78. Mono- and Dialkylation of Derivatives of (1*R*,2*S*)-2-Hydroxycyclopentanecarboxylic Acid and -cyclohexanecarboxylic Acid *via* Bicyclic Dioxanones: Selective Generation of Three Contiguous Stereogenic Centers on a Cyclohexane Ring[1])

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Dedicated to Dr. *Günther Ohloff* on the occasion of his 65th birthday

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Ethyl (1*R*,2*S*)-2-hydroxycyclopentanecarboxylate and -cyclohexanecarboxylate (**1a** and **2a**, respectively) obtained in 40 and 70% yield by reduction of 3-oxocyclopentanecarboxylate and cyclohexanecarboxylate, respectively *(Scheme 2)*, with non-fermenting yeast, are converted to bicyclic dioxanone derivatives **3** and **4** with formaldehyde, isobutyraldehyde, and pivalaldehyde *(Scheme 3)*. The Li-enolates of these dioxanones are alkylated (→**5a–5i, 5j, 6a–6g**), hydroxyalkylated (→ **5l,m, 6d,e**), acylated (→ **5k, 6c**) and phenylselenenylated (→**7–9**) with usually high yields and excellent diastereoselectivities (*Scheme 3*, *Tables 1* and *2*). All the major isomers formed under kinetic control are shown to have *cis*-fused bicyclic structures. Oxidation of the seleno compounds **7–9** leads to α,β-unsaturated carbonyl derivatives **10–13** *(Scheme 3)* of which the products **12a–c** with the C=C bond in the carbocyclic ring (exocyclic on the dioxanone ring) are most readily isolated (70–80% from the saturated precursors). *Michael* addition of Cu(I)-containing reagents to **12a–c** and subsequent alkylations afford dioxanones **14a–i** and **16a–d** with *trans*-fused cyclohexane ring *(Scheme 4)*. All enolate alkylations are carried out in the presence of the cyclic urea DMPU as a cosolvent. The configuration of the products is established by NMR measurements and chemical correlation. Some of the products are converted to single isomers of monocyclic hydroxycyclopentane (**17–19**) and cyclohexane derivatives (**20–23**; *Scheme 5*). Possible uses of the described reactions for EPC synthesis are outlined. The observed steric course of the reactions is discussed and compared with that of analogous transformations of monocyclic and acyclic derivatives.

Introduction. – In the course of our endeavour in the synthesis of enantiomerically pure compounds (EPC synthesis [3] [4]) from α- and β-amino- and hydroxyacids [5–8] we have recently studied the modification of (*R*)-3-hydroxybutanoic acid (**A**) *via* dioxanone derivatives *(Scheme 1)*. Thus, stereoselective alkylation at C(2) of this acid is possible *via* the enolate **B** [9] or the *Michael* acceptor **C** [10]. New substituents can be introduced at C(3) *via* the dioxinone **D** [11] [12] and at C(4) by generating the dienolate **E** [13–15].

Since it is highly desirable to have access to functionalized cyclopentane and cyclohexane derivatives with quaternary C-atoms [16] in enantiomerically pure form, we have investigated the reactions of bicyclic dioxinones from the readily available (1*R*,2*S*)-2-

[1]) Partially published in preliminary form [1] or mentioned in a previous paper [2].

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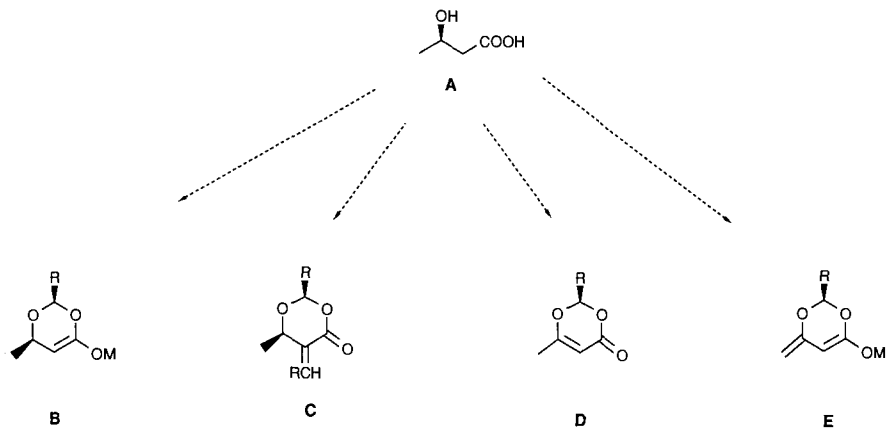
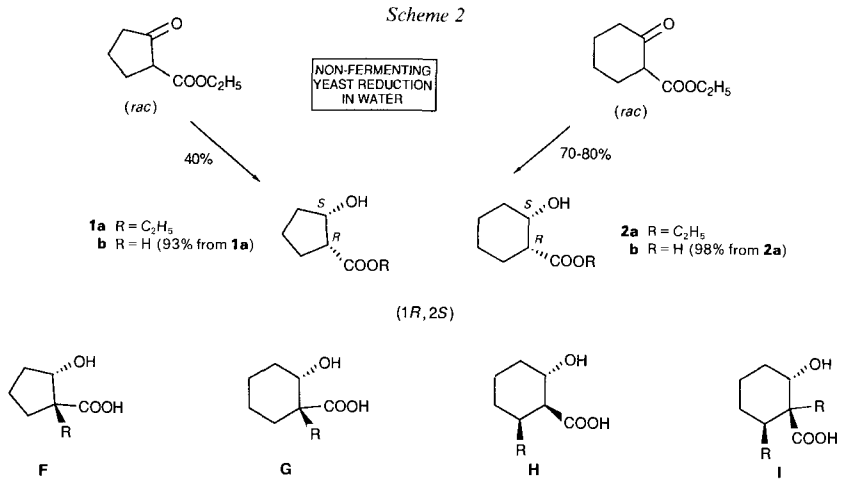
Scheme 1



hydroxycyclopentanecarboxylic acid (**1b**) and -cyclohexanecarboxylic acid (**2b**)[3][4] *(Scheme 2)*. In this paper, we will show that hydroxycycloalkanecarboxylic-acid derivatives of type **F**, **G**, **H**, and **I** can be prepared highly selectively[5]).

Inspite of the advent of a possibly more powerful method of reducing β-keto-esters enantioselectively [29], we made use of the yeast reduction of ethyl 2-oxocyclopentan-

Scheme 2



[3]) Recent examples of EPC syntheses of functionalized cyclopentanes are: [3 + 2] cycloadditions [17], cyclizations of 3,3-disubstituted 2,5-diones [18], transformations of camphor [19] and of suitable carbohydrates [20] [21], and a recent gingkolide synthesis [22].

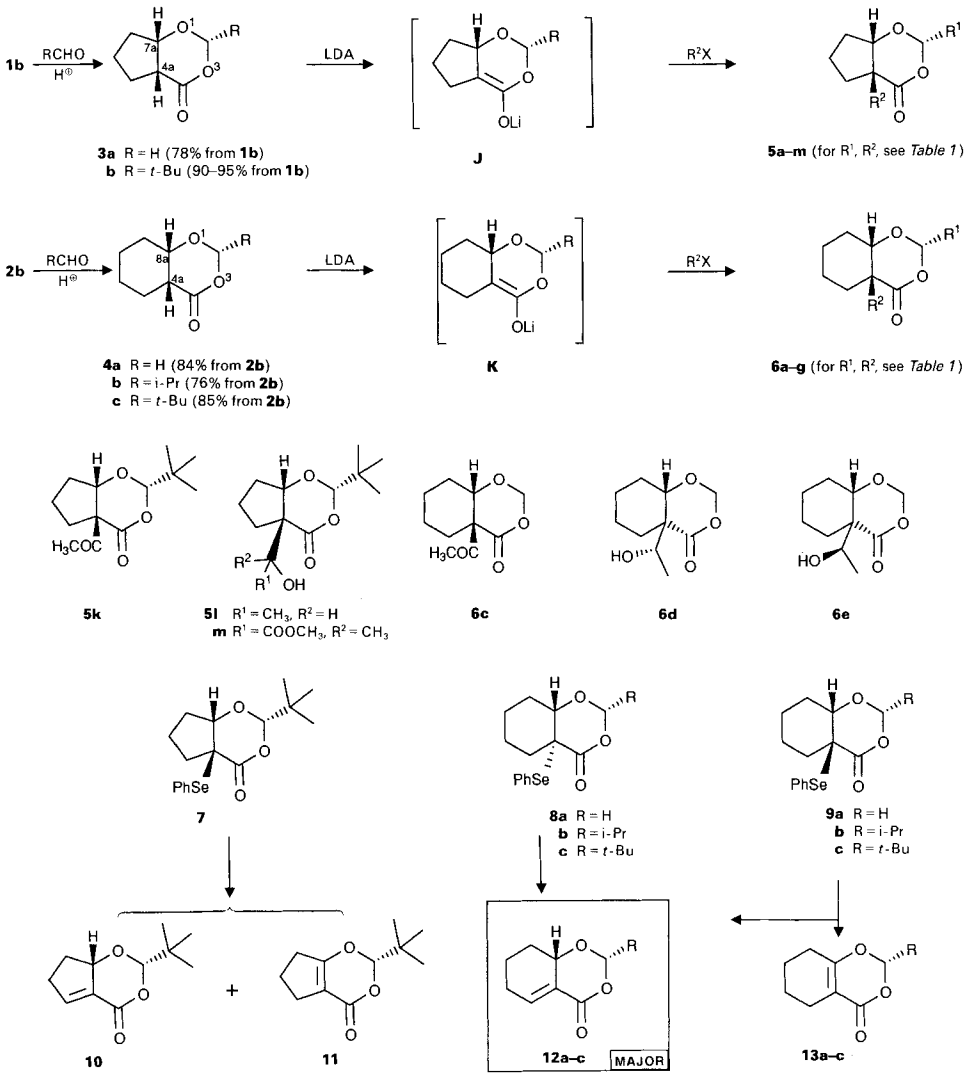
[4]) Enantiomerically pure cyclohexane derivatives have been recently synthesized by *Michael* addition of organocopper reagents to (*R*)- and (*S*)-5-(trimethylsilyl)cyclohex-2-enone [23], by diastereoselective *Birch* reduction and reductive alkylation of chiral benzoic- and anthranilic-acid derivatives [24], or from the pool of chiral building blocks [25], using monoterpenes [19a] [26] or carbohydrates [20] [27] as starting materials.

[5]) Structures of type **F**–**I** occur in a wide variety of natural products [28].

carboxylate [30] [31] and -cyclohexanecarboxylate[6]) [30a] [31] [33] [34]. The application of this reaction and its stereoselectivity were greatly improved by switching to non-fermenting conditions[7]) [31]. The esters **1a** and **2a** were saponified to the corresponding acids **1b** and **2b** [35], which were pure, single isomers.

Results. – The hydroxy-acids **1b** and **2b** were converted to the bicyclic dioxanones **3** and **4**, respectively, by acid-catalyzed acetalization with paraformaldehyde, isobutyralde-

Scheme 3



[6]) For analogous reactions of 2-oxothiacyclopentancarboxylates and -cyclohexanecarboxylates, see [32].

[7]) In a battery of 20 2-l flasks a total of 100 g of the keto-ester can be reduced by a total of 2.5 kg of yeast in 20 l H_2O within 1 day on a shaking apparatus (see *Exper. Part*).

hyde, or pivalaldehyde in benzene or toluene by heating under reflux in the presence of or under molecular sieve [36] [37], in yields exceeding 80% *(Scheme 3)*. In those cases which could have led to two stereoisomeric products, one isomer was formed preferentially (**3b**: > 98% ds; **4b**: 95% ds; **4c**: > 98% ds). The configuration of the newly formed acetal center was determined to be *S* by nuclear *Overhauser* effect (NOE) NMR measurements (positive NOE between H–C(2) and H–C(4) in **3b** and **4c**), as well as by an X-ray

Table 1. *Products* **5** *and* **6** *Obtained by Alkylation of the Bicyclic Dioxanones* **3** *and* **4** via *the Enolates* **J** *and* **K**, *Respectively*. The yields refer to purified products. The diastereoselectivities (ds) refer to the content of the *cis*-fused products **5** and **6** in the crude product, as determined by ^{1}H-NMR. Unless otherwise stated, the reactions were carried out in THF/DMPU by adding the electrophiles at −75°, and allowing to warm up to r.t. overnight.

Starting material	Electrophile	Product				
		No.	R^1	R^2	Yield [%]	Diastereoselectivity ds [%]
3a	CH_3I	**5a**	H	CH_3	63	> 95
3b	CH_3I	**5b**	*t*-Bu	CH_3	86	> 98
3b	CH_2Br_2	**5c**	*t*-Bu	CH_2Br	38	> 98
3b	CH_2=$CHCH_2CH_2Br$	**5d**	*t*-Bu	CH_2=$CHCH_2CH_2$	69	> 98
3b	CH_2=$CHCH_2Br$	**5e**	*t*-Bu	CH_2=$CHCH_2$	93	> 98
3b	CH_3=$C(Cl)CH_2Cl$	**5f**	*t*-Bu	CH_2=$C(Cl)CH_2$	42	> 98
3b	$CH_3C(Cl)$=$CHCH_2Cl$	**5g**	*t*-Bu	$CH_3C(Cl)$=$CHCH_2$	41	> 98
3b	$Br-CH_2COOCH_3$	**5h**	*t*-Bu	CH_3OOCCH_2	75	> 98
3b	$CH_3CH(Br)COOCH_3$	**5i**	*t*-Bu	$CH_3OOCCH(CH_3)$	42[b]	> 98[a]
3b	CH_2=$C(CH_2Br)COO(t\text{-Bu})$	**5j**	*t*-Bu	CH_2=$C(COO(t\text{-Bu}))CH_2$	45	> 98
3b	CH_3COCl	**5k**	*t*-Bu	CH_3CO	81	> 98
3b	CH_3CHO	**5l**	*t*-Bu	$CH_3CH(OH)$	[c]	[d]
3b	$CH_3COCOOCH_3$	**5m**	*t*-Bu	$CH_3C(OH)(COOCH_3)$	88[e]	[e]
4a	CH_3I	**6a**	H	CH_3	80	93
4a	CH_2=$CHCH_2Br$	**6b**	H	CH_2=$CHCH_2$	77	> 98
4a	CH_3COCl	**6c**	H	CH_3CO	42	> 95
4a	CH_3CHO	**6d**	H	$CH_3CH(OH)$	[f]	[f]
4b	CH_3I	**6f**	*i*-Pr	CH_3	82[g]	60
4c	CH_3I	**6g**	*t*-Bu	CH_3	80[g]	57[h]

[a]) Racemic electrophile was used. Kinetic resolution, to a small extent, occurred. The product **5i** was obtained as a 1.4:1 mixture of epimers at C-1′.

[b]) Corrected yield, 61%. *Ca.* 30% of starting material **3b** was detected in the crude reaction product (^{1}H-NMR).

[c]) Two diastereoisomers, epimeric at C(1′), were obtained, carrying out the reaction under the general conditions indicated in the head to the table, the overall yield was 79%; when the reaction was carried out in THF at −70° for 1.5 h, the yield was 91%. The same stereochemical outcome was realized under both sets of conditions.

[d]) Only two diastereoisomers, epimeric at C(1′), were detected in the crude product (facial selectivity of attack on enolate **J**, > 98%); the ratio was 2.3:1. The major compound was obtained in isomerically pure form by fractional crystallization.

[e]) Only two diastereoisomers, epimeric at C(1′), were detected, the ratio was 2:1. The major isomer was obtained in pure form by crystallization.

[f]) When the reaction was carried out at −75°, a 24:1 ratio of **6d** and **6e** *(Scheme 3)* was realized (90% overall yield; 69% of **6d**, after crystallization). Compounds **6d** and **6e** were obtained in a ratio of 3.5:1 (85% overall yield; 55% of **6d** and 9% of **6e**) when the reaction was performed in THF at −75° in the presence of $ZnCl_2$. The other diastereoisomers were present in less than 1% in the crude product.

[g]) The product gave rise to a single spot on TLC in several mixtures of solvents. The yield was determined by ^{1}H-NMR.

[h]) The reaction was carried out from −100 to −75° (3 h). When the reaction was performed at −70°, a 1:1 ratio of diastereoisomers was obtained (yield > 95% as determined by ^{1}H-NMR).

structure analysis of a product[8]) obtained from **4c**. The overall conversion[9]) of the yeast-reduction products **1a** and **2a** to the pure bicyclic acetals **3** and **4**, respectively, was carried out on a 20-to-30-g scale in yields above 70%.

For alkylations at C(4a) (α-carbonyl position) of the dioxanone, the lithium enolates **J** and **K** were generated from **3** and **4**, respectively, by addition to 1.1 equiv. of lithium diisopropyl amide (LDA) in THF at −75°. Then, the cyclic urea DMPU (=3,4,5-tetrahydro-1,3-dimethyl-2(1*H*)-pyrimidinone) [40] was added as a co-solvent, followed by an excess of an alkyl halide. After slow warming to room temperature and aqueous workup, the products **5a–j** and **6a,b,f,g** (*Scheme 3* and *Table 1*) were obtained in 40–90% yields and, in the case of the cyclopentane derivatives **3a,b** and of the formaldehyde acetal **4a**, with excellent diastereoselectivity. The much higher reactivity of the enolates **J** containing the five-membered ring allowed for alkylations with less reactive halides[10]) than in the case of enolates **K**. Both bicyclic enolates were thermally much more stable[11]) than the monocyclic analogues [9].

Addition of the enolates **J** and **K** to aldehydes and ketones and their acylation with AcCl led to products **5k–m** and **6c–e** (*Scheme 3*), the methyl ketones **5k** and **6c** being formed as single stereoisomers, the hydroxyalkylated derivatives **5l, m** and **6d,e** as two isomers epimeric at the carbinol center; the ratios were 2.3:1 to 24:1, depending on the ring size and on added salts such as $ZnCl_2$ (see *Table 1* and *Exper. Part*). Especially noteworthy is the formation of an aldol-type adduct **6d** with 95% ds (two new stereogenic centers, one of them quaternary [16] [41]).

Finally, we have phenylselenenylated [42] the enolates **J** and **K** to the bridgehead hetero-substituted bicyclic acetals **7–9** (see *Scheme 3* and *Table 2*). While we did not detect a second isomer in the case of the bicyclo[4.3.0]derivative (**7**), the *trans/cis* ratio (**8/9**) varied depending upon the reaction conditions in the case of bicyclo[4.4.0]-derivatives **8** and **9**: reaction without warming above the mixing temperature of the reagents (−75°) yielded mainly the *cis*-fused **9**, warming to room temperature[12]) overnight the *trans*-fused product **8** (see *Table 2*). The *cis/trans* isomers could be separated by chromatography, and some of them were fully characterized. Oxidation of the Se compounds under the usual conditions [42] [44] gives the α,β-unsaturated carbonyl compounds **10–13** (*Scheme 3*). There was essentially no regioselectivity of elimination with the cyclopentane derivative **7**(→ **10/11** *ca.* 2:1), while the isomer **12** with the double bond

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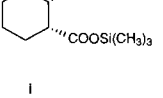
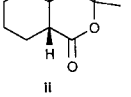
[8]) The X-ray structure analysis of **16b** (see below) was carried out by *B. Lamatsch* of our laboratory and will be reported separately.

[9]) The acetonide **ii** could only be obtained by applying *Noyori*'s method [38] to the reaction of the disilyl derivative **i** and acetone (*cf.* [37]). Since the silylation of **2b** was not successful with Me_3SiCl/Et_3N [37], we used bis(trimethylsilyl)acetamide in Et_2O or MeCN [39]. The acetonide **ii** is very unstable upon contact with air or upon heating. *Data for* **i**: b.p. 100–115°/0.15 Torr (bulb-to-bulb dist.). $[\alpha]_D = +31.1$ ($c = 0.64$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 2*s* at 0.10 and 0.30 ppm ($SiCH_3$). *Data for* **ii**: $[\alpha]_D = +49.4$ ($c = 1$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 2*s* at 1.57 and 1.60 ppm (CH_3), *dd* at 4.28 ppm ($J = 4$, 6 Hz, H–C(8a)).



i



ii

[10]) The 4-bromobut-1-ene does not react with **K** (R = H), but with **J** (R = *t*-Bu)!

[11]) We also noticed increasing stability with increasing bulk of R in the enolate **K**, see also the *Michael* additions to **12**, described below.

[12]) It is well known that phenylselenenylations of Li enolates may be reversible [43].

