# Intramolecular Diels–Alder Cycloaddition of *N*-Allyl-*N*-(2-furylmethyl)amides – First Step of a New Route Towards the Synthesis of a Densely Functionalized Pyrrolizidine Ring

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The intramolecular Diels–Alder reaction of *N*-allyl-*N*-(2-furylmethyl)amides to *exo*-*N*-acyl-3-aza-10-oxatricyclo[5.2.1.$0^{1,5}$]dec-8-enes is described. The cycloaddition is controlled not only by the size of the amide appendage, but also by electronegativity of the amide. An example of a new approach towards the synthesis of a highly functionalized pyrrolizidine ring, which links this Diels–Alder cycloaddition to an halogen atom transfer radical cyclization, is reported.

## Introduction

The proclivity of furans to undergo [4+2] cycloadditions[1] with various π-bonds is well established[2] and has attracted the attention of many research groups as a tool in the preparation of rigid oxygenated bicyclic systems en route to substituted arenes, carbohydrate derivatives and various natural products.[3] The appeal of the reaction stems from the impressive selectivity with which the intermediate 7-oxanorbornenes can be manipulated.[4] While the intermolecular approach was studied by Diels and Alder almost 70 years ago,[5] the intramolecular version, designated as IMDAF (Intra-Molecular Diels–Alder with Furan), appeared later, the first example was published at the beginning of the 1960s.[6] Since then, the IMDAF reaction has grown in importance, and it is now recognized as an attractive synthetic strategy for building complex products.[2,3,7]

The tether, which links the dienophile and furan, can be of different types and lengths,[2,3,7,8] and one of the most useful is the three-atom chain C(1)–N(2)–C(3).[9] These tethers allow the formation of tricyclic heterocycles, which can be elaborated into useful products.[9–17] Unfortunately, the furan ring is a relatively unreactive diene because of aromaticity,[18] and in order to favor cycloaddition, an oxo substituent has been introduced at C(1) or C(3)[8,18–20] (to exert an electronic contribution), while a bulky protecting group is generally required at N(2)[16] (steric contribution).[2,8,18] The bulky protecting group ensures that the furan and dienophile are held in the correct conformation for π-overlap (by the Thorpe–Ingold effect). In related work, Sternbach et al. observed that compounds with a furan ring and dienophile separated by a three-carbon chain can undergo the IMDAF reaction by introduction of geminal substituents at C(2).[21] In this case, the steric effect (often known as buttressing) influences the rotamer equilibrium so as to increase the population of the *cisoid* forms.[22] The introduction of a steric buttress is therefore crucial for a successful IMDAF reaction of dienes and dienophiles separated by C–N–C and related tethers. Indeed, IMDAF studies with allyl(furfuryl)amines have indicated that the cycloaddition does not proceed under mild conditions, unless an *N*-substituent, such as an aromatic ring[16,17,23] or a trityl group, is present;[24] alkyl appendages are also effective, but only if ammonium salts are used.[16]

Recently, during the study of the influence of benzylic protection on the CuCl/TMEDA-catalyzed rearrangement of *N*-allyl-*N*-benzyl-2,2-dichloroamides to pyrrolidin-2-ones,[25] we unexpectedly found that the IMDAF reaction [rather than halogen atom transfer radical cyclization (HATRC)] prevailed, under mild conditions, when a benzyl protecting group was replaced by a 2-furylmethyl group.[26] The 2,2-dichloroalkanoyl substituent on the N(2) position of the tether seemed to play a fundamental role in the activation of the intramolecular [4+2] cycloaddition. As the use of acyl groups as activators in the IMDAF reaction of *N*-allyl-*N*-(2-furylmethyl)amines has not been comprehensively studied,[24,27] this led us to examine, in detail, the use and mechanism of action of carbonyl activators. We now report our investigations, which include a new approach towards the synthesis of a heavily functionalized pyrrolizidine, using a novel IMDAF-HATRC reaction sequence.

## Results and Discussion

A range of *N*-allyl-*N*-(2-furylmethyl)amides **3** were synthesized following the retrosynthetic pathway depicted in Scheme 1. It was envisaged that a variety of R substituents would be incorporated in **3** so as to test both the steric and electronic effects of the acyl appendage on the IMDAF reaction.

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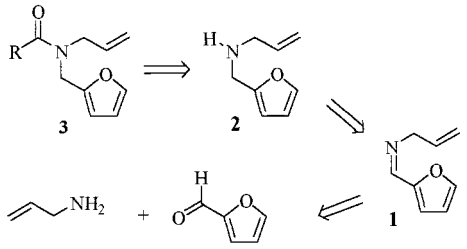
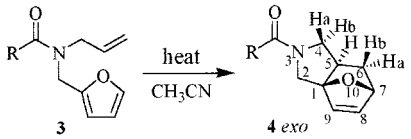


Scheme 1

Some problems were encountered by Sammes and coworkers during the synthesis of *N*-allyl-*N*-(2-furylmethyl)-amine (**2**)[24] as the one-pot reductive alkylation of allylamine [using $Na(CN)BH_3$], or the monoalkylation of *N*-(2-furylmethyl)amine with allyl bromide, gave poor yields. Unexpectedly, however, we observed that the two-step reductive alkylation of allylamine using $NaBH_4$ as the reducing agent, was able to afford **2** in high yields (80−89%).

Secondary amine **2** did not require purification, and subsequent acylation gave **3a**−**h** in 70−80% yield, although the reaction had to be carried out at 25 °C in order to prevent premature IMDAF reactions leading to **4**. As the cycloaddition occurred slowly, even on standing at room temperature, small amounts of each of the amides **3a**−**h** were prepared, purified and used immediately.

The intramolecular cycloadditions of **3a**−**h** were initially conducted in acetonitrile at 80 °C to afford, in almost all cases, the *N*-acyl-3-aza-10-oxatricyclo[5.2.1.$0^{1,5}$]dec-8-enes **4** (Scheme 2, Table 1) in high yields, generally as a mixture of two isomers. An NOESY experiment[28] performed on the amide **4d** (and discussed in the structural characterizations section) clearly revealed that the two isomers were indeed amide rotamers, and that the configuration of the tricyclic skeleton was *exo*. The other amides **4a**−**c**,**e**−**h** exhibited similar $^1$H NMR spectra and therefore the same (rotamer/*exo*) assignments were made. The presence of rotamers is a consequence of the large rotational barrier and thus the slow rotation around the amide bond,[29] while the *ortho* regioselectivity and the *exo* stereoselectivity are controlled by the short length of the tether which links the reacting functional groups.[24,30] Although the excellent yields of the IMDAF reactions at 80 °C are valuable from a preparative point of view, it is not possible to distinguish the influence of the R substituents on the cycloaddition reaction (Scheme 2). However, some differentiation became evident at 60 °C when, even after heating for 20 h, none of the substrates **3a**−**h** were totally converted into the IMDAF adduct **4a**−**h** (Table 1).



