Synthesis of Enantiomerically Pure Eight- and Nine-Membered Lactones by Copper(I) Chloride/2,2′-Bipyridine-Catalyzed Cyclization

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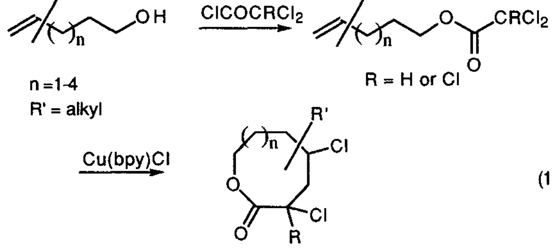
The stereocontrolled formation of eight- and nine-membered lactones by Cu(I)Cl/2,2′-bipyridine-catalyzed atom transfer cyclization of enantiomerically pure oxygen-substituted ω-alkenyl di- and trichloroacetates is described. The lactones are formed exclusively via the *endo*-cyclization mode and generally show a characteristic *cis*-relationship between the C-5 and C-6 substituents due to a highly stereoselective ring closure and chlorine transfer.

A considerable number of medium-sized heterocycles (eight- to twelve-membered) with interesting biological activities have been described.[1] Synthetic approaches towards these types of ring structures therefore receive much attention. Various macrocyclization methods have been developed for the synthesis of lactams,[2] cyclic ethers,[3] lactones[4] and other heterocycles.[5] The main challenge in the synthesis of these compounds proves to be the closure to the medium-sized ring itself.[6] Among the methods developed the cyclization by C–C bond formation via radical intermediates is rare, due to the slow cyclization rate to medium-sized systems.[7]

We recently developed a facile CuCl/2,2′-bipyridine-catalyzed *endo*-cyclization of ω-alkenyl di- and trichloroacetates to give eight- to eleven-membered lactones from readily available alkenols (eq 1).[8]



(1)

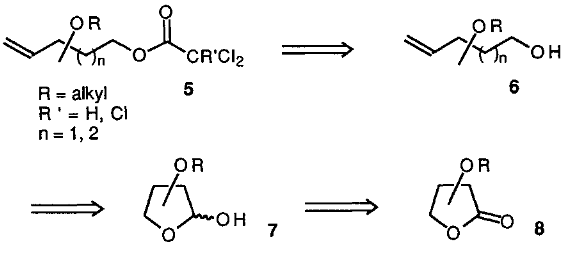
Precursors bearing substituents at various positions of the alkenyl chain were found to show remarkable differences with respect to the ease of cyclization. The results were explained on the basis of a template behavior of the Cu catalyst, which binds to the substrate in the coordination sphere via radical pairs. It was postulated that the success of the cyclization is dependent on the ability of the substrate molecule to fit into the geometry of the Cu(bpy)Cl complex.

To acquire additional information about this effect we set out to study the influence of allylic oxygen substituents in enantiopure precursors on the course of the cyclization reaction. It appeared convenient to synthesize these precursors starting with materials from the chiral pool. D-Mannose (**1**), D-isoascorbic acid (**2**), 2-deoxy-D-ribose (**3**) and (*R*)-pantolactone (**4**) were transformed into the desired chloroacetates by straightforward reaction sequences. The usefulness of these chiral precursors to analyze the steric and electronic effects of the oxygen substituents on product formation will be demonstrated.

Synthesis of the Cyclization Precursors

Scheme 1 shows the synthetic approach to most of the cyclization precursors. The chloroacetates **5** were obtained by esterification of the corresponding alkenols **6** with di- and trichloroacetyl chloride in the presence of a base (usually Et_3N) in dichloromethane.[9] The esterifications of acid labile compounds were carried out at −78 °C by using pyridine which led to higher yields of the desired esters.

The alkenols were obtained by a Wittig reaction of methylenetriphenylphosphorane on lactol derivative **7** at low temperature, usually −78 °C.[10] In most cases the lactol was accessible by reduction of the lactone **8** with diisobutylaluminum hydride (DIBAL-H) at −78 °C.[11]

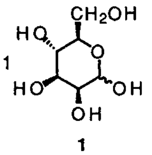
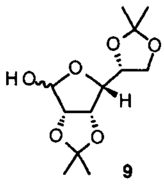
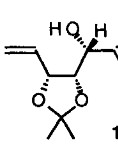
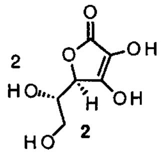
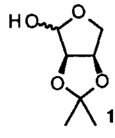
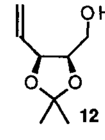
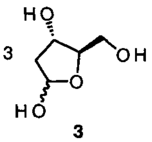
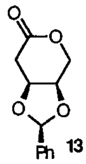
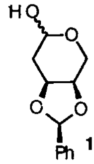
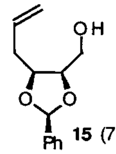
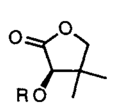
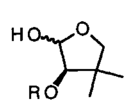
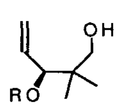


Scheme 1. General retrosynthesis

The lactol **9** was obtained directly from D-mannose (Table 1, entry 1).[12] Treatment with the Wittig ylide at −78 °C gave the enantiopure alkenol **10**. The synthesis of lactol **11** from D-isoascorbic acid (entry 2) is described in the literature.[11,13] The Wittig reaction afforded alkenol **12** in 85% isolated yield. Transformation of 2-deoxy-D-ribose into the benzylidene-protected ribono lactone **13**[14] was followed by reduction with DIBAL-H at −78 °C for 0.5 hours affording lactol **14**, from which alkenol **15** (71%) was obtained (entry 3).

(*R*)-Pantolactone (**4**) was treated with NaH in the presence of methoxymethyl chloride (MOMCl) to afford the enantiopure lactone **17** (entry 5). In a similar fashion (*R*)-pantolactone was treated with NaH and MeI. In this case MeI was not added immediately after the completion of the deprotonation, causing complete racemization of the acyloin to produce racemic lactone **16** (entry 4). Re-

Table 1. Synthesis of enantiopure alkenols

entry	precursor	lactone	lactol (yields of formation)	alkenol
1	 1		 9	 10 (93%)
2	 2		 11	 12 (85%)
3	 3	 13	 14 (96%)	 15 (71%)
4 5	R = H 4	 R = Me 16 (90%) R = MOM 17 (89%)	 R = Me 18 (71%) R = MOM 19 (95%)	 R = Me 20 (62%) R = MOM 21 (72%)

duction of the lactones with DIBAL-H at − 78 °C was followed by a Wittig reaction of the lactols **18** and **19** with methylenetriphenylphosphorane as described above to afford the ω-alkenols **20** (racemic) and **21** (enantiopure) in reasonable yields. The enantiomeric purity of the alkenols was determined by conversion to the diastereomeric Mosher esters[15] and comparison of the ^{1}H NMR spectra. The alkenols were converted to the di- and trichloroacetates as described above.

Results of the Cyclization Experiments

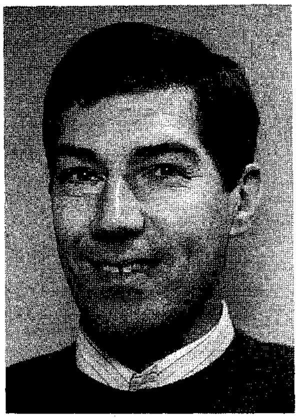
The presence of an inductively electron-withdrawing oxygen substituent on the allylic position of the cyclization precursors is assumed to benefit the cyclization. By lowering the LUMO of the olefin in this way, overlap with the SOMO of the alkyl radical should become more effective, enhancing the rate of cyclization.[16]

The dichloroacetate **22** was stirred in the presence of 30 mol of the Cu(bpy)Cl catalyst in a 0.1 M solution of 1,2-dichloroethane (DCE) for 18 hours at temperatures ranging between 80 and 150 °C, but only telomers were formed (Scheme 2). These conditions were developed in earlier work for the cyclizations of alkyl-substituted alkenyl chloroacetates.[8]

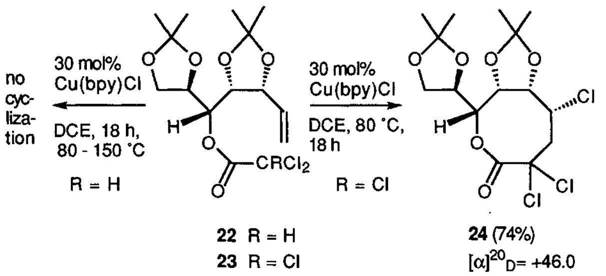
Biographical Sketches

W. Nico Speckamp (1933) received his Ph.D. degree with Professor H.O. Huisman at the University of Amsterdam in 1964. He was appointed full professor at the same university in 1980.

Frank Pirrung (1967) will obtain his Ph.D. degree with Professor W.N. Speckamp at the University of Amsterdam in 1995. Currently, he is working as a research chemist at EFKA Chemicals B.V., Hillegom (The Netherlands).



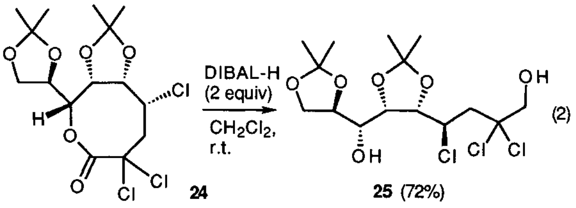
Henk Hiemstra (1952) received his Ph.D. degree with Professor H. Wynberg at the University of Groningen in 1980. After a post-doctoral stay with Professor B.M. Trost at the University of Wisconsin, Madison (USA), he joined the University of Amsterdam in 1982, where he is now a senior lecturer.



Scheme 2

The corresponding more reactive trichloroacetate **23** cyclized smoothly to the eight-membered lactone **24** in good yield (74%) under mild conditions (reflux in DCE for 18 h). Alternatively, **24** could be obtained in similar yield (71%) when heated in a sealed tube at 125 °C for 1.5 hours. From both experiments the cyclization product was obtained as a single isomer. Despite its crystallinity, **24** appeared unsuitable for an X-ray analysis. The stereochemistry of **24** could be inferred from its ^{1}H NMR spectrum. With the aid of a ^{1}H COSY experiment in C_6D_6 all signals of **24** could be assigned. A *cis*-relationship between the C-5 chlorine and the C-6 oxygen substitutent was concluded from the small coupling constant between H-5 and H-6 ($J = 1.0$ Hz). The conformation of the ring as well as the *cis*-relationship between C-5 and C-6 were also investigated by using NOE experiments. Irradiation of the protons of the lactone ring showed appreciable NOE effects between all vicinal protons and in addition a strong effect between H-5 and H-8. Thus, these protons are located on the same face of the molecule. From a Dreiding model study it was concluded that the eight-membered lactone ring of **24** adopts a chair–boat conformation in C_6D_6 solution. Due to the *cis*-ring junction of the acetal moiety at C-6 and C-7, the lactone cannot adopt the crown geometry.[17] The conformation of the lactone ring was confirmed by energy minimization using the CSC Chem3D Plus™ force field (Figure 1). In this chair–boat conformation the ester moiety has a dihedral angle of ca. 135°. The angles between H-5/6 and H-7/8 are ca. 60°, which is in agreement with the small coupling constants observed of 1.0 and 1.4 Hz, respectively.

Reduction of lactone **24** with 2 equiv of DIBAL-H at room temperature furnished the enantiopure diol **25** in 72% yield (eq 2). With DIBAL-H (1 equiv) at −78 °C no reaction was observed, probably due to steric hindrance by the two C-3 chlorine substituents. At room temperature half of the starting material was converted into diol **25**, meaning fast ring opening of the first reduction product to the aldehyde and further reduction.



(2)

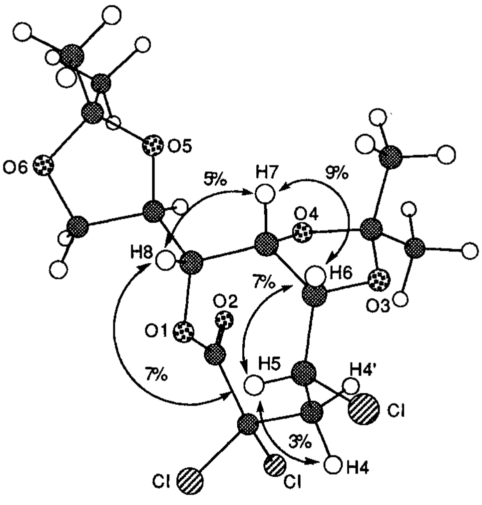
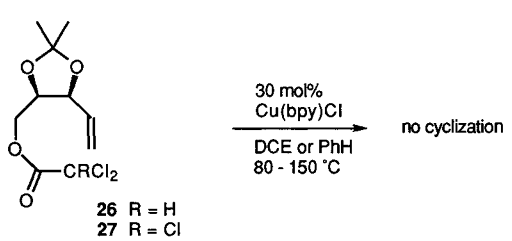


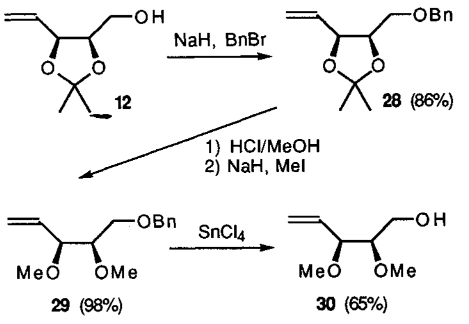
Figure 1. CSC Chem3D Plus™ minimized conformation of **24**. The observed NOE effects are indicated in this structure.

In order to get more insight into the highly stereoselective ring closure of acetate **23**, we synthesized the related chloroacetates **26** and **27** from D-isoascorbic acid (eq 3). These compounds lack the large substituent at C-1 as compared to the mannose-derived precursors. Unexpectedly, when treated with the copper catalyst at various temperatures under standard conditions, neither **26** nor **27** led to the formation of an eight-membered lactone. Starting material and telomers were obtained.



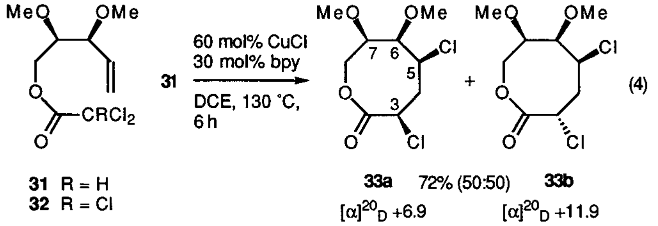
(3)

We then synthesized alkenol **30** with two methoxy groups (Scheme 3) increasing the flexibility of the chain as compared to **12**. Alkenol **12** was benzylated at the primary hydroxy function (**28**) and the diol was quantitatively liberated by using HCl/MeOH. Dimethylation of the diol **29** was followed by deprotection of the primary alcohol function through benzyl ether cleavage with $SnCl_4$[18] to give a satisfactory yield of the desired **30**. Esterification by the usual methods gave the di- and trichloroacetates **31** and **32** (eq 4).



Scheme 3

Using standard copper catalysis even at high temperatures, the dichloroacetate **31** could not be cyclized. However, the cyclization did occur on using an additional 0.3 equiv of CuCl (130 °C, 6 h) to give **33** in a yield of 72 % as a 1 : 1 mixture of diastereomers (eq 4), which could be separated by chromatography. Isomer **33a** was obtained crystalline (mp 88.0–88.5 °C, $[\alpha]_D^{20}$ + 6.9) and **33b** as an oil ($[\alpha]_D^{20}$ + 11.9).



