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Chiral Orthoesters in Organic Synthesis: Novel Reagents for the Enantioselective Acylation of Silylenolethers

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Abstract: *Dialkyl trans-2-alkoxy-2-alkyl-1,3-dioxolan-4,5-dicarboxylates and the corresponding N,N,N,N-tetramethyl-4,5-diamides have been prepared respectively from dialkyl tartrates or tartaric acid diamides. They smoothly reacted with silylenolethers in the presence of Lewis acids to give enantiomerically enriched (up to 90% d.e.) monoprotected 1,3-diketones. A dramatic dependence of the stereochemical outcome from the configuration of the enolic double bond of* **4** *has been observed. The products can be stereoselectively reduced to give configurationally defined monoprotected 3-ketols.*

The control of the absolute and relative stereochemistry in the preparation of 1,3-difunctional compounds (such as 3-ketols, 1,3-diols, homoallylic alcohols, aminols etc.) represents a very important goal in the field of asymmetric synthesis, owing to the occurrence of these subunits in the framework of several natural, pharmacologically active molecules.

Two approaches have been widely applied to this aim, namely the condensation of carbonyl compounds and related derivatives (imines etc.) with enolates or substituted allyl-metal reagents.[1] In both the cases enantio and diastereocontrol are achieved in a single reaction process. Chiral auxiliaries bound to the metal or to the substrate can induce facial preference in the approach of the electrophile; on the other had, if chelating metals are used, the process involves «pericyclic» transition states that generally ensure high diastereoselectivity.

Very satisfactory results have been obtained by these methodologies, but we believe that an alternative strategy merit to receive a deeper attention: the enantioselective acylation of enolates.

In Figure 1 alternative approaches to the synthesis of chiral 3-ketols containing two stereocenters are shown: while the aldol condensation route (**a**) directly affords the product, the allyl-metal route (**b**) requires an extra step for the refunctionalization of the C=C bond. In both the cases a single product (**A** or **B**) is obtained from a defined pair of substrates. On the other hand, the acylation route (**c**) affords an oxidized precursor (**C**) of the target ketols, containing a sole stereogenic centre, that in principle can give rise to both **A** and **B** upon stereoselective reduction; in this way an additional possibility in the control of the relative stereochemistry is allowed.

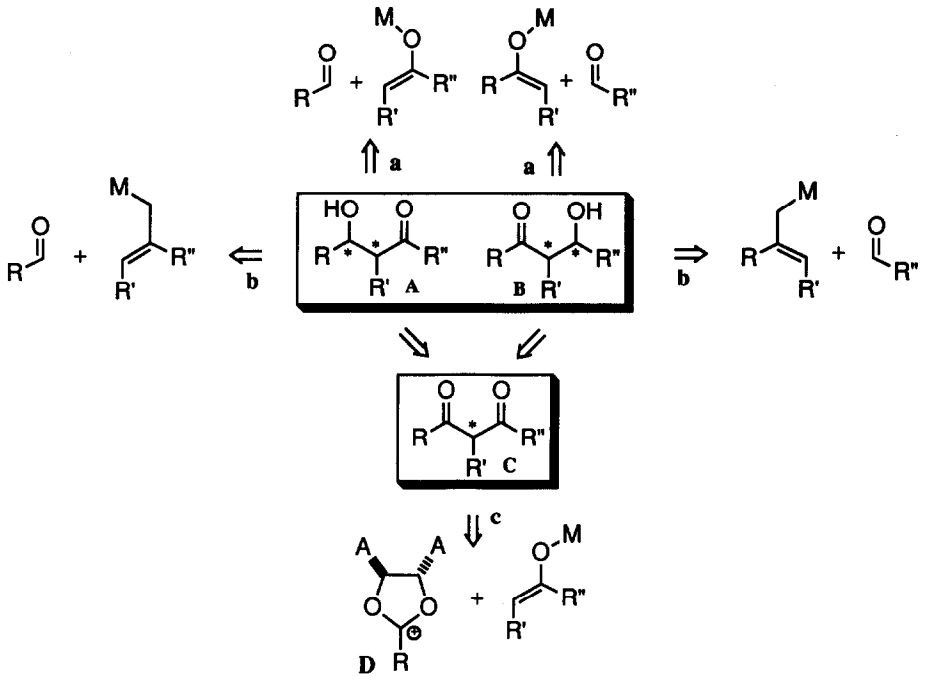


Fig. 1. Routes to the asymmetric synthesis of chiral ketols

The main drawback to this strategy is represented by the configurational lability of the 1,3-diketone **C** that has limited its applications to α,α-disubstituted enolates,[2] or to the special case of the sterically hindered amides employed by Evans.[3]

The use of suitably designed acyl cation equivalents should afford a protected derivative of **C**, so ensuring configurational stability and chemical flexibility. We have envisioned such synthetic templates into chiral 1,3-dioxolane-2-ilium ions[4] **D**, which, in turn, can be obtained from the interaction of Lewis acids with suitable orthoesters.

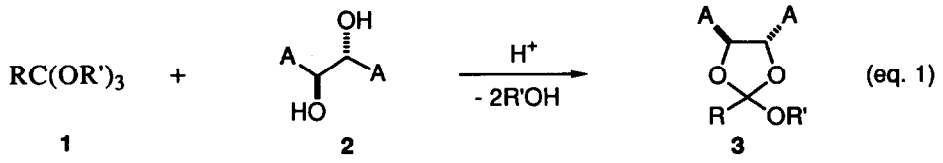
To this aim we recently reported preliminary results about the preparation of dialkyl *trans*-2-alkoxy-2-alkyl-1,3-dioxolan-4,5-dicarboxylates and their reaction with silylenolethers in the presence of Lewis acids.[5] In this paper we wish to fully describe this new type of enantioselective synthesis together with the problems and limitations found and some mechanistic implications that came into evidence.

Results and Discussion

The generation of 1,3-dioxolane-2-ilium ions from 2-alkoxy-1,3-dioxolanes and Lewis acids was discovered by Meerwein et al.;[6] they also highlighted the ambident electrophilic nature of these cations. Nevertheless their applications to organic synthesis have remained limited till now;[7] above all the use in asymmetric synthesis of homochiral 1,3-dioxolane-2-ilium ions or orthoesters was completely unknown.[8]

On the basis of previous experience on the use of tartaric acid based chiral auxiliaries in asymmetric synthesis,[9] we got convinced that tartaric acid derived 1,3-dioxolane-4,5-dicarboxylates-2-ilium ions could

represent good synthetic chiral equivalents of acyl cations. We succeeded in the preparation of the parent cyclic orthoesters by reacting dialkyl tartrates **2a** (R' = methyl, ethyl, isopropyl) with an excess of trimethyl or triethyl orthoesters **1**. Later we extended the preparation to 1,2-diols like **2b,c**. (eq. 1)

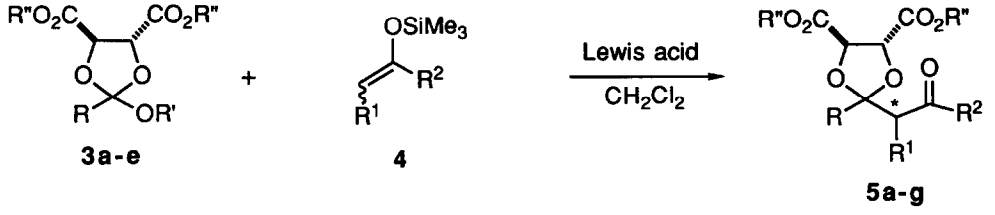


1 **2** **3**

1		2	3
R	R'	A	(yield %)
Me	Me	CO_2Me	**3a** (98)
Me	Me	CO_2Et	**3b** (98)
Me	Me	CO_2iPr	**3c** (60)
Et	Et	CO_2Et	**3d** (85)
Ph	Me	CO_2Et	**3e** (65)
Me	Me	$CONMe_2$	**3f** (65)
Me	Me	Ph	**3g** (70)

The cyclic orthoesters containing the tartaric acid moiety **3a-f** are stable and can be stored for months without decomposition (if care is taken to avoid the presence of traces of acids).; compound **3g** is poorly stable and is to be used within few days from the preparation.

With suitable chiral acyl cation equivalents in our hands we studied their use in enantioselective acylation reactions with silylenolethers **4**. A general picture of the reaction is highlighted in Scheme 1



Scheme 1. Reactions of Chiral Orthoesters **3a-e**

Acylation of Cyclic Ketones

A first crop of data, collected in Table 1, is related to cyclohexanone silylenolether **4** [R^1,R^2 = -$(CH_2)_4$-] and allowed to establish the efficiency of various Lewis acids in promoting the reaction and their effect on stereoselectivity. A diastereoisomeric mixture of acylated cyclohexanones **5b** is generally obtained; the isomers cannot be chromatographically separated, but their ratio can be determined by GC or by NMR through the integration of the peaks corresponding to the 4 and 5 position of the dioxolane ring.

Table 1. Reactions of **3b** with Silylenolether **4** [R^1,R^2 = -$(CH_2)_4$-] in the Presence of Various Lewis Acids[a]

Lewis Acid	T (°C)	t (h)	**5b** %[b]	D.e. %[c]
$TiCl_4$	-78	2	80	83
$BF_3{\cdot}OEt_2$	-60	3	75	80
$TfOSiMe_3$[d]	-40	12	68	50
$MgBr_2$[e]	0	120	0	—

[a] All the reactions were carried out in CH_2Cl_2 with a 1:2:2 **3b**:**4**:Lewis acid molar ratio according to the experimental procedure
[b] Relative to the chromatographically purified mixture of diastereoisomers
[c] Determined by NMR
[d] A catalytic amount (10% moles) of the Lewis acid is used
[e] Anhydrous $MgBr_2$ was prepared from Mg and 1,2-dibromoethane in Et_2O, then the solvent was evaporated and replaced with CH_2Cl_2

Strong Lewis acids like $BF_3{\cdot}OEt_2$ and $TiCl_4$ afford similar results, but the reaction temperature that must be kept slightly higher for the former; catalytic Me_3SiOTf gives lower stereoselectivity while weaker acids like $MgBr_2$ are totally ineffective. For this reason $TiCl_4$ or $BF_3{\cdot}OEt_2$ was used in further experiments.

