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Atom transfer radical cyclization of *O*-allyl-2,2-dichlorohemiacetal acetates: an expedient method to dichloro-γ-lactones

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ABSTRACT

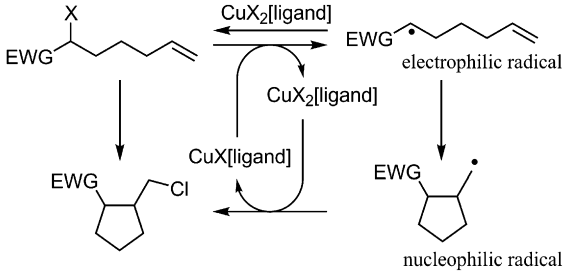
3-Alkyl-3-chloro-4-chloromethyl-γ-lactones were synthesized in acceptable yields, exploiting the CuCl-*N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine catalyzed atom transfer radical cyclization (ATRC) of *O*-allyl-2,2-dichlorohemiacetal acetates, starting materials easily prepared from 2,2-dichloroaldehydes. The oxidation of the intermediate dichloro-2-acetoxytetrahydrofurans was completed in a two-step, one-pot procedure: hydrolysis to γ-lactol and final oxidation to lactone with Jones' reagent.

1. Introduction

The use of radicals to build C–C bonds is today a well established and common practice.[1,2] In its infancy, however, this synthetic opportunity was underestimated by researchers, except for mechanistic studies, owing to the wild reactivity of the intermediate radicals, which was difficult to tame.[3] Nonetheless the improvement of experimental techniques has now allowed to overcome this difficulty and made the radical approach in the construction of complex molecules viable and equally trustworthy as the typical ionic procedures.[1–4]

Particularly attractive is the preparation of carbocycles,[5] *N*-heterocycles[6] or *O*-heterocycles[7] by transition metal catalyzed atom transfer radical cyclization (TMC-ATRC). The archetypal structures, which are the object of this reaction, comprise a carbon substituted with EWG groups and bound to at least one halide (the generating radical end), connected through a chain, usually of two/three/four atoms (the tether often incorporates the EWG group of the generating radical end), to a radicophilic vinyl appendage (see Scheme 1, for a generic example).

The main features of the ATRC, which makes the method particularly interesting and convenient, compared to other radical cyclizations, are: conservation of all the starting C–X bonds in the reaction product, convenience, high selectivity and high productivity.[8] The cyclization is usually promoted by the redox couple



Scheme 1. Mechanism of the TMC-ATRC.

$Cu^{(I)}/Cu^{(II)}$,[8] whose electrochemical properties are adjusted by a polydentate nitrogen ligand, added to the reaction mixture.[8,9] The reaction starts with a reversible removal of one halide from the C–X end of the starting material, by the $Cu^{(I)}X$[ligand], to afford an electrophilic radical, and the catalyst in its oxidized form: $Cu^{(II)}X_2$[ligand]. Afterwards the electrophilic radical closes on the radicophilic end to give a nucleophilic radical, which, promptly and irreversibly, is intercepted by the $Cu^{(II)}X_2$[ligand] complex, yielding the product and the catalyst in its reduced status. As a result, the regenerated $Cu^{(I)}X$[ligand] species begins a new reaction cycle (Scheme 1). The quenching action of the $Cu^{(II)}X_2$[ligand] towards the radical intermediates keeps their concentration at a low level with favourable effects on the reaction selectivity (i.e., the persistent radical effect), because in this way termination and side cross chain reactions are virtually suppressed.[10]

Although there are many reports on the synthetic use of TMC-ATRC,[5–8] one area that has been neglected is its employment in the Ueno–Stork reaction, an extremely important and versatile

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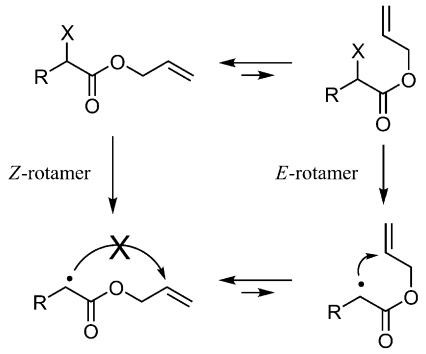
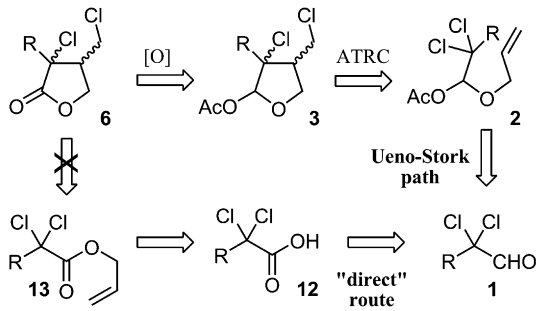
reaction, which concerns the radical cyclization of *O*-allyl α-haloacetals.[11] To the best of our knowledge there are only a few articles in the area and, in all, chloral was reported as the only aldehyde precursor.[12]

The most popular application of the radical cyclization of *O*-allyl α-haloacetals occurs in the method, developed independently by Ueno and Stork, for the preparation of γ-lactones.[13] Their approach, even if indirect, is still more reliable and versatile than the one involving the direct radical cyclization of α-haloesters; which, owing to the high barrier of rotation of the ester bond and to the instability of the (*E*)-rotamer (the sole conformer structurally suited for the intramolecular attack, Scheme 2),[11,14] has met with variable success, notwithstanding the number of solutions conceived to circumvent the problem.[14,15]



Scheme 2. Cyclization of 5-hexenyl radicals.

Following our interest in the copper catalyzed ATRC,[16] we have recently described its application to the target oriented syntheses of quercus lactones[17a] and pulchellalactam[17b] through appropriate 5-alkyl-3-chloro-4-chloromethyl-γ-lactones, directly generated from the corresponding allyl dichloroacetates. The TMC-ATRC, generally copper catalyzed, of allyl trichloroacetates to 3,3-dichloro-4-chloromethyl-γ-lactones was also experienced by other authors with usually satisfactory yields.[7a,b,d–g,i–k,n,o] Spurred by these promising results, on the direct radical cyclization of allyl α-polyhaloesters, we planned to extend the scope of TMC-ATRC to the higher homologues of acetate, which as far we are aware was never attempted by anyone (Scheme 3). Unfortunately, the cyclization of the allyl 2,2-dichloropentanoate (**13**, R=*n*-Pr), chosen as reference substrate, notwithstanding the efforts spent (ligands, solvents and reaction conditions were thoroughly changed), failed. As a consequence we turned our attention to the Ueno–Stork strategy. Now we report that this route led us to synthesize the 3-alkyl-3-chloro-4-chloromethyl-γ-lactones **6** in acceptable yields, from the cheap and easily accessible 2,2-dichloroaldehydes **1**,[18] through the CuCl–*N*,*N*,*N*′,*N*′,*N*″-pentamethyldiethylenetriamine (PMDETA) catalyzed ATRC of the *O*-allyl-2,2-dichlorohemiacetal acetate intermediates **2** (Scheme 3). It is interesting to note that from the point of view of



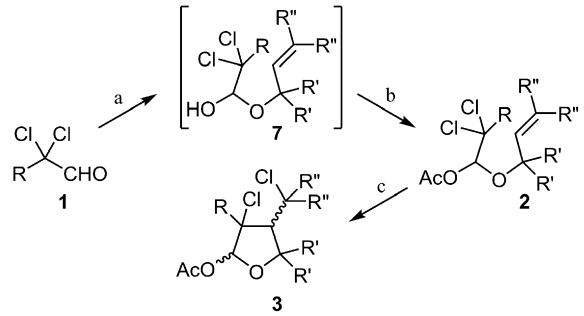
Scheme 3. Retrosynthetic path from dichloro-γ-lactones **6** to 2,2-dichloroaldehydes **1**.

the common starting material **1** (R≠H and Cl), both the 'direct' route and the Ueno–Stork path extend on the same number of steps. While this work was still in progress, we realized the synthetic potential of the radical cyclization of *O*-allyl α,α-dichloroacetals and announced its application to the synthesis of the botryodiplodin acetate.[19]

2. Results and discussion

The reported procedures for forming haloacetals, that is: the substitution of an α-haloether by an allyl alcohol or the halogenation of an enolether in the presence of an excess of an allylic alcohol (used in standard Ueno–Stork reactions),[11] appeared inappropriate for our starting materials, the α,α-dichloro aldehydes. However, the destabilization of the carbonyl function due to the electron-withdrawing action of the two α chlorine atoms, suggested us to exploit, for the construction of the *O*-allyl-α-perchloroacetals, the susceptibility of the α-perchloroaldehydes to form relatively stable hemiacetals.[20]

At the outset we studied the methylation of the hemiacetal **7d** (R=*n*-Pr; R′=R″=H), obtained in situ from 2,2-dichloropentanal (**1d**) and allyl alcohol, with methyl iodide in presence of a number of nitrogen bases (Scheme 4). Unfortunately all our efforts to get the acetal were frustrating, observing only the formation of methyl ammonium salts. We then considered the acylation of **7d** with acetyl chloride. In fact acyl halides not only react reversibly with nitrogen bases but the acylammonium salts present at the equilibrium are good acylating reagents too (conservation of the electrophilic potential). Gratifyingly, the addition of 2-propenol to α,α-dichloropentanal (**1d**) in CH_2Cl_2 at −13 °C and acetylation of the intermediate hemiacetal **7d** with acetyl chloride/Et_3N gave the expected haloacetal **2d** (R=*n*-Pr; R′=R″=H; Scheme 4) in good yield (73%). As side products allylacetate and unreacted **1d** were observed, indication that the equilibrium between the hemiacetal and the parent aldehyde is far to be complete.



Scheme 4. (a) AllOH, Et_3N, CH_2Cl_2, −13 °C, 2 h. (b) AcCl, CH_2Cl_2, 0 °C, 20 h. (c) CuCl/PMDETA, CH_3CN, 80 °C, 18 h.

To avoid the use of a stoichiometric amount of nitrogen base we, alternatively, tried the addition of sodium 2-propenolate to the carbonyl end followed by the acetylation of the intermediate thus generated. Owing to the potential interaction between the negatively charged oxygen and the vicinal halides,[21] the two steps were performed at −78 °C. Notwithstanding the almost complete conversion, the yield of **2d** was equivalent to the one obtained with the first method. Owing to the lower practicality of the second approach, the first one was preferred for carrying out the preparation of a set of hemiacetal acetates (Table 1). As clearly shown in Table 1, the yields appears greatly influenced by the steric hindrance of **1** and of the allyl alcohol; in fact, the outcomes progressively worsen on increasing the crowding around the reaction centres.

Since *O*-allyl-2,2-dichlorohemiacetal acetates have LUMOs of higher energy than the related 2,2,2-trichloro compounds, they should be less reactive (less able to undergo to a homolytic C–Cl

Table 1
Preparation of hemiacetal acetates **2**[a]

Entry	R	R′	R″	Prod	Yield[b,c] (%)
1	Me	H	H	**2a**	77 (95)
2	Me	Me	H	**2b**	48 (62)
3	Me	H	Me	**2c**	71 (89)
4	*n*-Pr	H	H	**2d**	73 (91)
5	*i*-Pr	H	H	**2e**	54 (68)

[a] **1** (0.875 mol), AllOH (0.875 mol), Et_3N (1.013 mol), AcCl (0.875 mol), CH_2Cl_2 (350 mL), T=−13 °C (2 h)→0 °C (20 h).
[b] Yields determined on isolated material.
[c] In parentheses the % of conversion (GC values) are reported.

cleavage).[22] Indeed, all the trials carried out on the ATRC of **2c** with CuCl/bipyridine (Bpy), the same catalyst used by Ram,[12] gave a poor outcome (Table 2, items 1–3). Neither *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) gave rise to an enough reactive complex (Table 2, Entries 4–6). Evidently, a more effective catalyst was required. This can be simply obtained increasing the number of the chelating nitrogen on the ligand that will catch the CuCl.[6n,8,23] The cheap aliphatic tripodal ligand PMDETA appeared a good candidate. Gratifyingly the ATRC with the new catalyst was carried out in high yield, under relatively mild reaction condition, using only a 10%$_{mol/mol}$ of the cuprous complex (Table 2, Entries 7–10). The best reaction conditions established for **2c** were then extended to the other hemiacetal acetates **2**, obtaining a good result in all cases (Table 3).

However, a modest stereoselectivity in the cyclization of **2** was observed (Table 3). In contrast to the configurational lability of the C-3 stereogenic centre in 3-alkyl-3-chloro-4-chloroalkyl-γ-lactams under the conditions of the ATRC reaction,[16a] the analogous position in **3** appears stable, thus excluding the possibility of reversible radical generation at this site by the redox catalyst. Indeed the ratio of the four produced diastereomers was virtually the same throughout the course of the reaction, even when purified **3** were subjected to the same ATRC conditions experienced by **2**. This observation suggests that the cyclization of **2** should proceed under kinetic control.