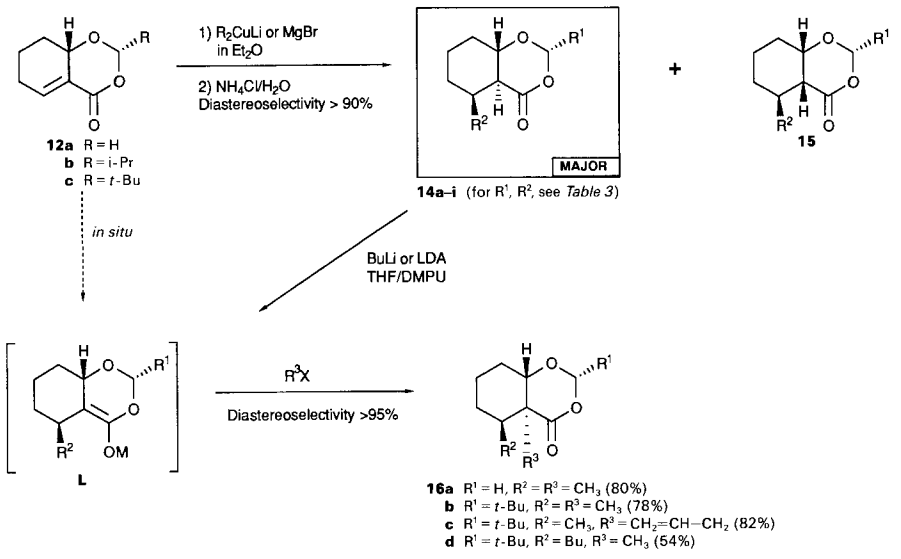
Table 2. *Products* **8** *and* **9** *Obtained by Selenation of the Bicyclic Dioxanones* **4**, via *Enolates* **K**. The reactions were carried out using a slight excess of PhSeBr or PhSeCl under the specified conditions; unless otherwise stated, the solvent was THF; the reactions were quenched by the addition of NH_4Cl/H_2O. The ratio of diastereoisomers was determined by ^{1}H-NMR.

Starting material	Conditions	Ratio **8**/**9**
4a	PhSeCl, −70° (15 min)	29:71
4a	PhSeCl, −70° to r.t.	83:17
4b	PhSeCl, THF/DMPU (2:1), −70° to r.t.	60:40
4b	PhSeBr, −70° to r.t.	55:45
4b	PhSeCl, −70° to r.t.	83:17
4c	PhSeCl, −70° (18 min)	31:69
4c	PhSeCl, THF/HMPA (2:1), −70° to r.t.	68:32
4c	PhSeCl, −70° to r.t.	87:13

exocyclic on the acetal ring was the sole product from the *trans*-fused precursors **8** and the major one from the *cis*-fused **9**. For large-scale preparation of the acetals **12** which we used for studying *Michael* additions (see below), the mixture of epimers **8**/**9** was oxidized directly and the desired product isolated by crystallization (70–80% overall from **4**).

The configurations of the products **5**–**9** shown in *Scheme 3* were determined mainly by NMR techniques[13]). Thus, NOE measurements of the methylated derivatives **5a**, **5b**, and **6a** indicate that the bridgehead Me group, the adjacent bridgehead H-atom, and the proton on the acetal center C(2) are *cis*-configurated. The splitting patterns of the signal from H–C(7a) and H–C(8a) in all compounds **5** and **6**, respectively, show that the products in each series must have the same configuration[14]). While we could not determine the configuration of C(1′) in **5l** and **m**, we

Scheme 4



[13]) The *cis*-fusion in **7** and **9**, and the *trans*-fusion in **8** also follow from the structure of the elimination products: only **7** and **9** give rise to the products **11** and **13**, respectively, with tetrasubstituted double bond between the bridgehead positions (*cis*-elimination of the intermediate selenoxides!).

[14]) In the crude alkylation products from **4**, we could detect the minor, *trans*-fused isomers of **6** by ^{1}H-NMR spectroscopy. While H–C(8a) appears at 3.70–3.75 ppm as a br. *s* in **6**, a *dd* ($J \approx 12$ and 4 Hz) centered at *ca.* 3.6 ppm is characteristic of the *trans*-isomer.

tentatively assign that in **6d** and **6e** from the application of *Horeau*'s method [45], see *Exper. Part.* The *cis*-fusion in both, **6d** and **6e** follows from the fact that their oxidation gives the same product[15]), *i.e.* **6c**.

The unsaturated carbonyl compounds **12** were tested extensively as *Michael* acceptors. We found that alkyl, allyl, vinyl, but also silyl groups can be introduced in the 5-position on the carbocyclic ring to give products **14** in usually better than 90% diastereoselectivity with formation of two new stereogenic centers *(Scheme 4)*. A few percent of the epimer **15** with *cis*-fusion of the two six-membered rings is detected by ^{1}H-NMR spectroscopy of the crude products. As indicated in *Table 3*, the yields of adducts **14** of conjugate addition range from 40 to 90%, independent of the reagent employed, *i.e.* R_2CuLi the Mg analogue, or a *Grignard* reagent doped with 5% CuI. The

Table 3. *Conjugate Additions to the α,β-Unsaturated Carbonyl Derivatives* **12**. With one exception (**14f**), the selectivity of formation of the diastereoisomers **14** is > 90%. The yields given refer to isolated and purified major products of type **14**. Diastereoselectivity (% ds) is the content of **14** in the crude product mixture of **14**/**15** (by ^{1}H-NMR).

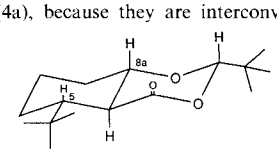
Starting material	Conditions for the conjugate addition			Product				
	Equivalent reagent	Temp. [°C]	Reaction time [h]	No.	R^1	R^2	Yield [%]	Diastereoselectivity ds [%]
12a	3 Me_2CuLi	−75	2.0	**14a**	H	CH_3	54	> 97
12a	3 Me_2CuLi	−10	0.03	**14a**	H	CH_3	29	> 97
12b	3 Me_2CuLi	0	1.5	**14b**	*i*-Pr	CH_3	60	91
12c	3 Me_2CuLi	−10	0.75	**14c**	*t*-Bu	CH_3	71	95
12c	3 Bu_2CuLi	−20 to 0	3.0	**14d**	*t*-Bu	Bu	78	> 95
12c	3 (*s*-Bu)$_2$CuLi	−75	4.0	**14e**	*t*-Bu	*s*-Bu	54	90
12c	3 (*t*-Bu)$_2$CuLi	−75	2.0	**14f**	*t*-Bu	*t*-Bu	43	80
12c	3 $(CH_2{=}CHCH_2)_2CuLi$	−75	2.5	**14g**	*t*-Bu	$CH_2{=}CHCH_2$	81	> 95
12c	3 $(CH_2{=}CH)_2CuMgBr$	0	1.5	**14h**	*t*-Bu	$CH_2{=}CH$	75	90
12c	3 $(CH_2{=}CH)_2CuMgBr$	−75 to −55	3.0	**14h**	*t*-Bu	$CH_2{=}CH$	72	> 95
12c	1.4 $(CH_2{=}CH)_2CuMgBr$	−75	4.0	**14h**	*t*-Bu	$CH_2{=}CH$	54	> 95
12c	3 $(CH_2{=}CH)MgBr$ + 0.15 CuI	0	2.0	**14h**	*t*-Bu	$CH_2{=}CH$	49	> 90
12c	3 $(PhMe_2Si)_2CuLi$	−75	2.5	**14i**	*t*-Bu	$PhMe_2Si$	76	92

only cuprate which added with low selectivity was the *t*-Bu derivative: besides **14f**, a second isomer was present in a ratio of 4:1, and the ^{1}H-NMR spectrum indicated that it was not **15f**, but another stereoisomer[16]) [17]). All products of type **14** were obtained in pure form mostly by crystallization sometimes by flash chromatography [47].

The primary adduct enolates **L** of the *Michael* additions to **12** can be trapped with alkyl halides[18]) in the following way: *in situ* addition of excess butyllithium, of the

[15]) Likewise, **5k** and **5l** must have the same configuration at C(4a), because they are interconvertible by oxidation/reduction, see *Table 1* and *Exper. Part.*

[16]) The ^{1}H-NMR analysis of this second isomer is compatible with the configuration shown in **iii**; H–C(8a) appears as a *dt* (J = 6 and 12 Hz) at 4.16 ppm, *i.e.* the two rings are *trans*-fused as in the major product and not *cis* as in the by-products **15** (H–C(8a) gives rise to a non-resolved, broad signal in **15**).



iii

[17]) The five-ring analogue **10** of the *Michael* acceptors **12** did not undergo the same reaction under identical conditions. Not even the Bu_3P-activated alkylcopper reagents [46] would add!

[18]) Usually cuprate-derived enolates can not be trapped *in situ* [48], except with very reactive electrophiles such as monomeric formaldehyde [49].

co-solvent DMPU [40], and of a large excess of MeI at −75° and warming up to 0° leads to the bridgehead methylated products **16b** and **d**, as the only detectable isomers! The activation of the cuprate enolate[18]) by BuLi was used previously [50] and is probably due to mixed-aggregate formation [51]; it works only after extensive optimization, in our hands. Alkylations of the *Michael* adducts **14** can also be achieved by enolate formation with BuLi – unperturbed by competing addition to the hindered C=O group – or with LDA, which worked well[19]) only in the case of **14a** (unsubstituted acetal center!), and subsequent addition of MeI or allyl bromide in the presence of DMPU, to give the same products **16** as above in 50–80% yield and as single stereoisomers[20]).

The assignment of configuration to the products **14**–**16** is based on NMR measurements, chemical correlation, and an X-ray analysis[8]). Thus, the bridgehead H-atoms of **14** must be antiperiplanar to each other, due to their coupling with $J \approx 11$ Hz (H–C(4a) at 2.35 ± 0.05 and H–C(8a) at 3.9 ± 0.1 ppm), while the coupling between the proton in α-position to C=O and the one on the newly formed stereogenic center ($J \approx 4$ Hz) proves their synclinal disposition. The assignment of *trans*-fusion of the rings and of *trans*-relationship between the substituents R^2 and R^3 in **16** is not as straightforward[21]). The similarity of the NMR spectra indicates that all four compounds of the general structure **16** have the *same* configuration, with R^2 and H–C(8a) *cis*-configurated to each other as in the monoalkylation products **14**. The *trans*-fusion in **16b** was definitely established from its crystal structure[8]) and by conversion to (−)-5-epi-dehydrofukinone [2] of known configuration [53]. Thus, we can savely assign the structure as shown in *Scheme 4* to all the bicyclic acetals of type **16**[22]). The assignments made here place all R^2 groups introduced in the *Michael*-addition step in an axial position of **14** and **16**, including the *t*-Bu group[23]) in **14f**.

To demonstrate that highly substituted hydroxycyclopentane and -cyclohexanecarboxylic-acid derivatives of types **F**–**I** are actually availably by the methodology described here, we cleaved some of the bicyclic acetals (**5**, **6**, **14**, and **16**) either by $LiAlH_4$ reduction (→ **18**, **23**) or by acidic or alkaline solvolysis (→ **17**, **19**–**22**; *Scheme 5*). The yields were usually in the 90% range, and the conditions mild enough for C=C bonds to survive. The allyl-substituted cyclohexane **20** has been described before and its configuration assigned, an additional structure proof for compound **6b**.

It appears that the α-alkylation and α-hydroxyalkylation of β-hydroxy-carboxylates both through the monocyclic (**B** in *Scheme 1*) and the bicyclic dioxanone enolates (**J**, **K** in *Scheme 3* and **L** in *Scheme 4*) is generally more stereoselective than through the open-chain lithioxy-lithium enolates [30b,c] [34] [57]. Furthermore, two practical advantages are that only 1 equiv. of strong base is required for the dioxanones, and that most of the

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[19]) This may be an extreme case of $(i\text{-Pr})_2NH$ acting as a proton source in Li-enolate reactions with electrophiles [51] [52]!

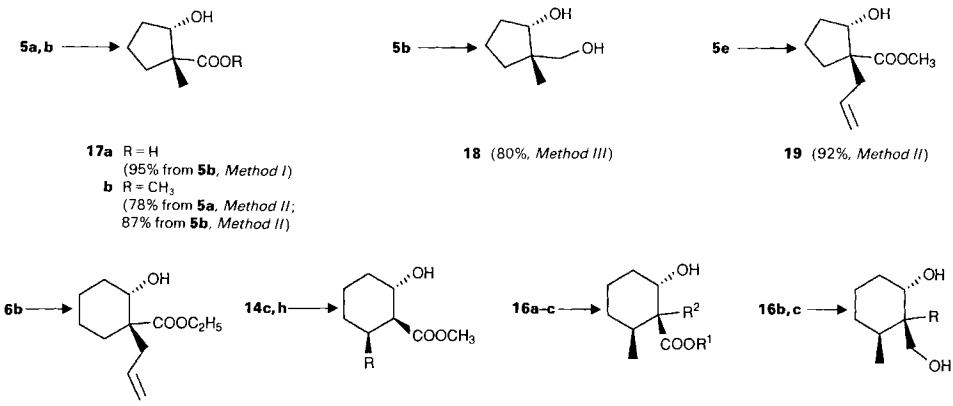
[20]) *Ca.* 50% of a second isomer was found to be present only with product **16a**, see also *Footnote 22*.

[21]) Indeed, we have originally [1] made a tentative assignment of the configuration of the compounds **16** which turned out to be wrong [2]!

[22]) The exceptionally high selectivity with which products **16b**–**d** were formed turned out to be a misfortune; had we obtained both, the *cis*- and the *trans*-fused isomers, it would have been easy to make a configurational assignment: we *later* prepared **16a** from pure **14a** and found 5% of the 4a-epimer of **16a** in the crude product; in the ^{1}H-NMR spectrum of this minor isomer, the CH_3–C(4a) appears as a *s* at 1.16 and CH_3–C(5) as a *d* at 0.91 ppm ($J = 6.9$ Hz); for **16a**, the corresponding values are: 1.41 (*s*) and 1.06 ppm (*d*, $J = 7.2$ Hz). The higher-field resonances of both Me groups in the minor and the lower-field ones in the major isomer are generally accepted clear-cut effects of synclinal *vs.* antiperiplanar relationships between Me groups on six-membered rings [54].

[23]) If the carbocyclic ring in **14f** would be a twist-boat rather than a chair, the *t*-Bu group would either be in an extremely unfavorable *'endo'*-type position or have massive *van-der-Waals* overlap with the O-atom of the C=O group (inspection of models recommended!). For a discussion of non-chair six-membered rings, see [55], for some previous cases of axial *t*-Bu groups in carbo- and heterocyclic six-membered rings, see [56].

Scheme 5



17a R = H (95% from **5b**, *Method I*)
b R = CH_3 (78% from **5a**, *Method II*; 87% from **5b**, *Method II*)

18 (80%, *Method III*)

19 (92%, *Method II*)

20 (82%, *Method IV*)

21a R = CH_3 (76% from **14c**, *Method V*)
b R = $CH{=}CH_2$ (86% from **14h**, *Method V*)

22a $R^1 = R^2 = CH_3$ (94% from **16b**, *Method V* or 82% from **16a**, *Method II*)
b $R^1 = CH_3$, $R^2 = CH_2{-}CH{=}CH_2$ (91% from **16c**, *Method V* or 79% from **16c**, *Method II*)
c R^1 = H, $R^2 = CH_2{-}CH{=}CH_2$ (90% from **16c**, *Method VI*)

23a R = CH_3 (90% from **16b**, *Method III*)
b R = $CH_2{-}CH{=}CH_2$ (83% from **16c**, *Method III*)

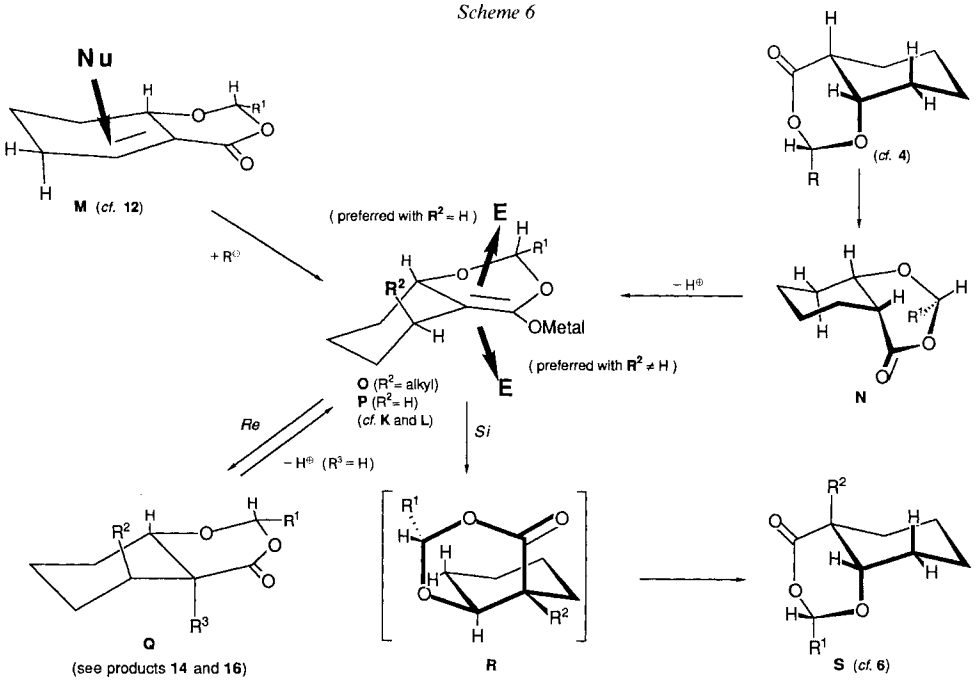
a) *Method I:* *Dowex 50 × 8*/MeOH/r.t.
Method II: MeONa/MeOH/r.t.
Method III: $LiAlH_4$/THF/0° to r.t.
Method IV: EtONa/EtOH/r.t.
Method V: a) *Method I;* b) CH_2N_2/Et_2O/0°.
Method VI: 1N HCl/THF/H_2O/r.t.

intermediates on the dioxanone route from the hydroxy acid to its alkyl derivative show a marked tendency to crystallize.

Discussion of the Steric Course of the Reactions. – The steric course of reactions of *Michael* acceptors and of enolates embedded in decaline and larger systems containing cyclohexane rings have been studied extensively [58]. Still, the results described above with the heterocyclic decaline analogues are somewhat surprising: inspite of the fact that one of the two six-membered rings in our system contains two O-atoms, *i.e.* atoms without substituents, the reactions are highly stereoselective in almost all cases. The observed course of the *Michael* additions is compatible with an axial attack on a cyclohexane half chair[24]), see **M** in *Scheme 6*. The subsequent protonation leads to the isolation of the *trans*-fused products **Q**, R^3 = H. The intermediate enolate **O** is protonated from the *Re*-face preferentially (≥ 91:9). Other electrophiles (RX, PhSeCl) approach from the same face, no matter whether the enolate is trapped *in situ* – after appropriate modification – or generated from **Q**, R^3 = H. The enolate **P** without a substituent at C(5) is formed by deprotonation of the bicyclic dioxanone and shows a very peculiar selectivity pattern: if R^1 is an i-Pr or *t*-Bu group the selectivity is poor, if it is an H-atom it is great (≥ 93:7), but in both cases the major product is *cis*-fused, *i.e.* the electrophiles approach from the

[24]) The most stable conformation of the dioxanone ring in monocyclic derivatives is known from NMR [59] and X-ray crystal-structure [12] investigations to be *sofa*-like, with one of the O-atoms out of the plane of the other five ring atoms. This is how we draw it in the formulae of *Scheme 6* for the following discussion. There is no structural information about the enolates of dioxanones.

Scheme 6



Si-face of the enolate double bond. It appears that the *Si*-face of enolate **P** – lacking a substituent at C(5) – is inherently more reactive than its *Re*-face.

