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π-Cyclizations of α-Methoxycarbonyl Oxycarbenium Ions; Synthesis of Oxacyclic Carboxylic Esters[1]

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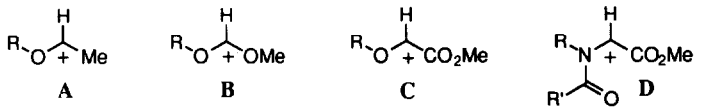
Dedicated with best personal congratulations to Professor L. Ghosez, a good collegue and friend

Abstract: Acid-mediated cyclization reactions are described of seven methyl 2-acetoxy-2-(3-alken-1-oxy)acetates with different chain substitution. The major product of the tin tetrachloride-induced cyclization reaction is in most cases a tetrahydropyran containing an equatorial carbomethoxy function at C2 and an axial chlorine atom at C4. The mechanism of its formation involves a net *cis*-addition of the intermediate α-ester oxycarbenium ion to the carbon-carbon double bond, most likely caused by a quasi axial orientation of the ester function in a chair-like transition state. The results are interpreted by invoking (1) the occurrence of a 2-oxonia-Cope rearrangement and (2) the participation of the ester function in the mechanism of cyclization by trapping the cyclic cationic intermediate. The cyclizations of two methyl 2-acetoxy-2-(4-alken-1-oxy)acetates and two methyl 2-acetoxy-2-(alkynoxy)acetates are also described.

INTRODUCTION

The intramolecular carbon-carbon bond formation between oxycarbenium[2] ions **A** and π-nucleophiles has been shown to be a powerful method in organic synthesis. This method has been applied to the preparation of (medium-sized) carbocyclic rings,[3] tetrahydropyrans[4] and medium-sized cyclic ethers.[5] In these cyclizations, the electronic and steric nature of the π-nucleophiles has been extensively varied. Besides alkenes, alkynes, aromatic rings, enols and enol ethers silicon-activated π-nucleophiles have also been used such as allylsilanes, vinylsilanes and silyl enol ethers. The essential characteristics of the oxycarbenium ion have, however, not been varied, except for the dioxycarbenium ions **B**[6] which are less reactive.



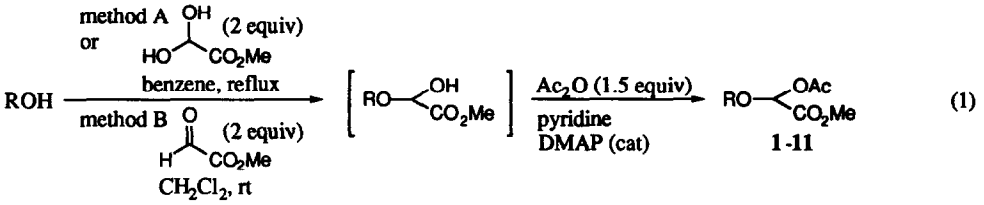
We now wish to report the results[7] of our study on the use of α-methoxycarbonyl oxycarbenium ions **C**, containing an electron-withdrawing ester function at the electrophilic carbon center. These α-ester oxycarbenium ions, which are more electrophilic than oxycarbenium ions of type **A**, provide cyclic ethers with an ester function at the 2-position. Our present results parallel earlier findings on the use of *N*-acyliminium ions **D**, bearing a carboxyl group at the cationic centre.[8] The utility of species **D** for the synthesis of α-amino acid derivatives has already been shown.[9]

RESULTS AND DISCUSSION

Preparation of precursors

Methyl 2-acetoxy-2-(alkenoxy)acetates **1-11** served as precursors for the α-ester oxycarbenium ions. The acetate function appeared to be a suitable leaving group. The precursors were prepared from the appropriate

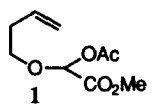
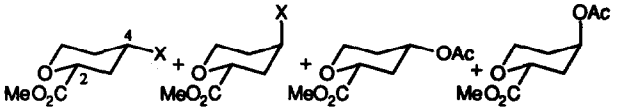
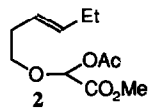
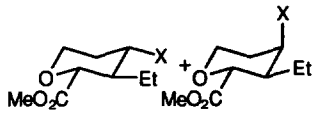
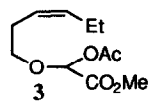
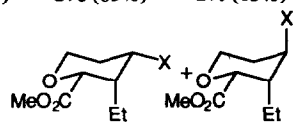
alcohol by treatment with either freshly distilled methyl glyoxylate hydrate[10] (2 equiv) in refluxing benzene using a Dean-Stark trap (method A) or with freshly distilled anhydrous methyl glyoxylate[11] (2 equiv) in dichloromethane at room temperature (method B, eq 1). The crude hemiacetal was immediately acylated with acetic anhydride in both methods giving the methyl 2-acetoxy-2-alkenoxyacetates **1-11** in moderate overall yields of 60-70% (Table I and III). The unreacted alcohol, which was also acylated with acetic anhydride in the second step (30-40%), could be regenerated by hydrolysis (K_2CO_3, MeOH). The low overall yield of the methyl 2-acetoxy-2-alkynoxyacetates (Table III) was probably caused by loss of the volatile alcohol in the first step (method A).



(1)

The starting alcohols were commercially available except for 1-*tert*-butyldiphenylsilyloxy-4-penten-2-ol[12] (**7**), 2-cyclohexene-1-methanol[13] (**10**) and 2-(1-cyclohexen-1-yl)ethanol[14] (**11**). All cyclization precursors were purified by using flash chromatography. Precursors **7-10** were isolated as mixtures of diastereoisomers. The ^1H NMR chemical shift of the proton adjacent to the acetoxy group in **1-11** was quite characteristic at 5.9-6.0 ppm. The ^{13}C NMR chemical shift of the acetal carbon atom was between 91.3 and 92.8 ppm.

Table I. Results of the Cyclizations of **1-3** with Several Acids

precursor (yield,[a,b] method[c])	acid	products (yield[a])			
 **1** (60%, A) (77%, B)					
	$BF_3{\cdot}OEt_2$ (X=F)	**12c** (18%)	**12t** (18%)	**13c** (9%)	**13t** (20%)
	$SnCl_4$ (X=Cl)	**14c** (30%)	**14t** (48%)	**13c** (2%)	**13t** (3%)
	$TiCl_4$ (X=Cl)	**14c** (34%)	**14t** (19%)	**13c** (5%)	**13t** (20%)
	HCOOH (X=OCHO)	**15c** (39%)	**15t** (8%)	-	-
 **2** (67%, A)					
	$SnCl_4$ (X=Cl)	**16c** (14%)	**16t** (68%)		
	HCOOH (X=OCHO)	**17c** (65%)	**17t** (13%)		
 **3** (64%, A)					
	$SnCl_4$ (X=Cl)	-	**18** (62%)		
	HCOOH (X=OCHO)	**19c** (60%)	**19t** (8%)		

a) Isolated yield of purified product. b) Overall yield from the corresponding alcohol. c) See equation 1.

Cyclizations and structural proof of the products

The generation of the α-ester oxycarbenium ion **C** from precursors **1-3** was investigated by using different acidic conditions as is shown in Table I. The addition of 'c' and 't' to the product numbers in Table I refers to the *cis*- or *trans*-relationship between the substituents at C2 and C4.

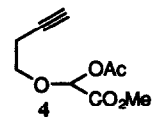
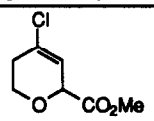
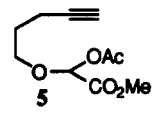
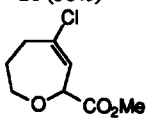
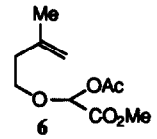
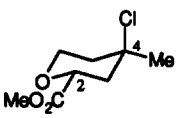
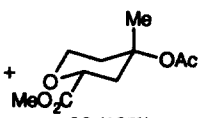
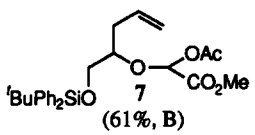
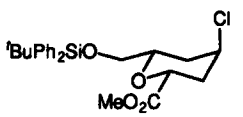
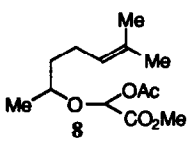
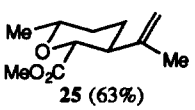
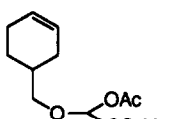
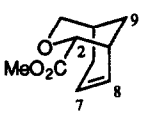
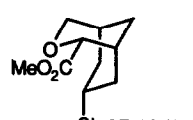
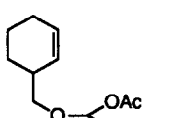
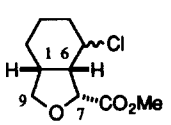
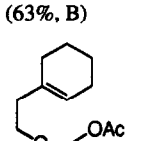
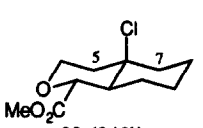
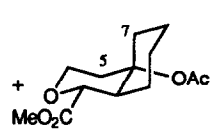
The Lewis acid-induced cyclizations were initiated at -78 °C with 2 equiv of the Lewis acid, allowed to slowly warm up to room temperature and stirred for 3 h. The products were purified by using flash chromatography. Although products **14t** and **14c** and products **16t** and **16c** could not be separated by this method, the mixture of **14t** and **14c** could be separated on a GC column. From precursor **1** 4-substituted 2-carbomethoxy-tetrahydropyrans were obtained as the sole products. Dihydropyrans, as a result of proton loss from a cyclic carbenium ion were not found. Termination of the reaction by incorporation of a nucleophile gave not only 4-halo-tetrahydropyrans (**12**, **14**), but also 4-acetoxytetrahydropyrans (**13**), in which case the leaving group of the precursor served as the nucleophile. Cyclization with boron trifluoride etherate gave, besides cyclization products, 13% of recovered starting material. The ratio 4-halo/4-acetoxytetrahydropyran depended on the Lewis acid used. With boron trifluoride etherate this ratio was about 1:1.[15] With tin tetrachloride much more incorporation of chloride was observed (16:1) than with titanium tetrachloride (2:1). For precursor **1** the stereoselectivity of the Lewis acid-induced cyclizations was rather low, but the tin tetrachloride-induced cyclization of **2** and **3** showed a preference for the formation of the 2,4-*trans*-compounds.

The formic acid-induced cyclizations of **1-3** gave after 2 days at room temperature the 4-formyl-tetrahydropyrans **15**, **17** and **19**. Remarkably, these reactions proceeded with high stereoselectivity to give the 2,4-*cis*-compounds as the major products.