To further check this hypothesis molecular mechanics calculations[24] have been performed to evaluate the relative energies of the four diastereoisomers (enantiomeric pairs) **3a**, depicted in Figure 1. While the parent tetrahydrofuran is known to show marked flexibility[25] in both bond angles and dihedrals,[26] polysubstituted tetrahydrofurans can be expected to exhibit a reduced number of conformations. The steric energies for the most stable conformation of each diastereoisomer are reported in Table 4, showing that α-*cis*-**3a** and β-*cis*-**3a** are ca. 2 kcal mol^{-1} more stable than α-*trans*-**3a** and β-*trans*-**3a**. A comparison with the relative yields reported in Table 3 supports the hypothesis that the ATRC does not progress under thermodynamic control.

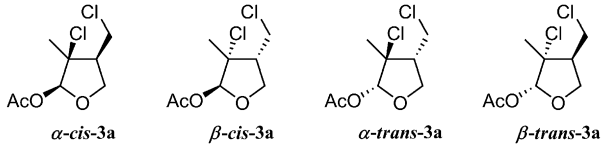


Figure 1. The four diastereomers of **3a**.

A more detailed inspection of molecular mechanics results shows that the most stable conformations of the four diastereoisomers are similar to envelopes with C(3) on the flap. This is reasonable as C(3), bearing both a chlorine atom and a methyl group, is the most congested ring carbon while the consequent location of the oxygen atom on the ring side opposite to the flap considerably reduces eclipsing of hydrogens and/or substituents in that critical part of the ring. The main factor determining the greater stability of α-*cis*-**3a** and β-*cis*-**3a** appears to be the trans relationship between the 3-CH_3 and the 4-CH_2Cl substituents (see Table 4), allowing a pseudoequatorial orientation of both these groups. As expected, in either diastereoisomer the C_3–C_4 bond is *anti* to both the CH_2–Cl and to a C(3)C–H bond, while the C=O double bond is eclipsed to both the C(2)–O and to a C(O)C–H bond. The conformations where the 3-CH_3 and 4-CH_2Cl groups are both axially oriented are ca. 4 kcal mol^{-1} less stable.

The stereochemical outcome of the radical haloacetal cyclization, carried out following the $Bu_3SnH/Et_3B/O_2$ method, has been explored by Renaud and co-workers.[27] They observed that in these reactions the acetal centre can fully control the stereochemistry at C-4 (the substituent at C-4 and the alkoxy at C-2 gain a cis relation) owing to the anomeric effect, which stabilizes the conformations where the exocyclic alkoxy group occupies a pseudoaxial position in the ring closure transition state.[27]

Since the anomeric effect of an acetoxy group should be greater than that of an alkoxy substituent,[28] we were surprised to see that the radical cyclization of **2** was not as selective, relatively to the positions C-2 and C-4, as expected; in fact the ratio of the diastereomers with the acetoxy and the substituent at C-4 in a cis arrangement against those with the same groups in a trans arrangement, (α-*cis*-**3**+α-*trans*-**3**)/(β-*cis*-**3**+β-*trans*-**3**), varied in the main from 63:37 to 70:30. Only **3b**, maybe owing to its higher steric congestion, gave a diastereomeric ratio (38:62) largely out from the reported interval.

Table 2
ATRC of hemiacetal acetate **2c**[a]

Entry	Ligand[b] (%)	CuCl[b] (%)	T (°C)	Conv[b] (%)	**3c** (%)[c,d]
1	Bpy (10)	10	80	0	0
2	Bpy (10)	10	100	20	19
3	Bpy (5)	5	100	0	0
4	TMEDA (20)	10	80	0	0
5	TMEDA (20)	10	100	40	38
6	TMEDA (10)	5	100	0	0
7	PMDETA (10)	10	80	99	98 (89)
8	PMDETA (5)	5	80	83	82
9	PMDETA (10)	10	100	64	26
10[e]	PMDETA (10)	10	80	98	97 (87)

[a] **2c** (10 mmol), CH_3CN (10 mL), 18 h.
[b] mol/mol of **2c**.
[c] GC values.
[d] In parentheses yields determined on isolated material.
[e] **2c** (16 mmol), CH_3CN (4 mL), 18 h.

Table 3
ATRC of hemiacetal acetates **2**[a]

Entry	Sub	Prod	Conv[b] (%)	Yield[c,d] (%)
1	**2a**	**3a**	100	84 (13:54:21:12)
2	**2b**	**3b**	100	91 (16:22:36:26)
3	**2c**	**3c**	100	89 (21:42:25:12)
5	**2d**	**3d**	100	88 (20:46:22:12)
6	**2e**	**3e**	100	93 (22:48:27:3)

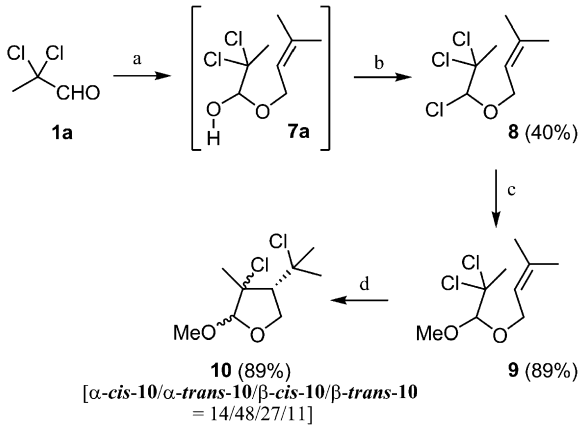
[a] **2** (10 mmol), CuCl (1.0 mmol), PMDETA (1.0 mmol), CH_3CN (10 mL), 18 h.
[b] GC values.
[c] Yields determined on isolated material.
[d] In parentheses the ratio α-*cis*-3/α-*trans*-3/β-*cis*-3/β-*trans*-3 determined by ^{1}H NMR.

Table 4
MMFF94[a] steric energies (kcal mol^{-1}) for diastereoisomers **3a**

Isomer	E_{st}	2-OAc/3-CH_3	3-CH_3/4-CH_2Cl
α-*cis*-**3a**	−5.768	*trans*	*trans*
β-*cis*-**3a**	−5.900	*cis*	*trans*
α-*trans*-**3a**	−3.917	*cis*	*cis*
β-*trans*-**3a**	−3.744	*trans*	*cis*

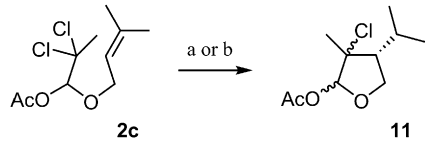
[a] See Ref. 24.

To comprehend if an alkoxy group, in place of the acetoxy one, could give rise to a different stereochemical outcome in the ATRC, we synthesized the *O*-allyl,*O*-methyl acetal **9** (Scheme 5). Since methylation of the hemiacetal **7a** proved to be an impassable route, we needed to develop an alternative method for the preparation of **9**. The starting point was always the hemiacetal **7a**, from aldehyde **1a** and 3-methyl-2-buten-1-ol, but now it was converted with methanesulfonyl chloride into the trichloroadduct **8** (yield 40%), which, after reaction with MeOLi, gave smoothly the target *O*-allyl,*O*-methyl acetal **9** (yield 89%). The ATRC of **9**, under the same reaction conditions we used to cyclize **2**, produced the 2-methoxy-tetrahydrofuran **10** (yield 89%) as a mixture of four diastereomers with a α-*cis*-**10**/α-*trans*-**10**/β-*cis*-**10**/β-*trans*-**10** ratio of 14:48:27:11 [(α-*cis*-**10**+α-*trans*-**10**):(β-*cis*-**10**+β-*trans*-**10**)=62:38], lined up with the product ratio we observed on the cyclization of **2** (see Table 3).



Scheme 5. (a) 3-Methyl-2-buten-1-ol, CH_2Cl_2, −13 °C, 1 h. (b) CH_3SO_2Cl, Et_3N, CH_2Cl_2, 0 °C, 20 h. (c) CH_3OLi, CH_3OH, 25 °C, 24 h. (d) CuCl/PMDETA, CH_3CN, 80 °C, 24 h.

Considering that the stereochemical outcome could be influenced by the cyclization method, we also tried the reaction of **2** with Bu_3SnH/AIBN in toluene at 110 °C (*Method a*, Experimental part). However, as shown in Scheme 6, the stereoselectivity of the obtained 2-acetoxy-3-chloro-4-isopropyl-3-methyl-tetrahydrofuran **11** (53% yield) was worse than the one issued by the TMC-ATRC method: α-*cis*-**11**/α-*trans*-**11**/β-*cis*-**11**/β-*trans*-**11**=27:28:25:20 (α-*cis*-**11**+α-*trans*-**11**):(β-*cis*-**11**+β-*trans*-**11**)=55:45. The reductive cyclization was then repeated at −78 °C, always in toluene, but using the system $Bu_3SnH/Et_3B/O_2$ (*Method b*, Experimental part). Under the new conditions a much better stereoselectivity was indeed noted: α-*cis*-**11**/α-*trans*-**11**/β-*cis*-**11**/β-*trans*-**11**=19:53:28:0 with a (α-*cis*-**11**+α-*trans*-**11**):(β-*cis*-**11**+β-*trans*-**11**) ratio of 72:28.[22b]



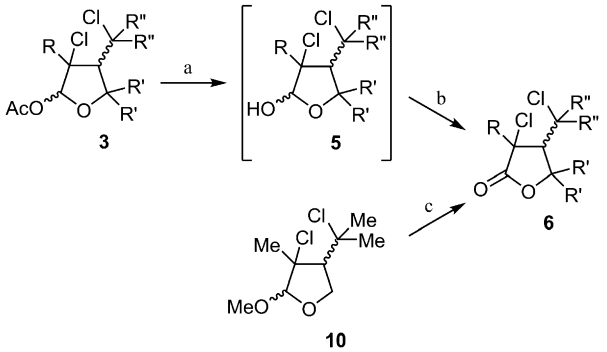
a) yield 53% ; α-***cis*-11**/α-***trans*-11**/β-***cis*-11**/β-***trans*-11** = 27/28/25/20

b) yield 43%; α-***cis*-11**/α-***trans*-11**/β-***cis*-11**/β-***trans*-11** = 19/53/28/0

Scheme 6. (a) Bu_3SnH, AIBN, toluene, 110 °C, 7 h; (b) Bu_3SnH, Et_3B/O_2, toluene, −78 °C, 2 h.

The partial selectivity we observed in the ATRC of **2** and **9** should not be attributed to the presence of a C(2)–Cl function in the cyclic radical intermediates. In fact, the cyclization, accomplished by Renaud and co-workers with the $Bu_3SnH/Et_3B/O_2$ method, of an analogous 2,2-dibromoacetal afforded a 2-alkoxy-tetrahydrofuran with complete cis-stereoselectivity between the substituents at C-2 and C-4.[29] Likely, the low temperature, under which the radical cyclizations with $Bu_3SnH/Et_3B/O_2$ were carried out, allowed the reaction to move solely through the most stable transition state structure; unfortunately the redox complex CuCl–PMDETA is unable to carry out the ATRC of **2** and **9** below 80 °C, and this prevents from delivering **3** or **10** with a more advantageous α/β ratio.

After a series of frustrating trials to accomplish the direct oxidation of **3a–e** and **10** with reagents based on $Cr^{(VI)}$ or H_2O_2/H^+ (evidently the electron-withdrawing action of the chloro atom bound at C-3 prevent a reaction otherwise possible[30]), we judged it more promising to perform the oxidation on the corresponding lactols (**5**, Scheme 7). Indeed we were only able to hydrolyze the acetates **3a–e** and not the methoxylate **10**, by heating in diluted aqueous H_2SO_4. Then the resulting lactols (**5**), without isolation, were oxidized, in the same pot, with Jones' reagent. This two-step procedure let the preparation of the expected dichloro-γ-lactones **6a**, **b**, **d** and **e** in satisfactory yields (Table 5).



Scheme 7. (a) H_2SO_4, H_2O, 80 °C, 6–24 h; (b) $K_2Cr_2O_7$, H_2SO_4, acetone/H_2O, 25 °C, 4–8 h; (c) O_3, 25 °C, EtOAc, 24 h.

Only with **3c** did the method fail, probably due to complications arising from the parasitic acid-catalyzed elimination of hydrogen chloride from the exocyclic substituent with the tertiary halogen,[19] during the hydrolysis step. A better way to obtain **6c** was successfully found, exploiting the oxidative ozonation of cyclic acetals like **10**.[31] In fact, the treatment with ozone at room temperature, for 24 h, was able to convert **10** into **6c**, in 33% yield.