Table 2. Reactions of Orthoesters **3a-e** with Cyclic Silylenolethers **4**[a]

Entry	Orthoester	[n-OSiMe$_3$] n	T (°C)	t (h)	R"O_2C, CO_2R' (Yield %)[c]	D.e. %[b]
1[d]	**3a**	1	-78	1	**5a** (80)	78
2	**3b**	1	-60	3	**5b** (75)	80
3	**3c**	1	-60	4	**5c** (80)	80
4	**3d**	1	-50	8	**5d** (75)	73
5	**3e**	1	-60	8	**5e** (93)	90
6	**3b**	0	-20[e]	24	**5f** (34)	43
7	**3b**	2	-60	2	**5g** (85)	71

[a] All the reactions were carried out in CH_2Cl_2 with a 1:2:2 **3**:**4**:$BF_3{\cdot}Et_2O$ molar ratio according to the experimental procedure
[b] Determined by NMR
[c] Relative to the chromatographically purified mixture of diastereoisomers
[d] $TiCl_4$ was used as Lewis acid
[e] At -60°C no product did form

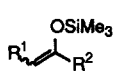
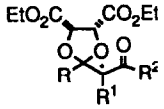
A more complete pattern of the acylation reaction of cyclic silylenolethers can be deduced from Table 2. Apart from the cyclopentanone derivative (entry 6) all the other experiments give yields superior to 70% and d.e. values from 70% to 89%. The effect of the substituent R of the orthoester is not very large, but a significant enhancement of stereoselectivity is found when passing from orthopropionate (entry 4) to orthoacetate (entry 2) to

orthobenzoate (entry 5). Significantly, an increasing in the size of the alkoxy substituent of the carboxylic groups do not affect stereoselectivity (entries 1,2,3).

Acylation of Open Chain Silylenolethers.

Moving to study open chain silylenolethers, the problem of the configuration of the enolic double bond has to be considered. To this aim we prepared some pure *Z* compounds by silylating the ketones with ethyl trimethylsilylacetate (ETSA) at low temperature,[10] and some *E* and *Z* mixtures of silylenolethers *via* metalation of the ketones with the lithium salt of 2,2,6,6-tetramethyl piperidine or diisopropyl amine, followed by silylation.[11] The following reaction with chiral orthoesters under usual conditions affords the expected products in good yields (Table 3). Again diastereoisomers were not separated but their ratio was determined as previously described.

Table 3. Reactions of Orthoesters **3b**, **3d**, **3e** with Open chain Silylenolethers **4**[a]

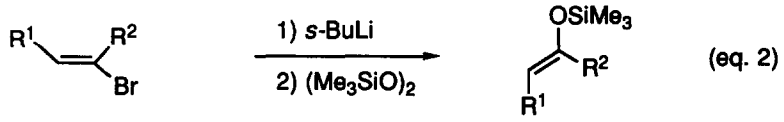
Entry	Orthoester				Lewis Acid	T (°C)	t (h)		D.e. %[b]
		R^1	R^2	E/Z[c]				(Yield %)[d]	
1	**3b**	Me	Et	2/98	$TiCl_4$	-78	2	**5h** (65)	0
2	**3b**	Me	Et	2/98	$BF_3{\cdot}OEt_2$	-60	5	**5h** (65)	0
3	**3b**	Et	*n*-Pr	2/98	$BF_3{\cdot}OEt_2$	-60	6	**5i** (61)	0
4	**3b**	Me	Ph	10/90	$BF_3{\cdot}OEt_2$	-60	3	**5j** (70)	50
5	**3b**	Me	Et	70/30	$TiCl_4$	-78	2	**5h** (75)	40
6	**3d**	Me	Et	82/18	$BF_3{\cdot}OEt_2$	-60	4	**5k** (70)	72
7	**3b**	Et	*n*-Pr	70/30	$TiCl_4$	-78	5	**5i** (60)	55
8	**3b**	Et	*n*-Pr	70/30	$BF_3{\cdot}OEt_2$	-60	4	**5i** (64)	66
9	**3b**	*n*-Pr	*n*-Pr	98/2	$BF_3{\cdot}OEt_2$	-60	2	**5l** (70)	90
10	**3d**	Et	Et	98/2	$BF_3{\cdot}OEt_2$	-60	5	**5m** (60)	84
11	**3e**	*n*-Pr	*n*-Pr	98/2	$BF_3{\cdot}OEt_2$	-60	5	**5n** (90)	88

[a] All the reactions were carried out in CH_2Cl_2 with a 1:2:2 3:4:Lewis acid molar ratio according to the experimental procedure
[b] Determined by NMR
[c] Ratio of *E* to *Z* silylenolethers isomers determined by GC
[d] Relative to the chromatographically purified mixture of diastereoisomers

The most impressive feature is the complete absence of stereoselectivity in the reactions of pure *Z* silylenolethers when R^1 and R^2 substituents have similar steric hindrance (entries 1, 2, 3). If the silylenolether's substituents are significantly different (entry 4), also in the case of *Z* enriched substrate, the product (**5j**) is formed in moderate diastereomeric excess. Mixtures of *E* and *Z* dialkyl silylenolethers (entries 5, 6, 7) do show stereoselectivity but afford d.e. values inferior to those of cyclic derivatives.

If we assume that in such mixtures the *Z* isomer gives a 1:1 ratio of products the *E* isomer results to react highly stereoselectively. To verify this assumption we prepared a few pure *E* silylenolethers: *E* vinylic bromides (from bromination-dehydrobromination of *E*-alkenes) were converted into *Z*-vinyllithium derivatives by treatment

with *s*-BuLi and allowed to react with *bis*-trimethylsilyl peroxide according to Davis et al.[12] (eq. 2). The geometrical purity of the so obtained silylenolethers, checked by GC and NMR, was higher than 97%.

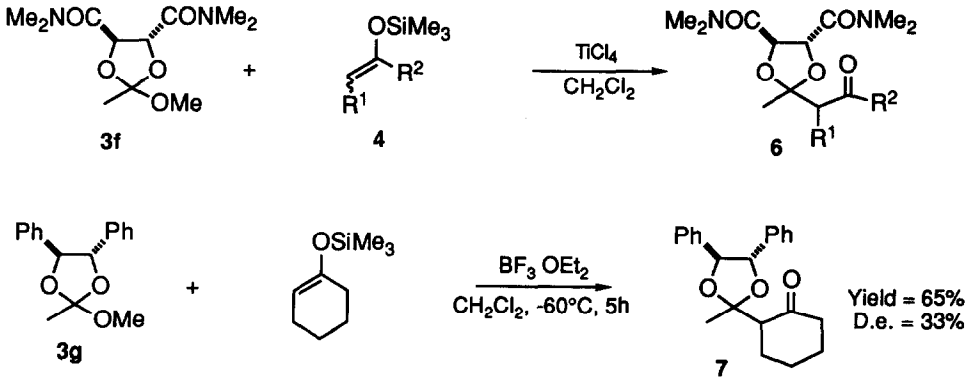


(eq. 2)

The results of the acylation of these enol derivatives are collected in Table 3 (entries 9, 10, 11). Stereoselectivities are good, even superior to those of cyclohexanone silylenolether and almost uneffected by the R group of orthoester; chemical yields are good too, expecially in the case of orthobenzoate (entry 11).

Use of Other Orthoesters.

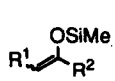
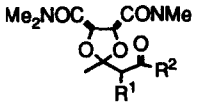
Orthoesters **3f** and **3g** have been tested in the reaction with silylenolethers (Scheme 2) and all gave the acylation products in satisfactory yield. In spite of the large steric hindrance, the diphenyl substituted substrate **3c** afforded the lower diastereomeric excess. Orthoester **3f**, derived from tartaric acid diamide, is completely unreactive in the presence of BF_3·OEt_2 but gives the expected products if $TiCl_4$ is used; stereoselectivity increases with respect to **3g**, but remains inferior to the values obtained from the ester containing substrates (Table 4).



Scheme 2. Reactions of Chiral Orthoesters **3b** and **3c**.

This trend reveals the importance of the carboxyl function as a substituent on the dioxolane ring to ensure high levels of asymmetric induction; the somewhat disappointing result afforded by **3f** with respect to **3b** was unexpected in consideration of the similarity of the ester and amide function and could be due to some change in the conformation of the intermediate 1,3-dioxolane-2-ilium ion.

Table 4. Reaction of Orthoester **3f** with Silylenolethers **4**[a]

Entry				Lewis Acid	T (°C)	t (h)		D.e. %[b]
	R^1	R^2	*E*/*Z*[c]				(Yield %)[d]	
1	-$(CH_2)_4$-		—	BF_3·OEt_2	25	40	—[e]	—
2	-$(CH_2)_4$-		—	$TiCl_4$	-78	15	**6a** (70)	60
3	Me	Et	70/30	$TiCl_4$	-78	15	**6b** (60)	33
4	Et	*n*-Pr	70/30	$TiCl_4$	-78	15	**6c** (66)	47

[a] All the reactions were carried out in CH_2Cl_2 with a 1:2:2 **3a**:4:Lewis acid molar ratio according to the experimental procedure
[b] Determined by NMR
[c] Ratio of E to Z silylenolethers isomers determined by GC
[d] Relative to the chromatographically purified mixture of diastereoisomers
[e] No product was formed

Mechanistic Aspects

The dramatic effect of the configuration of the silylenolether and the importance of the substituents of the dioxolane ring on the stereochemical outcome merit to be explained. A hypothetical transition state for the reaction of a silylenolether with orthoester **3a** could resemble the structure depicted in Fig. 2. Thanks to the C_2 symmetry of the chiral moiety of the orthoester, whatever will be the mechanism, i.e.if the attack of the nucleophile occur on a free dioxolane-2-ilium ion, or on an ion pair, or the reaction proceed through a concerted S_N2 pathway, it will not affect the main stereochemical features. The Neumann projections along the forming bond, corresponding to this transition structure are also shown in Fig. 2. The first upper two correspond to the attack of an *E* silylenolether from the *Si* face (**E**) and *Re* face (**F**) respectively. The structures for a *Z* nucleophile are shown in the lower part. In all the cases of the three staggered conformations only those having the hydrogen of the silylenolether facing the bulky dioxolane ring have been chosen to avoid large non-bonding interactions between reactants. The conformational problem deriving from the rotations around the CH—CO_2R" bond can be resolved if we take into account the absence of any effect from R" group; this means that the carboxylic substituent facing the incoming silylenolether points its carbonyl oxygen toward it and the alkoxy group in the opposite direction.[9] In the case of the *E* compound the transition structure **E** appears to be more stable than **F**, the latter suffering from a repulsive interaction between the carbonyl and the silylenolether oxygen's lone pairs. From these considerations it comes out that the product **E'** having the *S* configurations of the newly formed stereocentre should be preferentially obtained when *(R,R)* orthoesters are used.

Passing to *Z* nucleophiles we can see that no oxygen-oxygen interaction is present in the two transition structures shown in Fig. 2. The differences between the *Si* (**G**) and the *Re* (**H**) attack should come from weak steric interactions between the carbonyl group of the electrophile and the substituent of the silylenolether, respectively R^1 and R^2. The differences between these two groups are not very large in most of the cases examined and this fact can account for the lack of stereoselectivity generally exhibited by *Z* silylenolethers. When R^1 = Me and R^2 = Ph the 50% d.e. obtained (Table 3 entry 4) can be attributed to the greater steric hindrance of the phenyl group.