Si-Attack is equatorial on the cyclohexane ring (antiperiplanar to the ring bonds C(5)–C(6) and C(8a)–C(8)), *Re*-attack axial (antiperiplanar to the C–H bonds on C(5) and C(8a))[25]. In the case of introduction of a substituent at the *Re*-position of the enolates, the primary conformer formed is also the most stable one (**Q** in *Scheme 6*). In contrast, the conformer **R** resulting from a *Si*-attack (note that the R^2 group must [64] lie approximately in a plane perpendicular to that of the trigonal C-atom of the C=O group) suffers from repulsion between the R^1 group on the acetal center on C(2) and the axial H–C(8). This very fact is probably the reason for small selectivities of enolate *Si*-alkylations, unless the formaldehyde acetal is used ($R^1 = H$)[26]. The more stable conformer of the *cis*-fused products, including the starting material, is **S**, with the O-atom axial and the C=O group equatorial on the cyclohexane ring, and with the newly introduced R group almost exactly in plan with the C=O group. This is actually the conformer which is

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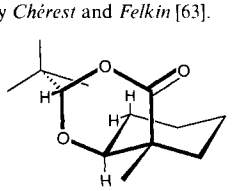
[25]) Compare the calculations on nucleophilic addition to cyclohexanones [60] and cyclohexenones [61] by *Houk* and his coworkers and previous work by *Anh* and *Eisenstein* [62], and by *Chérest* and *Felkin* [63].

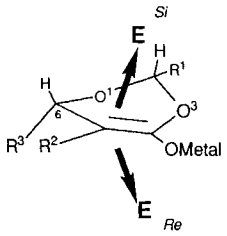
[26]) The following projection **iv** of the primary product conformer (with $R^1 = t$-Bu) shows the proximity of one of the Me groups to H_{ax}–C(8). The cyclopentane-derived enolate **J** gives rise to *cis*-fused products *exclusively*, independent of the substituent at C(2). This may be due not only to strain in the *trans*-fused isomers, but also to a much smaller repulsive interaction of the type indicated in **iv** for the 6-ring analogue.



iv

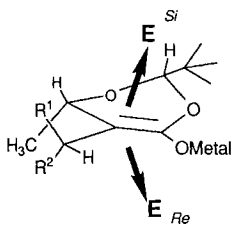
compatible with the ^{1}H-NMR spectra of compounds **4** and **6** (see discussion above, and *Exper. Part*).

It is interesting to compare the bicyclic enolates described here with those of monocyclic dioxanone derivatives [9] [10], see **T** and **U**. With Me group(s) at C(5) and/or C(6), the preferred trajectory of electrophile approach is always with relative topicity *like* (*Si* in **T**, antiperiplanar to the Me group). With CH_2R or CHR_2 at C(5), it is reversed (*unlike, Re* in **U**, antiperiplanar to H–C(6)). As suggested by *Tomioka et al.* [65] the reversal of relative topicity in reactions of α,β-disubstituted lactone enolates on going from an α-CH_3 (*cf.* **T**, $R^2 = CH_3$) to an α-RCH_2 group (*cf.* **U**, $R^2 = H$) may be caused by the RCH_2 group assuming a conformation with R shielding more effectively one face of the enolate plane than the β-substituent blocking the other.



T

Approach of	from	rel. top.	R^1	R^2	R^3
RX or D^+	*Si*	(*lk*)	*t*-Bu	H	Me
H^+	*Si*	(*lk*)	*t*-Bu	Me	Me
RX	*Si*	(*lk*)	H	H	Me
RX	*Re*	(*ul*)	*t*-Bu	H	H



U

Approach of H^- from *Re* face (*ul*)
R^1 = alkyl, Ph
R^2 = alkyl, silyl

Generous gifts of pivalaldehyde from the *BASF Aktiengesellschaft*, D-Ludwigshafen, are greatfully acknowledged. We thank *D. Manser* (elemental analysis) and *B. Brandenberg* (high-field NMR spectra) for technical assistance.

Experimental Part

General. Flasks, stirring bars, and hypodermic needles used for the generation and reactions of organometallic reagents were dried for *ca.* 12 h at 120° and allowed to cool in a dessicator over anh. $CaSO_4$. All reactions with sensible materials were conducted under a positive pressure of Ar. All solvents for reactions were of *purissimum* quality; THF and Et_2O were further distilled from potassium benzophenone ketyl. CuI was purified according to the method of *Posner et al.* [66]. Other reagents were purified by standard methods [67]. Organolithiums employed were titrated according to the method of *Kofron* and *Baclawski* [68]. The temp. refers to the reaction mixture and was measured by a *Pt-100* thermomether. Unless otherwise stated, org. extracts were dried ($MgSO_4$) and evaporated by using a rotary evaporator. Bulb-to-bulb distillations: air-bath temp., uncorrected. Melting points (uncorrected): *Büchi 510* apparatus. TLC: silica-gel plates *60 F_{254} (Merck)* developed with UV light and I_2. Flash chromatography (FC): *Fluka* silica gel (mesh size 0.040–0.063) according to the method of *Still et al.* [47]. Optical rotation: *Perkin-Elmer-241* polarimeter at r.t. and, unless otherwise stated, in $CHCl_3$ soln., *c* in g/100 ml. IR spectra (cm^{-1}): *Perkin-Elmer-983* spectrometer; film or KBr discs. ^{1}H- and ^{13}C-NMR spectra: *Varian-EM-390* or *XL-100* as well as *Bruker-300* apparatus; $CDCl_3$ solns., chemical shifts (δ) in ppm rel. to the internal reference TMS, coupling constants *J* in Hz. MS: 70 eV, *Hitachi-Perkin-Elmer-RMU-6M* instrument, *m/z* values with relative intensities (%) in parenthesis.

Workup Procedure 1. The reaction mixture was added to a sat. NH_4Cl soln. in H_2O at 0°. The mixture was diluted with H_2O and Et_2O, the phases separated, and the aq. phase thoroughly extracted with Et_2O. The combined Et_2O extracts were washed with 5% aq. HCl, sat. $NaHCO_3$ soln., and brine, and dried.

Workup Procedure 2. The reaction mixture was poured into a 10% aq. $NaHCO_3/CH_2Cl_2$ 1:1 and stirred for 30 min; the phases were separated, and the aq. phase extracted with CH_2Cl_2. The org. extracts were washed with 2N HCl and H_2O, and dried.

Workup Procedure 3. The mixture was added to a sat. NH_4Cl soln. in H_2O at 0°; stirring for 15 min was followed by the addition of H_2O and Et_2O, the phases were separated, the aq. phase was extracted with Et_2O, and the combined org. extracts were thoroughly washed with H_2O and brine, and dried.

Ethyl (1R,2S)-2-Hydroxycyclopentanecarboxylate (**1a**). A suspension of 126 g of baker yeast in 1 l of tap water was shaken for 0.5 h at 140 rpm and 30°. Then, 5.0 g (32.05 mmol) of *ethyl 2-oxocyclopentanecarboxylate* were added and the mixture shaken for 24 h. The soln. was thoroughly extracted (7 × 100 ml) with Et_2O. The org. extracts were washed with brine up to disappearance of the emulsion (5 or 7×) and dried, affording, after distillation, 2.7–3.7 g (33–45%) of **1a**. $[\alpha]_D = +13.1$ ($c = 1.16$) ([31]: +14.1).

(1R,2S)-2-Hydroxycyclopentanecarboxylic Acid (**1b**). At r.t., 380 ml of 1N LiOH in H_2O were added to a soln. of 10.0 g (0.063 mol) of **1a** in 760 ml of THF. The mixture was stirred at r.t. for 1 h, acidified with 6N HCl at 0°, saturated with NaCl, and extracted with Et_2O (at r.t. for 72 h or by heating at reflux in a continuous extractor for 36 h). The org. solvent was dried and evaporated giving 7.7 g (94%) of **1b**, chromatographically homogeneous, which could be used in the following reaction without further purification. An anal. pure sample could be obtained by crystallization. M.p. 44° (pentane/Et_2O at −20°). $[\alpha]_D = +26.4$ ($c = 1.4$). IR (KBr): 3400*s* (br.), 2960*s*, 1710*s*, 1415*m*, 1205*m*, 1100*m*, 1020*m*. ^{1}H-NMR (90 MHz): 1.30–2.20 (*m*, 6 H); 2.77 (*m*, H–C(1)); 4.77 (*m*, H–C(2)); 7.43 (br. *s*, OH, CO_2H). ^{13}C-NMR (20 MHz): 178.8; 73.9; 49.6; 34.0; 25.9; 21.9. MS: 118 (2.8, $M^+ - 18$), 102 (13.3), 86 (11.7), 84 (9.2), 73 (100). Anal. calc. for $C_6H_{10}O_3$: C 55.37, H 7.74; found: C 55.12, H 7.73.

Ethyl (1R,2S)-2-Hydroxycyclohexanecarboxylate (**2a**). As described for **1a**, with 126 g of baker yeast in 1 l of tap water and 5.0 g (29.4 mmol) of *ethyl 2-oxocyclohexanecarboxylate:* 3.5–4.1 (70–82%) of **2a**. $[\alpha]_D = +26.4$ ($c = 1.99$) ([31]: +28.06).

(1R,2S)-2-Hydroxycyclohexanecarboxylic Acid (**2b**). As described for **1b**, with 370 ml of 1N LiOH (0.37 mol) in H_2O and 10.15 g (0.059 mol) of **2a** in 720 ml of THF (1.5 h): 8.3 g (98%) of **2b** which was used in the following reaction without further purification.

(4aR,7aS)-5,6,7,7a-Tetrahydrocyclopenta[d]dioxin-4(4aH)-one (**3a**). A mixture of 2.02 g (15.6 mmol) of **1b**, 5.30 g (156 mmol) of paraformaldehyde, 1.2 g (4.7 mmol) of pyridinium *p*-toluenesulfonate (PPTS) and 10 g of 4-Å molecular sieve in 90 ml of dry toluene was heated at 90° for 6.5 h. The mixture was cooled, diluted with Et_2O and washed with sat. aq. $NaHCO_3$ soln. and H_2O. The org. soln. was dried and the solvent evaporated: 1.51 g (69%) of **3a**. Acidification of the aq. phase and extraction (Et_2O) allowed to recover 0.25 g of **1b** (corrected yield of **3a**: 78%). **3a**: M.p. 43° (pentane). $[\alpha]_D = -17.4$ ($c = 0.9$). IR (KBr): 2960*m*, 1730*s*, 1425*m*, 1370*m*, 1240*s*, 980*s*, 750*m*. ^{1}H-NMR (300 MHz): 1.53–2.18 (*m*, 6 H); 2.89 (*dt*, $J = 8.6, 6.5$, H–C(4a)); 4.44 (*m*, H–C(7a)); 5.31 (*d*, $J = 5.7$, H–C(2)); 5.37 (*d*, $J = 5.7$, H–C(2)). ^{13}C-NMR (75 MHz): 170.2 (*s*); 92.5 (*t*); 80.0 (*t*); 45.1 (*d*); 33.6 (*t*); 30.3 (*t*); 23.1 (*t*). MS: 112 (2.1, $M^+ - 30$), 84 (6.9), 69 (5.4), 68 (100), 67 (43.7), 55 (19.8), 53 (9.7), 41 (14.1), 39 (19.7), 27 (13.7). Anal. calc. for $C_7H_{10}O_3$: C 59.14, H 7.09; found: C 58.94, H 7.07.

(2S,4aR,7aS)-2-(tert-Butyl)-5,6,7,7a-tetrahydro-cyclopenta[d]dioxin-4(4H)-one (**3b**). A soln. of 5.92 g (45.54 mmol) of **1b**, 50 ml (440 mmol) of *t*-BuCHO, and 1.20 g (4.6 mmol) of PPTS in 260 ml of anh. C_6H_6 was heated in a *Soxhlet* containing 20 g of 4-Å molecular sieve for 1.25 h. The mixture was cooled, diluted with CH_2Cl_2, washed with sat. aq. $NaHCO_3$ soln. and H_2O, and dried. Evaporation of the solvent gave a crude product which was crystallized from pentane: 8.11–8.57 g (90–95%) of pure **3b**. M.p. 100–101°. $[\alpha]_D = +3.7$ ($c = 0.6$). IR (KBr): 2980*s*, 1735*s*, 1720*s*, 1360*s*, 1245*m*, 985*s*. ^{1}H-NMR (300 MHz): 0.98 (*s*, *t*-Bu); 1.60 (*m*, H–C(6)); 1.78 (*m*, H–C(6)); 1.94 (*m*, 2 H); 2.10 (*m*, 2 H); 2.82 (*m*, H–C(4a)); 4.39 (*m*, H–C(7a)); 4.87 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 172.1 (*s*); 107.6 (*d*); 79.2 (*d*); 44.3 (*d*); 35.1 (*s*); 33.5 (*t*); 30.1 (*t*); 23.9 (*q*, 3 C); 23.1 (*t*). MS: 141 (65.4, $M^+ - 57$), 95 (18.4), 87 (59.3), 85 (21.3), 68 (100), 67 (75.1), 57 (40.8), 55 (18.1), 43 (15.6), 41 (44.4), 39 (21.1), 29 (23.8), 28 (17.6), 27 (18). Anal. calc. for $C_{11}H_{18}O_3$: C 66.64, H 9.15; found: C 66.19, H 9.08.

(4aR,8aS)-Perhydro-2H,4H-[1,3]benzodioxin-4-one (**4a**). As described for **3a**, with 5.41 g (37.6 mmol) of **2b**, 12.0 g (376 mmol) of paraformaldehyde, 2.80 g (11.3 mmol) of PPTS, and 10 g of 4-Å molecular sieve in 180 ml of dry toluene (90° for 7 h; extraction with CH_2Cl_2): 4.0 g (69%) of **4a** and 1.0 g of **2b** (extracted with Et_2O; corrected yield of **4a**; 84%). **4a**: B.p. 90°/0.4 Torr. $[\alpha]_D = -1.7$ ($c = 0.73$). IR (film): 2920*s*, 1745*s*, 1245*s*, 1225*s*, 1215*s*, 995*s*.

^{1}H-NMR (300 MHz): 1.26–2.03 (*m*, 8 H); 2.68 (*m*, H–C(4a)); 4.08 (*dd*, *J* = 7.9, 4.0, H–C(8a)); 5.39 (*d*, *J* = 5.3, H–C(2)); 5.43 (*d*, *J* = 5.3, H–C(2)). ^{13}C-NMR (75 MHz): 170.7 (*s*); 92.7 (*t*); 73.3 (*d*); 42.5 (*d*); 29.9 (*t*); 25.5 (*t*); 23.7 (*t*); 20.6 (*t*). MS: 156 (0.3, M^+), 155 (1.1), 138 (0.5), 126 (4.4), 98 (6.4), 82 (100), 81 (22.1), 67 (72.8), 55 (24.5), 54 (44.3), 41 (27.8), 39 (19), 29 (10.1), 27 (16.1). Anal. calc. for $C_8H_{12}O_3$: C 61.52, H 7.74; found: C 61.24, H 8.09.

(2S,4aR,8aS)-Perhydro-2-isopropyl-2H,4H-[1,3]benzodioxin-4-one (**4b**). As described for **3b**, with 3.30 g (22.9 mmol) of **2b**, 20 ml (210 mmol) of i-PrCHO, 0.576 g (2.29 mmol) of PPTS in 150 ml of anh. C_6H_6, and 10 g of 4-Å molecular sieve (1.5 h): 4.7 g of crude product, consisting of a 95:5 mixture of **4b** and its epimer. FC (15–25% Et_2O/pentane) of the residue gave 0.236 g of a 1:1 mixture of **4b** and its epimer and 3.20 g (76%) of pure **4b** (decomposition on distillation). $[\alpha]_D$ = +9.7 (*c* = 1.06). ^{1}H-NMR (300 MHz): 1.012 (*d*, *J* = 6.9, 3 H, $(CH_3)_2CH$); 1.015 (*d*, *J* = 6.9, 3 H, $(CH_3)_2CH$); 1.17–1.94 (*m*, 8 H); 2.01 (*m*, $(CH_3)_2CH$); 2.58 (*m*, H–C(4a)); 4.05 (distorted *dd*, *J* = 7.0, 3.8, H–C(8a)); 5.16 (*d*, *J* = 3.8, H–C(2)). ^{13}C-NMR (20 MHz): 171.5 (*s*); 105.3 (*d*); 71.9 (*d*); 41.5 (*d*); 32.3 (*d*); 29.5 (*t*); 25.4 (*t*); 23.7 (*t*); 20.1 (*t*); 15.6 (*q*, 2 C). MS: 198 (< 0.8, M^+), 197 (1.3), 155 (74), 109 (10.9), 99 (26.6), 82 (100), 81 (93.7), 73 (23.7), 67 (63.5), 54 (26.2), 41 (23.9).

*(2S,4aR,8aS)-2-(*tert*-Butyl)perhydro-2H,4H-[1,3]benzodioxin-4-one* (**4c**). As described for **3b**, with 21.6 g (0.15 mol) of **2b**, 51 ml (0.45 mol) of *t*-BuCHO, 3.9 g (0.015 mol) of PPTS in 700 ml of anh. C_6H_6, and 40 g of 4-Å molecular sieve (6 h): 29.5 g of crude product, which was crystallized from pentane at –20°, affording 27.1 g (85%) of **4c**. M.p. 43–44° (pentane at –20°). $[\alpha]_D$ = +16.3 (*c* = 0.95). IR (KBr): 2970*s*, 1750*s*, 1730*s*, 1365*m*, 1245*m*, 1225*m*, 985*s*. ^{1}H-NMR (300 MHz): 1.00 (*s*, 9 H, *t*-Bu); 1.30–1.91 (*m*, 8 H); 2.56 (*m*, H–C(4a)); 4.02 (*dd*, *J* = 6.6, 3.8, H–C(8a)); 4.96 (*s*, H–C(2)). ^{13}C-NMR (20 MHz): 171.7 (*s*); 107.6 (*d*); 71.9 (*d*); 41.6 (*d*); 35.1 (*s*); 29.5 (*t*); 25.5 (*t*); 23.8 (*q*, 3 C); 23.2 (*t*); 20.1 (*t*). MS: 211 (0.8, $M^+ - 1$), 155 (100), 99 (28.5), 87 (46.6), 82 (85), 81 (82.8), 67 (43.8), 57 (28.6), 41 (53.9). Anal. calc. for $C_{12}H_{20}O_3$: C 67.89, H 9.50; found: C 67.68, H 9.30.

Alkylation of 3. – *General Method.* A soln. of 1 mmol of **3** in 2.4 ml of THF was dropwise added to a soln. of 1.2 mmol of LDA in 1.2 ml of THF at –70°; after stirring for 15 min, 1.8 ml of DMPU were added and stirring was continued for additional 15 min. Then, 1.5–10 equiv. of the electrophile were added (neat), and the temp. was kept at –70° for 1 h and slowly raised to r.t. (overnight). *Workup Procedure 3* afforded a residue, consisting of a single diastereoisomer, which was purified.

*(4aR,7aS)-5,6,7,7a-Tetrahydro-4a-methylcyclopenta[*d*]dioxin-4(4aH)-one* (**5a**). Electrophile: 10 equiv. of MeI. Purification by FC (pentane/Et_2O 4:1): 98 mg of **5a** (63%). B.p. 70–80°/0.15 Torr. $[\alpha]_D$ = –11.8 (*c* = 0.85). IR (film): 2975*m*, 1740*s*, 1380*m*, 1360*m*, 1265*m*, 1185*s*, 1005*s*. ^{1}H-NMR (300 MHz): 1.28 (*s*, CH_3–C(4a)); 1.66–2.12 (*m*, 5 H); 2.26 (*m*, H–C(7)); 3.99 (distorted *dd*, *J* = 5.6, 1.6, H–C(7)); 5.32 (*d*, *J* = 5.7, H–C(2)); 5.37 (*d*, *J* = 5.7, H–C(2)). ^{13}C-NMR (20 MHz): 173.4 (*s*); 92.2 (*t*); 85.8 (*d*); 49.9 (*s*); 37.7 (*t*); 31.8 (*t*); 21.6 (*q*); 21.4 (*t*). MS: 126 (4.5, $M^+ - 30$), 98 (21.6), 82 (73.9), 81 (18.7), 69 (10.6), 67 (100), 41 (29.5), 39 (22.6), 27 (12.1). Anal. calc. for $C_8H_{12}O_3$: C 61.52, H 7.74; found: C 61.55, H 7.78.