Table II. Selected ^{1}H NMR Data (ppm, *J* in Hz).

compound	O-C*H*-CO_2Me		*H*C-F/*H*C-Cl/*H*C-O	
	($CDCl_3$)	(C_6D_6)	($CDCl_3$)	(C_6D_6)
12c	3.81-4.27 (m)	3.79 (dd, 11.9, 4.4)	4.74 (dtt, 48.6, 10.0, 4.6)	3.89 (dseptet, 38.4, 4.46)
12t	4.37 (dd, 11.6, 2.7)	4.27 (dd, 10.4, 3.2)	5.03 (bd, 47.5)	4.39 (dm, 50.7)
13c	obscured	obscured	4.92 (tt, 10.6, 4.5)	4.72 (septet, 4.9)
13t	4.33 (dd, 10.9, 3.0)	4.24 (dd, 8.7, 4.3)	5.16 (m)	4.95 (quintet, 4.2)
14c	3.97 (dd, 11.5, 2.5)	3.43 (dd, 11.1, 2.6)	4.02 (m)	3.29 (tt, 11.1, 4.6)
14t	4.43-4.54 (m)	4.31 (dd, 7.3, 5.1)	4.43-4.54 (m)	3.88 (quintet, 4.3)
15c	4.00 (dd, 11.2, 2.6)	-	5.01 (tdd, 10.6, 5.0, 4.5)	-
15t	4.29 (dd, 10.8, 3.1)	-	5.27 (quintet, 3.4)	-
16c	obscured	-	obscured	-
16t	4.09 (d, 9.8)	-	4.53 (q, 3.0)	-
17c	3.95 (d, 7.8)	-	5.03 (td, 8.5, 4.2)	-
17t	obscured	-	5.41 (q, 2.8)	-
18	4.59 (d, 2.7)	4.56 (d, 3.1)	4.45 (q, 3.2)	4.12 (q, 4.0)
19c	4.03 (d, 2.4)	-	5.14 (dt, 11.1, 4.6)	-
19t	4.41 (d, 2.7)	-	obscured	-
20	4.75 (q, 2.7)	-	-	-
21	4.68 (m)	-	-	-
22	4.42 (dd, 11.5, 2.3)	-	-	-
23	4.21 (dd, 12.0, 2.3)	-	-	-
24	4.56 (dd, 11.5, 2.4)	-	4.68 (quintet, 3.0)	-
25	3.97 (d, 10.5)	-	-	-
26	4.06 (d, 1.9)	3.88 (d, 1.9)	-	-
27	4.32 (d, 2.3)	-	4.95 (septet, 5.8)	-
28	4.50 (d, 5.2)	-	-	-
29	4.09 (d, 9.9)	4.24 (d, 9.8)	-	-
30	4.05 (d, 10.1)	-	-	-

Table III. Results of the Tin Tetrachloride-induced Cyclizations of **4-11**.

precursor (yield,[a,b] method[c])	products (yield[a])
 **4** (23%, A)	 **20** (58%)
 **5** (26%, A)	 **21** (43%)
 **6** (60%, B)	 **22** (77%) +  **23** (13%)
 **7** (61%, B)	 **24** (56%)
 **8** (59%, A)	 **25** (63%)
 **9** (79%, A)	 **26** (67%) +  **27** (6%)
 **10** (63%, B)	 **28** (69%, 1:1)
 **11** (60%, B)	 **29** (34%) +  **30** (12%)

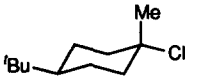
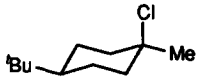
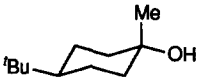
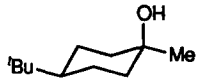
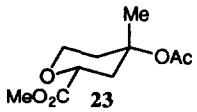
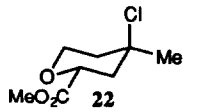
a) Isolated yield of purified product. b) Overall yield from the corresponding alcohol. c) See equation 1.

The stereochemical assignments of products **12-19** followed from the analyses of the ^{1}H NMR spectra with the aid of the nOe-difference technique. The coupling patterns of the hydrogens adjacent to the halide (or acetoxy) and ester substituent were particularly diagnostic and are shown in Table II. The ^{1}H NMR spectra were taken in both deuterated chloroform and deuterated benzene to solve the problem of overlapping signals. The benzene spectra showed more isolated signals in the area of 3-5 ppm, where the most characteristic signals are found. The stereochemical assignment of **14c**, **14t** and **18** was further established with the aid of the nOe-difference technique. Irradiation of H2 of **14c** gave an nOe on H3eq, H4 and H6ax and irradiation of H6ax gave an nOe on H2, H4, H5eq and H6eq. For **14t** an nOe was found for H3eq and H6ax upon irradiation of H2 and an nOe on H3 and H5 upon irradiation of H4. Irradiation of H2 of **18** gave an nOe on H3 and H6ax and irradiation of H4 gave an nOe on H3, H5 and the methylene protons of the ethyl substituent.

After examination of the several different reaction conditions, tin tetrachloride was selected for the cyclization of precursors **4-11**. This Lewis acid gave good yields and high chemoselectivity. The cyclization products obtained from precursors **4-11** are shown in Table III.

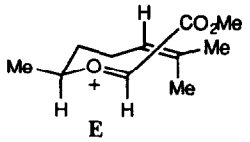
Cyclization of **4** and **5** with an alkyne function as π-nucleophile gave the unsaturated cyclic ethers **20** and **21**. The yields of pure **20** and **21** were moderate, because purification of these unsaturated cyclic ethers was accompanied by loss of material due to their sensitivity to air oxidation and/or their tendency to isomerize to the conjugated system. Cyclization of precursor **6**, proceeding via a tertiary carbenium ion, led to more of the 4-acetoxytetrahydropyran (**23**) compared to cyclization of **1**. The stereochemistry of the quaternary centres in chloride **22** and in acetate **23** is partly based on the ^{13}C NMR chemical shift of the methyl carbon atoms. Literature data[16] indicate that this chemical shift value is diagnostic for either an axial or equatorial orientation of the methyl group (Table IV). Product **22** (33.61 ppm) will have an equatorial methyl group, whereas product **23** (25.74 ppm) must have an axial methyl group. Cyclization of precursor **7** gave product **24** as a single isomer in a moderate yield. The *tert*-butyldiphenylsilyl function survived the acidic reaction conditions.

Table IV ^{13}C NMR Chemical Shifts of Ring Methyl Carbons.

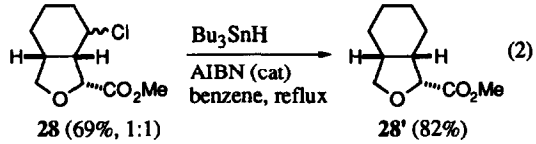
compound (axial Me-group)	δ(CH_3), ppm	compound (equatorial Me-group)	δ(CH_3), ppm
	28.1[a]		34.2[a]
	25.3[a]		31.5[a]
 **23**	25.7	 **22**	33.6

a) See reference 16.

In contrast to the cyclization products discussed so far, product **25** was a result of proton loss after formation of the tertiary (non-cyclic) carbenium ion. All substituents are in an equatorial position (nOe on H6 upon irradiation of H2) which can be explained by assuming a preference for a chair-like transition state and an *E*-oxycarbenium ion geometry (structure **E**).



E



28 (69%, 1:1) **28'** (82%) (2)

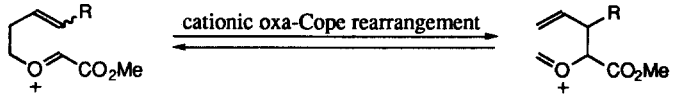
The cyclization of **9-11** resulted in the formation of bicyclic products. The remarkable reaction behaviour of precursor **9** has literature precedent.[17] The initially formed secondary carbenium ion at C8 readily underwent loss of a proton to give **26**, or a 1,2-hydride shift to form the secondary carbenium ion at C7 in order to relieve non-bonded interactions between the axial hydrogen at C7 and the ring oxygen atom. Termination by attack of chloride gave **27**. The position of the ester function in **26** was confirmed by a clear nOe on H4ax, H1 and H9ax upon irradiation of H2. Treatment of precursor **10** with tin tetrachloride gave a product mixture containing two chloride isomers in a 1:1 ratio in a yield of 69%. Because the two isomers could not be separated, it was difficult to elucidate their structures. Reduction of the product mixture with tributyltin hydride gave one product (eq 2) which was determined to be **28'** (nOe on H1 and H6 upon irradiation of H7).[18] A 5-*exo* cyclization had occurred instead of a 6-*endo* cyclization. The cyclization of **11** proceeded in a moderate yield. The tertiary carbenium ion formed after cyclization was trapped by both chloride and acetate (comparable to cyclization of **6**). The stereochemistry at the quarternary centres in products **29** and **30** is based on the ^{13}C NMR chemical shift of carbon atoms C5 and C7 in the same way as described for products **22** and **23**, according to the trend shown in Table IV. The chemical shifts of C5 and C7 of **29** (41.09 and 47.73 ppm) are shifted downfield in comparison with the chemical shifts for C5 and C7 of **30** (33.21 and 33.33). This suggests a *trans*-fused ring system with an axial chloride for compoud **29** and a *cis*-fused ring system with an equatorial acetoxy substituent for product **30**.

Discussion of the mechanism of cyclization

The cyclizations of precursors **1-3** in the presence of tin tetrachloride showed an unusual feature, which needs further explanation. There appears to be a preference for the formation of *trans*-2-carbomethoxy-4-chloro-tetrahydropyrans with an equatorial ester function and an axial chlorine atom. Cationic π-cyclizations to six-membered rings are usually assumed to proceed *via* π-complexes[19] as intermediates and to be terminated by equatorial attack of the nucleophile (chloride). The formation of the minor isomer **14c** from precursor **1** is in agreement with this theory. Thus, in the transition state the ester function adopts a quasi equatorial position and equatorial attack of chloride gives the *cis*-isomer. The transition state for the formation of the major *trans*-isomer **14t**, however, requires a quasi *axial* ester function. Equatorial attack of chloride then gives the *trans*-isomer. As the formation of the *trans*-2,4-disubstituted tetrahydropyrans appears to be favoured, the cyclizations must thus predominantly proceed *via* a transition state with a quasi axial ester function.

From the results of the cyclization of precursors **2** and **3** it is clear that the preferred reaction is a net *cis*-addition of the carbocation and the nucleophile to the carbon-carbon double bond. Starting with an *E*-alkene (**2**), a *cis*-relationship is obtained between H3 and H4 (**16t**). The same pathway is found for *Z*-alkene **3** leading to a *trans*-relationship in the cyclized product (**18**). The conformation of **18** (based on ^1H NMR) shows that the ester function has a strong preference for the equatorial position[20] thereby forcing the two other substituents to adopt an axial orientation. To be certain that the cyclization products are kinetic products, pure **14t** and pure **14c** were independently subjected to the reaction conditions and proved indeed to be stable. It is reasonable to assume that **16** and **18** are also kinetic products. Compounds **22**, **23**, **29** and **30** are formed from a tertiary carbenium ion and may be thermodynamic products. This may also explain why in these cases small amounts of the acetoxy compounds (**23**, **30**) were formed.