Somewhat surprisingly, the cis–trans ratio of the recovered γ-lactones **6** doesn't closely match with that of **3** and **10** (Table 5). An explanation of that comes from the observation, through GC–MS monitoring, of a different reactivity between the four diastereomers of **3**, during the hydrolysis and the oxidation steps. Also for **10**, it was evident that ozonation transformed faster some isomers in respect to others, resulting in a discrepancy between the diastereoisomeric ratio of the starting material and **6c**.

Table 5
Preparation of γ-lactones **6**

Entry	Sub	Prod	Method[a]	Conv[b] (%)	Yield[c,d] (%)
1	**3a**	**6a**	A	100	81 (33:67)
2	**3b**	**6b**	A	100	71 (65:35)
3	**3d**	**6d**	A	100	81 (41:59)
4	**3e**	**6e**	A	98	78 (53:47)
5	**10**	**6c**	B	99	33 (25:75)

[a] Method A: **3** (4 mmol); hydrolysis: 96% aq H_2SO_4 (eight drops), H_2O (4 mL), 80 °C, 6–24 h; oxidation: $K_2Cr_2O_7$ (3 mmol), acetone (2.8 mL), H_2O (2 mL), 96% aq H_2SO_4 (0.63 mL), 25 °C, 4–8 h; Method B: **10** (2 mmol), EtOAc (30 mL), O_3, 25 °C, 24 h.

[b] GC values.

[c] Yields determined on isolated material.

[d] In parentheses the cis:trans ratio determined by ^1H NMR.

3. Conclusions

In summary, an original two-step one-pot method for the assembly of a set of *O*-allyl-2,2-dichlorohemiacetal acetates (**2**) was developed, starting from cheap and easily available 2,2-dichloroaldehydes (**1**). Acetates **2**, subjected to a tin-free Ueno–Stork cyclization, catalyzed by a CuCl–PMDETA complex, were then transformed in a set of previously unreported 3-alkyl-3-chloro-4-chloromethyl-γ-lactol acetates (**3**) in good overall yield and moderate stereoselectivity. Finally, a two-step, one-pot hydrolysis–oxidation procedure was developed to transform the cyclic acetates **3** into the final γ-lactones (**6**). For the preparation of **6c**, a different route was necessary, being the cyclic acetate **3c** sensitive to acid hydrolysis conditions. Future development, especially oriented in the search to a more environmentally friendly oxidant, will follow.

4. Experimental part

4.1. General

Reagents and solvents were standard grade commercial products, purchased from Aldrich, Acros, Fluka or RdH, and used without further purification, except acetonitrile that was dried over three batches of 3 Å sieves (5% w/v, 12 h). The silica gel used for flash chromatography was Silica Gel 60 Merck (0.040–0.063 mm). 2,2-Dichloropropanal (**1a**), 2,2-dichloropentanal and 2,2-dichloro-3-methylbutanal were prepared following a published procedure and were fully characterized in Ref. 18. ^{1}H NMR, IR and MS spectra were recorded on Bruker DPX 200 and Bruker Avance 400, JASCO FT/IR-4200 and HP-G1800C Series II GC–MS instruments, respectively. ^{1}H and ^{13}C chemical shifts (δ) are reported in parts per million relative to TMS.

4.2. NMR spectroscopy details

The structural assignment of compounds **3a–d**, **6a–e**, **10** and **11** was determined by suitable two-dimensional techniques, applying standard pulse sequences implemented in the Bruker software. The most effective experiments in the determination of the molecular skeleton were the heteronuclear H,C inverse-detection multiple-quantum and multiple-bond NMR correlations (HMQC and HMBC). They permit the detection of one-bond and long-range H,C connectivities, respectively. These sequences were applied directly on mixtures of diastereoisomers (compounds **3a–d** and **6a–e**). Once established that the molecular skeleton was the same for all the components of a mixture, Nuclear Overhauser Enhancement Correlation Spectroscopy (NOESY) was used to determine the relative configuration of each component. Particularly, the stereochemistry of **3a–e**, **10** and **11** was assigned by NOE correlations between protons of R group and methine protons of C(2) and C(4) positions. Moreover, the NOE correlation between R and R′ protons was exploited in order to confirm the structural assignment. With regard to compounds **6a–e**, the relative configuration at the C(3) and C(4) positions was determined by NOE correlation between R, R′ and C(4) protons.

Parameters used in coupled HMQC experiments: spectral width=6 ppm with 4k complex points in f_2; spectral width=100 ppm in f_1, with 128 t_1 increments; two scans per increment; 3.45 ms evolution delay (corresponding to a ^1J=145 Hz). Parameters used in HMBC experiments: spectral width=6 ppm with 4k complex points in f_2; spectral width=170 ppm in f_1, with 256 t_1 increments; four scans per increment; 50 ms evolution delay (corresponding to a ^nJ=10 Hz), 3.45 ms delay for low-pass filter in order to reduce direct correlations. Parameters used in NOESY phase-sensitive (by time-proportional phase incrementation) experiments: spectral width=7 ppm with 4k complex points in f_2; 256 t_1 increments in f_1; eight scans per increment; mixing time=0.7 s.

4.3. Preparation of the 2,2-dichlorohemiacetal acetates 2 (Table 1)

*4.3.1. Preparation of 2,2-dichloro-1-(2-propenyloxy)propyl acetate (**2a**).* 2,2-Dichloropropanal **1a** (111.1 g, 0.875 mol) and 2-propen-1-ol (59.5 mL, 0.875 mol) were carefully mixed together (exothermic) in a 250 mL flat-bottomed conical flask, and left to stand for 2 h. In the meantime, a three-necked 1 L round bottom flask was equipped with a dropping funnel (sealed on the top with a $CaCl_2$ tube), a thermometer and a mechanical stirrer; then CH_2Cl_2 (350 mL) and triethylamine (141.2 mL, 1.013 mol) were introduced inside it. This solution, under stirring, was cooled to −13 °C and a solution of acetyl chloride (62.2 mL, 0.875 mol) in CH_2Cl_2 (20 mL), previously charged into the dropping funnel, was added. When the mixture was re-equilibrated at −13 °C, the content of the conical flask was introduced (washing the flask with 2×10 mL CH_2Cl_2), taking care to keep the temperature in the range 0–5 °C. Next, the reaction mixture was left at 0 °C for 20 h, and after warming at room temperature, diluted with HCl_{aq} 5% wt/v (150 mL). The organic phase was separated and washed with H_2O (3×50 mL), while the combined aqueous layers were further washed with CH_2Cl_2 (2×25 mL). The combined organic extracts were concentrated and dried through azeotropic distillation with toluene (20 mL). Distillation of the crude product under vacuum afforded the *title compound* **2a** (153.0 g, 77%) as a colourless liquid, bp 100–101 °C (9 mmHg). [Found: C, 41.4; H, 5.1. $C_8H_{12}Cl_2O_3$ requires C, 42.31; H, 5.33]; ^{1}H NMR ($CDCl_3$, 200 MHz): δ=2.10 (3H, s, C*H*$_3$), 2.16 (3H, s, C*H*$_3$), 4.22 (1H, ddt, *J*=12.4, 6.5, 1.6 Hz, OCH*H*), 4.34 (1H, ddt, *J*=12.4, 5.4, 1.6 Hz, OC*H*H), 5.24 (1H, dq, *J*=10.3, 1.6 Hz, CH=C*H*H), 5.35 (1H, dq, *J*=17.3, 1.6 Hz, CH=CH*H*), 5.80–6.05 (1H, m, C*H*=CH$_2$), 6.00 (1H, s, CCl$_2$C*H*). ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ=20.7 (*C*H$_3$C=O), 30.7 (*C*H$_3$CCl$_2$), 71.8 (OCH$_2$CH), 86.8 (*C*Cl$_2$), 97.6 (H*C*O), 118.4 (CH=*C*H$_2$), 132.7 (*C*H=CH$_2$), 169.9 (*C*=O). IR (film): 1751 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 41 (35), 43 (100), 57 (7), 72 (7), 110 (14), 131 (5), 167 (7, M$^+$−OAc).

*4.3.2. Preparation of 2,2-dichloro-1-(1,1-dimethyl-2-propenyloxy) propyl acetate (**2b**).* Starting from 2,2-dichloropropanal (111.1 g, 0.875 mol) and 2-methyl-3-buten-2-ol (91.5 mL, 0.875 mol), 107.2 g of the *title compound* **2b** were obtained (48%, colourless liquid, bp 92 °C at 10 mmHg) following the same procedure described for **2a**. [Found: C, 46.9; H, 6.2. $C_{10}H_{16}Cl_2O_3$ requires 47.08; H, 6.32]; ^{1}H NMR ($CDCl_3$, 200 MHz): δ=1.35 (3H, s, OC(C*H*$_3$)$_2$CH), 1.39 (3H, s, OC(C*H*$_3$)$_2$CH), 2.06 (3H, s, C*H*$_3$), 2.08 (3H, s, C*H*$_3$), 5.16 (1H, dd, *J*=11.2, 1.2 Hz, CH=C*H*H), 5.23 (1H, dd, *J*=17.6, 1.2 Hz, CH=C*H*H), 5.91 (1H, dd, *J*=17.6, 11.2 Hz, C*H*=CH$_2$), 6.16 (1H, s, CCl$_2$C*H*). ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ=21.0 (*C*H$_3$C=O), 25.5 (OC(*C*H$_3$)$_2$CH), 25.9 (OC(*C*H$_3$)$_2$CH), 30.7 (*C*H$_3$CCl$_2$), 78.5 (O*C*(CH$_3$)$_2$CH), 87.7 (*C*Cl$_2$), 93.4 (H*C*O), 115.0 (CH=*C*H$_2$), 141.8 (*C*H=CH$_2$), 169.2 (*C*=O). IR (film): 1749 (C=O), 1636 (C=C) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 41 (18), 43 (36), 69 (100), 86 (14), 113 (24), 128 (2).

*4.3.3. Preparation of 2,2-dichloro-1-(3-methyl-2-butenyloxy)propyl acetate (**2c**).* Starting from 2,2-dichloropropanal (111.1 g, 0.875 mol) and 3-methyl-2-buten-1-ol (89.8 mL, 0.875 mol), 158.5 g of the *title compound* **2c** were obtained (71%, colourless liquid, bp 94–96 °C at 4 mmHg) following the same procedure described for **2a**. [Found: C, 47.0; H, 6.3. $C_{10}H_{16}Cl_2O_3$ requires 47.08; H, 6.32]; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.67 (3H, br s, C*H*$_3$C=C), 1.75 (3H, br s, C*H*$_3$C=C), 2.07 (3H, s, C*H*$_3$), 2.15 (3H, s, C*H*$_3$), 4.15–4.40 (2H, m, OC*H*$_2$CH), 5.25–5.45 (1H, m, C*H*=C), 5.97 (1H, s, CCl$_2$C*H*); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 18.0 (*C*H$_3$C=C), 20.8 (*C*H$_3$C=O), 25.8 (*C*H$_3$C=C), 30.8 (*C*H$_3$CCl$_2$), 67.7 (OCH$_2$CH), 87.1 (*C*Cl$_2$), 97.6

(HCO), 119.2 (HC=C), 139.0 ($(CH_3)_2C$=C), 170.1 (C=O). IR (film): 1755 (C=O), 1674 (C=C) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 43 (44), 69 (100), 85 (89), 110 (14), 159 (29), 194 (3, M^+−60).

*4.3.4. Preparation of 2,2-dichloro-1-(2-propenyloxy)pentyl acetate (**2d**).* Starting from 2,2-dichloropentanal (135.6 g, 0.875 mol) and 2-propen-1-ol (59.5 mL, 0.875 mol), 163.0 g of the *title compound* **2d** were obtained (73%, colourless liquid, bp 94–97 °C at 1 mmHg) following the same procedure described for **2a**. [Found: C, 47.1; H, 6.4. $C_{10}H_{16}Cl_2O_3$ requires C, 47.08; H, 6.32]; ^{1}H NMR ($CDCl_3$, 200 MHz): δ=0.99 (3H, t, *J*=7.2 Hz, C*H*$_3$CH$_2$CH$_2$), 1.60–1.85 (2H, m, CH$_3$C*H*$_2$CH$_2$), 2.10–2.25 (2H, m, CH$_3$CH$_2$C*H*$_2$), 2.16 (3H, s, C*H*$_3$C=O), 4.20 (1H, ddt, *J*=12.7, 6.9, 1.4 Hz, OC*H*H), 4.33 (1H, ddt, *J*=12.7, 5.5, 1.4 Hz, OC*H*H), 5.24 (1H, dq, *J*=10.3, 1.4 Hz, CH=CH*H*), 5.34 (1H, dq, *J*=17.4, 1.4 Hz, CH=CH*H*), 5.80–6.05 (1H, m, C*H*=CH$_2$), 6.03 (1H, s, CCl$_2$C*H*). ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 13.6 (*C*H$_3$CH$_2$CH$_2$), 17.6 (CH$_3$*C*H$_2$CH$_2$), 20.8 (*C*H$_3$C=O), 43.4 (CH$_3$CH$_2$*C*H$_2$), 71.9 (O*C*H$_2$CH), 91.9 (CCl_2), 97.7 (HCO), 118.6 (CH=*C*H$_2$), 132.8 (*C*H=CH$_2$), 170.2 (*C*=O). IR (film): 1754 (C=O), 1674 (C=C) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 43 (100), 129 (13), 138 (23), 159 (5), 195 (12).