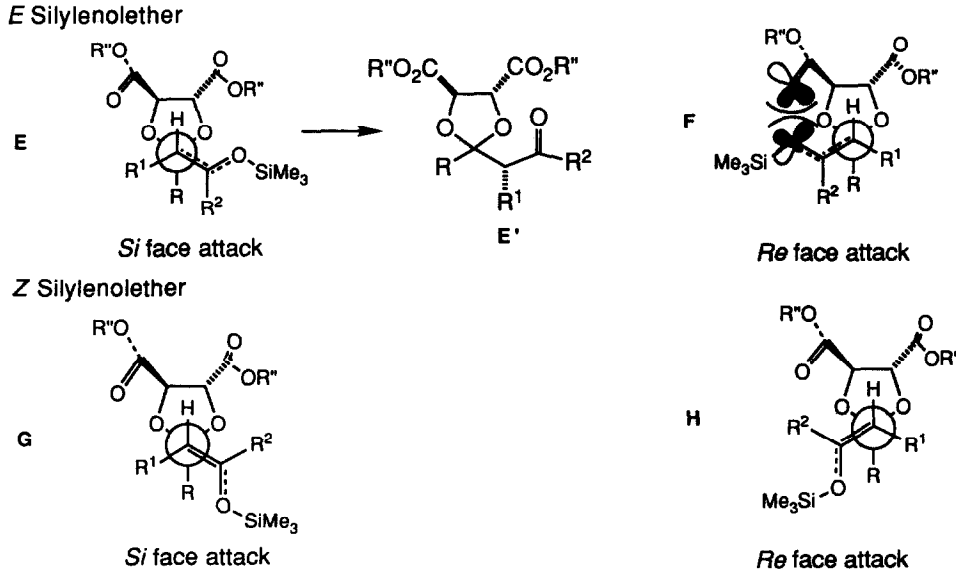
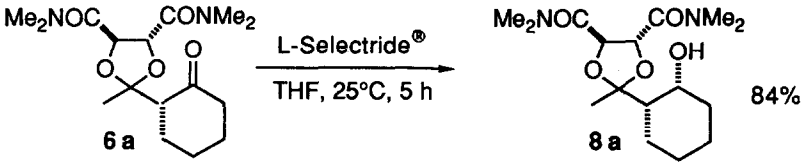


Fig 2. Hypothetical transition structures

Reductions of the Monoprotected Diketones 5 and 6 and Determination of the Absolute Configuration.

To complete the route toward the synthesis of configurationally defined 3-ketols we passed to study the possibility of stereoselectively reducing the free carbonyl function in compounds **5** and **6**.

Product **6a** cleanly reacts with L-Selectride® to give the monoprotected ketol **8a** as shown in Scheme 3.



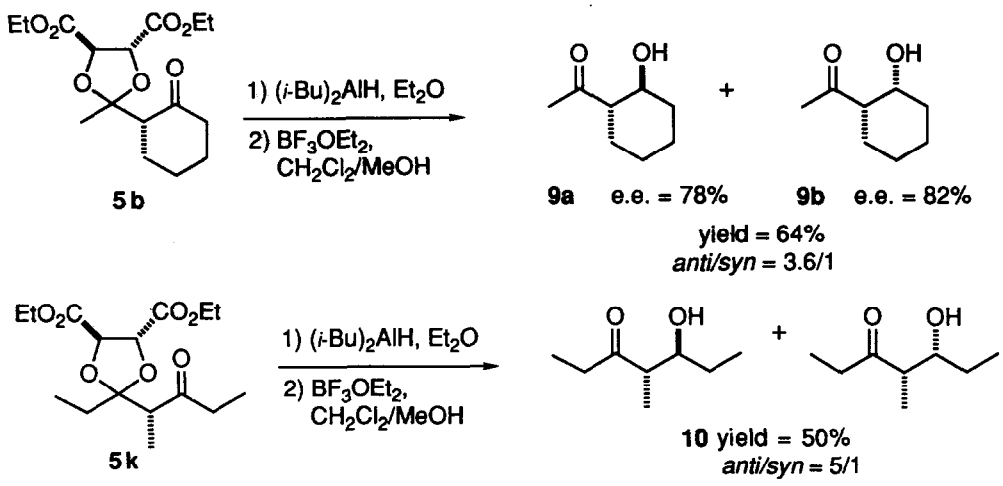
Scheme 3. Reduction of Product **6a**

Accordingly to the well known preference for the reductions of 2-substituted cyclohexanones with L-Selectride® to give exclusively the axial alcohol,[13] a single couple of products **8a** was formed in the same ratio of diastereoisomeric **6a**. On the basis of the ^{1}H-NMR spectrum we attribute the 1',2'-*syn* configuration to both these products.[14].

Compound **6b** and **6c** afford three alcohols when treated under the same conditions as **6a** in a 47 : 36 : 17 ratio for **8b** and 48: 25 : 27 for **8c**, but if the reaction temperature is lowered to -78° the formation of one of these product can be substantially depressed and **8b** is obtained in a 62 : 32 : 6 product ratio.

Attempts to apply the same reduction procedure to the ester containing substrates **5** always afforded unsatisfactory results, generally producing overreactivity and finally giving rise to very complex reaction mixtures. The change of the reducing agent was profitable; although no chemoselective C=O reduction could be

obtained, $LiAlH_4$ and expecially DIBAl-H were able to reduce both the carbonyl and the carboxyl C=O bonds, and, from these intermediates the deprotected 1,3-ketols were obtained by treatment with $BF_3{\cdot}OEt_2$ in $MeOH/CH_2Cl_2$ as depicted in Scheme 4.



Scheme 4. Reduction and deprotection of monoprotected 1,3-diketones **5**

Moderate stereoselectivity could be achieved from these transformations; significantly *anti* **9a** and *syn* **9b** 2-acetylcyclohexanols were easily separated, their relative stereochemistry was assigned keeping into account the presence of an axial coupling constant in the splitting pattern of the *CH*OH signal of the *anti* isomer and by comparison of the NMR chemical shifts with reported values[15] and the optical rotations of both the isomers were established. The enantiomeric excesses determined by the addition of chiral $Eu(hfc)_3$ was in agreement with the the diastereomeric excess of starting **5b**. Optically active 2-acetylcyclohexanol is not easily accessible from asymmetric aldol condensation and, at our knowledge, has never been previously prepared.

The same reaction sequence, when applied to **5k** afforded a mixture of *syn* and *anti* 4-methyl-5-hydroxy-3-heptanones **10** in a 1:5 ratio; the overall optical rotation of this mixtures was: $[\alpha]_D^{25} = +24.2$ (c 0.8 in Et_2O).

Since all the stereoisomeric 4-methyl-5-hydroxy-3-heptanones have been previously reported in the literature[16] we can definitively attribute the *(4S,5S)* configuration to the major isomer obtained. After excluding that significant isomerization could have occured in the reduction and deprotection steps[17] we concluded that the configuration of the newly formed stereocentre in **5k** is predominantly *S* and as a consequence, that the *Si* face of the silylenolether is preferentially acylated by *(R,R)* 4,5-dicarbethoxydioxolan-2-ilium ions as anticipated in the discussion of mechanistic aspects.

Conclusions

Optically active orthoesters derived from tartaric acid esters and amides have proved to be excellent precursors of chiral 1,3-dioxolan-2-ilium ions, being cheap, easily prepared and stable molecules. The acylation of silylenolethers by means of these reactants proceed in good yields and stereoselectivity when *E* substrates are

used, and represents a straightforward access to configurationally stable, monoprotected 1,3-diketones, that, in turn, appear to be extremely versatile precursors to a variety of 1,3-difunctional configurationally defined target molecules, 3-ketols being the most attractive ones.

Experimental

General. IR spectra were taken on a Perkin-Elmer PE 682 instrument and are reported in cm^{-1}. ^1H and ^{13}C-NMR spectra were all recorded with a Varian GEMINI-300 instrument in $CDCl_3$ solution, operating at 300 MHz for the former and 75.5 MHz for the latter; chemical shifts are given in δ units respect to TMS, coupling constants (J) are in Hz; in the case of inseparable pair of diastereoisomers, the full spectrum of the most abundant isomer is firstly reported, then, in square brackets, are shown only those peaks that can be unambiguously attributed to the minor component. MS spectra have been obtained with a Hewlett-Packard 5970 quadrupole instrument, using a HP 5890 gaschromatograph as the inlet system and electronic impact (70 eV) for ionization; spectra are reported in the order: m/e (relative abundance%).

All the compound prepared showed satisfactory microanalysis (C ± 0.2%, H ± 0.1%, N ±0.2%).

Routine TLC analyses were performed on silica gel plates (Kieselgel 60 F_{254}) purchased from Merck; the same company supplied silica gel for flash chromatography (230-400mesh).

All the reactions were carried out in oven-dried glassware and generally under Ar atmosphere. Anhydrous CH_2Cl_2 (<0.005% H_2O) was purchased by Fluka in Sure Seal™ bottles; other anhydrous solvents were dried: THF from Na-benzophenone ketyl, Et_2O from $LiAlH_4$, MeOH from Mg; anhydrous conditions were mantanied by means of standard syringe techniques.

Other commercially available chemical were obtained from Aldrich or Fluka and used without further purification. The preparation of silylenolethers by literature and standard procedures has been described in the text.

Preparation of Chiral Orthoesters **3a-g***: General Procedure.*

To a solution of a trialkyl orthoester **1** (120 mmol) and diol **2** (24 mmol) in benzene (30 ml) H_2SO_4 conc. (0.1 ml) is added and the reaction is heated at 80°C until TLC analysis shows the disappearance of **2**. After cooling, a saturated $NaHCO_3$ solution (10 ml) is added, the organic phase is separated and the aqueous layer extracted with $CHCl_3$ (3x20 ml), the combined organic fractions are then dried (Na_2SO_4) and concentrated. Purification of the product is performed by column chromatography using cyclohexane/EtOAc or $CHCl_3$/MeOH (**3f**) mixtures.

The following orthoesters have been prepared:

Dimethyl (4R)-trans-2-methoxy-2-methyl-1,3-dioxolan-4,5-dicarboxylate. **3a**: $[\alpha]_D^{25}$ = -28.45° (c 1.03 in $CHCl_3$). IR 2990, 1750, 1210, 1150, 1050, 740. ^1H-NMR 1.70 (s, 3H, CH_3C); 3.35 (s, 3H, OCH_3); 3.87 (s, 6H, $OCOCH_3$); 4.75 (d, 1H, J 5.4, CH); 5.00 (d, 1H, J 5.4, CH). MS 219 (3), 203 (34), 175 (79), 157 (3), 133 (5), 101 (16), 89 (12), 59 (47), 43 (100).