Via the characteristic splitting patterns[8] of H-3, H-4 and H-4′ in the ^{1}H NMR spectrum it was concluded that **33a** has a *cis*-relationship between the chlorine substituents in a crown shaped lactone ring, and **33b** a *trans*-relationship. The coupling constant between H-5 and H-6 was 0 Hz in both cases. Therefore, the substituents at C-5 and C-6 must be *cis* to obtain an angle of ca. 90° in a crown conformation of the eight-membered ring.[17] The dichloro *cis*-isomer **33a** was modeled with Chem3D Plus^{TM} and energy minimization via its force field (Figure 2) afforded a crown conformation, in which the C-6 methoxy substituent adopts the *pseudo*-axial and the C-5 chlorine the *pseudo*-equatorial orientation. The C-7 methoxy is found in the *pseudo*-equatorial position. The ester moiety has an s-*trans* geometry (dihedral angle 140°). The observed dihedral angles between H-5/6 and H-6/7 are 105° and 74°, respectively, and are in agreement with the corresponding ^{1}H NMR coupling constants of 0 Hz. These angles deviate from the 60° for an ideal crown, due to repulsion between the electronegative substituents attached to C-5, C-6 and C-7, caused by minimization of the dipole–dipole interactions. The C-5/C-6 *trans*-isomer would lead to a significantly larger dihedral angle between H-5/6 and H-6/7 and thus to larger coupling constants. The more reactive trichloroacetate **32** led only to the formation of telomeric material under standard conditions, even upon addition of extra CuCl as described above.

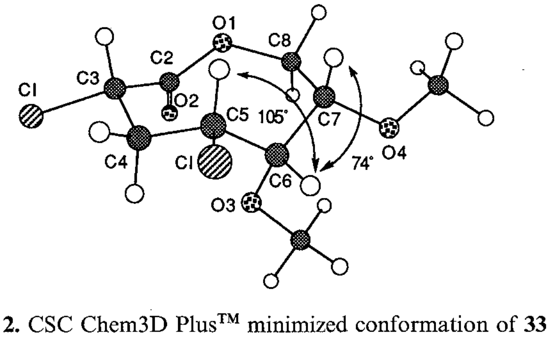


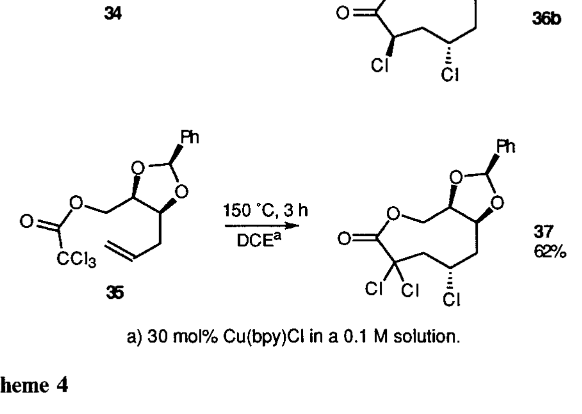
Figure 2. CSC Chem3D Plus^{TM} minimized conformation of **33a**.

The beneficial effect of an extra amount of CuCl was not observed with other substituted precursors. Presumably, the Cu catalyst acts as a Lewis acid[19] and complexes to the methoxy substituents of the starting material, so that extra CuCl is required to form a catalytically active species. During the attempted cyclization of **31** with CuCl and in equal amounts, free bipyridine ligand was detected on TLC.

The corresponding isopropylidene-protected acetate **26** could not be cyclized, however, with 60 mol% of CuCl and 30 mol% of bpy. Comparison with the D-mannose-derived trichloroacetate **23** shows, that the presence of the C-1 substituent in **23** is responsible for a successful cyclization probably by a favorable conformation of the starting material. The successful cyclization of the dimethoxy derivative might be due to the higher flexibility of the chain facilitating the cyclization.

Formation of nine-membered lactones by Cu(bpy)Cl-catalyzed cyclization of ω-hexenyl di- and trichloroacetates[8] was examined with enantiopure oxygen-substituted precursor **15** obtained from 2-deoxy-D-ribose (**3**) via the general procedure of Scheme 1.

Under standard conditions the dichloroacetate **34** cyclized at 150 °C to the crystalline nine-membered lactone **36** (63 %) as a mixture (80 : 20) of two inseparable diastereomers. Exclusive 9-*endo* cyclization took place. The major diastereomer **36a** has a *cis*-relationship between the two chlorine substituents, as could be inferred from the characteristic splitting pattern of the C-4 hydrogens similar to related nine-membered lactones.[8] In contrast to the eight-membered lactones the *trans*-stereochemistry between the C-5 chlorine and the C-7 oxygen substituent was found exclusively. This configuration followed from the analysis of the coupling constants of the protons at C-5, C-6 and C-7. The minor isomer **36b** is an epimer at C-3 with a *trans*-relationship between the two chlorines and a *trans*-relationship between C-5 and C-7.



a) 30 mol% Cu(bpy)Cl in a 0.1 M solution.

Scheme 4

The trichloroacetate **35** reacted under standard conditions to a single crystalline product **37** ($[\alpha]_D^{20}$ − 12.32) in 62 % yield as the result of *endo*-cyclization. The relative *trans*-stereochemistry between the C-5 chlorine and the C-7 oxygen substituent was determined in analogy to the dichloro derivative **36a**. In both cyclizations no epimer at C-5 could be detected. With a ^{1}H COSY experiment (C_6D_6) all signals of **37** were unambiguously assigned. From NOE experiments in combination with a Dreiding model study it was concluded that the molecule adopts a crown-like conformation except for the part that is connected via a *cis*-fusion to the acetal ring, and has an s-*trans* lactone geometry with a dihedral angle of ca. 140°. The NOE experiments proved that the C-5 chlorine occupies the *pseudo*-equatorial position, as H-5 shows an NOE effect of 6 % on H-4, while H-6′ shows a strong effect on H-4′ and H-9′ of 9 % and 7 %, respectively. The phenyl substituent of the acetal is situated above the plane through the lactone ring. Energy minimization via the CSC Chem3D Plus™ force field confirmed the proposed conformation (Figure 3).

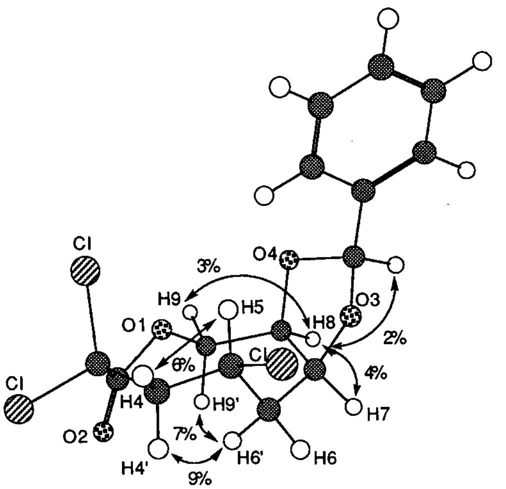


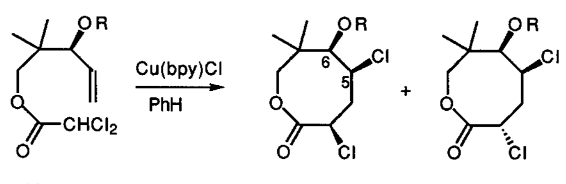
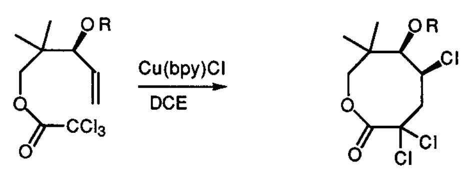
Figure 3. CSC Chem3D Plus™ minimized conformation of **37**. The observed NOE effects are indicated in this structure.

All precursors discussed so far possess two vicinal oxygen substituents. In order to rule out the influence of the more remote second chiral center on the stereoselective chloro transfer, a series of cyclization precursors was synthesized from (*R*)-(−)-pantolactone (**4**). These acetates, **38**–**41** (Table 2), have one stereocenter at the allylic position next to a geminal dimethyl group. Similar precursors having only geminal methyl substituents at C-2 cyclized smoothly to the eight-membered lactones.[8]

The racemic dichloroacetate **38**, upon treatment with 0.3 equiv of the Cu(bpy)Cl catalyst in a 0.1 M solution in benzene at 150 °C, cyclized readily to a mixture of two diastereomers of eight-membered lactone **42** in 75 % isolated yield in a 67 : 33 ratio. The isomers were separated by chromatography. The use of 0.6 equiv of catalyst gave a slightly higher yield of the product (78 %). In the ^{1}H NMR spectra of the two isomers, the major **42a** showed the characteristic signals of the H-4's and H-3 for the *cis*-dichloro lactone in a crown geometry. The coupling constant between H-5 and H-6 was 0 Hz for both isomers. The minor **42b** is an epimer at C-3 having a *trans*-relationship between the two chlorines. In analogy to previous examples this means an exclusive *cis*-relationship between the C-5/C-6 substituents.

The trichloroacetate **40** led to one diastereomer of the racemic eight-membered lactone **44** (34 %) at 170 °C. More telomers were observed than in the case of **38**, which is in agreement with earlier observations of trichloroacetate cyclizations.[8] At lower temperatures, the yield of **44** was lower. Again selective formation of the *cis*-C-5/C-6 isomer had taken place ($J = 0$ Hz). Lactone **44** was obtained as a crystalline compound (mp 79–81 °C) and a sample was subjected to an X-ray analysis[20] [Figure 4 and Tables 4, 5 (see experimental section)].

Table 2: Cyclizations of pantolactone derived precursors

entry	precursor	conditions[a]	products, yield, (*cis:trans*)		
					
1	R = Me **38**	150 °C, 4.5 h	**42a**	75% (67:33)	**42b**
2	R = MOM **39**	155 °C, 4 h	**43a**	91% (67:33)	**43b**
			+106.8[b]	$[\alpha]^{20}_{365}$	- 148.4[b]
					
3	R = Me **40**	170 °C, 2.5 h	**44** 34%		
4	R = MOM **41**	115 °C, 3 h	**45** 40%		$[\alpha]^{20}_{365}$= + 203.6[b]

a) 30 mol% Cu(bpy)Cl was employed in a 0.1 M solution. b) in $CHCl_3$.

The crystal structure of **44** proved the *cis*-relationship between the H-5 and H-6. In the solid state the C-5 chlorine adopts a *pseudo*-equatorial and the methoxy a *pseudo*-axial orientation in a crown conformation with an s-*trans* lactone geometry (140°).[21] The dihedral angle between H-5 and H-6 is 94°, which is in agreement with the value for the coupling constant expected from the Karplus equation.

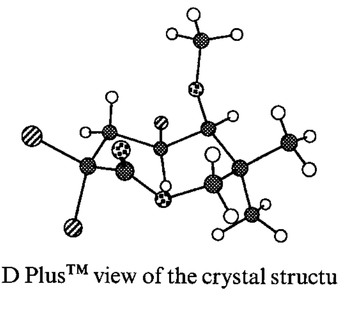
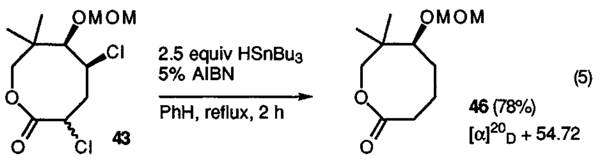


Figure 4. Chem3D Plus™ view of the crystal structure of lactone **44**.

The enantiopure MOMO-substituted derivatives **39** and **41** cyclized to the oxocan-2-ones **43** (91 %, 67 : 33, separated by chromatography) and **45** (40 %), respectively. All of the enantiopure products have a *cis*-relationship between H-5 and H-6 and the formation of the C-5/C-6 *trans*-substituted diastereomer or the seven-membered regioisomer[22] was never observed. The mixture of epimers of **43** was treated with $HSnBu_3$/2,2′-azobisisobutyronitrile (AIBN) (eq 5) to afford lactone **46**.



(5)

This series of experiments demonstrates that the stereoselective chlorine transfer is not influenced by the C-2 substituent of the cyclization precursor and solely depends on the stereochemistry of the C-3 substituent. For the eight-membered rings, the chlorine on C-5 of the product is introduced in a *syn*-fashion to the already present group on C-6. As most of the rings possess a crown conformation the relative stereochemistry can be inferred from the coupling constants in the ^1H NMR (Table 3). For the remaining lactones NOE techniques can be used to establish the conformation and relative stereochemistry.

Table 3: Selected ^1H NMR data of H-6 of some eight-membered lactones

Lactone	H-6
24	3.98 (dt, 1.0, 1.0, 8.1)[b]
33a	4.09 (d, 0.0, 1.5)[a]
33b	4.06 (s)[a]
42a	3.44 (s)[a]
42b	3.46 (s)[a]
43a	3.84 (s)[a]
43b	3.87 (s)[a]
44	3.41 (s)[a]
45	3.81 (s)[a]

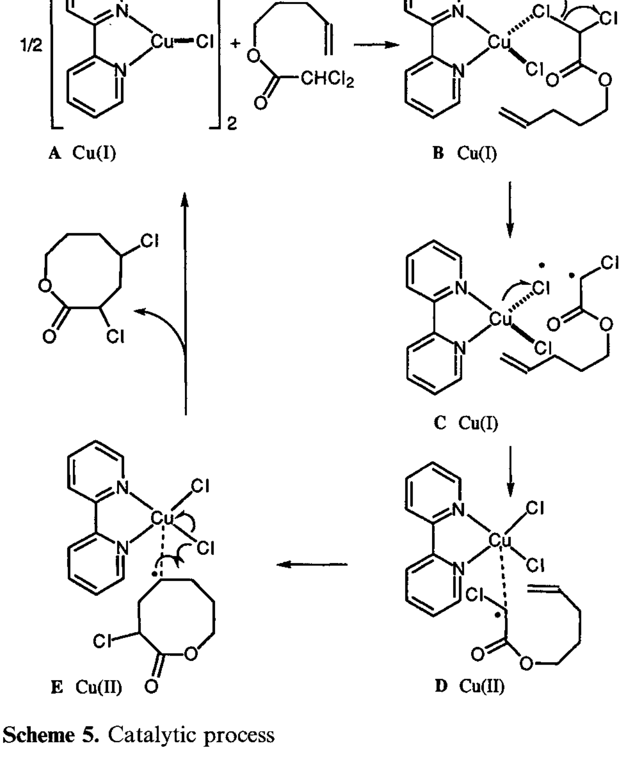
J in Hz, measured in $CDCl_3$[a], or C_6D_6[b].

Discussion

As has been said earlier[8] the cyclization reaction occurs via radicals coordinated to the Cu center whereby the C–C bond formation is taking place within the coordination sphere of the metal complex. This acts as a template for the reaction and causes the starting chloroester to fold according to the geometry of the complex. The proposed catalytic process is shown in Scheme 5 with the unsubstituted dichloroacetate as an example.

The coordinatively unsaturated monomeric catalytically active particle **A** initially complexes to one of the chlorine atoms of the precursor. This leads to a tetrahedral[23] encounter complex **B** activating the C–Cl bond and from which the chlorine atom abstraction takes place to furnish **C**, having a highly reactive chloro radical connected to the metal center. For stabilization, fast single electron transfer (SET) from Cu(I) to this ligand occurs, causing oxidation of the metal center to Cu(II) species with a square planar geometry.[24] The bipyridine ligand enhances the rate of SET by lowering the oxidation potential of the Cu center. The concomitantly formed carbon radical is stabilized by the captodative effect[25] and stays in the vicinity of the Cu atom forming a radical pair **D** in the coordination sphere. The C–C bond between the two reactive ends of the starting material is formed by a homolytic pathway after entering of the alkene into the coordination sphere, resulting in **E** where the new carbon radical remains coordinated to the metal center. Within **E** a chlorine ligand is transferred from the Cu atom to yield the product, which is expelled from the coordination sphere regenerating **A**.