*4.3.5. Preparation of 2,2-dichloro-3-methyl-1-(2-propenyloxy)butyl acetate (**2e**).* Starting from 2,2-dichloro-3-methylbutanal (135.6 g, 0.875 mol) and 2-propen-1-ol (59.5 mL, 0.875 mol), 120.6 g of the *title compound* **2e** were obtained (54%, colourless liquid, bp 91–92 °C at 2 mmHg) following the same procedure described for **2a**. [Found: C, 46.9; H, 6.0. $C_{10}H_{16}Cl_2O_3$ requires C, 47.08; H, 6.32]; ^{1}H NMR ($CDCl_3$, 200 MHz): δ=1.14 (3H, d, *J*=6.7 Hz, CH(C*H*$_3$)CH$_3$), 1.19 (3H, d, *J*=6.7 Hz, CH(C*H*$_3$)CH$_3$), 2.20 (3H, s, C*H*$_3$C=O), 2.52 (1H, ept, *J*=6.7 Hz, (CH$_3$)$_2$C*H*), 4.19 (1H, ddt, *J*=12.4, 5.9, 1.6 Hz, OC*H*H), 4.33 (1H, ddt, *J*=12.4, 5.4, 1.6 Hz, OC*H*H), 5.25 (1H, dq, *J*=10.2, 1.6 Hz, CH=C*H*H), 5.35 (1H, dq, *J*=17.1, 1.6 Hz, CH=C*H*H), 5.80–6.05 (1H, m, C*H*=CH$_2$), 6.12 (1H, s, CCl$_2$C*H*). ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ=18.0 ((*C*H$_3$)$_2$CH), 18.1 ((*C*H$_3$)$_2$CH), 20.9 (*C*H$_3$C=O), 39.3 ((CH$_3$)$_2$*C*H), 71.5 (O*C*H$_2$CH), 96.3 (HCO), 97.3 (CCl_2), 118.6 (CH=*C*H$_2$), 132.7 (*C*H=CH$_2$), 170.4 (*C*=O). IR (film): 1750 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 43 (100) 55 (10), 91 (5), 103 (9), 129 (4), 138 (9), 195 (3, M^+−OAc).

4.4. Preparation of the 2,2-dichlorolactol acetates 3 (Table 3)

*4.4.1. Preparation of 2-acetoxy-3-chloro-4-chloromethyl-3-methyl-tetrahydrofuran (**3a**).* CuCl (99 mg, 1 mmol) and **2a** (2.27 g, 10 mmol) were weighted into a Schlenk tube fitted with a perforable septum (blocked by a screw cap). Dry acetonitrile (10 mL) and PMDETA (209 μL, 1 mmol) were then added, under argon. The mixture was stirred at 80 °C and after 18 h it was diluted with HCl_{aq} 5% w/v (25 mL) and extracted with CH_2Cl_2 (2×15 mL). The combined organic layers were dried with toluene through azeotropic distillation. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2). This gave the *title compound* **3a** (1.91 g, 84%), as a 13:54:21:12 (α-*cis*/α-*trans*/β-*cis*/β-*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless thick oil. [Found: C, 42.2 H, 5.3 $C_8H_{12}Cl_2O_3$ requires C, 42.31; H, 5.33]; R_f (30% Et$_2$O/petroleum ether 40–60) 0.30 and 0.33; ^{1}H NMR ($CDCl_3$, 400 MHz): diastereomer α-*cis*-**3a** (13%) δ=1.71 (3H, s, C*H*$_3$C(3)), 2.12 (3H, s, C*H*$_3$C=O), 2.60 (1H, m, C(4)*H*), 3.65 (1H, t, *J*=11.0 Hz, C*H*$_2$Cl), 3.87 (1H, ddd, *J*=11.0, 4.6, 0.7 Hz, C*H*$_2$Cl), 4.09 (1H, dd, *J*=9.2, 6.3 Hz, C(5)*H*$_2$), 4.27 (1H, dd, *J*=9.2, 7.5 Hz, C(5)*H*$_2$), 6.05 (1H, s, C(2)*H*); diastereomer α-*trans*-**3a** (54%) δ=1.65 (3H, s, C*H*$_3$C(3)), 2.08 (3H, s, C*H*$_3$C=O), 2.90 (1H, m, C(4)*H*), 3.56 (1H, t, *J*=11.1 Hz, C*H*$_2$Cl), 3.72 (1H, ddd, *J*=10.8, 4.9, 1.2 Hz, C*H*$_2$Cl), 4.18 (1H, dd, *J*=9.3, 3.2 Hz, C(5)*H*$_2$), 4.46 (1H, ddd, *J*=9.3, 6.9, 1.2 Hz, C(5)*H*$_2$), 6.24 (1H, s, C(2)*H*); diastereomer β-*cis*-**3a** (21%) δ=1.68 (3H, s, C*H*$_3$C(3)), 2.08 (3H, s, C*H*$_3$C=O), 2.83 (1H, m, C(4)*H*), 3.64 (1H, dd, *J*=11.1, 8.9 Hz, C*H*$_2$Cl), 3.78 (1H, dd, *J*=11.2, 5.5 Hz, C*H*$_2$Cl), 3.88 (1H, ddd, *J*=10.0, 8.5, 0.4 Hz, C(5)*H*$_2$), 4.36 (1H, t, *J*=8.4 Hz, C(5)*H*$_2$), 6.24 (1H, s, C(2)*H*); diastereomer β-*trans*-**3a** (12%) δ=1.54 (3H, s, C*H*$_3$C(3)), 2.11 (3H, s, C*H*$_3$C=O), 3.13 (1H, m, C(4)*H*), 3.50 (1H, t, *J*=10.8 Hz, C*H*$_2$Cl), 3.84 (1H, dd, *J*=10.4, 4.4 Hz, C*H*$_2$Cl), 3.79 (1H, t, *J*=9.2 Hz, C(5)*H*$_2$), 4.37 (1H, t, *J*=8.9 Hz, C(5)*H*$_2$), 6.06 (1H, s, C(2)*H*). ^{13}C NMR ($CDCl_3$, 100.62 MHz): diastereomer α-*cis*-**3a** (13%) δ=20.9 (*C*H$_3$C=O), 28.9 (*C*H$_3$C(3)), 44.0 (*C*H$_2$Cl), 49.8 (*C*(4)), 71.4 (*C*(5)), 71.4 (*C*(3)), 100.6 (*C*(2)), 169.3 (C=O); diastereomer α-*trans*-**3a** (54%) δ=20.8 (*C*H$_3$C(3)), 21.1 (*C*H$_3$C=O), 43.3 (*C*H$_2$Cl), 52.6 (*C*(4)), 72.2 (*C*(5)), 73.4 (*C*(3)), 102.8 (*C*(2)), 169.0 (C=O); diastereomer β-*cis*-**3a** (21%) δ=21.1 (*C*H$_3$C=O), 23.1 (*C*H$_3$C(3)), 41.3 (*C*H$_2$Cl), 49.0 (*C*(4)), 72.3 (*C*(5)), 75.1 (*C*(3)), 103.6 (*C*(2)), 169.0 (C=O); diastereomer β-*trans*-**3a** (12%) δ=21.0 (*C*H$_3$C=O), 22.6 (*C*H$_3$C(3)), 41.0 (*C*H$_2$Cl), 48.9 (*C*(4)), 69.1 (*C*(3)), 71.5 (*C*(5)), 101.0 (*C*(2)), 169.4 (C=O). IR (film): 1758 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 67 (66), 75 (29), 83 (26), 89 (56), 103 (79), 148 (49), 167 (100, M^+−OAc).

*4.4.2. Preparation of 2-acetoxy-3-chloro-4-chloromethyl-3,5,5-trimethyl-tetrahydrofuran (**3b**).* Following the same procedure for the preparation of **3a**, **2b** (2.55 g, 10 mmol) gave, after flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2), the *title compound* **3b** (2.32 g, 91%), as a 16:22:36:26 (α-*cis*/α-*trans*/β-*cis*/β-*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil. [Found: C, 47.0; H, 6.2. $C_{10}H_{16}Cl_2O_3$ requires C, 47.08; H, 6.32]; R_f (30% Et$_2$O/petroleum ether 40–60) 0.35 and 0.41; ^{1}H NMR ($CDCl_3$, 400 MHz): diastereomer α-*cis*-3b (16%) δ=1.40 (3H, s, C(5)C*H*$_3$), 1.44 (3H, s, C(5)C*H*$_3$), 1.76 (3H, s, C*H*$_3$C(3)), 2.15 (3H, s, C*H*$_3$C=O), 2.34 (1H, dd, *J*=8.2, 6.0 Hz, C(4)*H*), 3.65 (1H, dd, *J*=11.6, 8.2 Hz, C*H*$_2$Cl), 3.82 (1H, dd, *J*=11.6, 6.0 Hz, C*H*$_2$Cl), 6.01 (1H, s, C(2)*H*); diastereomer α-*trans*-**3b** (22%) δ=1.35 (3H, s, C(5)C*H*$_3$), 1.53 (3H, s, C(5)C*H*$_3$), 1.59 (3H, s, C*H*$_3$C(3)), 2.11 (3H, s, C*H*$_3$C=O), 2.84 (1H, dd, *J*=9.6, 5.7 Hz, C(4)*H*), 3.56 (1H, dd, *J*=11.4, 9.6 Hz, C*H*$_2$Cl), 3.77 (1H, dd, *J*=11.4, 5.7 Hz, C*H*$_2$Cl), 6.24 (1H, s, C(2)*H*); diastereomer β-*cis*-**3b** (36%) δ=1.41 (3H, s, C(5)C*H*$_3$), 1.46 (3H, s, C(5)C*H*$_3$), 1.68 (3H, s, C*H*$_3$C(3)), 2.08 (3H, s, C*H*$_3$C=O), 2.53 (1H, dd, *J*=8.8, 5.3 Hz, C(4)*H*), 3.72 (1H, dd, *J*=11.6, 8.8 Hz, C*H*$_2$Cl), 3.79 (1H, dd, *J*=11.6, 5.3 Hz, C*H*$_2$Cl), 6.21 (1H, s, C(2)*H*); diastereomer β-*trans*-**3b** (26%) δ=1.34 (3H, s, C(5)C*H*$_3$), 1.52 (3H, s, C(5)C*H*$_3$), 1.56 (3H, s, C*H*$_3$C(3)), 2.13 (3H, s, C*H*$_3$C=O), 2.87 (1H, dd, *J*=11.3, 3.8 Hz, C(4)*H*), 3.57 (1H, t, *J*=11.3 Hz, C*H*$_2$Cl), 3.87 (1H, dd, *J*=11.3, 3.8 Hz, C*H*$_2$Cl), 6.03 (1H, s, C(2)*H*). ^{13}C NMR ($CDCl_3$, 100.62 MHz): diastereomer α-*cis*-**3b** (16%) δ=21.0 (*C*H$_3$C=O), 23.1 (C(5)CH$_3$), 29.4 (*C*H$_3$C(3)), 30.6 (C(5)CH$_3$), 41.1 (*C*H$_2$Cl), 59.4 (*C*(4)), 75.2 (*C*(3)), 84.0 (*C*(5)), 99.8 (*C*(2)), 169.8 (C=O); diastereomer α-*trans*-**3b** (22%) δ=21.1 (*C*H$_3$C=O), 21.4 (*C*H$_3$C(3)), 24.2 (C(5)CH$_3$), 31.6 (C(5)CH$_3$), 40.3 (*C*H$_2$Cl), 60.6 (*C*(4)), 73.4 (*C*(3)), 84.6 (*C*(5)), 101.6 (*C*(2)), 169.2 (C=O); diastereomer β-*cis*-**3b** (36%) δ=21.2 (*C*H$_3$C=O), 23.5 (C(5)CH$_3$), 24.7 (*C*H$_3$C(3)), 32.8 (C(5)CH$_3$), 40.6 (CH$_2$Cl), 56.7 (*C*(4)), 76.8 (*C*(3)), 86.6 (*C*(5)), 102.0 (*C*(2)), 169.4 (C=O); diastereomer β-*trans*-**3b** (26%) δ=21.2 (*C*H$_3$C=O), 23.6 (C(5)CH$_3$), 24.0 (*C*H$_3$C(3)), 33.3 (C(5)CH$_3$), 39.5 (CH$_2$Cl), 57.0 (*C*(4)), 70.9 (*C*(3)), 84.7 (*C*(5)), 99.3 (*C*(2)), 169.7 (C=O). IR (film): 1748 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 89 (34), 95 (34), 101 (32), 117 (100), 131 (49), 166 (18), 195 (50, M^+−AcO).

