (*C*), 130.0 (*C*), 129.6 (*C*H), 129.5 (*C*H), 128.1 (*C*H), 125.9 (C*H*), 123.7 (*C*H), 122.0 (*C*H), 121.1 (CH_2), 109.9 (*C*H), 84.2 (*C*), 64.1 (*C*), 36.8 (CH_2), 27.7 (CH_3). Anal. Calcd for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.18. Found: C, 70.79; H, 5.63; N, 7.48.

In this procedure, **3b** was obtained from **6b** (135 mg, 0.346 mmol) in 99% yield (99.5 mg, 0.343 mmol) as a white solid. R_f = 0.45 (silica gel, hexane/EtOAc = 1/2); m.p. 252–254 °C; IR (KBr) 3477 (N-H), 3177 (N-H), 3063 (C-H), 1735 (C=O), 1700 (C=O), 1658 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.71 (brs, 1H, N*H*), 7.59 (t, *J* = 7.2 Hz, 2H, Ar*H*), 7.48-7.42 (m, 4H, Ar*H*), 7.31 (t, *J* = 7.8 Hz, 1H, Ar*H*), 7.16 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.76 (d, *J* = 7.8 Hz, 1H, C*H*$_2$), 5.85 (s, 1H, C*H*$_2$), 5.44 (s, 1H, C*H*$_2$), 3.21 (d, *J* = 17.4 Hz, 1H, C*H*$_2$), 2.99 (d, *J* = 17.4 Hz, 1H, C*H*$_2$); ^{13}C NMR (75 MHz, DMSO-d_6) δ 176.0 (*C*), 169.5 (*C*), 143.1 (*C*), 139.0 (*C*), 134.0 (*C*), 129.8 (*C*H), 129.7 (*C*H), 128.3 (*C*H), 126.6 (*C*H), 124.2 (*C*H), 123.6 (*C*H), 115.2 (CH_2), 109.2 (*C*H), 60.5 (*C*), 37.6 (CH_2). Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.40; H, 4.85; N, 9.75.

Synthesis and characterization of 3c: According to the above synthetic procedure, **6c** was obtained from **2g** (106 mg, 0.260 mmol) in 93% yield (100 mg, 0.241 mmol) as a white solid. R_f = 0.35 (silica gel, hexane/EtOAc = 2/1); m.p. 55–57 °C; IR (KBr) 2983 (C-H), 1802 (C=O), 1791 (C=O), 1777 (C=O), 1735 (C=O), 1719 (C=O), 1609 (C=C) cm^{-1}; ^{1}H

NMR (300 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.43-7.37 (m, 1H, Ar*H*), 7.22-7.19 (m, *2*H, Ar*H*), 6.39 (t, *J* = 2.7 Hz, 1H, CH_2), 5.61 (t, *J* = 2.7 Hz, 1H, CH_2), 3.19 (td, *J* = 2.7, 17.1 Hz, 1H, CH_2), 2.81 (td, *J* = 2.7, 17.1 Hz, 1H, CH_2), 1.65 (s, 9H, CH_3), 1.20 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6 (*C*), 165.9 (*C*), 148.8 (*C*), 147.9 (*C*), 139.1 (*C*), 135.2 (*C*), 129.9 (*C*H), 129.0 (*C*), 125.2 (*CH*), 121.7 (*C*H), 121.4 (*C*H_2), 115.3 (*C*H), 84.8 (*C*), 84.5 (*C*), 64.0 (*C*), 37.1 (CH_2), 28.0 (CH_3), 27.2 (CH_3). Anal. Calcd for $C_{22}H_{26}N_2O_6$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.81; H, 6.27; N, 6.66.

In this procedure, **3c** was obtained from **6c** (62.2 mg, 0.150 mmol) in 98% yield (31.4 mg, 0.147 mmol) as a white solid. R_f = 0.16 (silica gel, hexane/EtOAc = 1/3); m.p. 235–237 °C; IR (KBr) 3288 (N-H), 3222 (N-H), 3062 (C-H), 3029 (C-H), 1725 (C=O), 1704 (C=O), 1662 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 7.32-7.25 (m, 2H, Ar*H*), 7.07 (dt, *J* = 0.9, 7.5 Hz, 1H, Ar*H*), 6.94 (d, *J* = 0.9, 7.5 Hz, 1H, Ar*H*), 6.02 (t, *J* = 2.7 Hz, 1H, CH_2), 5.52 (t, *J* = 2.7 Hz, 1H, CH_2), 3.15 (td, *J* = 2.7, 17.1 Hz, 1H, CH_2), 2.98 (td, *J* = 2.7, 17.1 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, CD_3OD) δ 180.5 (*C*), 172.9 (*C*), 142.7 (*C*), 140.0 (*C*), 131.8 (*C*), 131.1 (*C*H), 124.8 (*C*H), 124.3 (*C*H), 117.1 (*C*H_2), 111.5 (*C*H), 62.9 (*C*), 39.0 (*C*H_2). Anal. Calcd for $C_{12}H_{10}N_2O_2$: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.14; H, 4.81; N, 12.90.

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Keywords: α-methylene-γ-butyrolactam • electrophilic amide allylation • 3-heterosubstituted oxindoles • palladium catalyzed reaction • spirocyclic oxindole

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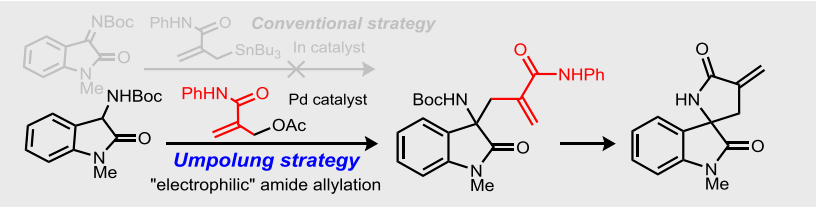

A new route to access spirocyclic 2-oxindole containing α-methylene-γ-butyrolactam structure via “electrophilic amide allylation” is reported. The key reaction was accomplished by using acetoxy methacrylamides and tetrakis(triphenylphosphine)palladium as a catalyst, affording a variety of the amide allylated products in excellent yields.

Electrophilic amide allylation

*Tetsuya Sengoku, Daichi Hayashi, Masaki Takahashi and Hidemi Yoda**

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Electrophilic amide allylation of 3-heterosubstituted oxindoles: a new route to spirocyclic 2-oxindole containing α-methylene-γ-butyrolactam structure