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Attempted Stereocontrol at C-2′ of Strigol-type Compounds by a Michael Reaction/Elimination Approach

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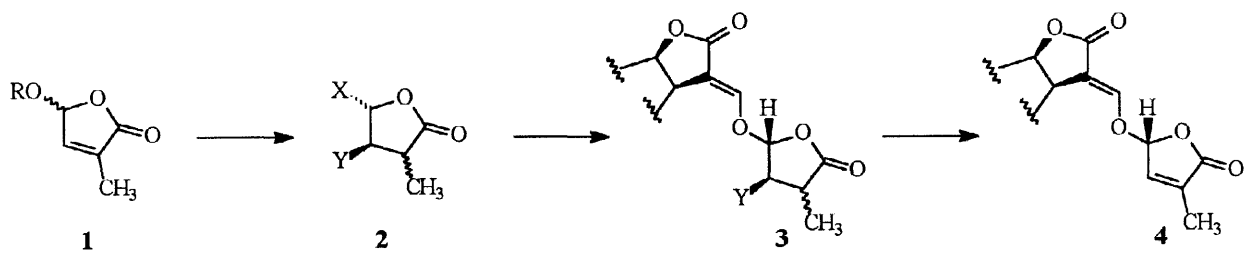
Abstract - By a Michael addition / nucleophilic substitution / elimination sequence the stereocontrol at C-2′ in strigol-typed compounds is in principle possible. However, the method is unsuitable for practical application since it has been shown that a stereolabile intermediate is involved.

Introduction

In the preceding publication we discussed the problem of controlling the configuration at C-2′ in the synthesis of strigol-type compounds.[1] In the present paper we describe results which were obtained using a Michael addition (**1** → **2**) / coupling under the stereocontrol of Y (**2** → **3**) / elimination (**3** → **4**) approach. In particular, we wanted to base this chemistry on Feringa's work.[2]



Scheme 1

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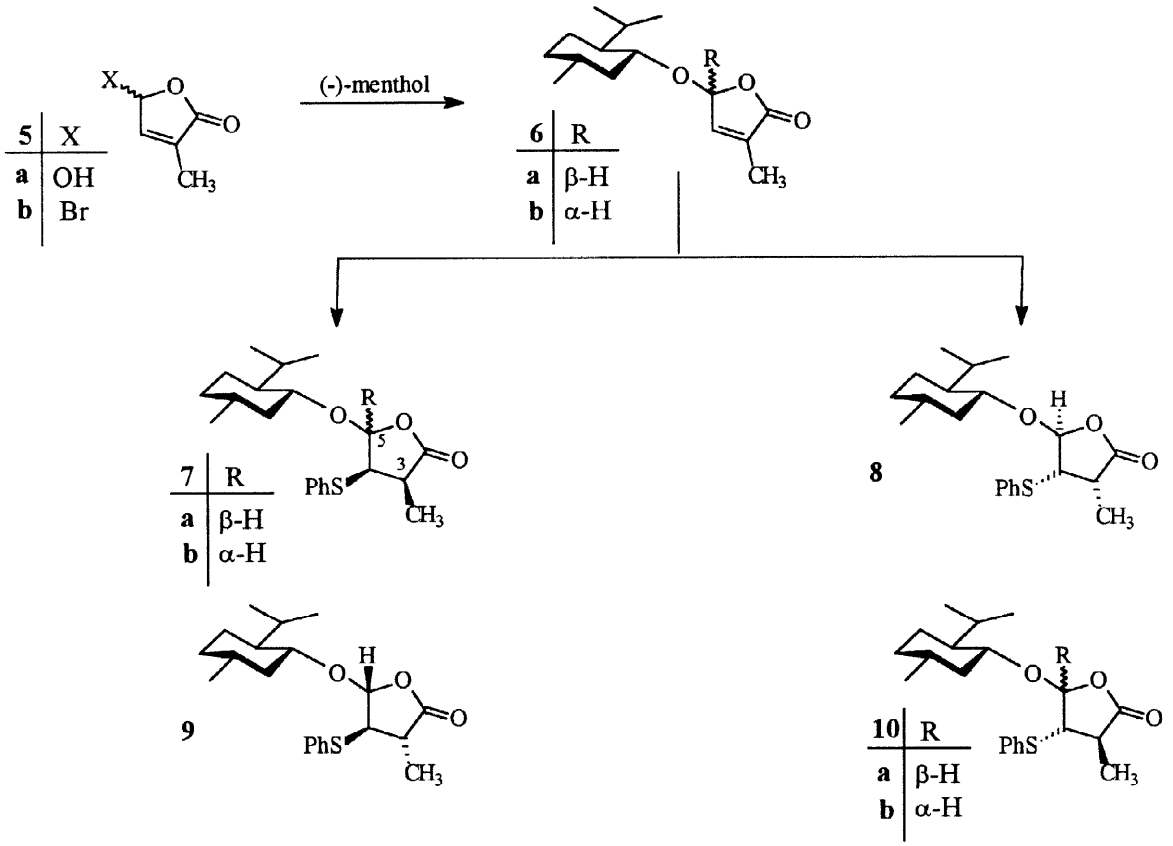