*4.4.3. Preparation of 2-acetoxy-3-chloro-4-[(1-chloro-1-methyl)-ethyl]-3-methyl-tetrahydrofuran (**3c**).* Following the same procedure for the preparation of **3a**, **2c** (2.55 g, 10 mmol) gave, after flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2), the *title compound* **3c** (2.27 g, 89%), as a 21:42:25:12 (α-*cis*/α-*trans*/β-*cis*/β-*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil. [Found: C, 47.2; H, 6.3. $C_{10}H_{16}Cl_2O_3$ requires C, 47.08; H, 6.32]; R_f (10% Et$_2$O/petroleum ether 40–60)

0.17 and 0.24; ^{1}H NMR ($CDCl_3$, 400 MHz): diastereomer α-*cis*-**3c** (21%) δ 1.77 (3H, s, C(3)C*H*$_3$), 1.79 (3H, s CH_3(C*H*$_3$)CCl), 1.88 (3H, s, C*H*$_3$(CH_3)CCl), 2.13 (3H, s, C*H*$_3$C=O), 2.78 (1H, dd, *J*=9.6, 8.2 Hz, C(4)*H*), 4.21 (1H, dd, *J*=9.6, 9.2 Hz, C(5)*H*), 4.29 (1H, dd, *J*=9.2, 8.2 Hz, C(5)*H*), 6.01 (1H, s, C(2)*H*); diastereomer α-*trans*-**3c** (42%) δ 1.64 (3H, s, C*H*$_3$(CH_3)CCl), 1.80 (6H, s CH_3(C*H*$_3$)CCl), 2.12 (3H, s, C*H*$_3$C=O), 3.05 (1H, dd, *J*=9.1, 8.6 Hz, C(4)*H*), 4.15 (1H, t, *J*=9.1 Hz, C(5)*H*), 4.30 (1H, dd, *J*=9.1, 8.6 Hz, C(5)*H*), 6.20 (1H, s, C(2)*H*); diastereomer β-*cis*-3c (25%) δ 1.76 (3H, s, C(3)C*H*$_3$), 1.79 (3H, s CH_3(C*H*$_3$)CCl), 1.83 (3H, s, C*H*$_3$(CH_3)CCl), 2.09 (3H, s, C*H*$_3$C=O), 3.01 (1H, dd, *J*=10.3, 8.4 Hz, C(4)*H*), 4.22 (1H, dd, *J*=10.3, 8.4 Hz, C(5)*H*), 4.34 (1H, t, *J*=8.4 Hz, C(5)*H*), 6.15 (1H, s, C(2)*H*); diastereomer β-*trans*-**3c** (12%) δ 1.61 (3H, s, C*H*$_3$(CH_3)CCl), 1.79 (3H, s, C(3)C*H*$_3$), 1.88 (3H, s CH_3(C*H*$_3$)CCl), 2.12 (3H, s, C*H*$_3$C=O), 3.00 (1H, t, *J*=9.4 Hz, C(4)*H*), 4.25 (1H, dd, *J*=9.4, 8.7 Hz, C(5)*H*), 4.30 (1H, dd, *J*=9.4, 8.7 Hz, C(5)*H*), 5.99 (1H, s, C(2)*H*); ^{13}C NMR ($CDCl_3$, 100.62 MHz): diastereomer α-*cis*-**3c** (21%) δ 20.9 (*C*H$_3$C=O), 29.1 (*C*H$_3$(CH_3)CCl), 32.0 (*C*H$_3$C(3)), 32.6 (CH_3(*C*H$_3$)CCl), 58.7 (*C*(4)), 70.0 (*C*(5)), 70.8 (*C*(3)), 71.3 (CH_3(CH_3)*C*Cl), 101.2 (C(2)), 169.5 (*C*=O); diastereomer α-*trans*-**3c** (42%) δ 21.0 (*C*H$_3$C=O), 21.4 (*C*H$_3$C(3)), 31.3 (*C*H$_3$(CH_3)CCl), 33.8 (CH_3(*C*H$_3$)CCl), 60.3 (*C*(4)), 68.6 (CH_3(CH_3)*C*Cl), 69.1 (*C*(5)), 72.8 (*C*(3)), 103.3 (*C*(2)), 169.3 (*C*=O); diastereomer β-*cis*-**3c** (25%) δ 21.2 (*C*H$_3$C=O), 25.4 (*C*H$_3$C(3)), 31.5 (CH_3(CH_3)CCl), 32.9 (CH_3(*C*H$_3$)CCl), 56.9 (*C*(4)), 69.6 (CH_3(CH_3)*C*Cl), 70.4 (*C*(5)), 73.8 (*C*(3)), 105.0 (*C*(2)), 169.4 (*C*=O); diastereomer β-*trans*-**3c** (12%) δ 21.1 (*C*H$_3$C=O), 24.9 (*C*H$_3$C(3)), 31.4 (*C*H$_3$(CH_3)CCl), 35.3 (CH_3(*C*H$_3$)CCl), 55.5 (*C*(4)), 68.8 (CH_3(CH_3)*C*Cl), 69.6 (*C*(5)), 71.0 (*C*(3)), 102.3 (*C*(2)), 169.6 (*C*=O). IR (film): 1757 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 43 (100), 90 (49), 95 (75), 117 (55), 130 (77), 159 (15), 176 (8), 195 (43, M^+−AcO).

*4.4.4. Preparation of 2-acetoxy-3-chloro-4-chloromethyl-3-propyl-tetrahydrofuran (**3d**).* Following the same procedure for the preparation of **3a**, **2d** (2.55 g, 10 mmol) gave, after flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2), the *title compound* **3d** (2.24 g, 88%), as a 20:46:22:12 (α-*cis*/α-*trans*/β-*cis*/β-*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil. [Found: C, 47.1; H, 6.1. $C_{10}H_{16}Cl_2O_3$ requires C, 47.08; H, 6.32]; R_f (30% Et_2O/petroleum ether 40–60) 0.44 and 0.50; ^{1}H NMR ($CDCl_3$, 400 MHz): diastereomer α-*cis*-**3d** (20%) δ=0.97 (3H, t, *J*=7.4 Hz, C*H*$_3$CH$_2$CH$_2$C(3)), 1.20–1.90 (2H, m, CH$_3$C*H*$_2$CH$_2$C(3)), 1.80–1.90 (1H, m, CH$_3$CH$_2$C*H*$_2$C(3)), 2.10–2.20 (1H, m, CH$_3$CH$_2$C*H*$_2$C(3)), 2.11 (3H, s, C*H*$_3$C=O), 2.64 (1H, m, C(4)*H*), 3.64 (1H, t, *J*=11.1 Hz, C*H*$_2$Cl), 3.85 (1H, dd, *J*=11.1, 1.8 Hz, C*H*$_2$Cl), 4.07 (1H, dd, *J*=9.2, 6.6 Hz, C(5)H_2), 4.22–4.28 (1H, m, C(5)H_2), 6.15 (1H, s, C(2)*H*); diastereomer α-*trans*-**3d** (46%) δ=0.99 (3H, t, *J*=6.0 Hz, C*H*$_3$CH$_2$CH$_2$C(3)), 1.20–1.90 (2H, m, CH$_3$C*H*$_2$CH$_2$C(3)), 1.79 (2H, t, *J*=8.4 Hz, CH$_3$CH$_2$C*H*$_2$C(3)), 2.08 (3H, s, C*H*$_3$C=O), 2.80–2.92 (1H, m, C(4)*H*), 3.60 (1H, t, *J*=10.7 Hz, C*H*$_2$Cl), 3.69 (1H, ddd, *J*=10.7, 4.4, 1.2 Hz, C*H*$_2$Cl), 4.26 (1H, dd, *J*=9.2, 1.6 Hz, C(5)H_2), 4.45 (1H, ddd, *J*=8.0, 6.8, 0.8 Hz, C(5)H_2), 6.23 (1H, s, C(2)*H*); diastereomer β-*cis*-**3d** (22%) δ=0.96 (3H, t, *J*=7.4 Hz, C*H*$_3$CH$_2$CH$_2$C(3)), 1.20–1.90 (2H, m, CH$_3$C*H*$_2$CH$_2$C(3)), 1.78–1.88 (1H, m, CH$_3$CH$_2$C*H*$_2$C(3)), 1.89–2.00 (1H, m, CH$_3$CH$_2$C*H*$_2$C(3)), 2.08 (3H, s, C*H*$_3$C=O), 2.80–2.92 (1H, m, C(4)*H*), 3.60–3.70 (1H, m, C*H*$_2$Cl), 3.78 (1H, dd, *J*=11.0, 5.0 Hz, C*H*$_2$Cl), 3.92 (1H, t, *J*=8.8 Hz, C(5)H_2), 4.37 (1H, t, *J*=8.8 Hz, C(5)H_2), 6.24 (1H, s, C(2)*H*); diastereomer β-*trans*-**3d** (12%) δ=0.93 (3H, t, *J*=7.6 Hz, C*H*$_3$CH$_2$CH$_2$C(3)), 1.20–1.90 (2H, m, CH$_3$C*H*$_2$CH$_2$C(3)), 1.50–1.70 (2H, m, CH$_3$CH$_2$C*H*$_2$C(3)), 2.11 (3H, s, C*H*$_3$C=O), 3.17 (1H, m, C(4)*H*), 3.52 (1H, t, *J*=10.8 Hz, C*H*$_2$Cl), 3.81 (1H, t, *J*=9.3 Hz, C(5)H_2), 3.84 (1H, dd, *J*=10.8, 2.0 Hz, C*H*$_2$Cl), 4.37 (1H, t, *J*=9.3 Hz, C(5)H_2), 6.26 (1H, s, C(2)*H*). ^{13}C NMR ($CDCl_3$, 100.62 MHz): diastereomer α-*cis*-**3d** (20%) δ=14.2 (*C*H$_3$CH$_2$CH$_2$C(3)), 18.1 (CH$_3$*C*H$_2$CH$_2$C(3)), 21.1 (*C*H$_3$C=O), 43.2 (CH$_3$CH$_2$*C*H$_2$C(3)), 44.6 (*C*H$_2$Cl), 48.0 (*C*(4)), 71.5 (*C*(5)), 75.5 (*C*(3)), 99.4 (*C*(2)), 168.9 (C=O); diastereomer α-*trans*-**3d** (46%) δ=14.1 (*C*H$_3$CH$_2$CH$_2$C(3)), 18.3 (CH$_3$*C*H$_2$CH$_2$C(3)), 21.1 (*C*H$_3$C=O), 35.0 (CH$_3$CH$_2$*C*H$_2$C(3)), 43.4 (*C*H$_2$Cl), 52.1 (*C*(4)), 72.4 (*C*(5)), 79.2 (*C*(3)), 101.9 (*C*(2)), 169.4 (C=O); diastereomer β-*cis*-**3d** (22%) δ=14.0 (*C*H$_3$CH$_2$CH$_2$C(3)), 17.8 (CH$_3$*C*H$_2$CH$_2$C(3)), 21.1 (*C*H$_3$C=O), 38.4 (CH$_3$CH$_2$*C*H$_2$C(3)), 41.9 (*C*H$_2$Cl), 49.2 (*C*(4)), 72.4 (*C*(5)), 79.4 (*C*(3)), 102.1 (*C*(2)), 169.1 (C=O); diastereomer β-*trans*-**3d** (12%) δ=13.9 (*C*H$_3$CH$_2$CH$_2$C(3)), 17.7 (CH$_3$*C*H$_2$CH$_2$C(3)), 21.1 (*C*H$_3$C=O), 36.2 (CH$_3$CH$_2$*C*H$_2$C(3)), 41.0 (*C*H$_2$Cl), 50.0 (*C*(4)), 71.3 (*C*(5)), 75.5 (*C*(3)), 98.1 (*C*(2)), 169.6 (C=O). IR (film): 1788 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 41 (27), 55 (27), 75 (27), 81 (70), 95 (37), 119 (100), 168 (65), 211 (2%, M^+).