**a**, R = $CF_3$ **c**, R = $C(CH_3)_3$ **e**, R = $CH(CH_3)_2$ **g**, R = $C(C_2H_5)Cl_2$
**b**, R = $CCl_3$ **d**, R = $CHCl_2$ **f**, R = $C(CH_3)Cl_2$ **h**, R = $CH_2Cl$

Scheme 2

A comparison of the results of Entries 3 and 5 with 4, 6, and 7 (Table 1), shows the importance of the size of the R substituent [at the N(2) position of the tether]. In general, the bulkier the substituent, the faster the rate of cyclization. While the incorporation of a steric buttress is expected to accelerate the rearrangement of the *N*-allyl-*N*-(2-furylmethyl)amines, nothing is known about the possible electronic effect of the electron-withdrawing amide groups. The large difference in rates of conversion between **3b** and **3c** suggests the involvement of this second factor. Indeed this difference in reactivity cannot only be attributed to steric factors, since the van der Waals radius of Cl (1.75 Å) is 13% smaller than that of $CH_3$ (2.0 Å).[31] A similar trend is seen for the related amides **3d** and **3e**, which have smaller R side chains than **3b** or **3c**, respectively. Further evidence of the electronic effect comes from a comparison of **3b** and **3f**. Hence, a change from a chlorine atom in **3b** to a methyl group in **3f** significantly slows down the rate of cycloaddition. It should also be noted that **3a**, a precursor with three small, but strongly electron-withdrawing fluorine atoms, is converted into **4a** in a reasonable 39% yield. This result further highlights the importance of the electronic effect (as well as the steric effect) in the acceleration of the rate of the IMDAF reactions investigated.

The likely rationale for the observed electronic effect resides in the structure of the amide group, which is suitably represented as a resonance hybrid of valence bond structures **I** and **II** (Figure 1).[32] Structure **I**, in which the nitrogen atom is $sp^3$-hybridized (Figure 1), is clearly more suited to the cycloaddition process than structure **II**, where the

Table 1. Intramolecular cycloaddition of **3** (2 mmol of substrate and 4 mL of $CH_3CN$ were used)

| Entry | R | Conversion [%][a][b] | Yield [%][a,b] | Rotamer ratio[c] | $\nu_{(C=O)}$ [$cm^{-1}$][d] |
|---|---|---|---|---|---|
| 1 | $CF_3$, **a** | 91 (42) | 88 (39) | 58:42 | 1696 |
| 2 | $CCl_3$, **b** | 100 (80) | 99 (76) | 62:38 | 1660 (1683) |
| 3 | $C(CH_3)_3$, **c** | 100 (47) | 98 (44) | 100:0 | 1602 (1636) |
| 4 | $CHCl_2$, **d** | 100 (41) | 97 (39) | 60:40 | 1663 (1682) |
| 5 | $CH(CH_3)_2$, **e** | 62 (9) | 60 (8) | 58:42 | 1623 |
| 6 | $C(CH_3)Cl_2$, **f** | 100 (52) | 98 (47) | 59:41 | 1645 |
| 7 | $C(C_2H_5)Cl_2$, **g** | 100 (61) | 98 (57) | 59:41 | 1647 |
| 8 | $CH_2Cl$, **h** | 43[e] (6) | 40[e] (5) | 58:42 | 1654 (1663) |

[a] At 80 °C (30 h) and, in parentheses, at 60 °C (20 h). − [b] Values determined on isolated material. − [c] Rotamer ratio: values determined by $^1$H NMR. − [d] ν(CO) stretching of **4**, in parentheses that of **3**. − [e] Reaction mixture heated at 80 °C for 40 h.

nitrogen atom is $sp^2$-hybridized. This is because the reacting furan and alkene groups are held closer together in **I** [C(1)−N(2)−C(3) tether angle 109°] than in **II** [C(1)−N(2)−C(3) tether angle 120°].[32,33] The reason for the electronic effect, which in its action is comparable to the Thorpe−Ingold effect,[33] is presumably related to the relative contributions of resonance structures **I** and **II**. The electronegativity of the R substituent is one of the key factors that governs the relative contributions, and it is known that an increase in the electron-withdrawing strength of R results in an apparent stabilization of structure **I**.[29] This is confirmed from the trend in C=O stretching frequencies in the IR spectrum of **3** and **4** (Table 1): as the C−O bond shortens, the C−N bond lengthens (as there is less conjugation)[32] and the reactivity increases. It must be stressed, however, that the electronic factor supplements, but cannot replace, the steric (buttress) effect of the *N*-substituents present in **3**.

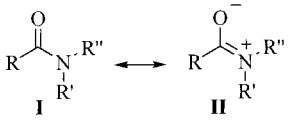
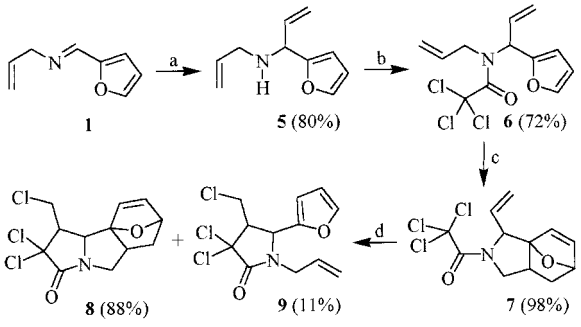


Figure 1. Resonance model for the amide group

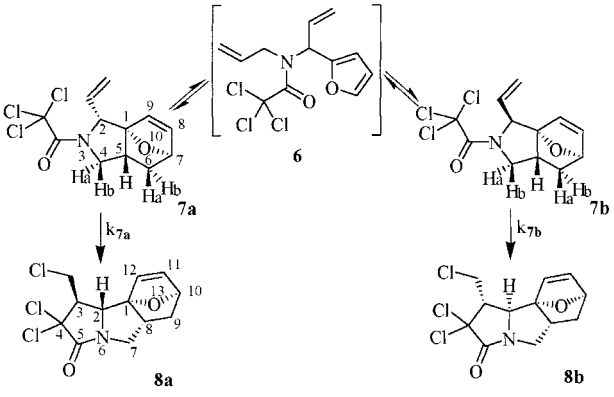
## Synthesis of the Pyrrolizidine Nucleus

Although the tandem IMDAF/radical cyclization sequence[34] has not been extensively utilized in synthesis, it does offer an extremely quick and efficient method for the construction of fused-ring systems. In this respect, we planned to exploit the homolytic cleavage of the C−Cl bond of the α-polychlorinated acyl substituent present in IMDAF adducts of type **4**. This could be promoted by a redox catalyst,[25,35] and if a radicophile (e.g. an alkene) was located at an appropriate distance from the radical center, a radical cyclisation could take place. Of particular interest was the attachment of a vinyl appendage at the C(2) or C(4) position of the tricycle as radical cyclisation could establish a new route to biologically important pyrrolizidine alkaloids. The development of new procedures for the preparation of these substances is an active area of research.[36]

