# Synthesis of 3-Alkyl-4-(chloromethyl)-1-RSO$_2$-1*H*-pyrrol-2(5*H*)-ones, Using a Sequential ATRC/[1,2]-Elimination, from 2,2-Dichloro-*N*-(2-chloroallyl)-*N*-RSO$_2$-amides

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**Abstract:** The preparation of 3-alkyl-4-(chloromethyl)-1-RSO$_2$-1*H*-pyrrol-2(5*H*)-ones was efficiently accomplished through a [1,2]-elimination of γ-lactams derived from the copper(I)-catalysed ATRC of 2,2-dichloro-*N*-(2-chloroallyl)-*N*-RSO$_2$-amides. The two reactions can be integrated into a sequential one-pot process.

**Key words:** copper, cyclization, elimination, lactams, radical reaction

The transition-metal-catalysed atom-transfer radical cyclization (TMC-ATRC) is a modern and powerful technique for the preparation of both N- and O-heterocycles.[1] One particularly useful application is the synthesis of polyhalogenated γ-lactams from N-protected *N*-allyl-α-haloamides.[1,2a,3] Attractive aspects of the method are: (i) high efficacy, (ii) easy execution and workup, (iii) high productivity, (iv) catalytic nature, and (vi) preservation of all the starting C–X functionalities on converting reactant into product. Additionally, the preparation of interesting natural or synthetic bioactive molecules, like chaetomellic anhydrides A and C,[4a–d] roccellic acid,[4d] tyromicin A,[4e] gabapentin,[4f,g] pilolactam,[4h] molecules with herbicidal activity,[4i] and the alkaloids trachelanthamine, haemantidine, and pretazzetine,[4j] has been achieved using a strategic TMC-ATRC step in the synthetic route.

Copper(I) halide complexes with polydentate nitrogen ligands are by far the preferred catalysts,[1a–f,2] being inexpensive and easy to prepare. Moreover they are versatile since the redox features of the complex can be adjusted by simply changing the ligand, whose number is large and ever increasing, thanks to the advancements in the sister technique of atom transfer radical polymerization.[5] With particularly reactive amides or when a nucleophilic solvent, like acetonitrile or *N*,*N*-dimethylformamide, is used, the ligand can be left out.[2a]

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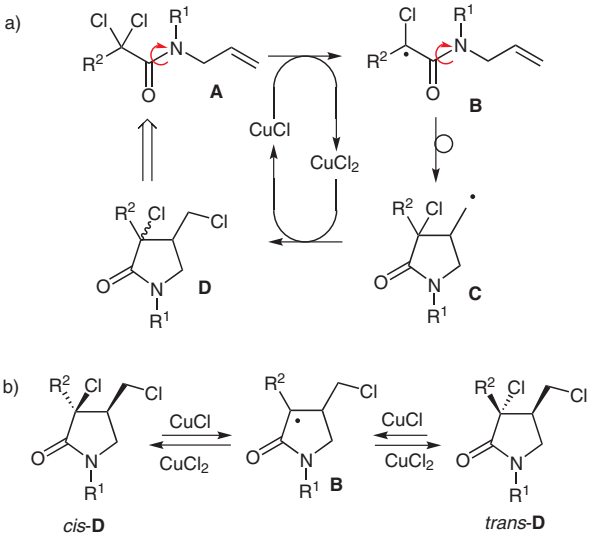
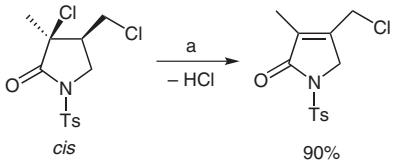
The recognized mechanism for the ATRC reaction consists of three elementary steps [Scheme 1 (a)].[1] First the Cu(I)X[L$_m$] metal complex reversibly abstracts a halogen atom from the substrate **A**, generating a radical species and increasing its oxidation state by one {Cu(II)X$_2$[L$_m$]}. The radical intermediate **B**, in the following step, adds to the tethered C=C bond, yielding a new radical **C**. Finally, this radical **C** is quenched by halogen transfer from the copper(II) complex, affording the reaction product **D**. In this way Cu(I)X[L$_m$], the active form of the catalyst, is regenerated. The atom transfers to and from the metal complex follow a concerted mechanism, via an inner-sphere single-electron-transfer process.[6]




**Scheme 1** (a) Copper-catalyzed ATRC of *N*-allyl-α-polychloroamides to form γ-lactams; (b) epimerization of the C3 centre of γ-lactams **D**

The substituent R$^1$ on the nitrogen atom of amide **A** plays a pivotal role in ensuring an efficient cyclization, since it, by influencing rotation around the amide bond, allows **A**, or the radical intermediate **B**, to adopt the appropriate con-

formation [Scheme 1 (a)].[7] This occurs because the N–CO rotational barrier is lowered as a result of a steric interaction, which can be also strengthened by an electronic effect. In fact, if the $R^1$ group is electronegative, the resonance stabilization between the lone pair on nitrogen and the neighbouring C=O is decreased, resulting in an amide bond having an enhanced single bond character. In addition, the electron-withdrawing substituent lowers the LUMO energy of the Cα–Cl bond, facilitating chlorine atom abstraction by the copper(I) complex.[2a,7a,b] Another important facet of the TMC-ATRC reaction is the configurational instability of the C3 stereogenic centre in the γ-lactam product **D**, which, under the reaction conditions, can be epimerized by the same ATRC catalyst [Scheme 1 (b)].[2a,4b,8]

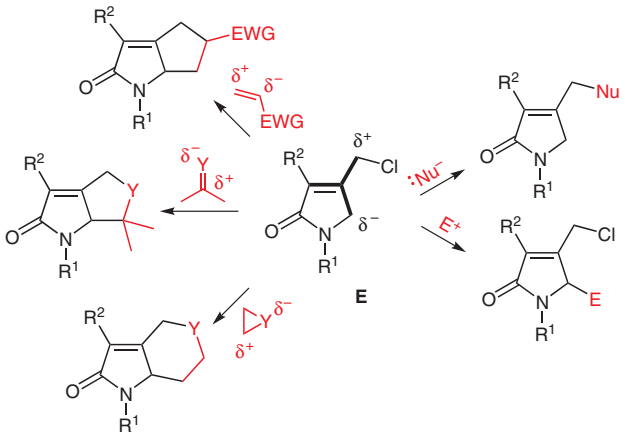



**Scheme 2** *Reagents and conditions*: (a) $(Ph_3P)_3RuCl_2$ (5 mol%), $C_6D_6$, argon, 100 °C, 72 h.

Although the preservation of all the halo functions in the final product is a key feature of the reaction,[1] the interest in the preparation of polychlorinated pyrrolidin-2-ones, using this technique, has essentially been confined to the testing of new catalysts, whereas the exploitation of the C–X functionalities in the cyclic products has been somewhat ignored. The few applications, reported in literature, excluding hydrodehalogenations, have regarded: stepwise or sequential radical processes,[8b,9] functional rearrangement into 5-methoxy-1*H*-pyrrol-2(5*H*)-ones or maleimides,[4a–4e,8a,10] preparation of bicyclo[3.2.0]hexan-2-ones,[11] dehydrohalogenations,[4j,8c,12] aromatization of bicyclic adducts,[8b,9b] and substitutions of the *exo*-Cl group with O-nucleophiles.[4j,13] Among these uses, the ruthenium-catalysed dehydrochlorination of *cis*-3-chloro-4-(chloromethyl)-1-tosylpyrrolidin-2-ones, reported by Slough and Rachita,[8c] captured our attention (Scheme 2).

In fact, 4-(chloromethyl)-1*H*-pyrrol-2(5*H*)-ones **E** (Scheme 3) are interesting molecules, which possess both a γ-*exo* electrophilic centre (the allylic chloro function) and a quiescent γ-*endo* nucleophilic site (the vinylogous C5–H hydrogens are relatively acidic), both conjugated to the α,β-unsaturated system. The synthetic potential of a structure like this, which in a sense mimics a trimethylenemethane arrangement, is enormous, as outlined by the examples in Scheme 3. In addition, the $\Delta^3$-unsaturation is a useful means to control the configuration of the substituents, at C3 and C4, through stereoselective hydrogenations.

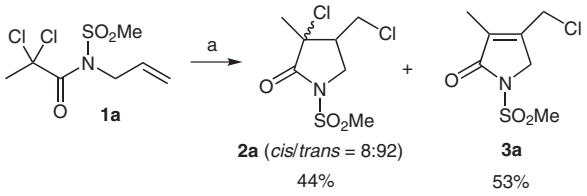
Nevertheless, and quite astonishingly, the study of the reactivity and of the synthetic potential of **E** has been completely neglected. Perhaps this is due to the absence of appropriate methods for their large-scale preparation. Indeed, to the best of our knowledge, the only viable process is still that published by Slough and Rachita (Scheme 2),[8c] but it uses a heavy (MW = 958.8) and expensive ruthenium catalyst, and it operates in a toxic solvent (benzene), under diluted conditions (substrate concentration = 0.12 M).




**Scheme 3** Some hypothetical uses of 4-(chloromethyl)-1*H*-pyrrol-2(5*H*)-ones following reaction with nucleophilic, electrophilic, or 1,2- or 1,3-dipolar reagents (in bold is the mimicked trimethylenemethane substructure)

We have recently demonstrated a tandem approach, involving an ATRC and a reductive [1,2]-elimination, both mediated by the system CuCl[PMDETA]/ascorbic acid/$Na_2CO_3$, to obtain **E** from *N*-(2-chloroallyl)-α-polychloroamides.[14] Unfortunately, the technique is devoid of any general applicability, yielding acceptable results in only a few cases.

