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Tin Powder-Promoted One-Pot Construction of α-Methylene-γ-lactams and Spirolactams from Aldehydes or Ketones, Acylhydrazines, and 2-(Bromomethyl)acrylate

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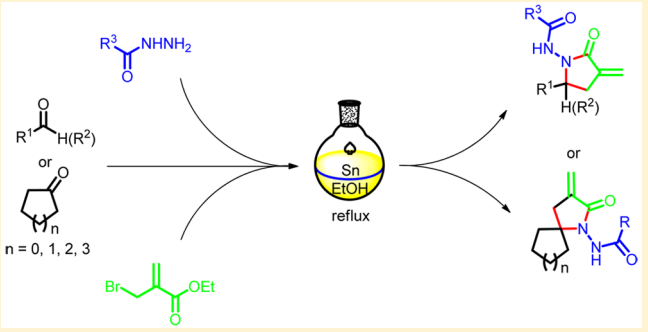
Supporting Information

ABSTRACT: A concise and efficient method for the synthesis of α-methylene-γ-lactams is developed from multicomponent one-pot reactions of aldehydes or ketones, hydrazides, and ethyl 2-(bromomethyl)acrylate promoted by tin powder. The reaction proceeds smoothly under mild reaction conditions without using any catalyst to give the corresponding products in high yields. α-Methylene-γ-spirolactams can also be prepared from cyclic ketones.



INTRODUCTION

α-Methylene-γ-lactam units are important scaffolds found in some biologically active molecules and natural products (Figure 1).[1−3] Compared with their isosteric α-methylene-γ-lactones, α-methylene-γ-lactams display much lower toxic side effects while maintaining similar bioactivities in antibacterial, antiinflammatory, antianaphylactic, and anticancer properties.[2] They are also versatile building blocks in organic synthesis. Thus, the development of appropriate synthetic strategies for obtaining these frameworks has received much attention over the past several decades.[3] For instance, intramolecular Baylis−Hillman reactions,[4] Baylis−Hillman alcohols and their derivatives as precursors,[5] addition of the allylic organometallic reagents to the imines,[6] Wittig or Horner−Wadsworth−Emmons reactions of functionalized α-(dialkoxyphosphoryl)-substituted lactams with carbonyl compounds,[2f,g,7] and radical chemistry[8] were the major approaches to obtaining α-methylene-γ-lactam moieties. Among these methodologies, addition of the allylic organometallic reagents to the imines is a fascinating method for producing α-methylene-γ-lactams. Metals such as zinc[5c,6b−d,9] and indium[6e] successfully promoted the addition of 2-(bromomethyl)acrylic acid or esters to aldimines to give the desired products. The allylboration of aldimines with 2-(alkoxycarbonyl)-allylboronates represents another facile route to α-methylene-γ-lactams.[10] However, additions of these reagents to ketimines have never been reported. In our research group, we are interested in metal tin-mediated organic reactions recently because organotin compounds usually display good stability toward heat, hydrolysis, and oxidation, tolerance to functional groups, and high selectivity in organic reactions.[11]

We found that one-pot reactions of aldehydes or ketones, acylhydrazine, 2-(bromomethyl)acrylic esters, and tin powder will give α-methylene-γ-lactams in good yields. In particular, α-methylene-γ-spirolactams[12] can be also obtained from cyclic ketones. Herein, we report a concise method for the construction of α-methylene-γ-lactams and α-methylene-γ-spirolactams (Scheme 1).

RESULTS AND DISCUSSION

In our initial investigations, the reactivity of *N*-acylhydrazones generated *in situ* was first examined (Table 1). Benzaldehyde (**1a**, 1 equiv) and benzoylhydrazine (**2a**, 1 equiv) were stirred at room temperature in ethanol for 3 h to form the corresponding *N*-benzoylhydrazone (**3a**) first, and then 2-(bromomethyl)acrylic ester (**4**, 1 equiv) and tin powder (1 equiv) were added. After the mixture had been stirred for an additional 8 h at room temperature, there was no desired product α-methylene-γ-lactam (**5a**) formed. Only *N*-benzoylhydrazone (**3a**) was recovered in 81% yield (Table 1, entry 1). Considering the lower reactivity of metal tin, the reaction was conducted again under reflux. To our delight, the reaction occurred to afford the desired product **5a** in 20% yield (Table 1, entry 2). To improve the yield, the reaction conditions were optimized (Table 1). The molar ratio of the substrates was examined first and found to influence the product yields greatly (Table 1, entries 2−10). In particular, a slight excess of tin was beneficial to the reaction. After careful optimization, 1 equiv of

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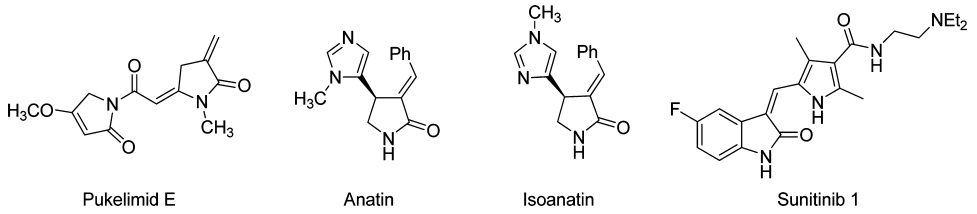


Figure 1. Natural products and biologically active molecules with an α-methylene-γ-lactam moiety.

Scheme 1. Tin Powder-Promoted One-Pot Reactions for the Construction of α-Methylene-γ-lactams and α-Methylene-γ-spirolactams

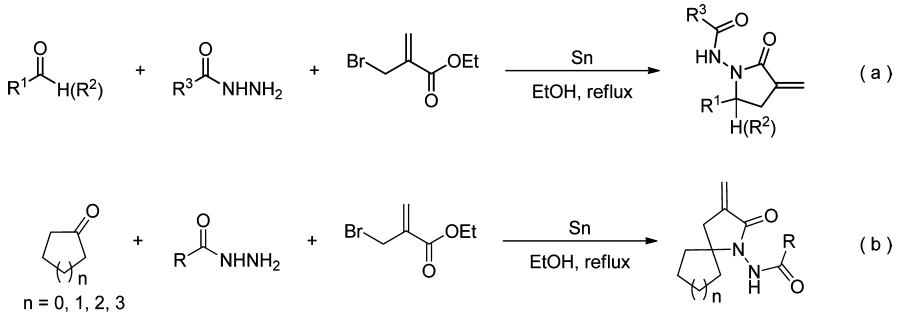
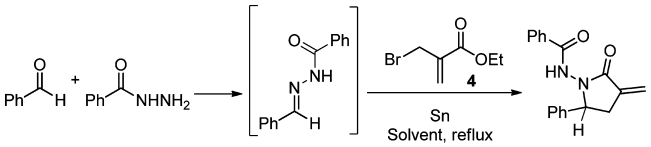


Table 1. Optimization of Reaction Conditions[a]



1a **2a** **3a** **5a**

entry	**1a**:**2a**:**4**:Sn mole ratio	solvent	time (h)	yield (%)
1	1:1:1:1	EtOH	11	0[b]
2	1:1:1:1	EtOH	6	20
3	1:1:1:1.5	EtOH	6	41
4	1:1:1:2	EtOH	6	47
5	1:1.2:1.5:1.5	EtOH	7	54
6	1:1.2:1.5:2	EtOH	6	56
7	1:1.2:2:2	EtOH	6	55
8	1:1.2:2:2.5	EtOH	7	62
9	1:1.2:3:2.5	EtOH	6	63
10	1:1.2:3:3.5	EtOH	6	73
11	1:1.2:3:3.5	MeOH	7	67
12	1:1.2:3:3.5	1,4-Dioxane	9	43
13	1:1.2:3:3.5	ethyl acetate	9	40
14	1:1.2:3:3.5	$CHCl_3$	8	52
15	1:1.2:3:3.5	CH_2Cl_2	7	48
16	1:1.2:3:3.5	toluene	8	55
17	1:1.2:3:3.5	THF	10	trace

[a]The reaction was conducted under reflux. [b]The reaction was conducted at room temperature, and *N*-benzoylhydrazone (**3a**) was obtained in 81% yield.

benzaldehyde, 1.2 equiv of benzoylhydrazine, 3.0 equiv of 2-(bromomethyl)acrylic ester, and 3.5 equiv of tin were determined to give the best molar ratio with an increase in product yield to 73% (Table 1, entry 10). Next, effects of solvent on the reaction were screened (Table 1, entries 10−17). Protic solvents such as ethanol and methanol were found to be the suitable solvents. The reactions in aprotic solvent such as 1,4-dioxane, ethyl acetate, chloroform, dichloromethane, and toluene gave the products in low yields; in particular, product **5a** could not be obtained in THF, which was usually the best solvent in other reactions that include metal. This indicated the different behavior of tin with other metals in organic reactions.

Under the optimized reaction conditions, the generality of substrates was checked next. Different aldehydes or ketones were reacted with benzoylhydrazine (Table 2). As shown in Table 2, most of the aromatic and aliphatic aldehydes would give the α-methylene-γ-lactams in good yields. However, the substituents on the phenyl ring of aromatic aldehydes had some influence on the yields. The aldehydes bearing an electron-withdrawing group on their phenyl rings usually gave the corresponding products in yields higher than that with electron-donating groups (Table 2, **5a**−**c** vs **5g**, **5h**, and **5j**). The reason was that the electron-withdrawing groups on the phenyl rings of aromatic aldehydes could increase the eletrophilicity of hydrazones (**3**) by an inductive effect. The position of substituents on the phenyl ring also affected the results. For instance, *o*-chlorobenzadehyde gave yields lower than that of the *p*-chlorobenzaldehyde or *m*-chlorobenzaldehyde because of steric hindrance (Table 2, **5e**−**g**). The aromatic aldehydes bearing amino, nitro, and hydroxyl groups on the phenyl ring could not afford the products (Table 2, **5d**, **5i**, and **5l**). Some less sterically hindered aliphalic ketones such as acetone or butan-2-one could produce the products in good yields (Table 2, **5r** and **5s**), but aromatic ketones or sterically hindered aliphatic ketones did not afford the products (Table 2, **5t**−**v**).

