Copper(I)-Catalyzed Intramolecular Addition of *N*-Chloroamides to Double Bonds; an Efficient Synthesis of Lactams from Unsaturated Amides

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Dedicated to Professor R. W. Hoffmann on the occasion of his 70th birthday.

Abstract: Copper(I) salts catalyse the intramolecular addition of *N*-chloramides to carbon–carbon double bonds leading to lactams in almost quantitative yield.

Key words: catalysis, copper, lactams, radical reactions

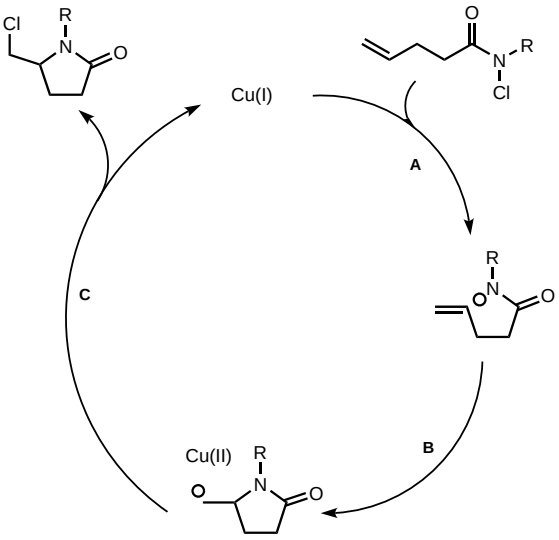
Lactams are important substructures of a variety of natural products and pharmacological active compounds.[1] One way to synthesise them is the intramolecular addition of the NH bond of an amide to a double bond, a process which is almost thermoneutral and therefore difficult to perform.[2] To circumvent this problem one can utilize the high energy content of an NCl bond and add *N*-chloroamides to double bonds. This reaction can be achieved via free radicals and the approach has been tried by a variety of groups.[3] However, the yield of lactams obtained in these cyclisations is unsatisfactory. A reason for this is undesired side reactions of the carbon radical formed in the cyclisation.

We recently reported, that copper(I) salts are efficient catalysts for the radical cyclisation of unsaturated *N*-chloroamines.[4] In these reactions the copper salt acts as the initiator of the radical reaction as well as the scavanger of the carbon radical formed as intermediate. As copper(II) chloride oxidises carbon radicals at a diffusion controlled rate,[5] we envisioned, that copper(I) salts should be efficient catalysts for a high yielding cyclisation of unsaturated *N*-chloroamides. Undesired reactions of the carbon radical formed should be minimised. The anticipated catalytic cycle is shown in Scheme 1.

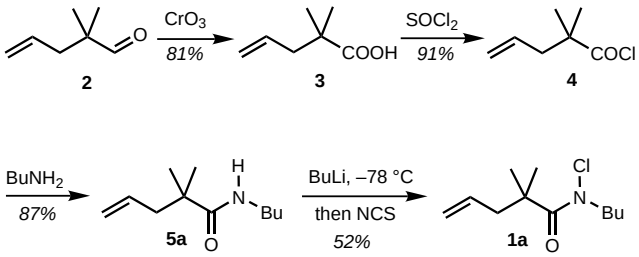
Copper(I) is oxidized by a chloroamide, giving copper(II) and an amidyl radical **A**. As the amidyl radical is electrophilic, it cyclises rapidly **B**, leading to a carbon radical, which in turn is quickly oxidised by copper(II) chloride **C**. In this last step the catalyst is regenerated and the product, a 5-chloromethyl-2-pyrrolidinone is formed.

To check wether this concept holds true, we synthesised chloroamide **1a** in the following way (Scheme 2).