During the course of the addition the reactive species are shielded from the bulk of the reaction suppressing the telomerization processes. The higher telomer formation with the trichloroacetates can be explained by a weaker coordination of the incipient radical to the Cu center.



Scheme 5. Catalytic process

The highly stereoselective introduction of the chlorine atom to C-5 of the eight-membered product regardless of the absolute stereochemistry of C-6, can be rationalized by assuming that the alkenyl chain will fold in accordance to the geometry of the complex and it is conceivable that the stereochemical orientation of the chain is determined by the configuration at C-3. The *syn*-introduction of the chlorine atom at C-5 of the product probably arises from transfer within the Cu complex to the carbon radical.

For the mannose-derived precursors, the presence of the large substituent at C-1 of the precursor will cause steric effects in the coordination sphere and only the higher reactivity of the trichloroacetate **31** results in ring closure. For the less reactive dichloroacetate **30** this substitution pattern might lead to a decrease in the cyclization rate.

In analogy to the eight-membered lactones, precursors for nine-membered rings are expected to arrange stereospecifically in the coordination sphere of the metal and chlorine transfer from the Cu center to the product might eventually lead to a C-5/7 *trans*-relationship.

Conclusion

We have shown that enantiomerically pure and oxygen-substituted di- and trichloroacetates can be used in Cu(bpy)Cl-catalyzed cyclizations to form various chiral eight- and nine-membered lactones expanding the scope of this reaction to synthesize enantiopure products in good yields. All of these possessed the configuration originating from the chiral starting material. The *cis*-relationship between the substituents at C-5 and C-6 in the series of the eight-membered rings is remarkable and is the result of highly stereocontrolled chlorine transfer to C-5. For the nine-membered lactones the chlorine atom is introduced stereospecifically at C-5 to give the C-5/C-7 *trans*-isomer in all cases. The ring closure is extremely regioselective for eight- and nine-membered ring formation. A template effect of the Cu catalyst and a reaction in the coordination sphere of the catalyst are a likely explanation.

All reactions were carried out under an inert atmosphere of dry N_2. Standard syringe techniques were applied to transfer dry solvents. IR spectra were obtained from $CHCl_3$ solutions using a Perkin-Elmer 1310 spectrophotometer and wavelengths (ν) are reported in cm^{-1}. ^1H NMR spectra were determined in $CDCl_3$, unless indicated otherwise, using a Bruker AC 200 (200 MHz), a Bruker WM 250 (250 MHz), a Bruker AMX 300 (300 MHz) or a Bruker AMX 400 (400 MHz) spectrometer. These instruments were also used for ^{13}C NMR (APT) spectra (50, 63, 75.5 and 100.6 MHz respectively) in $CDCl_3$ (unless indicated otherwise). Chemical shifts (δ) are given in ppm downfield from tetramethylsilane. Mass spectra and accurate mass measurements were carried out using a Jeol SX/SX 102 A Tandem Mass Spectrometer, a Varian MAT 711 or a VG Micromass ZAB-2HF instrument. Elemental analyses were performed by Dornis u. Kolbe Mikroanalytisches Laboratorium, Mülheim an der Ruhr, Germany. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. R_f values were obtained by using TLC on silica gel coated plastic sheets (Merck silica gel 60 F_{254}) with the indicated solvent mixture of EtOAc and hexanes. Chromatographic purification refers to flash chromatography[26] (fc) using the solvent mixture of EtOAc and hexanes in the given ratio (EtOAc : hexanes) and Janssen Chimica silica gel (0.030–0.075 mm). Melting points are uncorrected. CH_2Cl_2 and $(CH_2Cl)_2$ were distilled from P_2O_5 and stored over MS 3Å under an atmosphere of dry nitrogen. Benzene was distilled from P_2O_5 and stored over sodium wire. Dry THF and Et_2O were distilled from sodium benzophenone ketyl prior to use. CuCl was purified.[27] Reactions in sealed tubes were carried out in glass tubes (3 to 15 cm long and 0.5 to 4 cm wide) with a thread, which could be screwed tight with a plastic cap. X-ray crystal structure determinations[28] were performed on an Enraf-Nonius CAD-4 diffractiometer with graphite-monochromated CuKα radiation and ω-2Θ scan. Two reference reflections were measured hourly. Unit-cell parameters were refined by a least squares fitting procedure. Corrections for Lorentz and polarization effects were applied. The structure was solved by direct methods and the hydrogen atoms were calculated. An empirical absorption correction was applied. A final difference Fourier map revealed the residual electron density. Standard scattering factors were used. The anomalous scattering of Cl was taken into account. All calculations were performed with XTAL.

(*R*)-(−)-Pantolactone, D-mannose, D-isoascorbic acid, 2-deoxy-D-ribose, methyl iodide, MOMCl, TBDPSCl, imidazole, methyltriphenylphosphonium bromide, potassium sodium tartrate, $HSnBu_3$, AIBN, KHMDS 0.5 M in toluene, 1,1-dimethoxypropane, BnBr, $SnCl_4$, Bu_4NI, benzaldehyde (freshly distilled), CuCl, 2,2′-bipyridine, di- and trichloroacetyl chloride were commercially available.

Preparation of ω-Alkenols from Lactols by a Wittig Reaction; General Procedure A:[10]

To a stirred suspension of methyltriphenylphosphonium bromide (3.0 equiv) in THF (0.3 M) was added via syringe at −78 °C a 1.6 M hexane solution of BuLi (2.5 equiv) and the resulting yellow suspension was warmed to r.t. in 30 min. After cooling to −78 °C, a solution of the lactol (1 equiv) in THF (2 M solution) was added dropwise via syringe in 1 min. The resulting mixture was stirred at −78 °C, while the temperature increased to r.t. in 18 h. The mixture was refluxed for 15 min, then H_2O (10 % of the volume of THF) was added and the aqueous phase extracted with CH_2Cl_2 (3 ×). The combined organic phases were combined, washed with an equal volume of NaCl (aq) and H_2O, dried (Na_2SO_4) and concentrated in vacuo. The weight of the residue was determined, and an equal amount of silica gel was added, followed by the double volume of CH_2Cl_2 resulting in a homogenous slurry, which was concentrated in vacuo until dryness and transferred to the top of a column for chromatography (fc).

Esterification of ω-Alkenols to Di- and Trichloroacetates; General Procedure B:[9]

A solution of di- or trichloroacetyl chloride (1.0–1.3 equiv) in CH_2Cl_2 (0.3 M) was cooled in an ice-bath. The alkenol (1.0 equiv) was added in one portion, followed by dropwise addition of Et_3N (2 equiv) as a 3 M solution in CH_2Cl_2 over 20 min. The mixture was stirred for 1 h at 0 °C and then poured into an equal volume of 2 M HCl (aq). Acid labile compounds were poured into H_2O. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 ×). The combined organic phases were dried ($MgSO_4$ or Na_2SO_4) concentrated in vacuo and the residue was purified by fc.

Cu-Catalyzed Cyclization of Di- and Trichloroacetates to Medium-Sized Lactones; General Procedure C:[8]

The di- or trichloroacetate was dissolved in DCE or benzene (0.1 M solution) and placed into a flask under an N_2 atmosphere. CuCl (0.3 equiv) and 2,2-bipyridine (0.3 equiv) were added simultaneously, and the mixture was immediately brought to reflux (80 °C). If the reaction was carried out at temperatures between 80 and 190 °C, the acetate and solvent were placed into a sealable tube, equipped with a stirring bar, placed under an N_2 atmosphere and screwed tight after addition of the catalyst. The tube was immersed into an oil bath, which was preheated at the desired temperature and stirred for several hours. When the conversion was complete (TLC, the tube was cooled to r.t. prior to opening and rinsed with N_2 before closing), the mixture was concentrated in vacuo and the green residue was purified by fc without further workup. The lactone products were sensitive to humidity and were therefore kept under an N_2 atmosphere in an desiccator.

(2*R*,3*R*,4*R*,5*R*)-1,2 : 4,5-Di(isopropylidenedioxy)hept-6-en-3-ol (10): According to the general procedure A, Ph_3PCH_3Br (41.2 g, 115 mmol, 3.0 equiv) in THF (400 mL) was treated with BuLi (60 mL of a 1.6 M hexane solution, 96 mmol, 2.5 equiv) at −25 °C, followed by the addition of diacetone D-mannose **9**[12] (10.0 g, 38.4 mmol) in THF (250 mL) at −78 °C, and the resulting mixture was stirred for 10 h at −78 °C, and the resulting mixture was stirred for 10 h at −78 °C, followed by 2 days at r.t. After reflux, workup and fc (1:6, then 1:2), **10** was obtained (9.21 g, 35.65 mmol, 93%) as a colorless oil. R_f (1:2) 0.50; $[\alpha]_D^{20} = +33.0°$ ($c = 0.2$, EtOH).

IR: ν = 3550, 3080, 2980, 2930, 2880, 1450, 1425, 1380, 1260, 1160, 1110, 1070, 1040, 990, 880, 845 cm^{-1}.

^{1}H NMR (400 MHz): δ = 1.35 (s, 3H, Me), 1.39 (s, 3H, Me), 1.40 (s, 3H, Me), 1.53 (s, 3H, Me), 2.20 (d, 1H, J = 8.1 Hz, OH), 3.45 (t, 1H, J = 8.0 Hz, H-3), 3.95–4.05 (m, 2H, H-1), 4.05–4.15 (m, 1H, H-2), 4.38 (d, 1H, J = 7.5 Hz, H-4), 4.70 (t, 1H, J = 7.7 Hz, H-5), 5.33 (d, 1H, J = 9.9 Hz, H-7 *cis*), 5.40 (d, 1H, J = 17.2 Hz, H-7 *trans*), 6.09 (ddt, 1H, J = 7.8, 10.2, 17.5 Hz, H-6).

(2*R*,3*S*)-2,3-(Isopropylidenedioxy)pent-4-en-1-ol (12):

According to the general procedure A, Ph_3PCH_3Br (11.1 g, 31.2 mmol, 5.0 equiv) in THF (80 mL), was treated with BuLi (17.6 mL of a 1.6 M solution, 28.0 mmol, 4.5 equiv) at −25°C, followed by the addition of 2,3-*O*-isopropylidene-D-erythrose **11**[13] (1.0 g, 6.24 mmol) in THF (12 mL) at −78°C, and the resulting mixture was stirred for 18 h reaching r.t. After reflux for 3 h, workup and fc (1:20, then 1:3), **12** was obtained (835 mg, 5.28 mmol, 85%) as a colorless oil. R_f (1:1) 0.45; $[\alpha]_D^{20} = +1.5°$ ($c = 1.0$, EtOH).

IR: ν = 3500, 2970, 1700, 1455, 1430, 1375, 1370, 1360, 1325, 1230, 1170, 1140, 1115, 1040, 990 cm^{-1}.

^{1}H NMR (200 MHz): δ = 1.37 (s, 3H, Me), 1.48 (s, 3H, Me), 1.94 (s, 3H, OH), 3.55 (d, 2H, J = 5.6 Hz, H-1), 4.23 (dt, 1H, J = 5.7, 6.5 Hz, H-2), 4.61 (t, 1H, J = 7.0 Hz, H-3), 5.24 (dd, 1H, J = 1.1, 10.3 Hz, H-5 *cis*), 5.36 (dd, 1H, J = 1.1, 17.1 Hz, H-5 *trans*), 5.84 (ddd, 1H, J = 7.3, 10.3, 17.1 Hz, H-4).

(2*R*,4*S*,5*R*)- and (2*S*,4*S*,5*R*)-4,5-[(*S*)-Benzylidenedioxy]tetrahydropyran-2-ol (14):

According to the preparation of **18**, a solution of lactone **13**[14] (1.88 g, 8.5 mmol) in THF (17 mL) was treated with a 1.5 M toluene solution of DIBAL-H (7.4 mL, 11.1 mmol, 1.3 equiv) at −78°C and slowly warmed to r.t. in 0.5 h. After destruction of the excess DIBAL-H with EtOH (3 mL) a 1 M aq solution of potassium sodium tartrate (12 mL, 1.4 equiv) was added and the mixture was vigorously stirred for 1 h at r.t., washed with CH_2Cl_2 (3 × 25 mL), the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by fc (EtOAc) to yield **14** (1.81 g, 8.14 mmol, 96%) as a colorless oil as two diastereomers (*trans*:*cis* = 84:16). R_f (2:1) 0.50; $[\alpha]_D^{20} = -37.35°$ ($c = 1.17$, $CHCl_3$).

IR: ν = 3630, 3460, 3060, 2980, 1790, 1620, 1490, 1440, 1340, 1280, 1240, 1150, 1110, 1060, 990, 930, 860, 720 cm^{-1}.

(2*R*,4*S*,5*R*)-**14a** (*trans*):

^{1}H NMR (400 MHz): δ = 1.77 (ddd, 1H, J = 3.8 Hz, H-3), 2.34 (dt, 1H, J = 4.2, 15.1 Hz, H-3′), 3.76 (dd, 1H, J = 3.0, 12.8 Hz, H-6), 3.94 (dd, 1H, J = 3.0, 12.8 Hz, H-6′), 4.16 (dt, 1H, J = 3.5, 7.2 Hz, OC*H*), 4.42 (dt, 1H, J = 3.5, 7.2 Hz, OC*H*), 4.65 (d, 1H, J = 3.6 Hz, OH), 5.25 (dt, 1H, J = 4.2, 7.3 Hz, H-2), 5.76 (s, 1H, C*H*Ph), 7.30–7.60 (m, 5H, Ar).

^{13}C NMR (100.6 MHz): δ = 31.3 (C-3), 61.6 (C-6), 71.8 (CH), 72.0 (CH), 90.1 (C-2), 103.1 (*C*HPh), 126.6, 126.6, 128.1, 129.2, 129.2, 136.7 (6C–Ar).

(2*S*,4*S*,5*R*)-**14b** (*cis*):

^{1}H NMR (400 MHz): δ = 2.17 (m, 2H, 2H-3), 3.75 (dd, 1H, J = 4.7, 12.7 Hz, H-6), 4.05 (dd, 1H, J = 5.5, 12.7 Hz, H-6′), 4.29 (q, 1H, J = 5.2 Hz, OCH), 4.47 (q, 1H, J = 5.2 Hz, OCH), 5.11 (dt, 1H, J = 4.0, 8.5 Hz, H-2), 5.85 (s, 1H, C*H*Ph), 7.30–7.60 (m, 5H, Ar).

^{13}C NMR (100.6 MHz): δ = 33.3 (C-3), 60.8 (C-6), 71.6 (CH), 71.8 (CH), 91.3 (C-2), 103.1 (*C*HPh), 126.4, 126.4, 128.1, 129.2, 129.2, 136.6 (6C–Ar).