Scheme 2

Preparation of the menthyloxy lactones 7a, 9, 8, and 10b

A mixture of *rac*-**5a** and (-)-menthol was heated to provide the two diastereoisomers **6a** and **6b** from which **6a** was obtained by crystallization at low temperatures.[3] Treatment of **6a** with thiophenol in the presence of triethylamine furnished the two adducts **7a** and **9**. In a different set of experiments the mixture of **6a** and **6b** was treated directly with thiophenol and the adducts **7a/9** and **8/10b** were separated. In the latter case the separation was more complicated. Configurational assignment of these compounds turned out to be quite complicated since they adopt different conformations in solution and in the crystalline state. Figures 1 and 2 show the X-ray structures of **7a** and **9**. Obviously, thiophenoxide adds trans to the menthyloxy group of **6a**, and protonation of the intermediate anion is almost stereo-random, addition of the proton opposite to the phenylthio group being slightly preferred. According to the X-ray analysis **9** adopts a ^{4}E-conformation in the crystal. From the torsion angles, (3′-H-)C-3′-C-4′(-4′-H) = -98.4° and (4′-H-)C-4′-C-5′(-5′-H) = 99.4°, as calculated from the X-ray structure one would expect narrow multiplets for all ring protons in the ^{1}H NMR spectrum. This is, however, not the case: $J_{(4',5')}$ = 4.0 Hz and $J_{(3',4')}$ = 7.5 Hz are observed. Obviously, in solution the 5-membered ring adopts a twist conformation with the large substituents in pseudo-equatorial position rather than the envelope conformation. Similar results have been obtained for **7a** (see Experimental). In **9** a NOE between 3′-H and 5′-H demonstrates the cis relation between these protons. In **7a** this NOE is lacking. The configurations as depicted in **8** and **10b** were assigned on the basis of ^{1}H NMR results, again a NOE between 3′-H and 5′-H proves these two protons to be cis in **10b**.