As the vinyl appendage cannot be introduced at the C(4) position of **4b**, we carried out the synthesis of **7** from the *N*-allyl-*N*-(2-furylmethyl)amine **5** (Scheme 3). The route to **5** exploits the nucleophilic addition of vinylmagnesium bromide to imine **1**. However, because of the low reactivity of the C=N double bond, this reaction gave rise to a number of by-products.[37] Recently, Savoia et al. overcame the problem of low reactivity by using greater than stoichiometric amounts of Grignard reagents, or by using triorganozincates (prepared from dialkylzinc compounds/Grignard reagents).[38] Both variations proved successful in the facilitation of the nucleophilic attack[38] but, in our hands, the second variation gave a much better yield of **5** (80%).[39] The subsequent acylation to give amide **6** (72%),[40] followed by heating to promote the Diels−Alder reaction, gave **7** (98%) as an inseparable (60:40) mixture of **7a** (*exo-cis*) and **7b** (*exo-trans*) diastereomers (Scheme 4; for structural assignment see the next section).[41] Treatment of **7ab** with CuCl/TMEDA in $CH_3CN$ at 60 °C achieved an efficient radical rearrangement to **8** in 88% yield (Scheme 3). Only the two diastereomers **8a** and **8b** were observed in a ratio of 78:22 and, as expected, the radical closure was stereoselective; the chloromethyl appendage was located *trans* with respect to the C(2)−C(1) bond for both isomers.[25,42] The difference in stereochemistry between **8a** and **8b** arises from the relative disposition of the C(2)−C(3) and C(1)−O(13) bonds: *cis* for **8a** and *trans* for **8b**. As **8a** is prepared from **7a**, and **8b** from **7b**, the change in diastereomer ratio on conversion of **7** into **8** appears odd. However, the anomaly can be explained by consideration of an equilibration of compounds **7a** and **7b** under the conditions required for radical cyclisation (Scheme 4). Equilibration is expected to lead to an increase in the amount of **7a** and this is consistent with energy calculations which show that **7a** is thermodynamically more stable than **7b** ($E_{7a} - E_{7b} = -0.7$ kcal/mol).[43] The increased preference for **8a** thus arises from a faster rate of cyclization of diastereomer **7a** ($k_{7a} > k_{7b}$, Scheme 4). Interestingly, the radical cyclisation reaction also resulted in the formation of a small amount (11%) of the *trans*-pyrrolidinone **9**, presumably derived from a competitive retro Diels−Alder reaction of **8ab**.[44]



Scheme 3. (a) Vinylmagnesium bromide, diethylzinc, THF, −78 °C; (b) $CCl_3COCl$, $CH_2Cl_2$, 0 °C to room temp.; (c) $CH_3CN$, 60 °C; (d) CuCl/*N*,*N*,*N*′,*N*′-tetramethylethylenediamine, $CH_3CN$, 60 °C



Scheme 4

This regression is expected to be driven by the relief of steric strain on collapse of the tetracycle. Indeed, this was almost complete when **8ab** was heated at 120 °C for 20 h (conversion 82%, yield of **9** = 80%).

The high selectivity for the IMDAF and the radical steps suggested that both steps could be accomplished in one-pot. In an attempt to convert **6** into **8** both domino and consecutive approaches were investigated,[45] but only the second alternative proved viable, and gave the same outcome as the two-step protocol (see Exp. Sect.).

### Structural Characterizations of 4d, 7, and 8

$^1$H NMR NOESY is a very useful technique for derivation of structural information, such as conformations or relative configuration of chiral centers, in solution.[28] NOESY experiments were thus carried out in $CDCl_3$ solutions of **4d**, **7**, **8a**, and **8b** with a mixing time of 600 ms, and this enabled a number of structural features to be determined. The most useful NOE cross-peaks for determination of the *exo* configuration at the oxanorbornene/pyrrolidine junction in **4d**, **7a**,**b**, and **8a**,**b** were those detected between H-9 and H-5 in **4d**, **7a**,**b**, and H-12 and H-8 in **8a**,**b**. Moreover, the pattern of NOE cross-peaks showed that all the derivatives have similar chemical shifts for the hydrogen atoms close to the oxanorbornene/pyrrolidine ring junction. In particular, in **4d** and **7a**,**b** H-4a (high-field signal with respect to that of the geminal H-4b) and H-6b (low-field signal with respect to that of the geminal H-6a) are in a *trans* relationship with respect to the double bond hydrogen atoms of the oxanorbornene ring, whereas H-4b, H-5, and H-6a are in a *cis* relationship. A very similar situation holds for the corresponding hydrogen atoms of **8a**,**b**.

The two sets of signals present in the $^1$H NMR spectrum of **4d** were assigned to two (slow-exchanging) conformers derived from restricted rotation around the amide bond. The major conformer shows NOE cross-peaks between $CHCl_2$ and H-4ab hydrogen atoms, whereas the minor one displays NOE cross-peaks between $CHCl_2$ and H-2ab hydrogen atoms. These results clearly indicate that the dichloromethyl group is directed towards H-4ab in the first conformer and towards H-2ab in the second conformer.[46]

The different configuration of **7a** and **7b** at C-2 was proved by the H-2,H-9 NOESY cross-peak detected for **7a** (absent for **7b**), and by the H-9,H-11 cross-peak detected for **7b** (absent for **7a**). Thus the vinylic appendage is *cis* with respect to the oxygen bridge in **7a**, and *trans* in **7b**. Only one conformer was found to be present for each diastereoisomer in $CDCl_3$ solution.

Finally, the detection of NOE cross-peaks between H-2 (not H-3) and H-12 in **8a** and between H-3 (not H-2) and H-12 in **8b** enabled the relative configuration at C-2 and C-3 with respect to C-1 to be determined: H-2 is *cis* and H-3 is *trans* with respect to H-12 in **8a**, whereas H-3 is *cis* and H-2 is *trans* with respect to H-12 in **8b**. This NOE pattern shows that the chloromethyl appendage is located *trans* with respect to the C(2)−C(1) bond in both isomers.

## Conclusion

Amides **3a**−**h**, derived from acylation of *N*-allyl-*N*-(2-furylmethyl)amine (**2**) with various haloacetyl halides, have been shown to undergo efficient IMDAF reactions, which are controlled by both steric and electronic effects. This strategy was used to form chlorinated tricycle **7** which was then allowed to react in an HATRC reaction, to establish a new and effective method for the synthesis of a densely functionalized pyrrolizidine. We are currently investigating the application of this two-step procedure in the synthesis of biologically active compounds.

## Experimental Section

**General Remarks:** $^1$H NMR spectra were recorded on $CDCl_3$ solutions with Bruker DPX200 and 400AMX WB spectrometers, and the chemical shifts reported in ppm relative to tetramethylsilane as external standard. − IR spectra were obtained with a Perkin−Elmer 1600 Series FTIR. − Conditions for NOESY[28] phase-sensitive spectra by time-proportional phase incrementation (TPPI) were: mixing time = 600 ms, spectral width = 7 ppm with 2048 complex points in *f*2; 256 *t*1 values and 64 scans for *t*1 value. A squared sine function (SSB = 2) in *f*2 and gaussian multiplication (LB = −1, GB = 0.05) in *f*1 were applied before Fourier transformation. − Mass spectra were acquired with a combined HP 5890 GC/HP 5989A MS engine. − Reagents and solvents were standard grade commercial products, purchased from Aldrich or Fluka, and used without further purification. Acetonitrile (for the radical cyclizations) was dried over three batches of molecular sieves (3 Å) (5% w/v, 12 h), while THF (for the organometallic additions) was dehydrated in a continuous still using Na/K amalgam (1% w/v) and benzophenone (0.2% w/v). The 2,2-dichloropropanoic and 2,2-dichlorobutanoic acids were prepared and transformed into the respective acid chlorides according to literature methods.[25,47] The polycyclic compounds are named according to IUPAC rules.[48]