The preferred axial position of the ester function in the transition state may be due to the fact that an axial carbomethoxy function can trap the carbenium ion at C4 to form a more stable dioxycarbenium ion **L** (Scheme I). This type of ester participation is well-known in carbohydrate chemistry where the formation of β-(acetoxy)-oxycarbenium ions is a strategic tool to control the stereochemistry at the anomeric centre.[21] For the corresponding *N*-acyliminium ion **D** in which case the 2-carbomethoxy function always adopts an axial position as a result of pseudoallylic 1,3-strain, this type of ester participation was also suggested.[9b]

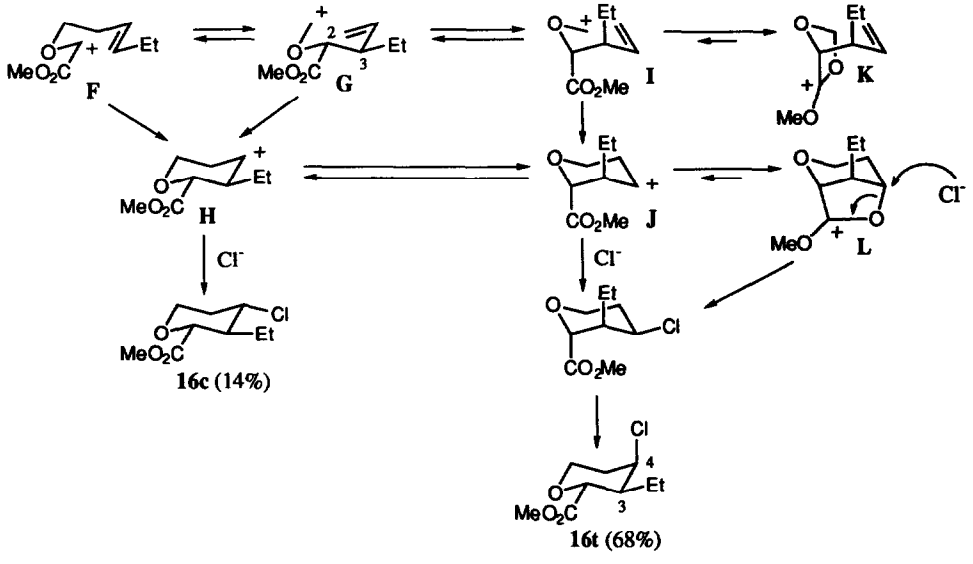


(3)

An important process which may affect the stereochemical outcome of oxycarbenium cyclizations of the 1,5-diene type is the cationic oxa-Cope rearrangement (eq 3).[22] Most probably, the equilibration of the incipient oxycarbenium ion to a mixture of oxa-Cope sigmatropisomers is relatively fast in comparison with cationic cyclization.[7]

A mechanistic proposal for the π-cyclizations of α-ester oxycarbenium ions is given in Scheme I, using the cyclization of **2** as an example. This proposal accounts for most of the experimental facts and assumes the occurrence of both the ester participation and the oxa-Cope rearrangement, where appropriate. The incipient α-methoxycarbonyl oxycarbenium ion **F** derived from **2**, with an *E*-alkene as π-nucleophile, can undergo a reversible cationic oxa-Cope rearrangement to form the oxycarbenium ion **G**. This rearrangement determines the relative stereochemistry at C2 and C3 before cyclization. Intermediates **F** and **G** can both cyclize to the cyclic carbenium ion **H** leading to the formation of **16c**. The uncyclized intermediate **G** can undergo a chair-chair interconversion to conformational isomer **I** with an axial ester function. This interconversion is probably followed by the (irrelevant) reversible formation of dioxycarbenium ion **K**. Cyclization of **I** should eventually lead to the major product **16t**. The intermediacy of the relatively stable dioxycarbenium ion **L** might be a reason for the predominant formation of **16t** from **F**. The formation of **16t** can also be accounted for without invoking the oxa-Cope rearrangement (**F** → **G**). A chair-chair interconversion of intermediate **H** to **J** would also lead to **16t** although this explanation seems less likely.

Scheme I



In conclusion, we have shown that 2-acetoxy-2-alkenoxyacetates (**1**-**11**) can be successfully cyclized upon treatment with tin tetrachloride and other acids to give cyclic ethers with an ester function at the 2-position. The mechanism proposed (Scheme I) provides an explanation for the predominant formation of the 2,4-*trans*-disubstituted tetrahydropyrans. The relevance of the cationic oxa-Cope rearrangement and the participation of the ester function in the mechanism of cyclization needs further study and is the subject of the following paper in this issue.[7]

ACKNOWLEDGEMENTS

We thank C. Kruk and his staff for their generous help in interpreting the NMR spectra. H.-J. Udding is kindly acknowledged for the conversion of 2-(1-cyclohexen-1-yl)ethanol into precursor **11**.

EXPERIMENTAL

General information. Infrared (IR) spectra were obtained from $CHCl_3$ solutions using a Perkin Elmer 1310 spectrophotometer and are reported in cm^{-1}. Proton nuclear magnetic resonance (^1H NMR) spectra were determined in $CDCl_3$ (unless indicated otherwise) as solvent using a Bruker AC 200 (200 MHz), a Bruker WM 250 (250 MHz) or a Bruker AMX 300 (300 MHz) instrument. The first two instruments were also used for the ^{13}C NMR (APT) spectra (50.3 MHz and 62.9 MHz) in $CDCl_3$ solution (unless indicated otherwise). Chemical shifts are given in ppm downfield from tetramethylsilane. Mass spectra and accurate mass measurements were carried out using a Varian MAT 711 or a VG Micromass ZAB-2HF instrument. R_f values were obtained by using thin-layer chromatography (TLC) on silica gel-coated plastic sheets (Merck silica gel 60 F_{254}) with the indicated solvent (mixture). Chromatographic purification refers to flash chromatography[23] using the same solvent as for TLC and Merck silica gel 60 (230-400 mesh) or Janssen Chimica silica gel (0.035-0.07 mm). Melting and boiling points are uncorrected. All reactions were carried out in an inert atmosphere of dry nitrogen (unless indicated otherwise). Standard syringe techniques were applied for transfer of Lewis acids, dry solvents and reagents.

Methyl glyoxylate hydrate.[10] To a solution of powdered dimethyl L-tartrate (34.68 g, 0.20 mol) in ether (500 mL) cooled in a cold water bath was added periodic acid (48.87 g, 0.21 mol) in 6 portions over 1 h with stirring. The milky reaction mixture was then stirred until the ether had become almost clear and a white solid separated. The ether phase was decanted, evaporated and distilled (45-50 °C/13 mmHg) to give methyl glyoxylate hydrate (16.10 g, 0.15 mol, 39%) as an orange oil. Methyl glyoxylate hydrate was used immediately for reactions with alcohols.

Anhydrous methyl glyoxylate.[11] The methyl hemiacetal of methyl glyoxylate[11] (8.20 g, 0.07 mol) was added to phosphorus pentoxide (9.70 g, 0.07 mol). The resulting mixture was distilled (30-50 °C/15 mmHg) to give anhydrous methyl glyoxylate (3.90 g, 0.04 mol, 65%) which was collected at -78 °C. After warm up to rt, the colourless viscous oil was used immediately for reactions with alcohols.

General procedure for the synthesis of precursors 1-11 (eq 1). Method A: Methyl glyoxylate hydrate (ca. 2 equiv) was added to a 0.1-0.2 M solution of the alcohol in benzene. The reaction mixture was refluxed for 16 h in the presence of a Dean-Stark trap. The reaction mixture was concentrated *in vacuo* and the residue was dissolved in pyridine (0.5-1.0 M) and treated with acetic anhydride (1.5 equiv calcd for both alcohol and glyoxylate) and DMAP (0.2 equiv). After being stirred for 16 h at rt, the reaction mixture was evaporated with benzene (3 ×) and CH_2Cl_2 (3 ×). The residue was chromatographed. Method B: Anhydrous methyl glyoxylate (ca. 2 equiv) was added to a 1.5 M solution of the alcohol in dry CH_2Cl_2. After being stirred overnight at rt, the reaction mixture was concentrated *in vacuo*. The residue was dissolved in pyridine (0.5-1.0 M) and treated with acetic anhydride (1.5 equiv calcd for both alcohol and glyoxylate) and a catalytic amount of DMAP. After being stirred for 16 h at rt, the reaction mixture was evaporated with benzene (3 ×) and CH_2Cl_2 (3 ×). The residue was chromatographed.

Methyl 2-acetoxy-2-(3-buten-1-oxy)acetate (1). Method A: 3-Buten-1-ol (2.00 g, 27.78 mmol) was treated with methyl glyoxylate hydrate (5.89 g, 55.56 mmol) in 150 mL of benzene to give the hemiacetal (4.56 g). The crude hemiacetal (4.30 g) was treated with acetic anhydride (4.1 g, 40.4 mmol) and DMAP (0.7 g, 5.4 mmol) in 30 mL of pyridine to give **1** (3.12 g, 15.45 mmol, 60%) as a colourless oil. R_f 0.45 (EtOAc:hexanes = 1:1.5). **IR** 1740-1760 (C=O), 1640 (C=C). **^1H NMR** (200 MHz) 2.16 (s, 3 H, CH_3), 2.38 (bq, J = 6.8 Hz, 2 H, CH_2CH=), 3.76 (m, 2 H, OCH_2), 3.80 (s, 3 H, OCH_3), 5.09 (m, 2 H, $=CH_2$), 5.79 (m, 1 H, CH=), 5.97 (s, 1 H, OCH). **^{13}C NMR** (50.3 MHz) 20.45 (CH_3), 33.43 (CH_2CH=), 52.44 (OCH_3), 69.21 (OCH_2), 92.25 (OCH), 116.80 ($=CH_2$), 133.68 (CH=), 165.97 (C=O), 169.70 (CO_2Me). **MS** (EI, 70 eV) 143 (M^+-OAc, 100), 131 (86), 55 (100), 43 (100). Preparative scale, method B: 3-Buten-1-ol (11.5 mL, 0.13 mol) was treated with anhydrous methyl glyoxylate (20 mL, 0.27 mol) in 120 mL of CH_2Cl_2. The crude hemiacetal was treated with acetic anhydride (80 mL, 0.85 mol) and DMAP (4.0 g, 0.03 mol) in 100 mL of pyridine. The crude product was distilled (88-93 °C/2 mbar) to give **1** (20.85 g, 0.10 mol, 77%) as a colourless oil.

Methyl 2-acetoxy-2-(3-(*E*)-hexen-1-oxy)acetate (2). Method A: 3-(*E*)-Hexen-1-ol (1.00 g, 10.00 mmol) was treated with methyl glyoxylate hydrate (2.12 g, 20.00 mmol) in 70 mL of benzene. The crude hemiacetal was treated with acetic anhydride (1.81 g, 17.79 mmol) and DMAP (0.29 g, 2.37 mmol) in 18 mL of pyridine to give **2** (1.54 g, 6.68 mmol, 67%) as a yellowish oil. R_f 0.47 (EtOAc:hexanes = 1:1.6). **IR** 1750 (C=O). **^1H NMR** (200 MHz) 0.94 (t, J = 7.4 Hz, 3 H, CH_2CH_3), 1.98 (m, 2 H, CH_2CH_3), 2.14 (s, 3 H, CH_3), 2.3 (m, 2 H, CH_2CH=), 3.7 (m, 2 H, OCH_2), 3.79 (s, 3 H, OCH_3), 5.3 (m, 1 H, CH=), 5.5 (m, 1 H, CH=), 5.96 (s, 1 H, OCH). **^{13}C NMR** (62.9 MHz) 13.63 (CH_2CH_3), 20.76 (CH_3), 25.55 (CH_2CH_3), 32.58 (CH_2CH=), 52.70 (OCH_3), 70.17 (OCH_2), 92.54 (OCH), 123.84 and 134.93 (CH=CH), 166.23 (C=O), 169.95 (CO_2Me).