*(2S,4aR,7aS)-2-(*tert*-Butyl)-5,6,7,7a-tetrahydro-4a-methylcyclopenta[*d*]dioxin-4(4aH)-one* (**5b**). Electrophile: 10 equiv. of MeI. Crystallization gave 182 mg of **5b** (86%). M.p. 53° (pentane at –20°). $[\alpha]_D$ = +4.9 (*c* = 0.85). IR (KBr): 2980*s*, 2960*s*, 1755*s*, 1725*s*, 1489*m*, 1415*m*, 1375*m*, 1360*s*, 1185*s*, 1120*s*, 1000*s*, 990*s*. ^{1}H-NMR (300 MHz): 0.97 (*s*, *t*-Bu); 1.26 (*s*, CH_3–C(4a)); 1.65–2.22 (*m*, 6 H); 3.93 (*dd*, *J* = 5.4, 1.7, H–C(7a)); 4.86 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 175.2 (*s*); 107.3 (*d*); 85.4 (*d*); 49.2 (*s*); 38.0 (*t*); 35.1 (*s*); 32.2 (*t*); 23.9 (*q*, 3 C); 21.9 (*q*); 21.8 (*t*). MS: 213 (0.3, $M^+ + 1$), 211 (0.5, $M^+ - 1$), 155 (41.9), 127 (24.9), 99 (67), 82 (100), 67 (96.5), 43 (22), 41 (50.8). Anal. calc. for $C_{12}H_{20}O_3$: C 67.89, H 9.50; found: C 67.94, H 9.35.

*(2S,4aS,7aS)-4a-(Bromomethyl)-2-(*tert*-butyl)-5,6,7,7a-tetrahydrocyclopenta[*d*]dioxin-4(4aH)-one* (**5c**). Electrophile: 3 equiv. of CH_2Br_2. Crystallization gave **5c** (111 mg, 38%). M.p. 97–99° (pentane). $[\alpha]_D$ = –12.4 (*c* = 1.5). IR (KBr): 2985*m*, 1735*s*, 1470*m*, 1410*m*, 1355*s*, 1195*s*, 970*s*. ^{1}H-NMR (300 MHz): 0.98 (*s*, *t*-Bu); 1.70–2.05 (*m*, 5 H); 2.32 (*m*, H–C(7)); 3.15 (*d*, *J* = 10.3, 1 H, BrCH_2); 3.93 (*d*, *J* = 10.3, 1 H, BrCH_2); 4.50 (*m*, H–C(7a)); 5.03 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 171.8 (*s*); 107.4 (*d*); 82.6 (*d*); 55.8 (*s*); 37.6 (*t*); 35.1 (*t*); 32.1 (*t*); 29.7 (*s*); 23.9 (*q*, 3 C); 22.3 (*t*). MS: 235 (21.8, $M^+ - 57$), 233 (22.1), 179 (11.4), 177 (11.7), 162 (11.2), 160 (11.9), 81 (100), 80 (61.3), 79 (18.1), 57 (21.8). Anal. calc. for $C_{12}H_{19}O_3Br$: C 49.50, H 6.58; found: C 49.20, H 6.63.

*(2S,4aS,7aS)-4a-(But-3′-enyl)-2-(*tert*-butyl)-5,6,7,7a-tetrahydrocyclopenta[*d*]dioxin-4(4aH)-one* (**5d**). Electrophile: 10 equiv. of 4-bromobut-1-ene. Distillation afforded 174 mg (69%) of **5d**. B.p. 90°/0.1 Torr. $[\alpha]_D$ = +34.9 (*c* = 0.9). IR (film): 2960*m*, 1740*s*, 1355*m*, 1235*m*, 1185*m*, 1035*m*, 990*m*. ^{1}H-NMR (90 MHz): 0.95 (*s*, *t*-Bu); 1.25–2.75 (*m*, 10 H); 4.10 (*m*, H–C(7a)); 4.80 (*s*, H–C(2)); 5.10–5.80 (*m*, CH_2=CH). MS: 252 (6.1, M^+), 195 (14.5), 166 (45.1), 149 (26.9), 139 (20.1), 137 (54.1), 122 (62.2), 121 (64.2), 112 (38.5), 93 (85.4), 67 (54.3), 57 (50.8), 55 (69.4), 41 (77.6), 28 (100).

*(2S,4aS,7aS)-4a-Allyl-2-(*tert*-butyl)-5,6,7,7a-tetrahydrocyclopenta[*d*]dioxin-4(4aH)-one* (**5e**). Electrophile: 5 equiv. of allyl bromide. Crystallization at low temp. gave **5e** (221 mg, 93%). M.p. < 30° (pentane at –20).

$[\alpha]_D = +40.2$ ($c = 1.3$). IR (film): 3040*w*, 2960*m*, 1740*s*, 1640*w*, 1355*m*, 1235*m*, 1180*m*, 1005*m*, 985*m*, 920*m*. ^{1}H-NMR (300 MHz): 0.95 (*s*, *t*-Bu); 1.56–1.88 (*m*, 3 H); 1.96 (*m*, 2 H); 2.12 (*dd*, $J = 13.9, 8.3$, 1 H, CH_2=CHCH_2); 2.25 (*m*, H–C(7)); 2.64 (*m*, 1 H, CH_2=CHCH_2); 4.14 (*t*, $J = 3.5$, H–C(7a)); 4.83 (*s*, H–C(2)); 5.09 (*dd*, $J = 2.6, 1.9$, 1 H, CH_2=CHCH$_2$); 5.15 (*m*, 1 H, CH_2=CHCH$_2$); 5.79 (*m*, CH_2=CHCH$_2$). ^{13}C-NMR (75 MHz): 174.1 (*s*); 133.3 (*d*); 119.4 (*t*); 107.1 (*d*); 82.5 (*d*); 53.6 (*s*); 40.5 (*t*); 37.6 (*t*); 35.1 (*s*); 32.4 (*t*); 23.8 (*q*, 3 C); 22.2 (*t*). MS: 181 (10.9, $M^+ - 57$), 135 (26.3), 125 (30.6), 108 (100), 93 (68.3), 79 (41.2), 67 (63.9), 41 (58.1). Anal. calc. for $C_{14}H_{22}O_3$: C 70.56, H 9.30; found: C 70.46, H 9.52.

*(2S,4aS,7aS)-2-(*tert*-Butyl)-4a-(2'-chloroprop-2'-enyl)-5,6,7,7a-tetrahydrocyclopenta[*d*]dioxin-4(4a*H*)-one* (**5f**). Electrophile: 8 equiv. of 2,3-dichloroprop-1-ene. FC (pentane/Et_2O 19:1) gave 114 mg of pure **5f** (42%). M.p. 76–77° (pentane). $[\alpha]_D = +19.8$ ($c = 0.87$). IR (KBr): 3060*w*, 2980*s*, 1735*s*, 1630*m*, 1410*m*, 1360*m*, 1350*m*, 1245*m*, 985*s*, 910*m*, 635*m*. ^{1}H-NMR (300 MHz): 0.97 (*s*, *t*-Bu); 1.61–1.93 (*m*, 3 H); 2.01 (*m*, 2 H); 2.17 (*m*, 1 H); 2.28 (distorted *d*, $J = 14.8$, 1 H, CH_2=C(Cl)CH_2); 3.32 (distorted *d*, $J = 14.8$, 1 H, CH_2=C(Cl)CH_2); 4.36 (*m*, 1 H, H–C(7a)); 4.95 (*s*, H–C(2)); 5.25 (*t*, $J = 1.3$, 1 H, CH_2=C(Cl)CH$_2$); 5.29 (*t*, $J = 0.6$, 1 H, CH_2=C(Cl)CH$_2$). ^{13}C-NMR (75 MHz): 173.1 (*s*); 138.2 (*s*); 116.6 (*t*); 107.5 (*d*); 81.6 (*d*); 53.6 (*s*); 43.4 (*t*); 38.0 (*t*); 35.2 (*s*); 31.8 (*t*); 23.9 (*q*, 3 C); 21.2 (*t*). MS: 272 (1.3, M^+), 237 (21.3), 186 (4.0), 171 (18.2), 169 (58.6), 151 (34.6), 142 (50.9), 141 (30.2), 107 (73.2), 95 (35.2), 81 (34.6), 79 (49.2), 67 (100), 65 (35.9), 57 (44.4), 41 (63.9), 39 (43.2). Anal. calc. for $C_{14}H_{21}O_3Cl$: C 61.65, H 7.76; found: C 61.79, H 7.84.

*(2S,4aS,7aS)-2-(*tert*-Butyl)-4a-(3'-chlorobut-2'-enyl)-5,6,7,7a-tetrahydrocyclopenta[*d*]dioxin-4(4a*H*)-one* (**5g**). Electrophile: 2 equiv. of 1,3-dichlorobut-2-ene. FC (pentane/Et_2O 97:3) gave **5g** (117 mg, 41%). B.p. 110°/0.3 Torr. $[\alpha]_D = +74.8$ ($c = 1.0$). IR (film): 2960*m*, 1735*s*, 1665*w*, 1355*m*, 1235*m*, 1185*m*, 995*m*. ^{1}H-NMR (300 MHz): 0.96 (*s*, *t*-Bu); 1.64–2.30 (*m*, 6 H); 2.13 (*s*, 3 H–C(4')); 2.43 (*dd*, $J = 14.4, 8.8$, H–C(1')); 2.57 (*m*, H–C(1')); 4.06 (*dd*, $J = 5.4, 1.4$, H–C(7a)); 4.81 (*s*, H–C(2)); 5.51 (*m*, H–C(2')). MS: 251 (43.9, $M^+ - 35$), 165 (58.9), 164 (40.4), 156 (38.5), 155 (37.9), 137 (55.6), 121 (88.7), 112 (44.3), 111 (49.3), 93 (42.5), 91 (35.6), 89 (55.3), 79 (46.2), 67 (68.1), 57 (61.1), 53 (54.8), 41 (76.8), 28 (100).

*Methyl (2S,4aS,7aS)-2-(*tert*-Butyl)-4,4a,5,6,7,7a-hexahydro-4-oxocyclopenta[*d*]dioxine-4-acetate* (**5h**). Electrophile: 1.5 equiv. of methyl bromoacetate. Crystallization at low temp. afforded 203 mg (75%) of **5h**. M.p. 60–62° (pentane at −20°). $[\alpha]_D = -54$ ($c = 0.9$). IR (KBr): 2980*s*, 1735*s*, 1480*m*, 1435*m*, 1410*m*, 1365*s*, 1220*s*, 985*s*. ^{1}H-NMR (300 MHz): 0.99 (*s*, *t*-Bu); 1.60–2.00 (*m*, 5 H); 2.15 (*m*, 1 H); 2.32 (*d*, $J = 17.8$, H–C(α)); 3.14 (*d*, $J = 17.8$, H–C(α)); 3.69 (*s*, $COOCH_3$); 4.26 (*t*, $J = 2.9$, H–C(7a)); 5.14 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 174.0 (*s*); 171.8 (*s*); 107.3 (*d*); 82.4 (*d*); 51.9 (*q*); 50.6 (*s*); 38.8 (*t*); 36.8 (*t*); 35.0 (*s*); 31.4 (*t*); 24.0 (*q*, 3 C); 21.4 (*t*). MS: 269 (0.7, $M^+ - 1$), 239 (5.9), 213 (52.5), 185 (16.4), 156 (16), 140 (100), 125 (48.7), 108 (59.9), 80 (60.5), 41 (49.2). Anal. calc. for $C_{14}H_{20}O_5$: C 62.20, H 8.20; found: C 61.93, H 8.07.

*Methyl (2S,4aS,7aS)-2-(*tert*-Butyl)-4,4a,5,6,7,7a-hexahydro-4-oxocyclopenta[*d*]dioxine-4a-acetate* (**5i**). Electrophile: 2 equiv. of racemic methyl 2-bromopropionate. FC (pentane/Et_2O 85:15) yielded 119 mg (isolated yield 42%) of **5i**, 1.4:1 mixture of epimers at C(α) (59 mg (30%) of **3b** could be recovered). B.p. 110–120°/0.4 Torr. $[\alpha]_D = -25.5$ ($c = 1.4$). IR (film): 2980*m*, 1735*s*, 1440*w*, 1355*m*, 1240*m*, 1180*m*, 1005*m*. ^{1}H-NMR (300 MHz; major epimer): 0.974 (*s*, *t*-Bu); 1.22 (*d*, $J = 7.6$, CH_3–C(α)); 1.75–2.12 (*m*, 6 H); 3.24 (*q*, $J = 7.6$, H–C(α)); 3.70 (*s*, $COOCH_3$); 4.39 (*dd*, $J = 4.0, 1.0$, H–C(7a)); 5.13 (*s*, H–C(2)). ^{1}H-NMR (300 MHz; minor epimer): 0.971 (*s*, *t*-Bu); 1.48 (*d*, $J = 7.3$, CH_3–C(α)); 1.75–2.12 (*m*, 6 H); 2.52 (*q*, $J = 7.3$, H–C(α)); 3.69 (*s*, $COOCH_3$); 4.20 (*t*, $J = 3.3$, H–C(7a)); 4.98 (*s*, H–C(2)). MS: 227 (13.3, $M^+ - 57$), 199 (19.3), 154 (59.8), 153 (25.6), 139 (36.4), 122 (40.2), 111 (32.2), 95 (87.8), 94 (75.3), 93 (50.3), 88 (26.3), 79 (32.2), 67 (94), 59 (34.5), 57 (57.6), 55 (56.2), 41 (100), 39 (50.5).

tert-*Butyl (2S,4aS,7aS)-2-(*tert*-Butyl)-4,4a,5,6,7,7a-hexahydro-α-methylidene-4-oxocyclopenta[*d*]dioxine-4a-proprionate* (**5j**). Electrophile: 5 equiv. of *tert*-butyl 2-(bromomethyl)acrylate. FC (pentane/Et_2O 9:1) gave 175 mg (45%) of **5j**. M.p. 54° (pentane at −20°). $[\alpha]_D = +24.8$ ($c = 0.6$). IR (KBr): 2985*s*, 1730*s*, 1715*s*, 1630*w*, 1485*m*, 1365*s*, 1355*s*, 1285*s*, 1195*s*, 1150*s*, 975*s*, 940*s*, 850*m*, 815*m*, 800*m*, 765*m*. ^{1}H-NMR (90 MHz): 0.93 (*s*, *t*-Bu); 1.50 (*s*, COO(*t*-Bu)); 1.60–2.40 (*m*, 6 H); 2.58 (*d*, $J = 13.5$, H–C(β)); 2.88 (*d*, $J = 13.5$, H–C(β)); 4.09 (*m*, H–C(7a)); 4.73 (*s*, H–C(2)); 5.67 (br. *s*, 1 H, CH_2=C(α)); 6.20 (*s*, 1 H, CH_2=C(α)). MS: 388 (2.1, M^+), 282 (1.9), 225 (46.3), 152 (62.1), 151 (46.5), 67 (48.4), 57 (100), 41 (47.9).

*(2S,4aR,7aS)-4a-Acetyl-2-(*tert*-butyl)-5,6,7,7a-tetrahydrocyclopenta[*d*]dioxin-4(4a*H*)-one* (**5k**). Electrophile: 5 equiv. of AcCl. FC (pentane/Et_2O 92:8) afforded 194 mg (81%) of **5k**. M.p. 54° (pentane). $[\alpha]_D = +135.9$ ($c = 1.1$). IR (KBr): 2980*s*, 1735*s*, 1710*s*, 1480*m*, 1415*m*, 1355*s*, 1235*s*, 1200*s*, 985*s*, 770*m*, 605*m*. ^{1}H-NMR (300 MHz): 0.96 (*s*, *t*-Bu); 1.60–1.96 (*m*, 4 H); 2.17 (*ddd*, $J = 13.5, 7.2, 1.3$, H–C(5)); 2.34 (*s*, Ac); 2.54 (*ddd*, $J = 13.5, 5.5, 1.1$, H–C(5)); 4.82 (*dd*, $J = 5.5, 2.9$, 1 H–C(7a)); 4.89 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 202.6 (*s*); 169.0 (*s*); 107.6 (*d*); 81.3 (*d*); 68.7 (*s*); 36.2 (*t*); 35.1 (*s*); 33.4 (*t*); 27.0 (*q*); 23.8 (*q*, 3 C); 23.3 (*t*). MS: 197 (0.8, $M^+ - 43$), 183

(17.4), 126 (29.9), 111 (23.9), 110 (24.1), 95 (100), 67 (17), 43 (44.1), 41 (19). Anal. calc. for $C_{13}H_{20}O_4$: C 64.98, H 8.39; found: C 65.04, H 8.23.

*(2S,4aS,7aS,1'ξ)-2-(*tert*-Butyl)-4a-(1'-hydroxyethyl)-5,6,7,7a-tetrahydrocyclopenta[*d*]dioxin-4(4aH)-one* (**5l**). Electrophile: 5 equiv. of CH_3CHO. The crude product (191 mg, 79%) consisted of a 2.3:1 mixture of epimers, part of which was oxidized to a single ketone, **5k** (see below). The major epimer was obtained in stereoisomerically pure form by crystallization. M.p. 134–135° (pentane). $[\alpha]_D = +19.7$ (MeOH, $c = 1.0$). IR (KBr): 3490*s* (br.), 2980*m*, 1710*s*, 1355*m*, 1245*m*, 1180*m*, 1000*m*. ^{1}H-NMR (300 MHz): 0.956 (*s*, *t*-Bu); 1.34 (*d*, $J = 6.4$, 3 H–C(2')); 1.58–2.30 (*m*, 7 H); 3.80 (*q*, $J = 6.4$, H–C(1')); 4.39 (*dd*, $J = 5.3$, 1.0, H–C(7a)); 5.03 (*s*, H–C(2)). ^{13}C-NMR (20 MHz): 173.4 (*s*); 106.5 (*d*); 82.5 (*d*); 71.6 (*d*); 59.6 (*s*); 35.3 (*t*); 34.7 (*s*); 33.9 (*t*); 23.7 (*q*, 3 C); 23.6 (*t*); 19.1 (*q*). MS: 244 (0.3, $M^+ + 2$), 243 (0.5, $M^+ + 1$), 185 (4.5), 139 (49.2), 113 (42.5), 112 (98.4), 111 (23.4), 97 (49.5), 95 (100), 94 (40.8), 71 (40.5), 67 (48.1), 45 (56.3), 43 (69.9), 41 (81.1). Anal. calc. for $C_{13}H_{22}O_4$: C 64.44, H 9.15; found: C 64.23, H 9.13.

Significant signals in the ^{1}H-NMR spectra (300 MHz) of the minor epimer: 0.965 (*s*); 1.28 (*d*, $J = 6.5$); 2.84 (br. *s*); 3.78 (br. *q*); 4.21 (distorted *d*, $J = 5.1$); 4.92 (*s*).

*Methyl (2S,4aR,7aS,1'ξ)-2-(*tert*-Butyl)-4,4a,5,6,7,7a-hexahydro-α-hydroxy-α-methyl-4-oxocyclopenta[*d*]-dioxine-4a-acetate* (**5m**). Electrophile: 5 equiv. of $CH_3COCOOCH_3$. The crude product (264 mg, 88%) consisted of a 2:1 mixture of epimers. The major one was obtained in stereoisomerically pure form by crystallization. M.p. 108–109° (pentane). $[\alpha]_D = +19.7$ (MeOH, $c = 1.0$). IR (KBr): 3450*s* (br.), 2970*s*, 1730*s*, 1715*s*, 1480*m*, 1455*m*, 1405*m*, 1380*m*, 1365*m*, 1350*m*, 1280*s*, 1240*s*, 1160*s*, 1105*s*, 1005*s*, 780*m*. ^{1}H-NMR (300 MHz): 0.94 (*s*, *t*-Bu); 1.45 (*s*, CH_3–C(α)); 1.72 (*m*, 3 H); 2.02 (*m*, 1 H); 2.16–2.28 (*m*, 1 H); 2.33–2.40 (*m*, 1 H); 3.81 (*s*, exchange with D_2O, OH); 3.85 (*s*, $COOCH_3$); 4.49 (*d*, $J = 4.7$, H–C(7a)); 4.88 (*s*, H–C(2)). MS: 241 (3.1, $M^+ - 59$), 215 (14), 127 (38.8), 112 (21.4), 111 (100), 95 (55.8), 43 (73.5), 41 (20.5). Anal. calc. for $C_{15}H_{24}O_6$: C 59.98, H 8.05; found: C 59.69, H 8.21.

Significant signals in the ^{1}H-NMR (300 MHz) of the minor epimer: 0.96 (*s*, *t*-Bu); 1.40 (*s*, CH_3–C(α)); 3.79 (*s*, $COOCH_3$); 4.41 (*d*, $J = 4.0$, H–C(7a)); 5.09 (*s*, H–C(2)).