*4.4.5. Preparation of 2-acetoxy-3-chloro-4-chloromethyl-3-isopropyl-tetrahydrofuran (**3e**).* Following the same procedure for the preparation of **3a**, **2e** (2.55 g, 10 mmol) gave, after flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2), the *title compound* **3e** (2.37 g, 93%), as a 22:48:27:3 (α-*cis*/α-*trans*/β-*cis*/β-*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil. [Found: C, 47.2; H, 6.2. $C_{10}H_{16}Cl_2O_3$ requires C, 47.08; H, 6.32]; R_f (30% Et_2O/petroleum ether 40–60) 0.41 and 0.49; ^{1}H NMR ($CDCl_3$, 400 MHz): diastereomer α-*cis*-**3e** (22%) δ=1.07 (3H, d, *J*=6.6 Hz, CH(C*H*$_3$)$_2$), 1.08 (3H, d, *J*=6.6 Hz, CH(C*H*$_3$)$_2$), 2.00 (1H, m, C*H*C(3)), 2.10 (3H, s, C*H*$_3$C=O), 2.74 (1H, m, C(4)*H*), 3.63 (1H, t, *J*=11.1 Hz, C*H*$_2$Cl), 3.81 (1H, dd, *J*=11.1, 4.3 Hz, C*H*$_2$Cl), 4.04 (1H, dd, *J*=9.2, 6.7 Hz, C(5)H_2), 4.26 (1H, dd, *J*=9.2, 7.7 Hz, C(5)H_2), 6.32 (1H, s, C(2)*H*); diastereomer α-*trans*-**3e** (48%) δ=0.97 (3H, d, *J*=6.6 Hz, CH(C*H*$_3$)$_2$), 1.14 (3H, d, *J*=6.6 Hz, CH(C*H*$_3$)$_2$), 2.07 (3H, s, C*H*$_3$C=O), 2.11 (1H, s, C*H*C(3)), 2.82 (1H, m, C(4)*H*), 3.66 (1H, t, *J*=10.7 Hz, C*H*$_2$Cl), 3.73 (1H, ddd, *J*=10.7, 3.8, 1.6 Hz, C*H*$_2$Cl), 4.33 (1H, dd, *J*=9.2, 1.5 Hz, C(5)H_2), 4.45 (1H, ddd, *J*=9.2, 6.1, 1.8 Hz, C(5)H_2), 6.21 (1H, s, C(2)*H*); diastereomer β-*cis*-**3e** (27%) δ=0.99 (3H, d, *J*=6.6 Hz, CH(C*H*$_3$)$_2$), 1.10 (3H, d, *J*=6.6 Hz, CH(C*H*$_3$)$_2$), 2.27 (1H, s, C*H*C(3)), 2.08 (3H, s, C*H*$_3$C=O), 2.94 (1H, m, C(4)*H*), 3.68 (1H, t, *J*=10.9 Hz, C*H*$_2$Cl), 3.90 (1H, dd, *J*=10.9, 3.9 Hz, C*H*$_2$Cl), 4.01 (1H, t, *J*=8.6 Hz, C(5)H_2), 4.42 (1H, t, *J*=8.6 Hz, C(5)H_2), 6.25 (1H, s, C(2)*H*); diastereomer β-*trans*-**3e** (3%) δ=0.98 (3H, d, *J*=6.6 Hz, CH(C*H*$_3$)$_2$), 1.14 (3H, d, *J*=6.6 Hz, CH(C*H*$_3$)$_2$), 2.12 (3H, s, C*H*$_3$C=O), 2.00 (1H, s, C*H*C(3)), 2.96 (1H, m, C(4)*H*), 3.51 (1H, t, *J*=11.1 Hz, C*H*$_2$Cl), 3.76 (1H, ddd, *J*=11.1, 3.9, 1.1 Hz, C*H*$_2$Cl), 4.07 (1H, dd, *J*=8.9, 3.3 Hz, C(5)H_2), 4.48 (1H, ddd, *J*=8.9, 5.8, 1.1 Hz, C(5)H_2), 6.15 (1H, s, C(2)*H*). ^{13}C NMR ($CDCl_3$, 100.62 MHz): diastereomer α-*cis*-**3e** (22%) δ=17.7 (CH(*C*H$_3$)$_2$), 17.9 (CH(*C*H$_3$)$_2$), 21.0 (*C*H$_3$C=O), 36.7 (*C*HC(3)), 45.0 (*C*H$_2$Cl), 46.2 (*C*(4)), 71.9 (*C*(5)), 80.5 (*C*(3)), 98.6 (*C*(2)), 169.3 (C=O); diastereomer α-*trans*-**3e** (48%) δ=17.7 (CH(*C*H$_3$)$_2$), 18.0 (CH(*C*H$_3$)$_2$), 21.1 (*C*H$_3$C=O), 29.3 (*C*HC(3)), 43.2 (*C*H$_2$Cl), 51.7 (*C*(4)), 72.6 (*C*(5)), 84.7 (*C*(3)), 101.2 (*C*(2)), 168.8 (C=O); diastereomer β-*cis*-**3e** (27%) δ=17.7 (CH(*C*H$_3$)$_2$), 18.1 (CH(*C*H$_3$)$_2$), 21.1 (*C*H$_3$C=O), 34.3 (*C*HC(3)), 44.1 (*C*H$_2$Cl), 48.3 (*C*(4)), 73.6 (*C*(5)), 83.8 (*C*(3)), 103.1 (*C*(2)), 169.1 (C=O); diastereomer β-*trans*-**3e** (3%) δ=17.7 (CH(*C*H$_3$)$_2$), 19.0 (CH(*C*H$_3$)$_2$), 21.0 (*C*H$_3$C=O), 32.3 (*C*HC(3)), 41.7 (*C*H$_2$Cl), 53.8 (*C*(4)), 70.7 (*C*(5)), 81.4 (*C*(3)), 98.50 (*C*(2)), 169.8 (C=O). IR (film): 1750 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 55 (66), 90 (100), 95 (99), 103 (37), 131 (88), 159 (51), 176 (55, M^+−OAc–*i*-Pr), 195 (69, M^+−OAc), 211 (1, M^+−*i*-Pr).

4.5. Preparation of 3-methyl-1-(1,2,2-trichloropropoxy)but-2-ene (8)

In a four-necked (one of which was threaded) round bottom flask (750 mL), fitted with a dropping funnel sealed on the top with a $CaCl_2$ tube, a perforable septum (blocked by a screw cap), a thermometer and a mechanical stirrer, 2,2-dichloropropanal **1a** (48.22 g, 0.38 mol), CH_2Cl_2 (300 mL) and 3-methyl-2-buten-1-ol (38.6 mL, 0.38 mol) were introduced at room temperature. The solution, under stirring, was then cooled to −13 °C. After 2 h,

triethylamine (64.0 mL, 0.46 mol) was added by a syringe. Then, a solution of methanesulfonyl chloride (29.4 mL, 0.38 mol) in CH_2Cl_2 (100 mL), previously charged into the dropping funnel, was added dropwise, taking care to keep the temperature below −5 °C. Next, the reaction mixture was left at 0 °C for other 20 h, after that it was diluted with HCl_{aq} 5% wt/v (100 mL). The organic phase was separated and washed with H_2O (2×50 mL), while the combined aqueous layers were further washed with CH_2Cl_2 (2×25 mL). The combined organic phases were dried with toluene through azeotropic distillation. Distillation of the crude product under vacuum afforded the *title compound* **8** (35.2 g, 40%), as a colourless liquid; bp 109–111 °C (3 mmHg); [Found: C, 41.6; H, 5.7. $C_8H_{13}Cl_3O$ requires C, 41.50; H, 5.66]; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.76 (3H, s, CH_3C═C), 1.83 (3H, s, CH_3C═C), 2.19 (3H, s, CH_3CCl$_2$), 4.34 (2H, m, CH_2), 5.36 (1H, m, C*H*═C), 5.69 (1H, s, *H*CO); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 18.2 (*C*H$_3$C═), 25.8 (*C*H$_3$C═), 31.6 (*C*H$_3$CCl$_2$), 67.2 (*C*H$_2$O), 88.3 (*C*Cl$_2$), 99.2 (*C*HClO), 117.8 (*C*H═C), 141.3 ((CH$_3$)$_2$*C*═C); MS (EI, 70 eV) *m*/*z* (%): 69 (100), 71 (84), 104 (60), 145 (4), 215 (3), 230 (2, M^+).

4.6. Preparation of 1-(2,2-dichloro-1-methoxypropoxy)-3-methylbut-2-ene (9)

In a four-necked round bottom flask, fitted with a thermometer, a dropping funnel and a reflux condenser closed on the top with a $CaCl_2$ tube, LiH (2.66 g, 330 mmol) was carefully dissolved in CH_3OH (250 mL). When the effervescence ceased, the alkaline solution was thermostated at 25 °C, after which it was added by the dropping funnel to a solution of **8** (30.10 g, 130 mmol) in CH_3OH (50 mL). The reaction mixture was stirred for 24 h. Then it was acidified with aqueous HCl 37%, diluted with water (400 mL) and extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were collected, concentrated and dried with toluene through azeotropic distillation. Distillation of the crude product under vacuum afforded the *title compound* **9** (26.28 g, 89%), as a colourless liquid; bp 78–80 °C (3 mmHg); [Found: C, 47.5; H, 7.2. $C_9H_{16}Cl_2O_2$ requires C, 47.59; H, 7.10]; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.70 (3H, m, CH_3C═C), 1.77 (3H, m, CH_3C═C), 2.06 (3H, m, CH_3CCl$_2$), 3.59 (3H, s, CH_3O), 4.30 (2H, m, CH_2), 4.50 (1H, s, *H*CO), 5.39 (1H, m, C*H*═C); ^{13}C NMR ($CDCl_3$, 100.62 MHz): δ 18.2 (*C*H$_3$C═), 25.8 (*C*H$_3$C═), 31.6 (*C*H$_3$CCl$_2$), 41.1 (*C*H$_3$O), 67.2 (*C*H$_2$O), 88.3 (*C*Cl$_2$), 99.2 (*C*HClO), 120.6 (*C*H═C), 141.3 ((CH$_3$)$_2$*C*═C); MS (EI, 70 eV) *m*/*z* (%): 69 (100), 106 (24), 141 (22), 226 (<1%, M^+).

4.7. Preparation of 1-(2,2-dichloro-1-methoxypropoxy)-3-methylbut-2-ene (10)

Following the same procedure for the preparation of **3a**, **9** (2.27 g, 10 mmol) gave, after flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2), the *title compound* **10** (2.02 g, 89%), as a 14:48:27:11 (α-*cis*/α-*trans*/β-*cis*/β-*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil. [Found: C, 47.7; H, 7.2. $C_9H_{16}Cl_2O_2$ requires C, 47.59; H, 7.10]; R_f (10% Et_2O/petroleum ether 40–60) 0.28 and 0.24; ^{1}H NMR ($CDCl_3$, 400 MHz): diastereomer α-*cis*-**10** (14%) δ 1.72 (3H, s, C(3)CH_3), 1.76 (3H, s CH$_3$(CH_3)CCl), 1.85 (3H, s, CH_3(CH$_3$)CCl), 2.74 (1H, dd, *J*=9.8, 8.1 Hz, C(4)*H*), 3.49 (3H, s, OCH_3), 4.10 (1H, dd, *J*=9.8, 8.8 Hz, C(5)*H*), 4.15 (1H, dd, *J*=8.8, 8.1 Hz, C(5)*H*), 4.60 (1H, s, C(2)*H*); diastereomer α-*trans*-**10** (48%) δ 1.70 (3H, s, C(3)CH_3), 1.76 (3H, s CH$_3$(CH_3)CCl), 1.63 (3H, s, CH_3(CH$_3$)CCl), 2.99 (1H, dd, *J*=9.3, 8.6 Hz, C(4)*H*), 3.46 (3H, s, OCH_3), 4.02 (1H, dd, *J*=9.3, 8.9 Hz, C(5)*H*), 4.17 (1H, dd, *J*=8.9, 8.6 Hz, C(5)*H*), 4.90 (1H, s, C(2)*H*); diastereomer β-*cis*-**10** (27%) δ 1.74 (3H, s, C(3)CH_3), 1.78 (3H, s CH$_3$(CH_3)CCl), 1.79 (3H, s, CH_3(CH$_3$)CCl), 3.00 (1H, dd, *J*=9.7, 8.6 Hz, C(4)*H*), 3.36 (3H, s, OCH_3), 4.16 (1H, dd, *J*=9.7, 8.6 Hz, C(5)*H*), 4.20 (1H, t, *J*=8.6 Hz, C(5)*H*), 4.74 (1H, s, C(2)*H*); diastereomer β-*trans*-**10** (11%) δ 1.55 (3H, s CH$_3$(CH_3)CCl), 1.74 (3H, s, C(3)CH_3), 1.86 (3H, s, CH_3(CH$_3$)CCl), 3.00 (1H, t, *J*=8.6 Hz, C(4)*H*), 3.43 (3H, s, OCH_3), 4.14 (1H, t, *J*=8.6 Hz, C(5)*H*), 4.17 (1H, t, *J*=8.6 Hz, C(5)*H*), 4.51 (1H, s, C(2)*H*); ^{13}C NMR ($CDCl_3$, 100.62 MHz): diastereomer α-*cis*-**10** (14%) δ 29.6 (*C*H$_3$(CH$_3$)CCl), 30.5 (*C*H$_3$C(3)), 32.7 (CH$_3$(*C*H$_3$)CCl), 56.1 (OCH$_3$), 58.9 (*C*(4)), 67.8 (*C*(5)), 71.4 (*C*(3)), 71.6 (CH$_3$(CH$_3$)*C*Cl), 109.3 (C(2)); diastereomer α-*trans*-**10** (48%) δ 20.7 (*C*H$_3$C(3)), 31.1 (*C*H$_3$(CH$_3$)CCl), 33.6 (CH$_3$(*C*H$_3$)CCl), 56.5 (OCH$_3$), 60.2 (*C*(4)), 67.2 (*C*(5)), 69.4 (CH$_3$(CH$_3$)*C*Cl), 73.2 (*C*(3)), 111.4 (C(2)); diastereomer β-*cis*-**10** (27%) δ 25.8 (*C*H$_3$C(3)), 31.2 (*C*H$_3$(CH$_3$)CCl), 33.1 (CH$_3$(*C*H$_3$)CCl), 54.9 (OCH$_3$), 56.9 (*C*(4)), 69.1 (*C*(5)), 70.4 (CH$_3$(CH$_3$)*C*Cl), 74.7 (*C*(3)), 112.7 (C(2)); diastereomer β-*trans*-**10** (11%) δ 25.5 (*C*H$_3$C(3)), 31.5 (*C*H$_3$(CH$_3$)CCl), 35.3 (CH$_3$(*C*H$_3$)CCl), 55.1 (OCH$_3$), 55.6 (*C*(4)), 67.9 (*C*(5)), 69.6 (CH$_3$(CH$_3$)*C*Cl), 71.2 (*C*(3)), 109.8 (C(2)). IR (film): 2973 (CH$_3$O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 41 (13), 69 (31), 77 (19), 90 (100), 195 (6%, M^+−OCH$_3$).