Methyl 2-acetoxy-2-(3-(*Z*)-hexen-1-oxy)acetate (3). Method A: 3-(*Z*)-Hexen-1-ol (2.00 g, 20.00 mmol) was treated with methyl glyoxylate hydrate (4.24 g, 40.00 mmol) in 100 mL of benzene to give the hemiacetal (3.95 g). The crude hemiacetal (3.70 g) was treated with acetic anhydride (3.0 g, 29.5 mmol) and DMAP (0.5 g, 3.9 mmol) in 30 mL of pyridine to give **3** (2.76 g, 12.0 mmol, 64%) as a colourless oil. R_f 0.57 (EtOAc:hexanes = 1:1.5). **IR** 1750 (C=O), 1760 (C=O). **^1H NMR** (200 MHz) 0.95 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 2.04 (m, 2 H, CH_2CH_3), 2.16 (s, 3 H, CH_3), 2.38 (m, 2 H, CH_2CH=), 3.7 (m, 2

H, OCH_2), 3.80 (s, 3 H, OCH_3), 5.30 (m, 1 H, CH=), 5.49 (m, 1 H, CH=), 5.98 (s, 1 H, OCH).

Methyl 2-acetoxy-2-(3-butyn-1-oxy)acetate (4). Method A: 3-Butyn-1-ol (1.00 g, 14.29 mmol) was treated with methyl glyoxylate hydrate (3.03 g, 28.58 mmol) in 70 mL of benzene to give the hemiacetal (1.02 g). The crude hemiacetal (378 mg) was treated with acetic anhydride (366 mg, 3.59 mmol) and DMAP (58.3 mg, 0.48 mmol) in 6 mL of pyridine to give **4** (243 mg, 1.22 mmol, 23%) as a yellow oil. R_f 0.40 (EtOAc:hexanes = 1:1.5). **IR** 3300 (C≡C), 1740 (C=O), 1760 (C=O). **^{1}H NMR** (200 MHz) 1.99 (t, J = 2.6 Hz, 1 H, ≡CH), 2.15 (s, 3 H, CH_3), 2.51 (td, J = 7.0, 2.6 Hz, 2 H, CH_2C≡), 3.79 (s, 3 H, OCH_3), 3.82 (m, 2 H, OCH_2), 5.99 (s, 1 H, OCH).

Methyl 2-acetoxy-2-(4-pentyn-1-oxy)acetate (5). Method A: 4-Pentyn-1-ol (1.00 g, 11.90 mmol) was treated with methyl glyoxylate hydrate (2.52 g, 23.80 mmol) in 50 mL of benzene to give the hemiacetal (0.95 g). The crude hemiacetal (800 mg) was treated with acetic anhydride (712 mg, 6.98 mmol) and DMAP (113 mg, 0.93 mmol) in 10 mL of pyridine to give **5** (557 mg, 2.60 mmol, 26%) as a colourless oil. R_f 0.50 (EtOAc:hexanes = 1:1.5). **IR** 3300 (C≡C), 1745 (C=O), 1760 (C=O). **^{1}H NMR** (200 MHz) 1.79 (quintet, J = 6.5 Hz, 2 H, OCH_2CH_2), 1.93 (t, J = 1.9 Hz, 1 H, ≡CH), 2.13 (s, 3 H, CH_3), 2.27 (td, J = 6.8, 2.3 Hz, 2 H, CH_2C≡), 3.77 (s, 3 H, OCH_3), 3.78 (m, 2 H, OCH_2), 5.94 (s, 1 H, OCH).

Methyl 2-acetoxy-2-(3-methyl-3-buten-1-oxy)acetate (6). Method B: 3-Methyl-3-buten-1-ol (712 mg, 8.28 mmol) was treated with anhydrous methyl glyoxylate (1.5 g, 17.0 mmol) in 5 mL of CH_2Cl_2. The crude hemiacetal was treated with acetic anhydride (3.6 mL, 38.2 mmol) and DMAP (0.5 g, 4.1 mmol) in 10 mL of pyridine to give **6** (1.08 g, 5.00 mmol, 60%) as a colourless oil. R_f 0.38 (EtOAc:hexanes = 1:1.3). **IR** 1745 (C=O), 1640 (C=C). **^{1}H NMR** (200 MHz) 1.74 (s, 3 H, $=CCH_3$), 2.16 (s, 3 H, CH_3), 2.35 (t, J = 7.0 Hz, 2 H, CH_2C=), 3.71-3.92 (m, 2 H, OCH_2), 3.80 (s, 3 H, OCH_3), 4.73 (bs, 1 H, $=CH_2$), 4.79 (bs, 1 H, $=CH_2$), 5.98 (s, 1 H, OCH).

Methyl 2-acetoxy-2-(1-[*tert*-butyldiphenylsilyloxy]-4-penten-2-oxy)acetate (7). Method B: 1-*tert*-Butyldiphenylsilyloxy-4-penten-2-ol[12] (1.47 g, 4.3 mmol) was treated with anhydrous methyl glyoxylate (1.2 mL, 16.4 mmol) in 10 mL of CH_2Cl_2. The crude hemiacetal was treated with acetic anhydride (2.9 mL, 30.8 mmol) and a catalytic amount of DMAP in 10 mL of pyridine to give **7** (1.25 g, 2.7 mmol, 61%) as a colourless oil. R_f 0.45 (EtOAc: hexanes = 1:3). **IR** 1750 (C=O). **^{1}H NMR** (200 MHz, mixture of diastereoisomers) 1.06 (s, 9 H, $SiC(CH_3)_3$), 2.01 and 2.14 (s, 3 H, CH_3), 2.1-2.6 (m, 2 H, CH_2CH=), 3.6-4.0 (m, 3 H, OCH_2CHO), 3.76 and 3.78 (s, 3 H, OCH_3), 5.08 (m, 2 H, $=CH_2$), 5.78 (m, 1 H, CH=), 6.04 and 6.31 (s, 1 H, CHOAc), 7.41 (m, 6 H, $Si(C_6H_5)_2$), 7.68 (m, 4 H, $Si(C_6H_5)_2$). **^{13}C NMR** (50.3 MHz, mixture of diastereoisomers) 18.85 and 19.00 ($SiCMe_3$), 20.58 and 20.72 (CH_3), 26.46 and 26.56 ($SiC(CH_3)_3$), 35.60 and 35.75 (CH_2CH=), 52.38 and 52.45 (OCH_3), 64.94 and 66.16 ($SiOCH_2$), 80.92 and 81.18 (CHO), 92.45 and 92.76 (CHOAc), 117.16 and 117.91 ($=CH_2$), 133.21 and 133.55 (CH=), 127.47, 127.52, 127.55, 129.38, 129.50, 129.58, 134.58, 135.35 and 135.40 ($Si(C_6H_5)_2$), 132.77 and 132.87 ($Si(C_6H_5)_2$), 166.35 and 167 (C=O), 170 (CO_2Me).

Methyl 2-acetoxy-2-(6-methyl-5-hepten-2-oxy)acetate (8). Method A: 6-Methyl-5-hepten-2-ol (1.50 g, 11.72 mmol) was treated with methyl glyoxylate hydrate (2.48 g, 23.44 mmol) in 90 mL of benzene. The crude hemiacetal was treated with acetic anhydride (2.08 g, 20.42 mmol) and DMAP (0.33 g, 2.72 mmol) in 20 mL of pyridine to give **8** (1.77 g, 6.86 mmol, 59%) as a colourless oil. R_f 0.50 (EtOAc:hexanes = 1:1.6). **IR** 1755 (C=O). **^{1}H NMR** (200 MHz, mixture of diastereoisomers) 1.21 (d, J =6.2 Hz, 3 H, $OCHCH_3$), 1.6 (m, 2 H, CH_2CH_2CH=), 1.59 (s, 3 H, $=CCH_3$), 1.66 (s, 3 H, $=CCH_3$), 2.04 (m, 2 H, CH_2CH=), 2.13 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 3.8 (m, 1 H, $OCHCH_3$), 5.06 (m, 1 H, CH=), 5.96 (s) and 6.00 (s, 1 H, OCH). **^{13}C NMR** (62.9 MHz, mixture of diastereoisomers) 17.56, 17.63, 19.73, 20.82, 20.87, 20.92 and 25.62 ($=C(CH_3)_2$, $OCHCH_3$, CH_3), 23.64 and 23.84 (CH_2CH_2CH=), 36.51 and 36.74 (CH_2CH=), 52.64 and 52.67 (OCH_3), 76.27 and 77.97 ($OCHCH_3$), 91.29 and 92.82 (OCH), 123.51 and 123.63 (CH=), 166.46 and 166.59 (C=O), 170.08 and 170.18 (CO_2Me).

Methyl 2-acetoxy-2-(3-cyclohexen-1-methoxy)acetate (9). Method A: 3-Cyclohexen-1-methanol (0.90 g, 8.04 mmol) was treated with methyl glyoxylate hydrate (1,70 g, 16.08 mmol) in 70 mL of benzene. The crude hemiacetal was treated with acetic anhydride (1.30 g, 12.75 mmol) and DMAP (0.21 g, 1.70 mmol) in 18 mL of pyridine to give **9** (1.53 g, 6.32 mmol, 79%) as a colourless oil. R_f 0.50 (EtOAc:hexanes = 1:1.7). **IR** 1750 (C=O). **^{1}H NMR** (200 MHz) 1.26 (m, 1 H, OCH_2CH), 1.75 (m, 2 H, $CHCH_2$), 1.96 (m, 4 H, CH_2CH=$CHCH_2$), 2.14 (s, 3 H, CH_3), 3.57 (m, 2 H, OCH_2), 3.79 (s, 3 H, OCH_3), 5.63 (bs, 2 H, CH=CH), 5.94 (s, 1 H, OCH). **^{13}C NMR** (62.9 MHz) 20.73 (CH_3), 24.24, 24.29 and 25.13 (CH_2CH_2, $=CHCH_2$), 33.56 (OCH_2CH), 52.63 (OCH_3), 74.75 (OCH_2), 92.80 (OCH), 125.48 and 126.92 (CH=CH), 166.26 (C=O), 169.90 (CO_2Me).

Methyl 2-acetoxy-2-(2-cyclohexen-1-methoxy)acetate (10). Method B: 2-Cyclohexen-1-methanol[13] (715 mg, 6.38 mmol) was treated with anhydrous methyl glyoxylate (1.2 g, 13.64 mmol) in 5 mL of CH_2Cl_2. The crude hemiacetal was treated with acetic anhydride (2.8 mL, 29.7 mmol) and DMAP (0.4 g, 3.3 mmol) in 10 mL of pyridine to give **10** (0.97 g, 4.01 mmol, 63%) as a colourless oil. R_f 0.45 (EtOAc:hexanes = 1:1.3). **IR** 1760 (C=O), 1745 (C=O). **^{1}H NMR** (200 MHz) 1.27-1.83 (m, 4 H, $CHCH_2CH_2$), 1.98 (m, 2 H, CH_2CH=), 2.16 (s, 3 H, CH_3), 2.46 (m, 1 H, CHCH=), 3.56 (m, 2 H, OCH_2), 3.81 (s, 3 H, OCH_3), 5.55 (m, 1 H, CH=), 5.77 (m, 1 H, CH=), 5.97 (s, 1 H, OCH).

