Synthesis of Functionalized γ-Lactams via Copper-Catalyzed Intramolecular C-Vinylation of Activated Methylene Compounds†

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With the catalysis of CuI/3,4,7,8-tetramethyl-1,10-phenanthroline, a number of *N*-(2-iodoallyl)-2-(ethoxycarbonyl)alkanamides underwent efficient intramolecular C-vinylation in THF at 50 ℃ leading to the synthesis of functionalized γ-lactams in 61%—99% yields.

Keywords lactams, copper, catalysis, vinylation

Introduction

Lactams are important structural motifs in many biologically active natural products and medicinal agents. They are also versatile intermediates in a number of areas ranging from organic synthesis to polymer chemistry. Preparations of lactams have long been an important topic in organic chemistry and continue to be actively pursued.[1] Our group has been focusing on the synthesis of lactams via C- or N-radical cyclization,[2] electrophilic halocyclization[3] or copper-catalyzed intramolecular N-vinylation.[4] Herein we report that the Cu(I)-catalyzed intramolecular vinylation of activated methylene compounds with vinyl iodides provides an simple and efficient entry to functionalized γ-lactams.

The past decade has witnessed a rapid progress in the formation of aryl (or vinyl) C—X bonds (X=N, O, S, *etc*.) via copper-catalyzed Ullmann coupling between aryl (or vinyl) halides and heteroatom-centered nucleophiles.[5] The high stability and low costs of the copper catalysts make these transformations attractive for industrial applications. By the appropriate choice of copper source, ligand, base and solvent, these reactions have been developed to include a wide range of substrates under mild conditions. This method was then successfully extended to the C—C bond formation via copper-catalyzed C-arylation of active methylene compounds (the Hurtley coupling[6]).[5] As a comparison, the analogous C-vinylation is far less explored.[7-9] Qian and Pei reported the intermolecular cross-coupling of activated methylene compounds with β-bromostyrenes.[7] We recently developed the efficient intramolecular C-vinylation of activated methylene compounds with vinyl halides leading to the facile synthesis of functionalized alkylidenecyclobutanes.[9] Driven by our interest in copper-catalyzed intramolecular vinylation reactions,[4,8-10] we envisioned that the intramolecular C-vinylation might be utilized for the synthesis of functionalized lactams starting from suitable *N*-(haloalkenyl)amides. Herein we disclose the details of our investigation.

Results and discussion

N-Benzyl-*N*-(2-iodoallyl)-2-(ethoxycarbonyl)propanamide (**1a**) was chosen as the model substrate for the optimization of reaction conditions (Table 1). Compound **1a** was first subjected to the following conditions previously developed by us in the synthesis of alkylidenecyclobutanes: CuI (20 mol%), *L*-proline (**L-1**, 80 mol%), Cs_2CO_3 (3 equiv.) in refluxing THF.[9] After 20 h, the expected product lactam **2a** was obtained in only about 10% yield while most of the starting material was recovered (Entry 1, Table 1). We then screened the ligands (Entries 2—7, Table 1). *N*,*N*′-Dimethylethylenediamine (**L-2**) showed the similar result. With the use of 1,10-phenanthroline (**L-3**) as the ligand, the yield of **2a** was increased to 50%. Switching the ligand to 3,4,7,8-tetramethyl-1,10-phenanthroline (**L-4**) resulted in a further improvement in the product yield (56%). A higher yield of **2a** was achieved when the temperature was lowered to 50 ℃ (Entry 7, Table 1), presumably because the product lactam was more stable at lower temperature. However, the yield was decreased when only 10 mol% of CuI was used (Entry 8, Table 1). The

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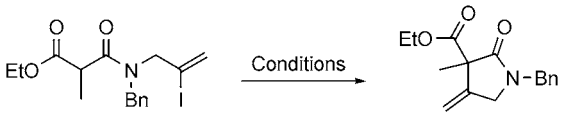
effect of bases was also examined and Cs_2CO_3 turned out to be superior to K_2CO_3 or K_3PO_4 (Entries 9 and 10, Table 1).