5k *by Oxidation of* **5l**. A suspension of 56 mg of a 2.3:1 epimeric mixture **5l**, 190 mg (0.88 mmol) of pyridinium chlorochromate (PCC), and 500 mg of 4-Å molecular sieve[27]) in 4 ml of dry CH_2Cl_2 was stirred at r.t. for 2.5 h. After addition of dry Et_2O, the mixture was filtered through a short path of silica gel *60 G* with Et_2O. Evaporation afforded 53 mg (96%) of diastereoisomerically pure **5k.**

$NaBH_4$ Reduction of **5k**. A soln. of 83 mg (0.35 mmol) of **5k** in 1 ml of MeOH was added to a suspension of 10 mg (0.26 mmol) of $NaBH_4$ in 0.5 ml of MeOH at –70°. The mixture was stirred at –70° for 1.25 h, quenched by the addition of 1 ml of a sat. NH_4Cl soln., and warmed up to r.t. Extractive workup (CH_2Cl_2) gave an org. soln. which was washed with brine, dried, and evaporated: 9:1 mixture of epimeric alcohols (65 mg, 78%); the major one was identical to the obtained in the reaction of **3b** with acetaldehyde.

(4aR,8aS)-Perhydro-4a-methyl-2H,4H-1,3-benzodioxin-4-one (**6a**). A soln. of 285 mg (1.85 mmol) of **4a** in 4 ml of THF was dropwise added to a soln. of 2.04 mmol of LDA in 2.8 ml of THF at –70° and stirred for 15 min. Then, 3.4 ml of DMPU were added, stirring was continued for additional 15 min, and 1.3 ml (20.3 mmol) of MeI were added. The temp. was kept at –70° for 1 h and slowly raised to r.t. (overnight). *Workup Procedure 3* afforded 295 mg of a residue which consisted of a 93:7 mixture of **6a** and its 4a-epimer. Crystallization furnished 247 (80%) of pure **6a**. M.p. 87–88° (pentane). $[\alpha]_D = +24.6$ ($c = 1.3$). IR (KBr): 2940*m*, 1725*s*, 1375*m*, 1240*s*, 1195*s*, 1150*s*, 1025*s*, 995*s*, 795*s*. ^{1}H-NMR (300 MHz): 1.23 (*s*, CH_3–C(4a)); 1.44–1.74 (*m*, 6 H); 1.82–1.94 (*m*, H–C(8)); 2.00–2.12 (*m*, H–C(8)); 3.74 (br. *s*, H–C(8a)); 5.39 (*d*, $J = 6.0$, H–C(2)); 5.47 (*d*, $J = 6.0$, H–C(2)). ^{13}C-NMR (75 MHz): 173.9 (*s*); 93.4 (*t*); 78.6 (*d*); 44.1 (*s*); 32.1 (*t*); 26.5 (*t*); 20.8 (*t*); 20.0 (*t*); 18.7 (*q*). MS: 171 (0.7, $M^+ + 1$), 140 (8.6), 112 (7.2), 97 (10.7), 96 (100), 95 (12.8), 81 (95.4), 69 (17.2), 68 (37.8), 67 (26.2), 55 (27), 41 (33.7), 38 (14.9). Anal. calc. for $C_9H_{14}O_3$: C 63.51, H 8.29; found: C 63.34, H 8.30.

(4aS,8aS)-4a-Allylperhydro-2H,4H-[1,3]benzodioxin-4-one (**6b**). As described for **6a**, with 744 mg (4.77 mmol) of **4a** in 15 ml of THF, 5.73 mmol of LDA in 7 ml of THF, 11 ml of DMPU, and 2.1 ml (23.85 mmol) of allyl bromide: 828 mg of a residue, > 98% of **6b**. Distillation gave 715 mg (77%) of pure **6b**. B.p. 110°/0.3 Torr. $[\alpha]_D = +71.4$ ($c = 1.8$). IR (film): 3035*w*, 2965*s*, 1740*s*, 1640*w*, 1435*m*, 1425*m*, 1370*m*, 1225*s*, 1150*s*, 1025*s*, 995*m*, 960*m*, 870*w*, 800*w*, 745*m*. ^{1}H-NMR (300 MHz): 1.44–1.74 (*m*, 6 H); 1.86 (*m*, H–C(8)); 2.01–2.10 (*m*, H–C(8)); 2.44 (*dd*, $J = 14.2$, 9.0, H–C(1')); 2.72 (*m*, H–C(1')); 3.93 (br. *s*, H–C(8a)); 5.11 (*m*, H–C(3')); 5.15 (*m*, H–C(3')); 5.35 (*d*, $J = 5.1$, H–C(2)); 5.43 (*d*, $J = 5.1$, H–C(2)); 5.76 (*m*, H–C(2')). MS: 196 (< 1, M^+), 166 (16.3), 124 (12.7), 122

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[27]) Before mixing, the solns. of PCC and of the epimeric mixture were stirred in the presence of molecular sieve [69].

(31.2), 121 (11.9), 107 (14.6), 95 (11.4), 94 (13.6), 93 (23.5), 91 (12.5), 81 (100), 79 (57.1), 77 (18.5), 67 (33.1), 53 (21), 41 (51.3), 39 (38.5), 27 (20.3). Anal. calc. for $C_{11}H_{16}O_3$: C 67.32, H 8.22; found: C 67.74, H 8.39.

(4aR,8aS)-4a-Acetylperhydro-2H,4H-[1,3]benzodioxin-4-one (**6c**). As described for **6a**, with 703 mg (4.51 mmol) of **4a** in 12 ml of THF, 5.41 mmol of LDA in 6 ml of THF, 6 ml of DMPU, and 1.6 ml (22.5 mmol) of AcCl: a 73:18:9 mixture **6c**/**4a**/4a-epimer of **4a** which was purified by FC (pentane/Et_2O 3:1) to give 360 mg (42%) of **6c**. M.p. 52–53° (pentane or pentane/Et_2O). $[\alpha]_D = +14.6$ ($c = 0.74$). IR (KBr): 2950*s*, 1730*s*, 1720*s*, 1710*s*, 1440*m*, 1240*s*, 1000*s*, 745*m*. ^{1}H-NMR (300 MHz): 1.25–2.30 (*m*, 8 H); 2.42 (*s*, Ac); 4.53 (br. *s*, H–C(8a)); 5.40 (*d*, $J = 5.2$, H–C(2)); 5.48 (*d*, $J = 5.2$, H–C(2)). ^{13}C-NMR (75 MHz): 204.4 (*s*); 168.2 (*s*); 93.1 (*t*); 74.3 (*d*); 61.2 (*s*); 29.9 (*t*); 28.0 (*q*); 27.3 (*t*); 22.4 (*t*); 20.1 (*t*). MS: 198 (< 1, M^+), 168 (1.2), 156 (16.2), 155 (47.5), 126 (74), 125 (40.9), 109 (38.6), 108 (20.7), 81 (87.6), 80 (39.4), 43 (100), 41 (28.6), 39 (27.5).

(4aS,8aS,1′S)-Perhydro-4a-(1′-hydroxyethyl)-2H,4H-[1,3]benzodioxin-4-one (**6d**) *and (4aS,8aS,1′R)-Perhydro-4a-(1′-hydroxyethyl)-2H,4H-1,3-benzodioxin-4-one* (**6e**) *from* **4a** *with Acetaldehyde in the Presence of* $ZnCl_2$. A soln. of 2.86 mg (18.3 mmol) of **4a** in 85 ml of THF was dropwise added to a soln. of 21.97 mmol of LDA in 45 ml of THF at −70°. The mixture was stirred for 30 min, and 1M soln. of $ZnCl_2$ in Et_2O (22 ml) were added. After stirring for 15 min, CH_3CHO (10.4 ml, 183 mmol) was added, the soln. stirred at −70° for 1.75 h, quenched by the addition of 30 ml of sat. aq. NH_4Cl soln., warmed up to r.t., and extracted with Et_2O. The org. phase was washed with H_2O and brine, dried and evaporated: 3.90 g of a residue which consisted of a 8:21:71: < 1 mixture **4a**/**6d**/**6e**/4a-epimers of **6d** and **6e** (^{1}H-NMR evidence). Part (0.68 mg) of this product was oxidized with PCC (see below), the rest was crystallized affording 1.40 g of **4a**. FC (pentane/Et_2O, 30–55%) of the mother liquor gave 255 mg (55% overall yield) of **6d** and 313 mg (9%) of **6e**.

6d: M.p. 109–110° (pentane/Et_2O). $[\alpha]_D = +27.5$ (MeOH, $c = 0.8$). IR (KBr): 3470*s* (br.), 3015*w*, 2950*s*, 1695*s*, 1445*m*, 1370*m*, 1240*s*, 1160*s*, 1100*s*, 1045*s*, 1035*s*, 995*s*, 950*s*, 740*s*. ^{1}H-NMR (300 MHz): 1.30 (*d*, $J = 6.4$, 3 H–C(2′)); 1.52–1.67 (*m*, 5 H); 1.90 (*m*, 2 H); 2.27 (*m*, H–C(8)); 3.48 (*d*, $J = 11.3$, exchange with D_2O, OH); 3.90 (br. *s*, H–C(8a)); 3.99 (*dq*, $J = 11.3, 6.4$, H–C(1′)); 5.40 (*d*, $J = 5.2$, H–C(2)); 5.49 (*d*, $J = 5.2$, H–C(2)). ^{13}C-NMR (75 MHz): 173.8 (*s*); 93.6 (*t*); 75.3 (*d*); 66.0 (*d*); 52.7 (*s*); 27.3 (*t*); 26.1 (*t*); 20.4 (*t*); 19.83 (*q*); 19.77 (*t*). MS: 185 (1.3, $M^+ - 15$), 156 (4.6), 127 (12.3), 126 (100), 111 (14.2), 108 (25.8), 97 (14.6), 82 (13.7), 81 (87.3), 80 (58.1), 67 (30.4), 43 (30.6), 41 (32.1). Anal. calc. for $C_{10}H_{16}O_4$: C 59.98, H 8.05; found: C 60.17, H 8.02.

6e: M.p. 67–68° (pentane/Et_2O). $[\alpha]_D = +22.5$ ($c = 0.69$). IR (KBr): 3380*s* (br.), 2930*s*, 1725*s*, 1390*m*, 1360*m*, 1235*s*, 1010*s*, 740*m*. ^{1}H-NMR (300 MHz): 1.53 (*d*, $J = 6.5$, 3 H–C(2′)); 1.21–2.08 (*m*, 8 H); 2.95 (br. *s*, exchange with D_2O, OH); 4.00 (*q*, $J = 6.5$, H–C(1′)); 4.22 (*t*, $J = 4.0$, H–C(8a)); 5.42 (*d*, $J = 5.1$, H–C(2)); 5.46 (*d*, $J = 5.1$, H–C(2)). ^{13}C-NMR (75 MHz): 171.6 (*s*); 92.9 (*t*); 75.9 (*d*); 70.0 (*d*); 53.4 (*s*); 28.9 (*t*); 26.4 (*t*); 21.4 (*t*); 20.2 (*t*); 19.1 (*q*). MS: 170 (1.5, $M^+ - 30$), 156 (8.8), 127 (16.9), 126 (100), 111 (19.5), 109 (1.1), 108 (26), 97 (15.5), 81 (77.3), 67 (28.9), 43 (28.9). Anal. calc. for $C_{10}H_{16}O_4$: C 59.98, H 8.05; found: C 59.73, H 8.19.

6d *from* **4a** *with Acetaldehyde in the Absence of* $ZnCl_2$. A soln. of 626 mg (4.01 mmol) of **4a** in 25 ml of THF was dropwise added to a soln. of 4.82 mmol of LDA in 10 ml of THF at −70° and stirred for 40 min. Then, CH_3CHO (2.4 ml, 40.1 mmol) was added, the soln. stirred at −70° for 1.5 h, quenched by the addition of 10 ml of sat. aq. NH_4Cl soln., warmed up to r.t., and extracted with Et_2O. The org. phase was washed with H_2O and brine, dried, and evaporated: 722 mg of 6:90:3: < 1 mixture **4a**/**6d**/**6e**/4a-epimers of **6d** and **6e** (^{1}H-NMR evidence). Crystallization from pentane/Et_2O gave 553 mg (69%) of diastereoisomerically pure **6d**.

Application of Horeau's *Method to* **6d**. To a soln. of 57.2 mg of **6d** in 1.50 ml of pyridine, 0.170 ml of 2-phenylbutyric anhydride were added. This soln. was kept at r.t. for 2.25 h, and 0.084 ml of H_2O were added. The mixture was allowed to stand at r.t. for 0.5 h, and the optical rotation a_1 was measured (= +1.74°). Then, 0.1 ml of Et_3N were added to a 1-ml aliquot of this soln., and the optical rotation a_2 was immediately measured (= +2.49°).

Application of Horeau's *Method to* **6e**. As described above with 37.6 mg of **6e** in 0.940 ml of pyridine, 0.110 ml of 2-phenylbutyric anhydride (2.5 h), H_2O (0.084 ml), and 0.1 ml of Et_3N: $a_1 = +0.60°$, $a_2 = +0.35°$.

6c *by Oxidation of* **6d** *and* **6e**. A suspension of 683 mg of a 3.5:1 mixture **6d**/**6e**, 2.30 g (10.2 mmol) of PCC, and 5 g of 4-Å molecular sieve[27]) in 100 ml of dry CH_2Cl_2 was stirred at r.t. for 2.75 h. After addition of dry Et_2O, the mixture was filtered through a short path of silica gel *60 G* with Et_2O. Evaporation afforded 500 mg of a single diastereoisomer along *ca.* 10% of **4a**, which was purified by FC (pentane/Et_2O 3:1) to give 460 mg (overall yield from **4a**, 72%) of **6c**.

(2S,4aR,8aS)-Perhydro-2-isopropyl-4a-methyl-2H,4H-[1,3]benzodioxin-4-one (**6f**). As described for **6a**, with 330 mg (1.74 mmol) of **4b** in 4.4 ml of THF, 1.90 mmol of LDA in 2 ml of THF, 3.2 ml of DMPU, and 1.1 ml (17.2 mmol) of MeI: 293 mg (82%) of an inseparable 3:2 mixture of **6f** and its 4a-epimer. ^{1}H-NMR: significant signals of **6f**: 1.016 (*d*, $J = 6.9$); 1.30 (*s*); 3.71 (br. *s*); 5.15 (*d*, $J = 3.6$); significant signals of the 4a-epimer: 1.020 (*d*, $J = 6.9$), 1.28 (*s*); 3.61 (*dd*, $J = 11.7, 4.2$); 5.19 (*d*, $J = 3.6$).

*(2S,4aR,8aS)-2-(*tert*-Butyl)-4a-methylperhydro-2*H,*4*H*-[1,3]benzodioxin-4-one* (**6g**). As described for **6a**, with 230 mg (1.09 mmol) of **4c** in 5.4 ml of THF, 1.24 mmol of LDA in 5.4 ml of THF, 5.4 ml of DMPU, and 0.7 ml (11.3 mmol) of MeI (addition at −100°) at −70° for 3 h, and then to r.t. (overnight): 208 mg (85%) of an inseparable 4:3 mixture of **6g** and its 4a-epimer. The ^{1}H-NMR: significant signals of **6g**: 1.001 (*s*); 1.29 (*s*); 3.71 (br. *s*); 4.94 (*s*); significant signals of the 4a-epimer: 0.996 (*s*); 1.27 (*s*); 3.58 (*dd*, *J* = 11.7, 4.2); 4.98 (*d*).

*(2S,4aS,8aS)-2-(*tert*-Butyl)-4a-(phenylselenenyl)-5,6,7,8-tetrahydrocyclopenta[*d*]dioxin-4(4a*H*)-one* (**7**). A soln. of 4.06 g (20 mmol) of **3b** in 70 ml of THF was dropwise added to a soln. of 22.7 mmol of LDA in 100 ml of THF at −70°. The mixture was stirred for 0.5 h, and a soln. of 5.10 g (27 mmol) of PhSeCl in 70 ml of THF was added. The soln. was kept at −70° for 1 h and warmed up to 0° for 6 h. *Workup Procedure 1* afforded a residue (7.76 g) consisting of **7** as a single diastereoisomer, along *ca.* 10% of **3b**, which was purified by FC (pentane/Et_2O 92:8): 5.72 g (81%, corrected yield 90%) of **7**. M.p. 68° (pentane at −20°). $[\alpha]_D$ = +43.3 (*c* = 0.84). IR (KBr): 2985*m*, 1720*s*, 1575*w*, 1570*w*, 1485*m*, 1435*m*, 1415*m*, 1365*m*, 1345*m*, 1245*s*, 1105*m*, 1030*m*, 995*s*, 970*m*, 775*m*, 745*s*, 695*m*. ^{1}H-NMR (300 MHz): 0.84 (*s*, *t*-Bu); 1.69–1.98 (*m*, 4 H); 2.24 (*m*, 1 H); 2.43 (*m*, 1 H); 4.28 (*s*, H–C(2)); 4.35 (*dd*, *J* = 6.6, 3.2, H–C(7a)); 7.26–7.47 (*m*, 3 arom. H); 7.68–7.72 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz): 171.3 (*s*); 137.7 (*d*, 2 C); 129.9 (*d*); 129.2 (*d*, 2 C); 127.0 (*s*); 106.7 (*d*); 85.7 (*d*); 53.5 (*s*); 38.0 (*t*); 34.9 (*s*); 33.4 (*t*); 23.8 (*q*, 3 C); 23.1 (*t*). MS: 355 (0.7, $M^+ + 2$), 354 (7.3, $M^+ + 1$), 352 (3.4), 226 (17.6), 225 (12.9), 224 (100), 222 (49.3), 221 (20.8), 157 (26.7), 143 (48.8), 95 (28.6), 83 (22.1), 77 (25.2), 67 (99.2), 57 (33.2), 55 (46), 41 (61.2), 39 (29.6). Anal. calc. for $C_{17}H_{22}O_3Se$: C 57.79, H 6.28; found: C 57.40, H 6.40.

*(4aR,8aS)-Perhydro-4a-(phenylselenenyl)-2*H,*4*H*-[1,3]benzodioxin-4-one* (**8a**) *and (4aS,8aS)-Perhydro-4a-(phenylselenenyl)-2*H,*4*H*-[1,3]benzodioxin-4-one* (**9a**). As described for **7**, with 1.20 g (7.70 mmol) of **4a** in 27 ml of THF, 8.47 mmol of LDA in 12 ml of THF, and 1.85 g (9.63 mmol) of PhSeCl in 15 ml of THF (1.5 h at −70° and slowly warmed up to r.t. overnight): 83:17 mixture of **8a**/**9a** (^{1}H-NMR) which was crystallized from pentane to give 795 mg of **8a**. FC (pentane/Et_2O, 30–40%) of the mother liquor furnished 245 mg of **9a** and additional 223 mg of **8a** (overall yield 53%).

8a: M.p. 108° (pentane). $[\alpha]_D$ = −75.9 (*c* = 0.71). IR (KBr): 3030*w*, 3005*w*, 2975*s*, 1735*s*, 1565*w*, 1450*m*, 1435*m*, 1425*m*, 1345*m*, 1235*s*, 1180*s*, 1005*s*, 870*w*, 850*w*, 830*w*, 745*s*, 695*s*. ^{1}H-NMR (90 MHz): 1.10–2.50 (*m*, 8 H); 3.74 (*dd*, *J* = 11.5, 4.2, H–C(8a)); 5.43 (*s*, H–C(2)); 7.13–7.40 (*m*, 3 arom. H); 7.50–7.72 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz): 169.0 (*s*); 138.1 (*d*, 2 C); 129.6 (*d*); 129.0 (*d*, 2 C); 125.6 (*s*); 94.4 (*t*); 80.3 (*d*); 56.0 (*s*); 28.7 (*t*); 27.6 (*t*); 24.1 (*t*); 20.9 (*t*). MS: 314 (3.2, $M^+ + 3$), 313 (2.4, $M^+ + 2$), 312 (16.9, $M^+ + 1$), 311 (<1, M^+), 157 (12.7), 125 (100), 109 (11.4), 97 (27.7), 81 (34.3), 79 (44.6), 78 (18.6), 77 (29.6), 69 (49.6), 55 (28.2), 51 (20.3), 41 (59.8), 39 (24.9). Anal. calc. for $C_{14}H_{16}O_3Se$: C 54.03, H 5.18; found: C 54.08, H 5.23.