In the investigations described above, *N*-acylhydrazones were generated in situ first and then reacted with 2-(bromomethyl)-acrylic ester and metal tin to produce the products in a cascade process. After the investigations mentioned above, it was clear that *N*-acylhydrazones were active enough to react with 2-(bromomethyl)acrylic ester and metal tin to give the desired products. Following these results, we just wondered if the one-pot reactions could also give the same results without preformation of *N*-acylhydrazones. Thus, benzaldehyde **1a**, benzoylhydrazine **2a**, 2-(bromomethyl)acrylic ester **4**, and tin powder were put into a flask simultaneously and then stirred and refluxed in ethanol. To our delight, the reaction occurred, and product **5a** was obtained in 76% yield after 10 h (Scheme

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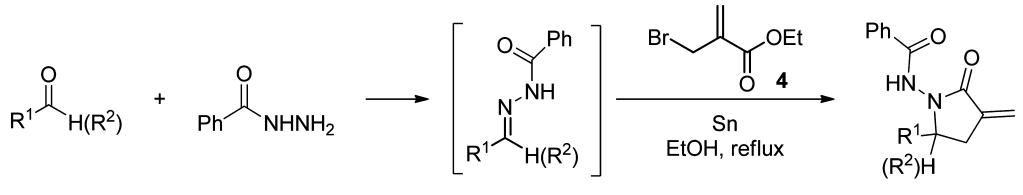
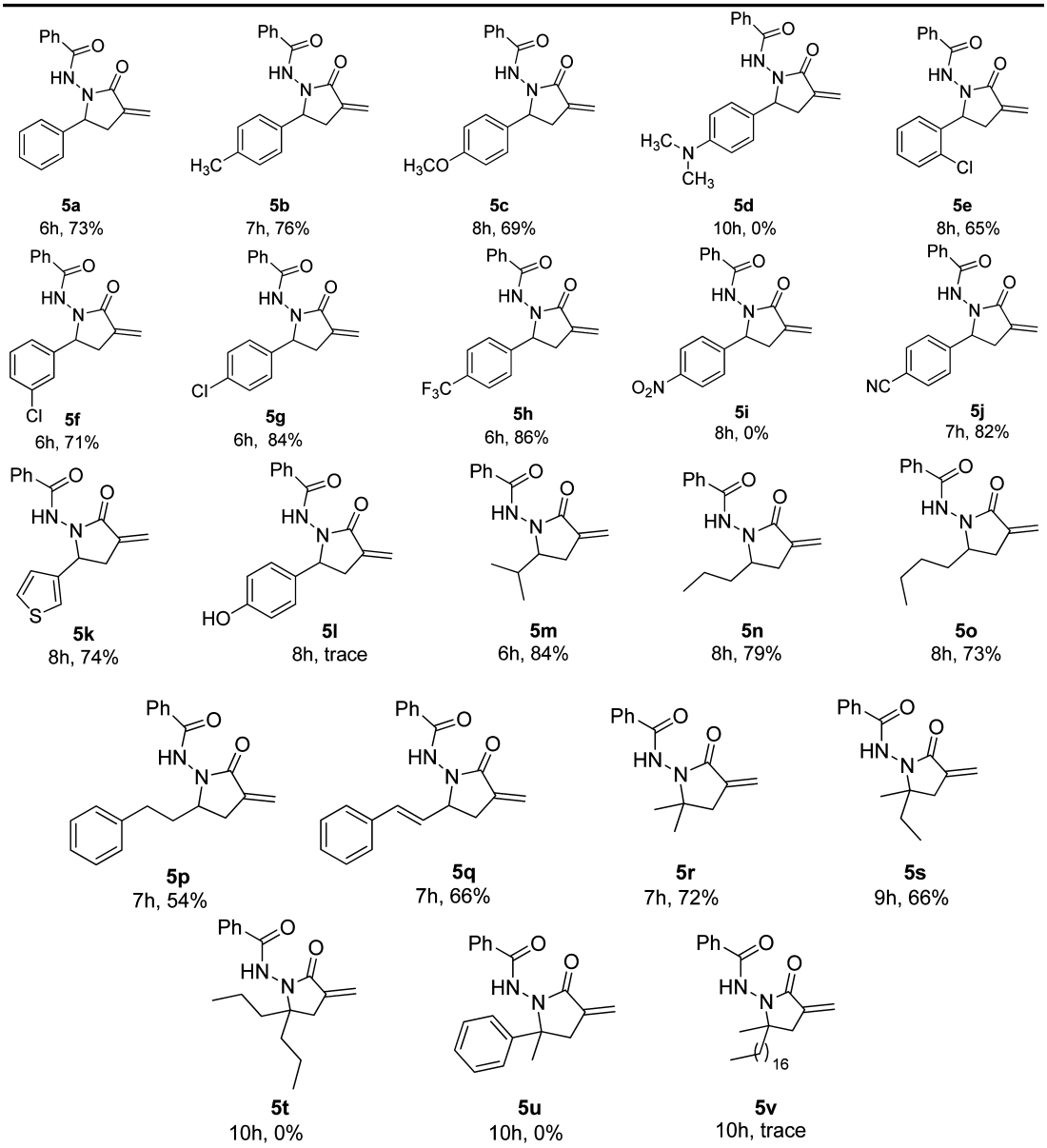
Table 2. Reaction of Different Aldehydes or Ketones for the Synthesis of α-Methylene-γ-lactam[a]



1 2a 3 5



[a]Aldehydes **1a–q** (0.5 mmol) and benzoyl hydrazine **2a** (0.6 mmol) or ketones **1r–v** (0.5 mmol) and benzoyl hydrazine **2a** (0.75 mmol) were refluxed in EtOH to generate hydrazone **3** monitored by analytical thin layer chromatography, and then tin powder (1.75 mmol) and ethyl 2-(bromomethyl)acrylate **4** (1.5 mmol) were added under reflux. Isolated yields.

2). This result was almost the same as the result of the cascade process described above. Therefore, the one-pot process was checked again with different aldehydes and acylhydrazines. The results are summarized in Table 3.

It was shown that both aromatic and aliphatic aldehydes could react with different aromatic acylhydrazines to afford the corresponding α-methylene-γ-lactams in good to excellent yields. The electron-withdrawing groups on both of the phenyl ring of aromatic aldehydes and acylhydrazines could increase the yields of α-methylene-γ-lactams (Table 3, **5ad–f**). However, when the groups on aromatic rings of both aldehydes and acylhydrazines were electron-donating groups, the yield of the products would be lower (Table 3, **5ag**). An acyclic aliphatic ketone such as acetone could also be used in the reaction to give γ,γ-disubstituted α-methylene-γ-lactams (Table 3, **5an** and **5ao**). Finally, it was found that the products could

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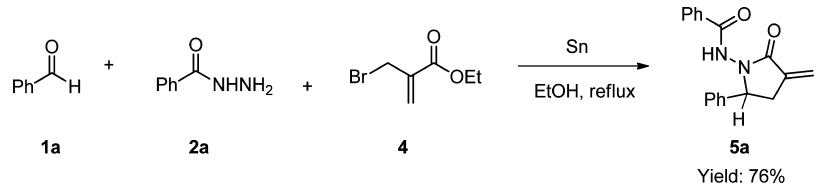
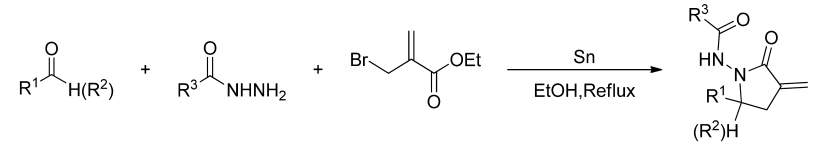
Scheme 2. One-Pot Reaction among 1a, 2a, 4, and Tin Powder



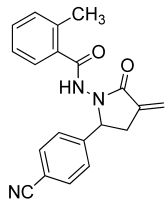
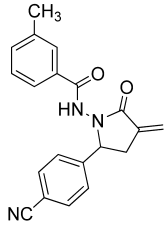
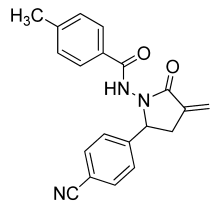
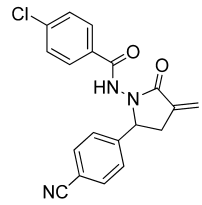
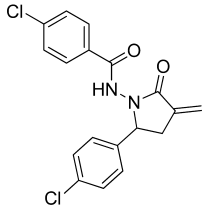
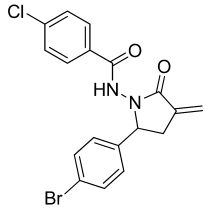
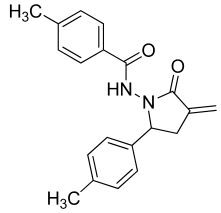
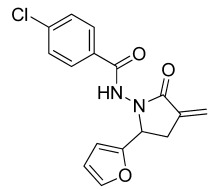
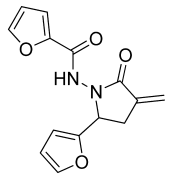
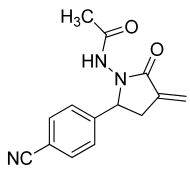
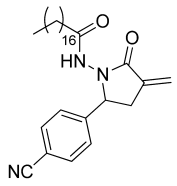
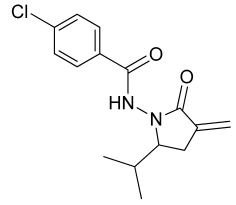
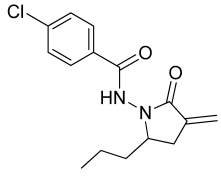
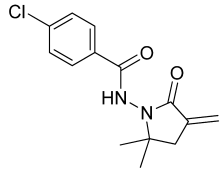
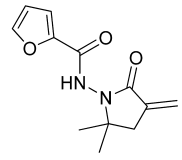
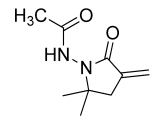
1a 2a 4 5a