Table 1 Intramolecular C-vinylation of amide **1a**



1a **2a**

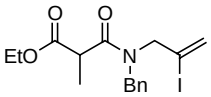
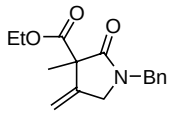
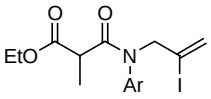
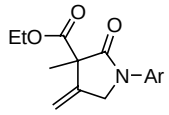
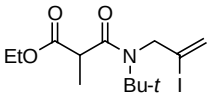
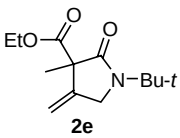
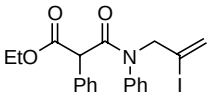
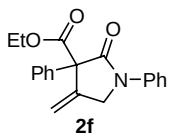
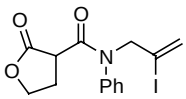
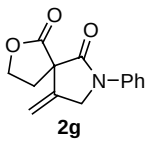
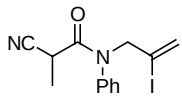
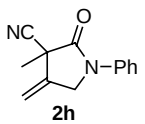
Entry[a]	Ligand[b]	Base	Yield[c]/%
1	**L-1**	Cs_2CO_3	10
2	**L-2**	Cs_2CO_3	10
3	**L-3**	Cs_2CO_3	50
4	**L-4**	Cs_2CO_3	56
5	**L-5**	Cs_2CO_3	27
6	**L-6**	Cs_2CO_3	21
7[d]	**L-4**	Cs_2CO_3	80 (61)
8[d,e]	**L-4**	Cs_2CO_3	55 (38)
9	**L-4**	K_2CO_3	5
10	**L-4**	K_3PO_4	0

[a] Reaction conditions: **1a** (0.30 mmol), CuI (0.06 mmol), ligand (0.24 mmol), base (0.90 mmol), THF (10 mL), reflux, 20 h. [b] **L-1**: *L*-proline; **L-2**: *N*,*N*′-dimethylethylenediamine; **L-3**: 1,10-phenanthroline; **L-4**: 3,4,7,8-tetramethyl-1,10-phenanthroline; **L-5**: 2-isobutyrylcyclohexanone; **L-6**: *N*,*N*-dimethylglycine hydrochloride. [c] ^{1}H NMR yield with the isolated yield in parentheses. [d] The reaction temperature was 50 ℃. [e] 10 mol% of CuI and 40 mol% of **L-4** were employed.

With the optimized conditions in hand (Entry 7, Table 1), we set out to explore the scope and limitation of this method. The results are summarized in Table 2. The *N*-aryl or *N*-*tert*-butyl-substituted analogs of **1a** all underwent smoothly the intramolecular C-vinylation to give the corresponding lactams in high yields (Entries 2—5, Table 2). The cyclization was also successful when the methyl group in **1a** was replaced by a bulky phenyl group (Entry 6, Table 2). When lactone **1g** was used as the substrate, the spiro-lactam **2g** was achieved in good yield (Entry 7, Table 2). Furthermore, the 2-cyanoamide **1h** also afforded the cyclization product **2h** in almost quantitative yield (Entry 8, Table 2). These results clearly demonstrate the efficiency of this C—C coupling strategy in the synthesis of functionalized lactams.

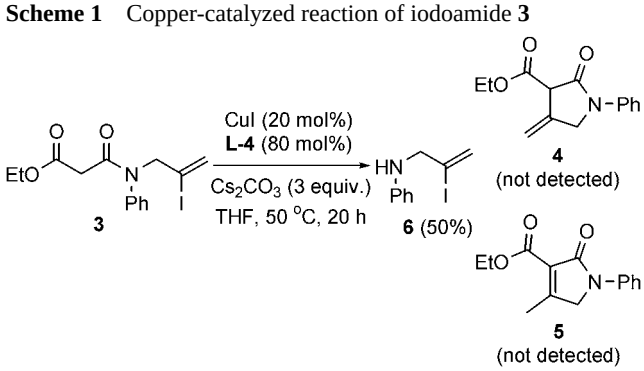
To further extend the scope of application, we prepared *N*-phenyl-*N*-(2-iodoallyl)-2-(ethoxycarbonyl)-acetamide (**3**) and subjected to the treatment with CuI/**L-4** under the above optimized conditions. We were surprised to find that no expected lactam **4** or its isomerized product **5** could be isolated. Instead, only *N*-(2-iodoallyl)aniline (**6**) was isolated in about 50% yield (Scheme 1). Apparently the *β*-elimination (to give **6**) rather than the C-vinylation (to give **4** or **5**) occurred for the carbanions of **3**. The reversed behavior in the reactions of **1** might be attributed to the *gem*-disubstituted pattern in **1**, which makes the cyclization conformationally more favorable. Further investigations on the above different mechanisms and on the control of enantioselectivity of C-vinylation are currently underway in our laboratory.