Diethyl (4R)-trans-2-methoxy-2-methyl-1,3-dioxolan-4,5-dicarboxylate. **3b**: $[\alpha]_D^{25}$ = -22.19° (c 0.96 in $CHCl_3$). IR 2990, , 1750, 1380, 1210, 1150, 1050, 740. ^1H-NMR 1.29 (t, 3H, J 7.1, CH_3CH_2O); 1.30 (t, 3H, J 7.1, CH_3CH_2O); 1.65 (s, 3H, CH_3C); 4.26 (q, 2H, J 7.1, CH_3CH_2O); 4.27 (m, 2H, CH_3CH_2O); 4.70 (d, 1H, J 5.4, CHO); 4.94 (d, 1H, J 5.4, CHO). ^{13}CNMR 13.78 (CH_3CH_2O); 20.93 (CH_3C); 50.29 (OCH_3); 61.83

(CH_3CH_2O); 76.37, 76.76 (CHO); 124.38 (OCO); 169.14, 169.31 (OC=O). MS 231 (18), 189 (87), 161 (5), 157 (5), 115 (13), 87 (14), 75 (14), 43 (100).

*Bis(1-methylethyl) (4R)-trans-2-methyl-2-methoxy-1,3-dioxolan-4,5-dicarboxylate.***3c**: $[\alpha]_D^{25}$ = -30.84° (c 1.07 in $CHCl_3$). IR 2990, 1750, 1385, 1375, 1220, 1160. ^{1}H-NMR 1.35 (d, 12H, J 6.0, CH_3CH); 1.70 (s, 3H, CH_3C), 3.40 (s, 3H, OCH_3); 4.65 (d, 1H, J 5.7, CHO); 4.90 (d, 1H, J 5.7, CHO); 5.15 (hept. 2H, CH_3CH). ^{13}C-NMR 21.30 (CH_3CH + CH_3C); 49.86 (OCH_3); 69.34 (CH_3CH); 76.27, 76.59 (CHO); 124.40 (OCO); 167.92, 168.23 (OC=O). MS 259 (12), 231 (2), 203 (80), 175 (25), 161 (90), 117 (100), 75 (65).

Diethyl (4R)-trans-2-ethoxy-2-ethyl-1,3-dioxolan-4,5-dicarboxylate. **3d**: $[\alpha]_D^{25}$ =-24.5° (c 1.15 in $CHCl_3$). IR 2980, 1750, 1380, 1210, 1150. NMR 0.97 (t, 3H, J 7.5, CH_3CH_2C); 1.11 (t, 3H, J 7.1, CH_3CH_2O); 1.27 (t, 3H, J 7.2, CH_3CH_2OC=O); 1.28 (t, 3H, J 7.2, CH_3CH_2OC=O) 1.89 (q, 2H, J 7.5, CH_3CH_2C); 3.50-3.66 (m, 2H, CH_3CH_2O); 4.16-4.32 (m, 4H, CH_3CH_2OC=O); 4.67 (d, 1H, J 5.7, CHO); 4.90 (d, 1H, J 5.7, CHO. ^{13}C-NMR 7.73 (CH_3CH_2O); 13.98, 14.84 (CH_3CH_2O); 20.05 (CH_3CH_2C); 58.11 (CH_3CH_2O); 61.79 (CH_3CH_2OC=O); 76.17, 76.80 (CHO); 126.00 (OCO); 168.83, 168.92 (OC=O). MS 261 (15), 245 (100), 217 (83), 171 (5), 143 (13), 115 (12), 89 (5), 57 (88).

Diethyl (4R)-trans-2-methoxy-2-phenyl-1,3-dioxolan-4,5dicarboxylate **3e**: $[\alpha]_D^{25}$ +10.17° (c 0.94 in $CHCl_3$. IR 2990, 2970, 2930, 1740, 1720, 1480, 1460, 1450, 1240, 1100, 1020, 700. ^{1}H-NMR 1.20 (t, 3H, J 7.1, CH_3CH_2O); 1.32 (t, 3H, J 7.1, CH_3CH_2O); 3.30 (s, 3H, OCH_3); 4.15 (q, 2H, J 7.1, CH_3CH_2O); 4.28 (q, 2H, J 7.1, CH_3CH_2O); 4.83 (d, 1H, J 6.0, CHO); 5.10 (d, 1H, J 6.0, CHO); 7.70-8.00 (m, 3H, Ar); 8.10-8.30 (m, 2H, Ar). ^{13}C-NMR 13.78, 13.92 (CH_3CH_2O); 51.06 (OCH_3); 61.79, 61.88 (CH_3CH_2O); 76.40, 76.76 (CHO); 123.63 (OCO); 126.33, 127.97, 129.33, 135.30 (Ar); 168.38, 168.60 (OC=O). MS 293 (100), 237 (3), 219 (3), 162 (2), 147 (2), 105 (63), 77(13).

(4R)-trans-N,N,N',N'-tetramethyl-2-methoxy-2-methyl-1,3-dioxolan-4,5-dicarboxamide **3f**: m.p. 58°C. = $[\alpha]_D^{25}$ = -1.12 (c 1.08 in $CHCl_3$); $[\alpha]_D^{365}$ = +17.7 (c 1.08 in $CHCl_3$). IR 3450, 2930, 1650, 1460, 1100. ^{1}H-NMR 1.60 (s, 3H, CH_3C); 3.05 (s, 6H, NCH_3); 3.25 (s, 6H, NCH_3); 3.35 (s, 3H, OCH_3); 5.27 (d, 1H, J 6.0, CHO); 5.45 (d, 1H, J 6.0, CHO). ^{13}C-NMR 22.16 (CH_3C); 35.41, 36.73 (NCH_3); 49.38 (OCH_3); 74.94, 75.54 (CHO); 123.62 (OCO); 167.53, 167.61 (NC=O). MS 245 (0.2), 229 (7), 186 (14), 156 (30), 114 (98), 98 (7), 72 (100).

trans-4,5-diphenyl-2-methoxy-2-methyl-1,3-dioxolane **3g**: ^{1}H-NMR 1.9 (s, 3H, CH_3C); 3.6 (s, 3H, OCH_3); 4.85 (d, 1H, J 9.0, CHO); 5.05 (d, 1H, J 9.0, CHO); 7.1-7.6 (m, 10H, Ar). MS 225 (0.4), 239 (8), 211 (2), 197 (16), 179 (25), 167 (56), 164 (89), 149 (25), 107 (54), 89 (29), 43 (100).

Acylation of silylenolethers with chiral orthoesters. Typical procedure: reaction of diethyl (4R)-trans-2-methoxy-2-methyl-1,3-dioxolan-4,5-dicarboxylate **3b** *with 1-(trimethylsilyloxy)cyclohex-1-ene (Table 1, entry 1).* A solution of **3b** (R = Me, R' = Me) (0.524 g, 2 mmol) and **4** [R^1,R^2 = $(CH_2)_4$] (0.68 g, 4 mmol) in anhydrous CH_2Cl_2 is cooled at -80°; after 5 min a solution of $TiCl_4$ (0.44 ml, 4 mmol) in CH_2Cl_2 (3 ml) is added dropwise with stirring. The resulting deep red solution is allowed to react at -80°C for 2 h then is quenched with a sat. $NaHCO_3$ solution (20 ml). The resulting mixture is filtered on celite pad and the solid is washed with CH_2Cl_2 (3x20 ml); the CH_2Cl_2 layer is separated and the aqueous layer extracted with $CHCl_3$ (2x20 ml). The combined organic phase is dried over anhydrous Na_2SO_4 and concentrated in vacuo, then the crude product is chromatographed using cyclohexane : EtOAc 8 : 2 to give a 91.5 : 8.5 (GC) mixture of diastereo-isomeric *diethyl*

(4R)-trans-2-methyl-2-(2-oxocyclohexyl)-1,3-dioxolan-4,5-dicarboxylate **5b** (0.525 g, 80% based on **3b**): IR 2990, 2970, 1750, 1720, 1450, 1440, 1380, 720. ^{1}H-NMR 1.22 (t, 3H, J 7.1, CH_3CH_2O) 1.25 (t, 3H, J 7.1, CH_3CH_2O); 1.55 (s, 3H, CH_3C), 1.55-1.80 (m, 3H); 1.80-2.10 (m, 2H); 2.10-2.45 (m, 3H); 2.79 (dd, 1H, J 5.0, 11.0, CHC=O); 4.25 (q, 2H, J 7.1, CH_3CH_2O); 4.27 (q, 2H, J 7.1, CH_3CH_2O); 4.65 (d, 1H, J 6.0, CHO); 4.74 (d, 1H, J 6.0, CHO); [4.61 (d, 1H, J 6.0, CHO); 4.76 (d, 1H, J 6.0, CHO)]. ^{13}C-NMR 14.17 (CH_3CH_2O); 22.71 (CH_3C); 24.81, 27.96, 29.60 (CH_2); 43.20 (CH_2C=O); 58.73 (*C*HC=O); 62.02 (CH_3CH_2O); 77.47, 78.14 (CHO); 115.03 (OCO); 169.76, 170.17 (OC=O); 209.47 (C=O); [22.80 (CH_3C); 24.88, 28.15, 29.33 (CH_2); 58.79 (*C*HC=O); 77.58, 77.87 (CHO)]. MS 313 (30), 255 (31), 231 (100), 203 (5), 161 (12), 95 (11), 67 (6).

The other acylation reactions have been carried out according to this procedure, in the presence of $TiCl_4$ or $BF_3{\cdot}OEt_2$, at the temperatures and for the times stated in Tables 1, 2, 3, and 4. Whenever $BF_3{\cdot}OEt_2$ or $TfOSiMe_3$ are used, no solid material is formed upon quenching and the filtration step is unnecessary. The following compounds have been obtained after column chromatography using cyclohexane/EtOAc mixtures as eluents, except for **6a,b,c** that require $CHCl_3$/MeOH elution.