Yield: 76%

Table 3. One-Pot Reaction of Different Carbonyl Compounds with Hydrazides for the Synthesis of α-Methylene-γ-lactams[a]



1 2 4 5

			
5aa	**5ab**	**5ac**	**5ad**
10h, 66%	13h, 65%	7h, 70%	9h, 80%
			
5ae	**5af**	**5ag**	**5ah**
11h, 83%	11h, 79%	9h, 42%	10h, 71%
			
5ai	**5aj**	**5ak**	**5al**
13h, 88%	10h, 0%	10h, 0%	12h, 90%
			
5am	**5an**	**5ao**	**5ap**
12h, 73%	10h, 80%	11h, 81%	12h, 0%

[a]Aldehydes **1** (0.5 mmol) and acylhydrazines **2aa−m** (0.6 mmol) or ketones **1** (0.5 mmol) and acylhydrazine **2an−p** (0.75 mmol), tin powder (1.75 mmol), and ethyl 2-(bromomethyl)acrylate **4** (1.5 mmol) were refluxed in EtOH (5 mL) under one-pot conditions. Isolated yields.

not be obtained if acyclic aliphatic acylhydrazines were used (Table 3, **5aj**, **5ak**, and **5ap**).

In the investigation described above, we noticed that some acyclic aliphatic ketones could be used as substrates to produce the corresponding γ,γ-disubstituted α-methylene-γ-lactams. We just wondered if the cyclic ketones could be used in the same reactions to produce the α-methylene-γ-spirolactams. Thus, cyclopentanone was tested as a substrate in the reaction described above. To our delight, the reaction occurred to give α-methylene-γ-spirolactam **7b** in 90% yield (Table 4, **7b**). Afterward, different cyclic ketones were examined, and the results are summarized in Table 4. It was shown that cyclic

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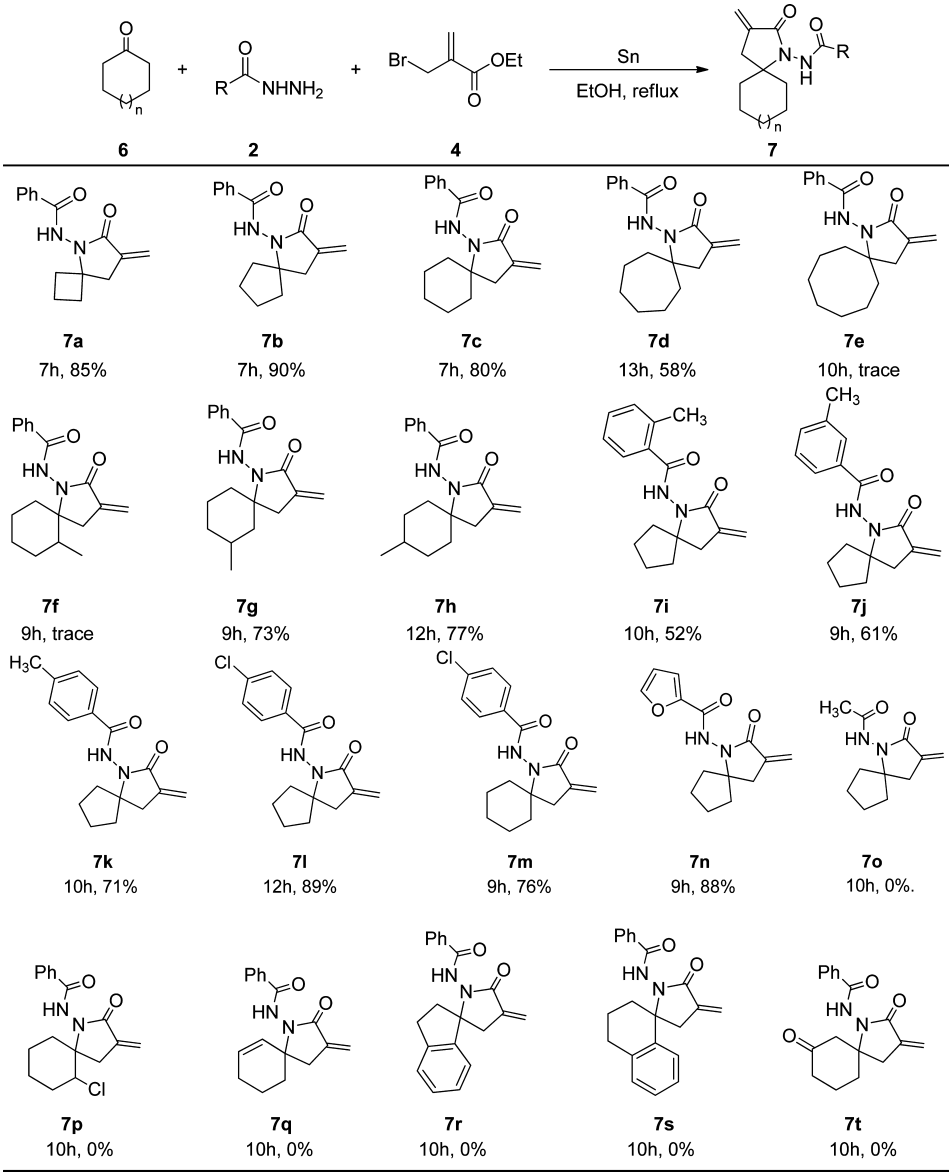
Table 4. One-Pot Reactions of Different Cyclic Ketones and Hydrazides for the Synthesis of α-Methylene-γ-spirolactams[a]



[a]Cyclic ketones **6** (0.5 mmol) and hydrazines **2** (0.75 mmol), tin powder (1.75 mmol), and ethyl 2-(bromomethyl)acrylate **4** (1.5 mmol) were refluxed in EtOH (6 mL) under one-pot conditions. Isolated yields.

ketones from small ring cyclobutanone to middle ring cycloheptanone could react with benzoyl hydrazine and 2-(bromomethyl)acrylic ester in the presence of tin powder to afford the corresponding α-methylene-γ-spirolactams **7** in high yields (Table 4, **7a–d**). With the growing size of the cyclic ketone ring, the yield of the products decreased. For instance, when cycloheptanone was used, the yield of product **7d** was decreased to 58% (Table 4, **7d**). If cyclooctanone was used, there was no product formed (Table 4, **7e**). We also found the position of substituents on cyclohexanone greatly influenced the reaction. For example, 2-methylcyclohexanone did not produce the product, but 3-methylcyclohexanone and 4-methylcyclohexanone afforded the products in good yields (Table 4, **7f–h**). Furthermore, different kinds of hydrazides also affected the reactions. All of the aromatic hydrazides, including heteroaromatic hydrazides such as furan-2-carbohydrazide, could be used to give the products in good to excellent yields. However, aliphatic hydrazides such as acetylhydrazide could not produce the product (Table 4, **7o**). In addition, 1,3-cyclohexanedione or unsaturated cyclic ketones such as 2-cyclohexenone, 1-indanone, and 1-tetralone could not produce the α-methylene-γ-spirolactams (Table 4, **7p–t**).

Finally, a possible mechanism was proposed on the basis of the literature[11] and experimental results (Scheme 3). First, *N*-acylhydrazones **3** were formed from aldehydes **1** and hydrazides **2** because product **5a** could also be obtained in 70% yield if *N*′-benzylidenebenzohydrazide **3a** was used as a substrate (Scheme 4). Intermediate **8**, which is in equilibrium with intermediate **9**,[11a] was generated from 2-(bromomethyl)acrylic ester **4** and tin metal. Afterward, the intermediate **8** would react with *N*-acylhydrazones **3** to give intermediate **10**, which was then cyclized to afford product **5**. *N*-Acylhydrazones **3** were more reactive than aldehydes **1** because the allylic alcohol products from aldehydes **1** and intermidate **8** were not obtained in the reaction. Furthermore, when an equal amount of benzaldehyde **1a** and *N*′-benzylidenebenzohydrazide **3a** were mixed together

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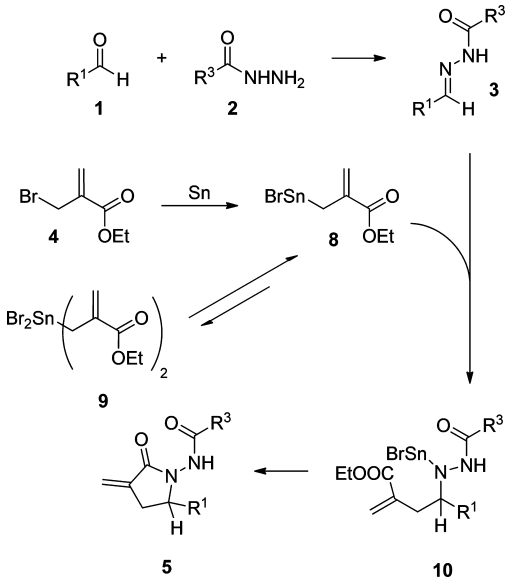
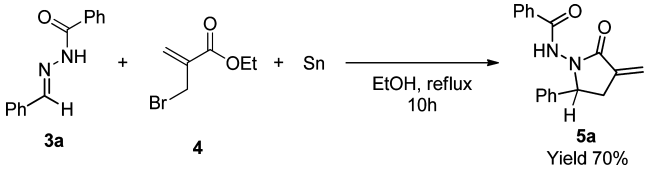
Scheme 3. Proposed Mechanism



Scheme 4. Reaction Using Hydrazone as a Substrate



and then reacted with 2-(bromomethyl)acrylic ester **4** in the presence of tin powder under standard conditions, only product **5a** from *N*′-benzylidenebenzohydrazide **3a** was obtained in 59% yield, and no product from benzaldehyde **1a** was detected (Scheme 5).