Table 2 Synthesis of γ-lactams **2**

Entry[a]	Substrate	Product	Yield[b]/%
1	 **1a**	 **2a**	61
			
2	**1b** (Ar = Ph)	**2b**	99
3	**1c** (Ar = 4-Cl-C_6H_4)	**2c**	86
4	**1d** (Ar = 2-Cl-C_6H_4)	**2d**	80
5	 **1e**	 **2e**	70
6	 **1f**	 **2f**	84
7	 **1g**	 **2g**	66
8	 **1h**	 **2h**	99

[a] Experimental conditions: **1** (0.30 mmol), CuI (0.06 mmol), **L-4** (0.24 mmol), Cs_2CO_3 (0.90 mmol), THF (10 mL), 50 ℃, 20 h. [b] Isolated yield based on **1**.

Scheme 1 Copper-catalyzed reaction of iodoamide **3**



Conclusion

The chemistry detailed above has clearly demonstrated that the Cu(I)-catalyzed intramolecular C-vinylation provides a simple and efficient entry to functionalized γ-lactams, which should be of important application in organic synthesis.

Experimental

Typical procedure for the copper-catalyzed intramolecular C-vinylation

The mixture of amide **1a** (0.12 g, 0.30 mmol), CuI (12 mg, 0.060 mmol), **L-4** (57 mg, 0.24 mmol) and Cs_2CO_3 (0.29 g, 0.90 mmol) in THF (10 mL) was stirred at 50 ℃ for 20 h under nitrogen atmosphere. The resulting mixture was cooled down to room temperature and filtered. The filtrate was then concentrated *in vacuo* and the crude product was purified by flash chromatography on silica gel with hexane/EtOAc (V∶V=10∶1) as the eluent to give the pure product **2a** as a colorless oil. Yield: 50 mg (61%).

***N*-Benzyl-2-(ethoxycarbonyl)-*N*-(2-iodoallyl)propanamide (1a)** Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.24/1.26 (2q, J=7.2 Hz, 3H), 1.42/1.47 (2d, J=6.9 Hz, 3H), 3.64—3.75 (1H, m), 3.82—5.14 (m, 6H), 5.90—5.97 (m. 1H), 6.24 (br, 1H), 7.16—7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 14.3/14.4, 14.5/14.7, 43.3/43.5, 48.4/50.7, 56.4/58.1, 61.8/62.0, 104.6/105.3, 126.6/126.8, 127.1/127.8, 128.2/128.3, 128.9/129.3, 136.0/136.8, 170.5/170.6, 170.7; IR (film) ν: 3065, 2983, 2939, 1738, 1659, 1427, 1186, 1098, 908, 737 cm^{-1}; EIMS m/z (%): 356 ($M^+-C_2H_5O$, 1), 274 (26), 234 (6), 200 (3), 146 (5), 129 (9), 106 (34), 91 (100); HRMS calcd for $C_{16}H_{20}INO_3$ (M) 401.0488, found 401.0489.

2-(Ethoxycarbonyl)-*N*-phenyl-*N*-(2-iodoallyl)propanamide (1b) Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.24 (t, J=7.2 Hz, 3H), 1.34 (d, J=7.2 Hz, 3H), 3.42 (q, J=7.2 Hz, 1H), 4.11 (q, J=6.9 Hz, 2H), 4.58 (AB, J=15.6 Hz, 2H), 5.84 (s, 1H), 6.22 (s, 1H), 7.30—7.46 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 14.3, 14.4, 44.1, 60.5, 61.5, 104.7, 128.0, 128.7, 128.9, 130.1, 141.6, 170.2, 170.7; IR (film) ν: 3065, 2982, 1743, 1667, 1595, 1494, 1389, 1222, 1191, 1095, 909, 701 cm^{-1}; EIMS m/z (%): 342 ($M^+-C_2H_5O$, 3), 260 (100), 232 (14), 160 (20), 130 (35), 119 (11), 106 (28), 77 (35); HRMS calcd for $C_{15}H_{18}INO_3$ (M) 387.0331, found 387.0331.