(2*R*,3*S*)-2,3-[(*S*)-Benzylidenedioxy]hex-5-en-1-ol (15):

According to the general procedure A, Ph_3PCH_3Br (4.20 g, 1.8 mmol, 3.0 equiv) in THF (16 mL) was treated with KHMDS (19.6 mL of a 0.5 M toluene solution, 9.8 mmol, 2.5 equiv), followed by the addition of lactol **14** (0.87 g, 3.92 mmol) in THF (1.5 mL) and the resulting mixture was stirred for 12 h at −78°C. Workup and fc (1:1) afforded **15** (764 mg, 3.47 mmol, 71%) as a colorless oil. R_f (1:1) 0.45; $[\alpha]_D^{20} = -10.66°$ ($c = 0.61$, $CHCl_3$).

IR: ν = 3580, 3460, 3000, 2870, 1640, 1460 cm^{-1}.

^{1}H NMR (400 MHz): δ = 1.98 (s, 1H, OH), 2.40–2.46 (m, 1H, H-4), 2.53–2.60 (m, 1H, H-4′), 3.75 (br s, 2H, 2H-1), 4.20–4.30 (m, 2H), 5.13 (d, 1H, J = 10.3 Hz, H-6 *cis*), 5.19 (d, 1H, J = 17.2 Hz, H-6 *trans*), 5.83 (s, 1H, C*H*Ph), 5.89 (ddt, 1H, J = 6.7, 10.2, 17.1, H-5), 7.30–7.60 (m, 5H, Ar).

^{13}C NMR (100.6 MHz): δ = 33.4 (C-4), 61.4 (C-1), 77.9 (CH), 78.3 (CH), 103.0 (*C*HPh), 117.3 (C-6), 126.6, 126.6, 128.2, 129.3, 129.3, 136.9 (6C–Ar), 133.9 (C-5).

3-Methoxy-4,4-dimethyldihydrofuran-2-(3*H*)-one (16):

To a stirred solution of (*R*)-(−)-pantolactone (**4**; 5.0 g, 38.4 mmol) in dry THF (64 mL) was added at 0°C NaH (1.7 g, 42.24 mmol, 1.1 equiv) in small portions. After 1 h MeI (2.86 mL, 46.1 mmol, 1.2 equiv) was added by syringe and the mixture was stirred at r.t. for 1 h. The excess of NaH was destroyed by addition of EtOH (3 mL), followed by H_2O (15 mL). The mixture was extracted with CH_2Cl_2 (3 × 25 mL) and the combined organic layers were dried (Na_2SO_4). After concentration in vacuo, the residue was purified by fc (1:5) to afford **16** (4.99 g, 34.6 mmol, 90%) as a colorless oil. R_f (1:3) 0.80.

IR: ν = 2960, 2920, 2890, 2820, 1780, 1460, 1385, 1365, 1340, 1290, 1150, 1125, 1090, 1020, 1010, 990, 940, 870 cm^{-1}.

^{1}H NMR (200 MHz): δ = 1.07 (s, 3H, Me), 1.20 (s, 3H, Me), 3.57 (s, 1H, H-3), 3.65 (s, 3H, OMe), 3.87 (d, 1H, J = 8.8 Hz, H-5), 3.97 (d, 1H, J = 8.8 Hz, H-5′).

(3*R*)-3-Methoxymethoxy-4,4-dimethyldihydrofuran-2-(3*H*)-one (17):

According to the preparation of **16**, **4** (15.6 g, 120 mmol) in dry THF (200 mL) was treated with NaH (5.3 g, 132 mmol, 1.1 equiv), followed directly by MOMCl (10 mL, 132 mmol, 1.1 equiv) and stirred at r.t. for 1 h. After workup the residue was purified by fc (1:3) to afford **17** (18.53 g, 106 mmol, 89%) as a colorless oil. R_f (1:3) 0.50; $[\alpha]_D^{20} = +122.0°$ ($c = 1.97$, $CHCl_3$).

IR: ν = 2960, 2930, 2895, 2820, 1780, 1460, 1395, 1370, 1345, 1290, 1260, 1190, 1145, 1120, 1060, 1020, 1005, 995, 935, 915, 890, 830, 810 cm^{-1}.

^{1}H NMR (400 MHz): δ = 1.08 (s, 3H, Me), 1.18 (s, 3H, Me), 3.41 (s, 3H, OMe), 3.90 (d, 1H, J = 8.8 Hz, H-5), 3.97 (d, 1H, J = 8.8 Hz, H-5′), 4.04 (s, 1H, H-3), 4.69 (d, 1H, J = 6.8 Hz, OC*H*HO), 4.98 (d, 1H, J = 6.8 Hz, OCH*H*O).

(2*R**,3*R**)- and (2*R**,3*S**)-3-Methoxy-4,4-dimethyltetrahydrofuran-2-ol (18):

To a solution of **16** (4.0 g, 27.7 mmol) in CH_2Cl_2 (93 mL) was slowly added by syringe a 1 M toluene solution of DIBAL-H (0.808 mL, 0.808 mmol, 1.2 equiv) at −78°C. The mixture was stirred for 2 h at −78°C. After warming to r.t., EtOH (3 mL) was added for destruction of the excess of DIBAL-H. This was followed by the addition of EtOAc (10 mL) and 1.5 M aq H_2SO_4 (20 mL) and stirred for 5 min. The aqueous phase was extracted with EtOAc (3 × 25 mL), and the combined organic layers were washed with aq $NaHCO_3$ (20 mL) and H_2O (20 mL) dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by fc (1:2) to afford **18** (2.88 g, 19.7 mmol, 71%) as a mixture of diastereomers (*trans*:*cis* = 75:25) as a colorless oil. R_f (1:2) 0.50.

IR: ν = 3590, 3440, 2960, 2930, 2870, 2830, 1775, 1730, 1465, 1365, 1350, 1330, 1295, 1220, 1120, 1040, 995, 980, 935, 905, 850, 815 cm^{-1}.

(2*R**,3*R**)-**18** (*trans*):

^{1}H NMR (400 MHz): 1.03 (s, 3H, Me), 1.07 (s, 3H, Me), 3.16 (d, 1H, J = 4.2 Hz, H-3), 3.42 (s, 3H, OMe), 3.55 (d, 1H, J = 8.4 Hz, H-5), 3.78 (d, 1H, J = 8.4 Hz, H-5′), 4.08 (s, 1H, OH), 5.42 (d, 1H, J = 3.6 Hz, H-2).

(2*R**,3*S**)-**18** (*cis*):

^{1}H NMR (400 MHz): δ = 1.07 (s, 3H, Me), 1.12 (s, 3H, Me), 3.27 (d, 1H, J = 2.9 Hz, H-3), 3.38 (d, 1H, J = 8.1 Hz, H-5), 3.48 (s, 3H, OMe), 3.65 (d, 1H, J = 8.1 Hz, H-5′), 4.08 (s, 1H, OH), 5.27 (d, 1H, J = 2.8 Hz, H-2).

(2*R*,3*R*)- and (2*S*,3*R*)-3-Methoxymethoxy-4,4-dimethyltetrahydrofuran-2-ol (19):
According to the preparation of **18**, a solution of **17** (4.27 g, 24.5 mmol) in THF (25 mL) was treated with DIBAL-H (9.8 mL, 14.7 mmol, 1.2 equiv) at -78 °C and slowly warmed to r.t. in 1 h. After destruction of the excess of DIBAL-H with EtOH (3 mL), sat. aq potassium sodium tartrate (5 mL) was added and the mixture was vigorously stirred for 1 h at r.t. and extracted with CH_2Cl_2 (3×25 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The resulting residue consisted of pure **19** (4.27 g, 24.2 mmol, 95%) as a colorless oil as two diastereomers (*trans*: *cis* = 75:25). R_f (1:2) 0.25.

IR: ν = 3595, 3405, 2960, 2880, 2820, 1465, 1440, 1400, 1365, 1350, 1330, 995, 945, 935, 915, 855, 815 cm^{-1}.

(2*R*,3*R*)-**19** (*trans*):

^{1}HNMR (200 MHz): 1.02 (s, 3H, Me), 1.05 (s, 3H, Me), 3.35 (s, 3H, OMe), 3.58 (d, 1H, J = 8.6 Hz, H-5), 3.59 (d, 1H, J = 2.8 Hz, H-3), 3.78 (d, 1H, J = 8.4 Hz, H-5′), 4.25 (d, 1H, J = 4.1 Hz, OH), 4.62 (d, 1H, J = 6.6 Hz, OC*H*HO), 4.73 (d, 1H, J = 6.6 Hz, OCH*H*O), 5.26 (t, 1H, J = 3.5 Hz, H-2.

(2*S*,3*R*)-**19** (*cis*):

^{1}HNMR (200 MHz): δ = 1.08 (s, 3H, Me), 1.15 (s, 3H, Me), 3.39 (s, 3H, OMe), 3.42 (d, 1H, J = 8.1 Hz, H-5), 3.60 (m, 1H, H-3), 3.70 (d, 1H, J = 8.1 Hz, H-5′), 4.05 (d, 1H, J = 9.0 Hz, OH), 4.66 (d, 1H, J = 7.9 Hz, OC*H*HO), 4.70 (d, 1H, J = 7.9 Hz, OCH*H*O), 5.41 (dd, 1H, J = 4.2, 9.0 Hz, H-2).

3-Methoxy-2,2-dimethylpent-4-en-1-ol (20):
According to the general procedure A, Ph_3PCH_3Br (7.33 g, 20.52 mmol, 3.0 equiv) in THF (68 mL) was treated with BuLi (11.0 mL of a 1.6 M solution, 17.0 mmol, 2.5 equiv), followed by the addition of lactol **18** (1.0 g, 6.8 mmol) in THF (3 mL) and stirred for 18 h at -78 °C. After workup and fc (1:8), pentenol **20** was obtained (610 mg, 4.27 mmol, 62%) as a colorless oil. R_f (1:8) 0.30.

IR: ν = 3500, 3090, 2960, 2940, 2880, 2830, 1640, 1470, 1450, 1420, 1380, 1365, 1345, 1320, 1230, 1180, 1160, 1115, 1080, 1040, 1025, 995, 970, 935 cm^{-1}.

^{1}HNMR (200 MHz): δ = 0.87 (s, 6H, 2Me), 2.89 (s, 1H, OH), 3.24 (s, 3H, OMe), 3.38 (d, 1H, J = 11.0 Hz, H-1), 3.49 (d, 1H, J = 10.9 Hz, H-1′), 3.39 (d, 1H, J = 8.1 Hz, H-3), 5.20 (dd, 1H, J = 1.8, 17.1 Hz, H-5 *cis*), 5.31 (dd, 1H, J = 1.9, 10.3 Hz, H-5 *trans*), 5.70 (ddd, 1H, J = 8.1, 10.3, 17.1 Hz, H-4).

(3*S*)-3-Methoxymethoxy-2,2-dimethylpent-4-en-1-ol (21):
According to the general procedure A, Ph_3PCH_3Br (12.7 g, 34.1 mmol, 3.0 equiv) in THF (115 mL) was treated with BuLi (17.7 mL of a 1.6 M solution, 28.4 mmol, 2.5 equiv), followed by the addition of lactol **19** (2.0 g, 11.4 mmol) in THF (5 mL) and the resulting mixture was stirred for 18 h at -78 °C. After workup and fc (1:4), pentenol **21** was obtained (1.42 g, 8.1 mmol, 72%) as a colorless oil. R_f (1:4) 0.35; $[\alpha]_D^{20} = +14.25°$ (c = 1.62, $CHCl_3$).

IR: ν = 3550, 3100, 2925, 2850, 1490, 1460, 1440, 1405, 1380, 1355, 1180, 1120, 1100, 1070, 1025, 990, 960, 940, 890 cm^{-1}.

^{1}HNMR (400 MHz): δ = 0.86 (s, 3H, Me), 0.94 (s, 3H, Me), 2.72 (s, 1H, OH), 3.33 (d, 1H, J = 11.0 Hz, H-1), 3.40 (s, 3H, OMe), 3.60 (d, 1H, J = 11.0 Hz, H-1′), 3.89 (d, 1H, J = 8.1 Hz, H-3), 4.52 (d, 1H, J = 6.5 Hz, OC*H*HO), 4.66 (d, 1H, J = 6.5 mmol, OCH*H*O), 5.22 (dd, 1H, J = 1.8, 17.2 Hz, H-5 *trans*), 5.31 (dd, 1H, J = 1.2, 10.4 Hz, H-5 *cis*), 5.70 (ddd, 1H, J = 8.1, 10.4, 17.2 Hz, H-4).

^{13}CNMR (63 MHz): δ = 19.3 (Me), 21.1 (Me), 38.3 (C-2), 55.0 (OMe), 69.0 (C-1), 82.4 (C-3), 93.5 (OCH_2O), 118.6 (C-5), 134.2 (C-4).

Dichloroacetic Acid (2*R*,3*R*,4*R*,5*R*)-1,2:4,5-Di(isopropylidenedioxy)hept-6-en-3-yl Ester (22):
According to the general procedure B, dichloroacetyl chloride (367 mg, 2.5 mmol, 2.2 equiv) and **10** (300 mg, 1.15 mmol) in CH_2Cl_2 (4.2 mL) were treated with Et_3N (233 mg, 2.3 mmol, 2 equiv) in CH_2Cl_2 (0.5 mL). The reaction was stirred for 1 h at 0 °C. Workup and fc (1:10) afforded **22** (341 mg, 0.93 mmol, 80%) as a light yellow oil. R_f (1:10) 0.40; $[\alpha]_D^{20} = +22.9°$ (c = 0.48, EtOH).

IR: ν = 3080, 2980, 2920, 2870, 1750, 1635, 1450, 1420, 1370, 1360, 1230, 1150, 1050, 970, 830, 800 cm^{-1}.

^{1}HNMR (200 MHz): δ = 1.35 (s, 3H, Me), 1.39 (s, 6H, 2Me), 1.42 (s, 3H, Me), 3.72 (t, 1H, J = 7.6 Hz, H-1), 4.05 (m, 4H, H-1′, H-2, H-4, H-5), 5.51 (m, 3H, 2H-7, H-3), 5.96 (m, 2H, H-6, $CHCl_2$), 5.94 (s, 1H, $CHCl_2$).

Trichloroacetic Acid (2*R*,3*R*,4*R*,5*R*)-1,2:4,5-Di(isopropylidenedioxy)hept-6-en-3-yl Ester (23):
To a solution of **10** (2.0 g, 7.74 mmol) and pyridine (674 mg, 8.51 mmol, 1.1 equiv) in CH_2Cl_2 (26 mL) was added dropwise via syringe a solution of trichloroacetyl chloride (1.55 g, 8.51 mmol, 1.1 equiv) at -78 °C and stirred for 15 min. After warming to r.t., the mixture was washed with H_2O (50 mL), the aqueous phase was extracted with CH_2Cl_2 (2×50 mL), the combined organic layers were dried ($MgSO_4$) and after concentration in vacuo the residue was purified by fc (1:5.5) to afford **23** (2.89 g, 7.16 mmol, 93%) as a viscous colorless oil, which solidified upon standing. Mp 64–65 °C (hexane); R_f (1:4) 0.30; $[\alpha]_D^{20} = -17.8°$ (c = 1.0, EtOH).

IR: ν = 3080, 2980, 2920, 2840, 1765, 1450, 1375, 1370, 1230, 1160, 1075, 1060, 1020, 980, 930, 890, 880, 840, 820, 670 cm^{-1}.