In conclusion, a novel method for the construction of α-methylene-γ-lactams is developed from multicomponent one-pot reactions of aldehydes or ketones, hydrazides, and ethyl 2-(bromomethyl)acrylate promoted by tin powder without using any transition metal catalysts. In particular, α-methylene-γ-spirolactams can also be obtained from cyclic ketones in good yields. This strategy is highly efficient with easy operation.

EXPERIMENTAL SECTION

General Methods. Flash chromatography was performed using silica gel 60 (230−400 mesh). Analytical thin layer chromatography (TLC) was conducted using silica gel GF254. TLC plates were analyzed by an exposure to ultraviolet (UV) light and/or submersion in a phosphomolybdic acid solution or in I_2. IR spectral absorption frequencies are reported in reciprocal centimeters. High-resolution mass spectra were recorded on a transform ion cyclotron resonance mass spectrometer. ^{1}H NMR spectra were measured on 600 MHz (**5aa−f**, **5ah−m**, **5ao**, **7g**, **7i**, **7j**, **7l**, and **7m**) and 400 MHz (**5a−s**, **5ag**, **5an**, **7a−d**, **7h**, **7k**, and **7n**) spectrometers. Chemical shifts were recorded as follows: chemical shift in parts per million from internal tetramethylsilane on the δ scale, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), coupling constant (hertz), integration, and assignment. ^{13}C NMR spectra were measured on 150 MHz (**5n**, **5aa−f**, **5ai−o**, **7a**, **7g**, **7i**, **7j**, and **7l−n**) and 100 MHz (**5a−m**, **5o−s**, **5ag**, **5ah**, **7b−d**, **7h**, and **7k**) spectrometers. Chemical shifts were recorded in parts per million from the solvent resonance employed as the internal standard (deuterochloroform at 77.0 ppm). The solvents were distilled by standard methods. Reagents were obtained from commercial suppliers and used without further purification unless otherwise noted.

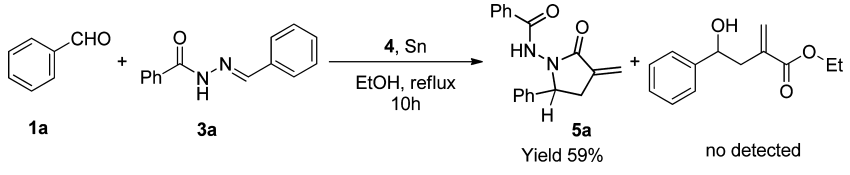
General Experimental Procedures for the Synthesis of Compounds 5 and 7. *Cascade Reactions of Carbonyl Compounds for the Synthesis of α-Methylene-γ-lactams **5a−v** Promoted by Tin Powder.* Aldehydes **1** (0.5 mmol, 1 equiv) and benzoyl hydrazine **2** (0.6 mmol, 1.2 equiv) or ketones **1** (0.5 mmol, 1 equiv) and benzoyl hydrazine **2** (0.75 mmol, 1.5 equiv) were put into a dried round-bottom flask (50 mL) fitted with a magnetic bar. Ethanol (3 mL) was then added. The mixture was stirred under reflux, and the reaction process was monitored by TLC. After formation of benzoyl hydrazone, tin powder (1.75 mmol, 3.5 equiv) and ethyl 2-(bromomethyl)acrylate **4** (1.5 mmol, 3 equiv) in 2 mL of ethanol were added to the flask. The resulting mixture was stirred under reflux for 6−13 h. The reaction mixture was cooled to room temperature, and ethanol was removed under vacuum. The saturated NH_4Cl solution (10 mL) was poured into the mixture and stirred for 10 min. The mixture was extracted with EtOAc (3 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. Purification of the residue by silica gel column chromatography using hexane and EtOAc (1:1) as the eluent furnished the pure products.

*One-Pot Synthesis of α-Methylene-γ-lactams (**5aa−m**) from Aldehydes Promoted by Tin Powder.* Aldehydes **1** (0.5 mmol, 1 equiv), acylhydrazines **2** (0.6 mmol, 1.2 equiv), tin powder (1.75 mmol, 3.5 equiv), and ethyl 2-(bromomethyl)acrylate **4** (1.5 mmol, 3 equiv) were placed in a dried round-bottom flask (50 mL) fitted with a magnetic bar. Ethanol (5 mL) was then added. The mixture was stirred under reflux for 6−13 h. The reaction mixture was cooled to room temperature, and ethanol was removed under vacuum. The saturated NH_4Cl solution (10 mL) was poured into the mixture and stirred for 10 min. The mixture was extracted with EtOAc (3 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. Purification of the residue by silica gel column chromatography using hexane and EtOAc (1:1) as the eluent furnished the pure products.

*One-Pot Synthesis of γ,γ-Disubstituted α-Methylene-γ-lactams (**5ao** and **5ap**) and α-Methylene-γ-spirolactams (**7a−t**) from Ketones Promoted by Tin Powder.* Ketones **1** (0.5 mmol, 1 equiv), acylhydrazines **2** (0.75 mmol, 1.5 equiv), tin powder (1.75 mmol, 3.5 equiv), and ethyl 2-(bromomethyl)acrylate **4** (1.5 mmol, 3 equiv) were placed in a dried round-bottom flask (50 mL) fitted with a magnetic bar. Ethanol (6 mL) was then added. The mixture was stirred under reflux for 6−13 h. The reaction mixture was cooled to room temperature, and ethanol was removed under vacuum. The saturated NH_4Cl solution (10 mL) was poured into the mixture and stirred for 10 min. The mixture was extracted with EtOAc (3 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. Purification of the residue by silica gel column chromatography using hexane and EtOAc (1:1) as the eluent furnished the pure products.

*N-(3-Methylene-2-oxo-5-phenylpyrrolidin-1-yl)benzamide **5a**.* White solid (115 mg, 73% yield): mp 118−120 °C; IR (KBr) ν 3188, 2992, 1713, 1677, 1525, 1402, 1272 cm^{-1}; ^{1}H NMR (400 MHz,

Scheme 5. Competitive Reactions between 1a and 3a



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$CDCl_3$) δ 10.08 (s, 1H), 7.60−7.58 (m, 2H), 7.36−7.24 (m, 6H), 7.18−7.15 (m, 2H), 6.20 (s, 1H), 5.53 (s, 1H), 5.22 (dd, J = 8.4, 4.8 Hz, 1H), 3.41 (dd, J = 17.2, 8.4 Hz, 1H), 2.76 (dt, J = 17.2, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 165.6, 140.0, 136.4, 132.0, 131.1, 129.1, 128.5, 128.4, 127.5, 126.8, 118.6, 60.5, 34.3; HRMS (ESI) calcd for $C_{18}H_{16}N_2O_2$ $[M + H]^+$ 293.1285, found 293.1294.

N-[3-Methylene-2-oxo-5-(p-tolyl)pyrrolidin-1-yl]benzamide **5b**. White solid (120 mg, 76% yield): mp 240−241 °C dec; IR (KBr) ν 3238, 2970, 2912, 1705, 1654, 1510, 1394, 1271 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 7.52 (d, J = 8.0 Hz, 2H), 7.23 (t, J = 8.0 Hz, 1H), 7.10−7.06 (m, 6H), 6.10 (s, 1H), 5.44 (s, 1H), 5.11−5.09 (m, 1H), 3.31 (dd, J = 17.2, 8.0 Hz, 1H), 2.66 (d, J = 17.2 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 165.6, 138.2, 136.9, 136.6, 132.0, 131.1, 129.7, 128.3, 127.5, 126.8, 118.4, 60.3, 34.3, 21.3; HRMS (ESI) calcd for $C_{19}H_{18}N_2O_2$ $[M + H]^+$ 307.1441, found 307.1438.

N-[5-(4-Methoxyphenyl)-3-methylene-2-oxopyrrolidin-1-yl]benzamide **5c**. White solid (109 mg, 69% yield): mp 92−93 °C; IR (KBr) ν 3230, 3006, 2839, 1712, 1668, 1610, 1509, 1401, 1235, 1183 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.34 (t, J = 8.0 Hz, 1H), 7.21−7.16 (m, 4H), 6.86 (d, J = 8.4 Hz, 2H), 6.18 (s, 1H), 5.52 (s, 1H), 5.16 (dd, J = 8.4, 4.8 Hz, 1H), 3.78 (s, 3H), 3.37 (dd, J = 17.2, 8.4 Hz, 1H), 2.77−2.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 165.7, 159.8, 136.6, 132.1, 131.8, 131.2, 128.4, 128.2, 127.5, 118.4, 114.4, 60.0, 55.4, 34.3; HRMS (ESI) calcd for $C_{19}H_{18}N_2O_3$ $[M + H]^+$ 323.1390, found 323.1387.