***N*-(4-Chlorophenyl)-2-(ethoxycarbonyl)-*N*-(2-iodoallyl)propanamide (1c)** Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.24 (t, J=7.2 Hz, 3H), 1.35 (d, J=6.9 Hz, 3H), 3.39 (q, J=6.9 Hz, 1H), 4.11 (q, J=7.2 Hz, 2H), 4.56 (AB, J=15.6 Hz, 2H), 5.84 (s, 1H), 6.19 (s, 1H), 7.27 (d, J=8.7 Hz, 2H), 7.41 (d, J=8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 14.1, 14.2, 43.9, 60.2, 61.4, 104.1, 128.4, 130.0, 130.1, 134.7, 139.8, 169.8, 170.3; IR (film) ν: 3100, 2983, 1738, 1672, 1492, 1388, 1323, 1156, 1094, 1013, 905, 841 cm^{-1}; EIMS m/z (%): 376 ($M^+-C_2H_5O$, 4), 294 (100), 266 (13), 193 (8), 164 (14), 140 (25), 130 (22), 111 (17); HRMS calcd for $C_{15}H_{17}ClINO_3$ (M) 420.9942, found 420.9940.

***N*-(2-Chlorophenyl)-2-(ethoxycarbonyl)-*N*-(2-iodoallyl)propanamide (1d)** Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.18—1.28 (m, 3H), 1.34—1.40 (m, 3H), 3.14—3.25 (m, 1H), 3.71—3.78 (m, 1H), 4.01—4.16 (m, 2H), 5.30—5.43 (m, 1H), 5.81/5.87 (2s, 1H), 6.11/6.32 (2s, 1H), 7.30—7.41 (m, 2H), 7.49—7.56 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.0/14.2, 14.6, 44.0/44.2, 58.1/59.2, 61.2/61.4, 103.5/104.5, 127.8/127.9, 128.1/129.2, 130.3, 130.7/131.1, 131.9/132.0, 133.0/133.4, 138.0/138.5, 169.7/169.8, 170.3; IR (film) ν: 3070, 2984, 2940, 1738, 1679, 1478, 1385, 1304, 1223, 1190, 1095, 910, 772 cm^{-1}; EIMS m/z (%): 376 ($M^+-C_2H_5O$, 4), 294 (100), 266 (16), 186 (7), 164 (12), 140 (16), 130 (20), 111 (11); HRMS calcd for $C_{15}H_{17}ClINO_3$ (M) 420.9942, found 420.9946.

***N*-(*tert*-Butyl)-2-(ethoxycarbonyl)-*N*-(2-iodoallyl)-propanamide (1e)** Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.25 (t, J=7.2 Hz, 3H), 1.37 (d, J=6.6 Hz, 3H), 1.47 (s, 9H), 3.43 (q, J=6.9 Hz, 1H), 4.04—4.34 (m, 4H), 6.00 (br, 1H), 6.42 (br, 1H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 14.1, 14.2, 43.3, 56.0, 58.2, 61.7, 103.8/104.6, 126.9/127.2, 170.1; IR (film) ν: 2980, 1746, 1664, 1393, 1186, 1095, 1032, 979, 904 cm^{-1}; EIMS m/z (%): 323 ($M^+-C_2H_5O$, 5), 267 (1), 242 (12), 193 (2), 164 (21), 143 (4), 114 (7), 57 (100); HRMS calcd for $C_{13}H_{22}INO_3$ (M) 367.0644, found 367.0641.