**Preparation of *N*-Allyl-*N*-(2-furylmethyl)amine (2):** Allylamine (5.71 g, 100 mmol), $CH_2Cl_2$ (150 mL), and $MgSO_4$ (15.00 g) were allowed to react, under argon, in a two-necked round bottom flask (250 mL) fitted with a dropping funnel. The stirred mixture was cooled in an ice/water bath, and after 1 h, furfural (9.61 g, 100 mmol) diluted in $CH_2Cl_2$ (10 mL) was added dropwise. After 3 h, the mixture was filtered to remove the hydrated $MgSO_4$, and concentrated under vacuum. The crude imine was then dissolved in $CH_3OH$ (300 mL), and under vigorous stirring the $NaBH_4$ (1.89 g, 50 mmol) was gradually added; the reaction temperature was controlled by a water bath. After 4−5 h, the mixture was diluted with water (600 mL) and extracted with ether (3 × 80 mL). The organic phases were collected, dried with $MgSO_4$ and concentrated under vacuum. The crude amine[24] **2** (12.21 g, 89%) was pure enough to be used for the preparation of amides **3**.

**Preparation of *N*-Allyl-*N*-(2-furylmethyl)trifluoroacetamide (3a):** In a two-necked round-bottomed flask (100 mL), fitted with a $CaCl_2$ tube and a dropping funnel, amine **2** (1.37 g, 10 mmol), $CH_2Cl_2$ (15 mL), and pyridine (1.19 g, 15 mmol) were added. The stirred mixture was cooled to 0 °C with an ice/water bath. A solution of trifluoroacetic anhydride (2.10 g, 10 mmol) in $CH_2Cl_2$ (5 mL) was then added dropwise, and after 1 h, the cooling bath was removed. The reaction mixture was stirred at room temperature for a further

4−5 h and then washed with 2.5% w/v aq. HCl (2 × 15 mL). The organic phase was dried with $MgSO_4$ and concentrated. The crude mixture was purified by silica gel chromatography with a petroleum ether (b.p. 40−60 °C)/diethyl ether gradient to give **3a** (1.70 g, 73%) as an oil. − $^1$H NMR ($CDCl_3$): δ = 4.06 (m, 2 H), 4.60 (m, 2 H), 5.23−5.41 (m, 2 H), 5.62−5.91 (m, 1 H), 6.29−6.42 (m, 2 H), 7.39−7.46 (m, 1 H). − MS (70 eV): *m*/*z* (%) = 233 (23) [M], 192 (100), 122 (13), 97 (59), 81 (63).

**Preparation of *N*-Allyl-*N*-(2-furylmethyl)amides 3b−3h:** The procedure described above was followed, but with acyl chlorides (10 mmol) instead of the trifluoroacetic anhydride (10 mmol). The crude amides were then purified by silica gel chromatography with a petroleum ether (b.p. 40−60 °C)/diethyl ether gradient to give **3b**−**h** in 70−80% yield. All products gave consistent spectroscopic analysis.

**Intramolecular Cycloaddition of Amides 3:** In a Schlenk tube, fitted with a rubber septum, was weighed the amide **3** (2 mmol) and under argon $CH_3CN$ (4 mL) was injected. The solution was heated at 60 °C for 20 h and the solvent was removed under vacuum. The crude Diels−Alder adducts **4** were isolated, generally as mixture of two rotamers, by silica gel chromatography with a petroleum ether (b.p. 40−60 °C)/diethyl ether gradient.

***N*-Trifluoroacetyl-3-aza-10-oxatricyclo[5.2.1.0$^{1,5}$]dec-8-ene (4a):** According to the general procedure, trifluoroacetamide **3a** (0.47 g, 2 mmol) was converted into **4a** (0.18 g, 39%, rotamer ratio 58:42) as an oil. − $^1$H NMR ($CDCl_3$): major rotamer: δ = 1.54 (dd, *J* = 7.6, 11.8 Hz, 1 H, H-6a), 1.85 (m, *J* = 2.8, 4.5, 11.8 Hz, 1 H, H-6b), 2.29 (m, *J* = 2.8, 7.6, 8.9, 11.4 Hz, 1 H, H-5), 3.35 (t, *J* = 11.4 Hz, 1 H, H-4a), 4.03 (d, *J* = 14.5 Hz, 1 H, H-2a), 4.10 (d, *J* = 14.5 Hz, 1 H, H-2b), 4.21 (dd, *J* = 8.9, 11.4 Hz, 1 H, H-4b), 5.16 (dd, *J* = 1.7, 4.5 Hz, 1 H, H-7), 6.43 (d, *J* = 5.8 Hz, 1 H, H-9), 6.51 (dd, *J* = 1.7, 5.8 Hz, 1 H, H-8); minor rotamer: δ = 1.58 (dd, *J* = 7.7, 11.8 Hz, 1 H, H-6a), 1.90 (m, *J* = 2.8, 4.5, 11.8 Hz, 1 H, H-6b), 2.15 (m, *J* = 2.8, 7.7, 8.9, 10.3 Hz, 1 H, H-5), 3.23 (dd, *J* = 10.3, 12.1 Hz, 1 H, H-4a), 4.15 (d, *J* = 12.2 Hz, 1 H, H-2a), 4.18 (d, *J* = 12.2 Hz, 1 H, H-2b), 4.21 (dd, *J* = 8.9, 12.1 Hz, 1 H, H-4b), 5.16 (dd, *J* = 1.7, 4.5 Hz, 1 H, H-7), 6.42 (d, *J* = 5.8 Hz, 1 H, H-9), 6.51 (dd, *J* = 1.7, 5.8 Hz, 1 H, H-8). − IR (film): ν(CO) [cm$^{-1}$]: 1696. − MS (70 eV): *m*/*z* (%) = 233 (23) [M], 192 (100), 122 (13), 97 (59), 81 (63). − $C_{10}H_{10}F_3NO_2$ (233.2): calcd. C 51.51, H 4.32, N 6.01; found C 51.55, H 4.47, N 6.17.