N-[5-(2-Chlorophenyl)-3-methylene-2-oxopyrrolidin-1-yl]benzamide **5e**. Colorless syrup (106 mg, 65% yield): IR (neat) ν 3238, 2999, 1705, 1668, 1516, 1278 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.56 (s, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.43−7.20 (m, 5H), 7.17−7.14 (m, 2H), 6.24 (s, 1H), 5.65 (d, J = 4.4 Hz, 1H), 5.55 (s, 1H), 3.57 (dd, J = 16.8, 8.8 Hz, 1H), 2.70 (d, J = 16.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 165.6, 137.6, 136.1, 133.3, 132.1, 130.9, 130.3, 129.3, 128.4, 127.6, 127.5, 119.0, 58.1, 32.7; HRMS (ESI) calcd for $C_{18}H_{15}ClN_2O_2$ $[M + H]^+$ 327.0895, found 327.0900.

N-[5-(3-Chlorophenyl)-3-methylene-2-oxopyrrolidin-1-yl]benzamide **5f**. White solid (162 mg, 71% yield): mp 153−155 °C; IR (KBr) ν 3166, 2999, 1712, 1683, 1532, 1401, 1278 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (s, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.34−7.24 (m, 4H), 7.17−7.13 (m, 3H), 6.29 (s, 1H), 5.56 (s, 1H), 5.23 (dd, J = 8.4, 4.4 Hz, 1H), 3.41 (dd, J = 17.2, 8.4 Hz, 1H), 2.75−2.69 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 165.5, 142.2, 135.7, 135.0, 132.1, 130.7, 130.3, 128.7, 128.4, 127.5, 126.7, 125.2, 119.3, 59.9, 34.1; HRMS (ESI) calcd for $C_{18}H_{15}ClN_2O_2$ $[M + H]^+$ 327.0895, found 327.0899.

N-[5-(4-Chlorophenyl)-3-methylene-2-oxopyrrolidin-1-yl]benzamide **5g**. Colorless syrup (131 mg, 84% yield): IR (neat) ν 3238, 3064, 3020, 2984, 1712, 1668, 1532, 1480, 1401, 1271, 1083 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 7.57 (d, J = 8.0 Hz, 2H), 7.35−7.30 (m, 3H), 7.20−7.15 (m, 4H), 6.20 (s, 1H), 5.56 (s, 1H), 5.21 (dd, J = 8.0, 4.8 Hz, 1H), 3.41 (dd, J = 17.2, 8.4 Hz, 1H), 2.73−2.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 165.6, 138.5, 136.1, 134.3, 132.2, 130.8, 129.3, 128.4, 128.3, 127.5, 118.9, 59.9, 34.2; HRMS (ESI) calcd for $C_{18}H_{15}ClN_2O_2$ $[M + H]^+$ 327.0895, found 327.0904.

N-{3-Methylene-2-oxo-5-[4-(trifluoromethyl)phenyl]pyrrolidin-1-yl}benzamide **5h**. Colorless syrup (160 mg, 86% yiled): IR (neat) ν 3252, 2999, 1720, 1654, 1532, 1329 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.33 (s, 1H), 7.62−7.56 (m, 4H), 7.41−7.31 (m, 3H), 7.17 (t, J = 7.6 Hz, 2H), 6.21 (s, 1H), 5.58 (s, 1H), 5.32 (dd, J = 8.0, 4.8 Hz, 1H), 3.46 (dd, J = 17.6, 8.0 Hz, 1H), 2.72 (dd, J = 17.6, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 165.7, 144.1, 135.8, 132.2, 130.8 (q, J = 33.0 Hz), 130.7, 128.4, 127.5, 127.2, 126.1 (q, $J_{C,F}$ = 3.6 Hz), 124.1 (q, $J_{C,F}$ = 270.6 Hz), 119.2, 60.1, 34.1; HRMS (ESI) calcd for $C_{19}H_{15}F_3N_2O_2$ $[M + H]^+$ 361.1158, found 361.1162.

N-[5-(4-Cyanophenyl)-3-methylene-2-oxopyrrolidin-1-yl]benzamide **5j**. White solid (148 mg, 82% yield): mp 181−183 °C; IR (KBr) ν 3260, 3057, 2233, 1705, 1668, 1532, 1271 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 7.58 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.33−7.26 (m, 3H), 7.12−7.08 (m, 2H), 6.15 (s, 1H), 5.53 (s, 1H), 5.25 (t, J = 4.0 Hz, 1H), 3.39 (dd, J = 17.2, 8.8 Hz, 1H), 2.63 (d, J = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 165.6, 145.3, 135.5, 132.9, 132.4, 130.6, 128.5, 127.6, 127.5, 119.4, 118.5, 112.5, 60.1, 33.9; HRMS (ESI) calcd for $C_{19}H_{15}N_3O_2$ $[M + H]^+$ 318.1237, found 318.1233.

N-[3-Methylene-2-oxo-5-(thiophen-3-yl)pyrrolidin-1-yl]benzamide **5k**. White solid (110 mg, 74% yield): mp 141−143 °C; IR (KBr) ν 3281, 3100, 2920, 1720, 1674, 1510, 1408, 1230, 1286 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.35−7.30 (m, 2H), 7.25 (s, 1H), 7.20 (t, J = 7.4 Hz, 2H), 6.98 (d, J = 4.0 Hz, 1H), 6.17 (s, 1H), 5.52 (s, 1H), 5.33 (dd, J = 8.4, 4.4 Hz, 1H), 3.37 (dd, J = 17.2, 8.4 Hz, 1H), 2.78 (dd, J = 17.2, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 165.6, 140.9, 136.2, 132.1, 131.0, 128.4, 127.5, 127.1, 125.5, 123.1, 118.7, 56.1, 33.5; HRMS (ESI) calcd for $C_{16}H_{14}N_2O_2S$ $[M + H]^+$ 299.0849, found 299.0845.

N-(5-Isopropyl-3-methylene-2-oxopyrrolidin-1-yl)benzamide **5m**. White solid (108 mg, 84% yield): mp 136−139 °C; IR (KBr) ν 3216, 2596, 1720, 1654, 1516, 1416, 1278 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.77 (s, 1H), 7.73 (d, J = 8.0 Hz, 2H), 7.36−7.33 (m, 1H), 7.22−7.19 (m, 2H), 6.05 (s, 1H), 5.43 (s, 1H), 4.10 (t, J = 4.0 Hz, 1H), 2.87 (dd, J = 17.2, 8.4 Hz, 1H), 2.58 (dd, J = 17.2, 2.0 Hz, 1H), 2.19−2.12 (m, 1H), 0.90 (d, J = 6.8 Hz, 3H), 0.77 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 165.6, 137.4, 132.0, 131.0, 128.4, 127.6, 117.6, 60.8. 28.7, 25.0, 18.1, 14.5; HRMS (ESI) calcd for $C_{15}H_{18}N_2O_2$ $[M + H]^+$ 259.1441, found 259.1441.

N-(3-Methylene-2-oxo-5-propylpyrrolidin-1-yl)benzamide **5n**. Colorless syrup (102 mg, 79% yield): IR (neat) ν 3245, 2956, 2869, 2355, 1712, 1668, 1524, 1422, 1278 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.38 (d, J = 6.8 Hz, 1H), 7.76 (d, J = 7.6 Hz, 2H), 7.37 (dd, J = 10.8, 4.0 Hz, 1H), 7.28−7.21 (m, 2H), 6.08 (s, 1H), 5.44 (s, 1H), 4.06 (s, 1H), 3.05 (dd, J = 17.2, 6.4 Hz, 1H), 2.50 (dd, J = 17.2, 2.0 Hz, 1H), 1.76 (dd, J = 15.6, 8.0 Hz, 1H), 1.44−1.25 (m, 3H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.6, 165.7, 137.0, 132.1, 131.1, 128.5, 127.6, 117.9, 56.6, 35.4, 30.3, 17.7, 14.2; HRMS (ESI) calcd for $C_{15}H_{18}N_2O_2$ $[M + Na]^+$ 281.1266, found 281.1273.

N-(5-Butyl-3-methylene-2-oxopyrrolidin-1-yl)benzamide **5o**. Colorless syrup (97 mg, 73% yield): IR (neat) ν 3224, 2927, 2854, 1726, 1647, 1516, 1278 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 2H), 7.37 (t, J = 7.6 Hz, 1H), 7.23 (t, J = 8.0 Hz, 2H), 6.08 (s, 1H), 5.43 (s, 1H), 4.05 (t, J = 4.0 Hz, 1H), 3.04 (dd, J = 16.8, 8.0 Hz, 1H), 2.50 (d, J = 16.8 Hz, 1H), 1.81−1.76 (m, 1H), 1.39−1.23 (m, 5H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 165.6, 137.1, 132.0, 131.1, 128.4, 127.6, 117.9, 56.7, 32.9, 30.3, 26.5, 22.8, 14.1; HRMS (ESI) calcd for $C_{16}H_{20}N_2O_2$ $[M + H]^+$ 273.1598, found 273.1595.