2,*N*-Diphenyl-2-(ethoxycarbonyl)-*N*-(2-iodoallyl)-acetamide (1f) Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.25 (d, J=7.5 Hz, 3H), 4.17 (q, J=7.2 Hz, 2H), 4.47—4.64 (m, 3H), 5.79 (s, 1H), 6.12 (s, 1H), 7.12—7.41 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.1, 56.1, 60.6, 61.9, 104.0, 127.7, 127.9, 128.3, 128.8, 129.7, 129.8, 133.2, 141.2, 167.8, 168.6; IR (film) ν: 3070, 3030, 2980, 1747, 1668, 1595, 1494, 1384, 1303, 1219, 1182, 1019, 910, 701 cm^{-1}; EIMS m/z (%): 448 (M^+-1, 5), 322 (100), 249 (7), 220 (3), 159 (10), 130 (15), 119 (9), 91 (13); HRMS calcd for $C_{20}H_{20}INO_3$ (M) 449.0488, found 449.0490.

***N*-(2-Iodoallyl)-2-oxo-*N*-phenyl-tetrahydrofuran-3-carboxamide (1g)** White solid; m.p. 124—126 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.20—2.38 (m, 1H), 2.72—2.85 (m, 1H), 3.56 (t, J=8.4 Hz, 1H), 4.19 (q, J=7.8 Hz, 1H), 4.48—4.56 (m, 1H), 4.62 (s, 2H), 5.85 (s, 1H), 6.26 (s, 1H), 7.44 (br, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 27.3, 43.7, 60.6, 67.4, 103.6, 128.0, 128.5, 128.9, 130.0, 141.1, 167.8, 173.5; IR (film) ν: 3065, 2926, 1766, 1661, 1594, 1494, 1396, 1159, 1019, 911, 700 cm^{-1}; EIMS m/z (%): 244 (M^+-I, 100), 200 (5), 167 (3), 158 (3), 130 (16), 119 (4), 106 (11), 77 (13); HRMS calcd for $C_{14}H_{14}NO_3$ (M−I) 244.0974, found 244.0980.

2-Cyano-*N*-(2-iodoallyl)-*N*-phenylpropanamide (1h) Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.50 (d, J=7.2 Hz, 3H), 3.46 (q, J=7.2 Hz, 1H), 4.52

(d, J=15.3 Hz, 1H), 4.66 (d, J=15.3 Hz, 1H), 5.84 (s, 1H), 6.10 (s, 1H), 7.34—7.52 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 15.9, 29.9, 60.5, 103.8, 118.1, 128.4, 129.2, 129.5, 130.3, 139.9, 165.7; IR (film) v: 3070, 2943, 2246, 1678, 1595, 1493, 1392, 1216, 1139, 1019, 912, 703 cm^{-1}; EIMS m/z (%): 339 (M^+−1, 1), 213 (100), 167 (6), 157 (5), 130 (16), 119 (7), 106 (6), 77 (14); HRMS calcd for $C_{13}H_{13}IN_2O$ (M) 340.0073, found 340.0070.

Ethyl 1-benzyl-3-methyl-4-methylene-2-oxopyrrolidine-3-carboxylate (2a) Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.13 (t, J=7.2 Hz, 3H), 1.48 (s, 3H), 3.75 (d, J=14.1 Hz, 1H), 3.95 (dt, J=14.1, 2.4 Hz, 1H), 4.08 (q, J=6.9 Hz, 2H), 4.26 (d, J=15.0 Hz, 1H), 4.76 (d, J=15.0 Hz, 1H), 5.02 (s, 1H), 5.12 (br, 1H), 71.9—7.27 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 14.1, 19.8, 46.7, 50.7, 55.7, 62.0, 110.1, 128.0, 128.3, 128.9, 136.0, 143.4, 170.6, 172.7; IR (film) v: 2984, 1741, 1703, 1664, 1431, 1247, 1119, 1022, 701 cm^{-1}; EIMS m/z (%): 273 (M^+, 10), 244 (5), 216 (2), 200 (32), 168 (1), 154 (1), 112 (2), 91 (100); HRMS calcd for $C_{16}H_{19}NO_3$ (M) 273.1365, found 273.1366.