For the sake of completeness, we have to mention two other reports on the isolation of compounds of type **E**: the preparation of a 4-(1-bromoethyl)-1*H*-pyrrol-2(5*H*)-one by bromination, with *N*-bromosuccinimide, of an N-substituted 4-ethyl-1,3-dimethyl-5-tosyl-1*H*-pyrrol-2(5*H*)-one (2 d, 70%),[15a] and the isolation of a 4-(chloromethyl)-1*H*-pyrrol-2(5*H*)-one as byproduct in the ATRC of *N*-propargyl-*N*-tosyltrichloroacetamide.[15b]




**Scheme 4** *Reagents and conditions*: (a) CuCl (10 mol%), DMF, argon, 80 °C, 24 h.

During our recent studies on the ATRC of *N*-alkyl-*N*-allyldichloroamides to γ-lactams, catalyzed by 'naked' copper(I) chloride ('ligand-free-like'-ATRC), we observed that, when *N*-mesyldichloroamide **1a** and copper(I) chloride (10 mol%) were heated at 80 °C in *N*,*N*-dimethylformamide (24 h), the γ-lactam **2a** was recovered along

**Table 1** [1,2]-Elimination from **2a** To Give 1*H*-Pyrrolidin-2-one **3a**

| Entry | Ratio *cis*/*trans* of **2a**[a] | Solvent (mL) | $Et_4NCl$ (mol%) | Temp (°C) | Time (h) | Conv.[b,c] (%) | Yield[b] (%) of **3a** |
|---|---|---|---|---|---|---|---|
| 1 | 58:42 | DMF (3) | 0 | 80 | 40 | 86 | 84 |
| 2 | 57:43 | DMF (3) | 5 | 80 | 40 | 88 | 84 |
| 3 | 57:43 | DMF (4) | 10 | 80 | 24 | 87 | 86 |
| 4 | 66:34 | DMF (3) | 20 | 80 | 23 | 90 | 90 |
| 5 | 55:45 | DMF (3) | 0 | 100 | 24 | 100 | 94 |
| 6 | 87:13 | DMF (3) | 0 | 100 | 24 | 100 | 93[d] |
| 7 | 87:13 | NMP (3) | 0 | 100 | 24 | 100 | 94[d] |
| 8[e] | 87:13 | DMF (45) | 0 | 100 | 24 | 100 | 94[d] |

[a] Reactions were performed using 5 mmol of substrate.
[b] Determined by GC.
[c] Unreacted material, which was always *trans*-**2a**.
[d] Determined on isolated material.
[e] This reaction was performed using 73.5 mmol of substrate.

with the 4-(chloromethyl)-1*H*-pyrrol-2(5*H*)-one **3a** (Scheme 4).[2a] To our surprise, the unsaturated γ-lactam **3a** was the main product: clearly, an *endo*-[1,2]-elimination (*E*) follows the ATRC. Furthermore the usual large preference for the *cis*-**2a** diastereomer was not observed as **2a** was isolated, almost exclusively, in the *trans* configuration. These experimental facts indicate, beyond any doubt, that **3a** is derived from the *anti*-dehydrochlorination of *cis*-**2a**.

We deemed that this attractive ATRC/[1,2]-elimination tandem transformation could have potential application as a new preparative method to form 4-(chloromethyl)-1*H*-pyrrol-2(5*H*)-ones. Our results are described herein.

At first, we tried to answer a preliminary question: what is the mechanism of the elimination step? The query was clarified by heating **2a** in *N*,*N*-dimethylformamide at 80 °C (Table 1, entry 1). The efficient formation of **3a** means that, contrary to the observations of Slough and Rachita, the dehydrohalogenation, in our case, is not metal-catalysed. Instead it is a typical *anti*-[1,2]-elimination mediated by *N*,*N*-dimethylformamide, which, therefore, plays the role of both solvent and base in the reaction mixture.[16]

Incidentally, this first test shed light on how to enhance the efficiency of the transformation. The fact that the yield of **3a** (84%) did not correspond to the percentage of the *cis*-isomer in the starting γ-lactam **2a** (58%) tells us two important things: (i) *trans*-**2a** epimerizes to *cis*-**2a**, and (ii) an ionic mechanism must be implicated, for the first time, in the configuration reversal.[17] Perhaps this involves an $S_N2$ reaction of the α-C–Cl group of *trans*-**2a** with chloride ions, freed during the facile elimination from the *cis* adduct (Scheme 5).

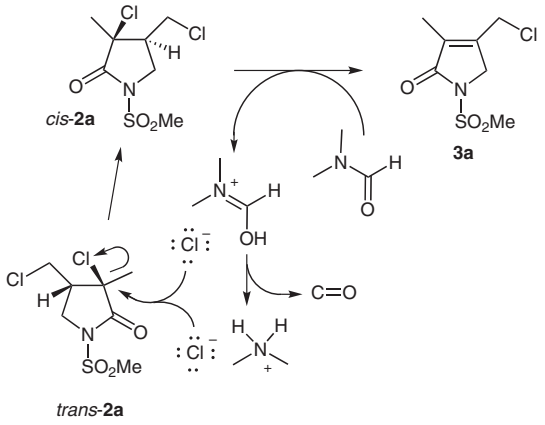
The unexpected epimerization can be fully understood if we take into account: (i) the polar aprotic nature of *N*,*N*-dimethylformamide, which exalts the chloride anion nucleophilicity,[18a] and (ii) the powerful electron-withdrawing effect of the sulfonyl group, which enforces the interaction between the π-LUMO of the C=O and the electron density that builds up, in the transition state of the $S_N2$ reaction, at the pentacoordinate C3 (this enhances the proclivity of the α-halogen in **2a** to be displaced).[18b] Both factors, cooperating synergistically, facilitate the inversion of configuration at C3.

Likely the increased reactivity of the α-chloro function, brought about by the sulfonyl substituent, is also a requisite for the smooth dehydrohalogenation of **2a**. The absence of any 4-(chloromethyl)-1*H*-pyrrol-2(5*H*)-one in the crude products obtained from the reaction of the *N*,*N*-diallyl- or *N*-allyl-*N*-benzyl-2,2-dichloropropanamides using copper(I) chloride in *N*,*N*-dimethylformamide at 100 °C,[2a] firmly corroborates this assumption.

Gratified by this first test, we tried to force the elimination in **2a** to completion. To this end, we thought it might be beneficial to add a source of chloride ion to the reaction mixture (Table 1, entries 2–4). However, no improvement was apparent, even when the chloride-carrier amounted to 20 mol%. In contrast, a modest increase of the reaction temperature to 100 °C was more rewarding: under these conditions, total conversion was indeed achieved (entries 5 and 6).

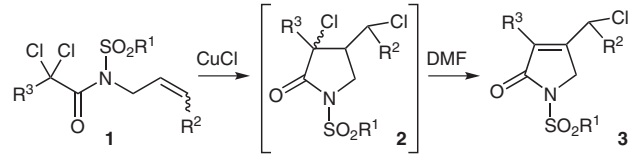
The dehydrochlorination works efficiently also on a preparative scale (entry 8) and *N*,*N*-dimethylformamide can be replaced by *N*-methylpyrrolidin-2-one without encountering any problems (entry 7).

The elimination was carried out in a sealed Schlenk reactor and an increase in pressure was evident inside the reaction tube. As we detected through the GC-MS of the reaction tube headspace, the pressure build-up is caused by the production of carbon monoxide. It originates from the decomposition of *N*,*N*-dimethylformamide (Scheme 5), a well-known phenomenon, whose rate increases at high temperatures and in the presence of acids or bases.[16a,19]




**Scheme 5** Mechanism of the elimination/epimerization of **2a** in *N*,*N*-dimethylformamide

To investigate the scope of the method, the starting *N*-allyl-*N*-sulfonyl-2,2-dichloroamides **1b–g** were synthesized. These substrates were then cycloisomerized using copper(I) chloride in acetonitrile, under 'ligand-free-like' conditions (Scheme 6 and Table 2).[2a] The desired γ-lactams **2** were secured in excellent yields and with a diastereomeric *cis*/*trans* ratio of ca. 60:40. For comparison, amides **1c** and **1d** were also cyclized, under standard conditions, using the redox complex CuCl[TMEDA]$_2$. As predicted, the diastereomeric ratio ameliorated consistently (85:15); the product yields were unaffected (Table 2, entries 3, 4 and 7, 8).[2a]




| | a | b | c | d | e | f | g | h | i | j |
|---|---|---|---|---|---|---|---|---|---|---|
| $R^1$ | Me | Me | Me | 4-tolyl | $CF_3$ | Me | Me | Me | Me | Me |
| $R^2$ | H | H | H | H | H | Me | Ph | H | H | H |
| $R^3$ | Me | H | Et | Et | Et | Me | Me | *i*-Pr | *n*-Hex | Cl |

**Scheme 6** Copper(I) chloride catalyzed ATRC/[1,2]-elimination of *N*-allyl-*N*-sulfonyl-α-polychloroamides

Owing to its thermal instability, substrate **1e** was unsuited to the ligand-free procedure at 100 °C. An ATRC catalysed by a copper(I) chloride complex that can operate at a lower temperature was, thus, needed. The powerful electron-withdrawing effect of the triflyl group ensures that **1e** has such a high activity, and an easy rotation around the amide bond, that it successfully undergoes complete cyclization using CuCl[TMEDA]$_2$ at even 0 °C (Table 2, entry 10).