N-(3-Methylene-2-oxo-5-phenethylpyrrolidin-1-yl)benzamide **5p**. White solid (88 mg, 54% yield): mp 139−141 °C; IR (KBR) ν 3260, 3035, 2847, 1705, 1668, 1516, 1437, 1286 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (s, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.30−7.28 (m, 1H), 7.19−7.10 (m, 7H), 5.95 (s, 1H), 5.32 (s, 1H), 4.07 (d, J = 3.6 Hz, 1H), 3.00 (t, J = 8.0 Hz, 1H), 2.58−2.47 (m, 3H), 2.09−1.97 (m, 1H), 1.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 165.6, 141.2, 136.7, 132.0, 130.9, 128.6, 128.4, 127.6, 126.2, 118.2, 56.4, 35.0, 30.6, 30.1; HRMS (ESI) calcd for $C_{20}H_{20}N_2O_2$ $[M + H]^+$ 321.1598, found 321.1594.

(E)-N-(3-Methylene-2-oxo-5-styrylpyrrolidin-1-yl)benzamide **5q**. Colorless syrup (127 mg, 66% yield): IR (neat) ν 3252, 2978, 1712, 1662, 1510, 1401, 1278 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.68 (d, J = 8.0 Hz, 2H), 7.37−7.34 (m, 3H), 7.31−7.19 (m, 5H), 6.58 (d, J = 15.6 Hz, 1H), 6.14 (s, 1H), 6.08 (q, J = 8.0 Hz, 1H), 5.48 (s, 1H), 4.75−4.69 (m, 1H), 3.22 (dd, J = 17.2, 8.0 Hz, 1H), 2.67 (dd, J = 17.2, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 165.8, 136.3, 136.1, 134.6, 132.1, 131.2, 128.7, 128.5, 128.3, 127.6, 127.5, 126.8, 118.4, 59.5, 31.8; HRMS (ESI) calcd for $C_{20}H_{18}N_2O_2$ $[M + H]^+$ 319.1441, found 319.1437.

N-(2,2-Dimethyl-4-methylene-5-oxopyrrolidin-1-yl)benzamide **5r**. White solid (100 mg, 72% yield): mp 242−243 °C; IR (KBr) ν 3166, 2970, 1705, 1676, 1532, 1401, 1278 cm^{-1}; ^{1}H NMR (400 MHz,

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$CDCl_3$) δ 10.06 (s, 1H), 7.77 (d, J = 7.2 Hz, 2H), 7.34−7.32 (m, 1H), 7.22−7.20 (m, 2H), 6.08 (s, 1H), 5.43 (s, 1H), 2.73 (s, 2H), 1.28 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 166.5, 136.9, 132.0, 128.4, 127.7, 118.2, 109.9, 60.9, 40.0, 26.5; HRMS (ESI) calcd for $C_{14}H_{16}N_2O_2$ $[M + H]^+$ 245.1285, found 245.1288.

N-(2-Ethyl-2-methyl-4-methylene-5-oxopyrrolidin-1-yl)-benzamide ***5s***. White solid (102 mg, 66% yield): mp >240 °C; IR (KBr) ν 3158, 2970, 1705, 1683, 1538, 1408, 1278 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.37 (t, J = 6.8 Hz, 1H), 7.26−7.21 (m, 2H), 6.07 (s, 1H), 5.41 (s, 1H), 2.78 (d, J = 16.8 Hz, 1H), 2.62 (d, J = 16.8 Hz, 1H), 1.66−1.60 (m, 2H), 1.27 (s, 3H), 0.83 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 166.6, 137.2, 132.0, 131.1, 128.4, 127.7, 117.8, 63.8, 36.7, 31.8, 24.6, 8.4; HRMS (ESI) calcd for $C_{15}H_{18}N_2O_2$ $[M + H]^+$ 259.1441, found 259.1438.

N-[5-(4-Cyanophenyl)-3-methylene-2-oxopyrrolidin-1-yl]-2-methylbenzamide ***5aa***. White solid (108 mg, 66% yield): mp 207−209 °C; IR (KBr) ν 3166, 2970, 2225, 1740, 1676, 1524, 1408, 1271 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.67 (d, J = 6.0 Hz, 2H), 7.42 (d, J = 6.0 Hz, 2H), 7.30−7.27 (m, 1H), 7.20 (d, J = 7.8 Hz, 1H), 7.15 (d, J = 7.2 Hz, 1H), 7.09 (t, J = 7.2 Hz, 1H), 6.14 (d, J = 1.8 Hz, 1H), 5.51 (s, 1H), 5.28−5.26 (m, 1H), 3.39 (dd, J = 16.8, 7.8 Hz, 1H), 2.72−2.64 (m, 1H), 2.25 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.3, 167.1, 145.3, 137.3, 135.0, 133.0, 132.3, 131.4, 131.1, 127.8, 127.4, 125.9, 119.6, 118.4, 112.7, 60.1, 33.8, 19.9; HRMS (ESI) calcd for $C_{20}H_{17}N_3O_2$ $[M + Na]^+$ 354.1213, found 354.1207.

N-[5-(4-Cyanophenyl)-3-methylene-2-oxopyrrolidin-1-yl]-3-methylbenzamide ***5ab***. Colorless syrup (107 mg, 65% yield): IR (neat) ν 3252, 2927, 2233, 1704, 1662, 1524, 1401, 1271 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.67−7.63 (m, 2H), 7.41−7.36 (m, 4H), 7.17−7.15 (m, 1H), 7.08−7.06 (m, 1H), 6.24 (d, J = 2.4 Hz, 1H), 5.60 (d, J = 2.4 Hz, 1H), 5.32−5.31 (m, 1H), 3.49−3.45 (m, 1H), 2.72−2.69 (m, 1H), 2.22 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8, 165.7, 145.4, 138.3, 135.5, 133.1, 133.0, 130.4, 128.4, 128.1, 127.6, 124.4, 119.4, 118.5, 112.5, 60.1, 34.0, 21.3; HRMS (ESI) calcd for $C_{20}H_{17}N_3O_2$ $[M + H]^+$ 332.1394, found 332.1390.

N-[5-(4-Cyanophenyl)-3-methylene-2-oxopyrrolidin-1-yl]-4-methylbenzamide ***5ac***. White solid (111 mg, 70% yield): mp 202−203 °C; IR (KBr) ν 3260, 3057, 2978, 2233, 1705, 1683, 1611, 1488, 1408, 1286 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.18 (s, 1H), 7.64 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 7.8 Hz, 2H), 6.21 (s, 1H), 5.58 (s, 1H), 5.32−5.30 (m, 1H), 3.45 (dd, J = 17.4, 8.4 Hz, 1H), 2.68 (d, J = 17.4 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 165.6, 145.4, 142.9, 135.6, 132.9, 129.0, 127.7, 127.6, 127.4, 119.3, 118.5, 112.4, 60.2, 33.9, 21.5; HRMS (ESI) calcd for $C_{20}H_{17}N_3O_2$ $[M + H]^+$ 332.1394, found 332.1390.

4-Chloro-N-[5-(4-cyanophenyl)-3-methylene-2-oxopyrrolidin-1-yl]benzamide ***5ad***. White solid (118 mg, 80% yield): mp 173−174 °C; IR (KBr) ν 3260, 2927, 2225, 1705, 1690, 1480, 1286 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.55 (s, 1H), 7.64 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 6.22 (t, J = 2.4 Hz, 1H), 5.62 (t, J = 2.4 Hz, 1H), 5.26 (dd, J = 8.4, 4.8 Hz, 1H), 3.48−3.44 (m, 1H), 2.71−2.67 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.2, 164.3, 145.1, 138.8, 135.4, 133.0, 128.8, 128.7, 128.5, 127.5, 119.8, 118.5, 112.6, 60.2, 34.0; HRMS (ESI) calcd for $C_{19}H_{14}ClN_3O_2$ $[M + H]^+$ 352.0847, found 352.0852.

4-Chloro-N-[5-(4-chlorophenyl)-3-methylene-2-oxopyrrolidin-1-yl]benzamide ***5ae***. White solid (149 mg, 83% yield): mp 157−159 °C; IR (KBr) ν 3202, 2992, 1976, 1676, 1596, 1488, 1401, 1271, 1288 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.43 (s, 1H), 7.51−7.49 (m, 2H), 7.33−7.31 (m, 2H), 7.18 (d, J = 8.4 Hz, 2H), 7.14−7.13 (m, 2H), 6.21 (t, J = 2.4 Hz, 1H), 5.59 (t, J = 1.8 Hz, 1H), 5.17 (dd, J = 8.4, 4.8 Hz, 1H), 3.45−3.40 (m, 1H), 2.74−2.70 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 164.3, 138.6, 138.2, 136.0, 134.4, 129.3, 128.9, 128.8, 128.6, 128.2, 119.2, 60.0, 34.2; HRMS (ESI) calcd for $C_{18}H_{14}Cl_2N_2O_2$ $[M + H]^+$ 361.0505, found 361.0506.

N-[5-(4-Bromophenyl)-3-methylene-2-oxopyrrolidin-1-yl]-4-chlorobenzamide ***5af***. White solid (156 mg, 79% yield): mp 164−166 °C; IR (KBr) ν 3238, 3064, 2934, 2862, 1712, 1662, 1532, 1386, 1278 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.92 (br, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 7.2 Hz, 2H), 7.18 (d, J = 3.6 Hz, 2H), 7.13 (d, J = 7.8 Hz, 2H), 6.22 (s, 1H), 5.59 (s, 1H), 5.16 (dd, J = 8.4, 4.8 Hz, 1H), 3.42 (dd, J = 17.4, 8.4 Hz, 1H), 2.72 (dd, J = 17.4, 2.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 164.4, 138.7, 135.9, 132.3, 128.9, 128.7, 128.5, 122.6, 119.3, 60.1, 34.2; HRMS (ESI) calcd for $C_{18}H_{14}BrClN_2O_2$ $[M + H]^+$ 405.0000, found 404.9997.