^{1}HNMR (400 MHz): δ = 1.34 (s, 3H, Me), 1.38 (s, 3H, Me), 1.39 (s, 3H, Me), 1.56 (s, 3H, Me), 3.95 (dd, 1H, J = 7.1, 8.7 Hz, H-1), 4.05 (dd, 1H, J = 6.2, 8.7 Hz, H-1′), 4.30 (dd, 1H, J = 4.9, 6.3 Hz, H-2), 4.40 (dd, 1H, J = 1.9, 7.1 Hz, H-4), 4.77 (t, 1H, J = 6.9 Hz, H-5), 5.23 (dd, 1H, J = 1.9, 4.9 Hz, H-3), 5.34 (dt, 1H, J = 1.3, 10.5 Hz, H-7 *cis*), 5.44 (dt, 1H, J = 1.3, 17.2 Hz, H-7 *trans*), 5.78 (ddt, 1H, J = 6.7, 10.5, 17.2 Hz, H-6).

^{13}CNMR (75.5 MHz): δ = 25.1 (2Me), 26.2 (2Me), 65.0 (C-1), 75.2 (CH), 75.4 (CH), 76.6 (CH), 77.7 (CH), 108.8 (2 OCO), 109.6 (CCl_3), 119.6 (C-7), 131.7 (C-6), 160.6 (CO).

(5*R*,6*S*,7*S*,8*R*)-3,3,5-Trichloro-6,7-(isopropylidenedioxy)-8-[(1*R*)-1,2-isopropylidenedioxy)ethyl]oxocan-2-one (24):
According to the general procedure C, trichloroacetate **23** (2.24 g, 5.56 mmol) in DCE (62 mL) was treated with 0.3 equiv of CuCl (1.67 mmol, 165 mg) and 0.3 equiv of 2,2′-bipyridine (1.67 mmol, 261 mg) and heated in a sealed tube at 125 °C for 1.5 h. Concentration in vacuo and purification by fc (1:5) afforded crude **24** (1.86 g, 4.62 mmol, 83%) as a light yellow solid, which was recrystallized from hexane to yield pure **24** (1.58 g, 3.92 mmol, 71%). R_f (1:3) 0.50; $[\alpha]_D^{20} = +46.0°$ (c = 0.1, EtOH).

IR: ν = 2980, 2930, 1770, 1450, 1430, 1375, 1260, 1175, 1070, 1010, 930, 880 cm^{-1}.

^{1}HNMR (400 MHz, C_6D_6): δ = 0.98 (s, 3H, Me), 1.18 (s, 3H, Me), 1.33 (s, H, Me), 1.38 (s, 3H, Me), 2.94 (ddd, 1H, J = 1.1, 2.1, 15.6 Hz, H-4), 3.49 (ddd, 1H, J = 1.1, 2.0, 5.4 Hz, H-5), 3.71 (dd, 1H, J = 5.4, 15.6 Hz, H-4′), 3.80 (dd, 1H, J = 6.3, 9.0 Hz, H-10), 3.98 (dt, 1H, J = 1.0, 8.1 Hz, H-6), 4.06 (dd, 1H, J = 1.4, 8.2 Hz, H-7), 4.14 (dd, 1H, J = 5.0, 9.0 Hz, H-10′), 4.19 (dd, 1H, J = 1.4, 8.1 Hz, H-8), 4.31 (ddd, 1H, J = 5.0, 6.3, 8.1 Hz, H-9).

^{13}CNMR (100.6 MHz, C_6D_6): δ = 23.0, 25.8, 26.6, 27.5 (4Me), 54.8 (C-4), 57.5 (C-5), 67.6 (C-10), 74.5 (CH), 78.0 (CH), 80.0 (CH), 81.9 (CH), 83.5 (C-3), 109.4 (OCO), 110.9 (OCO), 168.9 (C-2).

MS (FAB, 70 eV): m/z (%) = 403 (35, M$^+$ + 1), 391 (16), 389 (46), 387 (48), 347 (14), 345 (15), 289 (11), 138 (19), 137 (48), 136 (52), 115 (31), 107 (20), 101 (95), 85 (29), 77 (22), 69 (17), 59 (100).

Anal. Calc. for $C_{15}H_{21}O_6Cl_3$: C, 44.63; H, 5.24; Cl, 26.35. Found C, 44.48; H, 5.31; Cl, 26.28.

(4*R*,5*S*,6*S*,7*R*,8*R*)-5,6:8,9-Di(isopropylidenedioxy)-2,2,4-trichlorononane-1,7-diol (25):
A solution of **24** (100 mg, 0.25 mmol) in CH_2Cl_2 (0.75 mL) was treated with a 1.5 M toluene solution of DIBAL-H (0.75 mL, 0.50 mmol, 2 equiv) at -78 °C. The mixture was allowed to warm rapidly to r.t. and was stirred for 1 h. Aq potassium sodium tartrate (5 mL) was added and the mixture was vigorously stirred for 15 min at r.t. Extraction with CH_2Cl_2 (3×5 mL), drying (Na_2SO_4), concentration in vacuo and fc (1:3) gave **25** (73 mg, 0.18 mmol),

72%) as a colorless oil. R_f (1:3) 0.10; $[\alpha]_D^{20} = -17.96°$ ($c = 0.37$, $CHCl_3$).

IR: ν = 3550, 2980, 2930, 2880, 1450, 1380, 1370, 1250, 1160, 1080, 905, 880, 840 cm^{-1}.

^1H NMR (400 MHz): δ = 1.04, 1.24, 1.28 and 1.39 (4s, 12H, 4Me), 2.07 (d, 1H, J = 8.6 Hz, HO-C-7), 2.70 (dd, 1H, J = 7.8, 16.0 Hz, H-3), 2.74 (bt, 1H, J = 6.7 Hz, HO-C-1), 3.25 (dd, 1H, J = 2.0, 16.1 Hz, H-3'), 3.81 (dd, 1H, J = 6.6, 12.5 Hz, H-1), 3.87 (dd, 1H, J = 8.0, 12.3 Hz, H-1'), 3.90–4.00 (m, 2H, H-8, H-9), 4.03–4.10 (m, 1H, H-9'), 4.06 (dd, 1H, J = 6.9, 9.5 Hz, H-5), 4.16 (t, 1H, J = 7.5 Hz, H-7), 4.43 (d, 1H, J = 6.8 Hz, H-6), 4.92 (ddd, 1H, J = 2.0, 8.0, 9.9 Hz, H-4).

^{13}C NMR (100.6 MHz): δ = 24.5, 25.3, 26.3 and 26.8 (4Me), 48.8 (C-3), 53.8 (C-4), 66.4 (C-9), 69.1 (OCH), 71.1 (C-1), 75.6 (OCH), 76.3 (OCH), 79.3 (OCH), 91.0 (C-2), 109.2, 109.2 (2Cq).

Dichloroacetic Acid (2*R*,3*S*)-2,3-(Isopropylidenedioxy)pent-4-enyl Ester (26):
According to the general procedure B, a solution of dichloroacetyl chloride (560 mg, 3.8 mmol, 1.2 equiv) and **12** (500 mg, 3.16 mmol) in CH_2Cl_2 (13 mL) was treated at 0°C with Et_3N (630 mg, 6.3 mmol, 2 equiv) in CH_2Cl_2 (4 mL) and stirred at 0°C for 1 h. After workup and fc (1:10), **26** (135 mg, 0.050 mmol, 16%) was obtained as a yellow oil. R_f (1:10) 0.30; $[\alpha]_D^{20} = +15.5°$ (c = 1.06, EtOH).

IR: ν = 3080, 2980, 2940, 1760, 1715, 1450, 1380, 1370, 1300, 1165, 1110, 990, 930, 845, 815 cm^{-1}.

^1H NMR (300 MHz): δ = 1.40 (s, 3H, Me), 1.52 (s, 3H, Me), 4.16 (dd, 1H, J = 6.8, 11.4 Hz, H-1), 4.28 (dd, 1H, J = 4.6, 11.5 Hz, H-1'), 4.41 (dt, 1H, J = 4.5, 6.7 Hz, H-2), 4.71 (t, 1H, J = 6.7 Hz, H-3), 5.32 (d, 1H, J = 10.4 Hz, H-5 *cis*), 5.44 (d, 1H, J = 17.1 Hz, H-5 *trans*), 5.80 (ddd, 1H, J = 7.0, 10.3, 17.1 Hz, H-4), 5.97 (s, 1H, $CHCl_2$).

Trichloroacetic Acid (2*R*,3*S*)-2,3-(Isopropylidenedioxy)pent-4-enyl Ester (27):
To a solution of **12** (176 mg, 1.1 mmol) and pyridine (60.8 mg, 0.8 mmol, 0.7 equiv) in CH_2Cl_2 (5 mL) was added via syringe at −78°C trichloroacetyl chloride (145 mg, 0.8 mmol, 0.7 equiv). The reaction was stirred for 1.5 h at −78°C. After addition of 2 M aq HCl (5 mL), extraction of the aq phase with CH_2Cl_2 (3 × 5 mL), drying of the organic layers (Na_2SO_4) and concentration in vacuo, the residue was purified by fc (1:10) to afford **27** (238 mg, 0.78 mmol, 98%) as a colorless oil. R_f (1:8) 0.40; $[\alpha]_D^{20} = +36.4°$ (c = 0.5, EtOH).

IR: ν = 3080, 2980, 2930, 1765, 1450, 1380, 1370, 1250, 1165, 1080, 1070, 1050, 990, 930, 840, 825 cm^{-1}.

^1H NMR (200 MHz): δ = 1.39 (s, 3H, Me), 1.51 (s, 3H, Me), 4.25–4.35 (m, 2H, 2H-1), 4.43 (q, 1H, J = 6.0 Hz, H-2), 4.74 (t, 1H, J = 6.5 Hz, H-3), 5.32 (d, 1H, J = 10.3 Hz, H-5 *cis*), 5.45 (d, 1H, J = 17.1 Hz, H-5 *trans*), 5.86 (ddd, 1H, J = 6.9, 10.3, 17.1 Hz, H-4).

(2*R*,3*S*)-1-Benzyloxy-2,3-(isopropylidenedioxy)pent-4-ene (28):
Pentenol **12** (100 mg, 0.63 mmol) was dissolved in THF (1 mL), cooled to 10°C and NaH (15.6 mg, 0.65 mmol, 1.02 equiv) was added in small portions. After 15 min Bu_4NI (5 mg, 0.02 equiv) and BnBr (111 mg, 0.65 mmol, 1.02 equiv) were added and the mixture was stirred for 18 h at r.t. Addition of H_2O (10 mL), extraction of the aq phase with CH_2Cl_2 (3 × 15 mL), drying (Na_2SO_4), concentration in vacuo and purification by fc (1:8) gave **28** (134 mg, 0.54 mmol, 86%) as a colorless oil. R_f (1:6) 0.40; $[\alpha]_D^{20} = -89°$ (c = 1.3, $CHCl_3$).

IR: ν = 3070, 3050, 2980, 2920, 2940, 1720, 1485, 1445, 1370, 1360, 1230, 1160, 1075, 1035, 985, 920 cm^{-1}.

^1H NMR (200 MHz): δ = 1.40 (s, 3H, Me), 1.51 (s, 3H, Me), 3.46 (d, 2H, 2H-1), 4.40 (q, 1H, J = 6.2 Hz, H-2), 4.50–4.70 (m, 3H, J = 6.5 Hz, H-3 and CH_2Ph), 5.23 (d, 1H, J = 10.2 Hz, H-5 *cis*), 5.35 (d, 1H, J = 17.5 Hz, H-5 *trans*), 5.82 (ddd, 1H, J = 7.2, 10.2, 17.2 Hz, H-4), 7.30–7.45 (m, 5H, Ar).

(2*R*,3*S*)-1-Benzyloxy-2,3-dimethoxypent-4-ene (29):
Pentene **28** (134 mg, 0.54 mmol) was dissolved in 0.2 M HCl/MeOH (6 mL) and stirred for 2 d at r.t. The solvent was evaporated, the residue was taken up in aq $NaHCO_3$ (10 mL) and the product was extracted with CH_2Cl_2 (3 × 5 mL). The organic phases were washed with H_2O (5 mL), dried ($MgSO_4$) and concentrated in vacuo. This afforded pure (2*S*,3*S*)-1-benzyloxypent-4-ene-2,3-diol (112 mg, 0.54 mmol, 100%) as a viscous colorless oil. R_f (1:1) 0.20; $[\alpha]_D^{20} = -6.4°$ (c = 1.0, $CHCl_3$).

IR: ν = 3560, 3440, 3080, 3060, 3000, 2920, 2860, 1720, 1490, 1450, 1380, 1360, 1220, 1090, 990, 930, 910 cm^{-1}.

^1H NMR (200 MHz): δ = 2.53 (br s, 2H, 2OH), 3.61 (d, 2H, J = 4.9 Hz, 2H-1), 3.81 (q, 1H, J = 4.7 Hz, H-2), 4.27 (dt, 1H, J = 1.2, 4.5 Hz, H-3), 4.54 (s, 2H, CH_2Ph), 5.23 (td, 1H, J = 1.4, 10.5 Hz, H-5 *cis*), 5.35 (td, 1H, J = 1.4, 17.3 Hz, H-5 *trans*), 5.89 (ddd, 1H, J = 5.8, 10.5, 17.2 Hz, H-4), 7.30–7.40 (m, 5H, Ar).

To a solution of the above diol (541 mg, 2.6 mmol) in THF (4.3 mL) at 10°C was added a suspension of NaH (137 mg, 5.72 mmol, 2.2 equiv) in THF (1 mL) in small portions via a pasteur pipette. After 15 min of stirring, the resulting suspension of the disodium salt was treated with MeI (1.84 g, 13 mmol, 5 equiv) and stirred for 2 h at r.t. The excess of NaH was treated with EtOH (1 mL) and H_2O (50 mL) was added. Extraction of the aq phase with CH_2Cl_2 (3 × 40 mL), drying (Na_2SO_4), concentration in vacuo and fc (1:6) afforded **29** (600 mg, 2.54 mmol, 98%) as a light yellow oil. R_f (1:6) 0.35; $[\alpha]_D^{20} = +8.75°$ (c = 0.48, $CHCl_3$).

IR: ν = 3090, 3070, 2980, 2920, 2880, 2800, 1440, 1355, 1180, 1080, 980, 920 cm^{-1}.

^1H NMR (200 MHz): δ = 3.29 (s, 3H, OMe), 3.49 (s, 3H, OMe), 3.40–3.50 (m, 1H, H-2), 3.58 (d, 2H, J = 5.1 Hz, 2H-1), 3.73 (dd, 1H, J = 4.2, 7.7 Hz, H-3), 4.55 (s, 2H, CH_2Ph), 5.20–5.35 (m, 2H, 2H-5), 5.78 (ddd, 1H, J = 7.7, 10.6, 17.1 Hz, H-4), 7.30–7.40 (m, 5H, Ar).

(2*R*,3*S*)-2,3-Dimethoxypent-4-en-1-ol (30):
To a solution of **29** (200 mg, 0.84 mmol) in CH_2Cl_2 (5 mL) was slowly added via syringe 1.2 M $SnCl_4$ in CH_2Cl_2 (5 mL, 6 mmol, 7 equiv) and the mixture was stirred for 3 d. It was poured into aq $NaHCO_3$ (20 mL) and the aq layer was extracted with CH_2Cl_2 (3 × 20 mL), the organic layers were dried (Na_2SO_4), concentrated in vacuo and purified by fc (1:3) to give **30** (80 mg, 0.55 mmol, 65%) as a colorless oil. Small quantities of **29** (ca. 15%) were isolated. R_f (1:3) 0.10; $[\alpha]_D^{20} = +35.0°$ (c = 0.8, $CHCl_3$).