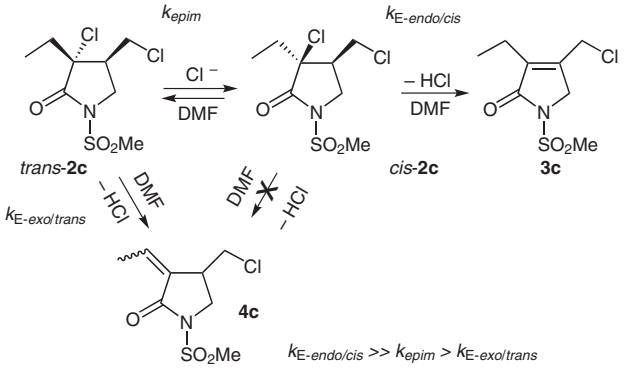
The γ-lactams **2b–g** (Scheme 6) were then subjected to the elimination protocol established for **2a**. The impact of the $R^3$ group at C3, on the reaction progress, was immediately apparent. When no substituent was present, as in **2b** ($R^3$ = H), harsher conditions (120 °C) were required although this resulted in an unselective reaction. Instead,

**Table 2** Preparation of the γ-Lactams **2** by Copper-Catalyzed ATRC

| Entry | Substrate (mmol) | Solvent (mL) | CuCl (mol%) | Temp (°C) | Time (h) | Conv.[a] (%) | Yield[b] (%) (ratio[c] *cis*/*trans*) |
|---|---|---|---|---|---|---|---|
| 1 | **1a** (5) | MeCN (2.5) | 10 | 100 | 23 | 100 | 97 (57:43) |
| 2 | **1b** (5) | MeCN (2.5) | 10 | 120 | 24 | 99 | 92 (27:73) |
| 3 | **1c** (15) | MeCN (7.5) | 10 | 100 | 24 | 100 | 96 (67:33) |
| 4 | **1c** (5) | MeCN (4) | 10[d] | 35 | 20 | 100 | 97 (86:14) |
| 5 | **1c** (5) | DMF (4) | 10[d] | 35 | 20 | 100 | 94 (86:14) |
| 6 | **1c** (5) | DMF (4) | 5[d] | 35 | 20 | 100 | 92 (85:15) |
| 7 | **1d** (5) | MeCN (2.5) | 10 | 100 | 22 | 100 | 98 (61:39)[e] |
| 8 | **1d** (5) | MeCN (4) | 10[d] | 35 | 23 | 100 | 95 (85:15)[e] |
| 9 | **1e** (5) | MeCN (4) | 10[d] | 20 | 20 | 100 | 80 (84:16)[e] |
| 10 | **1e** (5) | MeCN (4) | 10[d] | 0 | 20 | 100 | 93 (75:25)[e] |
| 11 | **1f** (5) | MeCN (2.5) | 10 | 100 | 24 | 100 | 93 (75:25) |
| 12 | **1g** (5) | MeCN (2.5) | 10 | 100 | 24 | 100 | 93 (93:7) |
| 13 | **1j** (5) | MeCN (2.5) | 10 | 80 | 4 | 100 | 98 |

[a] Determined by GC.
[b] Determined on isolated material.
[c] Ratio *cis*/*trans* determined by $^1$H NMR.
[d] CuCl[TMEDA]$_2$ was used.
[e] Ratio c*is*/*trans* determined by GC.

when $R^3$ was a larger sized group, such as in **2c** ($R^3$ = Et), a moderate regioselectivity problem arose. In addition to the lactam **3c**, derived from the expected *endo* dehydrochlorination, a small amount of the 3-ethylidene-γ-lactam **4c** (as a mixture of *E*/*Z* diastereomers) (Figure 1) was also afforded through a competing *exo*-elimination process (Table 3, entry 2). It is likely that, for steric reasons, the larger size of $R^3$ (β-branching) slows down the epimerization of *trans*-**2c** sufficiently so that the alternative *exo*-dehydrohalogenation pathway becomes competitive (Scheme 7).




**Scheme 7** Full reaction scheme for the sequential ATRC/[1,2]-elimination

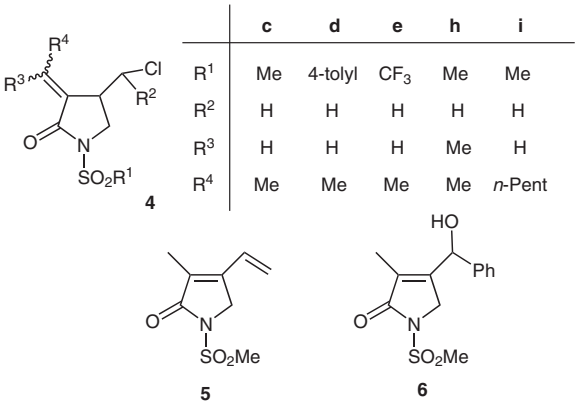



**Figure 1** Other products provided by the elimination step of γ-lactams **2**

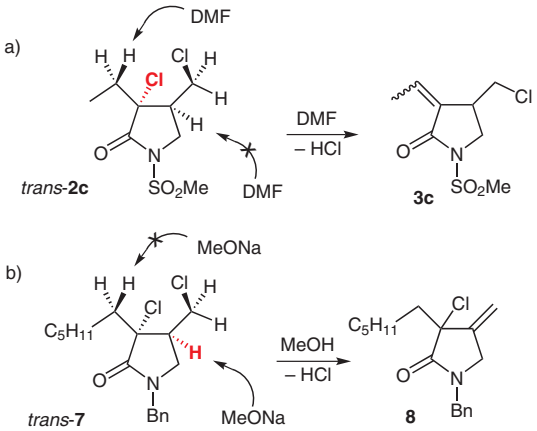
We tried to suppress the side reaction by changing the reaction conditions. Unfortunately, higher dilution (Table 3, entry 3), harsher conditions (entry 4), the addition of a chloride ion carrier (entry 5), or the use of more electronegative sulfonyl groups (entries 8 and 10) had no effect on the regioselectivity.

When stopping the dehydrohalogenation of **2c** after only 4.5 hours (entry 6), we observed that the transformation of the *cis* isomer was virtually complete, the unreacted material was essentially *trans*, and **4c** was formed in only 1% yield. This result demonstrates that the *endo*-elimination of *cis*-**2c** is by far the fastest process and that **4c** cannot be derived from *cis*-**2c** (Scheme 7). This last point was definitively corroborated by the quantitative transformation of the single isomer *cis*-**2e** into **3e** (entry 11). Under the same conditions **3e** and **4e** were recovered from the reaction of *trans*-**2e** (entry 12). The ratio $yield_{3e}/yield_{4e} \approx 4$ means the epimerization is only slightly faster than the *exo*-elimination (Scheme 7).

At this point the only remaining chance to substantially ameliorate the selectivity toward γ-lactams **3** was to use, as starting materials, dichloro-γ-lactams **2** with a higher *cis*/*trans* ratio (Table 3, entries 2, 7 and 8, 9). As mentioned earlier, this can be accomplished by carrying out the ATRC in the presence of copper(I) chloride complexes using nitrogen ligands (Table 2, entry 3, 4 and 7, 8).

Some years ago, during our studies on the functional rearrangement of polyhalogenated γ-lactams,[4a–c] we noted that, in sodium methoxide/methanol, molecules like *trans*-**7**, although unable to undergo *endo*-elimination, underwent dehydrohalogenation all the same, affording the 4-methylene-γ-lactam **8** [Scheme 8 (a)].[4b,c,10] Astonishingly this *exo*-regioselectivity at the C4 position is at odds with the *exo*-regioselectivity at C3, reported here, for the similar molecule *trans*-**2c** [Scheme 8 (b)]. These findings can be rationalized by considering that for *trans*-**7**, where a 'strong' base is involved and the α-Cl is not particularly activated, the elimination involved the more acidic C4–H hydrogen (E2-E1$_{cb}$ like),[20] while for *trans*-**2c**, where the base is weak and the α-Cl is instead strongly activated, elimination involved the more labile C3–Cl bond (Scheme 8).

In spite of the higher susceptibility towards the C4 *exo*-elimination, substrates **2f** and **2g**, which have a secondary *exo* C–Cl function, also gave the lactams **3**. However, the conversion of **2g** was not as selective as usual, and the yield of **3g** was only fair (Table 3, entry 14). For **2f**, the reaction did not stop at the stage of **3f** and, in part, a second elimination occurred, delivering the conjugated dienone **5** (Table 3, entry 13 and Figure 1).




**Scheme 8** Rationalization of the different *exo*-regioselectivity in the elimination of analogous *trans*-3-chloro-4-(chloromethyl)-γ-lactams

**Table 3** Preparation of the α,β-Unsaturated γ-Lactams **3**

| Entry | Substrate (mmol) | Substrate (dr) | Solvent (mL) | CuCl (%) | TMEDA (%) | Temp (°C) | Time (h) | Conv.[a] (%) | Yield (%) **3**[b] | **4**[b,c] | Other[b] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **2a** (3) | 87:13 | DMF (3) | 0 | 0 | 100 | 24 | 100 | 93 | 0 | – |
| 2 | **2c** (5) | 67:33 | DMF (3) | 0 | 0 | 100 | 24 | 100 | 75 | 11 (60:40) | – |
| 3 | **2c** (5) | 67:33 | DMF (10) | 0 | 0 | 100 | 24 | 99 | 75 | 14 (82:18) | – |
| 4 | **2c** (5) | 67:33 | DMF (3) | 0 | 0 | 120 | 18 | 100 | 76 | 10 (86:14) | – |
| 5[d] | **2c** (5) | 67:33 | DMF (3) | 0 | 0 | 100 | 24 | 100 | 76 | 14 (78:22) | – |
| 6 | **2c** (5) | 67:33 | DMF (3) | 0 | 0 | 100 | 4.5 | 72[b] | 66 | 1 | – |
| 7 | **2c** (3) | 85:15 | DMF (1.8) | 0 | 0 | 100 | 24 | 100 | 84 | 7 (68:32) | – |
| 8 | **2d** (3) | 61:39 | DMF (1.8) | 0 | 0 | 100 | 24 | 100 | 74 | 23 (81:19) | – |
| 9 | **2d** (3) | 86:14 | DMF (1.8) | 0 | 0 | 100 | 24 | 100 | 89 | 9 (80:20) | – |
| 10 | **2e** (3) | 50:50 | DMF (1.8) | 0 | 0 | 100 | 24 | 100 | 85 | 9 (87:13) | – |
| 11 | *cis*-**2e** (3) | – | DMF (1.8) | 0 | 0 | 100 | 23 | 100 | 91 | 0 | – |
| 12 | *trans*-**2e** (1) | – | DMF (1.8) | 0 | 0 | 100 | 23 | 100 | 76 | 20 (82:18) | – |
| 13 | **2f** (5) | 42:33:21:4 | DMF (3) | 0 | 0 | 100 | 24 | 100 | 46 | 0 | 46 (**5**) |
| 14 | **2g** (5) | 62:31:7 | DMF (3) | 0 | 0 | 100 | 24 | 100 | 53 | 0 | – |
| 15 | **2j** (5) | – | DMF (3) | 0 | 0 | 80 | 6 | 100 | 87 | – | – |
| 16 | **1a** (5) | – | DMF (4) | 10 | 0 | 100 | 24 | 100 | 92 | 0 | – |
| 17 | **1c** (5) | – | DMF (4) | 10 | 0 | 100 | 24 | 100 | 78 | 6 (77:23) | – |
| 18 | **1c** (5) | – | NMP (4) | 10 | 0 | 100 | 24 | 100 | 94 | 0 | – |
| 19 | **1d** (5) | – | DMF (4) | 10 | 0 | 100 | 24 | 100 | 80 | 15 (82:18) | – |
| 20 | **1d** (5) | – | DMF (4) | 5 | 10 | –[e] | –[e] | 100 | 86 | 9 (76:24) | – |
| 21 | **1d** (5) | – | DMF (4) | 5 | 10 | –[f] | –[f] | 100 | 83 | 11 (78:22) | – |
| 22 | **1f** (5) | – | DMF (4) | 10 | 0 | 100 | 24 | 100 | 48 | 0 | 43 (**5**) |
| 23 | **1g** (5) | – | DMF (4) | 10 | 0 | 100 | 24 | 100 | 0 | 0 | 49 (**6**) |
| 24 | **1h** (5) | – | DMF (4) | 10 | 0 | 100 | 24 | 100 | 77 | 14 | – |
| 25 | **1i** (5) | – | DMF (4) | 10 | 0 | 100 | 24 | 100 | 76 | 10 (80:20) | – |