Methyl 2-acetoxy-2-[2-(1-cyclohexen-1-yl)-ethoxy]acetate (11). Method B: 2-(1-cyclohexen-1-yl)-ethanol[14] (2.58 g, 20.5 mmol) was treated with anhydrous methyl glyoxylate (2.7 g, 30.68 mmol) in 7 mL of CH_2Cl_2. The crude hemiacetal was treated with acetic anhydride (2.9 mL, 30.8 mmol) and DMAP (50 mg, 0.41 mmol) in 21 mL of pyridine to give **11** (3.15 g, 12.3 mmol, 60%) as a colourless oil. R_f 0.55 (EtOAc:hexanes = 1:4). **IR** 1745 (C=O). **^{1}H NMR** (200 MHz) 1.40-1.65 (m, 4 H, CH_2CH_2), 1.85-2.05 (m, 4 H, CH_2CH=$CHCH_2$), 2.16 (s, 3 H, CH_3), 2.26 (t, J = 7.2 Hz, 2 H, OCH_2CH_2), 3.69-3.87 (m, 2 H,

OCH_2), 3.80 (s, 3 H, OCH_3), 5.45 (bs, 1 H, =CH), 5.97 (s, 1 H, OCH).

Boron trifluoride etherate-induced cyclization of 1. To a solution of **1** (252 mg, 1.25 mmol) in 7 mL of dry CH_2Cl_2 was added at -70 °C $BF_3{\cdot}OEt_2$ (0.30 mL, 2.44 mmol). The reaction mixture was allowed to slowly warm up to rt and stirred for 3 h at rt. The reaction mixture was poured into icewater and an excess of $NaHCO_3$ was added. The resulting mixture was stirred at rt for 30 min and then filtered over celite. The residue was rinsed with 150 mL of CH_2Cl_2. After the layers were separated, the water layer was extracted (3 ×) with CH_2Cl_2 (30 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed to give three fractions. The first fraction was starting material (34 mg, 0.17 mmol, 13%). The second fraction consisted of two isomers (ratio 1:1) of **2-carbomethoxy-4-fluorotetrahydropyran (12)** (71 mg, 0.44 mmol, 35%, colourless oil). R_f 0.20 (EtOAc:hexanes = 1:2). **IR** 1745 (C=O). **^{1}H NMR** (200 MHz, mixture of isomers) 1.69-2.46 (m, 8 H, H3 and H5), 3.48 (td, J = 10.9, 1.3 Hz, 1 H, H6ax), 3.76 (s) and 3.78 (s, 6 H, CH_3), 3.81-4.27 (m, 4 H, H2 and H6), 4.37 (dd, J = 11.6, 2.7 Hz, 1 H, H2ax), 4.74 (tt, J = 10.0, 4.6 Hz, d, J_{HF} = 48.6 Hz, 1 H, H4ax), 5.03 (bd, J_{HF} = 47.5 Hz, 1 H, H4eq). **^{13}C NMR** (50.3 MHz, mixture of isomers) 29.99 (d, $^2J_{CF}$ = 20.4 Hz), 31.82 (d, $^2J_{CF}$ = 18.4 Hz), 33.36 (d, $^2J_{CF}$ = 20.8 Hz) and 34.70 (d, $^2J_{CF}$ = 19.8 Hz) (C3 and C5), 51.94 and 52.06 (CH_3), 62.39 (d, $^3J_{CF}$ = 10.3 Hz) and 63.97 (d, $^3J_{CF}$ = 10.4 Hz) (C6), 70.94 and 73.33 (d, $^3J_{CF}$ = 10.1 Hz) (C2), 85.40 (d, $^1J_{CF}$ = 170.6 Hz) and 87.52 (d, $^1J_{CF}$ = 176.9 Hz) (C4), 170.40 and 171.25 (C=O). **MS** (EI, 70 eV) 114 (12), 103 (M^+-CO_2Me, 100), 55 (46). The third fraction consisted of two isomers (*trans*/*cis* = 2.4:1) of **4-acetoxy-2-carbomethoxytetrahydropyran (13)** (73 mg, 0.36 mmol, 29%, yellowish oil). R_f 0.15 (EtOAc:hexanes = 1:2). **IR** 1740 (C=O), 1730 (C=O). **^{1}H NMR** (200 MHz, major isomer) 1.6-2.4 (m, 4 H, H3 and H5), 2.08 (s, 3H, CH_3), 3.4-4.2 (m, 2 H, H6), 3.75 (s, 3 H, OCH_3), 4.33 (dd, J = 10.9, 3.0 Hz, 1 H, H2ax), 5.16 (m, 1H, H4eq), (minor isomer, isolated signals) 2.03 (s, 3 H, CH_3), 4.92 (tt, J = 10.6, 4.5 Hz, 1 H, H4ax). **^{13}C NMR** (50.3 MHz, major isomer) 20.92 (CH_3), 29.30 and 32.62 (C3 and C5), 51.94 (OCH_3), 62.83 (C6), 66.04 and 71.46 (C2 and C4), 169.78 and 171.32 (C=O and CO_2Me), (minor isomer) 20.82 (CH_3), 30.81 and 33.78 (C3 and C5), 65.00 (C6), 68.77 and 73.98 (C2 and C4). **MS** (EI, 70 eV) 143 (M^+-CO_2Me, 12), 114 (22), 83 (M^+-CO_2Me -AcOH, 100), 55 (35), 43 (59). Accurate mass 143.0720 (calcd for $C_7H_{11}O_3$ (M^+-CO_2Me) 143.0708).

General procedure for the tin tetrachloride-induced cyclization of 1-11. A 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (2 equiv) was added at -78 °C to a 0.1 M solution of the precursor in dry CH_2Cl_2. The reaction mixture was allowed to warm up to rt and stirred for 3 h at rt. The reaction mixture was poured into icewater and an excess of $NaHCO_3$ was added. The resulting mixture was stirred at rt for 30 min and then filtered over celite. The residue was rinsed with 150-250 mL of CH_2Cl_2. After the layers were separated, the water layer was extracted (3 ×) with CH_2Cl_2 (20-50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed.

Tin tetrachloride-induced cyclization of 1. According to the general procedure, precursor **1** (704 mg, 3.49 mmol) in 20 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (5.8 mL, 6.96 mmol) to give two fractions. The first fraction consisted of two isomers (**14t**:**14c** = 1.6:1) of **2-carbomethoxy-4-chlorotetrahydropyran (14)** (483 mg, 2.71 mmol, 78%, colourless oil). R_f 0.40 (EtOAc:hexanes = 1:1.5). **IR** 1750 (C=O). The two isomers were separated with GLC (carbowax 20 M, 15% on gaschrom P, 2.5 m × 8 mm, 160 °C). **14t**: **^{1}H NMR** (250 MHz) 1.77 (m, 1 H, H5), 2.01-2.22 (m, 3 H, H3 and H5), 3.72 (s, 3 H, CH_3), 3.93 (m, 2 H, H6), 4.43-4.54 (m, 2 H, H2 and H4). **^{1}H NMR** (250 MHz, C_6D_6) 1.30 (m, 1 H, H5), 1.48 (m, 1 H, H5), 1.88 (m, 2 H, H3), 3.28 (s, 3 H, CH_3), 3.53 (dt, J = 11.9, 4.4 Hz, 1 H, H6eq), 3.65 (ddd, J = 12.1, 9.3, 3.1 Hz, 1 H, H6ax), 3.88 (quintet, J = 4.3 Hz, 1 H, H4eq), 4.31 (dd, J = 7.3, 5.1 Hz, 1 H, H2ax). **^{13}C NMR** (50.3 MHz) 33.27 (C5), 36.37 (C3), 52.12 (CH_3), 54.71 (C4), 62.52 (C6), 71.01 (C2), 171.29 (C=O). **14c**: **^{1}H NMR** (250 MHz) 1.89 (m, 2 H, H5), 2.09 (m, 1 H, H3ax), 2.48 (m, 1 H, H3eq), 3.46 (td, J = 12.0, 2.4 Hz, 1 H, H6ax), 3.76 (s, 3 H, CH_3), 3.97 (dd, J = 11.5, 2.5 Hz, 1 H, H2ax), 4.02 (m, 1 h, H4), 4.15 (ddd, J = 12.0, 4.7, 2.1 Hz, 1 H, H6eq). **^{1}H NMR** (250 MHz, C_6D_6) 1.47 (m, 2 H, H5), 1.79 (dt, J = 12.9, 11.2 Hz, 1 H, H3ax), 2.12 (dquintet, J = 12.9, 2.2 Hz, 1 H, H3eq), 2.70 (td, J = 11.6, 2.7 Hz, 1 H, H6ax), 3.28 (s, 3 H, CH_3), 3.29 (tt, J = 11.1, 4.6 Hz, 1 H, H4ax), 3.43 (dd, J = 11.1, 2.6 Hz, 1 H, H2ax), 3.59 (ddd, J = 12.0, 4.6, 2.5 Hz, 1 H, H6eq). **^{13}C NMR** (50.3 MHz) 36.05 (C5), 38.91 (C3), 52.25 (CH_3), 54.23 (C4), 66.56 (C6), 75.34 (C2), 170.12 (C=O). **MS** (EI, 70 eV) 119/121 (M^+-CO_2Me, 100/32), 55 (90). The second fraction consisted of two isomers (**13t**:**13c**) = 1.6:1) of **13** (36 mg, 0.18 mmol, 5%, colourless oil). R_f 0.25 (EtOAc:hexanes = 1:1.5). Preparative scale: To a solution of **1** (18.00 g, 89.11 mmol) in 500 mL of dry CH_2Cl_2 was added pure $SnCl_4$ (21 mL, 0.18 mol) at -78 °C. The reaction mixture was allowed to slowly warm up to rt and stirred for 16 h at rt. The reaction mixture was poured into icewater and $NaHCO_3$ was added (pH = 8-9). The resulting mixture was stirred for 30 min at rt and then filtered over celite. The residue was rinsed with CH_2Cl_2 (200 mL). After the layers were separated, the water layer was extracted (3 ×) with $CHCl_3$ (200 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (100 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude product (15.85 g) was distilled (70-90 °C/1 mbar) to give **14** (12.11 g, 67.84 mmol, 76%, **14t**:**14c** = 1.3:1) as a colourless oil. The residue was distilled (bulb to bulb, 150-200 °C/0.06 mbar) to give **13** (1.27 g, 6.29 mmol, 7%, **13c**:**13t** = 1:1.5) as a yellowish oil.

Titanium tetrachloride-induced cyclization of 1. To a solution of **1** (161 mg, 0.80 mmol) in 5 mL of dry CH_2Cl_2 was added at -78 °C a 1.2 M solution of $TiCl_4$ in CH_2Cl_2 (1.6 mL, 1.9 mmol). The reaction mixture was allowed to warm up to rt

and stirred for 3 h at rt. The reaction mixture was poured into icewater and an excess of $NaHCO_3$ was added. The resulting mixture was stirred at rt for 30 min and then filtered over celite. The residue was rinsed with 125 mL of CH_2Cl_2. After the layers were separated, the water layer was extracted (3 ×) with CH_2Cl_2 (25 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed to give two fractions. The first fraction consisted of two isomers (**14c**:**14t** = 1.8:1) of **14** (75 mg, 0.42 mmol, 53%, colourless oil). The second fraction consisted of two isomers (**13t**:**13c**) = 4:1) of **13** (40 mg, 0.20 mmol, 25%, colourless oil).