IR: ν = 3480, 3080, 2980, 2940, 2880, 2820, 1460, 1445, 1415, 1180, 1100, 990, 930, 905 cm^{-1}.

^1H NMR (200 MHz): δ = 2.00 (s, 1H, OH), 3.23 (q, 1H, J = 4.8 Hz, H-2), 3.32 (s, 3H, OMe), 3.46 (s, 3H, OMe), 3.72 (d, 2H, J = 4.6 Hz, 2H-1), 3.60–3.80 (m, 1H, H-3), 5.30 (d, 1H, J = 9.7 Hz, H-5 *cis*), 5.32 (d, 1H, J = 17.7 Hz, H-5 *trans*), 5.76 (ddd, 1H, J = 7.2, 9.6, 17.2 Hz, H-4).

Dichloroacetic Acid (2*R*,3*S*)-2,3-Dimethoxypent-4-enyl Ester (31):
According to the general procedure B, dichloroacetyl chloride (160 mg, 1.09 mmol, 1.1 equiv) and **30** (145 mg, 0.99 mmol) in CH_2Cl_2 (3 mL) was treated with Et_3N (200 mg, 1.98 mmol, 2 equiv) in $CHCl_2$ (1 mL) at −10°C. The reaction was stirred for 2 d at r.t. Workup and fc (1:6) afforded **31** (204 mg, 0.79 mmol, 80%) as a light yellow oil. R_f (1:6) 0.30; $[\alpha]_D^{20} = +16.41°$ (c = 0.53, $CHCl_3$).

IR: ν = 3080, 2990, 2930, 2890, 2820, 1765, 1460, 1445, 1300, 1170, 1110, 1085, 1020, 910, 815, 645 cm^{-1}.

^1H NMR (200 MHz): δ = 3.29 (s, 3H, OMe), 3.40–3.50 (m, 1H, H-2), 3.46 (s, 3H, OMe), 3.67 (dd, 1H, J = 5.0, 7.0 Hz, H-3), 4.33 (dd, 1H, J = 5.9, 11.7 Hz, H-1), 4.46 (dd, 1H, J = 3.5, 11.7 Hz, H-1'), 5.33 (d, 1H, J = 17.3 Hz, H-5 *trans*), 5.35 (d, 1H, J = 10.5 Hz, H-5 *cis*), 5.76 (ddd, 1H, J = 7.4, 10.7, 17.0 Hz, H-4), 5.98 (s, 1H, $CHCl_2$).

(2*R*,3*S*)-Trichloroacetic Acid 2,3-Dimethoxypent-4-enyl Ester (32):
According to the general procedure B, trichloroacetyl chloride (68 mg, 0.38 mmol, 1.1 equiv) and **30** (50 mg, 0.34 mmol) in CH_2Cl_2

(1 mL) was treated with Et_3N (69 mg, 0.68 mmol, 2 equiv) in CH_2Cl_2 (0.5 mL). The reaction was stirred for 2 h at 0 °C. Workup and fc (1:6) afforded **32** (87 mg, 0.30 mmol, 88 %) as a colorless oil. R_f (1:6) 0.60; $[\alpha]_D^{20} = +18.67°$ ($c = 0.83$, $CHCl_3$).

IR: ν = 3080, 2990, 2930, 2890, 2820, 1765, 1460, 1445, 1230, 1110, 1090, 990, 935, 840, 825, 680 cm^{-1}.

^{1}H NMR (200 MHz): δ = 3.29 (s, 3 H, OMe), 3.45 (s, 3 H, OMe), 3.40–3.50 (m, 1 H, H-2), 3.66 (dd, 1 H, J = 5.8, 6.5 Hz, H-3), 4.40 (dd, 1 H, J = 6.1, 11.6 Hz, H-1), 4.53 (dd, 1 H, J = 3.3, 11.5 Hz, H-1′), 5.32 (d, 1 H, J = 17.8 Hz, H-5 *trans*), 5.34 (d, 1 H, J = 10.5 Hz, H-5 *cis*), 5.75 (ddd, 1 H, J = 7.4, 10.6, 18.1 Hz, H-4).

(2*R*,5*S*,6*R*,7*R*)- and (2*S*,5*S*,6*R*,7*R*)-3,5-Dichloro-6,7-dimethoxyoxocan-2-one (33a,b):

According to the general procedure C, dichloroacetate **31** (64 mg, 0.25 mmol) in DCE (2.5 mL) was treated with 0.6 equiv of CuCl (0.15 mmol, 14.9 mg) and 0.3 equiv of 2,2′-bipyridine (0.075 mmol, 11.7 mg) and heated in a sealed tube at 130 °C for 6 h. Concentration in vacuo and fc over a short column (1:3) afforded pure **33** (46 mg, 0.18 mmol, 72 %) as a colorless oil, which consisted of two diastereomers in the ratio of 50:50. The two isomers were separated by fc (1:10) to yield (2*S*,5*S*,6*R*,7*R*)-**33b** (20 mg, 31 %) as a colorless oil and (2*R*,5*S*,6*R*,7*R*)-**33a** (17.2 mg, 27 %) as white crystals.

33a (*cis*-dichloro): R_f (1:6) 0.25; white crystals; mp 88.0–88.5 °C (hexane); $[\alpha]_D^{20} = +6.9°$ ($c = 0.85$, $CHCl_3$).

IR: ν = 2990, 2940, 2900, 2830, 1785, 1460, 1435, 1370, 1345, 1250, 1190, 1160, 1130, 1100, 1060, 1040, 1020, 1000, 940, 880, 845, 815 cm^{-1}.

^{1}H NMR (400 MHz): δ = 2.58 (ddd, 1 H, J = 1.5, 6.5, 13.7 Hz, H-4), 2.91 (dt, 1 H, J = 11.5, 13.7 Hz, H-4′), 3.43 (s, 3 H, OMe), 3.60 (s, 3 H, OMe), 3.60–3.68 (m, 1 H, H-7), 4.06 (s, 1 H, H-6), 4.08 (dd, 1 H, J = 5.7, 10.3 Hz, H-8), 4.25 (dd, 1 H, J = 1.5, 11.1 Hz, H-5), 4.39 (dd, 1 H, J = 6.5, 11.8 Hz, H-3), 4.70 (t, 1 H, J = 10.5 Hz, H-8′).

^{13}C NMR (75.5 MHz): δ = 41.2 (C-4), 54.8 (OMe), 58.1 (CHCl), 58.5 (OMe), 61.7 (CHCl), 63.7 (C-8), 82.7 (OCH), 86.3 (OCH), 169.0 (C-2).

MS (EI, 70 eV): m/z (%) = 215 (10), 213 (20), 212 (8), 185 (8), 162 (23), 142 (100), 119 (13), 111 (21), 87 (7), 71 (22), 58 (56), 45 (10), 43 (9), 29 (4).

HRMS calc for $C_9H_{14}O_4Cl$ ($M^+ - {}^{35}Cl$) 221.0580, found 221.0578.

Anal. Calc. for $C_9H_{142}Cl_2$: C, 42.04; H, 5.49; Cl, 27.58. Found C, 42.15; H, 5.54; Cl, 27.69.

33b (*trans*-dichloro): R_f (1:6) 0.35; $[\alpha]_D^{20} = +11.9°$ ($c = 1.0$, $CHCl_3$).

IR: ν = 2990, 2940, 2900, 2830, 1760, 1460, 1390, 1370, 1260, 1170, 1155, 1100, 1060, 1030, 960, 925, 880, 840 cm^{-1}.

^{1}H NMR (300 MHz): δ = 2.38 (ddd, 1 H, J = 2.1, 5.2, 14.6 Hz, H-4), 3.15 (ddd, 1 H, J = 4.9, 10.8, 14.6 Hz, H-4′), 3.44 (s, 3 H, OMe), 3.60 (ddd, 1 H, J = 1.5, 5.4, 10.2 Hz, H-7), 3.66 (s, 3 H, OMe), 4.09 (d, 1 H, J = 1.5 Hz, H-6), 4.24 (dd, 1 H, J = 2.1, 10.8 Hz, H-3), 4.33 (dd, 1 H, J = 5.4, 10.9 Hz, H-8), 4.40 (dd, 1 H, J = 10.2, 10.9 Hz, H-8′), 4.70 (dd, 1 H, J = 4.9, 5.1 Hz, H-5).

^{13}C NMR (75.5 MHz): δ = 40.9 (C-4), 53.9 (OMe), 56.4 (OMe), 58.3 (CHCl), 62.2 (CHCl), 64.1 (C-8), 81.3 (OCH), 85.9 (OCH), 169.4 (C-2).

MS (EI, 70 eV): m/z (%) = 221 ($M^+ - {}^{35}Cl$, 5), 194 (14), 185 (12), 119 (10), 101 (46), 92 (20), 71 (53), 59 (23), 58 (100), 45 (25), 43 (42), 41 (22), 32 (32), 31 (43), 29 (27).

HRMS calc for $C_9H_{14}O_4$ ($M^+ - {}^{35}Cl$) 221.0580, found 221.0619.

Dichloroacetic Acid (2*R*,3*S*)-2,3-[(*S*)-Benzylidenedioxy]hex-5-enyl Ester (34):

A solution of pyridine (154 mg, 1.95 mmol, 1.5 equiv) and **15** (286 mg, 1.30 mmol) in CH_2Cl_2 (4.3 mL) was treated with dichloroacetyl chloride (211 mg, 14.3 mmol, 1.1 equiv) by dropwise addition at −78 °C. The mixture was stirred for 2 h at −78 °C, poured into H_2O (10 mL), the aq phase was extracted with CH_2Cl_2 (3 × 5 mL), the combined organic layers were dried (Na_2SO_4), concentrated in vacuo and the residue was purified by fc (1:3) to afford **34** (396 mg, 1.20 mmol, 92 %) as a colorless oil. R_f (1:3) 0.60; $[\alpha]_D^{20} = +16.10°$ ($c = 0.82$, $CHCl_3$).

IR: ν = 3500, 3000, 2800, 1760, 1640, 1590, 1490, 1460, 1400, 1290, 1160, 1090, 990, 920, 810, 690 cm^{-1}.

^{1}H NMR (400 MHz): δ = 2.40–2.47 (m, 1 H, H-4), 2.50–2.58 (m, 1 H, H-4′), 4.32–4.37 (m, 4 H), 5.16 (d, 1 H, J = 10.4 Hz, H-6 *cis*), 5.25 (d, 1 H, J = 17.5 Hz, H-6 *trans*), 5.84 (s, 1 H, C*H*Ph), 5.91 (ddt, 1 H, J = 3.2, 10.8, 17.6 Hz, H-5), 5.96 (s, 1 H, C*H*Cl_2), 7.20–7.60 (m, 5 H, Ar).

^{13}C NMR (100.6 MHz): δ = 33.4 (C-4), 64.0 ($CHCl_2$), 65.7 (C-1), 74.8 (CH), 78.1 (CH), 103.5 (*C*HPh), 117.8 (C-6), 126.6, 126.6, 128.3, 129.5, 129.5, 136.7 (6 C–Ar), 133.4 (C-5), 164.1 (CO).

MS EI (70 eV): m/z (%) = 331 ($M^+ + 1$, 25), 330 (M^+, 16), 329 (30), 291 (24), 289 (35), 262 (13), 185 (45), 183 (68), 162 (14), 105 (100), 77 (19).

Trichloroacetic Acid (2*R*,3*S*)-2,3-[(*S*)-Benzylidenedioxy]hex-5-enyl Ester (35):

A solution of pyridine (324 mg, 4.10 mmol, 1.5 equiv) and **15** (600 mg, 2.73 mmol) in CH_2Cl_2 (8 mL) was treated with trichloroacetyl chloride (682 mg, 3.75 mmol, 1.4 equiv) by dropwise addition at −78 °C. The mixture was stirred for 2 h at −78 °C, poured into H_2O (10 mL), the aq phase was extracted with CH_2Cl_2 (3 × 5 mL), the combined organic layers were dried (Na_2SO_4), concentrated in vacuo and the residue was purified by fc (1:3) to afford **35** (980 mg, 2.68 mmol, 98 %) as a white solid. R_f (1:5) 0.50; mp 35 °C; $[\alpha]_D^{20} = +14.56°$ ($c = 0.67$, $CHCl_3$).

IR: ν = 3000, 2880, 1760, 1640, 1460, 1400, 1230, 1090, 1000, 920, 840, 820, 680 cm^{-1}.

^{1}H NMR (400 MHz): δ = 2.40–2.60 (m, 2 H, 2 H-4), 4.20–4.50 (m, 2 H), 4.49 (br s, 2 H), 5.10–5.20 (m, 1 H, H-6 *cis*), 5.15–5.25 (m, 1 H, H-6 *trans*), 5.85 (s, 1 H, C*H*Ph), 5.80–6.00 (m, 1 H, H-5), 7.30–7.60 (m, 5 H, Ar).

^{13}C NMR (100.6 MHz): δ = 33.3 (C-4), 67.2 (C-1), 74.6 (CH), 78.1 (CH), 103.5 (*C*HPh), 117.8 (C-6), 126.6, 126.6, 128.3, 129.4, 129.4, 136.6 (6 C–Ar), 33.4 (C-5), 161.6 (CO).

MS EI (70 eV): m/z (%) = 365 ($M^+ + 1$, 25), 364 (M^+, 13), 363 (25), 325 (30), 323 (32), 262 (8), 221 (28), 217 (87), 133 (18), 119 (27), 105 (100), 79 (67), 77 (44), 41 (17).

(3*S*,5*S*,7*S*,8*R*)- and (3*R*,5*S*,7*S*,8*R*)-7,8-[(*S*)-Benzylidenedioxy]-3,5-dichloro-7,8-dihydroxyoxonan-2-one (36a,b):

According to the general procedure C, dichloroacetate **34** (100 mg, 0.30 mmol) in benzene (3 mL) was treated with 0.3 equiv of CuCl (0.09 mmol, 8.9 mg) and 0.3 equiv of 2,2′-bipyridine (0.09 mmol, 15.5 mg) and heated in a sealed tube at 150 °C for 3 h. Concentration in vacuo and purification by fc (1:6) afforded **36** (63 mg, 0.19 mmol, 63 %) of a white solid, which consisted of two diastereomers in the ratio 80:20. R_f (1:5) 0.30; mp 127–145 °C; $[\alpha]_D^{20} = -39.70°$ ($c = 1.00$, $CHCl_3$).

IR: ν = 3000, 2920, 2000, 1760, 1500, 1370, 1345, 1160, 1090, 1060, 1030, 1010, 975, 690 cm^{-1}.

MS EI (70 eV): m/z (%) = 331 ($M^+ + 1$, 64), 227 (15), 225 (20), 179 (12), 153 (14), 107 (90), 105 (100), 91 (52), 79 (45), 78 (18), 59 (15).

Anal. Calc. for $C_{15}H_{16}Cl_2O_4$: C, 54.40; H, 4.87; Cl, 21.41. Found: C, 54.57; H, 4.92; Cl, 21.29.