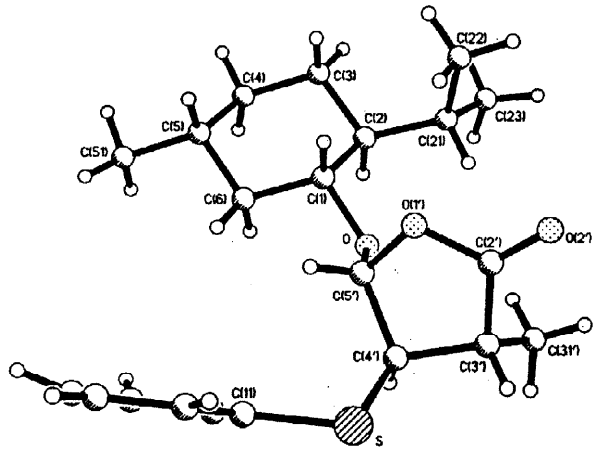


Figure 1. X-ray structure of **9**

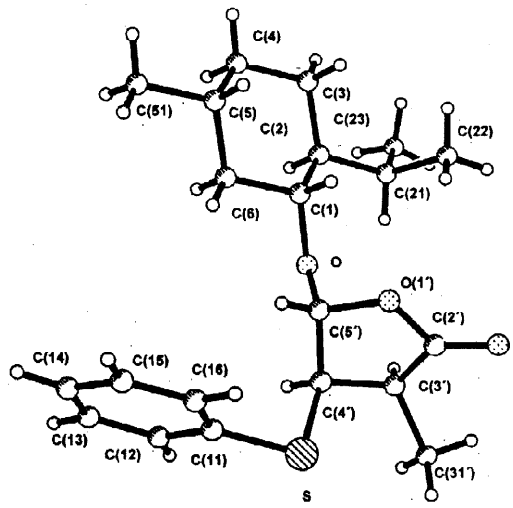


Figure 2. X-ray structure of **7a**

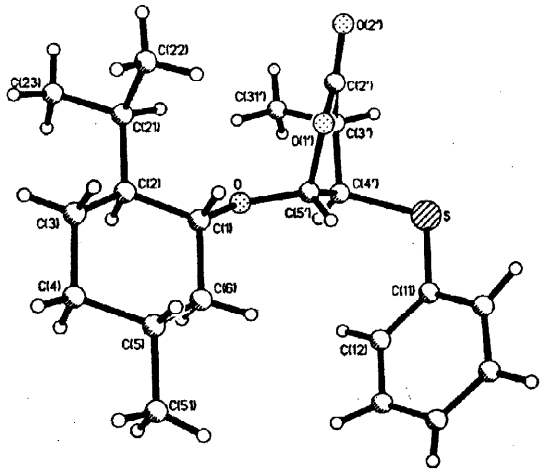


Figure 3. Projection of the X-ray structure of **9** showing the ^{4}E-conformation

Formation of the hydroxy lactones 11

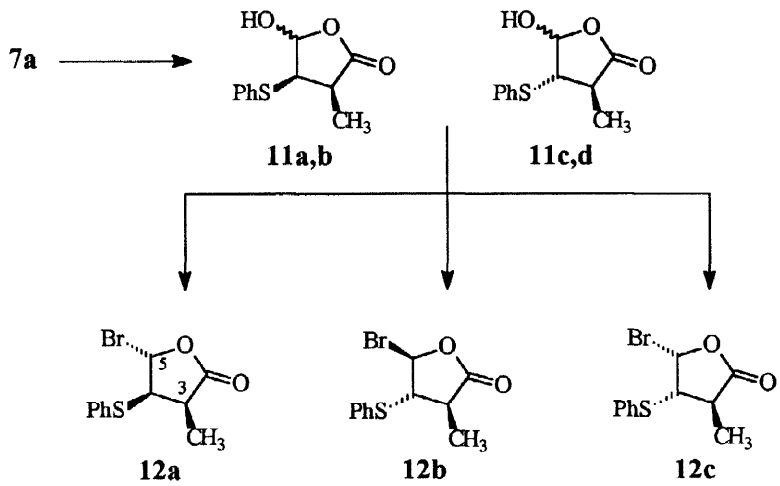
Removal of the auxiliary menthyl group was then achieved from **7a** and **8** by treatment with HCl in acetone. In each experiment a mixture of compounds was formed which contained more components than expected and which could not be separated. In the case of **7a** the ^{1}H NMR spectrum (200 MHz, DMSO-d_6) of the hydrolysis products displayed in a temperature range between 26°C and 75°C (studied at 10° intervals) broad signals that could not be analyzed. However, at -50°C (400 MHz, $CDCl_3$) a nicely resolved spectrum was obtained which showed the presence of a 2:1:3 mixture of three hemiacetals. The spectra of the individual compounds could be analyzed in the mixture by means of H,H COSY. The results are collected in Table 1. A detailed configurational analysis based on the NMR data was not attempted but on the basis of arguments detailed below it is clear that in two of them the substituents at C-3 and at C-4 are trans and in the third one they are cis. It may be noted at this point that in the presence of triethylamine also well-resolved spectra were obtained. The analysis of these spectra seemed to indicate that under these conditions the mixture contained only two stereoisomers (see Experimental).