[a] Determined by GC.
[b] Determined on isolated material.
[c] In parentheses is the *E*/*Z* ratio determined by $^1$H NMR.
[d] $Et_4NCl$ was added (20 mol%).
[e] $T_I$ = 35 °C (12 h) and $T_{II}$ = 100 °C (24 h).
[f] $T_I$ = 35 °C (5 min) to 100 °C in 25 min and $T_{II}$ = 100 °C (23.5 h).

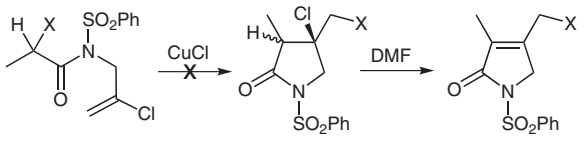
Finally, we explored the integration of ATRC and [1,2]-elimination into a one-pot process. As both reactions can be carried out in the same solvent, this was very easy to accomplish. In fact, it was just enough to heat at 100 °C a mixture of the starting amide and copper(I) chloride in *N*,*N*-dimethylformamide (or NMP), to obtain the 4-(chloromethyl)-1*H*-pyrrol-2(5*H*)-ones **3**, with the same effectiveness observed with the step-by-step procedure (Table 3, entries 16–25). Unexpectedly, with substrate **1g** (entry 23), rather than isolate **3g**, the hydroxy analogue **6** was recovered (this result was not examined further).

The trichloroacetamide **1j** was unsuited to the sequential one-pot procedure. In fact, at 70–80 °C, the elimination product **3j**, likely owing to the presence of copper(I) chloride, came up against a number of side-transformations, whereas at lower temperature (60 °C, 17 h) the dehydrohalogenation was partial. Thus we opted for the stepwise strategy and prepared in high yield, through the ligand-

free ATRC of **1j**, the trichlorolactam **2j** (Table 2, entry 13). Owing to the double substitution with halogens at C3, the elimination step of **2j** was facilitated, and the reaction could be effectively completed at 80 °C in only six hours, giving the functionalised lactam **3j**, which features one allylic and one vinylic chlorine (Table 3, entry 15). The low reaction temperature, in this case, prevented the decomposition of *N*,*N*-dimethylformamide hydrochloride and the subsequent pressure build-up, inside the Schlenk tube.

Since the best outcome of the elimination step requires γ-lactams **2** with a higher content of *cis* diastereomer (see above), we tried to reach such a goal, also in the sequential process. To this aim we first established that the CuCl[TMEDA]$_2$ catalysed ATRCs in *N*,*N*-dimethylformamide or in acetonitrile were alike (Table 2, entries 4–6). Then, the cycloisomerization in *N*,*N*-dimethylformamide, catalysed by the copper(I) complex, was successfully joined to the elimination step, having the forethought to let the ATRC to go to completion at 'low' temperature (Table 3, entry 19 and 20).

To bypass the regioselectivity problem we also tried the ATRC of the *N*-(2-chloroallyl)-α-monohalopropanamides **9**.[21] The corresponding γ-lactams **10**, in fact, have an α-H adjacent to the C=O function, which, reasonably, can be easily epimerized under basic conditions, affording the desired configuration for the *endo*-elimination step (Scheme 9). Unfortunately, we were unable to achieve any cyclization of **9**, under a variety of reaction conditions. Likely, as we observed in the case of the *N*-benzyl-2,2-dichloro-*N*-(2-chloroallyl)acetamide,[14] the alleged intramolecular hydrogen bond, between the α-H and the vinylic chlorine, forces the amide **9** to adopt a conformation unsuitable for the cyclization, opening the door to side reactions.




**Scheme 9** ATRC/[1,2]-elimination of *N*-(2-chloroallyl)-α-monohalopropanamides

In this work we have shown that the 3-alkyl-4-(chloromethyl)-1-RSO$_2$-1*H*-pyrrol-2(5*H*)-ones can be efficiently prepared through a [1,2]-elimination of γ-lactams derived from the copper-catalysed ATRC of 2,2-dichloro-*N*-(2-chloroallyl)-*N*-RSO$_2$-amides. The reactivity of these products, although not fully assessed as yet, seems very appealing. We also deem that the use of the carbon monoxide, released by decomposition of *N*,*N*-dimethylformamide, in a consecutive carbonylative reaction of the unsaturated lactams **3**, might turn out to be synthetically useful.[22] Attractive features of the method are: simplicity, inexpensive, high productivity, and the possibility to integrate ATRC and elimination into a sequential one-pot process. We urge parties who are interested in developing the chemistry of 4-(chloromethyl)-1*H*-pyrrol-2(5*H*)-ones to contact us for a supply of these products.

Reagents and solvents were standard grade commercial products, and generally used without further purification. CuCl was a product of purity grade puriss. p.a. ACS ≥97%. Flash chromatography was performed using Silica Gel 60 Merck (0.040–0.063 mm); PE = petroleum ether. 10% HCl was w/v.

The amides **1a–j** were efficiently assembled by reaction of acyl chlorides with sodium allyl(sulfonyl)amides, following or adapting standard procedures.[2a,8a,23] Only in the case of **1e**, was the acylation[24] of the *N*-allyltrifluoromethanesulfonamide carried out in the presence of pyridine [since **1e** is prone to hydrolysis, the reaction mixture was concentrated and directly purified as fast as possible by chromatography (PE–Et$_2$O, 100:0 to 70:30); notwithstanding the problem was only partially contained, and the product was recovered in only fair yield, 51%]. Commercial anhyd THF or CH$_2$Cl$_2$, dried over three batches of 3 Å molecular sieves (5% w/v, 12 h), were used as solvents in these reactions.

The starting *N*-allyl sulfonamides were easily obtained by sulfonylation, with commercial reagents, of allylamine, using or adapting literature methods.[25] Cinnamylamine and crotylamine were prepared from the corresponding allyl chloride by the Delèpine method.[26]

Products **2a**, **3a**, and **2b** are known compounds.[2a,8a] IR and MS spectra were recorded, respectively, on Perkin Elmer 1600 Series FTIR, or Avatar 320 FT/IR, and HP 5890 GC–HP 5989A MS (for EI 70 eV) or Bruker Esquire 4000 (for ESI) instruments. NMR spectra were recorded on a Varian 500 MHz spectrometer. Signal attributions were based on gCOSY and gHSQC spectroscopy; only in the case of **2j** and **3j** were signals assigned by analogy with related products. The relative configurations of γ-lactams **2** and **4** were determined by NOESY experiments. Elemental analyses were performed on the EA 1110 Carlo Erba.

**3-Chloro-4-(chloromethyl)-3-methyl-1-(methylsulfonyl)pyrrolidin-2-one (2a); Typical Procedure 1**

CuCl (0.050 mg, 0.5 mmol) and 2,2-dichloroamide **1a** (1.301 g, 5 mmol) were weighed in a Schlenk tube fitted with a pierceable septum (blocked by a screw cap) and a magnetic stirring bar. MeCN (2.5 mL) was then added under argon. The mixture was stirred at 100 °C and after 23 h was diluted with H$_2$O (30 mL), acidified with 10% HCl, and extracted with CH$_2$Cl$_2$ (4 × 5 mL). The combined organic layers were concentrated. Flash chromatography of the crude (silica gel, PE–Et$_2$O, 100:0 to 10:90) gave the pyrrolidinone **2a** (1.262 g, 97%) as a white powder; inseparable mixture of diastereomers *cis*/*trans* 57:43 ($^1$H NMR).

**3-Chloro-4-(chloromethyl)-1-(methylsulfonyl)pyrrolidin-2-one (2b)**

Following typical procedure 1, **1b** (1.231 g, 5 mmol) was treated with CuCl (0.050 mg, 0.5 mmol) in MeCN (2.5 mL) at 120 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–Et$_2$O, 100:0 to 10:90) gave **2b** (1.133 g, 92%) as a pale brownish powder; inseparable mixture of diastereomers *cis*/*trans* 27:73 ($^1$H NMR).

**3-Chloro-4-(chloromethyl)-3-ethyl-1-(methylsulfonyl)pyrrolidin-2-one (2c)**

Following typical procedure 1, **1c** (4.113 g, 15 mmol) was treated with CuCl (0.150 mg, 1.5 mmol) in MeCN (7.5 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–Et$_2$O, PE–Et$_2$O, 80:20 to 20:80 gradient) gave **2c** (3.948 g, 96%) as

a pale yellow oil; inseparable mixture of diastereomers *cis*/*trans* 67:33 ($^1$H NMR).