(3*S*,5*S*,7*S*,8*R*)-**36a** (*cis*-dichloro):

^{1}H NMR (400 MHz, C_6D_6): δ = 1.59 (dd, 1 H, J = 12.3, 16.4 Hz, H-6), 1.95 (dt, 1 H, J = 11.4, 13.4 Hz, H-4), 2.22 (ddt, 1 H, J = 0.6, 7.7, 13.4 Hz, H-4′), 2.27 (ddd, 1 H, J = 3.6, 7.7, 16.4 Hz, H-6′), 3.32 (ddt, 1 H, J = 1.1, 7.8, 11.4 Hz, H-5), 3.43 (ddd, 1 H, J = 08, 4.1, 11.0 Hz, H-9), 3.54 (dd, 1 H, J = 7.0, 11.3 Hz, H-3), 3.83 (ddd, 1 H, J = 4.1, 5.9, 11.4 Hz, H-8), 4.00 (ddd, 1 H, J = 3.6, 5.9, 11.7 Hz, H-7), 4.54 (t, 1 H, J = 11.2 Hz, H-9), 5.50 (s, 1 H, C*H*Ph), 7.10–7.40 (m, 5 H, Ar).

^{13}C NMR (100.6 MHz, C_6D_6): δ = 39.9 (C-6), 47.0 (C-4), 52.6 (C-5), 54.6 (C-3), 64.0 (C-9), 73.7 (CH), 77.3 (CH), 104.6 (*C*HPh), 127.5, 127.5, 129.3, 129.3, 130.4, 137.8 (6 C–Ar), 168.8 (C-2).

(3*R*,5*S*,7*S*,8*R*)-**36b** (*trans*-dichloro):

^{1}H NMR (400 MHz, C_6D_6): δ = 1.87 (dd, 1 H, *J* = 2.2, 16.2 Hz, H-6), 2.37 (dt, 1 H, *J* = 11.4, 13.3 Hz, H-4), 2.56 (ddd, 1 H, *J* = 3.4, 7.6, 16.3 Hz, H-6′), 2.75 (dd, 1 H, *J* = 6.9, 13.4 Hz, H-4′), 3.90–4.00 (m, 2 H, H-7, H-8), 4.45 (dd, 1 H, *J* = 6.9, 11.2 Hz, H-3), 4.40–4.60 (m, 2 H, H-5 and H-9), 4.69 (t, 1 H, *J* = 11.0 Hz, H-9′), 5.81 (s, 1 H, CHPh), 7.30–7.50 (m, 5 H, Ar).

^{13}C NMR (100.6 MHz, C_6D_6): δ = 40.7 (C-6), 46.2 (C-4), 51.4 (C-5), 55.2 (C-3), 64.4 (C-9), 73.8 (CH), 77.4 (CH), 104.4 (*C*HPh), 127.8, 127.8, 129.2, 129.2, 130.4, 137.8 (6 C-Ar), 168.7 (C-2).

(5*S*,7*S*,8*R*)-7,8-[(*S*)-Benzylidenedioxy]-3,3,5-trichloro-7,8-dihydroxyoxonan-2-one (37):

According to the general procedure C, trichloroacetate **35** (144 mg, 0.39 mmol) in DCE (3.9 mL) was treated with 0.3 equiv of CuCl (0.12 mmol, 11.6 mg) and 0.3 equiv of 2,2′-bipyridine (0.12 mmol, 18.3 mg) and heated in a sealed tube at 150 °C for 3 h. Concentration in vacuo and purification by fc (1 : 5) afforded **37** (89 mg, 0.24 mmol, 62 %) as white crystals after recrystallization. R_f (1 : 5) 0.60; mp 135 °C (Et_2O); $[\alpha]_D^{20}$ = – 12.32° (*c* = 0.69, $CHCl_3$).

IR: *v* = 3020, 2920, 2860, 2000, 1760, 1450, 1370, 1220, 1090, 1070, 1020, 980, 860, 840, 690 cm^{-1}.

^{1}H NMR (400 MHz, C_6D_6): δ = 1.44 (dd, 1 H, *J* = 12.2, 16.3 Hz, H-6), 2.25 (ddd, 1 H, *J* = 3.3, 7.8, 16.5 Hz, H-6′), 2.39 (dd, 1 H, *J* = 10.8, 14.8 Hz, H-4), 2.83 (d, 1 H, *J* = 14.7 Hz, H-4′), 3.48 (dd, 1 H, *J* = 4.0, 9.6 Hz, H-9), 3.60–3.70 (m, 1 H, H-8), 3.80–4.00 (m, 2 H, H-5 and H-7), 4.40 (t, 1 H, *J* = 10.9 Hz, H-9′), 5.41 (s, 1 H, C*H*Ph), 7.00–7.30 (m, 5 H, Ar).

^{13}C NMR (100.6 MHz, C_6D_6): δ = 39.1 (C-6), 46.4 (C-4), 51.5 (C-5), 53.9 (C-3), 63.5 (C-9), 73.0 (CH), 76.6 (CH), 103.8 (*C*HPh), 126.5, 126.5, 128.5, 129.8, 129.8, 136.1 (6 C-Ar), 168.5 (C-2).

MS (EI, 70 eV): *m*/*z* (%) = 365 (M^+ + 1, 100), 364 (M^+, 36), 363 (64), 312 (12), 262 (35), 212 (15), 182 (14), 162 (50), 107 (55), 105 (100), 79 (37), 78 (31), 77 (33), 59 (11).

Anal. calc. for $C_{15}H_{15}Cl_3O_4$: C, 49.45; H, 4.15; Cl, 28.82. Found C, 49.18; H, 4.29; Cl, 29.18.

Dichloroacetic Acid 3-Methoxy-2,2-dimethylpent-4-enyl Ester (38):

According to the general procedure B, dichloroacetyl chloride (360 mg, 2.45 mmol, 1.4 equiv) and **20** (250 mg, 1.75 mmol) in CH_2Cl_2 (3 mL) was treated with Et_3N (676 mg, 3.5 mmol, 2 equiv) in CH_2Cl_2 (1 mL). The reaction was stirred for 20 min at 0 °C. Workup and fc (1 : 20) afforded **38** (377 mg, 1.48 mmol, 84 %) as a colorless oil. R_f (1 : 10) 0.90; $[\alpha]_D^{20}$ = 0.0° (*c* = 2.35, $CHCl_3$).

IR: *v* = 3080, 2930, 2910, 2830, 2800, 1750, 1460, 1410, 1390, 1360, 1290, 1160, 1110, 1090, 990, 925, 810 cm^{-1}.

^{1}H NMR (250 MHz): δ = 0.91 (s, 3 H, Me), 0.92 (s, 3 H, Me), 3.21 (s, 3 H, OMe), 3.34 (d, 1 H, *J* = 8.1 Hz, H-3), 4.01 (d, 1 H, *J* = 10.5 Hz, H-1), 4.20 (d, 1 H, *J* = 10.5 Hz, H-1′), 5.21 (dd, 1 H, *J* = 1.9, 17.1 Hz, H-5 *trans*), 5.31 (dd, 1 H, *J* = 1.8, 10.2 Hz, H-5 *cis*), 5.67 (ddd, 1 H, *J* = 8.1, 10.2, 17.1 Hz, H-4), 5.95 (s, 1 H, $CHCl_2$).

^{13}C NMR (63 MHz): δ = 19.3 (Me), 21.1 (Me), 38.2 (C-2), 56.6 (OMe), 64.3 ($CHCl_2$), 72.8 (C-1), 86.5 (C-3), 119.5 (C-5), 134.1 (C-4), 164.1 (CO).

Dichloroacetic Acid (3*S*)-3-Methoxymethoxy-2,2-dimethylpent-4-enyl Ester (39):

A solution of pyridine (1.09 g, 13.8 mmol, 1.2 equiv) and **21** (2.0 g, 11.5 mmol) in CH_2Cl_2 (38 mL) was treated with dichloroacetyl chloride (2.71 g, 18.4 mmol, 1.6 equiv) by dropwise addition at 0 °C. The reaction was stirred for 3 h at 0 °C. The mixture was poured into H_2O (10 mL) and the aq phase was extracted with CH_2Cl_2 (3 × 25 mL), the combined organic layers were dried (Na_2SO_4), concentrated in vacuo and the residue was purified by fc (1 : 10) affording **39** (2.83 g, 9.93 mmol, 86 %) as a colorless oil. R_f (1 : 10) 0.90.

IR: *v* = 3080, 2930, 2910, 2830, 2800, 1750, 1460, 1410, 1390, 1360, 1290, 1160, 1090, 990, 925, 810 cm^{-1}.

^{1}H NMR (200 MHz): δ = 0.96 (s, 3 H, Me), 0.99 (s, 3 H, Me), 3.36 (s 3 H, OMe), 3.88 (d, 1 H, *J* = 8.2 Hz, H-3), 4.09 (d, 1 H, *J* = 10.6 Hz, H-1), 4.21 (d, 1 H, *J* = 10.6 Hz, H-1′), 4.49 (d, 1 H, *J* = 6.8 Hz, OC*H*HO), 4.68 (d, 1 H, *J* = 6.8 Hz, OCH*H*O), 5.25 (dd, 1 H, *J* = 1.4, 17.1 Hz, H-5 *trans*), 5.33 (dd, 1 H, *J* = 1.7, 10.3 Hz, H-5 *cis*), 5.70 (ddd, 1 H, *J* = 8.3, 10.4, 17.1 Hz, H-4), 5.98 (s, 1 H, $CHCl_2$).

^{13}C NMR (63 MHz): δ = 19.3 (Me), 20.8 (Me), 37.7 (C-2), 55.1 (OMe), 64.2 ($CHCl_2$), 72.2 (C-1), 80.5 (C-3), 93.4 (OCH_2O), 119.6 (C-5), 133.4 (C-4), 163.7 (CO).

Trichloroacetic Acid 3-Methoxy-2,2-dimethylpent-4-enyl Ester (40):

According to the general procedure B, trichloroacetyl chloride (535 mg, 3.0 mmol, 1.4 equiv) and **20** (300 mg, 2.1 mmol) in CH_2Cl_2 (3 mL) was treated with Et_3N (424 mg, 4.2 mmol, 2 equiv) in CH_2Cl_2 (3 mL). The reaction was stirred for 30 min at 0 °C. Workup and fc (1 : 20) afforded **40** (410 mg, 1.42 mmol, 68 %) as a colorless oil. R_f (1 : 10) 0.75; $[\alpha]_D^{20}$ = 0.0° (*c* = 2.0, $CHCl_3$).

IR: *v* = 2990, 2915, 2810, 2760, 2465, 2365, 1250, 1170, 1120, 1090, 990, 930, 880, 840, 820 cm^{-1}.

^{1}H NMR (400 MHz): δ = 0.95 (s, 3 H, Me), 0.96 (s, 3 H, Me), 3.23 (s, 3 H, OMe), 3.38 (d, 1 H, *J* = 8.1 Hz, H-3), 4.10 (d, 1 H, *J* = 10.4 Hz, H-1), 4.29 (d, 1 H, *J* = 10.4 Hz, H-1′), 5.23 (dd, 1 H, *J* = 1.8, 17.1 Hz, H-5), 5.33 (dd, 1 H, *J* = 1.8, 10.4 Hz, H-5′), 5.69 (ddd, 1 H, *J* = 8.1, 10.3, 17.1 Hz, H-4).

^{13}C NMR (63 MHz): δ = 19.4 (Me), 21.3 (Me), 38.5 (C-2), 56.8 (OMe), 74.9 (C-1), 86.6 (C-3), 91.1 (CCl_3), 119.8 (C-5), 134.2 (C-4), 161.8 (CO).

Trichloroacetic Acid (3*S*)-3-Methoxymethoxy-2,2-dimethylpent-4-enyl Ester (41):

A solution of Et_3N (289 mg, 2.86 mmol, 2.0 equiv) and **21** (250 mg, 1.43 mmol) in CH_2Cl_2 (4.8 mL) was treated with trichloroacetyl chloride (362 mg, 2.0 mmol, 1.4 equiv) by dropwise addition at 0 °C. The reaction was stirred for 3 h at 0 °C. The mixture was poured into H_2O (10 mL) and the aq phase was extracted with CH_2Cl_2 (3 × 25 mL), the combined organic layers were dried (Na_2SO_4), concentrated in vacuo and the residue was purified by fc (1 : 10) to afford **41** (390 mg, 1.20 mmol, 85 %) as a colorless oil. R_f (1 : 6) 0.80; $[\alpha]_D^{20}$ = + 112° (*c* = 1.5, $CHCl_3$).

IR: *v* = 3065, 3020, 2955, 2880, 2810, 1760, 1460, 1420, 1365, 1250, 1145, 1090, 1035, 1015, 990, 930, 910, 875, 835, 670 cm^{-1}.

^{1}H NMR (200 MHz): δ = 0.99 (s, 3 H, Me), 1.02 (s, 3 H, Me), 3.36 (s, 3 H, OMe), 3.90 (d, 1 H, *J* = 8.2 Hz, H-3), 4.17 (d, 1 H, *J* = 10.5 Hz, H-1), 4.30 (d, 1 H, *J* = 10.5 Hz, H-1′), 4.50 (d, 1 H, *J* = 6.8 Hz, OC*H*HO), 4.69 (d, 1 H, *J* = 6.8 Hz, OCH*H*O), 5.26 (dd, 1 H, *J* = 1.8, 17.1 Hz, H-5 *trans*), 5.34 (ddd, 1 H, *J* = 1.9, 10.3 Hz, H-5 *cis*), 5.71 (ddd, 1 H, *J* = 8.3, 10.4, 17.1 Hz, H-4).

(3*R,5*S**,6*R**)- and (3*R**,5*R**,6*S**)-3,5-Dichloro-6-methoxy-7,7-dimethyloxocan-2-one (42a,b):**

According to the general procedure C, dichloroacetate **38** (300 mg, 1.17 mmol) in benzene (11.7 mL) was treated with 0.6 equiv of CuCl (0.70 mmol, 69 mg) and 0.3 equiv of 2,2′-bipyridine (0.70 mmol, 117 mg) and heated in a sealed tube at 150 °C for 4.5 h. Concentration in vacuo and purification by fc (1 : 50) afforded (3*R**,5*S**,6*R**)-**42a** (*cis*-dichloro) (155 mg, 0.61 mmol, 52 %) as a colorless oil [R_f (1 : 20) 0.85] and (3*R**,5*R**,6*S**)-**42b** (*trans*-dichloro) (77 mg, 0.30 mmol, 26 %) as a white solid, which was recrystallized form hexane [R_f (1 : 20) 0.80]. Ratio of diastereomers (*cis* : *trans* = 67 : 33).

42a:

IR: *v* = 2960, 2900, 2830, 1775, 1460, 1435, 1380, 1360, 1340, 1290, 1160, 1100, 1035, 985, 950, 860, 820 cm^{-1}.

^{1}H NMR (400 MHz): δ = 0.93 (s, 3 H, Me), 1.17 (s, 3 H, Me), 2.67 (ddd, 1 H, *J* = 1.5, 6.2, 7.8 Hz, H-4), 2.89 (dt, 1 H, *J* = 2.2, 11.4 Hz, H-4′), 3.42 (d, 1 H, *J* = 9.3 Hz, H-8), 3.44 (s, 1 H, H-6), 3.58 (s, 3 H, OMe), 4.46 (dd, 1 H, *J* = 6.2, 11.8 Hz, CHCl), 4.64 (d, 1 H, *J* = 10.6 Hz, H-8′), 4.66 (dd, 1 H, *J* = 11.7, 15.6 Hz, CHCl).

^{13}C NMR (100.6 MHz): $\delta = 22.5$ (Me), 26.3 (Me), 42.1 (C-4), 42.7 (C-7), 52.1 (CH), 55.0 (CH), 62.2 (C-6), 72.2 (C-8), 93.1 (OMe), 169.6 (C-2).

42b: white crystals; mp 72–74 °C (hexane).