9a: Thick oil. $[\alpha]_D$ = +67 (*c* = 1.2). IR (film): 3025*w*, 2940*s*, 1735*s*, 1435*m*, 1220*s*, 1020*s*, 820*w*, 760*w*, 740*m*, 695*m*. ^{1}H-NMR (300 MHz): 1.00–2.40 (*m*, 8 H); 4.00 (*dd*, *J* = 7.1, 3.9, H–C(8a)); 5.24 (*d*, *J* = 5.1, H–C(2)); 5.42 (*d*, *J* = 5.1, H–C(2)); 7.10–7.40 (*m*, 3 arom. H); 7.40–7.80 (*m*, 2 arom. H). MS: 315 (1, $M^+ + 4$), 314 (6.7, $M^+ + 3$), 313 (5.1, $M^+ + 2$), 312 (35.7, $M^+ + 1$), 311 (2.7, M^+), 310 (17.7), 238 (16.1), 158 (24.9), 157 (34), 156 (15.7), 155 (22.2), 125 (100), 109 (30.7), 97 (57), 81 (75), 79 (84.8), 78 (30.8), 77 (53.3), 69 (47), 55 (37.9), 51 (32.7), 41 (69.8), 39 (33.1).

*(2S,4aR,8aS)-Perhydro-2-isopropyl-4a-(phenylselenenyl)-2*H,*4*H*-[1,3]benzodioxin-4-one* (**8b**) *and (2S,4aS,8aS)-Perhydro-2-isopropyl-4a-(phenylselenenyl)-2*H,*4*H*-[1,3]benzodioxin-4-one* (**9b**). As described for **7**, with 765 mg (3.86 mmol) of **4b** in 12 ml of THF, 4.29 mmol of LDA in 6 ml of THF, and 934 mg (4.88 mmol) of PhSeCl in 10 ml of THF (1.5 h at −70° and slowly warmed up to r.t. overnight): 11:73:16 mixture **4b**/**8b**/**9b** (^{1}H-NMR) which was separated by FC (5–20% Et_2O/pentane) to give 145 mg (11%) of **9b** and 696 mg (51%) of **8b**.

8b: M.p. 84–86° (pentane). $[\alpha]_D$ = −45.3 (*c* = 0.69). IR (KBr): 3025*w*, 2970*s*, 1735*s*, 1580*w*, 1470*m*, 1445*m*, 1435*m*, 1370*m*, 1255*s*, 1230*s*, 1005*m*, 980*m*, 915*w*, 875*w*, 850*w*, 740*m*, 690*m*. ^{1}H-NMR (90 MHz): 1.07 (*d*, *J* = 7, $(CH_3)_2$CH); 1.10–2.30 (*m*, 9 H); 3.70 (*dd*, *J* = 11.4, H–C(8a)); 5.21 (*d*, *J* = 4, H–C(2)); 7.05–7.30 (*m*, 3 arom. H); 7.40–7.60 (*m*, 2 arom. H). MS: 356 (1.1, $M^+ + 3$), 355 (0.9, $M^+ + 2$), 354 (6.2, $M^+ + 1$), 353 (0.5, M^+), 238 (34.4), 236 (18), 98.5 (21.6), 81 (100), 80.5 (28.5), 73 (67.1), 54.5 (29.6), 40 (69.1).

9b: Thick oil. $[\alpha]_D$ = +75.5 (*c* = 0.85). IR (film): 3025*w*, 2970*s*, 1740*s*, 1575*w*, 1470*m*, 1435*m*, 1405*m*, 1355*m*, 1225*s*, 1170*s*, 1020*m*, 995*m*, 925*w*, 740*m*, 690*m*. ^{1}H-NMR (90 MHz): 0.94 (*d*, *J* = 7, $(CH_3)_2$CH); 1.40–2.30 (*m*, 9 H); 3.80 (distorted *t*, *J* = 3, H–C(8a)); 4.88 (*d*, *J* = 4, H–C(2)); 7.20–7.45 (*m*, 3 arom. H); 7.50–7.70 (*m*, 2 arom. H). MS: 356 (2.7, $M^+ + 3$), 355 (2.4, $M^+ + 2$), 354 (14.6, $M^+ + 1$), 353 (1.4, M^+), 352 (7), 282 (4.6), 255 (5.8), 240 (13.9), 239 (10.1), 238 (76.9), 236 (38), 157 (30.3), 125 (29.2), 109 (23.5), 97 (29.2), 81 (100), 79 (46), 77 (34.2), 69 (27.1), 43 (34.2), 41 (55.6).

*(2S,4aR,8aS)-2-(*tert*-Butyl)perhydro-4a-(phenylselenenyl)-2*H,*4*H*-[1,3]benzodioxin-4-one* (**8c**) *and (2S,4aS,8aS)-2-(*tert*-Butyl)perhydro-4a-(phenylselenenyl)-2*H,*4*H*-[1,3]benzodioxin-4-one* (**9c**). As described for

7, with 355 mg (1.67 mmol) of **4c** in 7 ml of THF, 1.52 mmol of LDA in 3 ml of THF, and 347 mg (1.81 mmol) of PhSeCl in 10 ml of THF/HMPTA 1:1 (1 h at −70° and slowly warmed up to r.t.): 32:68 mixture of **8c**/**9c**, which was separated by FC (pentane/Et_2O 5:1) to give 220 mg (45%) of **9c** and 102 mg (21%) of **8c**.

8c: M.p. 138–140° (pentane). $[\alpha]_D = -43$ ($c = 0.43$). ^{1}H-NMR (300 MHz): 1.07 (*s*, *t*-Bu); 1.26–1.50 (*m*, 3 H); 1.72–1.98 (*m*, 4 H); 2.24 (*m*, 1 H); 3.71 (*dd*, $J = 11.5, 4.2$, H–C(8a)); 5.06 (*s*, H–C(2)); 7.24–7.42 (*m*, 3 arom. H); 7.58–7.64 (*m*, 2 arom. H).

9c: M.p. 76–79° (pentane). $[\alpha]_D = +70$ ($c = 0.95$). ^{1}H-NMR (300 MHz): 0.92 (*s*, *t*-Bu); 1.52–1.82 (*m*, 5 H); 2.01 (*m*, 2 H); 2.22 (*m*, 1 H); 3.80 (*t*, $J = 3.6$, H–C(8a)); 4.72 (*s*, H–C(2)); 7.28–7.42 (*m*, 3 arom. H); 7.64–7.70 (*m*, 2 arom. H).

*(2S,7aS)-2-(*tert*-Butyl)-7,7a-dihydrocyclopenta[*d*]dioxin-4(6*H*)-one* (**10**) *and (2S)-2-(*tert*-Butyl)-6,7-dihydrocyclopenta[*d*]dioxin-4(5*H*)-one* (**11**). A soln. of 3.13 g (18.8 mmol) of **3b** in 50 ml of THF was dropwise added to 20.6 mmol of LDA in 50 ml of THF at −70°. After stirring for 0.5 h, a soln. of 4.00 g (20.6 mmol) of PhSeCl in 40 ml of THF was added. The mixture was kept at −70° for 1 h and warmed up to 0° (for 7 h). *Workup Procedure 1* afforded a crude product which was dissolved in 150 ml of CH_2Cl_2 and 2.6 ml (31.6 mmol) of pyridine and treated dropwise at < 10° with 4.9 ml (42.7 mmol) of 30% H_2O_2. The soln. was further stirred at 0° for 40 min. *Workup Procedure 2* gave 2.85 g of a residue which was chromatographed (FC, 15–20% Et_2O/pentane) to afford 1.15 g (37%) of **10** and 0.57 g (18%) of **11**.

10: M.p. 120–122° (pentane). $[\alpha]_D = +74.4$ ($c = 1.1$). IR (KBr): 2990*s*, 1725*s*, 1645*s*, 1480*m*, 1405*m*, 1365*m*, 1345*s*, 1245*s*, 1195*s*, 1080*s*, 955*s*, 755*s*, 740*s*. ^{1}H-NMR (300 MHz): 1.00 (*s*, *t*-Bu); 2.03 (*m*, 1 H); 2.54 (*m*, 3 H); 4.86 (*m*, H–C(7a)); 5.09 (*s*, H–C(2)); 6.98 (br. *s*, H–C(5)). ^{13}C-NMR (75 MHz): 144.0 (*d*); 133.0 (*s*); 109.8 (*d*); 82.4 (*d*); 35.4 (*s*); 32.0 (*t*); 30.3 (*t*); 24.2 (*q*, 3 C). MS: 195 (0.6, $M^+ - 1$), 152 (2.8), 141 (12.2), 139 (75.2), 93 (88), 66 (100). Anal. calc. for $C_{11}H_{16}O_3$: C 67.32, H 8.22; found: C 66.92, H 8.44.

11: M.p. 76° (pentane at −20°). $[\alpha]_D = +179.8$ ($c = 0.78$). IR (KBr): 2980*m*, 1730*s*, 1635*s*, 1400*s*, 1120*s*, 1005*s*, 915*m*, 760*m*. ^{1}H-NMR (300 MHz): 1.07 (*s*, *t*-Bu); 2.04 (*m*, 2 H–C(6)); 2.51–2.68 (*m*, 2 H–C(5), 2 H–C(7)); 5.09 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 174.9 (*s*); 161.9 (*s*); 107.7 (*d*); 106.2 (*s*); 34.5 (*s*); 31.0 (*t*); 25.9 (*t*); 24.2 (*q*, 3 C); 19.6 (*t*). MS: 196 (5.9, M^+), 168 (1.4), 139 (7.5), 111 (100), 110 (45.8), 82 (14.6), 57 (37.5), 55 (28.5), 41 (58.4), 39 (39.3). Anal. calc. for $C_{11}H_{16}O_3$: C 67.32, H 8.22; found: C 67.23, H 8.45.

*(8aS)-6,7,8,8a-Tetrahydro-2*H*,4*H*-[1,3]benzodioxin-4-one* (**12a**). As described for **10**/**11**, with 3.03 g (18.5 mmol) of **4a** in 65 ml of THF, 22.2 mmol of LDA in 30 ml of THF, 4.80 g (24.9 mmol) of PhSeCl in 30 ml of THF (1 h, at −70° and slowly warmed up to r.t. within 12 h), 100 ml of CH_2Cl_2 and 3.0 ml (37.0 mmol) of pyridine, and 6.0 ml (52.9 mmol) of 30% H_2O_2 (1.5 h at 0°): 3.20 g of a residue consisting of > 85% of **12a** (< 5% of regioisomer **13a**; 5–10% of **4a**). FC (30–45% Et_2O/pentane) of the residue furnished 2.00 g (67%) of **12a**. M.p. 58–59° (pentane). $[\alpha]_D = +71$ ($c = 0.7$). IR (KBr): 3010*w*, 2970*m*, 2955*m*, 2935*m*, 1725*s*, 1645*s*, 1415*m*, 1360*m*, 1260*s*, 1245*s*, 1215*m*, 1115*m*, 1025*s*, 970*s*, 880*m*, 860*w*, 815*w*, 775*m*, 725*m*, 705*m*. ^{1}H-NMR (300 MHz): 1.50–1.76 (*m*, 2 H–C(7)); 1.95 (*m*, H–C(8)); 2.21 (*m*, H–C(8)); 2.34 (*m*, 2 H–C(6)); 4.40 (br. *m*, H–C(8a)); 5.43 (*d*, $J = 5.7$, H–C(2)); 5.46 (*d*, $J = 5.7$, H–C(2)); 7.16 (br. *m*, H–C(5)). ^{13}C-NMR (75 MHz): 142.2 (*d*); 128.0 (*s*); 93.1 (*t*); 75.4 (*d*); 28.0 (*t*); 26.0 (*t*); 19.2 (*t*). MS: 154 (1.4, M^+), 153 (1.2), 126 (16), 124 (100), 97 (15), 96 (61.9), 80 (11.4), 79 (48.4), 77 (13.1), 68 (95.4), 55 (16.3), 53 (13), 52 (16.1), 51 (15.5), 41 (17.3), 39 (33.1), 27 (16.9). Anal. calc. for $C_8H_{10}O_3$: C 62.33, H 6.54; found: C 62.29, H 6.61.

*(2S,8aS)-6,7,8,8a-Tetrahydro-2-isopropyl-2*H*,4*H*-[1,3]benzodioxin-4-one* (**12b**). As described for **10**/**11**, with 2.89 g (14.6 mmol) of **4b** in 45 ml of THF, 16.1 mmol of LDA in 20 ml of THF, 3.64 g (16.1 mmol) of PhSeCl in 30 ml of THF (1 h at −70° for 1 h and warmed up to r.t. within 12 h), 90 ml of CH_2Cl_2 and 2.4 ml (29.2 mmol) of pyridine, and 4.5 ml (39.4 mmol) of 30% H_2O_2 (2 h at 0°): 2.64 g of a residue consisting of > 95% of **12b**. FC (pentane/Et_2O 4:1) gave 2.01 g (70%) of pure **12b**. M.p. 28° (pentane at −20°). $[\alpha]_D = +18.3$ ($c = 2.15$). IR (film): 2980*m*, 1730*s*, 1645*s*, 1475*m*, 1420*m*, 1375*m*, 1355*s*, 1260*s*, 1240*s*, 1210*m*, 1025*m*, 985*m*, 890*m*, 865*m*, 780*m*, 735*m*, 715*m*. ^{1}H-NMR (300 MHz): 1.00 (*d*, $J = 6.9$, 3 H, $(CH_3)_2CH$); 1.01 (*d*, $J = 6.9$, 3 H, $(CH_3)_2CH$); 1.47–2.04 (*m*, 2 H–C(7), 2 H–C(8)); 2.19 (*m*, $(CH_3)_2CH$); 2.32 (*m*, 2 H–C(6)); 4.36 (br. *m*, H–C(8a)); 5.19 (*d*, $J = 4.3$, H–C(2)); 7.17 (br. *m*, H–C(5)). ^{13}C-NMR (75 MHz): 164 (*s*); 141.6 (*d*); 127.6 (*s*); 106.3 (*d*); 74.6 (*d*); 32.9 (*d*); 28.0 (*t*); 26.1 (*t*); 19.4 (*t*); 16.1 (*q*, 2 C). MS: 196 (< 0.3, M^+), 195 (2), 153 (100), 125 (11.5), 124 (15.5), 109 (11.8), 107 (71), 97 (53), 96 (11), 81 (10.3), 80 (26.3), 79 (91.8), 77 (13.2), 68 (24.8), 55 (13.4), 43 (20.1), 41 (22.5).

*(2S,8aS)-2-(*tert*-Butyl)-6,7,8,8a-tetrahydro-2*H*,4*H*-[1,3]benzodioxin-4-one* (**12c**) *and (2S)-2-(*tert*-Butyl)-5,6,7,8-tetrahydro-2*H*,4*H*-[1,3]benzodioxin-4-one* (**13c**). As described for **10**/**11**, with 5.45 g (25.8 mmol) of **4c** in 70 ml of THF, 28.5 mmol of LDA in 35 ml of THF, 6.40 g (33.5 mmol) of PhSeCl in 70 ml of THF (1 h at −70° and slowly warmed up to r.t. within 12 h), 90 ml of CH_2Cl_2 and 4.2 ml (52.2 mmol) of pyridine, and 8 ml (70.6 mmol) of 30% H_2O_2 (1.75 h at 0° and 0.75 h at r.t.): a solid which was crystallized from pentane affording 2.20 g of **12c**. FC

(pentane/Et_2O 4:1) of the mother liquor gave 1.35 g of **12c** and 0.48 g of **13c** (overall yield 80%; ratio **12c**/**13c** 7.4:1).

12c: M.p. 93–94° (pentane). $[\alpha]_D = +31.9$ ($c = 0.8$). IR (KBr): 2980*m*, 1725*s*, 1645*s*, 1360*m*, 1260*s*, 1240*s*, 1220*s*, 1030*m*, 980*s*, 785*m*. ^{1}H-NMR (90 MHz): 1.00 (*s*, *t*-Bu); 1.20–2.08 (*m*, 4 H); 2.30 (*m*, 2 H–C(6)); 4.33 (*m*, H–C(8a)); 5.00 (*s*, H–C(2)); 7.10 (br. *s*, H–C(5)). ^{13}C-NMR (20 MHz): 162.7 (*s*); 141.5 (*d*); 127.4 (*s*); 108.1 (*d*); 74.4 (*d*); 35.1 (*s*); 27.7 (*t*); 25.9 (*t*); 23.9 (*q*, 3 C); 19.2 (*t*). MS: 210 (< 0.2, M^+), 209 (1), 153 (100), 125 (9), 123 (8), 107 (76.6), 98 (12.4), 97 (72.1), 80 (20.3), 79 (77), 57 (20.3), 41 (30.3). Anal. calc. for $C_{12}H_{18}O_3$: C 68.55, H 8.63; found: C 68.12, H 8.68.

13c: M.p. 67–69° (pentane at −60°). $[\alpha]_D = +38.4$ ($c = 0.39$). IR (KBr): 2970*m*, 1725*s*, 1645*s*, 1395*s*, 1295*s*, 1115*s*, 1085*s*. ^{1}H-NMR (90 MHz): 1.03 (*s*, *t*-Bu); 1.20–2.10 (*m*, 2 H–C(6), 2 H–C(7)); 2.27 (*m*, 2 H–C(5), 2 H–C(8)). MS: 211 (1.9, $M^+ + 1$), 210 (12.5, M^+), 155 (10.1), 153 (21.0), 125 (100), 124 (71.1), 109 (27.2), 68 (33.7), 41 (35.9).

Michael *Addition of Dialkylcuprates to* **12**. *General Method.* A soln. of 1 mmol of **12** in 5 ml of Et_2O was dropwise added to 3 mmol of R_2CuM in 15 ml of Et_2O (Et_2O/THF 2:1 in the case of bromomagnesium divinylcuprate), stirred at the temp. and for the times indicated in *Table 3*, and quenched by the addition of 1 ml of sat. aq. NH_4Cl soln. at the temp. indicated in *Table 3*. The mixture was warmed up to r.t. and diluted with Et_2O and H_2O, the phases were separated and the aq. soln. was extracted with Et_2O; the combined org. extracts were washed with H_2O and brine, dried, and evaporated and the residue crystallized or chromatographed, as indicated below.

(4aS,5S,8aS)-Perhydro-5-methyl-2H,4H-[1,3]benzodioxin-4-one (**14a**). Crystallization afforded 92 mg (54%) of **14a** from **12a**. M.p. 91° (pentane). $[\alpha]_D = +118.2$ ($c = 0.9$). IR (KBr): 2940*s*, 1735*s*, 1425*m*, 1395*m*, 1385*m*, 1370*m*, 1310*s*, 1230*s*, 1005*s*, 730*m*. ^{1}H-NMR (300 MHz): 0.99 (*d*, $J = 7.2$, CH_3–C(5)); 1.39–1.70 (*m*, 5 H); 2.13 (*m*, H–C(8)); 2.48 (*dd*, $J = 11.3, 4.0$, H–C(4a)); 2.68 (*m*, H–C(5)); 3.83 (*td*, $J = 11.3, 4.3$, H–C(8a)); 5.39 (*d*, $J = 5.3$, H–C(2)); 5.41 (*d*, $J = 5.3$, H–C(2)). ^{13}C-NMR (75 MHz): 168.4 (*s*); 93.6 (*t*); 74.2 (*d*); 51.3 (*d*); 32.6 (*t*); 31.7 (*t*); 28.4 (*d*); 19.0 (*t*); 14.0 (*q*). MS: 170 (0.8, M^+), 140 (3.2), 123 (4.8), 96 (72.7), 95 (14), 81 (100), 79 (10.4), 69 (22.5), 68 (33.8), 67 (27.3), 55 (25.1), 54 (12), 53 (14.8), 41 (34.5), 39 (32.1), 27 (17.1). Anal. calc. for $C_9H_{14}O_3$: C 63.51, H 8.29; found: C 63.18, H 8.36.

(2S,4aS,5S,8aS)-Perhydro-2-isopropyl-(5-methyl)-2H,4H-[1,3]benzodioxin-4-one (**14b**). FC (pentane/Et_2O 9:1) gave 127 mg (60%) of **14b** from **12b**. M.p. 40–42° (pentane at −20°). $[\alpha]_D = +81.6$ ($c = 0.82$). IR (KBr): 2970*s*, 1740*s*, 1385*s*, 1370*s*, 1220*s*, 1010*s*, 990*s*, 880*m*, 860*m*, 750*m*. ^{1}H-NMR (300 MHz): 0.97 (*d*, $J = 7.2$, CH_3); 0.98 (*d*, $J = 6.9$, CH_3); 0.99 (*d*, $J = 6.8$, CH_3); 1.50–1.74 (*m*, 6 H); 1.95 (*m*, 1 H); 2.09 (*m*, 1 H); 2.33 (*dd*, $J = 11.2, 4.1$, H–C(4a)); 3.80 (*td*, $J = 11.2, 4.2$, H–C(8a)); 5.16 (*d*, $J = 4.0$, H–C(2)). MS: 213 (0.2, $M^+ + 1$), 212 (< 0.2, M^+), 169 (9.8), 123 (99.4), 97 (11.8), 96 (100), 95 (49.6), 82 (10.4), 81 (97.3), 69 (11), 68 (24.8), 67 (26.1), 55 (20.5), 43 (16.9), 41 (30.5), 39 (11.9), 27 (10.3).