Dimethyl (4R)-trans-2-methyl-2-(2-oxocyclohexyl)-1,3-dioxolan-4,5-dicarboxylate **5a**: IR 2980, 1750, 1720, 1380, 720. ^{1}H-NMR 1.54 (s, 3H, CH_3C); 1.60-1.80 (m, 3H); 1.85-2.15 (m, 2H); 2.15-2.45 (m, 3H); 2.78 (dd, 1H, J 5.0, 11.0, CHC=O); 3.80 (s, 3H, OCH_3); 3.81 (s, 3H, OCH_3); 4.72 (d, 1H, J 5.9, CHO); 4.80 (d, 1H, J 5.9, CHO); [1.55 (s, 3H, CH_3C); 3.79 (s, 3H, OCH_3); 3.80 (s, 3H, OCH_3); 4.67 (d, 1H, J 5.9, CHO); 4.84 (d, 1H, J 5.9, CHO)]. ^{13}C-NMR 22.94 (CH_3C); 25.14, 28.23, 29.70 (CH_2); 43.47 (CH_2C=O); 53.12 (OCH_3); 58.97 (*C*HC=O); 77.48, 78.17 (CHO); 115.41 (OCO); 170.47, 170.84 (OC=O); 209.62 (C=O); [22.85 (CH_3C); 28.43, 29.93 (CH_2); 77.63, 77.88 (CHO). MS 285 (10), 241 (10), 203 (100), 175 (2), 143 (5), 85 (9), 43 (26).

Bis(1-methyethyl) (4R)-trans-2-methyl-2-(2-oxocyclohexyl)-1,3-dioxolan-4,5-dicarboxylate **5c**: IR 2990, 1760, 1720, 1380, 720. ^{1}H-NMR 1.30 (d, 12H, J 6.2, CH_3CH); 1.56 (s, 3H, CH_3C); 1.60-1.85 (m, 3H); 1.85-2.15 (m, 2H); 2.15-2.50 (m, 3H); 2.82 (dd, 1H, J 5.0, 11.0, CHC=O); 4.60 (d, 1H, J 6.1, CHO); 4.70 (d, 1H, J 6.1, CHO); 5.12 (hept, 1H, J 6.2, CH_3CH); 5.13 (hept, 1H, J 6.2, CH_3CH); [4.57 (d, 1H, J 6.2, CHO); 4.71 (d, 1H, J 6.2, CHO)]. ^{13}C-NMR 22.00, 22.05, 23.06 (CH_3); 25.04, 28.28, 29.54 (CH_2); 43.53 (CH_2C=O); 59.01 (*C*HC=O); 70.17, 70.23 (CH_3CH); 77.86, 78.49 (CHO); 115.23 (OCO); 169.68, 170.13 (OC=O); 210.25 (C=O); [22.87 (CH_3); 29.86 (CH_2); 58.92 (*C*HC=O); 77.93 (CHO)]. MS 341 (11), 259 (100), 217 (26), 175 (53), 147 (18), 85 (11), 43 (61).

Diethyl (4R)-trans-2-ethyl-2-(2-oxocyclohexyl)-1,3-dioxolan-4,5-dicarboxylate **5d**: IR 2980, 1750, 1720, 1230. ^{1}H-NMR 0.94 (t, 3H, J 7.3, CH_3CH_2C); 1.31 (t, 6H, J 7.1, CH_3CH_2O); 1.60-1.90 (m, 4H); 1.90-2.15 (m, 3H); 2.15-2.50 (m, 3H); 2.84 (dd, 1H, J 5.0, 11.0, CHC=O); 4.28 (q, 4H, J 7.1, CH_3CH_2O); 4.68 (d, 1H, J 7.1, CHO); 4.72 (d, 1H, J 7.1, CHO);[0.92 (t, 3H, J 7.3, CH_3CH_2C); 1.30 (t, 6H, J 7.1, CH_3CH_2O); 4.26 (q, 4H, J 7.1, CH_3CH_2O); 4.65 (d, 1H, J 7.2, CHO); 4.70 (d, 1H, J 7.2, CHO)]. ^{13}C-NMR 7.63 (CH_3CH_2C); 14.37 (CH_3CH_2O); 24.99, 28.13, 28.90, 28.99 (CH_2); 43.50 (CH_2C=O); 56.30 (*C*HC=O); 62.21 (CH_3CH_2O); 78.33, 78.38 (CHO); 117.07 (OCO); 169.81, 169.91; (OC=O); 209.90 (C=O); [7.46 (CH_3CH_2C); 28.40, 28.74, 29.47 (CH_2); 56.62 (*C*HC=O)]. MS 313 (79), 269 (11), 245 (100), 161 (10), 125 (28), 97 (10), 57 (36).

Diethyl (4R)-trans-2-phenyl-2-(2-oxocyclohexyl)-1,3-dioxolan-4,5-dicarboxylate **5e**: IR 2990, 1740, 1720, 1240, 1100. ^{1}H-NMR 1.16 (t, 3H, J 7.1, CH_3CH_2O); 1.31 (t, 3H, J 7.1, CH_3CH_2O); 1.55-2.10 (m, 6H,

CH_2); 2.20-2.45 (m, 2H, CH_2C=O); 3.10 (dd, 1H J 4.6, 9.7, CHC=O); 4.00 (m, 2H, CH_3CH_2O); 4.28 (q, 2H, J 7.1, CH_3CH_2O); 4.73 (d, 1H, J 6.3, CHO); 4.84 (d, 1H, J 6.3, CHO); 7.25-7.40 (m, 3H, Ar); 7.50-7.60 (m, 2H, Ar); [4.71 (s, 2H, CHO)]. ^{13}C-NMR 14.27, 14.47 (CH_3CH_2O); 24.53, 28.14, 29.24 (CH_2); 43.50 (CH_2C=O); 58.96 (*CH*C=O); 62.09, 62.33 (CH_3CH_2O); 77.15, 77.28 (CHO); 114.30 (OCO); 127.58, 128.35, 129.21, 140.37 (Ar); 169.20, 169.69 (OC=O); 208.61 (C=O); [23.74, 28.91 (CH_2); 42.16 (CH_2C=O)]. MS 345 (1), 293 (100), 265 (5), 219 (1), 147 (2), 105 (60), 77 (8).

Diethyl (4R)-trans-2-methyl-2-(2-oxocyclopentyl)-1,3-dioxolan-4,5-dicarboxylate **5f**: IR 2990, 1730, 1370. ^{1}H-NMR 1.28 (t; 6H, J 7.1, CH_3CH_2O); 1.55 (s, 3H, CH_3C); 1.60-2.30 (m, 6H, CH_2); 2.45-2.60 (m, 1H, CHC=O); 4.25 (q, 2H, J 7.1, CH_3CH_2O); 4.26 (q, 2H, J 7.1, CH_3CH_2O); 4.63 (d, 1H, J 6.5, CHO); 4.70 (d, 1H, J 6.5, CHO); [1.53 (s, 3H, CH_3C); 4.67 (d, 2H, J 6.6, CHO); 4.75 (d, 1H, J 6.6, CHO)]. ^{13}C-NMR 14.51 (CH_3CH_2O); 20.92 (CH_2); 23.96 (CH_3C); 25.85 (CH_2); 40.13 (CH_2C=O); 56.57 (*CH*C=O); 62.47 (CH_3CH_2O); 77.70, 78.52 (CHO); 115.32 (OCO); 169.59, 170.49 (OC=O); 209.42 (C=O); [20.60 (CH_2); 24.27 (CH_3C); 26.27 (CH_2); 56.28 (*CH*C=O)]. MS 299 (22), 241 (14), 231 (100), 157 (5), 117 (11), 85 (10), 43 (27).

Diethyl (4R)-trans-2-methyl-2-(2-oxocycloheptyl)-1,3-dioxolan-4,5-dicarboxylate **5g**: IR 2990, 1730, 1370. ^{1}H-NMR 1.33 (t, 3H, J 7.1, CH_3CH_2O); 1.35 (t, 3H, J 7.1, CH_3CH_2O); 1.52 (s, 3H, CH_3C); 1.60-2.20 (m, 8H, CH_2); 2.40-2.85 (m, 2H, CH_2C=O); 2.93 (dd, 1H, J 4.0, 11.2, CHC=O); 4.30 (q, 2H, J 7.1, CH_3CH_2O); 4.32 (q, 2H, J 7.1, CH_3CH_2O);4.68 (d, 1H, J 6.3, CHO); 4.78 (d, 1H, J 6.3, CHO); [1.55 (s, 3H, CH_3C); 4.66 (d, 1H, J 5.7, CHO); 4.76 (d, 1H, J 5.7, CHO)]. ^{13}C-NMR 14.43 (CH_3CH_2O); 23.66 (CH_3C); 25.95, 28.03, 30.18 (CH_2); 43.79 (CH_2C=O); 61.32 (*CH*C=O); 62.48, 62.54 (CH_3CH_2O); 77.72, 78.23 (CHO); 115.77 (OCO); 169.87, 170.42 (OC=O); 214.15 (C=O); [23.30 (CH_3C); 24.32, 25.17, 28.74, 29.65 (CH_2); 44.12 (CH_2C=O); 60.28 (*CH*C=O); 77.57 (CHO); 115.99 (OCO); 213.99 (C=O)]. MS 327 (8), 269 (10), 231 (100), 203 (4), 161 (13), 117 (4), 85 (2), 43 (21).

Diethyl (4R)-trans-2-methyl-2-(3-oxopent-2-yl)-1,3-dioxolan-4,5-dicarboxylate **5h**: IR 2990, 1750, 1710, 1370, 1100. ^{1}H-NMR 1.02 (t, 3H, J 7.3, CH_3CH_2C=O); 1.20 (d, 3H, J 7.1, CH_3CH); 1.32 (t, 3H, J 7.1, CH_3CH_2O); 1.35 (t, 3H, J 7.1, CH_3CH_2O); 1.45 (s, 3H, CH_3C); 2.49 (dq, 1H, J 7.3, 18.5, CH_3CH_2C=O); 2.70 (dq, 1H, J 7.3, 18.5, CH_3CH_2C=O); 3.04 (q, 1H, J 7.1, CHC=O); 4.28 (q, 2H, J 7.1, CH_3CH_2O); 4.30 (q, 2H, J 7.1, CH_3CH_2O); 4.78 (s, 2H, CHO); [1.18 (d, 3H, J 7.1, CH_3CH); 4.70 (d, 1H, J 6.4, CHO); 4.28 (d, 1H, J 6.4, CHO)]. ^{13}C-NMR 7.62, 12.58 (CH_3); 14.17 (CH_3CH_2O); 21.83 (CH_3C); 37.24 (CH_2C=O); 54.07 (*CH*C=O); 62.13 (CH_3CH_2O); 77.62, 77.94 (CHO); 115.98 (OCO); 169.77, 169.97 (OC=O); 212.37 (C=O); [12.71 CH_3CH_2); 21.49 (CH_3C); 36.95 (CH_2C=O); 54.27 (*CH*C=O); 77.73, 77.86 (CHO)]. MS 301 (8), 245 (7), 231 (100), 203 (5), 161 (10), 57 (24), 43 (25).