***N*-Trichloroacetyl-3-aza-10-oxatricyclo[5.2.1.0$^{1,5}$]dec-8-ene (4b):** According to the general procedure, trichloroacetamide **3b** (0.57 g, 2 mmol) was converted into **4b** (0.43 g, 76%, rotamer ratio 62:38), m.p. 88−90 °C. − $^1$H NMR ($CDCl_3$): major rotamer: δ = 1.52 (dd, *J* = 7.5, 11.7 Hz, 1 H, H-6a), 1.86 (m, *J* = 2.7, 4.5, 11.7 Hz, 1 H, H-6b), 2.28 (m, *J* = 2.7, 7.5, 7.8, 10.9 Hz, 1 H, H-5), 3.43 (t, *J* = 10.9 Hz, 1 H, H-4a), 4.02 (d, *J* = 14.6 Hz, 1 H, H-2a), 4.22 (d, *J* = 14.6 Hz, 1 H, H-2b), 4.61 (dd, *J* = 7.8, 10.9 Hz, 1 H, H-4b), 5.16 (dd, *J* = 1.6, 4.5 Hz, 1 H, H-7), 6.43 (d, *J* = 5.8 Hz, 1 H, H-9), 6.50 (dd, *J* = 1.6, 5.8 Hz, 1 H, H-8); minor rotamer: δ = 1.60 (dd, *J* = 7.5, 11.7 Hz, 1 H, H-6a), 1.92 (m, *J* = 2.7, 4.5, 11.7 Hz, 1 H, H-6b), 2.16 (m, *J* = 2.7, 7.5, 8.9, 9.6 Hz, 1 H, H-5), 3.37 (dd, *J* = 9.6, 12.3 Hz, 1 H, H-4a), 4.21 (dd, *J* = 8.9, 12.3 Hz, 1 H, H-4b), 4.34 (d, *J* = 13.1 Hz, 1 H, H-2a), 4.59 (d, *J* = 13.1 Hz, 1 H, H-2b), 5.16 (dd, *J* = 1.6, 4.5 Hz, 1 H, H-7), 6.43 (d, *J* = 5.8 Hz, 1 H, H-9), 6.51 (dd, *J* = 1.6, 5.8 Hz, 1 H, H-8). − IR (film): ν(CO) [cm$^{-1}$]: 1663. − MS (70 eV): *m*/*z* (%) = 281 (1) [M$^{35}$], 246 (40), 210 (39), 176 (12), 136 (7), 122 (10), 81 (100). − $C_{10}H_{10}Cl_3NO_2$ (282.6): calcd. C 42.51, H 3.52, N 4.96 ; found C 42.63, H 3.21, N 5.11.

***N*-Pivaloyl-3-aza-10-oxatricyclo[5.2.1.0$^{1,5}$]dec-8-ene (4c):** According to the general procedure, trimethylacetamide **3c** (0.44 g, 2 mmol) was converted into **4c** (0.20 g, 44%, rotamer ratio 100:0), m.p. 111−113 °C. − $^1$H NMR ($CDCl_3$): δ = 1.30 [s, 9 H, $C(CH_3)_3$], 1.49 (dd, *J* = 7.5, 11.7 Hz, 1 H, H-6a), 1.82 (m, *J* = 2.8, 4.4, 11.7 Hz, 1 H, H-6b), 2.12 (broad, 1 H, H-5), 3.21 (t, *J* = 10.4 Hz, 1 H, H-4a), 3.95 (broad, 1 H, H-2a), 4.10 (d, *J* = 13.4 Hz, 1 H, H-2b), 4.20 (t, *J* = 9.3 Hz, 1 H, H-4b), 5.11 (dd, *J* = 1.5, 4.5 Hz, 1 H, H-7), 6.40 (d, *J* = 5.8 Hz, 1 H, H-9), 6.44 (d, *J* = 1.5, 5.8 Hz, 1 H, H-9). − IR (film): ν(CO) [cm$^{-1}$]: 1605. − MS (70 eV): *m*/*z* (%) = 221 (12) [M], 180 (56), 96 (32), 81 (67), 57 (100). − $C_{13}H_{19}NO_2$ (221.3): calcd. C 70.56, H 8.65, N 6.33; found C 70.41, H 8.51; N 6.31.

***N*-Dichloroacetyl-3-aza-10-oxatricyclo[5.2.1.0$^{1,5}$]dec-8-ene (4d):** According to the general procedure, dichloroacetamide **3d** (0.50 g, 2 mmol) was converted into **4d** (0.19 g, 39%, rotamer ratio 60:40), m.p. 111−113 °C. − $^1$H NMR ($CDCl_3$): major rotamer: δ = 1.51 (dd, *J* = 7.5, 11.7 Hz, 1 H, H-6a), 1.83 (m, *J* = 2.7, 4.6, 11.7 Hz, 1 H, H-6b), 2.26 (m, *J* = 2.7, 7.5, 8.5, 10.2 Hz, 1 H, H-5), 3.32 (t, *J* = 10.3 Hz, 1 H, H-4a), 3.96 (d, *J* = 14.4 Hz, 1 H, H-2a), 4.04 (d, *J* = 14.4 Hz, 1 H, H-2b), 4.24 (dd, *J* = 8.5, 10.4 Hz, 1 H, H-4b), 5.11 (dd, *J* = 1.7, 4.6 Hz, 1 H, H-7), 6.10 (s, 1 H, $CHCl_2$), 6.38 (d, *J* = 5.8 Hz, 1 H, H-9), 6.45 (dd, *J* = 1.7, 5.8 Hz, 1 H, H-8); minor rotamer: δ = 1.54 (dd, *J* = 7.5, 11.7 Hz, 1 H, H-6a), 1.85 (m, *J* = 2.7, 4.7, 11.7 Hz, 1 H, H-6b), 2.11 (m, *J* = 2.7, 7.5, 8.9, 9.7 Hz, 1 H, H-5), 3.16 (dd, *J* = 9.7, 12.1 Hz, 1 H, H-4a), 4.15 (dd, *J* = 8.9, 12.1 Hz, 1 H, H-4b), 4.17 (d, *J* = 12.2 Hz, 1 H, H-2a), 4.21 (d, *J* = 12.2 Hz, 1 H, H-2b), 5.11 (dd, *J* = 1.7, 4.6 Hz, 1 H, H-7), 6.12 (s, 1 H, $CHCl_2$), 6.39 (d, *J* = 5.8 Hz, 1 H, H-9), 6.46 (dd, *J* = 1.7, 5.8 Hz, 1 H, H-8). − IR (film): ν(CO) [cm$^{-1}$]: 1655. − MS (70 eV): *m*/*z* (%) = 247 (1) [M$^{35}$], 212 (34), 206 (33), 176 (28), 96 (64), 81 (100). − $C_{10}H_{11}Cl_2NO_2$ (248.1): calcd. C 48.41, H 4.47, N 5.65; found C 48.56, H 4.45, N 5.54.