Table 1. Characteristic ^{1}H NMR data of hydroxy lactones **11** at -50°C in $CDCl_3$ solution

	3-CH_3, $J_{(3,3\text{-}CH_3)}$	3-H, $J_{(3,4)}$	4-H, $J_{(4,5)}$	5-H
isomer a	1.33, d 7.2 Hz	2.78 - 2.87, dq 11.6 Hz	3.58, dd 4.4 Hz	5.83 - 5.89, m
isomer b	1.37, d 7.2 Hz	3.45, dq 7.2 Hz	4.09, d -	5.63, s
isomer c	1.42, d 7.2 Hz	2.50 - 2.59, dq 9.6 Hz	3.32, dd 6.0 Hz	5.67 - 5.74, m

When the hydrolysis products of **7a** were treated with (-)-menthol in the presence of p-toluenesulfonic acid a mixture of four compounds resulted. Two of them could be readily identified to be **7a** and **10b**. The formation of **10b** can be explained assuming the hemiacetals formed from **7a** to be in equilibrium with the ring opened aldehyde, the α-position of which is of course stereo-labile.[4]

Supposing that under the acidic conditions the configuration at C-3 is not affected, the remaining acetals obtained from the hydrolysis products of **7a** and (-)-menthol must be **10a** and **7b**. In one of these compounds (believed to be **10a**), $J_{(3,4)}$ is 11.5 Hz and $J_{(4,5)}$ = 5.0 Hz and the chemical shift of 3-H indicates a trans relation of the substituents at C-3 and C-4. On the other hand in the second compound (**7b**) the corresponding coupling constants are 8.5 Hz and 5.0 Hz, and from the chemical shifts of 3-H and 4-H it may be deduced that in this compound with all substituents cis to each other a unique conformation of the ring is adopted not encountered in any other compound obtained in the course of the present work.



Scheme 3

Formation of the bromo lactones 12a, 12b, and 12c from the hydrolysis products of 7a

In keeping with the results dicussed above treatment of the hydrolysis products of **7a** with CBr_4 / PPh_3[5] led to the formation of three bromo derivatives which were separated by careful chromatography. Working with these compounds was hampered by the fact that they were quite unstable. The relative disposition of the SPh group was easily identified by the chemical shift of 3-H. As Table 2 shows, when 3-CH_3 and SPh are trans a strong shielding effect of the aromatic ring on 3-H is being exerted. This holds both for the menthyloxy and the bromo compounds. From this discussion it follows that in two of the three bromides 3-H and the SPh substituent are cis. Although it must be assumed that each of the bromo compounds is composed of interconverting conformers, from the known relative configuration at C-3 and C-4 and the observed coupling constants the relative configuration at C-5 could be determined. The coupling constants as observed are in each case incompatible with the reversed configuration at C-5.[6]

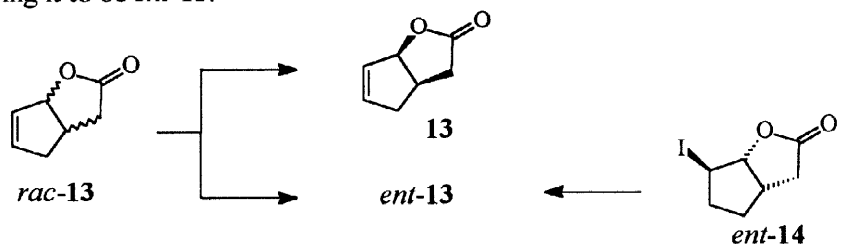
Table 2. Comparison of characteristic ^1H NMR data of bromides **12a-c** and menthyloxy compounds **7a** and **9**

	3-CH_3, $J_{(3,3\text{-}CH_3)}$	3-H, $J_{(3,4)}$	4-H, $J_{(4,5)}$	5-H
7a	1.30, d 7.5 Hz	3.22, dq 7.5 Hz	3.92, d -	5.37, s
9	1.39, d 7.5 Hz	2.50, dq 7.1 Hz	3.32, d 3.9 Hz	5.46, d
12a	1.44, d 7.3 Hz	3.50, dq 7.3 Hz	4.42, d -	6.32, s
12b	1.62, d 7.5 Hz	2.66, dq 4.6 Hz	4.00, dd 2.6 Hz	6.23, d
12c	1.38, d 7.0 Hz	2.81, dq 12.1 Hz	3.56, dd 4.6 Hz	6.57, d