Ethyl 3-methyl-4-methylene-2-oxo-1-phenylpyrrolidine-3-carboxylate (2b) Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.21 (t, J=7.2 Hz, 3H), 1.62 (s, 3H), 4.13—4.22 (m, 2H), 4.44 (d, J=15.0 Hz, 1H), 4.63 (dt, J=15.0, 2.1 Hz, 1H), 5.28 (br, 2H), 7.20 (t, J=7.2 Hz, 1H), 7.41 (t, J=7.5 Hz, 2H), 7.69 (d, J=8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 14.2, 19.8, 52.7, 57.2, 62.1, 110.3, 120.5, 125.4, 129.3, 138.9, 142.3, 170.3, 171.8; IR (film) v: 2984, 2937, 1737, 1710, 1598, 1495, 1392, 1229, 1119, 1093, 1020, 906, 759 cm^{-1}; EIMS m/z (%): 259 (M^+, 21), 230 (12), 186 (100), 160 (23), 130 (12), 106 (20), 91 (14), 77 (39); HRMS calcd for $C_{15}H_{17}NO_3$ (M) 259.1208, found 259.1206.

Ethyl 1-(4-chlorophenyl)-3-methyl-4-methylene-2-oxopyrrolidine-3-carboxylate (2c) Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.13 (t, J=7.2 Hz, 3H), 1.54 (s, 3H), 4.05—4.13 (m, 2H), 4.33 (d, J=13.2 Hz, 1H), 4.52 (dt, J=13.2, 2.4 Hz, 1H), 5.21 (s, 2H), 7.30 (d, J=8.7 Hz, 2H), 7.57 (d, J=8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 14.0, 19.5, 52.4, 57.0, 62.0, 110.5, 121.3, 129.1, 130.3, 137.3, 141.7, 169.8, 171.7; IR (film) v: 2984, 1744, 1708, 1668, 1494, 1388, 1295, 1227, 1085, 1101, 829 cm^{-1}; EIMS m/z (%): 293 (M^+, 24), 264 (10), 220 (100), 190 (6), 156 (5), 138 (14), 111 (23), 81 (29); HRMS calcd for $C_{15}H_{16}ClNO_3$ (M) 293.0819, found 293.0820.

Ethyl 1-(2-chlorophenyl)-3-methyl-4-methylene-2-oxopyrrolidine-3-carboxylate (2d) Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.26 (t, J=7.2 Hz, 3H), 1.61 (s, 3H), 4.19 (q, J=7.2 Hz, 2H), 4.35 (d, J=13.2 Hz, 1H), 4.50 (dt, J=13.2, 2.4 Hz, 1H), 5.22 (s, 1H), 5.27 (s, 1H), 7.25—7.33 (m, 3H), 7.45—7.47 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 14.0, 19.5, 53.3, 55.3, 61.8, 110.1, 127.9, 129.4, 129.5, 130.5, 132.2, 135.4, 143.1, 170.1, 172.3; EIMS m/z (%): 293 (M^+, 18), 272 (13), 264 (18), 258 (40), 220 (100), 184 (16), 138 (12), 112 (16); HRMS calcd for $C_{15}H_{16}ClNO_3$ (M) 293.0819, found 293.0823.

Ethyl 1-(*tert*-butyl)-3-methyl-4-methylene-2-oxopyrrolidine-3-carboxylate (2e) Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.20 (t, J=7.2 Hz, 3H), 1.43 (s, 9H), 1.45 (s, 3H), 3.99—4.17 (m, 4H), 5.09—5.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 14.1, 19.1, 27.9, 50.1, 54.6, 57.0, 61.7, 109.3, 143.6, 170.8, 172.8; IR (film) v: 2979, 1743, 1697, 1663, 1223, 1119, 1023, 909 cm^{-1}; EIMS m/z (%): 239 (M^+, 14), 224 (22), 210 (7), 183 (14), 166 (21), 150 (48), 137 (22), 110 (100); HRMS calcd for $C_{13}H_{21}NO_3$ (M) 239.1521, found 239.1524.