4.8. Preparation of 2-acetoxy-3-chloro-4-isopropyl-3-methyltetrahydrofuran (11)

Method a. In a three-necked round bottom flask, equipped with a condenser with bubbler (in one neck), 2,2-dichloro-1-[(3-methyl-2-butenyl)oxy]propyl acetate **2c** (0.51 g, 2 mmol) and toluene (20 mL) were introduced. A syringe pump 'charged' with AIBN (16 mg, 0.1 mmol), dissolved in toluene (10 mL), was connected to the second neck, together with inert gas (Ar) inlet. A second syringe pump 'charged' with Bu_3SnH (0.58 mL, 2.2 mmol), dissolved in toluene (20 mL), was connected to the third neck. The argon valve was opened, assuring a gentle flow through the system, monitored by moderate bubbling, then the heater and the magnetic stirrer were turned on. When a stable temperature was obtained (110 °C), both syringe pumps were turned on, adjusted so to drive the complete addition of reagents in 1 h. The reaction mixture was then stirred for additional 2 h at 110 °C and, once allowed to cool down to room temperature, a 10% wt/v aqueous solution of KF (1.45 mL, 2.5 mmol) was added under stirring so to facilitate the removal of the formed Bu_3SnCl. Filtration on Celite and flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 2:8), afforded the *title compound* **11** (0.234 g, 53%), as an 27:28:25:20 (α-*cis*/α-*trans*/β-*cis*/β-*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil.

Method b. To a solution of 2,2-dichloro-1-[(3-methyl-2-butenyl) oxy]propyl acetate **2c** (0.11 g, 0.41 mmol, 1 equiv) and Bu_3SnH (0.12 mL, 0.45 mmol, 1.1 equiv) in toluene (1 mL) at −78 °C triethylborane (0.36 mL, 0.41 mmol, 1 equiv) was added. The solution was stirred at room temperature for 2 h before the solvent was removed in vacuo. The product was purified by column chromatography (9 petrol/1 Et_2O) using a 10% KF/90% silica column. This afforded a mixture of products: 2-chloro-1-[(3-methyl-2-butenyl)oxy]propyl acetate (0.029 g, 34%) as a colourless oil and the *title compound* **11** (0.027 g, 43%) as a 19:53:28:0 (α-*cis*/α-*trans*/β-*cis*/β-*trans*, from the ^{1}H NMR spectrum) as an inseparable mixture of diastereomers; colourless oil.

[Found: C, 54.2; H, 7.6. $C_{10}H_{17}ClO_3$ requires C, 54.42; H, 7.76]; R_f (20% Et_2O/petroleum ether 40–60) 0.26 and 0.30; ^{1}H NMR ($CDCl_3$, 400 MHz): diastereomer α-*cis*-**11** (27%) δ 0.88 (3H, d, *J*=6.5 Hz, CH$_3$(CH_3)CH), 1.08 (3H, d, *J*=6.5 Hz, CH_3(CH$_3$)CH), 1.71 (3H, s, C(3)CH_3), 1.92 (1H, ddd, *J*=10.6, 9.4, 7.4 Hz, C(4)*H*), 2.01 (1H, m, *J*=9.4, 6.5 Hz, CH$_3$(CH$_3$)C*H*), 2.16 (3H, s, CH_3C═O), 3.86 (1H, dd, *J*=10.6, 8.4 Hz, C(5)*H*), 4.07 (1H, dd, *J*=8.4, 7.4 Hz, C(5)*H*), 5.96 (1H, s, C(2)*H*); diastereomer α-*trans*-**11** (28%) δ 0.87 (3H, d, *J*=6.6 Hz, CH$_3$(CH_3)CH), 1.12 (3H, d, *J*=6.6 Hz, CH_3(CH$_3$)CH), 1.57 (3H, s, C(3)CH_3), 1.81 (1H, m, *J*=9.8, 6.6 Hz, CH$_3$(CH$_3$)C*H*), 2.12 (3H, s, CH_3C═O), 2.38 (1H, dt, *J*=9.8, 8.1 Hz, C(4)*H*), 3.70 (1H, dd, *J*=9.8,

8.7 Hz, C(5)*H*), 4.13 (1H, dd, *J*=8.7, 8.1 Hz, C(5)*H*), 6.21 (1H, s, C(2)*H*); diastereomer β-*cis*-**11** (25%) δ 0.91 (3H, d, *J*=6.4 Hz, $CH_3(CH_3)CH$), 1.09 (3H, d, *J*=6.4 Hz, $CH_3(CH_3)CH$), 1.68 (3H, s, C(3)CH_3), 1.99 (1H, m, *J*=9.9, 6.4 Hz, $CH_3(CH_3)CH$), 2.05 (1H, dt, *J*=9.9, 8.2 Hz, C(4)*H*), 2.07 (3H, s, CH_3C=O), 3.84 (1H, dd, *J*=9.9, 8.2 Hz, C(5)*H*), 4.25 (1H, t, *J*=8.2 Hz, C(5)*H*), 6.18 (1H, s, C(2)*H*); diastereomer β-*trans*-**11** (20%) δ 0.88 (3H, d, *J*=6.6 Hz, $CH_3(CH_3)CH$), 1.16 (3H, d, *J*=6.6 Hz, $CH_3(CH_3)CH$), 1.57 (3H, s, C(3)CH_3), 1.76 (1H, m, *J*=10.0, 6.6 Hz, $CH_3(CH_3)CH$), 2.11 (3H, s, CH_3C=O), 2.38 (1H, dt, *J*=10.0, 8.8 Hz, C(4)*H*), 3.63 (1H, dd, *J*=10.0, 8.8 Hz, C(5)*H*), 4.23 (1H, t, *J*=8.8 Hz, C(5)*H*), 6.00 (1H, s, C(2)*H*); ^{13}C NMR ($CDCl_3$, 100.62 MHz): diastereomer α-*cis*-**11** (27%) δ 21.0 (CH_3C=O), 21.4 ($CH_3(CH_3)CH$), 21.7 ($CH_3(CH_3)CH$), 28.0 ($CH_3C(3)$), 28.5 ($CH_3(CH_3)CH$), 55.9 (*C*(4)), 71.4 (*C*(5)), 74.6 (*C*(3)), 102.0 (*C*(2)), 170.0 (*C*=O); diastereomer α-*trans*-**11** (28%) δ 21.0 (CH_3C=O), 21.0 ($CH_3(CH_3)CH$), 21.7 ($CH_3(CH_3)CH$), 19.4 ($CH_3C(3)$), 27.2 ($CH_3(CH_3)CH$), 56.2 (*C*(4)), 70.6 (*C*(5)), 71.8 (*C*(3)), 103.8 (*C*(2)), 169.6 (*C*=O); diastereomer β-*cis*-**11** (25%) δ 21.1 (CH_3C=O), 21.7 ($CH_3(CH_3)CH$) , 22.3 ($CH_3(CH_3)CH$), 24.8 ($CH_3C(3)$), 28.7 ($CH_3(CH_3)CH$), 53.0 (*C*(4)), 73.8 (*C*(5)), 76.1 (*C*(3)), 104.9 (*C*(2)), 169.6 (*C*=O); diastereomer β-*trans*-**11** (20%) δ 21.1(CH_3C=O), 21.2($CH_3(CH_3)CH$), 22.2 ($CH_3(CH_3)CH$), 22.4 ($CH_3C(3)$), 24.9 ($CH_3(CH_3)CH$), 51.6 (*C*(4)), 72.7 (*C*(5)), 69.8 (*C*(3)), 102.0 (*C*(2)), 169.9 (*C*=O). IR (film): 1751 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 43 (81), 56(68), 83(100), 126 (17), 161 (8, M^+-AcO).

4.9. One-pot hydrolysis–oxidation of dichlorolactols 3 towards lactones 6

*4.9.1. Preparation of 3-chloro-4-chloromethyl-3-methyldihydrofuran-2(3H)-one (**6a**).* γ-Lactol acetate **3a** (0.91 g, 4 mmol) and distilled water (4 mL) were weighted into a Schlenk tube, and under vigorous magnetic stirring, 96% aqueous H_2SO_4 was added (eight drops). Then the tube was closed with a Teflon septum (blocked by a screw cap) and the mixture was stirred at 80 °C until complete conversion was detected by GC monitoring (6 h). During that time, $K_2Cr_2O_7$ (0.88 g, 3 mmol), H_2O (2 mL) and 96% aqueous H_2SO_4 (0.63 mL) were weighted in a second Schlenk tube fitted with a perforable septum (blocked by a screw cap) and thermostated at 25 °C. At the end of hydrolysis time, the content of the first Schlenk tube was poured into the second one under magnetic stirring, together with acetone (11.2 mL, freshly distilled). The reaction mixture was stirred for 4 h at 25 °C, then it was diluted with H_2O (10 mL) and CH_2Cl_2 (10 mL) and the organic phase was concentrated and dried with toluene through azeotropic distillation. Chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2) gave the *title compound* **6a** (0.59 g, 81%) as a 33:67 (*cis*/*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil. [Found: C, 39.4; H, 4.5. $C_6H_8Cl_2O_2$ requires C, 39.37; H, 4.41]; R_f (30% Et_2O/petroleum ether 40–60) 0.19 and 0.23; ^{1}H NMR ($CDCl_3$, 400 MHz): *cis*-**6a** (33%) δ 1.80 (3H, s C(3)CH_3), 2.81 (1H, m, C(4)*H*), 3.66 (1H, dd, *J*=11.4, 8.5 Hz, C(4)CH_2Cl), 3.80 (1H, dd, *J*=11.4, 6.0 Hz, C(4)CH_2Cl), 4.03 (1H, dd, *J*=10.2, 9.2 Hz, C(5)H_2), 4.48 (1H, dd, *J*=9.2, 7.2 Hz, C(5)H_2); *trans*-**6a** (67%) δ 1.72 (3H, s, C(3)CH_3), 3.08 (1H, m, C(4)*H*), 3.49 (1H, dd, *J*=11.5, 8.0 Hz, C(4)CH_2Cl), 3.70 (1H, dd, *J*=11.5, 4.6 Hz, C(4)CH_2Cl), 4.28 (1H, dd, *J*=9.7, 3.5 Hz, C(5)H_2), 4.61 (1H, dd, *J*=9.7, 6.4 Hz, C(5)H_2). ^{13}C NMR ($CDCl_3$, 100.62 MHz): *cis*-**6a** (33%) δ 24.6 (C(3)CH_3), 40.3 (C(4)CH_2Cl), 49.4 (*C*(4)), 64.6 (*C*(3)), 68.5 (*C*(5)), 173.2 (*C*=O); *trans*-**6a** (67%) δ 20.9 (C(3)CH_3), 41.5 (C(4)CH_2Cl), 50.0 (*C*(4)), 63.5 (*C*(3)), 68.4 (*C*(5)), 173.4 (*C*=O). IR (film): 1781 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 89 (74), 103 (100), 105 (31), 168 (46), 182 (1%, M^+).