Preparation and configurational assignment of hydroxymethylene lactone 15a and reference samples of 27, 28, and their enantiomers

As already mentioned, for reasons of convenience we decided to study the stereoselective coupling of the strigol butenolide ring equivalents using hydroxymethylene lactone **15a**, thus aiming the synthesis at GR28 (**27**) and its stereoisomers.[7] Racemic **15a** was prepared via *rac*-**13** as described previously.[8] When we started our work no enantioselective synthesis of **13** was available. We could, however, resolve *rac*-**13** by cellulose triacetate chromatography. The optical rotations of the two enantiomers were $[\alpha]_D$ = +133 and -131, respectively. In the meantime elegant Pd-mediated enantioselective syntheses of 2-cyclopenten-1-yl acetic acid have been developed in the laboratories of Trost[9] and of Helmchen[10]. Helmchen and coworkers achieved enantiomeric enrichment by crystallization of iodo lactone *ent*-**14** and its enantiomer, respectively. Thanks to a generous gift by Professor Helmchen at this stage we could use *ent*-**14** for configurational assignment of the

two **13** enantiomers. Dehydrohalogenation with DBU converted *ent*-**14** into the dextrorotatory enantiomer ($[\alpha]_D = +134$) showing it to be *ent*-**13**.[11]



Scheme 4

Using known and conventional methods[12] **13** and *ent*-**13** were converted into GR28 (**27**), the 2′-*epi*-isomer (**28**) and their enantiomers. In this sequence of reactions bromo butenolide *rac*-**5b** was used as coupling reagent. The CD curves of the four compounds are displayed in Figure 4. The curves are quite similar to those of the strigol isomers.[13] Most specifically, the curve of GR28 shows great similarities to that of (+)-strigol in keeping with the configurational assignment for **13**.

In addition, based on previous work, the configuration at C-2′could be determined from the sign of the CD at 270 nm. The compounds with a negative sign have been shown to have (*R*)-configuration at C-2′. This analysis requires that there is no overlap with the CD bands from the remaining part of the molecule as discussed in detail for the strigol series.[13] This requirement is fullfilled in the present case, too, as can be seen from the CD spectra of **16b** and *ent*-**16b** (see Figure 5). The correctness of this assignment in the GR28 series is confirmed by X-ray analysis (in the racemic series).[13]