IR (film): 1743 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ (*cis*) = 1.06 (t, *J* = 7.4 Hz, 3 H, C*H*$_3$CH$_2$), 2.22, 2.21 (dq, *J* = 7.4 Hz, 2 H, CH$_2$CH$_3$), 2.84 (m, 1 H, H4), 3.27 (s, 3 H, $CH_3SO_2$), 3.49 (dd, *J* = 11.3, 10.0 Hz, 1 H, H5), 3.67 (dd, *J* = 11.4, 9.0 Hz, 1 H, CHCl), 3.80 (dd, *J* = 11.4, 5.2 Hz, 1 H, CHCl), 4.15 (dd, *J* = 10.0, 7.0 Hz, 1 H, H5); δ (*trans*) = 1.18 (t, *J* = 7.3 Hz, 3 H C*H*$_3$CH$_2$), 1.97, 2.15 (2 m, 2 H, CH$_2$CH$_3$), 2.97 (m, 1 H, H4), 3.28 (s, 3 H, $CH_3SO_2$), 3.52 (dd, *J* = 11.6, 11.4 Hz, 1 H, CHCl), 3.73 (dd, *J* = 11.6, 3.8 Hz, 1 H, CHCl), 3.87 (dd, *J* = 10.6, 3.1 Hz, 1 H, H5), 4.11 (dd, *J* = 10.6, 6.4 Hz, 1 H, H5).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ (*cis*) = 9.3, 28.8, 39.9, 41.3, 43.0, 47.0, 72.8, 169.6; δ (*trans*) = 8.3, 25.8, 40.3, 41.8, 46.1, 46.8, 72.2, 169.6.

MS (EI, 70 eV): *m*/*z* (%) = 245 (55) [(M + 1) – 29]$^+$, 238 (6), 196 (100), 79 (31).

Anal. Calcd for $C_8H_{13}Cl_2NO_3S$: C, 35.05; H, 4.78; N, 5.11; S, 11.70. Found: C, 34.92; H, 4.84; N, 5.11; S, 11.67.

**3-Chloro-4-(chloromethyl)-3-ethyl-1-tosylpyrrolidin-2-one (2d)**
Following typical procedure 1, **1d** (1.751 g, 5 mmol) was treated with CuCl (0.050 mg, 0.5 mmol) in MeCN (2.5 mL) at 100 °C for 22 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 80:20 to 20:80) gave **2d** (1.716 g, 98%) as a white powder; inseparable mixture of diastereomers *cis*/*trans* 61:39 (GC).

IR (KBr): 1745 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ (*cis*) = 0.98 (t, *J* = 7.3 Hz, 3 H, C*H*$_3$CH$_2$), 2.06, 2.12 (2 dq, *J* = 14.8, 7.3 Hz, 1 H each, CH$_2$CH$_3$), 2.44 (s, 3 H, C*H*$_3$PhSO$_2$), 2.77 (m, 1 H, H4), 3.44 (t, *J* = 10.0, 9.7 Hz, 1 H, H5), 3.59 (dd, *J* = 11.3, 9.1 Hz, 1 H, CHCl), 3.75 (dd, *J* = 11.1, 5.2 Hz, 1 H, CHCl), 4.21 (dd, *J* = 10.0, 7.3 Hz, 1 H, H5), 7.35 (d, *J* = 8.2 Hz, 2 H, ArH), 7.90 (d, *J* = 8.4 Hz, 2 H, ArH); δ (*trans*) = 1.06 (t, *J* = 7.3 Hz, 3 H, C*H*$_3$CH$_2$), 1.68 (dq, *J* = 14.8, 7.3 Hz, 1 H, CH$_2$CH$_3$), 1.98 (dq, *J* = 14.8, 7.3 Hz, 1 H, CH$_2$CH$_3$), 2.44 (s, 3 H, $CH_3$Ph), 2.85 (m, 1 H, H4), 3.32 (dd, *J* = 11.2, 9.8 Hz, 1 H, CHCl), 3.64 (dd, *J* = 11.2, 4.0 Hz, 1 H, CHCl), 3.94 (dd, *J* = 10.6, 3.1 Hz, 1 H, H5), 4.09 (dd, *J* = 10.6, 6.3 Hz, 1 H, H5), 7.35 and 7.92 (2 d, *J* = 8.2 Hz, 2 H each, Ph).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ (*cis*) = 9.2, 21.6, 29.6, 41.3, 42.6, 47.5, 72.9, 127.9, 129.8, 133.7, 145.8, 168.3; δ (*trans*) = 8.0, 21.6, 25.8, 42.6, 46.2, 47.3, 72.1, 128.0, 129.8, 134.0, 145.7, 168.3.

MS (EI, 70 eV): *m*/*z* (%) = 321 (3) [(M + 1) – 29]$^+$, 285 (14), 272, (6), 257 (5), 250 (7), 208 (14), 155 (35), 91 (100).

Anal. Calcd for $C_{14}H_{17}Cl_2NO_3S$: C, 48.01; H, 4.89; N, 4.00; S, 9.15. Found: C, 48.24; H, 4.91; N, 4.02; S, 9.14.

**3-Chloro-4-(chloromethyl)-3-ethyl-1-(trifluoromethylsulfonyl)pyrrolidin-2-one (2e) in the Presence of a Nitrogen Ligand; Typical Procedure 2**
CuCl (50 mg, 0.5 mmol) and amide **1e** (1.641 g, 5 mmol) were weighed in a Schlenk tube fitted with a pierceable septum (blocked by a screw cap) and a magnetic stirring bar. The tube was thermostatted at 0 °C. MeCN (4 mL) was added under argon and, then, TMEDA (151 μL, 0.10 mmol) was injected through the septum with a microsyringe. The mixture was stirred for 20 h. Afterwards it was diluted with $H_2O$ (20 mL), acidified with 10% HCl and extracted with $CH_2Cl_2$ (3 × 10 mL). Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 30:70) gave the γ-lactams *cis*-**2e** and *trans*-**2e**).

**Diastereomer *cis*-2e**
Brownish oil; yield: 1.152 g (70%).

IR (film): 1748 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.5 Hz, 3 H, C*H*$_3$CH$_2$), 2.19, 2.28 (2 dq, *J* = 14.6, 7.5 Hz, 1 H each, 2 H, CH$_2$CH$_3$), 2.90 (m, 1 H, H4), 3.65 (t, *J* = 10.1 Hz, 1 H, H5), 3.68 (dd, *J* = 11.5, 9.0 Hz, 1 H, CHCl), 3.82 (dd, *J* = 11.5, 5.1 Hz, 1 H, CHCl), 4.22 (dd, *J* = 10.1, 7.2 Hz, 1 H, H5).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 9.1, 29.4, 40.7, 42.8, 48.7, 71.9, 119.4, 167.8.

MS (EI, 70 eV): *m*/*z* (%) = 299 (38) [(M + 1) – 29]$^+$, 250 (100), 69 (36).

Anal. Calcd for $C_8H_{10}Cl_2F_3NO_3S$: C, 29.28; H, 3.07; N, 4.27; S, 9.77. Found: C, 29.31; H, 3.08; N, 4.28; S, 9.82.

**Diastereomer *trans*-2e**
Brownish oil; yield: 0.378 g (23%).

IR (film): 1745 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.8 Hz, 3 H, C*H*$_3$CH$_2$), 1.88, 2.20 (2 dq, *J* = 14.8, 7.8 Hz, 1 H each, 2 H, CH$_3$CH$_2$), 3.00 (m, 1 H, H4), 3.48 (dd, *J* = 12.0, 8.6 Hz, 1 H, CHCl), 3.73 (dd, *J* = 12.0, 3.9 Hz, 1 H, CHCl), 4.03 (dd, *J* = 11.0, 2.4 Hz, 1 H, H5), 4.26 (dd, *J* = 11.0, 6.7 Hz, 1 H, H5).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 8.2, 25.7, 41.5, 45.8, 48.6, 71.3, 119.3, 167.8.

MS (EI, 70 eV): *m*/*z* (%) = 299 (29) [(M + 1) – 29]$^+$, 250 (100), 69 (43).

Anal. Calcd for $C_8H_{10}Cl_2F_3NO_3S$: C, 29.28; H, 3.07; N, 4.27; S, 9.77. Found: C, 29.19; H, 3.09; N, 4.29; S, 9.80.

**3-Chloro-4-(1-chloroethyl)-3-methyl-1-(methylsulfonyl)pyrrolidin-2-one (2f)**
Following typical procedure 1, **1f** (1.371 g, 5 mmol) was treated with CuCl (0.050 mg, 0.5 mmol) in MeCN (2.5 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 20:80) gave **2f** (1.278 g, 93%) as a pale-yellow oil; inseparable mixture of diastereomers, *cis*/*trans* 75:25, (*cis*$_I$ + *cis*$_{II}$)/(*trans*$_I$ + *trans*$_{II}$) (42 + 33):(21 + 4) ($^1$H NMR).

IR (film): 1743 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ (*cis I*) = 1.71 (d, *J* = 6.7 Hz, 3 H, C*H*$_3$CH), 1.85 (s, 3 H, C3-CH$_3$), 2.48 (dt, *J* = 10.5, 6.9 Hz, 1 H, H4), 3.28 (s, 3 H, $CH_3SO_2$), 3.53 (dd, *J* = 10.5, 9.5 Hz, 1 H, H5), 4.21 (dd, *J* = 10.5, 7.1 Hz, 1 H, H5), 4.27 (m, 1 H, CHCl); δ (*cis II*) = 1.57 (d, *J* = 6.5 Hz, 3 H, C*H*$_3$CH), 1.96 (s, 3 H, C3-CH$_3$), 2.54 (dt, *J* = 10.5, 6.9 Hz, 1 H, H4), 3.28 (s, 3 H, $CH_3SO_2$), 3.36 (dd, *J* = 10.5, 9.5 Hz, 1 H, H5), 3.94 (dd, *J* = 10.5, 7.1 Hz, 1 H, H5), 4.33 (m, 1 H, CHCl); δ (*trans I*) = 1.65 (d, *J* = 6.8 Hz, 3 H, C*H*$_3$CH), 1.81 (s, 3 H, C3-CH$_3$), 2.81 (dt, *J* = 10.5, 6.9 Hz, 1 H, H4), 3.28 (s, 3 H, $CH_3SO_2$), 3.85 (dd, *J* = 10.5, 9.5 Hz, 1 H, H5), 4.14 (dd, *J* = 10.5, 7.1 Hz, 1 H, H5), 4.27 (m, 1 H, CHCl); δ (*trans II*) = 1.48 (d, *J* = 6.5 Hz, 3 H, C*H*$_3$CH), 1.78 (s, 3 H, C3-CH$_3$), 3.01 (dt, *J* = 10.5, 6.9 Hz, 1 H, H4), 3.28 (s, 3 H, $CH_3SO_2$), 3.81 (dd, *J* = 10.5, 9.5 Hz, 1 H, H5), 4.02 (dd, *J* = 10.5, 7.1 Hz, 1 H, H5), 4.21 (overlapped, 1 H, CHCl).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ (*cis I*) = 23.9, 25.3, 39.9, 47.7, 51.9, 56.6, 68.0, 170.3; δ (*cis II*) = 22.9, 25.0, 39.8, 45.8, 51.9, 53.8, 69.9, 170.5; δ (*trans I*) = 20.4, 23.5, 40.5, 44.4, 51.3, 55.5, 67.8, 170.4; δ (*trans II*) = 20.9, 23.9, 40.3, 44.4, 51.7, 54.3, 67.2, 170.45.