(2S,4aS,5S,8aS)-2-(tert-Butyl)perhydro-5-methyl-2H,4H-[1,3]benzodioxin-4-one (**14c**). Crystallization gave 170 mg (75%) of **14c** from **12c**. M.p. 89–91° (pentane at −20°). $[\alpha]_D = +85.3$ ($c = 0.46$). IR (KBr): 2985*s*, 1735*s*, 1360*s*, 1215*s*, 1000*s*, 755*m*. ^{1}H-NMR (300 MHz): 0.965 (*s*, *t*-Bu); 0.972 (*d*, $J = 7.2$, CH_3–C(5)); 1.38 (*m*, H–C(7)); 1.50–1.72 (*m*, 2 H–C(6), H–C(7), H–C(8)); 2.09 (*m*, H–C(8)); 2.31 (*dd*, $J = 11.2, 4.1$, H–C(4a)); 2.67 (*m*, H–C(5)); 3.78 (*td*, $J = 11.2, 4.2$, H–C(8a)); 4.98 (*s*, H–C(2)). ^{13}C-NMR (20 MHz): 169.7 (*s*); 108.9 (*d*); 73.1 (*d*); 50.3 (*d*); 35.3 (*s*); 32.2 (*t*); 31.5 (*t*); 28.2 (*d*); 23.9 (*q*, 3 C); 18.8 (*t*); 13.9 (*q*). MS: 226 (< 0.3, M^+), 169 (19.8), 123 (100), 96 (100), 95 (33.1), 81 (49.4), 41 (26.9). Anal. calc. for $C_{13}H_{22}O_3$: C 68.99, H 9.80; found: C 68.95, H 9.76.

(2S,4aS,5S,8aS)-5-Butyl-2-(tert-butyl)perhydro-2H,4H-[1,3]benzodioxin-4-one (**14d**). Crystallization gave 209 mg (78%) of **14d** from **12c**. M.p. 62–63° (pentane at −20°). $[\alpha]_D = +60$ ($c = 1.0$). IR (KBr): 2970*s*, 1740*s*, 1380*m*, 1365*m*, 1220*s*, 1200*m*, 995*m*. ^{1}H-NMR (300 MHz): 0.89 (*t*, $J = 6.4$, $CH_3(CH_2)_3$); 0.96 (*s*, *t*-Bu); 1.14–1.74 (*m*, 10 H); 1.80 (*m*, 1 H); 2.08 (*m*, H–C(8)); 2.32 (*dd*, $J = 11.1, 4.0$, H–C(4a)); 2.43 (br. *s*, H–C(5)); 3.74 (*td*, $J = 11.1, 4.2$, H–C(8a)); 4.97 (*s*, H–C(2)). ^{13}C-NMR: 169.5; 108.7; 73.5; 51.0; 35.1; 33.7; 31.9; 30.1; 27.4; 27.2; 23.8 (3 C); 22.5; 18.8; 13.7. MS: 269 (1, $M^+ + 1$), 268 (< 0.4, M^+), 211 (7.9), 182 (1.9), 165 (100), 138 (65.2), 96 (77.2), 95 (19.3), 82 (36.4), 81 (57.4), 67 (14.6). Anal. calc. for $C_{16}H_{28}O_3$: C 71.60, H 10.52; found: C 71.39, H 10.11.

(2S,4aS,5R,8aS)-5-(sec-Butyl)-2-(tert-butyl)perhydro-2H,4H-[1,3]benzodioxin-4-one (**14e**). FC (pentane/Et_2O 19:1) afforded 145 mg (54%) of **14e**, from **12c**, as a 1:1 mixture of 1′-epimers. M.p. 64–65° (pentane at −20°). $[\alpha]_D = +41.3$ ($c = 0.62$). IR (KBr): 2980*s*, 2970*s*, 1730*s*, 1485*m*, 1465*m*, 1360*s*, 1250*m*, 1235*m*, 1220*s*, 1000*s*, 960*s*, 755*m*. ^{1}H-NMR (300 MHz): 0.85–0.95 (*d* and *t*, 2 CH_3); 0.98 (*s*, *t*-Bu); 1.04–1.74 (*m*, 7 H); 1.91 (*m*, 1 H); 2.10 (*m*, 1 H); 2.28–2.40 (*m*, H–C(4a), H–C(5)); 3.78 (*m*, H–C(8a)); 4.98, 4.99 (*s*, 1 H, H–C(2) of both epimers). ^{13}C-NMR (75 MHz): 170.0 (*s*); 108.5 (*d*); 108.4 (*d*); 73.6 (*d*); 50.1 (*d*); 39.9 (*d*); 38.6 (*d*); 35.4 (*s*); 33.3 (*d*); 32.8 (*d*); 32.5 (*t*); 29.0 (*t*); 27.9 (*t*); 27.8 (*t*); 24.1 (*q*); 19.6 (*t*); 17.6 (*q*); 12.1 (*q*); 11.0 (*q*). MS: 269 (< 0.4,

$M^+ + 1$), 211 (1.6), 183 (2.7), 182 (6.1), 167 (1.5), 166 (12), 165 (100), 147 (15.3), 138 (60.8), 126 (11.3), 122 (11.9), 110 (10.9), 109 (75), 82 (39.4), 81 (73.7). Anal. calc. for $C_{16}H_{28}O_3$: C 71.60, H 10.52; found: C 71.51, H 10.57.

*(2S,4aS,5R,8aS)-2,5-Di(*tert*-butyl)perhydro-2H,4H-[1,3]benzodioxin-4-one* (**14f**). Crystallization furnished 115 mg (43%) of **14f** from **12c**. M.p. 122–123° (pentane at −20°). $[\alpha]_D = +71.5$ ($c = 0.9$). IR (KBr): 2980*s*, 1730*s*, 1370*s*, 1360*s*, 1240*s*, 1000*s*, 960*s*, 755*m*. ^{1}H-NMR (90 MHz): 1.00 (*s*, *t*-Bu); 1.05 (*s*, *t*-Bu); 1.25–1.78 (*m*, 6 H); 2.42 (*dd*, $J = 11.2, 4.1$, H–C(4a)); 2.58 (*m*, H–C(5)); 3.99 (*td*, $J = 11.2, 4.2$, H–C(8a)); 5.00 (*s*, H–C(2)). ^{13}C-NMR: 170.0 (*s*); 108.2 (*d*); 73.7 (*d*); 51.3 (*d*); 42.6 (*d*); 35.3 (*s*); 34.6 (*s*); 32.6 (*t*); 31.9 (*q*, 3 C); 27.9 (*t*); 24.0 (*q*, 3 C); 21.4 (*t*). MS: 211 (3.3, $M^+ - 57$), 165 (100), 138 (24.7), 127 (22), 126 (66.5), 81 (47.9), 80 (40.4), 57 (98.7), 41 (77.2). Anal. calc. for $C_{16}H_{28}O_3$: C 71.60, H 10.52; found: C 71.87, H 10.88.

*(2S,4aS,5R,8aS)-5-Allyl-2(*tert*-butyl)perhydro-2H,4H-[1,3]benzodioxin-4-one* (**14g**). FC (pentane/Et_2O 19:1) afforded 204 mg (81%) of **14g** from **12c**. M.p. 90° (pentane). $[\alpha]_D = +63.7$ ($c = 0.3$). IR (KBr): 2975*m*, 1745*s*, 1640*w*, 1365*s*, 1355*s*, 1210*s*, 1010*s*, 995*s*, 915*s*, 860*m*, 820*w*, 805*w*, 760*w*. ^{1}H-NMR (300 MHz): 0.97 (*s*, *t*-Bu); 1.31–1.83 (*m*, 5 H); 2.02–2.25 (*m*, H–C(8), 2 H–C(1′)); 2.37 (*dd*, $J = 11.2, 4.0$, H–C(4a)); 2.56 (br. *m*, H–C(5)); 3.76 (*td*, $J = 11.2, 4.2$, H–C(8a)); 4.97 (*s*, H–C(2)); 5.00 (*m*, H–C(3′)); 5.04 (*m*, H–C(3′)); 5.73 (*m*, H–C(2′)). ^{13}C-NMR (75 MHz): 169.5 (*s*); 137.0 (*d*); 116.2 (*t*); 108.9 (*d*); 73.5 (*d*); 50.4 (*d*); 35.3 (*s*); 33.4 (*d*); 32.3 (*t*); 32.1 (*t*); 27.3 (*t*); 24.0 (*q*, 3 C); 18.8 (*t*). MS: 252 (0.8, M^+), 195 (2.1), 166 (16), 149 (62.3), 122 (15.4), 121 (27.1), 81 (100), 79 (18.5). Anal. calc. for $C_{15}H_{24}O_3$: C 71.39, H 9.59; found: C 71,53, H 9.96.

*(2S,4aS,5R,8aS)-2-(*tert*-Butyl)perhydro-5-vinyl-2H,4H-[1,3]benzodioxin-4-one* (**14h**). FC (pentane/Et_2O 92:8) afforded 172–117 mg (72–49%; depending upon the experimental conditions collected in *Table 3*) of **14h** from **12c**. M.p. 50–51° (pentane at −20°). $[\alpha]_D = +116.2$ ($c = 0.94$)[28]). IR (KBr): 3990*m*, 3980*m*, 3965*m*, 1845*w*, 1740*s*, 1640*w*, 1365*m*, 1220*s*, 995*s*, 920*m*, 755*m*. ^{1}H-NMR (300 MHz): 0.96 (*s*, *t*-Bu); 1.40–1.72 (*m*, 4 H); 1.91 (*m*, 1 H); 2.11 (*m*, H–C(8)); 2.39 (*dd*, $J = 11.3, 4.1$, H–C(4a)); 3.26 (br. *s*, H–C(5)); 3.79 (*td*, $J = 11.3, 4.2$, H–C(8a)); 4.97 (*s*, H–C(2)); 5.14 (*d*, $J = 1.6$, H–C(2′)); 5.19 (*dt*, $J = 7.3, 1.6$, H–C(2′)); 5.80 (*m*, H–C(1′)). ^{13}C-NMR (20 MHz): 168.9 (*s*); 136.0 (*d*); 117.4 (*t*); 108.8 (*d*); 73.6 (*d*); 50.1 (*d*); 36.9 (*d*); 35.3 (*s*); 32.1 (*t*); 29.5 (*t*); 23.9 (*q*, 3 C); 19.4 (*t*). MS: 239 (1.4, $M^+ + 1$), 238 (3, M^+), 181 (24.2), 152 (20), 135 (100), 108 (66), 107 (53.9), 93 (81), 91 (26.5), 80 (28.2), 79 (84.7), 57 (25), 41 (32.5). Anal. calc. for $C_{14}H_{22}O_3$: C 70.56, H 9.30; found: C 70.26, H 9.34.

*(2S,4aS,5S,8aS)-2-(*tert*-Butyl)-5-[dimethyl(phenyl)silyl]perhydro-2H,4H-[1,3]benzodioxin-4-one* (**14i**). FC (pentane/Et_2O 19:1) furnished 264 mg (76%) of **14i** from **12c**. B.p. 160°/1 Torr. $[\alpha]_D = +57.2$ ($c = 1.07$). IR (film): 3035*m*, 3025*m*, 2980*m*, 1740*s*, 1640*w*, 1485*m*, 1425*m*, 1375*m*, 1355*s*, 1250*m*, 1215*s*, 995*s*, 835*m*, 815*w*, 770*m*, 735*w*, 705*w*. ^{1}H-NMR (90 MHz): 0.38 (*s*, CH_3Si); 0.45 (*s*, CH_3Si); 1.08–2.23 (*m*, 7 H); 2.38 (*dd*, $J = 11, 4.5$, H–C(4a)); 3.20 (*td*, $J = 11, 4$, H–C(8a)); 4.20 (*s*, H–C(2)); 7.25–7.62 (*m*, 5 arom. H). ^{13}C-NMR (20 MHz): 170.5; 138.3; 134.6 (2 C); 129.0; 127.8 (2 C); 108.2; 75.2; 49.3; 34.8; 32.0; 28.2; 23.8 (3 C); 23.1; 22.7; –0.58; –2.31. MS: 331 (0.3, $M^+ - 15$), 269 (1.4), 245 (100), 243 (24.8), 183 (99.8), 137 (34.3), 135 (98.1). Anal. calc. for $C_{20}H_{30}O_3Si$: C 69.32, H 8.73; found: C 69.11, H 8.58.

(4aS,5S,8aS)-Perhydro-4a,5-dimethyl-2H,4H-[1,3]benzodioxin-4-one (**16a**). As described for **6a**, with 175 mg (1.03 mmol) of **14a** in 3.5 ml of THF, 1.27 mmol of LDA in 1.5 ml of THF at −70° (20 min), 2.5 ml of DMPU, and 0.66 ml (10.6 mmol) of MeI: 195 mg of a residue consisting of a 95:5 mixture of **16a** and its 4a-epimer. Crystallization furnished 152 mg (80%) of diastereoisomerically pure **16a**. M.p. 95–96° (pentane). $[\alpha]_D = +119.9$ ($c = 0.8$). IR (KBr): 2980*s*, 1745*s*, 1385*m*, 1375*m*, 1265*s*, 1255*s*, 1205*s*, 1010*s*, 735*s*. ^{1}H-NMR (300 MHz): 1.06 (*d*, $J = 7.2$, CH_3); 1.37 (*m*, 1 H); 1.41 (*s*, CH_3–C(4a)); 1.56–1.88 (*m*, 5 H); 2.31 (*m*, H–C(5)); 3.94 (*dd*, $J = 11.2, 4.4$, H–C(8a)); 5.39 (*d*, $J = 4.9$, H–C(2)); 5.41 (*d*, $J = 4.9$, H–C(2)). MS: 154 (3.8, $M^+ - 30$), 111 (10.4), 110 (100), 109 (11), 95 (78.8), 91 (11.1), 83 (20.8), 82 (22), 81 (54.8), 79 (10.7), 69 (18.1), 68 (26.3), 67 (39.1), 55 (49.1), 53 (20), 41 (41.2), 39 (35.2), 27 (20.9). Anal. calc. for $C_{10}H_{16}O_3$: C 65.19, H 8.75; found: C 64.94, H 8.61.

*(2S,4aS,5S,8aS)-2-(*tert*-Butyl)perhydro-4a,5-dimethyl-2H,4H-[1,3]benzodioxin-4-one* (**16b**). As described for **6a**, with 2.50 g (11.05 mmol) of **14c** in 12 ml of THF, 12.15 mmol of BuLi (instead of LDA) in 16 ml of 1:1 THF/hexane, 10 ml of DMPU, and 7 ml (110 mmol) of MeI: 2.56 g (97%) of a residue consisting of **16b** as a single diastereoisomer. Crystallization furnished 2.06 g (78%) of pure **16b**. M.p. 124–125° (pentane). $[\alpha]_D = +77.5$ ($c = 1.3$). IR (KBr): 2985*m*, 1735*s*, 1380*m*, 1365*m*, 1260*s*, 1195*s*, 975*s*. ^{1}H-NMR (300 MHz): 0.98 (*s*, *t*-Bu); 1.05 (*d*, $J = 7.0$, CH_3–C(5)); 1.34 (*s*, CH_3–C(4a)); 1.52–2.04 (*m*, 6 H); 2.31 (*m*, H–C(5)); 3.90 (*dd*, $J = 11.2, 4.2$, H–C(8a)); 4.98 (*s*, H–C(2)). ^{13}C-NMR (20 MHz): 173.8 (*s*); 109.2 (*d*); 74.6 (*d*); 47.2 (*s*); 35.1 (*s*); 33.9 (*d*); 26.0 (*t*); 25.6 (*t*); 23.7 (*q*, 3 C); 19.2 (*t*); 18.8 (*q*); 14.9 (*q*). MS: 240 (< 0.6, M^+), 183 (4.1), 111 (8.7), 110 (100), 109 (66), 95 (44.3), 81 (38.8), 67 (18.7). Anal. calc. for $C_{14}H_{24}O_3$: C 69.96, H 10.07; found: C 69.81, H 9.86.

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[28]) In [1], $[\alpha]_D$ of this compound was erroneously reported to be +60°.

*(2S,4aS,5S,8aS)-4a-Allyl-2-(*tert*-butyl)perhydro-5-methyl-2H,4H-[1,3]benzodioxin-4-one* (**16c**). As described for **6a**, with 4.71 g (20.8 mmol) of **14c** in 70 ml of THF, 24.0 mmol of BuLi (instead of LDA) in 45 ml of 2:1 THF/hexane, 50 ml of DMPU, and 18 ml (208 mmol) of allyl bromide: **16c** as a single diastereoisomer. Crystallization furnished 4.54 g (82%) of pure **16c**. M.p. 98–99° (pentane at −20°). $[\alpha]_D = +71.1$ ($c = 1.0$). IR (KBr): 3030*w*, 2980*s*, 1735*s*, 1635*w*, 1485*m*, 1365*m*, 1355*m*, 1210*s*, 1185*s*, 1005*s*, 985*s*, 965*m*, 930*m*, 760*m*. ^{1}H-NMR (300 MHz): 0.99 (*s*, *t*-Bu); 1.04 (*d*, $J = 7.2$, CH_3); 1.25–1.83 (*m*, 6 H); 2.37 (*m*, H–C(5)); 2.50 (br. *dd*, $J = 14.7, 6.5$, H–C(1′)); 2.62 (br. *dd*, $J = 14.7, 6.5$, H–C(1′)); 4.00 (*dd*, $J = 11.1, 4.6$, H–C(8a)); 4.98 (*s*, H–C(2)); 5.04–5.12 (*m*, 2 H–C(3′)); 5.79 (*m*, H–C(2′)). ^{13}C-NMR (20 MHz): 171.2; 132.8; 117.8; 109.5; 75.0; 50.5; 35.1; 33.9; 29.9; 25.6 (2 C); 23.9 (3 C); 18.6; 14.9. MS: 267 (0.2, $M^+ + 1$), 266 (0.2, M^+), 209 (21), 181 (16.9), 180 (41.5), 153 (21.7), 139 (20.7), 136 (51.4), 135 (62.6), 121 (32.8), 96 (30.8), 95 (100), 93 (36.9), 81 (32.5). Anal. calc. for $C_{16}H_{26}O_3$: C 72.14, H 9.84; found: C 72.10, H 10.11.

*(2S,4aS,5S,8aS)-5-Butyl-2-(*tert*-butyl)perhydro-4a-methyl-2H,4H-[1,3]benzodioxin-4-one* (**16d**). As described for **6a**, with 340 mg (1.27 mmol) of **14c** in 7 ml of THF, 1.80 mmol of BuLi (instead of LDA) in 8 ml of 6:1 THF/hexane, 7 ml of DMPU, and 0.22 ml (3.53 mmol) of MeI: 349 (98%) of a residue consisting of **16d** as a single diastereoisomer. Crystallization furnished 190 mg (54%) of pure **16d**. M.p. 64–65° (pentane at −20°). $[\alpha]_D = +48.6$ ($c = 1.6$). IR (KBr): 2980*s*, 2965*s*, 1725*s*, 1375*m*, 1275*m*, 1230*s*, 1195*s*, 1080*m*, 980*s*, 760*m*. ^{1}H-NMR (300 MHz): 0.88 (distorted *t*, $J = 6.6$, $CH_3(CH_2)_3$); 0.98 (*s*, *t*-Bu); 1.33 (*s*, CH_3); 1.19–1.82 (*m*, 12 H); 2.03 (br. *s*, H–C(5)); 3.84 (*dd*, $J = 11.3, 4.4$, H–C(8a)); 4.98 (*s*, H–C(2)). ^{13}C-NMR (75 MHz): 174.2 (*s*); 109.5 (*d*); 75.5 (*d*); 48.5 (*s*); 40.1 (*d*); 35.4 (*s*); 31.1 (*t*); 28.6 (*t*); 25.5 (*t*); 24.1 (*q*, 3 C); 22.7 (*t*); 22.0 (*t*); 19.4 (*q*); 19.2 (*t*); 14.0 (*q*). MS: 225 (4.2, $M^+ - 57$), 197 (1.8), 152 (66), 151 (45.6), 109 (24.3), 96 (61.1), 95 (100), 81 (21.6), 67 (21), 55 (24.7), 41 (27.8). Anal. calc. for $C_{17}H_{30}O_3$: C 72.30, H 10.71; found: C 72.06, H 10.92.