The known aldehyde **2** was oxidised under Jones conditions[6] to acid **3**. From this the amide **5a** was via the acid chloride **4** in good yield. This amide **5a** was transformed to *N*-chloroamide **1a** by deprotonation and reaction with NCS.[3,7]

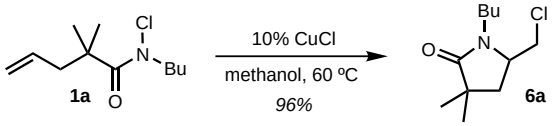


Scheme 1



Scheme 2

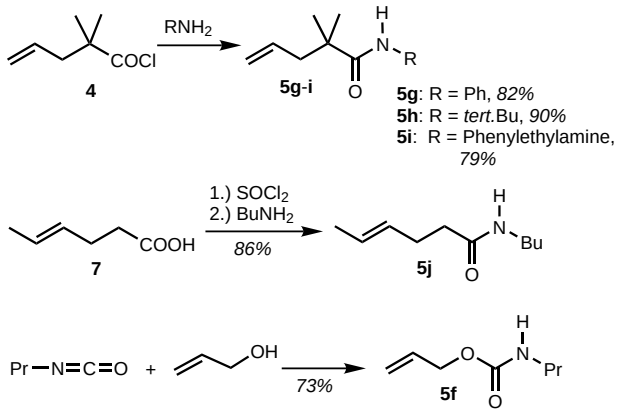
Upon addition of catalytic amounts of copper(I) chloride to this chloroamide we obtained lactam **6a** in very good yield (Scheme 3).



Scheme 3

Synthesis 2003, No. 12, Print: 02 09 2003. Web: 07 08 2003.
Art Id.1437-210X,E;2003,0,12,1886,1890,ftx,en;T10902SS.pdf.
DOI: 10.1055/s-2003-40997

Amongst various solvents tested for the cyclisation, methanol proved to be most suitable, probably because it dissolves the catalyst best. To check the scope of this reaction, we prepared the amides **5g–i** (Scheme 4).[8] For the synthesis of **5g–i**, we reacted the acid chloride **4** with different amines whilst **5j** was obtained from the known acid **7**[9] via the acid chloride. The carbamate **5f** was obtained by a straightforward reaction of propylisocyanate with allylic alcohol.[10]



Scheme 4

The amides **5b–i** were transformed to the corresponding *N*-chloroamides **1b–i** by deprotonation and reaction with NCS. To our surprise the yields of chloroamides varied significantly depending on the substrate used (Table 1). In the reaction of **5g**, the chloroamide was formed together with a mixture of (3,3-dimethyldihydrofuran-2-ylidene)phenylamine and 3,3-dimethyl-1-phenylpyrrolidin-2-one. Due to the electron withdrawing phenyl group in this substrate, the deprotonated amide seems to be not nucleophilic enough to react efficiently with NCS. Instead the NCS attacks the double bond forming a chloronium ion, which in turn is opened by nucleophilic attack of either the oxygen or the nitrogen of the deprotonated amide, leading to the products observed.

We next cyclised the chloroamides **1b–i** using catalytic amounts of copper(I) chloride (Table 1).

As anticipated, mostly good yields of cyclic amides **6b–i** were obtained. Even when a severe steric hindrance is present, as in the case of **1h**, a good yield of lactam **6h** could be isolated. However, **1e** and **1f** produced lower yields of the cyclisation products **6e** and **6f**, showing the limitations of the reaction. In both cases conformational effects, disfavouring the conformation required for the cyclisation, are present. This result is in accordance with the observations of other groups performing amidyl-radical cyclisations.[11] This also holds true for the observed diastereomeric ratio (dr, Table 1) in the cyclisation of **1b**, **1c** and **1i** which is in the range one expects for a relatively unselective radical cyclisation. Surprisingly, in the case of the addition to a 1,2-disubstituted double bond (**1j** to **6j**) a high diastereomeric ratio is observed. This might result from the quick reaction of the intermediate carbon radical with copper(II) chloride. Further studies to clarify this unusual high diastereomeric ratio are currently being performed in our group.