Formic acid-induced cyclization of 1. Precursor **1** (170 mg, 0.84 mmol) was dissolved in 3 mL of formic acid and stirred for 2 days at rt. The reaction mixture was concentrated *in vacuo* and evaporated with benzene (3 × 5 mL) and CH_2Cl_2 (3 × 5 mL). The residue was chromatographed to give two isomers (**15c**:**15t** = 5:1) of **2-carbomethoxy-4-formyltetrahydropyran (15)** (74 mg, 0.39 mmol, 47%) as a yellowish oil. R_f 0.40 (EtOAc:hexanes = 1.5:1). **^{1}H NMR** (200 MHz, major isomer) 1.66 (m, 2 H, H5), 1.91 (m, 1 H, H3ax), 2.29 (dquintet, J = 12.6, 2.3 Hz, 1 H, H3eq), 3.48 (td, J = 11.8, 2.5 Hz, 1 H, H6ax), 3.70 (s, 3 H, CH_3), 4.00 (dd, J = 11.2, 2.6 Hz, 1 H, H2), 4.12 (ddd, J = 12.0, 4.7, 2.7 Hz, 1 H, H6eq), 5.01 (tdd, J = 10.6, 5.0, 4.5 Hz, 1 H, H4), 7.96 (s, 1 H, CHO), (minor isomer, isolated signals) 3.75 (s, 3 H, CH_3), 4.29 (dd, J = 10.8, 3.1 Hz, 1 H, H2), 5.27 (quintet, J = 3.4 Hz, 1 H, H4), 8.04 (s, 1 H, CHO).

Tin tetrachloride-induced cyclization of 2. According to the general procedure, precursor **2** (165 mg, 0.72 mmol) in 10 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (1.19 mL, 1.43 mmol) to give two isomers (*rel*-(2*R*, 3*S*,4*R*) (**16t**):*rel*-(2*R*,3*S*,4*S*) (**16c**) = 5:1) of **2-carbomethoxy-4-chloro-3-ethyltetrahydropyran (16)** (122 mg, 0.59 mmol, 82%) as a colourless oil. R_f 0.35 (EtOAc:hexanes = 1:1.4). **IR** 1740 (C=O). **^{1}H NMR** (200 MHz, major isomer) 0.87 (t, J = 7.3 Hz, 3 H, CH_3), 1.34 (m, 2 H, CH_2Me), 1.92 (m, 2 H, H5), 2.20 (m, 1 H, H3), 3.74 (s, 3 H, OCH_3), 3.90 (m, 2 H, H6), 4.09 (d, J = 9.8 Hz, 1 H, H2), 4.53 (q, J = 3.0 Hz, 1 H, H4), (minor isomer, isolated signals) 0.89 (t, J = 7.5 Hz, 3 H, CH_3), 3.46 (td, J = 11.3, 3.0 Hz, 1 H, H6ax), 3.75 (s, 3 H, OCH_3). **^{13}C NMR** (62.9 MHz, major isomer) 10.04 (CH_3), 20.39 (CH_2Me), 33.83 (C5), 44.24 (C3), 52.03 (OCH_3), 58.26 (C4), 62.12 (C6), 76.58 (C2), 170.81 (C=O), (minor isomer) 9.41 (CH_3), 20.95 (CH_2Me), 35.70 (C5), 46.80 (C3), 52.15 OCH_3), 58.65 (C4), 65.82 (C6), 79.06 (C2). **MS** (EI, 70 eV) 206/208 (M^+, 7/3), 147/149 (M^+-CO_2Me, 100/43). Accurate mass 206.0712 (calcd for $C_9H_{15}O_3{}^{35}Cl$ 206.0709).

Formic acid-induced cyclization of 2. Precursor **2** (21 mg, 0.09 mmol) was dissolved in 0.5 mL of formic acid and stirred for 2 days at rt. The reaction mixture was concentrated *in vacuo* and evaporated with benzene (3 × 3 mL) and CH_2Cl_2 (3 × 3 mL) to give the crude product which consisted of two isomers (*rel*-(2*R*,3*S*,4*S*) (**17c**):*rel*-(2*R*,3*S*,4*R*) (**17t**) = 5:1) of **2-carbomethoxy-3-ethyl-4-formyl-tetrahydropyran (17)** (15 mg, 0.07 mmol, 78%, yellowish oil). R_f 0.15 (EtOAc:hexanes = 1.3:1). **^{1}H NMR** (200 MHz, major isomer) 0.92 (t, J = 7.5 Hz, 3 H, CH_3), 1.19-2.36 (m, 5 H, H3, H5, CH_2Me), 3.58 (ddd, J = 12.3, 9.3, 3.3 Hz, 1 H, H6ax), 3.78 (s, 3 H, OCH_3), 3.95 (d, J = 7.8 Hz, 1 H, H2), 4.14 (m, 1 H, H6eq), 5.03(td, J = 8.5, 4.2 Hz, 1 H, H4), 8.05 (s, 1 H, CHO), (minor isomer, isolated signals) 5.41 (q, J = 2.8 Hz, 1 H, H4), 8.14 (s, 1 H, CHO).

Tin tetrachloride-induced cyclization of 3. According to the general procedure, precursor **3** (380 mg, 1.65 mmol) in 15 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2CL_2 (2.80 mL, 3.36 mmol) to give *rel*-(2*R*,3*R*,4*R*)-**2-carbomethoxy-4-chloro-3-ethyltetrahydropyran (18)** (210 mg, 1.02 mmol, 62%) as a colourless oil. R_f 0.50 (EtOAc:hexanes = 1:2). **IR** 1745 (C=O). **^{1}H NMR** (200 MHz) 0.88 (t, J = 7.5 Hz, 3 H, CH_3), 1.32-1.66 (m, 3 H, CH_2Me and H5), 1.98-2.27 (m, 2 H, H3 and H5), 3.72 (s, 3 H, OCH_3), 3.90 (m, 2 H, H6), 4.45 (q, J = 3.2 Hz, 1 H, H4), 4.59 (d, J =2.69 Hz, 1 H, H2). **^{1}H NMR** (250 MHz, C_6D_6) 0.60 (t, J = 7.5 Hz, 3 H, CH_3), 1.19-1.47 (m, 3 H, CH_2Me and H5), 1.68 (m, 1 H, H5), 2.00 (septet, J = 3.5 Hz, 1 H, H3), 3.29 (s, 3 H, OCH_3), 3.64 (m, 2 H, H6), 4.12 (q, J = 4.0 Hz, 1 H, H4), 4.56 (d, J = 3.1 Hz, 1 H, H2). **^{13}C NMR** (50.3 MHz) 11.77 (CH_3), 20.57 (CH_2Me), 28.84 (C5), 45.64 (C3), 51.85 (OCH_3), 57.85 (C4), 62.81 (C6), 73.84 (C2), 171.16 (C=O). **MS** (EI, 70 eV) 206/208 (M^+, 16/4), 147/149 (M^+-CO_2Me, 100/32). Accurate mass 206.0712 (calcd for $C_9H_{15}O_3{}^{35}Cl$ 206.0709).

Formic acid-induced cyclization of 3. Precursor **3** (54 mg, 0.23 mmol) was dissolved in 1 mL of formic acid and stirred for 2 days at rt. The reaction mixture was concentrated *in vacuo* and evaporated with benzene (3 × 3 mL) and CH_2Cl_2 (3 × 3 mL). The residue was chromatographed to give two isomers (*rel*-(2*R*,3*R*,4*S*) (**19c**):*rel*-(2*R*,3*R*,4*R*) (**19t**) = 7.5:1) of **2-carbomethoxy-3-ethyl-4-formyltetrahydropyran (19)** (34 mg, 0.16 mmol, 68%) as a yellowish oil. R_f 0.40 (EtOAc:hexanes = 1.5:1). **IR** 1740 (C=O), 1720 (C=O). **^{1}H NMR** (200 MHz, major isomer) 0.85 (t, J = 7.6 Hz, 3H, CH_3), 1.4-2.0 (m, 4 H, H5 and CH_2CH_3), 2.26 (m, 1 H, H3eq), 3.50 (td, J = 11.7, 3.1 Hz, 1 H, H6ax), 3.74 (s, 3 H, OCH_3), 4.03 (d, J = 2.4 Hz, 1 H, H2), 4.16 (ddd, J = 12.0, 5.1, 2.5 Hz, 1 H, H6eq), 5.14 (dt, J = 11.1, 4.6 Hz, 1 H, H4), 8.03 (d, J = 0.8 Hz, 1 H, CHO), (minor isomer, isolated signals) 1.23 (t, J = 7.2 Hz, 3 H, CH_3), 4.41 (d, J = 2.7 Hz, 1 H, H2), 8.10 (s, 1 H, CHO). **^{13}C NMR** (50.3 MHz, major isomer) 13.53 (CH_3), 16.37 (CH_2CH_3), 26.83 (C5), 42.63 (C3), 51.88 (OCH_3), 65.40 (C6), 72.17 (C2), 77.27 (C4), 160.05 (CHO), 170.41 (C=O).

Tin tetrachloride-induced cyclization of 4. According to the general procedure, precursor **4** (176 mg, 0.88 mmol) in 8 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (1.47 mL, 1.76 mmol) to give **2-carbomethoxy-4-chloro-5,6-dihydro-2H-pyran (20)** (90 mg, 0.51 mmol, 58%) as a yellowish oil. R_f 0.50 (EtOAc:hexanes = 1.2:1). **IR** 1745

(C=O). ^{1}H NMR (200 MHz) 2.41 (m, 2 H, H5), 3.77 (s, 3 H, CH_3), 3.90 (m, 1 H, H6), 4.10 (ddd, J = 11.5, 6.5, 5.1 Hz, 1 H, H6), 4.75 (q, J = 2.7 Hz, 1 H, H2), 6.00 (dt, J = 3.1, 1.6 Hz, 1 H, H3). ^{13}C NMR (50.3 MHz) 32.22 (C5), 52.33 (CH_3), 62.95 (C6), 73.14 (C2), 120.59 (C3), 131.88 (C4), 169.81 (C=O).

Tin tetrachloride-induced cyclization of 5. According to the general procedure, precursor **5** (253 mg, 1.18 mmol) in 10 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (1.97 mL, 2.36 mmol) to give **2-carbomethoxy-4-chloro-2,5,6,7-tetrahydrooxepin (21)** (97 mg, 0.51 mmol, 43%) as a yellowish oil. R_f 0.40 (EtOAc:hexanes = 1:1.3). IR 1745 (C=O). ^{1}H NMR (200 MHz) 1.93 (m, 2 H, H6), 2.69 (m, 2 H, H5), 3.76 (s, 3 H, CH_3), 3.78(m, 1 H, H7), 4.08 (m, 1 H, H7), 4.68 (m, 1 H, H2), 6.01 (d, J = 3.4 Hz, 1 H, H3). ^{13}C NMR (62.9 MHz) 27.31 (C6), 35.72 (C5), 52.55 (CH_3), 70.38 (C7), 75.33 (C2), 125.41 (C3), 138.30 (C4), 169.90 (C=O). MS (EI, 70 eV) 155 (M^+-Cl, 10), 131/133 (M^+-CO_2Me, 100/32).