4-Methyl-N-[3-methylene-2-oxo-5-(p-tolyl)pyrrolidin-1-yl]-benzamide ***5ag***. White solid (68 mg, 42% yield): mp 181−183 °C; IR (KBr) ν 3288, 3028, 1705, 1676, 1495, 1394, 1264 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80−9.73 (m, 1H), 7.50 (dd, J = 8.4 Hz, 2H), 7.16−7.11 (m, 4H), 6.98−6.95 (m, 2H), 6.18 (d, J = 2.4 Hz, 1H), 5.52 (s, 1H), 5.17 (dd, J = 8.4, 4.8 Hz, 1H), 3.42−3.35 (m, 1H), 2.76−2.70 (m, 1H), 2.33 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 165.7, 142.5, 138.2, 137.0, 136.6, 129.7, 129.0, 128.4 127.5, 126.8, 118.3, 60.3, 34.3, 21.5, 21.3; HRMS (ESI) calcd for $C_{20}H_{20}N_2O_2$ $[M + Na]^+$ 343.1417, found 343.1415.

4-Chloro-N-[5-(furan-2-yl)-3-methylene-2-oxopyrrolidin-1-yl]-benzamide ***5ah***. White solid (110 mg, 71% yield): mp 190−191 °C; IR (KBr) ν 3440, 3274, 2920, 1720, 1668, 1596, 1474, 1408, 1271 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.61 (d, J = 8.4 Hz, 2H), 7.38 (s, 1H), 7.26−7.23 (m, 2H), 6.33 (d, J = 1.2 Hz, 2H), 6.15 (s, 1H), 5.54 (s, 1H), 5.19 (dd, J = 8.4, 4.8 Hz, 1H), 3.28 (dd, J = 17.4, 8.4 Hz, 1H), 3.08−3.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 164.3, 150.8, 143.1, 138.4, 135.5, 129.0, 128.9, 128.5, 118.8, 110.4, 109.2, 53.8, 30.0; HRMS (ESI) calcd for $C_{16}H_{13}ClN_2O_3$ $[M + H]^+$ 317.0687, found 317.0685.

N-[5-(Furan-2-yl)-3-methylene-2-oxopyrrolidin-1-yl]furan-2-carboxamide ***5ai***. White solid (120 mg, 88% yield): mp 178−179 °C; IR (KBr) ν 3216, 3144, 1712, 1668, 1582, 1502, 1394, 1155 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.49 (s, 1H), 7.38 (s, 1H), 7.36−7.35 (m, 1H), 7.05 (d, J = 3.6 Hz, 1H), 6.37−6.35 (m, 2H), 6.32−6.31 (m, 1H), 6.17 (s, 1H), 5.52 (s, 1H), 5.18 (dd, J = 8.4, 4.8 Hz, 1H), 3.29−3.24 (m, 1H), 3.05−3.01 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 156.8, 151.1, 145.6, 145.1, 143.2, 135.6, 118.8, 116.0, 111.9, 110.6, 109.4, 54.1, 30.2; HRMS (ESI) calcd for $C_{14}H_{12}N_2O_4$ $[M + H]^+$ 273.0870, found 273.0870.

4-Chloro-N-(5-isopropyl-3-methylene-2-oxopyrrolidin-1-yl)-benzamide ***5al***. White solid (131 mg, 90% yield): mp 159−160 °C; IR (KBr) ν 3180, 2963, 1698, 1668., 1596, 1524, 1430, 1278 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.03 (br, 1H), 7.68−7.67 (m, 2H), 7.20−7.17 (m, 2H), 6.06 (d, J = 3.0 Hz, 1H), 5.45 (d, J = 1.8 Hz, 1H), 4.06 (dd, J = 8.4, 3.6 Hz, 1H), 2.91−2.86 (m, 1H), 2.57 (d, J = 17.4 Hz, 1H), 2.15−2.13 (m, 1H), 0.91−0.90 (m, 3H), 0.77−0.75 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.2, 164.1, 138.3, 137.0, 129.0, 128.8, 128.4, 117.8, 60.9, 28.5, 24.8, 17.9, 14.2; HRMS (ESI) calcd for $C_{15}H_{17}ClN_2O_2$ $[M + H]^+$ 293.1051, found 293.1049.

4-Chloro-N-(3-methylene-2-oxo-5-propylpyrrolidin-1-yl)-benzamide ***5am***. White solid (107 mg, 73% yield): mp 122−124 °C; IR (KBr) ν 3230, 2956, 1712, 1647, 1589, 1474, 1292 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.48 (s, 1H), 7.69 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 7.2 Hz, 2H), 6.08 (t, J = 2.4 Hz, 1H), 5.46 (t, J = 2.4 Hz, 1H), 4.05−4.01 (m, 1H), 3.08−3.03 (m, 1H), 2.54−2.49 (m, 1H), 1.77−1.71 (m, 1H), 1.42−1.37 (m, 1H), 1.33−1.26 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 164.5, 138.6, 136.9, 129.3, 129.0, 128.7, 118.2, 56.8, 35.4, 30.3, 17.6, 14.2; HRMS (ESI) calcd for $C_{15}H_{17}ClN_2O_2$ $[M + H]^+$ 293.1051, found 293.1049.

4-Chloro-N-(2,2-dimethyl-4-methylene-5-oxopyrrolidin-1-yl)-benzamide ***5an***. White solid (111 mg, 80% yield): mp 189−191 °C; IR (KBr) ν 3252, 2970, 1698, 1676, 1596, 1516, 1474, 1401, 1264, 1090 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 7.71 (d, J = 6.4 Hz, 2H), 7.19 (d, J = 7.2 Hz, 2H), 6.07 (s, 1H), 5.44 (s, 1H), 2.74 (d, J = 1.6 Hz, 2H), 1.27 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.9, 165.2, 138.5, 136.7, 129.2, 129.1, 128.6, 118.5, 61.0, 40.0, 26.5; HRMS (ESI) calcd for $C_{14}H_{15}ClN_2O_2$ $[M + H]^+$ 279.0895, found 279.0892.

N-(2,2-Dimethyl-4-methylene-5-oxopyrrolidin-1-yl)furan-2-carboxamide ***5ao***. White solid (95 mg, 81% yield): mp 160−163 °C; IR (neat) ν 3210, 2970, 1720, 1683, 1582, 1516, 1459, 1300, 1177 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.39 (s, 1H), 7.41 (s, 1H), 7.12 (d, J =

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J. Org. Chem. 2015, 80, 12224−12233

3.6 Hz, 1H), 6.39 (s, 1H), 6.10 (s, 1H), 5.43 (s, 1H), 2.75 (s, 2H), 1.31 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.3, 157.8, 145.9, 144.9, 136.5, 118.2, 115.7, 111.8, 60.5, 39.7, 26.3; HRMS (ESI) calcd for $C_{12}H_{14}N_2O_3$ $[M + H]^+$ 235.1077, found 235.1074.

N-(7-Methylene-6-oxo-5-azaspiro[3.4]octan-5-yl)benzamide ***7a***. White solid (109 mg, 85% yield): mp 171−173 °C; IR (KBr) ν 3252, 2999, 1720, 1662, 1516, 1408, 1278, 1119 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.83 (d, J = 7.6 Hz, 2H), 7.36−7.34 (m, 1H), 7.23 (t, J = 7.6 Hz, 2H), 6.05 (d, J = 2.4 Hz, 1H), 5.42 (s, 1H), 3.04 (s, 2H), 2.50−2.47 (m, 2H), 1.88−1.85 (m, 2H), 1.69−1.65 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.8, 166.5, 136.5, 132.1, 131.1, 128.5, 127.7, 117.9, 63.5, 38.5, 33.1, 13.3; HRMS (ESI) calcd for $C_{15}H_{16}N_2O_2$ $[M + H]^+$ 257.1285, found 257.1283.

N-(3-Methylene-2-oxo-1-azaspiro[4.4]nonan-1-yl)benzamide ***7b***. White solid (122 mg, 90% yield): mp 152−154 °C; IR (KBr) ν 3202, 2978, 2869, 1712, 1662, 1495, 1401, 1271 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.32−7.30 (m, 1H), 7.20−7.17 (m, 2H), 6.06 (s, 1H), 5.41 (s, 1H), 2.76 (s, 2H), 1.95 (s, 2H), 1.72 (s, 2H), 1.60 (s, 2H), 1.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 166.3, 136.9, 131.9, 130.9, 128.3, 127.6, 117.8, 70.3, 39.6, 35.5, 22.8; HRMS (ESI) calcd for $C_{16}H_{18}N_2O_2$ $[M + H]^+$ 271.1441, found 271.1443.

N-(3-Methylene-2-oxo-1-azaspiro[4.5]decan-1-yl)benzamide ***7c***. White solid (116 mg, 80% yield): mp 227−228 °C; IR (KBr) ν 3216, 2920, 2840, 1712, 1654, 1532, 1230 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.72 (d, J = 7.2 Hz, 2H), 7.24 (d, J = 6.8 Hz, 1H), 7.13 (d, J = 7.2 Hz, 2H), 6.00 (s, 1H), 5.36 (s, 1H), 2.67 (s, 2H), 1.62 (s, 2H), 1.57 (d, J = 14.0 Hz, 2H), 1.45 (s, 2H), 1.24 (d, J = 13.2 Hz, 2H), 1.18 (s, 1H), 1.02 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 166.3, 136.8, 131.7, 130.9, 128.2, 127.5, 118.0, 63.8, 35.5, 34.5, 24.6, 22.9; HRMS (ESI) calcd for $C_{17}H_{20}N_2O_2$ $[M + H]^+$ 285.1598, found 285.1595.