MS (ESI): *m*/*z* = 274.1 [M + H]$^+$.

Anal. Calcd for $C_8H_{13}Cl_2NO_3S$: C, 35.05; H, 4.78; N, 5.11; S, 11.70. Found: C, 35.22; H, 4.80; N, 5.08; S, 11.69.

**3-Chloro-4-[chloro(phenyl)methyl]-3-methyl-1-(methylsulfonyl)pyrrolidin-2-one (2g)**

Following typical procedure 1, **1g** (1.681 g, 5 mmol) was treated with CuCl (0.050 mg, 0.5 mmol) in MeCN (2.5 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 0:100) gave **2g** (1.563 g, 93%) as a pale-yellow oil; inseparable mixture of diastereomers, *cis*/*trans* 93:7, (*cis*$_I$ + *cis*$_{II}$)/(*trans*) (65 + 28):7 ($^1$H NMR).

IR (film): 1744 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ (*cis I*) = 0.96 (s, 3 H, C3-$CH_3$), 2.99 (m, 1 H, H4), 3.30 (s, 3 H, $CH_3SO_2$), 3.68 (dd, *J* = 10.3, 10.0 Hz, 1 H, H5), 4.38 (dd, *J* = 10.3, 6.7 Hz, 1 H, H5), 5.16 (d, *J* = 10.2 Hz, 1 H, CHCl), 7.41 (m, 5 H, Ph); δ (*cis II*) = 2.00 (s, 3 H, C3-$CH_3$), 2.99 (m, 1 H, H4), 3.12 (t, *J* = 10.0 Hz, 1 H, H5), 3.23 (s, 3 H, $CH_3SO_2$), 3.27 (m, 1 H, H5), 5.13 (d, *J* = 9.8 Hz, 1 H, CHCl), 7.41 (m, 5 H, Ph); δ (*trans*) = 1.90 (s, 3 H, C3-$CH_3$), 3.26 (m, 1 H, H4), 3.32 (s, 3 H, $CH_3SO_2$), 3.88 (dd, *J* = 4.2, 11.1 Hz, 1 H, H5), 4.07 (dd, *J* = 7.3, 11.1 Hz, 1 H, H5), 5.20 (d, *J* = 4.9 Hz, 1 H, CHCl), 7.41 (m, 5 H, Ph).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ (*cis I*) = 23.5, 40.0, 47.8, 52.1, 61.4, 69.0, 128.0, 129.1, 129.8, 138.4, 170.2; δ (*cis II*) = 25.1, 39.9, 46.2, 51.7, 59.9, 69.9, 127.4, 129.5, 129.8 137.7, 170.4; δ (*trans*) = 21.0, 40.6, 44.6, 51.8, 61.0, 70.1, 127.3, 129.3, 129.7, 137.5, 170.4.

MS (ESI): *m*/*z* = 336.1 $[M + H]^+$.

Anal. Calcd for $C_{13}H_{15}Cl_2NO_3S$: C, 46.44; H, 4.50; N, 4.17; S, 9.54. Found: C, 46.65; H, 4.51; N, 4.16; S, 9.58.

**3,3-Dichloro-4-(chloromethyl)-1-(methylsulfonyl)pyrrolidin-2-one (2j)**

Following typical procedure 1, **1j** (1.403 g, 5 mmol) was treated with CuCl (0.050 mg, 0.5 mmol) in MeCN (2.5 mL) at 80 °C for 4 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 20:80) gave **2j** (1.380 g, 98%) as a white powder; mp 88–90 °C.

IR (KBr): 1764 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 3.19 (m, 1 H, H4), 3.33 (s, 3 H, $CH_3SO_2$), 3.60 (dd, *J* = 10.5, 9.1 Hz, 1 H, H5), 3.76 (dd, *J* = 11.9, 9.6 Hz, 1 H, CHCl), 3.97 (dd, *J* = 11.9, 4.6 Hz, 1 H, CHCl), 4.19 (dd, 10.5, 7.8 Hz, 1 H, H5).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 40.1, 40.4, 46.8, 50.7, 82.5, 164.5.

MS (EI, 70 eV): *m*/*z* (%) = 279 (2) $[M]^+$, 158 (13), 122 (22), 109 (100), 79 (15).

Anal. Calcd for $C_6H_8Cl_3NO_3S$: C, 25.69; H, 2.87; N, 4.89; S, 11.43. Found: C, 25.71; H, 2.89; N, 5.00; S, 11.38.

**4-(Chloromethyl)-3-methyl-1-(methylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (3a) by Elimination; Typical Procedure 3**

[WARNING!! High pressure develops inside the reaction tube due to release of CO]. γ-Lactam **2a** (1.301 g, 5 mmol) was weighed in a Schlenk tube fitted with a pierceable septum (blocked by a screw cap) and a magnetic stirring bar. DMF (3 mL) was then added. The mixture was stirred at 100 °C and after 24 h was diluted with $H_2O$ (30 mL), acidified with 10% HCl, and extracted with $CH_2Cl_2$ (4 × 5 mL). The combined organic layers were concentrated. Flash chromatography of the crude (silica gel, PE–$Et_2O$, 90:10 to 20:80) gave the pyrrolidinone **3a** (1.040 g, 93%) as a white powder.

**4-(Chloromethyl)-3-methyl-1-(methylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (3a) by a Sequential Process; Typical Procedure 4**

[WARNING!! High pressure develops inside the reaction tube due to release of CO]. CuCl (0.050 g, 0.5 mmol) and 2,2-dichloroamide **1a** (1.301 g, 5 mmol) were weighed in a Schlenk tube fitted with a pierceable septum (blocked by a screw cap) and a magnetic stirring bar. DMF (4 mL) was then added under argon. The mixture was stirred at 100 °C and after 24 h was diluted with $H_2O$ (30 mL), acidified with 10% w/v HCl, and extracted with $CH_2Cl_2$ (4 × 5 mL). The combined organic layers were concentrated. Flash chromatography of the crude (silica gel, PE–$Et_2O$, 90:10 to 20:80) gave the pyrrolidinone **3a** (1.029 g, 92%) as a white powder.

**4-(Chloromethyl)-3-ethyl-1-(methylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (3c)**

Following typical procedure 4, **1c** (1.371 g, 5 mmol) was treated with CuCl (0.050 g, 0.5 mmol) in DMF (4 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 0:100) gave an inseparable mixture of **3c** and α-alkylidene-γ-lactams **4c** (constitutional isomers) [1.003 g, 84%; **3c**/**4c** = 93:7; *E*/*Z* = 73:23 ($^1$H NMR)] as a white powder. A clean sample of **3c** was obtained by crystallization ($Et_2O$–PE).

White needles; mp 75–77 °C.

IR (KBr): 1715 (C=O), 1756 cm$^{-1}$ (C=C).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 7.6 Hz, 3 H, C$H_3$CH$_2$), 2.33 (q, *J* = 7.6 Hz, 2 H, CH$_2$CH$_3$), 3.30 (s, 3 H, $CH_3SO_2$), 4.35 (s, 2 H, $CH_2Cl$), 4.40 (s, 2 H, H5).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 12.7, 17.0, 36.6, 40.8, 50.0, 137.0, 148.0, 169.1.

MS (EI, 70 eV): *m*/*z* (%) = 237 (45) $[M]^+$, 202 (41), 188 (8), 158 (100), 124 (49), 79 (50).

Anal. Calcd for $C_8H_{12}ClNO_3S$: C, 40.42; H, 5.09; N, 5.89; S, 13.49. Found: C, 40.32; H, 5.1; N, 5.90; S, 13.43.

**(*E*)- and (*Z*)-4-(Chloromethyl)-3-ethylidene-1-(methylsulfonyl)pyrrolidin-2-one (4c)**

$^1$H NMR (500 MHz, $CDCl_3$): δ (*E*) = 1.93 (dd, *J* = 7.4, 1.0 Hz, 3 H, C$H_3$CH), 3.28 (s, 3 H, $CH_3SO_2$), 3.43 (br m, 1 H, H4), 3.53 (dd, *J* = 11.1, 8.2 Hz, 1 H, CHCl), 3.63 (dd, *J* = 11.1, 4.0 Hz, 1 H, CHCl), 3.89 (m, 2 H, H5), 6.90 (dq, *J* = 7.4, 1.8 Hz, 1 H, =C*H*CH$_3$); δ (*Z*) = 2.22 (dd, *J* = 7.6, 1.8 Hz, 3 H, C$H_3$CH), 3.23 (br m, 1 H, H4), 3.29 (s, 3 H, $CH_3SO_2$), 3.55 (dd, *J* = 11.4, 7.5 Hz, 1 H, CHCl), 3.63 (overlapped, 1 H, CHCl), 3.73 (dd, *J* = 10.4, 3.7 Hz, 1 H, H5), 3.89 (overlapped, 1 H, H5), 6.35 (dq, *J* = 7.6, 1.8 Hz, 1 H, =C*H*CH$_3$).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ (*E*) = 15.0, 36.0, 40.4, 45.8, 47.2, 131.2, 138.1, 166.2; δ (*Z*) = 14.0, 38.7, 40.5, 46.9, 47.3, 129.6, 142.0, 166.6.