In summary, we have presented a copper(I) chloride catalysed cyclisation of unsaturated *N*-chloroamides that produces superior yields as compared to the known cyclisations of chloroamides. We are currently investigating this reaction in further detail and applying the procedure to natural product synthesis.

All solvents were purified by distillation and dried, if necessary, prior to use. As a standard solvent instead of Et_2O in many cases *tert*-butyl methyl ether (TBME) was used. The reactions were carried out in vacuum heat dried glassware under an argon atmosphere. Products were purified by flash chromatography on silica gel (40–63 μm). NMR spectra were recorded on a Bruker WM 300 and a Bruker AMX 400 spectrometer in $CDCl_3$ using TMS as internal standard. Elemental analyses were performed on a CHN-O Rapid from Foss-Heraeus and a Vario EL III from Elementar Analysensysteme.

Amides from Acids; General Procedure

To a solution of the unsaturated acid (0.33 mol) in CH_2Cl_2 (50 mL), thionyl chloride (26.2 mL, 0.36 mol) was added slowly at 0 °C. The mixture was stirred 14 h at r.t., after which the reaction was complete. The so obtained solution of acid chloride was added slowly to the corresponding amine (1.64 mol) at 0 °C. After stirring the reaction overnight, solvent and excess amine were removed in vacuo and the remainder taken up in TBME and aq hydrochloric acid (2 M) (150 mL each). The layers were separated and the organic layer washed again with aq hydrochloric acid (2 M; 150 mL). After drying (Na_2SO_4), the solvent was removed in vacuo and the product was obtained from the residue either by distillation or crystallisation.

***N*-Butyl-2,2-dimethylpent-4-enoic Acid Amide (5a)**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.2 Hz, 3 H), 1.16 (s, 6 H), 1.34 (m, 2 H), 1.47 (m, 2 H), 2.27 (dt, *J* = 7.4, 1.2 Hz, 2 H), 3.24 (m, 2 H), 5.05 (m, 2 H), 5.67 (br s, 1 H), 5.74 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 20.1, 25.1, 31.7, 39.2, 41.9, 45.2, 117.6, 134.5, 193.4.

Anal. Calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.55; N, 7.64. Found: C, 71.75; H, 11.79; N, 7.61.

Propylcarbamic Acid Allyl Ester (5f)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.2 Hz, 3 H), 1.52 (sx, *J* = 7.2 Hz, 2 H), 3.14 (t, *J* = 6.0 Hz, 2 H), 4.56 (dt, *J* = 6.0, 3.6 Hz, 2 H), 4.72 (br s, 1 H), 5.24 (m, 2 H), 5.92 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.1, 23.2, 42.9, 65.4, 117.4, 133.1, 157.2.

***N*-Phenyl-2,2-dimethylpent-4-enoic Acid Amide (5g)**

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 6 H), 2.36 (d, *J* = 8.0Hz, 2 H), 5.17 (m, 2 H), 5.82 (m, 1 H), 7.08 (t, *J* = 7.2 Hz, 1 H), 7.28 (m, 2 H), 7.39 (s, 1 H), 7.50 (d, *J* = 7.6 Hz, 2 H).