***N*-Isobutanoyl-3-aza-10-oxatricyclo[5.2.1.0$^{1,5}$]dec-8-ene (4e):** According to the general procedure, isobutanamide **3e** (0.42 g, 2 mmol) was converted into **4e** (0.03 g, 6%, rotamer ratio 58:42), m.p. 81−82 °C. − $^1$H NMR ($CDCl_3$): major rotamer: δ = 1.14 (d, *J* = 6.8 Hz, 3 H, $CH_3$), 1.17 (d, *J* = 6.8 Hz, 3 H, $CH_3$), 1.50 (dd, *J* = 7.5, 11.7 Hz, 1 H, H-6a), 1.82 (m, *J* = 2.8, 4.5, 11.7 Hz, 1 H, H-6b), 2.21 (m, *J* = 2.8, 7.5, 8.9, 9.9 Hz, 1 H, H-5), 2.66 (m, *J* = 6.7 Hz, 1 H, CH), 3.21 (t, *J* = 9.9 Hz, 1 H, H-4a), 3.94 (d, *J* = 14.1 Hz, 1 H, H-2a), 3.97 (d, *J* = 14.1 Hz, 1 H, H-2b), 4.00 (dd, *J* = 8.9, 9.9 Hz, 1 H, H-4b), 5.12 (dd, *J* = 1.5, 4.5 Hz, 1 H, H-7), 6.40 (d, *J* = 5.8 Hz, 1 H, H-9), 6.44 (dd, *J* = 1.5, 5.8 Hz, 1 H, H-8); minor rotamer: δ = 1.15 (d, *J* = 6.7 Hz, 3 H, $CH_3$), 1.18 (d, *J* = 6.7 Hz, 3 H, $CH_3$), 1.52 (dd, *J* = 7.6, 11.7 Hz, 1 H, H-6a), 1.85 (m, *J* = 2.8, 4.5, 11.7 Hz, 1 H, H-6b), 2.09 (m, *J* = 2.8, 7.6, 8.8, 9.8 Hz, 1 H, H-5), 2.66 (m, *J* = 6.7 Hz, 1 H, CH), 3.04 (dd, *J* = 9.8, 11.8 Hz, 1 H, H-4a), 3.95 (d, *J* = 12.1 Hz, 1 H, H-2a), 4.02 (d, *J* = 12.1 Hz, 1 H, H-2b), 4.16 (dd, J = 8.8, 11.8 Hz, 1 H, H-4b), 5.12 (dd, *J* = 1.5, 4.5 Hz, 1 H, H-7), 6.40 (d, *J* = 5.8 Hz, 1 H, H-9), 6.45 (dd, *J* = 1.6, 5.8 Hz, 1 H, H-8). − IR (film): ν(CO) cm$^{-1}$: 1623. − MS (70 eV): *m*/*z* (%) = 207 (19) [M], 166 (33), 96 (100), 81 (47). − $C_{12}H_{17}NO_2$ (207.3): calcd. C 69.54, H 8.27, N 6.76; found C 69.53, H 8.15; N 6.68.

***N*-(2,2-Dichloropropanoyl)-3-aza-10-oxatricyclo[5.2.1.0$^{1,5}$]dec-8-ene (4f):** According to the general procedure, 2,2-dichloropropanamide **3f** (0.52 g, 2 mmol) was converted into **4f** (0.25 g, 47%, rotamer ratio 59:41), m.p. 73−75 °C. − $^1$H NMR ($CDCl_3$): major rotamer: δ = 1.50 (dd, *J* = 7.5, 11.7 Hz, 1 H, H-6a), 1.86 (m, *J* = 2.8, 4.5, 11.7 Hz, 1 H, H-6b), 2.25 (m, *J* = 2.8, 7.5, 7.9, 10.8 Hz, 1 H, H-5), 2.36 (s, 3 H, $CH_3$), 3.44 (t, *J* = 10.9 Hz, 1 H, H-4a), 3.93 (d,

$J$ = 14.6 Hz, 1 H, H-2a), 4.16 (d, $J$ = 14.6 Hz, 1 H, H-2b), 4.78 (dd, $J$ = 7.9, 11.0 Hz, 1 H, H-4b), 5.14 (dd, $J$ = 1.6, 4.5 Hz, 1 H, H-7), 6.42 (d, $J$ = 5.8 Hz, 1 H, H-9), 6.47 (dd, $J$ = 1.6, 5.8 Hz, 1 H, H-8); minor rotamer: δ = 1.57 (dd, $J$ = 7.6, 11.7 Hz, 1 H, H-6a), 1.89 (m, $J$ = 2.8, 4.5, 11.7 Hz, 1 H, H-6b), 2.11 (m, $J$ = 2.8, 7.6, 9.0, 9.6 Hz, 1 H, H-5), 2.36 (s, 3 H, $CH_3$), 3.27 (dd, $J$ = 9.6, 12.2 Hz, 1 H, H-4a), 4.15 (dd, $J$ = 9.0, 12.2 Hz, 1 H, H-4b), 4.41 (d, $J$ = 13.1 Hz, 1 H, H-2a), 4.72 (d, $J$ = 13.1 Hz, 1 H, H-2b), 5.14 (dd, $J$ = 1.6, 4.5 Hz, 1 H, H-7), 6.43 (d, $J$ = 5.8 Hz, 1 H, H-9), 6.48 (dd, $J$ = 1.6, 5.8 Hz, 1 H, H-8). − IR (film): ν(CO) [$cm^{-1}$]: 1645. − MS (70 eV): $m/z$ (%) = 261 (2) [$M^{35}$], 226 (28), 190 (27), 81 (100). − $C_{11}H_{13}Cl_2NO_2$ (262.1): calcd. C, 50.02, H 5.72, N 5.30; found C 49.88, H 5.77; N 5.36.

***N*-(2,2-Dichlorobutanoyl)-3-aza-10-oxatricyclo[5.2.1.0$^{1,5}$]dec-8-ene (4g):** According to the general procedure, 2,2-dichlorobutanamide **3g** (0.55 g, 2 mmol) was converted into **4g** (0.31 g, 57%, rotamer ratio 59:41), m.p. 77−79 °C. − $^1$H NMR ($CDCl_3$): major rotamer: δ = 1.28 (t, $J$ = 7.2 Hz, 3 H, $CH_3$), 1.51 (dd, $J$ = 7.5, 11.7 Hz, 1 H, H-6a), 1.87 (m, $J$ = 2.8, 4.5, 11.7 Hz, 1 H, H-6b), 2.26 (m, $J$ = 2.8, 7.5, 8.0, 10.9 Hz, 1 H, H-5), 2.55 (q, $J$ = 7.2 Hz, 2 H, $CH_2$), 3.44 (t, $J$ = 10.9 Hz, 1 H, H-4a), 3.93 (d, $J$ = 14.5 Hz, 1 H, H-2a), 4.17 (d, $J$ = 14.5 Hz, 1 H, H-2b), 4.79 (dd, $J$ = 8.0, 10.9 Hz, 1 H, H-4b), 5.15 (dd, $J$ = 1.6, 4.5 Hz, 1 H, H-7), 6.43 (d, $J$ = 5.8 Hz, 1 H, H-9), 6.47 (dd, $J$ = 1.6, 5.8 Hz, 1 H, H-8); minor rotamer: δ = 1.28 (t, $J$ = 7.2 Hz, 3 H, $CH_3$), 1.58 (dd, $J$ = 7.6, 11.7 Hz, 1 H, H-6a), 1.90 (m, $J$ = 2.8, 4.5, 11.7 Hz, 1 H, H-6b), 2.12 (m, $J$ = 2.8, 7.6, 9.6, 9.6 Hz, 1 H, H-5), 2.55 (q, $J$ = 7.2 Hz, 2 H, $CH_2$), 3.28 (dd, $J$ = 9.7, 11.7 Hz, 1 H, H-4a), 4.15 (dd, $J$ = 9.6, 11.7 Hz, 1 H, H-4b), 4.42 (d, $J$ = 13.2 Hz, 1 H, H-2a), 4.74 (d, $J$ = 13.2 Hz, 1 H, H-2b), 5.15 (dd, $J$ = 1.6, 4.5 Hz, 1 H, H-7), 6.45 (d, $J$ = 5.8 Hz, 1 H, H-9), 6.48 (dd, $J$ = 1.6, 5.8 Hz, 1 H, H-8). − IR (film): ν(CO) $cm^{-1}$: 1647. − MS (70 eV): $m/z$ (%) = 275 (2) [$M^{35}$], 240 (20), 234 (13), 204 (30), 170 (11), 136 (19), 81 (100). − $C_{12}H_{15}Cl_2NO_2$ (276.1): calcd. C 52.19, H 5.47, N 5.07; found C 52.13, H 5.47; N 5.07.