MS (EI, 70 eV): *m*/*z* (%) (*E*) = 237 (17) $[M]^+$, 202 (18); 188 (21), 158 (21), 130 (60), 110 (40), 95 (100), 79 (15).

**4-(Chloromethyl)-3-ethyl-1-tosyl-1*H*-pyrrol-2(5*H*)-one (3d)**

Following typical procedure 4, **1d** (1.751 g, 5 mmol) was treated with CuCl (0.050 g, 0.5 mmol) in DMF (4 mL) at 100 °C for 24 h. Chromatography of the crude product (silica gel, $CH_2Cl_2$–PE–$Et_2O$, 50:50:0 to 50:0:50) gave a mixture of **3d** and α-alkylidene-γ-lactams **4d** (constitutional isomers) [1.491 g, 95%; **3d**/**4d** 82:18, *E*/*Z* 80:20 ($^1$H NMR)] as a white powder. A clean sample of **3d** was obtained by crystallization ($Et_2O$).

White powder; mp 143–145 °C.

IR (KBr): 1714 (C=O), 1665 cm$^{-1}$ (C=C).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.03 (t, *J* = 7.6 Hz, 3 H, C$H_3$CH$_2$), 2.25 (q, *J* = 7.4 Hz, 2 H, CH$_2$CH$_3$), 2.43 (s, 3 H, C$H_3$PhSO$_2$), 4.33 (s, 2 H, $CH_2Cl$), 4.44 (s, 2 H, H5), 7.35 (d, *J* = 8.2 Hz, 2 H, ArH), 7.96 (d, *J* = 8.2 Hz, 2 H, ArH).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 12.4, 16.9, 21.4, 37.0, 50.5, 128.0, 129.8, 135.2, 137.3, 145.3, 147.6, 168.3.

MS (EI, 70 eV): *m*/*z* (%) = 313 (1) [M]$^+$, 278 (3), 264 (1), 249 (36), 234 (19), 214 (67), 91 (100).

Anal. Calcd for $C_{14}H_{16}ClNO_3S$: C, 53.59; H, 5.14; N, 4.46; S, 10.22. Found: C, 53.67; H, 5.11; N, 4.45; S, 10.28.

**(*E*)- and (*Z*)-4-(Chloromethyl)-3-ethylidene-1-tosylpyrrolidin-2-one (4d)**

$^1$H NMR (500 MHz, $CDCl_3$): δ (*E*) = 1.85 (dd, *J* = 7.4, 1.1 Hz, 3 H, C*H*$_3$CH), 2.43 (s, 3 H, C*H*$_3$PhSO$_2$), 3.34 (br m, 1 H, H4), 3.41 (dd, *J* = 11.1, 9.6 Hz, 1 H, CHCl), 3.56 (dd, *J* = 11.1, 3.8 Hz, 1 H, CHCl), 3.88 (dd, *J* = 10.5, 7.5 Hz, 1 H, H5), 4.04 (dd, *J* = 10.5, 1.7 Hz, 1 H, H5), 6.78 (dq, *J* = 7.5, 1.8 Hz, 1 H, =C*H*CH$_3$), 7.35 (d, *J* = 8.2 Hz, 2 H, ArH), 7.93 (d, *J* = 8.2 Hz, 2 H, ArH); δ (*Z*) = 2.13 (dd, *J* = 7.4, 1.8 Hz, 3 H, C*H*$_3$CH), 2.43 (s, 3 H, C*H*$_3$PhSO$_2$), 3.15 (br m, 1 H, H4), 3.45 (dd, *J* = 11.2, 8.5 Hz, 1 H, CHCl), 3.62 (overlapped, 1 H, CHCl), 3.83 (dd, *J* = 10.3, 3.4 Hz, 1 H, H5), 4.07 (dd, *J* = 10.2, 6.9 Hz, 1 H, H5), 6.23 (dq, *J* = 7.6, 1.8 Hz, 1 H, =C*H*CH$_3$), 7.35 (d, *J* = 8.2 Hz, 2 H, ArH), 7.96 (d, *J* = 8.2 Hz, 2 H, ArH).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ (*E*) = 14.7, 36.1, 45.3, 47.6, 128.1, 129.7, 131.3, 137.6, 165.2; δ (*Z*) = 13.7, 38.6, 41.2, 46.9, 132.6, 141.4, 169.0.

MS (EI, 70 eV): *m*/*z* (%) (*E*) = 264 (1) [M – 49]$^+$, 249 (80), 234 (37), 200 (42), 95 (84), 91 (100).

**4-(Chloromethyl)-3-ethyl-1-(trifluoromethylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (3e)**

Following typical procedure 3, **2e** (1.641 g, 5 mmol, *cis*/*trans* 50:50) was heated in DMF (4 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:00 to 20:80) gave **3e** and **4e**.

White flakes; yield: 1.237 g (85%); mp 83–85 °C.

IR (KBr): 1752 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.14 (t, *J* = 7.3 Hz, 3 H, $CH_2CH_3$), 2.39 (q, *J* = 7.3 Hz, 2 H, $CH_2CH_3$), 4.39 (s, 2 H, H5), 4.51 (s, 2 H, $CH_2Cl$).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 12.5, 17.3, 36.5, 51.5, 136.4, 149.6, 166.7.

MS (EI, 70 eV): *m*/*z* (%) = 291 (15) [M]$^+$, 256 (22), 222 (11), 158 (100).

Anal. Calcd for $C_8H_9ClF_3NO_3S$: C, 32.94; H, 3.11; N, 4.80; S, 10.99. Found: C, 32.97; H, 3.05; N, 4.80; S, 11.04.

**(*E*)- and (*Z*)-4-(Chloromethyl)-3-ethylidene-1-(trifluoromethylsulfonyl)pyrrolidin-2-one (4e)**

Colourless oil that gets brownish; yield: 0.137 g (9%); *E*/*Z* 87:13 ($^1$H NMR).

IR (film): 1758 (C=O), 1670 cm$^{-1}$ (C=C).

$^1$H NMR (500 MHz, $CDCl_3$): δ (*E*) = 2.00 (dd, *J* = 7.4, 1.0 Hz, 3 H, C*H*$_3$CH=), 3.49 (br m, 1 H, H4), 3.53 (dd, *J* = 10.5, 8.7 Hz, 1 H, CHCl), 3.65 (dd, *J* = 10.5, 3.4 Hz, 1 H, CHCl), 3.99 (dd, *J* = 10.4, 7.3 Hz, 1 H, H5), 4.07 (dd, *J* = 10.4, 1.5 Hz, 1 H, H5), 7.09 (dq, *J* = 7.4, 1.0 Hz, 1 H, CHC*H*$_3$); δ (*Z*) = 2.28 (dd, *J* = 7.4, 1.7 Hz, 3 H, =CHC*H*$_3$), 3.30 (m, 1 H, H4), 3.56 (dd, *J* = 10.9, 7.5 Hz, 1 H, CHCl), 3.65 (overlapped, 1 H, CHCl), 3.88 (dd, *J* = 10.5, 3.5 Hz, 1 H, H5), 4.03 (overlapped, 1 H, H5), 6.52 (dq, *J* = 7.4, 1.0 Hz, 1 H, =C*H*CH$_3$).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ (*E*) = 15.4, 36.2, 45.1, 48.9, 119.6, 129.6, 141.6, 164.3; δ (*Z*) = 13.9, 39.0, 46.4, 48.7, 119.6, 132.6, 145.9, 164.3.

MS (EI, 70 eV): *m*/*z* (%) (*E*) = 291 (14) [M]$^+$, 256 (13), 242 (100), 222 (33), 95 (95); *m*/*z* (%) (*Z*) = 291 (10) [M]$^+$, 256 (4), 242 (100).

**4-(1-Chloroethyl)-3-methyl-1-(methylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (3f)**

Following typical procedure 4, **1f** (1.441 g, 5 mmol) was reacted with CuCl (0.050 g, 0.5 mmol) in DMF (4 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 20:80) gave an inseparable mixture of **3f** and **5** [1.010 g; **3f**/**5** 1:1 ($^1$H NMR), yield: 46%/46%] as a pale-yellow oil.

**3f**

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.71 (d, *J* = 6.9 Hz, 3 H, C*H*$_3$CHCl), 1.88 (t, $^5J$ = 2.0 Hz, 3 H, $CH_3C$=), 3.33 (s, 3 H, $CH_3SO_2$), 4.38 (part A of an $ABX_3$, $^2J$ = 16.6 Hz, $^5J$ = 2.0 Hz, 1 H, H5), 4.52 (part B of an $ABX_3$, $^2J$ = 16.6 Hz, $^5J$ = 2.0 Hz, 1 H, H5), 5.06 (q, *J* = 6.9 Hz, 1 H, CHCl).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 8.7, 23.6, 41.0, 48.0, 49.7, 129.5, 152.9, 169.7.

MS (ESI): *m*/*z* = 238.1 [M + H]$^+$.

**3-Methyl-1-(methylsulfonyl)-4-vinyl-1*H*-pyrrol-2(5*H*)-one (5)**

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.90 (t, *J* = 1.7 Hz, 3 H, $CH_3C$=), 3.31 (s, 3 H, $CH_3SO_2$), 4.56 (s, 2 H, H5), 5.53 (d, *J* = 11.0 Hz, 1 H, C*H*$_2$=CH), 5.59 (d, *J* = 17.7 Hz, 1 H, C*H*$_2$=CH), 6.72 (dd, *J* = 17.7, 11.0 Hz, 1 H, C*H*=CH$_2$).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 8.6, 40.9, 48.9, 126.1, 129.4, 130.0, 148.1, 170.6.

MS (ESI): *m*/*z* = 202.3 [M + H]$^+$.