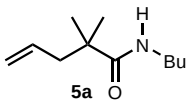
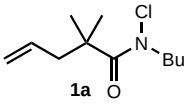
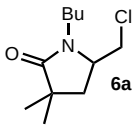
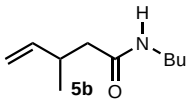
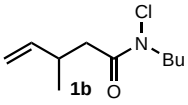
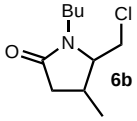
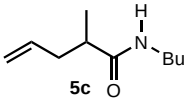
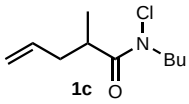
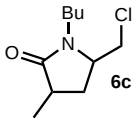
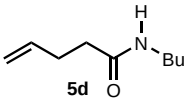
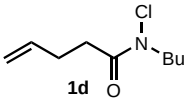
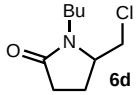
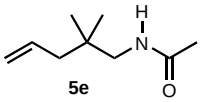
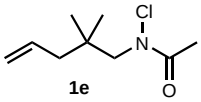
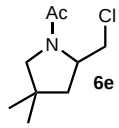
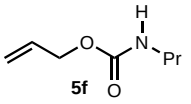
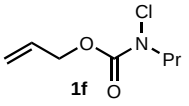
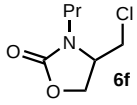
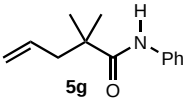
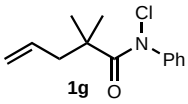
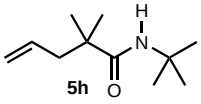
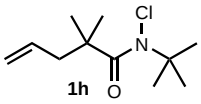
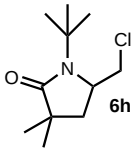
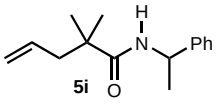
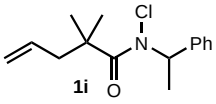
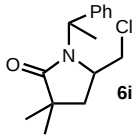
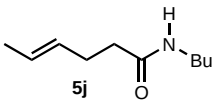
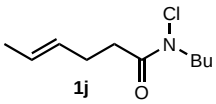
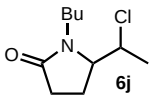
^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.2, 42.8, 45.2, 118.4, 120.1, 124.2, 128.9, 134.2, 137.9, 175.4.

Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.58; H, 8.31; N, 6.69.

***N*-*tert*-Butyl-2,2-dimethylpent-4-enoic Acid Amide (5h)**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (s, 6 H), 1.34 (s, 9 H), 2.24 (dt, *J* = 7.5, 1.2 Hz, 2 H), 5.06 (m, 2 H), 5.41 (s, 1 H), 5.76 (m, 1 H).

Table 1 Yields of *N*-Chloroamides and of the Cyclisations

Amide	Chloroamide	Yield (%)	Lactam	Yield (%) (dr)
 **5a**	 **1a**	52	 **6a**	96
 **5b**	 **1b**	75	 **6b**	91 (4:1)
 **5c**	 **1c**	51	 **6c**	75 (2:1)
 **5d**	 **1d**	43	 **6d**	70
 **5e**	 **1e**	42	 **6e**	34
 **5f**	 **1f**	64	 **6f**	12
 **5g**	 **1g**	-		
 **5h**	 **1h**	47	 **6h**	79
 **5i**	 **1i**	61	 **6i**	63 (2:1)
 **5j**	 **1j**	45	 **6j**	76 (10:1)

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.3, 28.8, 42.2, 45.4, 50.9, 117.7, 134.6, 176.4.

Anal. Calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.55; N, 7.64. Found: C, 71.72; H, 11.56; N, 7.52.

***N*-Phenylethyl-2,2-dimethylpent-4-enoic Acid Amide (5i)**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (s, 6 H), 1.46 (d, *J* = 6.9 Hz, 3 H), 2.26 (quin, *J* = 7.2 Hz, 1 H), 5.01 (dt, *J* = 2.7, 1.2 Hz, 2 H), 5.11 (m, 2 H), 5.70 (m, 1 H), 5.82 (s, 1 H), 7.29 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6, 25.1, 41.8, 45.2, 48.5, 117.9, 126.1, 127.2, 128.6, 134.4, 143.4, 176.1.

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.83; H, 9.24; N, 6.01.

(*E*)-*N*-Butylhex-4-enoic Acid Amide (5j)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.2 Hz, 3 H), 1.35 (m, 2 H), 1.48 (m, 2 H), 1.63 (d with fine splitting, *J* = 4.8 Hz, 3 H), 2.22 (m, 2 H), 2.30 (m, 2 H), 3.23 (q, *J* = 6.9 Hz, 2 H), 5.45 (m, 2 H), 6.10 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 17.6, 19.9, 28.5, 31.6, 36.4, 39.0, 125.9, 129.5, 172.5.