Ethyl 4-methylene-2-oxo-1,3-diphenylpyrrolidine-3-carboxylate (2f) Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.28 (t, J=7.2 Hz, 3H), 4.29 (q, J=7.2 Hz, 2H), 4.59 (AB, J=13.2 Hz, 2H), 5.43 (s, 1H), 5.62 (s, 1H), 7.18 (t, J=7.5 Hz, 1H), 7.26—7.41 (m, 5H), 7.58 (d, J=8.4 Hz, 2H), 7.79 (d, J=8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.0, 52.3, 62.2, 66.4, 113.8, 120.2, 125.2, 128.1, 128.3, 128.4, 129.0, 135.9, 138.7, 140.0, 169.6, 169.7; EIMS m/z (%): 321 (M^+, 74), 292 (100), 248 (63), 220 (28), 129 (35), 115 (52), 104 (35), 77 (32); HRMS calcd for $C_{20}H_{19}NO_3$ (M) 321.1365, found 321.1359.

4-Methylene-2,2'-dioxo-1-phenyl-spiro(pyrrolidin-3,3'-tetrahydrofuran) (2g) White solid, m.p. 112—114 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.47—2.57 (m, 1H), 2.94—3.04 (m, 1H), 4.39—4.53 (m, 2H), 4.65—4.80 (m, 2H), 5.31 (s, 1H), 5.38 (s, 1H), 7.21 (t, J=7.2 Hz, 1H), 7.40 (t, J=8.1 Hz, 2H), 7.65 (d, J=7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 32.2, 52.7, 57.8, 66.9, 110.5, 120.4, 125.6, 129.1, 138.3, 140.2, 169.3, 173.6; EIMS m/z (%): 243 (M^+, 39), 199 (100), 184 (67), 170 (57), 156 (34), 130 (11), 104 (40), 77 (68); HRMS calcd for $C_{14}H_{13}NO_3$ (M) 243.0895, found 243.0892.

3-Cyano-3-methyl-4-methylene-2-oxo-1-phenylpyrrolidine (2h) White solid, m.p. 72—74 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.78 (s, 3H), 4.53 (AB, J=14.1 Hz, 2H), 5.49 (d, J=1.2 Hz, 1H), 5.60 (d, J=1.2 Hz, 1H), 7.23 (t, J=7.5 Hz, 1H), 7.41 (t, J=8.1 Hz, 2H), 7.64 (d, J=7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 23.7, 45.4, 51.3, 113.2, 118.3, 120.3, 125.9, 129.2, 137.9, 138.6, 167.0; IR (film) v: 2990, 2240, 1712, 1673, 1495, 1398, 1277, 1223, 1094, 916, 761 cm^{-1}; EIMS m/z (%): 212 (M^+, 100), 197 (41), 183 (27), 169 (26), 158 (8), 119 (47), 106 (19), 91 (26); HRMS calcd for $C_{13}H_{12}N_2O$ (M) 212.0950, found 212.0948.

2-(Ethoxycarbonyl)-*N*-(2-iodoallyl)-*N*-phenylacetamide (3) White solid, m.p. 44—46 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.23 (t, J=7.2 Hz, 3H), 3.25 (s, 2H), 4.12 (q, J=7.2 Hz, 2H), 4.60 (s, 2H), 5.84 (s, 1H), 6.24 (d, J=1.2 Hz, 1H), 7.29—7.42 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.1, 41.8, 60.3, 61.4, 104.0, 128.0, 128.3, 128.8, 129.9, 141.4, 166.0, 167.5; EIMS m/z (%): 246 (M^+−I, 100), 218 (18), 200 (3), 172 (3), 159 (6), 130 (20), 106 (17), 77 (13); HRMS calcd for

$C_{14}H_{16}INO_3$ (M) 373.0175, found 373.0170.

***N*-(2-Iodoallyl)aniline (6)** Yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.98 (s, 2H), 4.23 (br, 1H), 5.84 (d, J=1.5 Hz, 1H), 6.33 (d, J=1.8 Hz, 1H), 6.60 (d, J=8.7 Hz, 2H), 6.74 (t, J=7.5 Hz, 1H), 7.18 (t, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ: 55.9, 109.8, 113.1, 118.3, 125.2, 129.4, 146.6; EIMS *m*/*z* (%): 259 (M^+, 55), 132 (40), 117 (16), 106 (100), 93 (6), 77 (22), 65 (20), 51 (10); HRMS calcd for $C_9H_{10}IN$ (M) 258.9858, found 258.9855.