**4-[Hydroxy(phenyl)methyl]-3-methyl-1-(methylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (6)**

Following typical procedure 4, **1g** (1.681 g, 5 mmol) was reacted with CuCl (0.050 g, 0.5 mmol) in DMF (4 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 0:100) gave **6** (0.689 g, 49%) as a white powder; mp >200 °C (dec.).

IR (Nujol): 3399 (OH), 1716 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.60 (br s, 1 H, OH), 1.88 (s, 3 H, C3-$CH_3$), 3.16 (s, 3 H, $CH_3SO_2$), 4.19 (pseudo q *J* = 17.0 Hz, 2 H, H5), 4.69 (s, 1 H, C*H*OH), 7.23 (t, 2 H, Ph), 7.34 (d, 1 H, Ph), 7.39 (d, 2 H, Ph).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 9.1, 40.8, 46.9, 48.5, 127.2, 128.8, 129.8, 129.9, 137.1, 153.2, 169.7.

MS (EI, 70 eV): *m*/*z* (%) = 265 (19) [(M + 1) – 17]$^+$, 187 (30), 91 (100).

Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50; H, 5.37; N, 4.98; S, 11.40. Found: C, 55.30; H, 5.42; N, 4.96; S, 11.46.

**4-[Chloro(phenyl)methyl]-3-methyl-1-(methylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (3g)**

Following typical procedure 3, **2g** (1.681 g, 5 mmol) was heated in DMF (4 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 0:100) gave **3g** (0.789 g, 53%) as a brownish oil.

IR (liquid): 1720 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.93 (s, 3 H, C3-$CH_3$), 3.32 (s, 3 H, $CH_3SO_2$), 4.17 and 4.55 (2 dq, *J* = 18.4, 1.8 Hz, 1 H each, H5), 6.02 (s, 1 H, CHCl), 7.41 (s, 5 H, Ph).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 8.9, 41.0, 48.7, 56.0, 126.8, 129.2, 130.1, 136.7, 151.8, 169.6.

MS (EI, 70 eV): *m*/*z* (%) = 299 (8) [M]$^+$, 264 (100), 221 (19), 143 (82), 129 (75), 125 (73).

Anal. Calcd for $C_{13}H_{14}ClNO_3S$: C, 52.09; H, 4.71; N, 4.67; S, 10.70. Found: C, 51.99; H, 4.72; N, 4.70; S, 10.75.

**4-(Chloromethyl)-3-isopropyl-1-(methylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (3h)**

Following typical procedure 4, **1h** (1.323 g, 5 mmol) was reacted with CuCl (0.050 g, 0.5 mmol) in DMF (4 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 0:100) gave an inseparable mixture of **3h** and α-alkylidene-γ-lactam **4h** (constitutional isomers) [1.142 g, 91%; **3h/4h** 85:15 ($^1$H NMR)] as a white powder. A clean sample of **3h** was obtained by crystallization ($Et_2O$–*i*-$Pr_2O$).

White needles; mp 106–108 °C.

IR (KBr): 1717 (C=O), 1659 cm$^{-1}$ (C=C).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.26 [d, *J* = 7.0 Hz, 6 H, $(CH_3)_2CH$], 2.89 [sept, *J* = 7.0 Hz, 1 H, $CH(CH_3)_2$], 3.32 (s, 3 H, $CH_3SO_2$), 4.36 (s, 2 H, $CH_2Cl$), 4.39 (s, 2 H, H5).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 19.9, 25.4, 36.6, 40.6, 49.5, 139.7, 147.3, 168.4.

MS (EI, 70 eV): *m*/*z* (%) = 251 (61) [M]$^+$, 236 (9), 222 (21), 216 (39), 188 (16), 172 (90), 158 (22), 130 (100), 79 (47).

Anal. Calcd for $C_9H_{14}ClNO_3S$: C, 42.94; H, 5.61; N, 5.56; S, 12.74. Found: C, 43.08; H, 5.57; N, 5.59; S, 12.80.

**4-(Chloromethyl)-3-isopropylidene-1-(methylsulfonyl)pyrrolidin-2-one (4h)**

$^1$H NMR (500 MHz, $CDCl_3$): δ = 1.96 (s, 3 H, $CH_3$ *cis* to $CH_2Cl$), 2.25 (s, 3 H, $CH_3$ *trans* to $CH_2Cl$), 3.28 (s, 3 H, $CH_3SO_2$), 3.33 (m, 1 H, H4), 3.47 (dd, *J* = 11.2, 9.0 Hz, 1 H, CHCl), 3.57 (dd, *J* = 11.2, 3.5 Hz, 1 H, CHCl), 3.79 (dd, *J* = 11.4, 7.4 Hz, 1 H, H5), 3.91 (dd, *J* = 11.4, 1.1 Hz, 1 H, H5).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 19.9, 23.7, 37.9, 40.1, 45.8, 46.0, 123.4, 154.0, 166.4.

MS (EI, 70 eV): *m*/*z* (%) = 251 (17) [M]$^+$, 216 (12), 202 (79), 124 (35), 79 (24).

**4-(Chloromethyl)-3-hexyl-1-(methylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (3i)**

Following typical procedure 4, **1i** (1.651 g, 5 mmol) was reacted with CuCl (0.050 g, 0.5 mmol) in DMF (4 mL) at 100 °C for 24 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 80:20 to 20:80) gave an inseparable mixture of **3i** and α-alkylidene-γ-lactams **4i** (constitutional isomers) [1.267 g, 86%; **3i/4i** 88:12, *E*/*Z* 80:20, ($^1$H NMR)] as yellowish flakes. A clean sample of **3i** was obtained by crystallization ($Et_2O$–PE).

White powder; mp 49–51 °C.

IR (KBr): 1715 (C=O), 1660 cm$^{-1}$ (C=C).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 0.88 (br t, 3 H, $CH_3CH_2$), 1.29 [m, 6 H, $(CH_2)_3$], 1.49 (m, 2 H, $CH_2$), 2.31 (t, *J* = 7.7 Hz, 2 H, $CH_2C$=), 3.33 (s, 3 H, $CH_3SO_2$), 4.35 (s, 2 H, $CH_2Cl$), 4.43 (s, 2 H, H5).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 14.0, 22.4, 23.7, 28.0, 29.1, 31.4, 36.9, 40.9, 50.1, 135.9, 148.5, 169.3.

MS (EI, 70 eV): *m*/*z* (%) = 293 (7) [M]$^+$, 258 (30), 250 (10), 244 (50), 188 (100), 79 (13).

Anal. Calcd for $C_{12}H_{20}ClNO_3S$: C, 49.05; H, 6.86; N, 4.77; S, 10.91. Found: C, 49.38; H, 6.79; N, 4.81; S, 10.87.

**(*E*)- and (*Z*)-4-(Chloromethyl)-3-hexylidene-1-(methylsulfonyl)pyrrolidin-2-one (4i)**

$^1$H NMR (500 MHz, $CDCl_3$): δ (*E*) = 0.88 (br t, 3 H, $CH_3CH_2$), 1.29 [m, 4 H, $(CH_2)_2$], 1.49 (m, 2 H, $CH_2$), 2.25 (dq, *J* = 8.6, 1.8 Hz, 2 H, $CH_2CH$=), 3.30 (s, 3 H, $CH_3SO_2$), 3.41 (br m, 1 H, H4), 3.52 (dd, *J* = 11.2, 6.5 Hz, 1 H, CHCl), 3.62 (dd, *J* = 11.2, 3.9 Hz, 1 H, CHCl), 3.89 (dd, *J* = 10.6, 7.8 Hz, 1 H, H5), 3.94 (dd, *J* = 10.6, 1.8 Hz, 1 H, H5), 6.86 (dt, *J* = 8.6, 1.2 Hz, 1 H, CHC=C); δ (*Z*) = 0.88 (br t, 3 H, $CH_3CH_2$), 1.29 [m, 4 H, $(CH_2)_2$], 1.49 (m, 2 H, $CH_2$), 2.74, (br q, *J* = 7.8 Hz, 2 H, $CH_2CH$=), 3.30 (s and m, 4 H, $CH_3SO_2$ , H4), 3.56 (dd, *J* = 11.2, 8.0 Hz, 1 H, CHCl), 3.64 (overlapped, 1 H, CHCl), 3.74 (dd, *J* = 10.4, 3.4 Hz, 1 H, H5), 3.93 (overlapped, 1 H, H5), 6.26 (t, *J* = 7.6, 1.4 Hz, 1 H, CHC=C).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ (*E*) = 13.9, 22.4, 28.2, 29.3, 31.4, 36.2, 40.4, 46.1, 47.2, 130, 143.4, 166.3; δ (*Z*) = 13.4, 27.4, 28.7, 32.5, 38.6, 40.3, 46.9, 47.3, 128.5, 139.0, 160.1.

MS (EI, 70 eV): (*E*) *m*/*z* (%) = 244 (100) [M – 49]$^+$, 224 (76); 211 (43), 162 (71), 79 (36).

**4-(Chloromethyl)-3-chloro-1-(methylsulfonyl)-1*H*-pyrrol-2(5*H*)-one (3j)**

Following typical procedure 3, **2j** (1.403 g, 5 mmol) was heated in DMF (4 mL) at 80 °C for 6 h. Flash chromatography of the crude product (silica gel, PE–$Et_2O$, 100:0 to 0:100) gave **3j** (1.067 g, 87%) as a white solid; mp 67–69 °C.

IR (KBr): 1722 cm$^{-1}$ (C=O).

$^1$H NMR (500 MHz, $CDCl_3$): δ = 3.27 (s, 3 H, $CH_3SO_2$), 3.40 (s, 2 H, $CH_2Cl$), 3.47 (s, 2 H, H5).

$^{13}$C NMR (125.68 MHz, $CDCl_3$): δ = 36.1, 40.6, 49.8, 124.9, 148.7, 163.2.

MS (EI, 70 eV): *m*/*z* (%) = 243 (26) [M]$^+$, 208 (37), 194 (100), 164 (41), 130 (74), 116 (92), 79 (48).

Anal. Calcd for $C_6H_7Cl_2NO_3S$: C, 29.52; H, 2.89; N, 5.74; S, 13.14. Found: C, 29.43; H, 2.97; N, 5.69; S, 13.22.

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