Tin tetrachloride-induced cyclization of 6. According to the general procedure, precursor **6** (456 mg, 2.11 mmol) in 15 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (3.50 mL,4.20 mmol) to give two fractions. The first fraction consisted of ***rel*-(2*R*,4*R*)-2-carbomethoxy-4-chloro-4-methyltetrahydropyran (22)** (314 mg, 1.63 mmol, 77%, colourless oil). R_f 0.20 (EtOAc:hexanes = 1:3). IR 1745 (C=O). ^{1}H NMR (200 MHz) 1.67 (s, 3 H, CH_3), 1.69-1.86 (m, 3 H, H3 and H5), 2.24 (d, J = 14.1 Hz, 1 H, H3), 3.76 (s, 3 H, OCH_3), 3.80-4.08 (m, 2 H, H6), 4.42 (dd, J = 11.5, 2.3 Hz, 1 H, H2). ^{13}C NMR (50.3 MHz) 33.61 (CH_3), 39.78 and 42.98 (C3 and C5), 52.12 (OCH_3), 64.02 (C6), 67.76 (C4), 72.43 (C2), 171.27 (C=O). MS (EI, 70 eV) 133/135 (M^+-CO_2Me, 100/30), 97 (16), 69 (82), 41 (26). Accurate mass 133.0446 (calcd for $C_6H_{10}O^{35}Cl$ (M^+-CO_2Me) 133.0420). The second fraction consisted of ***rel*-(2*R*,4*R*)-4-acetoxy-2-carbomethoxy-4-methyltetrahydropyran (23)** (60 mg, 0.28 mmol, 13%, colourless oil). R_f 0.10 (EtOAc:hexanes = 1:3). IR 1740 (C=O), 1725 (C=O). ^{1}H NMR (200 MHz) 1.54 (s, 3 H, CH_3), 1.49-1.69 (m, 2 H, H5), 2.05 (s, 3 H, (C=O)CH_3), 2.29 (dd, J = 14.4, 1.7 Hz, 1 H, H3), 2.51 (dt, J = 14.0, 2.3 Hz, 1 H, H3), 3.65 (td, J = 12.2, 2.0 Hz, 1 H, H6), 3.76 (s, 3 H, OCH_3), 3.97 (dd, J = 12.4, 4.7 Hz, 1 H, H6), 4.21 (dd, J = 12.0, 2.3 Hz, 1 H, H2). ^{13}C NMR (50.3 MHz) 22.06 ((C=O)CH_3), 25.74 (CH_3), 34.92 and 39.12 (C3 and C5), 52.07 (OCH_3), 63.44 (C6), 72.01 (C2), 78.07 (C4), 170.00 and 171.47 (C=O and CO_2Me). MS (EI, 70 eV) 156 (M^+-AcOH, 15), 97 (M^+-CO_2Me -AcOH, 100), 43 (60).

Tin tetrachloride-induced cyclization of 7. According to the general procedure, precursor **7** (1.12 g, 3.2 mmol) in 20 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (4.0 mL, 4.8 mmol) to give ***rel*-(2*R*,4*R*,6*S*)-6-(*tert*-butyldiphenylsilyloxymethyl)-2-carbomethoxy-4-chlorotetrahydropyran (24)** (809 mg, 1.8 mmol, 56%) as a colourless oil. R_f 0.70 (EtOAc:hexanes = 1:1.4). IR 1750 (C=O). ^{1}H NMR (200 MHz) 1.06 (s, 9 H, $SiC(CH_3)_3$), 1.77-2.27 (m, 4 H, H3 and H5), 3.63-3.89 (m, 2 H, $SiOCH_2$), 3.76 (s, 3 H, CH_3), 4.08 (m, 1 H, H6), 4.56 (dd, J = 11.5, 2.4 Hz, 1 H, H2), 4.68 (quintet, J = 3.0 Hz, 1 H, H4), 7.26-7.76 (m, 10 H, $Si(C_6H_5)_2$). ^{13}C NMR (50.3 MHz) 19.05 ($SiCMe_3$), 26.60 ($SiC(CH_3)_3$), 35.11 and 35.94 (C3 and C5), 51.95 (CH_3), 55.33 ($SiOCH_2$), 66.03 (C4), 70.77 and 72.25 (C2 and C6), 127.43, 129.45, 134.58, 135.41 and 135.47 ($Si(C_6H_5)_2$), 133.2 ($Si(C_6H_5)_2$), 171.09 (C=O). MS (EI, 70 eV) 389/391 (M^+-$C(CH_3)_3$, 100/40), 213 (54), 199 (87), 31 (65).

Tin tetrachloride-induced cyclization of 8. According to the general procedure, precursor **8** (134 mg, 0.52 mmol) in 8 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (0.87 mL, 1.04 mmol) to give ***rel*-(2*R*,3*S*,6*R*)-2-carbomethoxy-6-methyl-3-propenyltetrahydropyran (25)** (65 mg, 0.33 mmol, 63%) as a colourless oil. R_f 0.50 (EtOAc:hexanes = 1:1.4). IR 1740 (C=O). ^{1}H NMR (200 MHz) 1.23 (d, J = 6.2 Hz, 3 H, (C6)CH_3), 1.13-1.87 (m, 4 H, H4 and H5), 1.69 (s, 3 H, CH_3), 2.35 (td, J = 11.0, 3.8 Hz, 1 H, H3), 3.43-3.76 (m, 1 H, H6), 3.67 (s, 3 H, OCH_3), 3.97 (d, J = 10.5 Hz, 1 H, H2), 4.72 (bs, 2 H, =CH_2). ^{13}C NMR (62.9 MHz) 19.61 and 21.47 (CH_3 and (C6)CH_3), 29.00 and 32.55 (C4 and C5), 46.85 (C3), 51.44 (OCH_3), 73.98 (C6), 80.81 (C2), 112.41 (=CH_2), 144.66 (=C), 170.49 (C=O). MS (EI, 70 eV) 198 (M^+, 8), 139 (M^+-CO_2Me, 88), 68 (100). Accurate mass 198.1281 (calcd for $C_{11}H_{18}O_3$ 198.1256).

Tin tetrachloride-induced cyclization of 9. According to the general procedure, precursor **9** (200 mg, 0.83 mmol) in 10 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (1.38 mL, 1.66 mmol) to give ***rel*-(1*R*,2*R*,5*R*)-2-carbomethoxy-3-oxabicyclo-[3.3.1]-7-nonene (26)** and ***rel*-(1*R*,2*R*,5*S*,7*R*)-2-carbomethoxy-7-chloro-3-oxabicyclo-[3.3.1]-nonane (27)** (109 mg, 0.60 mmol, 73%, colourless oil) in a 92:8 ratio as an inseparable mixture. R_f 0.35 (EtOAc:hexanes = 1:1). IR 1745 (C=O). ^{1}H NMR (200 MHz, major component) 1.84 (m, 3 H, H5 and H9), 2.26 (m, 2 H, H6), 2.66 (m, 1 H, H1), 3.71 (s, 3 H, CH_3), 3.73 (m, 1 H, H4), 4.01 (d, J = 11.4 Hz, 1 H, H4), 4.06 (d, J = 1.9 Hz, 1 H, H2), 5.55 (m, 1 H, H8), 5.95 (dt, J = 9.8, 3.4 Hz, 1 H, H7), (minor component, isolated signals) 4.21 (bs, 1 H, H4), 4.32 (d, J = 2.3 Hz, 1 H, H2), 4.95 (septet, J = 5.8 Hz, 1 H, H7). ^{13}C NMR (50.3 MHz, **26**) 26.60 (C5), 29.43 and 31.53 (C6 and C9), 32.52 (C1), 51.88 (CH_3), 75.21 (C4), 77.13 (C2), 124.23 and 132.08 (C7 and C8), 170.88 (C=O). MS (EI, 70 eV) 182 (M^+ for **26**, 20), 123 (M^+-CO_2Me, 86), 79 (100). Accurate mass 182.0925 (calcd for **26** $C_{10}H_{14}O_3$ 182.0943).

Tin tetrachloride-induced cyclization of 10. According to the general procedure, precursor **10** (529 mg, 2.19 mmol) in 15 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (3.70 mL, 4.44 mmol) to give a mixture (1:1) of ***rel*-(1*R*,6*S*,7*R*)-7-carbomethoxy-5-chloro-8-oxabicyclo-[4.3.0]-nonane (28)** (329 mg, 1.51 mmol, 69% colourless oil). R_f 0.15 (EtOAc:hexanes = 1:3). ^{1}H NMR (200 MHz, two isomers) 0.15-2.25 (m, 6 H, H2, H3 and H4), 2.55-2.80 (m, 2 H, H1 and H6), 3.68 and 3.71 (s, 3 H, CH_3), 3.65-4.35 (m, 3 H, H5 and H9), 3.91 (d, J = 7.3 Hz, 1 H, H7), 4.41 (d, J = 6.8 Hz, 1 H, H7). ^{13}C NMR (50.3 MHz, two isomers) 19.10, 19.74, 20.51, 21.32, 23.43 and 30.97 (C2, C3 and C4), 35.99, 38.37, 39.27 and 47.24 (C1 and C6), 51.69 and 51.99 (CH_3), 57.25 and 62.36 (C5), 69.88 and 72.81 (C9), 79.70 and 79.87 (C7), 170.02 and

171.68 (C=O). To this mixture (47 mg, 0.22 mmol) in 5 mL of refluxing benzene, a solution of Bu_3SnH (115 μL, 0.43 mmol) and a catalytic amount of AIBN in 2 mL of benzene was added dropwise. After 1 h of reflux the reaction mixture was concentrated *in vacuo*. The residue was chromatographed to give ***rel*-(1*R*,6*S*,7*R*)-7-carbomethoxy-8-oxabicyclo-[4.3.0]-nonane (28')** (33 mg, 0.18 mmol, 82%) as a colourless oil. ^{1}H NMR (200 MHz) 1.2-1.9 (m, 8 H, H2, H3, H4 and H5), 2.15-2.65 (m, 2 H, H1 and H6), 3.73 (s, 3 H, CH_3), 3.92 (d, J = 9.5 Hz, 2 H, H9), 4.50 (d, J = 5.2 Hz, 1 H, H7).