Anal. Calcd for $C_{10}H_{19}NO$: C, 70.96; H, 11.31; N, 8.27. Found: C, 70.70; H, 11.67; N, 8.21.

_N_-Chloroamides; General Procedure

To a solution of amide (55 mmol) in anhyd Et_2O (200 mL) was added butyllithium solution (34.5 mL at 1.6 M; 55 mmol) at –78 °C. The reaction was stirred 30 min at 0 °C and then NCS (8.9 g, 67 mmol) was added. After 2 h stirring at 0 °C, H_2O (200 mL) was added and the layers separated. The aq layer was washed with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), the solvent was removed in vacuo and the product isolated from the residue by flash chromatography.

_N_-Butyl-_N_-chloro-2,2-dimethylpent-4-enoic Acid Amide (1a)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.5Hz, 3 H), 1.25 (s, 6 H), 1.52 (m, 2 H), 3.15 (m, 2 H), 3.72 (m, 2 H), 4.56 (dt, *J* = 5.4, 1.2 Hz, 2 H), 5.25 (m, 2 H), 5.92 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 20.5, 26.3, 26.8, 32.8, 42.3, 46.1, 117.8, 134.3, 177.3.

_N_-Butyl-_N_-chloro-3-methylpent-4-enoic Acid Amide (1b)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.2 Hz, 3 H), 1.08 (d, *J* = 6.8 Hz, 3 H), 1.34 (m, 2 H), 1.65 (m, 2 H), 2.52 (m, 2 H), 2.75 (m, 1 H), 3.71 (t, *J* = 7.2 Hz, 2 H), 5.01 (m, 2 H), 5.82 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 19.3, 19.6, 29.3, 34.2, 40.1, 52.1, 113.1, 142.7, 176.1.

_N_-Butyl-_N_-chloro-2-methylpent-4-enoic Acid Amide (1c)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 7.2 Hz, 3 H), 1.16 (d, *J* = 6.9 Hz, 3 H), 1.34 (m, 2 H), 1.65 (m, 2 H), 2.15 (m, 2 H), 2.45 (m, 1 H), 3.72 (m, 2 H), 5.05 (m, 2 H), 5.77 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5, 16.8, 19.3, 29.3, 36.1, 37.8, 52.0, 116.6, 135.5, 176.6.

_N_-Butyl-_N_-chloropent-4-enoic Acid Amide (1d)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.2 Hz, 3 H), 1.38 (m, 2 H), 1.70 (dt, *J* = 7.6 Hz, 2 H), 2.43 (m, 2 H), 2.64 (t, *J* = 7.6 Hz, 2 H), 3.74 (t, *J* = 7.2 Hz, 2 H), 5.07 (m, 2 H), 5.89 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.6, 19.3, 29.3, 31.7, 35.9, 52.0, 115.4, 137.1, 173.2.

_N_-Acetyl-_N_-chloro-3,3-dimethylpent-4-enamine (1e)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (s, 6 H), 2.07 (dt, *J* = 7.2, 1.2 Hz, 2 H), 2.28 (s, 3 H), 3.59 (s, 2 H), 5.05 (m, 2 H), 5.84 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0, 25.3, 26.9, 36.3, 44.9, 117.7, 134.4, 178.3.

_N_-Chloro-_N_-propylcarbamic Acid Allyl Ester (1f)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.2 Hz, 3 H), 1.65 (sx, *J* = 7.2 Hz, 2 H), 3.54 (t, *J* = 6.9Hz, 2 H), 4.60 (dt, *J* = 5.7, 1.8 Hz, 2 H), 5.24 (m, 2 H), 5.88 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.2, 20.5, 55.8, 67.7, 118.2, 132.0, 175.7.