***N*-Chloroacetyl-3-aza-10-oxatricyclo[5.2.1.0$^{1,5}$]dec-8-ene (4h):** According to the general procedure, monochloroacetamide **3h** (0.43 g, 2 mmol) was converted into **4h** (0.02 g, 5%, rotamer ratio 58:42) as an oil. − $^1$H NMR ($CDCl_3$): major rotamer: δ = 1.45 (dd, $J$ = 7.5, 11.8 Hz, 1 H, H-6a), 1.76 (m, 1 H, H-6b), 2.18 (m, 1 H, H-5), 3.18 (t, $J$ = 9.9 Hz, 1 H, H-4a), 3.80−4.14 (m, 5 H), 5.04 (dd, $J$ = 1.6, 4.4 Hz, 1 H, H-7), 6.33 (d, $J$ = 5.8 Hz, 1 H, H-9), 6.38 (dd, $J$ = 1.6, 5.8 Hz, 1 H, H-8); minor rotamer: δ = 1.46 (dd, $J$ = 7.5, 11.6 Hz, 1 H, H-6a), 1.77 (m, 1 H, H-6b), 2.04 (m, 1 H, H-5), 3.00 (dd, $J$ = 10.1, 11.6 Hz, 1 H, H-4a), 3.80−4.14 (m, 5 H), 5.04 (dd, $J$ = 1.6, 4.4 Hz, 1 H, H-7), 6.34 (d, $J$ = 5.8 Hz, 1 H, H-9), 6.37 (dd, $J$ = 1.6, 5.8 Hz, 1 H, H-8). − IR (film): ν(CO) [$cm^{-1}$]: 1663. − MS (70 eV): $m/z$ (%) = 213 (10) [$M^{35}$], 178 (11), 172 (52), 96 (100), 81 (60). − $C_{10}H_{12}ClNO_2$ (213.7): calcd. C 56.21, H 5.66, N 6.56; found C 56.31, H 5.68, N 6.75.

**Preparation of *N*-Allyl-*N*-(2-furyl)prop-2-en-1-amine (5):** A solution of distilled imine **1** (0.81 g, 6 mmol) in anhydrous THF (20 mL) was prepared under argon. After cooling to −78 °C, diethylzinc (1 M in hexane, 9 mL) and, 10 min later, vinylmagnesium bromide (1 M in THF, 9 mL) were added. The stirred solution was kept for 1 h at −78 °C, afterwards the cooling bath was removed. When the reaction mixture reached room temperature, dilution with 5% w/v aq. NaOH (10 mL) and extraction with ethyl ether (2 × 15 mL) followed. The organic phases were collected, dried ($MgSO_4$) and concentrated under vacuum. The crude amine **5** was purified by silica gel chromatography, with a petroleum ether (b.p. 40−60 °C)/diethyl ether gradient; 0.78 g of clean product was recovered, yield 80% as an oil. − MS (70 eV): $m/z$ (%) = 163 (4) [M], 162 (7) [M − 1], 136 (100), 122 (54), 107 (73), 94 (19), 79 (56), 77 (47), 41 (35).

**Preparation of *N*-Allyl-*N*-[1-(2-furyl)prop-2-enyl]trichloroacetamide (6):** In a two-necked round-bottomed flask (100 mL) fitted with a $CaCl_2$ tube and a dropping funnel, amine **5** (0.60 g, 3.69 mmol), $CH_2Cl_2$ (15 mL), and pyridine (1.19 g, 15 mmol) were added. The mixture was stirred and cooled to 0 °C with an ice/water bath. A solution of trichloroacetyl chloride (0.62 g, 3.69 mmol) in $CH_2Cl_2$ (5 mL) was then added dropwise. After 1 h, the cooling bath was removed. The reaction mixture was stirred at room temperature for a further 4−5 h and then washed with 2.5% w/v aq. HCl (2 × 15 mL). The organic phase was dried with $MgSO_4$ and concentrated. The crude product was purified by silica gel chromatography, with a petroleum ether (b.p. 40−60 °C)/diethyl ether gradient, to give amide **6** (0.82 g, 72%) as an oil. − MS (70 eV): $m/z$ (%) = 307 (1) [$M^{35}$], 272 (28) [$M^{35}$ − 35], 266 (47) [$M^{35}$ − 41], 236 (18), 202 (13), 162 (19), 107 (100), 79 (59), 77 (56), 41 (34).

**Preparation of *N*-(Trichloroacetyl)-2-vinyl-10-oxa-3-azatricyclo-[5.2.1.0$^{1,5}$]dec-8-ene (7):** Into a Schlenk tube, fitted with a rubber septum, was weighed the amide **6** (0.93 g, 3 mmol), and dried $CH_3CN$ (4 mL) was injected under argon. The solution was heated at 60 °C for 20 h, and the solvent was then removed under vacuum. The Diels−Alder adduct **7** (0.91 g, 98%) was isolated as an inseparable mixture (solid) of the diastereomers **7a** (*exo-cis*) and **7b** (*exo-trans*) (in a ratio of 60:40) by silica gel chromatography, using a petroleum ether (b.p. 40−60 °C)/diethyl ether gradient. − $^1$H NMR ($CDCl_3$): **7a**: δ = 1.45 (dd, $J$ = 7.4, 11.8 Hz, 1 H, H-6a), 1.78 (m, $J$ = 2.8, 4.3, 11.8 Hz, 1 H, H-6b), 2.15 (m, $J$ = 2.8, 7.4, 7.4, 11.2 Hz, 1 H, H-5), 3.38 (t, $J$ = 11.2, 11.2 Hz 1 H, H-4a), 4.65 (dd, $J$ = 7.5, 11.2 Hz, 1 H, H-4b), 5.04 (broad d, $J$ = 7.1 Hz, 1 H, H-2), 5.14 (dd, $J$ = 1.7, 4.5, Hz, 1 H, H-7), 5.33 (dt, $J$ = 1.1, 1.1, 10.3 Hz, 1 H, H-12a), 5.37 (dt, $J$ = 1.1, 1.1, 17.2 Hz, 1 H, H-12b), 5.75 (m, $J$ = 7.1, 10.3, 17.2 Hz, 1 H, H-11), 6.40 (d, $J$ = 5.8 Hz, 1 H, H-9), 6.45 (dd, $J$ = 1.7, 5.8 Hz, 1 H, H-8); **7b**: δ = 1.53 (dd, $J$ = 7.3, 11.7 Hz, 1 H, H-6a), 1.86 (m, $J$ = 2.4, 4.5, 11.7 Hz, 1 H, H-6b), 2.35 (m, $J$ = 2.4, 7.6, 8.9, 9.7 Hz, 1 H, H-5), 3.65 (dd, $J$ = 9.7, 10.5 Hz, 1 H, H-4a), 4.53 (dd, $J$ = 8.9, 10.5 Hz, 1 H, H-4b), 4.97 (broad d, $J$ = 6.4 Hz, 1 H, H-2), 5.10 (dd, $J$ = 1.7, 4.5 Hz, 1 H, H-7), 5.36 (dt, $J$= 1.1, 1.1, 10.4, 1 H, H-12a), 5.40 (dt, $J$= 1.1, 1.1, 17.2, 1 H, H-12b), 5.91 (m, $J$ = 6.4, 10.4, 17.2 Hz, 1 H, H-11), 6.33 (d, $J$ = 5.8 Hz, 1 H, H-9), 6.46 (dd, $J$ = 1.7, 5.8 Hz, 1 H, H-8). − IR (film): ν(CO) [$cm^{-1}$]: 1665. − MS (70 eV): $m/z$ (%) = 307 (1) [$M^{35}$], 272 (28), 266 (46), 236 (18), 107 (100), 79 (60), 77 (56). − $C_{12}H_{12}Cl_3NO_2$ (308.6): calcd. C, 46.71, H 3.92, N 4.54; found C 46.77, H 4.00, N 4.62.