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References

1 For reviews, see: (a) Nubbemeyer, U. *Top. Curr. Chem.* **2001**, *216*, 125.
(b) Groaning, M. D.; Meyers, A. I. *Tetrahedron* **2000**, *56*, 9843.
(c) Shiraki, R.; Tadano, K.-I. *Rev. Heteroat. Chem.* **1999**, *20*, 283.
(d) Robin, S.; Rousseau, G. *Tetrahedron* **1998**, *54*, 13681.
(e) Ley, S. V.; Cox, L. R.; Meek, G. *Chem. Rev.* **1996**, *96*, 423.

2 (a) Liu, L.; Wang, X.; Li, C. *Org. Lett.* **2003**, *5*, 361.
(b) Tang, Y.; Li, C. *Org. Lett.* **2004**, *6*, 3229.
(c) Liu, L.; Chen, Q.; Wu, Y.-D.; Li, C. *J. Org. Chem.* **2005**, *70*, 1539.
(d) Chen, Q.; Shen, M.; Tang, Y.; Li, C. *Org. Lett.* **2005**, *7*, 1625.
(e) Lu, H.; Li, C. *Tetrahedron Lett.* **2005**, *46*, 5983.
(f) Hu, T.; Shen, M.; Chen, Q.; Li, C. *Org. Lett.* **2006**, *8*, 2647.
(g) Yuan, X.; Liu, K.; Li, C. *J. Org. Chem.* **2008**, *73*, 6166.
(h) Fang, X.; Liu, K.; Li, C. *J. Am. Chem. Soc.* **2010**, *132*, 2274.

3 (a) Shen, M.; Li, C. *J. Org. Chem.* **2004**, *69*, 7906.
(b) Tang, Y.; Li, C. *Tetrahedron Lett.* **2006**, *47*, 3823.
(c) Hu, T.; Liu, K.; Shen, M.; Yuan, X.; Tang, Y.; Li, C. *J. Org. Chem.* **2007**, 72, 8555.

4 (a) Hu, T.; Li, C. *Org. Lett.* **2005**, *7*, 2035.
(b) Lu, H.; Li, C. *Org. Lett.* **2006**, *8*, 5365.
(c) Zhao, Q.; Li, C. *Org. Lett.* **2008**, *10*, 4037.
(d) Lu, H.; Yuan, X.; Zhu, S.; Sun, C.; Li, C. *J. Org. Chem.* **2008**, *73*, 8665.

5 For reviews, see: (a) Kunz, K.; Scholz, U.; Ganzer, D. *Synlett* **2003**, 2428.
(b) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400.
(c) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337.
(d) Deng, W.; Liu, L.; Guo, Q.-X. *Chin. J. Org. Chem.* **2004**, *24*, 150.
(e) Dehli, J. R.; Legros, J.; Bolm, C. *Chem. Commun.* **2005**, 973.
(f) Chemler, S. R.; Fuller, P. H. *Chem. Soc. Rev.* **2007**, *36*, 1153.
(g) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054.
(h) Ma, D.; Cai, Q. *Acc. Chem. Res.* **2008**, *41*, 1450.
(i) Evano, G.; Toumi, M.; Coste, A. *Chem. Commun.* **2009**, 4166.

6 Hurtley, W. R. H. *J. Chem. Soc.* **1929**, 1870.

7 Pei, L.; Qian, W. *Synlett* **2006**, 1719.

8 Fang, Y.; Li, C. *Chem. Commun.* **2005**, 3574.

9 Chen, L.; Shi, M.; Li, C. *Org. Lett.* **2008**, *10*, 5285.

10 (a) Fang, Y.; Li, C. *J. Am. Chem. Soc.* **2007**, *129*, 8092.
(b) Pan, Y.; Lu, H.; Fang, Y.; Fang, X.; Chen, L.; Qian, J.; Wang, J.; Li, C. *Synthesis* **2007**, 1242.
(c) Zhao, Q.; Li, L.; Fang, Y.; Sun, D.; Li, C. *J. Org. Chem.* **2009**, *74*, 459.
(d) Sun, C.; Fang, Y.; Li, S.; Zhang, Y.; Zhao, Q.; Zhu, S.; Li, C. *Org. Lett.* **2009**, *11*, 4084.

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