Tin tetrachloride-induced cyclization of 11. According to the general procedure, precursor **11** (521 mg, 2.04 mmol) in 15 mL of CH_2Cl_2 was treated with a 1.2 M solution of $SnCl_4$ in CH_2Cl_2 (3.50 mL, 4.20 mmol) to give two fractions. The first fraction consisted of ***rel*-(1*R*,2*S*,6*S*)-2-carbomethoxy-6-chloro-3-oxabicyclo-[4.4.0]-decane (29)** (162 mg, 0.70 mmol, 34%, colourless oil). R_f 0.23 (EtOAc:hexanes = 1:3). IR 1740 (C=O). ^{1}H NMR (300 MHz) 1.2-2.1 (m, 11 H, H1, H5, H7, H8, H9, and H10), 3.75 (s, 3 H, CH_3), 3.98 (ddd, J = 11.8, 5.1, 1.4 Hz, 1 H, H4), 4.09 (td, J = 11.7, 2.4 Hz, 1 H, H4), 4.09 (d, J = 9.9 Hz, 1 H, H2). ^{13}C NMR (62.9 MHz) 21.11, 22.64 and 25.08 (C8, C9 and C10), 40.99 and 41.09 (C5 and C7), 47.73 (C1), 51.95 (CH_3), 63.89 (C4), 74.40 (C6), 77.35 (C2), 170.78 (C=O). The second fraction consisted of ***rel*-(1*R*,2*R*,6*S*)-6-acetoxy-2-carbomethoxy-3-oxabicyclo-[4.4.0]-decane (30)** (63 mg, 0.25 mmol, 12%, colourless oil). R_f 0.18 (EtOAc:hexanes = 1:3). IR 1735 (C=O), 1725 (C=O). ^{1}H NMR (200 MHz) 1.08-1.75 (m, 9 H, H5, H7, H8, H9 and H10), 2.08 (s, 3 H, CH_3), 2.60 (bd, J = 14.5 Hz) and 2.73 (bd, J = 11.5 Hz, 2 H, H1 and H5), 3.62 (td, J = 12.3, 2.1 Hz, 1 H, H4ax), 3.73 (s, 3 H, OCH_3), 3.89 (ddd, J = 11.7, 5.2, 1.3 Hz, 1 H, H4eq), 4.05 (d, J = 10.1 Hz, 1 H, H2). ^{13}C NMR (62.9 MHz) 20.80, 21.95, 22.01 and 24.90 (C8, C9, C10 and CH_3), 33.21 and 33.33 (C5 and C7), 46.80 (C1), 51.97 (OCH_3), 63.56 (C4), 76.98 (C2), 79.81 (C6), 169.74 and 170.96 (C=O and CO_2Me).

REFERENCES AND NOTES

1. For a preliminary account, see: Lolkema, L. D. M.; Hiemstra, H.; Mooiweer, H. H.; Speckamp, W. N. *Tetrahedron Lett.* **1988**, *29*, 6365.
2. The term 'oxonium ion' is frequently used for this type of intermediate. This name is incorrect, however because the positive charge is on carbon (a carbenium ion), resonance-stabilized by an oxygen substituent. The name 'oxocarbenium ion' is also used, but as the oxygen atom is part of an alk*oxy* group we prefer the term 'oxycarbenium ion' for this type of intermediate.
3. (a) Cockerill, G. S.; Kocienski, P. *J. Chem. Soc., Chem. Commun.* **1983**, 705; (b) Cockerill, G. S.; Kocienski, P.; Treadgold, R. *J. Chem. Soc., Perkin Trans. I* **1985**, 2093, 2101; (c) Yamada, J.; Asano, T.; Kadota, I.; Yamamoto, Y. *J. Org. Chem.* **1990**, *55*, 6066; (d) Kadota, I.; Gevorgyan, V.; Yamada, J.; Yamamoto, Y. *Synlett* **1991**, 823.
4. (a) Adams, D. R.; Bhatnagar, S. P. *Synthesis* **1977**, 661; (b) Coppi, L. Ricci, A.; Taddei, M. *Tetrahedron Lett.* **1987**, *28*, 973; Coppi, L. Ricci, A.; Taddei, M. *J. Org. Chem.* **1988**, *53*, 911; (c) Wei, Z. Y.; Li, J. S.; Wang, D.; Chan, T. H. *Tetrahedron Lett.* **1987**, *28*, 3441; Chan, T. H.; Arya, P *Tetrahedron Lett.* **1989**, *30*, 4065; Arya, P.; Chan, T. H. *J. Chem. Soc., Chem. Commun.* **1990**, 967; (d) Wei, Z. Y.; Wang, D.; Li, J. S.; Chan, T. H. *J. Org. Chem.* **1989**, *54*, 5768; (e) Hoppe, D.; Krämer, T.; Erdbrügger, C. F.; Egert, E. *Tetrahedron Lett.* **1989**, *30*, 1233; (f) Nishiyama, H.; Narimatsu, S.; Sakuta, K.; Itoh, K. *J. Chem. Soc., Chem. Commun.* **1982**, 459; Nishiyama, H.; Itoh, K. *J. Org. Chem.* **1982**, *47*, 2498; (g) Overman, L. E.; Castañeda, A.; Blumenkopf. T. A. *J. Am. Chem. Soc.* **1986**, *108*, 1303; (h) Bunnelle, W. H.; Seamon, D. W.; Mohler, D. L.; Ball, T. F.; Thompson, D. W *Tetrahedron Lett.* **1984**, *25*, 2653; Melany, M. L.; Lock, G. A.; Thompson, D. W. *J. Org. Chem.* **1985**, *50*, 3925; Winstead, R. C.; Simpson, T. H.; Lock, G. A.; Schiavelli, M. D.; Thompson, D. W. *J. Org. Chem.* **1986**, *51*, 275; Mohler, D. L.; Thompson, D. W. *Tetrahedron Lett.* **1987**, *28*, 2567; Nikolic, N. A.; Gonda, E.; Longford, C. P. D.; Lane, N. T.; Thompson, D. W. *J. Org. Chem.* **1989**, *54*, 2748; (i) Kay, I. T.; Williams, E. G. *Tetrahedron Lett.* **1983**, *24*, 5915; (j) Wagner, A.; Heitz, M. P.; Mioskowski C. *Tetrahedron Lett.* **1989**, *30*, 1971; See also reference 22.
5. (a) Overman, L. E.; Blumenkopf, T. A.; Castañeda, A.; Thompson, A. S. *J. Am. Chem. Soc.* **1986**, *108*, 3516; Overman, L. E.; Thompson, A. S. *J. Am. Chem. Soc.* **1988**, *110*, 2248; Castañeda, A.; Kucera, D. J.; Overman. L. E. *J. Org. Chem.* **1989**, *54*, 5695; Blumenkopf, T. A.; Bratz, M.; Castañeda, A.; Look, G. C.; Overman, L. E.; Rodriguez, D.; Thompson, A. S. *J. Am. Chem. Soc.* **1990**, *12*, 4386; Blumenkopf, T. A.; Look, G. C.; Overman, L. E. *J. Am. Chem. Soc.* **1990**, *112*, 4399; Berger, D.; Overman, L. E. *Synlett* **1992**, 811; (b) Mortimore, M.; Cockerill, G. S.; Kocienski, P.;

Treadgold, R. *Tetrahedron Lett.* **1987**, *28*, 3747; see also reference 3.

6. (a) Li, T.-T.; Lesko, P.; Ellison, R. H.; Subramanian, N.; Fried, J. H. *J. Org. Chem.* **1981**, *46*, 111; (b) Perron, F.; Albizati, K. F. *J. Org. Chem.* **1987**, *52*, 4128; Perron-Sierra, F.; Promo, M. A.; Martin, V. A.; Albizati, K. F. *J. Org. Chem.* **1991**, *56*, 6188.
7. For more results on the π-cyclizations of α-ester oxycarbenium ions, see: Lolkema, L. D. M.; Semeyn, C.; Ashek, L.; Hiemstra, H.; Speckamp, W. N., following paper in this issue.
8. Mooiweer, H. H.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron* **1989**, *45*, 4627; Mooiweer, H. H.; Ettema, K. W. A.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron* **1990**, *46*, 2991.
9. (a) Mooiweer, H. H.; Hiemstra, H.; Fortgens, H. P.; Speckamp, W. N. *Tetrahedron Lett.* **1987**, *28*, 3285; Mooiweer, H. H.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron* **1991**, *47*, 3451; (b) Esch, P. M.; Boska, I. M.; Hiemstra, H.; Speckamp, W. N. *Synlett* **1989**, 38; Esch, P. M.; Boska, I. M.; Hiemstra, H.; De Boer, R. F.; Speckamp, W. N. *Tetrahedron* **1991**, *47*, 4039, 4063.
10. Kelly, T. R.; Schmidt, T. E.; Haggerty, J. G. *Synthesis* **1972**, 544.
11. Methyl glyoxylate was generated from the methyl hemiacetal of methyl glyoxylate through distillation from phosphorus pentoxide, Hook, J. M. *Synth.Commun.* **1984**, *14*, 83. The methyl hemiacetal of methyl glyoxylate was obtained from Chemie Linz Ges. m.b.H., Linz, Austria.
12. Obtained by lithium aluminium hydride reduction of ethyl 2-acetoxy-4-pentenoate,[7] followed by treatment of the formed 4-penten-1,2-diol (83%) with *tert*-butyldiphenylsilyl chloride [1 equiv, Et_3N (1 equiv), DMAP (cat), CH_2Cl_2, 0 °C → rt, 5 h, 93%].
13. Obtained by lithium aluminium hydride reduction of methyl 2-cyclohexenecarboxylate, Davies, S. G.; Whitham, G. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2279.
14. Belleau, B.; Gulini, U.; Gour-Salin, B.; Ahmed, F. R. *Can. J. Chem.* **1985**, *63*, 1268.
15. For other examples of incorporation of fluoride see references 4d and 6a.
16. Schneider, H.-J.; Hoppen, V. *J. Org. Chem.* **1978**, *43*, 3866.
17. Schoemaker, H. E.; Dijkink, J.; Speckamp, W. N. *Tetrahedron* **1978**, *34*, 163.
18. For structural proof of the corresponding ethyl ester, see: Lolkema, L. D. M.; Hiemstra, H.; Al Ghouch, A. A.; Speckamp, W. N. *Tetrahedron Lett.* **1991**, *32*, 1491.
19. Dewar, M. J. S.; Reynolds, C. H. *J. Am. Chem. Soc.* **1984**, *106*, 1744.
20. Anderson, C. B.; Sepp, D. T. *J. Org. Chem.* **1968**, *33*, 3272; Eliel, E. L.; Hargrave, K. D.; Pietrusiewicz, K. M.; Manoharan, M. *J. Am. Chem. Soc.* **1982**, *104*, 3635.
21. Reviews: Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155. Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212; for an example of ester participation, see: Brückner, C.; Holzinger, H.; Reissig, H.-U. *J. Org. Chem.* **1988**, *53*, 2450.
22. Herrinton, P. M.; Hopkins, M. H.; Mishra, P.; Brown, M. J.; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 3711; Hirst, G. C.; Howard, P. N.; Overman, L. E. *J. Am. Chem. Soc.* **1989**, *111*, 1514; Hopkins, M. H.; Overman, L. E.; Rishton, G. M. *J. Am. Chem. Soc.* **1991**, *113*, 5354; Brown, M. J.; Harrison, T.; Herrinton, P. M.; Hopkins, M. H.; Hutchinson, K. D.; Mishra, P.; Overman, L. E. *J. Am. Chem. Soc.* **1991**, *113*, 5365; Brown, M. J.; Harrison, T.; Overman, L. E. *J. Am. Chem. Soc.* **1991**, *113*, 5378; Johnson, T. O.; Overman, L. E. *Tetrahedron Lett.* **1991**, *32*, 7361; Overman, L. E. *Acc. Chem. Res.* **1992**, *25*, 352.
23. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

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