***N*-*tert*-Butyl-*N*-chloro-2,2-dimethylpent-4-enoic Acid Amide (1h)**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (s, 6 H), 1.43 (s, 9 H), 2.49 (dt, *J* = 7.5, 1.2 Hz, 2 H), 5.06 (m, 2 H), 5.76 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.3, 29.4, 41.8, 45.1, 64.3, 117.5, 134.7, 181.9.

_N_-Chloro-_N_-phenylethyl-2,2-dimethylpent-4-enoic Acid Amide (1i)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 6 H), 1.57 (d, *J* = 6.3 Hz, 3 H), 2.53 (m, 2 H), 5.05 (m, 2 H), 5.73 (m, 1 H), 6.13 (q, *J* = 6.9 Hz, 1 H), 7.32 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.9, 25.8, 43.6, 43.8, 56.6, 117.8, 127.6, 128.2, 128.7, 134.0, 139.6, 177.5.

(*E*)-*N*-Butyl-*N*-chlorohex-4-enoic Acid Amide (1j)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 7.2 Hz, 3 H), 1.36 (sx, *J* = 7.6 Hz, 2 H), 1.67 (m, 5 H), 2.34 (m, 2 H), 2.57 (t, *J* = 8.4 Hz, 2 H), 3.72 (t, *J* = 7.2 Hz, 2 H), 5.49 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.6, 17.8, 19.3, 27.9, 29.3, 33.6, 52.0, 126.1, 129.4, 172.5.

Cyclisation of *N*-Chloroamides; General Procedure

To a solution of chloroamide (3 mmol) in MeOH (7 mL) was added at 60 °C copper(I) chloride (30 mg, 0.3 mmol) and the reaction mixture stirred at this temperature for 36 h. Then TBME and aq ammonia (2 M) (10 mL each) were added, the layers separated and the aq layer was washed with TBME (3 × 10 mL). After drying the combined organic layers (Na_2SO_4), the solvent was removed in vacuo. From the residue the lactams were isolated by flash chromatography.

1-Butyl-5-chloromethyl-3,3-dimethylpyrrolidin-2-one (6a)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.2 Hz, 3 H), 1.13 (s, 3 H), 1.21 (s, 3 H), 1.33 (m, 2 H), 1.48 (m, 2 H), 1.78 (dd, *J* = 13.2, 7.3 Hz, 1 H), 2.03 (dd, *J* = 13.2, 7.8 Hz, 1 H), 2.93 (ddd, *J* = 13.8, 8.1, 5.3 Hz, 2 H), 3.62 (m, 2 H), 3.83 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 20.1, 25.5, 25.8, 29.2, 38.2, 39.9, 40.1, 45.5, 54.5, 179.9.

Anal. Calcd for $C_{11}H_{20}NOCl$: C, 60.68, H, 9.26, N, 6.43. Found: C, 60.80, H, 9.64, N, 6.33.

1-Butyl-5-chloromethyl-4-methylpyrrolidin-2-one (6b)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.2 Hz, 3 H), 1.16 (t, *J* = 7.2 Hz, 3 H), 1.34 (m, 2 H), 1.49 (m, 2 H), 1.99 (dd, *J* = 17.1, 4.8 Hz, 1 H), 2.35 (m, 1 H), 2.69 (m, 1 H), 2.89 (m, 2 H), 3.62 (m, 2 H), 3.69 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 19.9, 20.4, 29.3, 38.2, 40.1, 42.1, 44.3, 65.4, 174.2.

1-Butyl-5-chloromethyl-3-methylpyrrolidin-2-one (6c)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 6.8 Hz, 3 H), 1.27 (d, *J* = 6.0 Hz, 3 H), 1.35 (m, 2 H), 1.52 (m, 3 H), 2.46 (m, 2 H), 2.97 (m, 1 H), 3.68 (d, *J* = 4.4 Hz, 2 H), 3.72 (m, 1 H), 3.88 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.6, 16.4, 20.0, 29.2, 30.8, 35.7, 40.1, 45.4, 55.7, 177.4. Minor isomer, selected signals: δ = 16.8, 20.1, 31.5, 35.2, 40.4, 45.5, 56.1.