'One-Pot' Synthesis of **16b**. A soln. of 720 mg (3.43 mmol) of **12c** and 10.44 mmol of Me_2CuLi in 42 ml of Et_2O was stirred at −10 to 0° for 2 h and cooled to −70°. Then, as described for **6a**, with 4.4 ml (6.96 mmol) of 1.6M BuLi (instead of LDA) in hexane, 21 ml of DMPU, and 2.2 ml (34.8 mmol) of MeI (1 h at −70° and warmed up to 0° within 8 h): 726 mg of crude product. Crystallization from pentane gave 515 mg (64%) of **16b**.

Cleavage of Acetal Ring. Method I. A soln. of 1 mmol of **5** in 10 ml of MeOH was stirred with 120 mg of *Dowex 50 × 8* at r.t. for the time indicated. Pure hydroxy acid was obtained by filtration, washing (MeOH) of the solid residue, and evaporation of the solvent.

Method II. A soln. of 1 mmol of **5** or **16** and a cat. amount of NaOMe in 20 ml of dry MeOH was stirred for the time indicated. The solvent was evaporated and the residue dissolved in Et_2O/H_2O. The phases were separated, the aq. phase was extracted with Et_2O, and the combined org. extracts were washed with brine and dried. Evaporation furnished the hydroxy esters **17**, **19**, and **22**, which were purified as indicated below.

Method III. A soln. of 1 mmol of **5** or **16** in 6 ml of THF was dropwise added to a suspension of 2 mmol of $LiAlH_4$ in 6 ml of THF at 0°. The mixture was kept at 0° or warmed up to r.t. for the time indicated. When all starting material was consumed, the excess hydride was destroyed by the sequential addition of 5 ml of wet Et_2O and 2 ml of sat. aq. Na_2SO_4 soln. at −40°; the mixture was warmed to r.t. (1 h) and the white solid filtered off and washed with Et_2O and CH_2Cl_2/MeOH 5:1. Evaporation furnished the diols **18** or **23**, which were purified by the method reported below.

Method IV. A soln. of 1 mmol of **6** and a cat. amount of NaOEt in 20 ml of dry EtOH was stirred for the time indicated. The solvent was evaporated and the residue dissolved in Et_2O/H_2O. The phases were separated, the aq. phase was extracted with Et_2O, and the combined org. extracts were washed with brine and dried. Evaporation furnished the hydroxy ester **20**, which was purified as indicated below.

Method V. A soln. of 1 mmol of **14** or **16** in 10 ml of MeOH was stirred with 120 mg of *Dowex 50 × 8* at r.t. for the time indicated. The mixture was filtered, the resin washed with MeOH, and the solvent evaporated to give a residue (mixture of the hydroxy acid and the corresponding methyl ester), which was dissolved in Et_2O and treated with ethereal CH_2N_2 at 0°. The excess of CH_2N_2 was destroyed by the addition of AcOH. Evaporation furnished **21** and **22**, which were further purified as indicated.

Method VI. At 0°, 1.7 ml of conc. HCl were dropwise added to a soln. of 1 mmol of **16** in 18.6 ml of THF, and further stirred at r.t. for the time indicated. Addition of H_2O was followed by extraction with Et_2O. The org. phase was washed with brine, dried, and evaporated: pure hydroxy-acid.

(1R,2S)-2-Hydroxy-1-methylcyclopentanecarboxylic Acid (**17a**). It was prepared by *Method I* from **5b** (19 h): 137 mg (95%) of **17a**. ^{1}H-NMR (90 MHz): 1.25 (*s*, CH_3–C(1)); 1.35–2.40 (*m*, 6 H); 4.03 (*m*, H–C(2)); 6.80 (br. *s*, exchange with D_2O, COOH, OH).

Methyl (1R,2S)-2-Hydroxy-1-methylcyclopentanecarboxylate (**17b**). It was prepared from **5a** (1 h; 124 mg, 78%) or **5b** (1.5 h; 137 mg, 87%) according to *Method II*. B.p. 85°/0.15 Torr. $[\alpha]_D = +34.9$ ($c = 2.53$). IR (film): 3480*s* (br.), 2960*s*, 1740*s*, 1465*m*, 1435*m*, 1375*m*, 1120*s* (br.), 900*m*. ^{1}H-NMR (90 MHz): 1.20 (*s*, CH_3–C(1));

1.30–2.30 (*m*, 6 H); 3.00 (br. *s*, exchange with D_2O, OH); 3.72 (*s*, $COOCH_3$); 3.98 (br. *s*, H–C(2)). ^{13}C-NMR (75 MHz): 177.7 (*s*); 80.0 (*d*); 54.3 (*s*); 51.9 (*q*); 33.2 (*t*); 32.0 (*t*); 22.4 (*q*); 20.5 (*t*). MS: 158 (> 0.7, M^+), 130 (21.6), 101 (100), 99 (11.9), 98 (27.8), 87 (25.3), 81 (22.8), 73 (41.9), 69 (24.6), 41 (36.6), 39 (20.5), 28 (32.2).

(1S,2S)-2-(Hydroxymethyl)-2-methylcyclopentanol (**18**). It was synthesized from **5b** by *Method III* (0° for 1 h): 104 mg (80%) of **5b** as a thick oil. $[\alpha]_D = +32.5$ (MeOH, $c = 0.43$). IR (film): 3350*s* (br.), 2975*s*, 1460*m*, 1055*s*. ^{1}H-NMR (90 MHz): 0.97 (*s*, CH_3–C(2)); 1.20–2.25 (*m*, 6 H); 3.50 (*d*, $J = 12$, 1 H, CH_2OH); 3.70 (*d*, $J = 12$, 1 H, CH_2OH); 3.88 (br. *m*, H–C(1)); 4.05 (br. *s*, exchange with D_2O, 2 OH). ^{13}C-NMR (75 MHz): 82.1 (*d*); 68.7 (*t*); 46.5 (*s*); 34.8 (*t*); 33.7 (*t*); 23.3 (*q*); 21.3 (*t*). MS: 112 (7, $M^+ - 18$), 97 (24.3), 94 (59.8), 81 (22.5), 79 (34.7), 69 (29), 68 (100), 67 (53.9), 57 (36.7), 56 (79.1), 55 (46.5), 43 (37.6), 41 (73.1), 39 (44.5), 31 (35.1), 27 (32).

Methyl (1S,2S)-1-Allyl-2-hydroxycyclopentanecarboxylate (**19**). Using *Method II* for 14 h, 169 mg (92%) of **19** were obtained from **5e**. B.p. 110°/0.25 Torr. $[\alpha]_D = +26.3$ ($c = 1.87$). IR (film): 3480*s* (br.), 2950*s*, 1720*s*, 1640*w*, 1220*s*, 915*m*. ^{1}H-NMR (300 MHz): 1.56–1.76 (*m*, 3 H); 1.78–1.91 (*m*, 1 H); 1.92–2.08 (*m*, 1 H); 2.13–2.26 (*m*, 2 H); 2.39 (*dd*, $J = 13.9$, 7.2, H–C(1′)); 2.85 (*d*, $J = 4.4$, OH); 3.71 (*s*, $COOCH_3$); 4.07 (distorted *dd*, $J = 8.9$, 4.4, H–C(2)); 5.01–5.08 (*m*, 2 H–C(3′)); 5.65–5.79 (*m*, H–C(2′)). ^{13}C-NMR (75 MHz): 176.1 (*s*); 133.6 (*d*); 177.9 (*t*); 78.7 (*d*); 58.6 (*s*); 51.7 (*q*); 40.5 (*t*); 32.3 (*t*); 31.0 (*t*); 20.5 (*t*). MS: 184 (2.2, M^+), 156 (6.6), 152 (7.2), 127 (76.7), 125 (13.3), 124 (41.7), 113 (12), 96 (29.8), 95 (63.6), 81 (25.5), 79 (35), 67 (100), 55 (47.8), 53 (35.1), 41 (75.4), 39 (63.3), 27 (33).

Ethyl (1S,2S)-1-Allyl-2-hydroxycyclohexanecarboxylate (**20**). *Method IV* (9 h) afforded 174 mg (82%) of **20** (from **6b**), identical with authentic material [33]. $[\alpha]_D = -19.2$ ($c = 1.8$). ^{1}H-NMR (300 MHz): 1.20–1.37 (*m*, 2 H); 1.28 (*t*, $J = 7.1$, 3 H); 1.41–1.56 (*m*, 1 H); 1.66–1.74 (*m*, 1 H); 1.85–1.94 (*m*, 1 H); 2.10–2.16 (*m*, 1 H); 2.39 (*ddd*, $J = 13.7$, 7.6, 0.9, H–C(1′)); 2.55 (*ddd*, $J = 13.7$, 7.6, 0.9, H–C(1′)); 3.44 (*td*, $J = 10.1$, 3.7; *dd* on D_2O addition, H–C(2)); 3.54 (br. *d*, $J = 10.1$, exchange with D_2O, OH); 4.18 (*m*, 2 H); 5.05 (*m*, H–C(3′)); 5.09 (*m*, H–C(3′)); 5.74–5.88 (*m*, H–C(2′)).

Methyl (1S,2S,6S)-2-Hydroxy-6-methylcyclohexanecarboxylate (**21a**). This compound was synthesized from **14c** by *Method V* (5 h for *Method I*): 131 mg (76%). M.p. 56–57° (pentane). $[\alpha]_D = +73$ ($c = 0.2$). IR (KBr): 3210*s* (br.), 2930*s*, 1735*s*, 1355*m*, 1165*s*, 1065*s*. ^{1}H-NMR (300 MHz): 0.86 (*d*, $J = 7.2$, CH_3–C(6)); 1.28 (*m*, 1 H); 1.56 (*m*, 4 H); 2.01 (*m*, 1 H); 2.43 (*m*, H–C(1), H–C(6)); 2.80 (br. *s*, exchange with D_2O, OH); 3.72 (*s*, CO_2CH_3); 4.02 (*ddd*, $J = 11.0$, 9.5, 4.6, H–C(2)). MS: 172 (< 1, M^+), 154 (8.8), 144 (8.2), 141 (4.9), 112 (11.4), 101 (100), 97 (10.7), 95 (27.8), 94 (14.4), 69 (43.6), 55 (16.8), 43 (10.9), 41 (33.2), 39 (18.2).

Methyl (1S,2S,6R)-2-Hydroxy-6-vinylcyclohexanecarboxylate (**21b**). This compound was synthesized from **14h** by *Method V* (3.5 h for *Method I*): 158 mg (86%). M.p. 40° (pentane). $[\alpha]_D = +45.8$ ($c = 1.06$). IR (KBr): 3210*s* (br.), 2940*s*, 1735*s*, 1640*w*, 1195*s*, 1165*s*, 915*m*, 850*m*. ^{1}H-NMR (90 MHz): 1.10–1.80 (*m*, 5 H); 2.00 (*m*, 1 H); 2.50 (*dd*, $J = 10$, 4.5, H–C(1)); 2.95 (br. *m*, H–C(6)); 3.20 (*s*, exchange with D_2O, OH); 3.66 (*s*, CO_2CH_3); 4.05 (*m*, H–C(2)); 4.93 (*m*, H–C(2′)); 5.08 (*m*, H–C(2′)); 5.87 (*m*, H–C(1′)). ^{13}C-NMR (20 MHz): 173.8 (*s*); 137.1 (*d*); 115.8 (*t*); 66.1 (*d*); 54.3 (*d*); 51.1 (*q*); 40.8 (*d*); 32.6 (*t*); 29.9 (*t*); 19.4 (*t*). MS: 184 (4.5, M^+), 166 (21.9), 153 (20.7), 151 (22.3), 116 (39.5), 113 (98), 107 (100), 106 (35.3), 96 (26.2), 81 (45.1), 67 (30.1), 41 (30.1). Anal. calc. for $C_{10}H_{16}O_3$: C 65.19, H 8.75; found: C 65.18, H 8.69.

Methyl (1S,2S,6S)-2-Hydroxy-1,6-dimethylcyclohexanecarboxylate (**22a**). It was prepared from **16b** (*Method V*, 2.5 h; 175 mg, 94%) or from **16a** (*Method II*, 6 h; 153 mg, 82%). B.p. 100–105°/0.25 Torr. $[\alpha]_D = +65.4$ ($c = 0.9$). IR (KBr): 3500*s* (br.), 2950*s*, 1715*s*, 1380*m*, 1280*m*, 1245*m*, 1125*m*. ^{1}H-NMR (90 MHz): 0.90 (*d*, $J = 7$, CH_3); 1.27 (*s*, CH_3); 1.30–2.20 (*m*, 7 H); 3.03 (*s*, exchange with D_2O, OH); 3.70 (*s*, CO_2CH_3); 4.17 (*m*, H–C(2)). ^{13}C-NMR (75 MHz): 178.5 (*s*); 68.4 (*d*); 51.5 (*q*); 51.3 (*s*); 36.6 (*d*); 28.8 (*t*); 27.2 (*t*); 19.3 (*t*); 16.9 (*q*); 15.9 (*q*). MS: 186 (5.5, M^+), 171 (1.9), 168 (5.7), 158 (6.8), 154 (20.2), 126 (16.3), 115 (100), 109 (23.9), 83 (33.3), 55 (30.7). Anal. calc. for $C_{10}H_{18}O_3$: C 64.49, H 9.74; found: C 64.08, H 10.11.

Methyl (1S,2S,6S)-1-Allyl-2-hydroxy-6-methylcyclohexanecarboxylate (**22b**). This compound was prepared from **16c**, using *Method V* (6 h; 193 mg, 91%) or *Method II* (28 h; 167 mg, 79%). B.p. 110/0.2 Torr. $[\alpha]_D = +89.5$ ($c = 0.5$). IR (KBr): 3550*s* (br.), 2930*s*, 1720*s*, 1635*w*, 1220*s*, 1205*s*, 1135*m*, 1085*m*, 910*m*. ^{1}H-NMR (300 MHz): 0.92 (*d*, $J = 7.2$, CH_3); 1.27 (*m*, 1 H); 1.58 (*m*, 4 H); 1.84 (*m*, 1 H); 2.13 (*m*, H–C(6)); 2.37 (*dd*, $J = 14.3$, 8.6, H–C(1′)); 2.68 (*dd*, $J = 14.3$, 6.3, H–C(1′)); 2.91 (*d*, $J = 2.8$, exchange with D_2O, OH); 3.70 (*s*, CO_2CH_3); 4.23 (br. *m*, H–C(2)); 4.98–5.08 (*m*, 2 H–C(3′)); 5.97 (*m*, H–C(2′)). ^{13}C-NMR (75 MHz): 177.2 (*s*); 135.7 (*d*); 116.9 (*t*); 68.7 (*d*); 54.8 (*s*); 51.3 (*q*); 36.6 (*t*); 35.1 (*d*); 28.9 (*t*); 27.4 (*t*); 19.2 (*t*); 16.2 (*q*). MS: 212 (12.2, M^+), 197 (2), 194 (8.3), 184 (5.4), 180 (12.7), 171 (13.8), 155 (15.5), 153 (17.2), 141 (100), 109 (79), 93 (36.2), 81 (66.8), 55 (40.9), 41 (54.4), 28 (42.7). Anal. calc. for $C_{12}H_{20}O_3$: C 67.89, H 9.50; found: C 67.68, H 9.80.

(1S,2S,6S)-1-Allyl-2-hydroxy-6-methylcyclohexanecarboxylic Acid (**22c**). Application of *Method VI* (3.5 h) to **16c** afforded 178 mg (90%) of **22c** as a thick oil. $[\alpha]_D = +52.4$ (MeOH, $c = 1.4$); $[\alpha]_D = +85.3$ ($CHCl_3$, $c = 1.2$). IR (film): 3600–2600*s* (br.), 1695*s*, 1640*w*, 1385*m*, 1240*m*, 1085*m*, 1000*m*, 915*m*, 860*w*, 735*w*. ^{1}H-NMR (300 MHz):

1.02 (*d*, *J* = 7.2, CH_3); 1.35 (*m*, 1 H); 1.60 (*m*, 4 H); 1.87 (*m*, 1 H); 2.15 (*m*, H–C(6)); 2.45 (*dd*, *J* = 14.2, 8.1, H–C(1')); 2.68 (*dd*, *J* = 14.2, 6.5, H–C(1')); 4.24 (*m*, H–C(2)); 5.04–5.15 (*m*, 2 H–C(3')); 6.02 (*m*, H–C(2')). MS: 198 (2.3, M^+), 180 (33.3), 152 (23.9), 141 (28.1), 137 (22.3), 127 (100), 123 (22), 111 (24.4), 109 (94.8), 95 (32.7), 93 (40.9), 82 (38.4), 81 (84), 79 (35.8), 67 (37.3), 55 (58.9), 41 (94.6), 39 (52).

(1S,2S,3S)-2-(Hydroxymethyl)-2,3-dimethylcyclohexanol (**23a**). It was synthesized from **16b** by *Method III* (0°, 4 h): 142 mg (90%) of **5b**, which was crystallized from pentane. M.p. 71°. $[\alpha]_D$ = +40.9 (MeOH, *c* = 0.79); $[\alpha]_D$ = +34.7° ($CHCl_3$, *c* = 0.92). IR (KBr): 3350*s* (br.), 2930*s*, 1465*m*, 1445*m*, 1375*m*, 1020*s*. ^{1}H-NMR (300 MHz): 0.88 (*d*, *J* = 7.4, CH_3–C(3)); 1.09 (*s*, CH_3–C(2)); 1.16–1.28 (*m*, 1 H); 1.40–1.80 (*m*, 6 H); 2.44 (*m*, exchange with D_2O, OH); 3.44 (*dd*, *J* = 10.6, 6.3, H–C(1')); 3.87 (*dd*, *J* = 10.6, 3.9, H–C(1')); 3.90 (*m*, H–C(1)). ^{13}C-NMR (75 MHz): 73.3 (*d*); 71.3 (*t*); 41.2 (*s*); 36.5 (*d*); 30.8 (*t*); 29.0 (*t*); 19.5 (*t*); 16.3 (*q*); 14.6 (*q*). MS: 140 (5.1, M^+ – 18), 127 (2.9), 122 (19.5), 109 (45.5), 96 (100), 83 (43.9), 81 (37.6), 71 (23), 70 (47.8), 69 (51.3), 67 (36), 57 (31.3), 55 (65.7), 43 (43.5), 41 (75), 29 (32). Anal. calc. for $C_9H_{18}O_2$: C 68.31, H 11.47; found: C 68.32, H 11.50.

(1S,2S,3S)-2-Allyl-2-(hydroxymethyl)-3-methylcyclohexanol (**23b**). It was synthesized from **16c** by *Method III* (r.t., 13 h): 153 mg (83%) of **23b**. B.p. 130°/0.25 Torr. $[\alpha]_D$ = +38.1 (MeOH, *c* = 1.1). IR (film): 3460*s* (br.), 2930*s*, 1635*m*, 995*m*, 970*m*, 910*m*. ^{1}H-NMR (300 MHz): 0.83 (*d*, *J* = 7.3, CH_3–C(3)); 1.25 (*m*, 1 H); 1.46–1.78 (*m*, 5 H); 1.87 (*m*, H–C(3)); 2.29 (br. *m*, exchange with D_2O, OH); 2.30 (*dd*, *J* = 14.1, 7.5, H–C(1')); 2.44 (*d*, *J* = 3.2, exchange with D_2O, OH); 2.60 (*dd*, *J* = 14.1, 7.1, H–C(1')); 3.62 (*dd*, *J* = 11.1, 7.1; *d* on D_2O addition, 1 H, CH_2OH); 3.80 (*dd*, *J* = 11.1, 6.5; *d* on D_2O addition, 1 H, CH_2OH); 4.03 (*m*, H–C(1)); 5.09–5.21 (*m*, 2 H–C(3')); 5.97 (*m*, H–C(2')). ^{13}C-NMR: 135.9 (*d*); 117.3 (*t*); 73.5 (*d*); 68.9 (*t*); 43.7 (*s*); 32.2 (*d*, *t*, 2 C); 30.2 (*t*); 28.5 (*t*); 19.2 (*t*); 14.4 (*q*). MS: 169 (1.1, M^+ – 15), 166 (5.6), 153 (5.7), 135 (15.5), 125 (29.5), 107 (58.8), 97 (24.5), 95 (49.5), 93 (26.3), 83 (36.2), 81 (82.3), 79 (38.6), 69 (30.3), 67 (47.8), 57 (22.6), 55 (100), 43 (36.5), 41 (65).

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