IR: $\nu = 2950$, 1730, 1460, 1430, 1385, 1360, 1280, 1150, 1095, 1030, 980, 940, 860 cm^{-1}.

^{1}H NMR (400 MHz): $\delta = 0.96$ (s, 3 H, Me), 1.20 (s, 3 H, Me), 2.49 (ddd, 1 H, $J = 3.4$, 7.7, 13.7 Hz, H-4), 2.91 (ddd, 1 H, $J = 4.9$, 11.4, 13.7 Hz, H-4′), 3.46 (s, 1 H, H-6), 3.58 (d, 1 H, $J = 11.9$ Hz, H-8), 3.65 (s, 3 H, OMe), 4.50 (d, 1 H, $J = 11.9$ Hz, H-8′), 4.63 (dd, 1 H, $J = 3.4$, 11.3 Hz, CHCl), 4.78 (dd, 1 H, $J = 4.9$, 7.7 Hz, CHCl).

^{13}C NMR (100.6 MHz): $\delta = 22.2$ (Me), 23.1 (Me), 42.7 (C-7), 43.0 (C-4), 55.2 (C), 57.5 (CH), 61.7 (C-6), 71.9 (C-8), 93.7 (OMe), 169.8 (C-2).

MS (EI, 70 eV): m/z (%) = 213 ($M^+ - C_3H_4$, 100), 210 (30), 198 (41), 192 (42), 181 (43), 153 (14), 142 (16), 131 (32), 117 (99), 105 (22), 99 (50), 69 (60), 58 (53), 54 (52), 53 (43), 34 (29).

HRMS calcd for $C_7H_{11}O_3Cl_2$ ($M^+ - C_3H_4$) 213.0085, found 213.0075.

Anal. Calc. for $C_{10}H_{15}O_3Cl_2$: C, 47.26; H, 5.95; Cl, 27.90. Found C, 46.26; H, 6.13; Cl, 27.26.

(3*R*,5*S*,6*R*)- and (3*S*,5*S*,6*R*)-3,5-Dichloro-6-methoxymethoxy-7,7-dimethyloxocan-2-one (43a, b):

According to the general procedure C, dichloroacetate **39** (500 mg, 1.75 mmol) in benzene (17.5 mL) was treated with 0.6 equiv of CuCl (1.05 mmol, 104 mg) and 0.3 equiv of 2,2′-bipyridine (1.05 mmol, 164 mg) and heated in a sealed tube at 155 °C for 4 h. Concentration in vacuo and purification by fc (1:10) afforded (3*R*,5*S*,6*R*)-**43a** (302 mg, 1.06 mmol, 60%) and (3*S*,5*S*,6*R*)-**43b** (151 mg, 0.53 mmol, 31%) as colorless oils. Ratio of diastereomers (*cis*: *trans* = 67:33).

43a (*cis*-dichloro): R_f (1:10) 0.40; $[\alpha]_{365}^{20} = +106.84°$ ($c = 0.76$, CHCl$_3$).

IR: $\nu = 2960$, 2900, 2830, 1775, 1460, 1435, 1380, 1360, 1340, 1290, 1160, 1100, 1035, 985, 950, 860, 820 cm^{-1}.

^{1}H NMR (400 MHz): $\delta = 0.94$ (s, 3 H, Me), 1.21 (s, 3 H, Me), 2.67 (ddd, 1 H, $J = 1.7$, 8.1, 13.7 Hz, H-4), 2.88 (ddd, 1 H, $J = 2.2$, 11.5, 13.7 Hz, H-4′), 3.44 (s, 3 H, OMe), 3.47 (d 1 H, $J = 10.8$ Hz, H-8), 3.84 (s, 1 H, H-6), 4.47 (dd, 1 H, $J = 6.4$, 11.7 Hz, H-3), 4.66 (d, 1 H, $J = 10.8$ Hz, H-8′), 4.69 (m, 1 H, H-5), 4.71 (d, 1 H, $J = 6.5$ Hz, OC*H*HO), 4.90 (d, 1 H, $J = 6.5$ Hz, OCH*H*O).

^{13}C NMR (100.6 MHz): $\delta = 23.0$ (Me), 23.6 (Me), 42.7 (C-7), 43.9 (C-4), 55.2 (CH), 56.9 (CH), 57.6 (C-3), 72.2 (C-8), 90.2 (OMe), 98.3 (OCH$_2$O), 170.0 (C-2).

43b (*trans*-dichloro): R_f (1:10) 0.35; $[\alpha]_{365}^{20} = -148.43°$ ($c = 0.76$, CHCl$_3$).

IR: $\nu = 2960$, 1750, 1480, 1470, 1440, 1370, 1340, 1290, 1260, 1150, 1100, 1020, 990 cm^{-1}.

^{1}H NMR (400 MHz): $\delta = 0.98$ (s, 3 H, Me), 1.23 (s, 3 H, Me), 2.49 (ddd, 1 H, $J = 3.5$, 8.0, 11.5 Hz, H-4), 2.89 (ddd, 1 H, $J = 5.0$, 11.4, 13.8 Hz, H-4′), 3.46 (s, 3 H, OMe), 3.63 (d, 1 H, $J = 12.1$ Hz, H-8), 3.87 (s, 1 H, H-6), 4.53 (dd, 1 H, $J = 12.1$ Hz, H-8′), 4.64 (dd, 1 H, $J = 3.5$, 11.4 Hz, CH), 4.74 (d, 1 H, $J = 6.4$ Hz, OC*H*HO), 4.81 (dd, 1 H, $J = 5.0$, 7.9 Hz, CH), 4.98 (d, 1 H, $J = 6.4$ Hz, OCH*H*O).

^{13}C NMR (100.6 MHz): $\delta = 22.6$ (Me), 24.7 (Me), 42.0 (C-7), 42.9 (C-4), 52.1 (CH), 55.1 (CH), 57.0 (C-3), 72.6 (C-8), 89.4 (OMe), 98.4 (OCH$_2$O), 169.9 (C-2).

(5*R**,6*S**)-3,3,5-Trichloro-6-methoxy-7,7-dimethyloxocan-2-one (44):

According to the general procedure C, trichloroacetate **40** (200 mg, 0.69 mmol) in DCE (6.9 mL) was treated with 0.3 equiv of CuCl (0.21 mmol, 20 mg) and 0.3 equiv of 2,2′-bipyridine (0.21 mmol, 32.3 mg) and heated in a sealed tube at 170 °C for 2.5 h. Concentration in vacuo and purification by fc (1:100) afforded **44** (93 mg, 0.32 mmol, 34%) as a white solid, which was recrystallized from Et$_2$O to give white crystals; mp 79–81 °C; one crystal (approx. 0.05 × 0.40 × 0.50 mm) was subjected to an X-ray analysis;[20] R_f (1:100) 0.35.

IR: $\nu = 2950$, 2930, 2820, 1770, 1460, 1410, 1390, 1360, 1315, 1280, 1255, 1190, 1175, 1100, 1050, 1030, 1010, 990, 975, 945, 885, 860, 835 cm^{-1}.

^{1}H NMR (400 MHz): $\delta = 0.93$ (s, 3 H, Me), 1.20 (s, 3 H, Me), 2.99 (dd, 1 H, $J = 1.2$, 15.0 Hz, H-4), 3.33 (dd, 1 H, $J = 10.6$, 15.0 Hz, H-4′), 3.41 (s, 1 H, H-6), 3.56 (s, 3 H, OMe), 3.58 (d, 1 H, $J = 10.5$ Hz, H-8), 4.59 (d, 1 H, $J = 10.5$ Hz, H-8′), 4.82 (d, 1 H, $J = 10.6$ Hz, H-5).

^{13}C NMR (100.6 MHz): $\delta = 22.7$ (Me), 23.2 (Me), 43.3 (C-7), 53.2 (C-4), 56.4 (C-5), 62.0 (C-6), 73.8 (C-8), 81.9 (C-3), 93.6 (OMe), 166.0 (C-2).

Crystallographic data for **44**: triclinic, $P\bar{1}$, $a = 6.334(3)$ Å, $b = 8.876(1)$ Å, $c = 12.538(2)$ Å, $\alpha = 92.84(1)°$; $\beta = 92.626(9)°$; $\gamma = 106.93°$; $V = 661.6(4)$ Å^3; z = 2; $D_x = 1.45$ gcm^{-3}, λ (CuKα) = 1.5418 Å, μ (CuKα) = 63.53 cm^{-1}, T = −25 °C, $(\sin\Theta)/\lambda = 0.63$ Å^{-1}, t = 33 h, $R_w = 0.066$, $(\Delta/\sigma)_{max} = 0.30$, F(000) = 300. Final R = 0.053 for 2427 reflections.

Table 4: Bond distances (standard deviations) of the non-hydrogen atoms (Å) of **44**

Cl(3)-C(3)	1.785 (3)	*C(3)-C(4)*	1.537 (5)	*C(7)-C(10)*	1.533 (4)
Cl(3)′-C(3)	1.776 (4)	*C(4)-C(5)*	1.532 (5)	*C(7)-C(11)*	1.541 (5)
Cl(5)-C(5)	1.825 (3)	*C(5)-C(6)*	1.562 (4)	*C(8)-O(1)*	1.457 (4)
C(2)-C(3)	1.521 (4)	*C(6)-C(7)*	1.552 (4)	*C(9)-O(3)*	1.432 (4)
C(2)-O(1)	1.335 (4)	*C(6)-O(3)*	1.420 (3)		
C(2)-O(2)	1.193 (4)	*C(7)-C(8)*	1.519 (5)		

Table 5: Bond angles (standard deviations) of the non-hydrogen atoms (°) of **44**

C(3)-C(2)-O(1)	107.8 (3)	*C(3)-C(4)-C(5)*	116.6 (2)	*C(6)-C(7)-C(11)*	108.1 (2)
C(3)-C(2)-O(2)	125.5 (3)	*Cl(5)-C(5)-C(4)*	104.5 (2)	*C(8)-C(7)-C(10)*	110.8 (2)
O(1)-C(2)-O(2)	126.6 (3)	*Cl(5)-C(5)-C(6)*	107.4 (2)	*C(8)-C(7)-C(11)*	107.5 (3)
Cl(3)-C(3)-Cl(3)′	108.8 (2)	*C(4)-C(5)-C(6)*	117.4 (3)	*C(10)-C(7)-C(11)*	108.6 (3)
Cl(3)-C(3)-C(2)	109.4 (2)	*C(5)-C(6)-C(7)*	117.2 (2)	*C(7)-C(8)-O(1)*	106.2 (2)
Cl(3)-C(3)-C(4)	111.2 (2)	*C(5)-C(6)-O(3)*	110.9 (2)	*C(2)-O(1)-C(8)*	117.7 (2)
Cl(3)′-C(3)-C(2)	109.7 (2)	*C(7)-C(6)-O(3)*	107.2 (2)	*C(6)-O(3)-C(9)*	114.4 (3)
Cl(3)′-C(3)-C(4)	107.4 (2)	*C(6)-C(7)-C(8)*	111.3 (3)		
C(2)-C(3)-C(4)	100.3 (2)	*C(6)-C(7)-C(10)*	110.4 (3)		

(5*S*,6*R*)-3,3,5-Trichloro-6-methoxymethoxy-7,7-dimethyloxocan-2-one (45):

According to the general procedure C, trichloroacetate **41** (500 mg, 1.56 mmol) in DCE (16 mL) was treated with 0.3 equiv of CuCl (0.47 mmol, 46 mg) and 0.3 equiv of 2,2′-bipyridine (0.47 mmol, 73 mg) and heated in a sealed tube at 115 °C for 3 h. Concentration in vacuo and purification by fc (1:20) afforded **45** (200 mg, 0.63 mmol, 40%) as a colorless oil. R_f (1:6) 0.30; $[\alpha]_{365}^{20} = +203.64°$ ($c = 0.68$, CHCl$_3$).

IR: $\nu = 2960$, 2890, 2820, 1770, 1735, 1590, 1460, 1415, 1390, 1365, 1255, 1185, 1145, 1100, 1060, 1030, 1020, 1005, 980, 930, 890, 860, 835 cm^{-1}.

^{1}H NMR (400 MHz): $\delta = 0.94$ (s, 3 H, Me), 1.24 (s, 3 H, Me), 2.98 (dd, 1 H, $J = 1.5$, 15.0 Hz, H-4), 3.38 (dd, 1 H, $J = 10.6$, 15.0 Hz, H-4′), 3.43 (s, 3 H, OMe), 3.62 (d, 1 H, $J = 10.5$ Hz, H-8), 3.81 (s, 1 H, H-6), 4.63 (d, 1 H, $J = 10.5$ Hz, H-8′), 4.68 (d, 1 H, $J = 6.4$ Hz, OCHHO), 4.85 (dt, 1 H, $J = 1.3$, 10.5 Hz, H-5), 4.89 (d, 1 H, $J = 6.4$ Hz, OCHHO).

^{13}C NMR (100.6 MHz): $\delta = 22.8$ (Me), 23.4 (ME), 43.0 (C-7), 54.0 (C-4), 56.4 (CH), 56.9 (CH), 73.8 (C-8), 81.8 (C-3), 90.3 (OMe), 98.5 (OCH$_2$O), 166.0 (C-2).

(6*S*)-6-Methoxymethoxy-7,7-dimethyloxocan-2-one (46):

To a refluxing solution of lactone **43** (265 mg, 0.93 mmol) in 9 mL of benzene was added via syringe pump a solution of $HSnBu_3$ (0.62 mL, 2.33 mmol, 2.5 equiv) and AIBN (7.7 mg, 0.05 mmol, 0.05 equiv) in benzene (3 mL) over a period of 1 h. After 1 h of reflux, the solvent was evaporated and the residue taken up in CH_2Cl_2 (20 mL). This solution was washed with aq KF (8 mL). The organic phase was separated and the aq phase was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, dried (Na_2SO_4), concentrated in vacuo and the residue was purified by fc (1 : 3) affording **46** (157 mg, 0.55 mmol, 78 %) as a colorless oil. R_f (1 : 3) 0.35; $[\alpha]_D^{20} = +54.72°$ ($c = 0.88$, $CHCl_3$).

IR: ν = 2950, 2920, 1720, 1475, 1450, 1370, 1330, 1315, 1300, 1240, 1260, 1245, 1220, 1190, 1110 cm^{-1}.

^1H NMR (400 MHz): δ = 0.93 (s, 3 H, Me), 1.09 (s, 3 H, Me), 1.72–1.78 (m, 1 H, H-5), 1.75–1.82 (m, 1 H, H-4), 1.82–1.92 (m, 1 H, H-5′), 1.95–2.05 (m, 1 H, H-4′), 2.49 (ddd, 1 H, J = 4.0, 6.4, 10.3 Hz, H-3), 2.60 (dt, 1 H, J = 6.5, 10.6 Hz, H-3′), 3.32 (d, 1 H, J = 8.3 Hz, H-6), 3.37 (s, 3 H, OMe), 3.81 (d, 1 H, J = 12.5 Hz, H-8), 4.18 (d, 1 H, J = 8.5 Hz, H-8′), 4.54 (d, 1 H, J = 6.8 Hz, OCHH), 4.65 (d, 1 H, J = 6.8 Hz, OCHHO).

^{13}C NMR (100.6 MHz): δ = 13.8 (Me), 17.5 (C-4), 24.4 (Me), 27.8 (C-5), 31.2 (C-3), 40.5 (C-7), 56.1 (C-6), 74.8 (C-8), 81.1 (OMe), 96.0 (OCH_2O), 175.1 (C-2).

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