*4.9.2. Preparation of 3-chloro-4-chloromethyl-3,5,5-trimethyldihydrofuran-2(3H)-one (**6b**).* Following the same procedure for the preparation of **6a**, **3b** (1.02 g, 4 mmol) was processed for an appropriate reaction time (6 h for the hydrolysis and 4 h for the oxidation). Then, flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2), gave the *title compound* **6b** (0.60 g, 71%), as a 65:35 (*cis*/*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil. [Found: C, 45.7; H, 5.6. $C_8H_{12}Cl_2O_2$ requires C, 45.52; H, 5.73]; R_f (30% Et_2O/petroleum ether 40–60) 0.22 and 0.32; ^{1}H NMR ($CDCl_3$, 200 MHz): *cis*-**6b** (65%) δ 1.48 (3H, s, C(5)CH_3), 1.54 (3H, s, C(5)CH_3), 1.83 (3H, s, C(3)CH_3), 2.54 (1H, m, C(4)*H*), 3.69 (1H, dd, *J*=11.8, 7.6 Hz, C(4)CH_2Cl), 3.82 (1H, dd, *J*=11.8, 7.9 Hz, C(4)CH_2Cl); *trans*-**6b** (35%) δ 1.40 (3H, s, C(5)CH_3), 1.61 (3H, s, C(5)CH_3), 1.71 (3H, s, C(3)CH_3), 3.04 (1H, m, C(4)*H*), 3.60 (1H, dd, *J*=11.5, 9.4 Hz, C(4)CH_2Cl), 3.81 (1H, dd, *J*=11.5, 5.9 Hz, C(4)CH_2Cl); ^{13}C NMR ($CDCl_3$, 50.32 MHz): *cis*-**6b** (65%) δ 21.8 (CH_3), 27.4 (CH_3), 30.0 (CH_3), 39.9 (C(4)CH_2Cl), 57.0 (*C*(4)), 65.7 (*C*(3)), 84.8 (*C*(5)), 172.1 (*C*=O); *trans*-**6b** (35%) δ 22.7 (CH_3), 23.8 (CH_3), 30.9 (CH_3), 38.6 (C(4)CH_2Cl), 58.8 (*C*(4)), 65.4 (*C*(3)), 84.2 (*C*(5)), 172.8 (*C*=O). IR (film): 1781 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 89 (49), 117 (100), 131 (27), 195 (13).

*4.9.3. Preparation of 3-chloro-4-chloromethyl-3-propyldihydrofuran-2(3H)-one (**6d**).* Following the same procedure for the preparation of **6a**, **3d** (1.02 g, 4 mmol) was processed for an appropriate reaction time (6 h for the hydrolysis and 4 h for the oxidation). Then, flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2), gave the *title compound* **6d** (0.68 g, 81%), as a 41:59 (*cis*/*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil. [Found: C, 45.4; H, 5.5. $C_8H_{12}Cl_2O_2$ requires C, 45.52; H, 5.73]; R_f (30% Et_2O/petroleum ether 40–60) 0.32 and 0.39; ^{1}H NMR ($CDCl_3$, 400 MHz): *cis*-**6d** (41%) δ=0.97 (3H, t, *J*=7.3 Hz, $CH_2CH_2CH_3$), 1.25–1.40 (1H, m, $CH_2CH_2CH_3$), 1.50–1.60 (1H, m, $CH_2CH_2CH_3$), 2.05–2.15 (2H, m, $CH_2CH_2CH_3$), 2.94 (1H, m, *J*=9.7, 9.0, 7.3, 5.4 Hz, C(4)*H*), 3.65 (1H, dd, *J*=11.4, 9.0 Hz, CH_2Cl), 3.80 (1H, dd, *J*=11.4, 5.4 Hz, CH_2Cl), 4.05 (1H, dd, *J*=9.7, 9.2 Hz, C(5)H_2), 4.50 (1H, dd, *J*=9.2, 7.3 Hz, C(5)H_2); *trans*-**6d** (59%) δ=0.99 (3H, t, *J*=7.3 Hz, $CH_2CH_2CH_3$), 1.40–1.50 (1H, m, $CH_2CH_2CH_3$), 1.65–1.75 (1H, m, $CH_2CH_2CH_3$), 1.70–1.75 (1H, m, $CH_2CH_2CH_3$), 1.95–2.05 (1H, m, $CH_2CH_2CH_3$), 3.03 (1H, m, *J*=9.1, 5.9, 4.1, 3.1 Hz, C(4)*H*), 3.43 (1H, dd, *J*=11.4, 9.1 Hz, CH_2Cl), 3.67 (1H, dd, *J*=11.4, 4.1 Hz, CH_2Cl), 4.34 (1H, dd, *J*=9.6, 3.1 Hz, C(5)H_2), 4.60 (1H, dd, *J*=9.6, 5.9 Hz, C(5)H_2). ^{13}C NMR ($CDCl_3$, 100.62 MHz): *cis*-**6d** (41%) δ=13.9 ($CH_2CH_2CH_3$), 18.2 ($CH_2CH_2CH_3$), 39.3 ($CH_2CH_2CH_3$), 40.9 (CH_2Cl), 46.2 (C(4)), 68.0 (C(3)), 68.5 (C(5)), 172.7 (C(2)); *trans*-**6d** (59%) δ=13.8 ($CH_2CH_2CH_3$), 17.4 ($CH_2CH_2CH_3$), 34.9 ($CH_2CH_2CH_3$), 41.1 (CH_2Cl), 49.7 (C(4)), 67.6 (C(3)), 68.4 (C(5)), 172.6 (C(2)). IR (film): 1788 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 41 (27), 55 (27), 75 (27), 81 (70), 95 (37), 119 (100), 168 (65), 211 (2%, M^+).

*4.9.4. Preparation of 3-chloro-4-chloromethyl-3-isopropyldihydrofuran-2(3H)-one (**6e**).* Following the same procedure for the preparation of **6a**, **3e** (1.02 g, 4 mmol) was processed for an appropriate reaction time (24 h for the hydrolysis and 8 h for the oxidation). Then, flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2), gave the *title compound* **6e** (0.66 g, 78%), as a 53:47 (*cis*/*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless oil. [Found: C, 45.5; H, 5.7. $C_8H_{12}Cl_2O_2$ requires C, 45.52; H, 5.73]; R_f (30% Et_2O/petroleum ether 40–60) 0.34 and 0.42; ^{1}H NMR ($CDCl_3$, 400 MHz): *cis*-**6e** (53%) δ 1.09 (3H, d, *J*=6.9 Hz, C(3)CH(CH_3)CH_3), 1.18 (3H, d, *J*=6.9 Hz, C(3)CH(CH_3)CH_3), 2.46 (1H, ept, *J*=6.9 Hz, C(3)CH(CH_3)CH_3), 2.90–3.10 (1H, m, C(4)*H*), 3.68 (1H, dd, *J*=11.4, 10.3 Hz, C(4)CH_2Cl) , 3.83 (1H, dd, *J*=11.4, 4.3 Hz, C(4)CH_2Cl), 4.10 (1H, t, *J*=9.2 Hz, C(5)*H*), 4.55 (1H, dd, *J*=9.2, 7.5 Hz, C(5)*H*); *trans*-**6e** (47%) δ 1.13 (3H, d, *J*=6.5 Hz, C(3)CH(CH_3)CH_3), 1.34 (3H, d, *J*=6.5 Hz, C(3)CH(CH_3)CH_3), 2.15 (1H, ept, *J*=6.5 Hz, C(3)CH(CH_3)CH_3), 2.90–

3.10 (1H, m, C(4)*H*), 3.43 (1H, dd, *J*=11.4, 10.1 Hz, C(4)C*H*$_2$Cl), 3.74 (1H, ddd, *J*=11.4, 3.7, 1.2 Hz, C(4)C*H*$_2$Cl), 4.39 (1H, dd, *J*=9.6, 1.5 Hz, C(5)*H*), 4.62 (1H, ddd, *J*=9.6, 5.2, 1.2 Hz, C(5)*H*); ^{13}C NMR ($CDCl_3$, 100.62 MHz): *cis*-**6e** (53%) δ 17.3 (C(3)CH(*C*H$_3$)CH$_3$), 18.2 (C(3)CH(CH$_3$)*C*H$_3$), 35.1 (C(3)*C*H(CH$_3$)CH$_3$), 42.4 (C(4)CH$_2$Cl), 43.3 (*C*(4)), 68.9 (*C*(5)), 72.1 (*C*(3)), 172.7 (*C*=O); *trans*-**6e** (47%) δ 16.6 (C(3)CH(*C*H$_3$)CH$_3$), 18.5 (C(3)CH(CH$_3$)*C*H$_3$), 30.7 (C(3)*C*H(CH$_3$)CH$_3$), 41.1 (C(4)CH$_2$Cl), 50.7 (*C*(4)), 67.8 (*C*(5)), 71.7 (*C*(3)), 171.7 (*C*=O). IR (film): 1789 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 89 (49), 119 (100), 131 (29), 168 (47, M$^+$−CH(CH$_3$)$_2$), 175 (1, M$^+$−Cl•).

4.10. Preparation of 3-chloro-4-(1-chloro-1-methylethyl)-3-methyldihydrofuran-2(3*H*)-one (6c)

In a cylindrical flask, 2-methoxy-tetrahydrofuran **10** (0.45 g, 2 mmol, a 14:48:27:11 mixture of diastereomers) was dissolved in EtOAc (30 mL) at room temperature. An effluent stream of O_3/O_2 from an ozone generator (10 mmol O_3/h) was bubbled into it, under vigorous stirring. After 24 h, the ozone generator was turned off and, after purging for 20 min with air, the crude reaction mixture was directly concentrated. Flash chromatography on silica gel, eluting with petroleum ether (bp 40–60 °C)/ethyl ether gradient (from 10:0 to 8:2) gave the *title compound* **6a** (0.14 g, 33%) as a 25:75 (*cis*/*trans*, from the ^{1}H NMR spectrum) inseparable mixture of diastereomers; colourless thick oil. [Found: C, 45.6; H, 5.7. $C_8H_{12}Cl_2O_2$ requires C, 45.52; H, 5.73]; R_f (50% Et$_2$O/petroleum ether 40–60) 0.44 and 0.49; ^{1}H NMR ($CDCl_3$, 400 MHz): *cis*-**6c** (25%) δ 1.82 (3H, s, ClC(CH$_3$)C*H*$_3$), 1.83 (3H, s, ClC(C*H*$_3$)CH$_3$), 1.92 (3H, s, C(3)C*H*$_3$), 2.85 (1H, dd, *J*=10.6, 7.0 Hz, C(4)*H*), 4.30–4.40 (1H, m, C(5)*H*), 4.54 (1H, dd, *J*=9.0, 7.0 Hz, C(5)*H*); *trans*-**6c** (75%) δ 1.66 (3H, s, ClC(CH$_3$)C*H*$_3$), 1.79 (3H, s, ClC(C*H*$_3$)CH$_3$), 1.91 (3H, s, C(3)C*H*$_3$), 3.06 (1H, t, *J*=7.8 Hz, C(4)*H*), 4.30–4.40 (1H, m, C(5)*H*), 4.57 (1H, dd, *J*=9.6, 7.6 Hz, C(5)*H*); ^{13}C NMR ($CDCl_3$, 100.62 MHz): *cis*-**6c** (25%) δ 26.9 (C(3)*C*H$_3$), 30.7 (ClC(CH$_3$)CH$_3$), 32.8 (ClC(*C*H$_3$)CH$_3$), 58.3 (*C*(4)), 63.3 (*C*(3)), 67.0 (*C*(5)), 68.3 (ClC(CH$_3$)CH$_3$), 173.2 (*C*=O); *trans*-**6c** (25%) δ 23.2 (C(3)CH$_3$), 30.7 (ClC(CH$_3$)CH$_3$), 33.2 (ClC(*C*H$_3$)CH$_3$), 58.8 (*C*(4)), 65.3 (*C*(3)), 67.4 (*C*(5)), 67.6 (ClC(CH$_3$)CH$_3$), 174.1 (*C*=O). IR (film): 1791 (C=O) cm^{-1}; MS (EI, 70 eV) *m*/*z* (%): 41 (48), 55 (26), 77 (97), 90 (44), 117 (57), 131 (100), 151 (5), 175 (1, M$^+$−Cl), 195 (<1).

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