Diethyl (4R)-trans-2-methyl-2-(4-oxohept-3-yl)-1,3-dioxolan-4,5-dicarboxylate **5i** IR 2990, 1750, 1370, 1100. ^{1}H-NMR 0.80 (t, 3H, J 7.5, CH_3CH_2); 0.90 (t, 3H, J 7.5, CH_3CH_2); 1.28 (t, 3H, J 7.1, CH_3CH_2O); 1.31 (t, 3H, J 7.1, CH_3CH_2O); 1.38 (s, 3H, CH_3C), 1.45-1.90 (m, 4H, CH_3CH_2); 2.25-2.50 (m, 1H, CH_2C=O); 2.50-2.70 (m, 1H, CH_2C=O); 2.85 (dd, 1H, J 2.6, 8.5, CHC=O); 4.25 (q, 2H, J 7.1, CH_3CH_2O); 4.28 (q, 2H, J 7.1, CH_3CH_2O); 4.74 (d, 1H, J 6.4, CHO); 4.76 (d, 1H, J 6.4, CHO); [1.36 (s, 3H, CH_3C); 4.64 (d, 1H, J 6.4, CHO); 4.70 (d, 1H, J 6.4, CHO)]. ^{13}C-NMR 12.84, 14.10, 14.51, 14.54 (CH_3) 17.07 (CH_2); 21.79 (CH_3C); 22.29 (CH_2); 48.46 (CH_2C=O); 62.49 (*CH*C=O + CH_3CH_2O); 77.94, 78.13 (CHO); 116.16 (OCO); 170.15, 170.27 (OC=O); 212.22 (C=O); [17.01, 21.91, 22.04, 48.22; 62.86 (CH_3CH_2O)]. MS 329 (4), 271 (8), 259 (8), 231 (100), 203 (4), 161 (8), 117 (6), 89 (4), 43 (12).

Diethyl (4R)-trans-2-methyl-2-(3-oxo-3-phenylprop-2-yl)-1,3-dioxolan-4,5-dicarboxylate **5j**: IR 2990, 1750, 1680, 1590, 1450, 1380, 720. ^{1}H-NMR 1.28 (t, 3H, J 7.1, CH_3CH_2O); 1.30 (t, 3H, J 7.1, CH_3CH_2O); 1.35 (d, 3H, J 7.1, CH_3CH); 1.60 (s, 3H, CH_3C); 4.07 (q, 1H, J 7.1, CHC=O); 4.23 (m, 2H, CH_3CH_2O); 4.28 (q, 2H, J 7.1, CH_3CH_2O); 4.76 (d, 1H, J 5.1, CHO); 4.82 (d, 1H, J 5.1, CHO); 7.44-7.64 (m, 3H, Ar); 7.94-8.08 (m, 2H, Ar); [1.20 (t, 3H, J 7.1, CH_3CH_2O); 4.73 (s, 2H, CHO)]. ^{13}C-NMR 13.60, 13.76 (CH_3); 22.21 (CH_3C); 48.59 (CHC=O); 61.87, 61.95 (CH_3CH_2O); 76.58, 77.01 (CHO); 116.34 (OCO); 128.63, 128.75, 135.15, 137.77 (Ar); 169.85 (OC=O); 201.30 (C=O); [21.65 (CH_3C); 48.56 (CHC=O); 61.89 (CH_3CH_2O); 77.26 (CHO); 128.96, 133.20 (Ar)]. MS 349 (5), 291 (5), 231 (100), 161 (13), 105 (87), 77 (21), 43 (29).

Diethyl (4R)-trans-2-ethyl-2-(3-oxopent-2-yl)-1,3-dioxolan-4,5-dicarboxylate **5k**: IR 2990, 2970, 1760, 1370. ^{1}H-NMR 0.92 (t, 3H, J 7.3, CH_3CH_2C); 1.01 (t, 3H, J 7.2, CH_3CH_2C=O); 1.16 (d, 3H, J 7.0, CH_3CH); 1.30 (t, 3H, J 7.1, CH_3CH_2O); 1.31 (t, 3H, J 7.1, CH_3CH_2O); 1.67-1.85 (m, 2H, CH_3CH_2C); 2.50 (dq, 1H, J 7.2, 18.5, CH_3CH_2C=O); 2.68 (dq, 1H, J 7.2, 18.5, CH_3CH_2C=O); 3.06 (q, 1H, J 7.0, CHC=O); 4.27 (q, 4H, J 7.1, CH_3CH_2O); 4.65 (d, 1H, J 7.4, CHO); 4.73 (d, 1H, J 7.4 CHO); [1.04 (t, 3H, J 7.2, CH_3CH_2C=O); 3.11 (q, 1H, J 7.1, CH_3CH); 4.59 (d, 1H, J 7.8, CHO); 4.64 (d, 1H, J 7.8, CHO)]. ^{13}C-NMR 6.98, 7.60, 12.18 (CH_3); 14.15 (CH_3CH_2O); 27.87 (CH_2C); 37.18 (CH_2C=O); 52.35 (CHC=O) 62.18 (CH_3CH_2O); 77.73, 78.23 (CHO); 117.40 (OCO); 169.40 (OC=O)169.52 (OC=O); 212.63 (C=O); [6.63, 12.57 (CH_3); 27.02 (CH_3CH_2C); 36.82 (CH_2C=O); 53.14 (CHC=O); 78.47 (CHO)]. MS 301 (15), 257 (6), 245 (100), 217 (3), 57 (40).

Diethyl (4R)-trans-2-methyl-2-(5-oxooct-4-yl)-1,3-dioxolan-4,5-dicarboxylate **5l**: IR 2990, 2970, 1760, 1370. ^{1}H-NMR 0.88 (t, 3H, J 7.4, CH_3CH_2); 0.89 (t, 3H, J 7.4, CH_3CH_2); 1.12-1.26 (m, 2H); 1.30 (t, 3H, J 7.2, CH_3CH_2O); 1.33 (t, 3H, J 7.2, CH_3CH_2O); 1.40 (s, 3H, CH_3C); 1.46-1.63 (m, 3H); 1.72-1.87 (m, 1H); 2.37 (ddd, 1H, J 6.5,7.9, 18.0, CH_2C=O); 2.61 (ddd, 1H, J 6.7, 7.9, 18.0); 2.95 (dd, 1H, J 3.0, 11.3, CHC=O); 4.26 (q, 2H, J 7.2, CH_3CH_2O); 4.28 (m, 2H, CH_3CH_2O); 4.76 (d, 1H, J 5.6, CHO); 4.78 (d, 1H, J 5.6, CHO); [4.67 (d, 1H, J 5.6, CHO); 4.72 (d, 1H, J 5.6, CHO)]. ^{13}C-NMR 13.37, 13.81, 13.93 (CH_3); 16.28, 21.00 (CH_2) 21.51 (CH_3C); 30.17 (CH_2); 47.79 (CH_2C=O); 59.78 (CHC=O); 61.90 (CH_3CH_2O); 77.13, 77.32 (CHO); 115.16 (OCO); 169.56, 169.71 (OC=O); 211.54 (C=O). MS 343 (1) 285 (5), 231 (100), 161 (10), 89 (13, 43 (38).

Diethyl (4R)-trans-2-ethyl-2-(4-oxohex-3-yl)-1,3-dioxolan-4,5-dicarboxylate **5m**: IR 2990, 2970, 1760, 1370. 0.81 (t, 3H, J 7.4, CH_3CH_2C); 0.90 (t, 3H, J 7.3, CH_3CH_2CH); 1.02 (t, 3H, J 7.2, CH_3CH_2C=O); 1.30 (t, 3H, J 7.1, CH_3CH_2O); 1.32 (t, 3H, J 7.1, CH_3CH_2O); 1.75 (q, 2H, J 7.4, CH_3CH_2C); 1.78- 1.95 (m, 2H, CH_3CH_2CH); 2.40 (dq, 1H, J 7.2, 18.0, CH_3CH_2C=O); 2.68 (dq, 1H, J 7.2, 18.0, CH_3CH_2C=O); 2.91 (dd, 1H, J 3.1, 11.3, CHC=O); 4.28 (m, 4H, CH_3CH_2O); 4.65 (d, 1H, J 7.3, CHO); 4.75 (d, 1H, J 7.3, CHO); [0.89 (t, 3H, J 7.3, CH_3CH_2CH); 1.01 (t, 3H, J 7.2, CH_3CH_2C=O); 4.54 (d, 1H, J 8.7, CHO); 4.64 (d, 1H, J 8.7, CHO)]. ^{13}C-NMR 6.32, 6.93, 12.03, 13.62 (CH_3); 20.37, 27.43 (CH_2) 38,52 (CH_2C=O); 60.09 (CHC=O); 64.64 (CH_3CH_2O); 77.27, 77.71 (CHO); 116.78 (OCO); 168.81, 169.12 (OC=O); 211.98 (C=O);. MS 315 (13), 260 (22), 245 (100), 217 (2), 161 (4), 99 (6), 57 (73).

Diethyl (4R)-trans-2-phenyl-2-(5-oxooct-4-yl)-1,3-dioxolan-4,5-dicarboxylate **5n**: IR 2990, 2970, 1740, 1720, 1480, 1240, 1100, 700. ^{1}H-NMR 0.80 (t, 3H, J 7.2, $CH_3CH_2CH_2$); 0.85 (t, 3H, J 7.3, $CH_3CH_2CH_2$); 1.21 (t, 3H, J 7.4, CH_3CH_2O); 1.30 (t, 3H, J 7.4, CH_3CH_2O); 1.31-1.60 (m, 5H); 1.65-1.95 (m, 1H); 2.37 (ddd, 1H, J 6.6, 8.1, 17.9, CH_2C=O); 2.55 (ddd, 1H, J 6.6, 8.1, 17.9, CH_2C=O); 3.16 (dd, 1H, J 3.2, 11.6, CHC=O); 4.03 (m, 2H, CH_2CH_2O); 4.26 (q, 2H, J 7.4, CH_3CH_2O); 4.58 (d, 1H, J 6.9, CHO); 4.67 (d, 1H, J 6.9,

CHO); 7.25-7.40 (m, 3H, Ar); 7.40-7.55 (m, 2H, Ar); [4.68 (d, 1H, J 6.9, CHO); 4.70 (d, 1H, J 6.9, CHO)]. ^{13}C-NMR 13.40 (CH_3), 13.62 (CH_3); 13.78 (CH_3CH_2O); 14.98 (CH_2), 16.29 (CH_2); 20.64 (CH_2); 47.10 (CH_2C=O); 60.18 (CHC=O); 61.55, 61.81 (CH_3CH_2O); 76.58, 77.43 (CHO); 113.92 (OCO); 126.81, 127.97, 128.91, 139.40 (Ar); 168.19 (OC=O); 168.81 (OC=O); 210.43 (C=O). MS 347 (2), 293 (100), 265 (5), 161 (10), 105 (50), 43 (20).