N-(3-Methylene-2-oxo-1-azaspiro[4.6]undecan-1-yl)benzamide ***7d***. White solid (74 mg, 58% yield): mp 201−202 °C; IR (KBr) ν 3245, 3064, 2927, 2854, 1712, 1654, 1532, 1401, 1278, 1191, 1097 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.33 (s, 1H), 7.20 (s, 2H), 6.04 (s, 1H), 5.42 (s, 1H), 2.71 (s, 2H), 2.04 (s, 2H), 1.60 (d, J = 11.2 Hz, 4H), 1.53 (s, 4H), 1.38 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 166.4, 137.1, 131.9, 131.0, 128.4, 127.6, 118.0, 66.8, 38.5, 38.2, 29.5, 22.5; HRMS (ESI) calcd for $C_{18}H_{22}N_2O_2$ $[M + H]^+$ 299.1754, found 299.1751.

N-(7-Methyl-3-methylene-2-oxo-1-azaspiro[4.5]decan-1-yl)-benzamide ***7g***. Colorless syrup (109 mg, 73% yield): IR (neat) ν 3238, 2927, 2370, 1712, 1668, 1516, 1408, 1278 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.71 (d, J = 7.8 Hz, 2H), 7.30 (t, J = 7.2 Hz, 1H), 7.17 (t, J = 7.8 Hz, 2H), 6.03 (s, 1H), 5.38 (s, 1H), 2.69 (q, J = 16.2 Hz, 2H), 2.02−1.96 (m, 2H), 1.90 (d, J = 12.6 Hz, 1H), 1.67 (d, J = 6.0 Hz, 1H), 1.56 (s, 2H), 1.36 (t, J = 12.0 Hz, 1H), 1.23 (dd, J = 8.4, 6.0 Hz, 1H), 0.99 (d, J = 9.0 Hz, 1H), 0.89 (d, J = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.2, 166.4, 137.1, 131.9, 131.1, 128.4, 127.6, 117.6, 62.9, 44.1, 41.2, 36.4, 32.5, 28.1, 22.1, 21.0; HRMS (ESI) calcd for $C_{18}H_{22}N_2O_2$ $[M + H]^+$ 299.1754, found 299.1750.

N-(8-Methyl-3-methylene-2-oxo-1-azaspiro[4.5]decan-1-yl)-benzamide ***7h***. White solid (112 mg, 77% yield): mp 187−188 °C; IR (KBr) ν 3245, 3065, 2934, 2862, 1726, 1662, 1532, 1401, 1278 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.78 (d, J = 7.6 Hz, 2H), 7.33 (s, 1H), 7.20 (s, 2H), 6.06 (s, 1H), 5.41 (s, 1H), 2.73 (s, 2H), 1.95 (t, J = 12.4 Hz, 2H), 1.81 (s, 1H), 1.60 (s, 2H), 1.51 (s, 2H), 1.32 (d, J = 12.4 Hz, 2H), 0.91 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 166.5, 136.9, 131.9, 131.1, 128.4, 127.6, 118.0, 63.8, 36.4, 30.2, 28.7, 26.4, 17.7; HRMS (ESI) calcd for $C_{18}H_{22}N_2O_2$ $[M + H]^+$ 299.1754, found 299.1768.

2-Methyl-N-(3-methylene-2-oxo-1-azaspiro[4.4]nonan-1-yl)-benzamide ***7i***. White solid (74 mg, 52% yield): mp 181−182 °C; IR (KBr) ν 3166, 2963, 1678, 1668, 1524, 1401, 1278 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.49 (d, J = 3.0 Hz, 1H), 7.32−7.31 (m, 1H), 7.18 (s, 2H), 5.95 (s, 1H), 5.32 (s, 1H), 2.71 (s, 2H), 2.38 (s, 3H), 1.94 (s, 2H), 1.77 (s, 2H), 1.65 (s, 1H), 1.56 (s, 2H), 1.31 (d, J = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.2, 166.4, 137.9, 137.0, 132.6, 130.7, 128.3, 128.2, 124.6, 117.7, 70.3, 39.7, 35.5, 22.8, 21.3; HRMS (ESI) calcd for $C_{17}H_{20}N_2O_2$ $[M + H]^+$ 285.1598, found 285.1595.

3-Methyl-N-(3-methylene-2-oxo-1-azaspiro[4.4]nonan-1-yl)-benzamide ***7j***. White solid (101 mg, 61% yield): mp 120−122 °C; IR (KBr) ν 3252, 2970, 2876, 1712, 1668, 1524, 1408, 1286, 1184 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.64−7.59 (m, 2H), 7.12 (d, J = 7.2 Hz, 1H), 7.08 (t, J = 7.8 Hz, 1H), 6.07 (s, 1H), 5.41 (s, 1H), 2.77 (s, 2H), 2.24 (s, 3H), 1.96 (s, 2H), 1.72 (s, 2H), 1.60 (s, 2H), 1.53 (d, J = 11.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.0, 166.3, 137.9, 136.9, 132.5, 130.7, 128.2, 128.1, 124.5, 117.5, 70.2, 39.6, 35.4, 22.7, 21.2; HRMS (ESI) calcd for $C_{17}H_{20}N_2O_2$ $[M + H]^+$ 285.1598, found 285.1595.

4-Methyl-N-(3-methylene-2-oxo-1-azaspiro[4.4]nonan-1-yl)-benzamide ***7k***. White solid (118 mg, 71% yield): mp 153−154 °C; IR (KBr) ν 3238, 2947, 1712, 1668, 1524, 1416, 1292 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (d, J = 13.2 Hz, 1H), 7.64−7.59 (m, 2H), 7.13−7.07 (m, 2H), 6.07 (s, 1H), 5.41 (s, 1H), 2.77 (s, 2H), 2.25 (s, 3H), 1.97−1.94 (m, 2H), 1.72 (s, 2H), 1.60 (d, J = 4.4 Hz, 2H), 1.54 (d, J = 11.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 166.3, 142.3, 136.9, 128.8, 128.1, 127.5, 117.5, 70.1, 39.6, 35.5, 22.7, 21.4; HRMS (ESI) calcd for $C_{17}H_{20}N_2O_2$ $[M + H]^+$ 285.1598, found 285.1597.

4-Chloro-N-(3-methylene-2-oxo-1-azaspiro[4.4]nonan-1-yl)-benzamide ***7l***. White solid (135 mg, 89% yield): mp 191−193 °C; IR (KBr) ν 3180, 2956, 1712, 1668, 1589, 1394, 1264, 1083 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.28 (s, 1H), 7.72 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 8.4 Hz, 2H), 6.07 (s, 1H), 5.44 (s, 1H), 2.78 (s, 2H), 1.96 (s, 2H), 1.74 (d, J = 6.6 Hz, 2H), 1.63 (d, J = 4.8 Hz, 2H), 1.54 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.2, 165.0, 138.4, 136.7, 129.0, 128.9, 128.5, 117.9, 70.3, 39.6, 35.5, 22.8; HRMS (ESI) calcd for $C_{16}H_{17}ClN_2O_2$ $[M + K]^+$ 343.0610, found 343.0606.

4-Chloro-N-(3-methylene-2-oxo-1-azaspiro[4.5]decan-1-yl)-benzamide ***7m***. White solid (121 mg, 76% yield): mp 185−186 °C; IR (KBr) ν 3180, 2941, 2840, 1705, 1668, 1589, 1524, 1401, 1271, 1162 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.00 (s, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 6.07 (s, 1H), 5.45 (s, 1H), 2.75 (s, 2H), 1.72 (d, J = 12.0 Hz, 2H), 1.63−1.61 (m, 3H), 1.50 (d, J = 12.0 Hz, 2H), 1.32 (d, J = 13.2 Hz, 2H), 1.09 (d, J = 12.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.0, 165.3, 138.5, 136.7, 129.3, 129.1, 128.6, 118.5, 64.1, 35.7, 34.7, 24.8, 23.0; HRMS (ESI) calcd for $C_{17}H_{19}ClN_2O_2$ $[M + H]^+$ 319.1208, found 319.1204.

N-(3-Methylene-2-oxo-1-azaspiro[4.4]nonan-1-yl)furan-2-carboxamide ***7n***. White solid (133 mg, 88% yield): mp 215−216 °C; IR (KBr) ν 3224, 3035, 2970, 1720, 1668, 1574, 1459, 1394, 1314, 1170 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.38 (s, 1H), 7.09 (d, J = 2.4 Hz, 1H), 6.35 (dd, J = 3.2, 1.6 Hz, 1H), 6.08 (s, 1H), 5.41 (s, 1H), 2.77 (s, 2H), 1.96 (dd, J = 11.2, 7.6 Hz, 2H), 1.73 (s, 2H), 1.66−1.54 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.8, 157.8, 145.8, 145.0, 136.6, 117.7, 115.5, 111.7, 70.1, 39.5, 35.4, 22.7; HRMS (ESI) calcd for $C_{14}H_{16}N_2O_3$ $[M + H]^+$ 261.1234, found 261.1233.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02154.

Copies of the IR, ^{1}H NMR, ^{13}C NMR and HRMS spectra of **5** and **7** (PDF)

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The authors declare no competing financial interest.

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