**Preparation of 4,4-Dichloro-3-chloromethyl-5-oxo-13-oxa-6-aza-tetracyclo[8.2.1.0$^{1,8}$.0$^{2,6}$]tridec-11-ene (8):** Into a Schlenk tube, fitted with a rubber septum, were weighed the amide **7** (0.62 g, 2 mmol) and CuCl (0.02 g, 0.2 mmol). Dried $CH_3CN$ (4 mL), followed by TMEDA (60 μL, 0.4 mmol), were then injected under argon. The stirred solution was heated at 60 °C for 20 h and then filtered. The filtrate was concentrated and chromatographed, eluting with a petroleum ether (b.p. 40−60 °C)/diethyl ether gradient, to give **8a** (0.42 g, 69%), **8b** (0.12, 19%), and *N*-allyl-3,3-dichloro-4-chloromethyl-5-(2-furyl)pyrrolidin-2-one (**9**) (0.07 g, 11%).

**8a:** M.p. 116−117 °C. − $^1$H NMR ($CDCl_3$): δ = 1.66 (dd, $J$ = 7.8, 11.7 Hz, 1 H, H-9a), 1.87 (m, $J$ = 3.0, 4.5, 11.7 Hz, 1 H, H-9b), 2.44 (m, $J$ = 3.0, 7.8, 7.8, 9.6 Hz, 1 H, H-8), 3.30 (m, $J$ = 4.7, 7.7, 9.7 Hz, 1 H, H-3), 3.30 (dd, $J$ = 7.7, 12.2 Hz, 1 H, H-7a), 3.65 (m, $J$ = 0.6, 9.7, 12.2 Hz, 1 H, H-7b), 3.91 (dd, $J$ = 9.7, 11.5 Hz, 1 H, H-14a), 3.99 (dd, $J$ = 4.7, 11.5 Hz, 1 H, H-14b), 4.20 (dd, $J$ = 0.6,

7.7 Hz, 1 H, H-2), 5.12 (dd, *J* = 1.6, 4.5 Hz, 1 H, H-10), 6.38 (dd, *J* = 1.6, 5.9 Hz, 1 H, H-11), 6.40 (d, *J* = 5.9 Hz, 1 H, H-12). − IR (film): ν(CO) [$cm^{-1}$]: 1729. − MS (70 eV): *m/z* (%) = 307 (3) [$M^{35}$], 272 (17), 258 (13), 189 (58), 175 (15), 108 (100). − $C_{12}H_{12}Cl_3NO_2$ (308.6): calcd. C 46.71, H 3.92, N 4.54; found C 46.62, H 3.96, N 4.48.

**8b:** M.p. 121−123 °C. − $^1H$ NMR ($CDCl_3$): δ = 1.44 (dd, *J* = 7.7, 11.7 Hz, 1 H, H-9a), 1.78 (m, *J* = 3.2, 4.5, 11.7 Hz, 1 H, H-9b), 2.02 (m, *J* = 3.2, 7.7, 7.7, 10.4 Hz, 1 H, H-8), 2.80 (dd, *J* = 10.4, 11.6 Hz, 1 H, H-7a), 3.06 (m, *J* = 6.1, 7.2, 9.3 Hz, 1 H, H-3), 3.83 (d, *J* = 9.3 Hz, 1 H, H-2), 3.92 (dd, *J* = 7.2, 12.0 Hz, 1 H, H-14a), 4.12 (dd, *J* = 6.1, 12.0 Hz, 1 H, H-14b), 4.24 (dd, *J* = 7.6, 11.6 Hz, 1 H, H-7b), 5.14 (dd, *J* = 1.7, 4.5, Hz, 1 H, H-10), 6.39 (dd, *J* = 1.7, 5.9 Hz, 1 H, H-11), 6.54 (d, *J* = 5.9 Hz, 1 H, H-12). − IR (film): ν(CO) [$cm^{-1}$]: 1729. − MS (70 eV): *m/z* (%) = 307 (3) [$M^{35}$], 272 (17), 258 (13), 189 (58), 175 (15), 108 (100). − $C_{12}H_{12}Cl_3NO_2$ (308.6): calcd. C 46.71, H 3.92, N 4.54; found C 46.78, H 3.85, N 4.60.

***trans*-*N*-Allyl-3,3-dichloro-4-chloromethyl-5-(2-furyl)pyrrolidin-2-one (9):** M.p. 75−77 °C. − $^1H$ NMR ($CDCl_3$): δ = 3.19 (m, 1 H), 3.41 (dt, *J* = 6.8, 8.6 Hz, 1 H), 3.69 (dd, *J* = 6.7, 11.9 Hz, 1 H), 3.99 (dd, *J* = 6.7, 11.9 Hz, 1 H), 4.19 (m, 1 H), 4.44 (d, *J* = 8.6 Hz, 1 H), 5.02 (m, 1 H), 5.14 (m, 1 H), 5.57 (m, 1 H), 6.39 (m, 1 H), 6.46 (m, 1 H), 7.46 (m, 1 H). − IR (film): ν(CO) [$cm^{-1}$]: 1726. − MS (70 eV): *m/z* (%) = 307 (1) [$M^{35}$], 272 (10), 191 (34), 189 (55), 108 (100). − $C_{12}H_{12}Cl_3NO_2$ (308.6): calcd. C 46.71, H 3.92, N 4.54; found C 46.82, H 3.80, N 4.64.

**Sequential Preparation of 8:** Into a Schlenk tube, fitted with a rubber septum, the amide **6** (0.62 g, 2 mmol) was weighed, and $CH_3CN$ (4 mL) was injected under argon. After 20 h at 60 °C, a fresh solution of CuCl (0.02 g, 0.2 mmol) and TMEDA (60 μL, 0.4 mmol) in dried $CH_3CN$ (2 mL) was added via cannule (under argon). The reaction mixture was stirred at 60 °C for a further 20 h. The same reaction workup procedure (reported above) was followed, to give **8** (0.56 g, 90%) and **9** (0.06 g, 10%).

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