(4R)-trans N,N,N',N'-tetramethyl-2-methyl-2-(2-oxocyclohexyl)-1,3-dioxolan-4,5-dicarboxamide **6a**: IR 3450, 2920, 1710, 1645, 1050. ^{1}H-NMR 1.51 (s, 3H, CH_3); 1.60-1.80 (m, 3H) 1.85-2.05 (m, 2H); 2.15-2.40 (m, 3H); 2.80 (dd, 1H, J 3.2, 11.0, CHC=O); 2.95 (s, 3H, NCH_3); 2.96 (s, 3H, NCH_3); 3.14 (s, 3H, NCH_3); 3.18 (s, 3H, NCH_3); 5.08 (d, 1H, J 6.7, CHO); 5.31 (d, 1H, J 6.7, CHO); [2.94 (s, 3H, NCH_3); 3.16 (s, 3H, NCH_3); 3.17 (s, 3H, NCH_3); 5.09 (d, 1H, J 6.7, CHO); 5.32 (d, 1H, J 6.7, CHO)].^{13}C-NMR 22.25(CH_3C); 24.39, 27.62, 28.91 (CH_2); 35.62, 36.96 (NCH_3); 42.91 (CH_2C=O); 58.17 (CHC=O); 74.62, 76.09 (CHO); 112.82 (OCO); 168.26, 168.34 (NC=O); 209.78 (C=O); [27.85, 29.34 (CH_2); 43.16 (CH_2C=O); 74.95, 75.77 (CHO)]. MS 326 (1), 229 (11), 186 (21), 156 (8), 114 (100), 72 (71).

(4R)-trans N,N,N',N'-tetramethyl-2-methyl-2-(3-oxopent-2-yl)-1,3-dioxolan-4,5-dicarboxamide **6b**: IR 2920, 1710, 1645, 1050, ^{1}H-NMR 1.02 (t, 3H, J 7.3, CH_3CH_2); 1.13 (d, 3H, J 7.1, CH_3CH); 1.37 (s, 3H, CH_3C); 2.48 (dq, 1H, J 7.3, 18.5, CH_3CH_2); 2.62 (dq, 1H, J 7.3, 18.5, CH_3CH_2); 2.71 (q, 1H, J 7.1, CHC=O); 2.96 (s, 3H, NCH_3); 2.97 (s, 3H, NCH_3); 3.15 (s, 3H, NCH_3); 3.17 (s, 3H, NCH_3); 5.25 (d, 1H, J 6.0, CHO); 5.32 (d, 1H, J 6.0, CHO); [1.01 (t, 3H, J 7.3, CH_3CH_2); 1.14 (d, 3H, J 7.1, CH_3CH); 1.39 (s, 3H, CH_3C); 2.96 (s, 3H, NCH_3); 3.16 (s, 3H, NCH_3); 3.18 (s, 3H, NCH_3); 5.19 (d, 1H, J 6.0, CHO); 5.29 (d, 1H, J 6.0, CHO). ^{13}C-NMR 7.98 (CH_3CH_2); 12.88 (CH_3CH); 22.11 (CH_3C); 36.29, 37.56 (NCH_3); 37.56 (CH_3CH_2); 54.39 (CH_3CH); 75.93, 76.49 (CHO); 114.46 (OCO); 168.67, 168.93 (NC=O); 212.96 (C=O); [13.11 (CH_3CH); 21.62 (CH_3C); 37.29 (CH_3CH_2); 54.03 (CH_3CH); 75.77, 76.37 (CHO); 114.53 (OCO); 168.48, 168.67 (NC=O); 213.15 (C=O)]. MS 314 (0.4), 242 (0.5), 229 (9), 186 (16), 156 (4), 114 (89), 72 (100).

(4R)-trans N,N,N',N'-tetramethyl-2-methyl-2-(4-oxohept-3-yl)-1,3-dioxolan-4,5-dicarboxamide **6c**: IR 2920, 1710, 1645, 1050. ^{1}H-NMR 0.77 (t, 3H, J 7.5, CH_3CH_2); 0.86 (t, 3H, J 7.5, CH_3CH_2); 1.32 (s, 3H, CH_3C); 1.45-1.61 (m, 3H); 1.64-1.81 (m, 1H), 2.28-2.42 (m, 1H, CH_2C=O); 4.48-2.66 (m, 1H, CH_2C=O); 2.83 (dd, 1H, J 3.6, 11.0, CHC=O); 2.93 (s, 3H, NCH_3); 2.95 (s, 3H, NCH_3); 3.12 (s, 3H, NCH_3); 3.15 (s, 3H, NCH_3); 5.28 (d, 1H, J 6.1, CHO); 5.32 (d, 1H, J 6.1, CHO); [0.85 (t, 3H, J 7.2, CH_3CH_2); 1.34 (s, 3H, CH_3C); 2.94 (s, 3H, NCH_3); 3.11 (s, 3H, NCH_3); 3.14 (s, 3H, NCH_3), 5.21 (s, 2H, CHO)]. ^{13}C-NMR: 12.19, 13.45 (CH_3CH_2);16.28, 21.05 (CH_2); 21.49 (CH_3C); 35.63, 36.86 (NCH_3); 47.66 (CH_2C=O); 61.82 (CHC=O); 75.73, 75.66 (CHO); 113.75 (OCO); 168.14, 168.40 (NC=O); 211.76 (C=O); [16.21, 21.21 (CH_2); 21.30 (CH_3C); 35.49, 35.58 (NCH_3); 47.43 (CH_2C=O); 61.54 (CHC=O); 75.01, 75.53 (CHO); 113.75 (OCO); 167.80, 168.40 (NC=O); 211.76 (C=O); [16.21, 21.21 (CH_2); 21.30 (CH_3C); 35.49, 35.58 (NCH_3); 47.43 (CH_2C=O); 61.54 (CHC=O); 75.01, 75.53 (CHO); 113.83 (OCO); 167.81 (NC=O); 211.99 (C=O)]. MS 342 (3), 270 (2), 229 (29), 186 (18), 142 (8), 114 (100), 72 (79).

Trans-2-methyl-2-(2-oxocyclohexyl)-4,5-diphenyl-1,3-dioxolane **7**: ^{1}H- NMR 1.7- 2.15 (m, 5H); 1.77 (s, 3H, CH_3); 2.33-2.58 (m, 3H); 2.93 (dd, 1H, J 2.7, 10.5, CHC=O); 4.76 (d, J 9.5, CHO); 4.80 (d, 1H, J 9.5, CHO); 7.18-7.36 (m, 10H, Ar); [1.74 (s, 3H, CH_3); 4.70 (d, 1H, J 8.1, CHO); 4.73 (d, 1H, J 8.1, CHO)]. ^{13}C-NMR 23.61 (CH_3); 24.45, 27.60, 28.80 (CH_2); 42.99 (CH_2C=O); 58.96 (CHC=O); 84.75, 85.82 (CHO); 109.82 (OCO); 126.74, 126.99, 128.44, 136.11, 137.11 (Ar); 209.80 (C=O); [23.32 (CH_3); 24.34, 27.78,

29.21 (CH_2); 59.12 (*CH*C=O); 84.89, 85.67 (CHO); 126.83, 128.25), 128.30, 136.25 (Ar); 210.21 (C=O]. MS 239 (18), 230 (74), 197 (32), 187 (39), 143 (13), 124 (100), 91 (71), 67 (32), 43 (92).

Reduction of compounds **6a**, **6b**, **6c** *with L-Selectride®. Typical Procedure: Preparation of (4R)-trans-N,N,N',N'-tetramethyl-2-methyl-2-(2-hydroxycyclohexyl)-1,3-dioxolan-4,5-dicarboxamide* (**8a**). To a cooled (0°C), stirred solution of **6a** (80 : 20 diastereomeric mixture) (0.490 g, 1.5 mmol) in anhydrous THF (10 ml), a 1 M solution of L-Selectride® in THF (1.65 ml) is added dropwise. The reaction mixture is then allowed to reach room temperature and mantained for 5 h at this temperature. A 10% aqueous NH_4Cl solution (10 ml) is then added and the product extracted with $CHCl_3$ (3x20 ml). The combined organic phase is dried (Na_2SO_4), concentrated in vacuo, and the crude product chromatographed on silica gel ($CHCl_3$: MeOH 95 : 5), affording **8a** as a 80 :20 mixture of diastereoisomers (0.413 g, 84%): IR 3450, 2930, 1685, 1500, 1400, 1150, 1055, 970. ^{1}H-NMR (after D_2O exchange) 1.15-1.50 (m, 2H, CH_2); 1.43 (s, 3H, CH_3C); 1.55-1.95 (m, 7H); 2.97 (s, 3H, NCH_3), 2.98 (s, 3H, NCH_3); 3.17 (s, 3H, NCH_3); 3.19 (s, 3H, NCH_3); 4.25-4.29 (m, 1H, *CH*OH); 5.03 (d, 1H, J 6.6, CHO); 5.44 (d, 1H, J 6.6, CHO); [1.39 (s, 3H, CH_3C); 2.98 (s, 3H, NCH_3); 3.16 (s, 3H, NCH_3); 3.18 (s, 3H, NCH_3); 4.34-4.38 (m, 1H, *CH*OH); 4.86 (d, 1H, J 6.9, CHO); 5.47 (d, 1H, J 6.9, CHO)]. ^{13}C-NMR 19.70, 20.51 (CH_2); 24.23 (CH_3); 26.04 (CH_2); 33.19 (CH_2); 35.98, 37.31 (NCH_3); 49.69 (*CH*CHOH); 65.89 (CHOH); 75.14, 76.32 (CHO); 115.73 (OCO); 168.38, 169.03 (NC=O); [19.63, 20.91 (CH_2); 23.81 (CH_3); 26.35 (CH_2); 36.14, 37.13 (NCH_3); 49.28 (*CH*CHOH); 65.16 (CHOH); 73.98, 77.61 (CHO); 115.90 (OCO). MS 328 (0.4), 256 (0.7), 229 (21), 186 (15), 142 (7), 114 (100), 72 (70).