Anal. Calcd for $C_{10}H_{18}NOCl$: C, 58.96; H, 8.91; N, 6.88. Found: C, 58.71; H, 9.13; N, 6.49.

1-Butyl-5-chloromethylpyrrolidin-2-one (6d)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.2 Hz, 3 H), 1.34 (m, 2 H), 1.50 (m, 2 H), 1.99 (m, 2 H), 2.19 (m, 2 H), 2.93 (m, 1 H), 3.63 (d, *J* = 4.8 Hz, 2 H), 3.64 (m, 1 H), 3.93 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 20.1, 22.2, 29.4, 29.8, 40.2, 45.5, 57.8, 174.9.

Anal. Calcd for $C_9H_{16}NOCl$: C, 56.99, H, 8.50, N, 7.38. Found: C, 57.26, H, 8.23, N, 7.11.

1-Acetyl-2-chloromethyl-4,4-dimethylpyrrolidine (6e)

This reaction was performed with chloroamide (0.3 mmol). Due to the low yield a ^{13}C NMR was not obtained.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (s, 6 H), 1.86 (dd, *J* = 7.8, 3.0 Hz, 2 H), 2.00 (s, 3 H), 3.23 (s, 2 H), 3.73 (dd, *J* = 10.8, 2,1 Hz, 1 H), 4.05 (dd, *J* = 10.8, 6.0 Hz, 1 H), 4.33 (m, 1 H).

3-Butyl-4-chloromethyloxazolidin-2-one (6f)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 8.0 Hz, 3 H), 1.66 (m, 2 H), 1.91 (m, 1 H), 3.08 (m, 1 H), 3.46 (m, 1 H), 3.65 (m, 2 H), 4.24 (dd, *J* = 8.4, 4.4 Hz, 1 H), 4.41 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.1, 20.7, 29.9, 43.9, 55.6, 65.3, 160.2.

1-*tert*-Butyl-5-chloromethyl-3,3-dimethylpyrrolidin-2-one (6h)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (s, 3 H), 1.22 (s, 3 H), 1.45 (s, 9 H), 1.99 (d, *J* = 2.7 Hz, 2 H), 3.40 (dd, *J* = 10.8, 9.6 Hz, 1 H), 3.73 (m, 1 H), 3.88 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.8, 28.5, 28.6, 37.0, 40.1, 47.5, 54.2, 56.2, 179.9.

Anal. Calcd for $C_{11}H_{20}NOCl$: C, 60.68; H, 9.26; N, 6.43. Found: C, 60.69; H, 9.22; N, 6.31.

1-Phenylethyl-5-chloromethyl-3,3-dimethylpyrrolidin-2-one (6i)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (s, 3 H), 1.28 (s, 3 H), 1.65 (t, *J* = 7.2 Hz, 3 H), 1.86 (m, 2 H), 3.39 (m, 2 H), 3.48 (m, 1 H), 5.43 (m, 1 H), 7.32 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.1, 25.6, 25.9, 38.1, 39.7, 46.6, 46.9, 54.4, 126.7, 127.3, 128.6, 138.8, 179.4. Minor isomer, selected signals: δ = 25.7, 26.0, 39.0, 49.3, 50.6, 54.3.

Anal. Calcd for $C_{15}H_{20}NOCl$: C, 67.79; H, 7.58; N, 5.27. Found: C, 67.55; H, 7.86; N, 4.98.

1-Butyl-5-(1-chloroethyl)pyrrolidin-2-one (6j)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 7.6 Hz, 3 H), 1.37 (m, 2 H), 1.55 (d, *J* = 6.8 Hz, 3 H), 2.07 (m, 2 H), 2.37 (m, 2 H), 2.54 (m, 2 H), 2.96 (m, 1 H), 3.76(m, 2H), 4.41 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.6, 18.3, 20.0, 20.5, 29.0, 30.1, 40.0, 57.3, 62.1, 174.9.

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