According to this procedure the following products have been obtained. The complete spectrum of the major diastereoisomer present is firstly reported, then, in square brackets the peaks that can be unambiguously attributed to the second most abundant isomer, and finally in brace the peaks of the minor one:

(4R)-Trans-N,N,N',N',-tetramethyl-2-methyl-2-(3-hydroxypent-2-yl)-1,3-dioxolan-4,5-dicarboxamide **8b**: IR 3450, 2930, 1685, 1500, 1400, 1150, 1055, 970. ^{1}H-NMR (after D_2O exchange) 0.93 (t, 3H, J 7.1, CH_3CH_2); 0.98 (d, 3H, J 7.1, CH_3CH); 1.25-1.50 (m, 1H, CH_2), 1.44 (s, 3H, CH_3C); 1.50-1.70 (m, 1H, CH_2); 1.82 (dq, 1H, J 1.4, 7.1, CH_3CH); 2.95 (s, 6H, NCH_3); 3.15 (s, 6H, NCH_3); 3.91 (ddd, 1H, J 1.4, 5.8, 7.4, *CH*OH); 5.10 (d, 1H, J 6.9, CHO); 5.42 (d, 1H, J 6.9, CHO); [1.42 (s, 3H, CH_3C); 1.94 (dq, 1H, J 7.1, 8.7, CH_3CH); 3.52 (ddd, 1H, J 3.1, 7.9, 8.7 *CH*OH); 5.14 (d, 1H, J 6.7, CHO); 5.38 (d, 1H, J 6.7, CHO)]; {1.04 (d, 3H, J 7.1, CH_3CH); 1.39 (s, 3H, CH_3C); 4.02 (ddd, 1H, J 1.0, 5.7, 6.8, *CH*OH); 4.83 (d, 1H, J 7.1, CHO); 5.52 (d, 1H, J 7.1, CHO)}. ^{13}C-NMR 7.55 (CH_3CH_2); 11.06 (CH_3CH); 24.07 (CH_3C); 28.25 (CH_2); 36.21, 37.49 (NCH_3); 45.32 (CH_3CH); 72.13 (CHOH); 75.54, 76.31 (CHO); 116.67 (OCO); 168.63,169.23 (NC=O); [9.38 (CH_3CH_2); 13.29 (CH_3CH); 20.86 (CH_3C); 27.58 (CH_2); 37.35 (NCH_3); 46.08 (CH3*CH*); 73.97 (CHOH); 75.87 (CHO); 117.48 (OCO); 168.52 (NC=O)]; {7.99 (CH_3CH_2); 11.26 (CH_3CH); 28.18 (CH_2); 36.47 (NCH_3); 44.95 (CH_3CH); 70.92 (CHOH); 74.15, 77.93 (CHO); 116.99 (OCO)}. MS 316 (0.5), 243 (0.6), 229 (20), 186 (17), 156 (1), 114 (100), 98 (5), 72 (48).

(4R)-Trans-N,N,N',N'-tetramethyl-2-methyl-2-(4-hydroxyhept-3-yl)-1,3-dioxolan-4,5-dicarboxamide **8c** IR 3450, 2930, 1685, 1500, 1400, 1150, 1055, 970, ^{1}H-NMR (after D_2O exchange) 0.93 (t, 3H, J 7.1, CH_3CH_2); 1.02 (t, 3H, J 7.1, CH_3CH_2); 1.20-1.80 (m, 7H); 1.42 (s, 3H, CH_3C); 2.97 (s, 3H, NCH_3); 2.98 (s, 3H, NCH_3); 3.17 (s, 6H, NCH_3); 3.96-4.03 (m, 1H, *CH*OH); 5.12 (d, 1H, J 6.6, CHO); 5.42 (d, 1H, J 6.6, CHO); [0.94 (t, 3H, J 7.1, CH_3CH_2); 1.03 (t, 3H, J 7.1, CH_3CH_2); 1.45 (s, 3H, CH_3C); 3.15 (s, 3H, NCH_3); 3.18 (s, 3H, NCH_3); 4.08-4.15 (m, 1H, *CH*OH); 4.86 (d, 1H, J 6.6, CHO); 5.51 (d, 1H, J 6.6, CHO)]; {3.16 (s, 3H, NCH_3); 3.19 (s, 3H, NCH_3); 3.63-3.74 (m, 1H, *CH*OH); 5.16 (d, 1H, J 6.6, CHO), 5.37 (d, 1H, J

6.6, CHO)}. ^{13}C-NMR 13.73, 14.93 (*CH$_3$*CH$_2$); 16.73, 19.38 (CH$_2$); 23.80 (*CH$_3$*C); 35.59, 36.80, 36.86 (NCH$_3$); 37.27 (*CH$_2$*CHOH); 52.64 (*CH*CHOH); 70.48 (CHOH); 74.83, 75.49 (CHO); 116.59 (OCO); 168.03, 168.38 (NC=O); [13.85, 15.40 (*CH$_3$*CH$_2$); 16.90 (CH$_2$); 23.68 (CH$_3$C); 36.75, 37.14 (NCH$_3$); 52.27 (*CH*CHOH); 69.02 (CHOH); 73.59, 75.76 (CHO); 116.87 (OCO); 168.69, 168.90 (NC=O)]; {13.02 (*CH$_3$*CH$_2$); 18.56, 20.73 (CH$_2$); 22.24 (CH$_3$C); 35.85 (NCH$_3$) 36.98 (*CH$_2$*CHOH); 52.55 (*CH*CHOH); 71.37 (CHOH); 74.23 (CHO); 116.71 (OCO); 168.19, 168.69 (NC=O)}. MS 344 (0.3), 301 (0.6), 272 (0.7), 229 (57), 186 (27), 142 (8), 114 (99), 72 (100).

Trans-1-(2-hydroxycyclohexyl)ethanone **9a** and *cis-1-(2-hydroxycyclohexyl)ethanone* **9b.** A solution of **5b** (0.328 g, 1 mmol) in anhydrous Et$_2$O (5 ml) is cooled at -100°C. Diisobutylaluminum hydride (0.8 ml, 5 mmol), dissolved in Et$_2$O (5 ml) is added dropwise with stirring. After keeping at -100°C for 1h, the reaction is quenched by addition of 3 N HCl up to pH 2-3. The reaction mixture is extracted with EtOAc (3 x 20 ml), and the combined organic layers are dried (Na$_2$SO$_4$) and concentrated in vacuo. The residue is then dissolved in 3 ml of dry CH$_2$Cl$_2$ and 1 ml of dry MeOH under Ar atmosphere. BF$_3$·OEt$_2$ (0.16 ml, 1 mmol) is added as CH$_2$Cl$_2$ solution (2 ml) at room temperature. After 24 h a sat. aq. NaHCO$_3$ solution (5 ml) is added and the mixture is extracted with EtOAc (3 x 20 ml). After drying and concentration, column chromatography allowed to separate: **9a** (0.071 g, 50%) $[\alpha]_D^{25}$ +39.1 (c 0.69 in Et$_2$O). IR 3440, 1700. ^{1}H-NMR 1.20-1.30 (m, 4H, CH$_2$); 1.70-1.80 (m, 2H, CH$_2$); 1.90-2.10 (m, 2H, CH$_2$); 2.18 (s, 3H, CH$_3$); 2.35 (ddd, 1H, J 3.1, 9.4, 11.6, CHC=O); 2.63 (br. s, 1H, OH); 3.75-3.85 (m, 1H, *CH*OH); upon addition of (+)-Eu(hfc)$_3$ two peaks at δ 5.50, and δ 5.78 in a 89 : 11 ratio were detected. ^{13}C-NMR 24.49, 25.47, 28.05, 29.23 (CH$_2$); 33.82 (CH$_3$); 59.12 (*CH*C=O); 70.96 (CHOH); 213.71 (C=O). MS 142 (5), 124 (20), 109 (10), 81 (40), 71 (62), 67 (37), 43 (100). **9b** (0.020 g, 14%): $[\alpha]_D^{25}$ -13.1° (c 0.84 in Et$_2$O). IR 3440, 1700. ^{1}H-NMR 1.24-1.28 (m, 3H); 1.40-1.50 (m, 1H); 1.62-1.90 (m, 4H); 2.20 (s, 3H, CH$_3$); 2.48 (ddd, 1H, J 2.2, 6.0, 9.5, CHC=O); 3.20 (br. s, 1H, OH); 4.18-4.24 (m, 1H, *CH*OH); upon addition of Eu(hfc)$_3$ two peaks at δ 4.85, and δ 5.00 in a 9 : 91 ratio were detected. ^{13}C-NMR 23.32, 25.37, 28.81, 29.68 (CH$_2$); 31.83 (CH$_3$); 53.89 (*CH*C=O); 66.19 (CHOH); 213.23.

4-Methyl-5-hydroxyheptan-3-one **10** Compound **5k** (0.330 g, 1 mmol) was subjected to the same reduction procedure described for the cyclohexanone derivative **5b**. Column chromatography of the crude reaction product afforded an inseparable mixture of *anti* and *syn* **10** (0.72 g, 50%): $[\alpha]_D^{25}$ +24.2 (c 0.8 in Et$_2$O). Comparison of the ^{1}H and ^{13}C-NMR spectra with those reported by Mori et al.[16] allowed us to attribute the *anti* configuration to the most abundant isomer.

References and Notes

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14. The 300 MHz ^{1}H-NMR spectrum of compound **8a**, after D_2O exchange, showed two not well resolved peaks corresponding to the *CH*OH signals of the two diastereoisomeric products respectively coming from diastereoisomeric starting ketones. Although it was not possible to exactly establish the H1'-H2' cyclohexanol coupling constant, from the width of those peaks (7.5.Hz at half height, 14 Hz at the base) we can judge that, for an ABC*X* system, only small coupling constant are present. So the H1' proton must be in an equatorial position, otherwise large axial-axial coupling constant should be present, and the OH group must be axial. Since the very large dioxolane substituent should adopt an equatorial arrangement we can conclude that the configuration of cyclohexanol is *cis* and so the relative stereochemistry of the reduction is *syn*.
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16. Mori, K.; Ebata, T. *Tetrahedron* **1986**, *42*, 4421. The following specific rotation values were reported for the four stereoisomers of 4-methyl-5-hydroxyheptan-3-one: *(4R,5R)* $[\alpha]_D^{23}$ -37.8° (c 1.20 in ether), *(4S,5S)* $[\alpha]_D^{22}$ +36.8° (C 1.25 in ether), *(4R,5S)* $[\alpha]_D^{20}$ -26.7° (c 1.52 in ether), *(4S,5R)* $[\alpha]_D^{20}$ +27.0° (c 1.24 in ether)
17. To ascertain that no *syn/anti* epimerization could have occurred during the deprotection step, pure *syn*-4-(1-hydroxyhexyl)hexan-3-one, independently prepared according to: Boldrini, G. P.; Mancini, F.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Chem. Soc., Chem. Commun.* **1990**, 1680, was treated with a five fold excess of $BF_3{\cdot}OEt_2$ in MeOH-CH_2Cl_2 for 24h at room temperature and then with sat. aq. $NaHCO_3$ solution. Although some decomposition occurred, the ^{1}H-NMR spectrum showed that no *anti* isomer was formed.

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