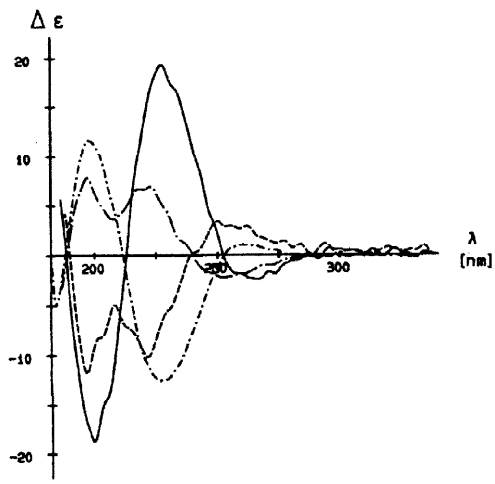


Figure 4. CD of **27** (—), *ent*-**27**, **28** (---), and *ent*-**28**

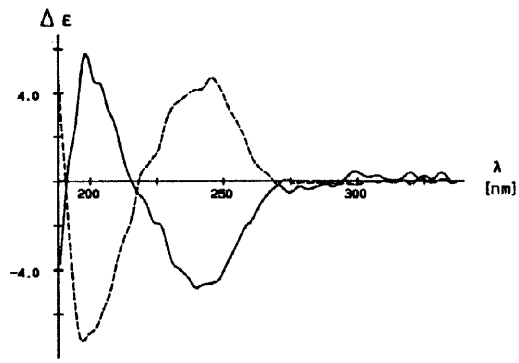


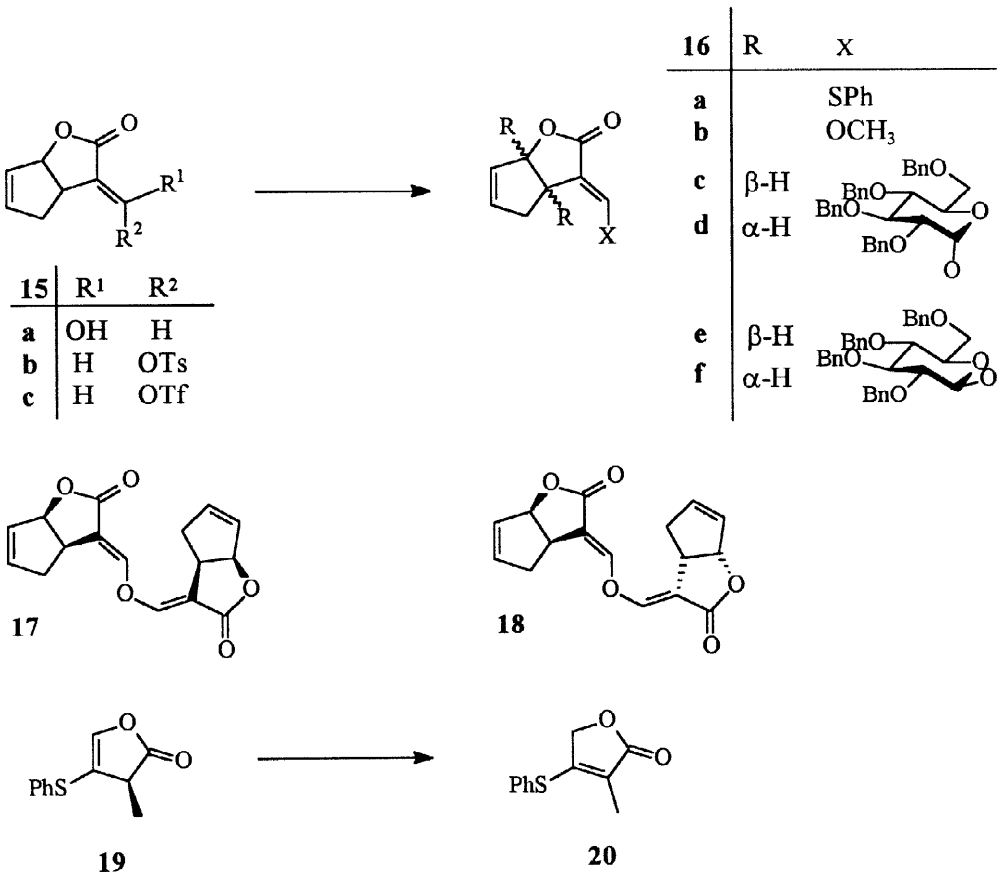
Figure 5. CD of methyl enolethers **16b** (—), *ent*-**16b**

The curves of **27** and *ent*-**27** are not completely enantiomorphic, as the sample of *ent*-**27** contained some impurity that could not be removed because of lack of material. The same is true for **28** and *ent*-**28**. When **28** was prepared by a different route (see accompanying publication) the CD effects were larger than that of the present sample (λ_{max} ($\Delta\varepsilon$) = 198 (16.9), 209 (8.3), 221 (14.6), 253 (-4.6), 270 nm (< 0)).[11]

Coupling experiments

First it was tried to use *rac*-**15a** as electrophilic species. Compound *rac*-**15a** was, therefore, converted into tosylate *rac*-**15b** and triflate *rac*-**15c**, respectively. Reaction of *rac*-**15b** with thiophenol gave straightforwardly *rac*-**16a**. Similarly, from *rac*-**15c** and sodium methoxide methyl enolether *rac*-**16b** was obtained. Methanol alone proved unreactive. It should be mentioned at this stage, that we also prepared the methyl enol ethers in non-racemic form. The CD spectra are displayed in Figure 5.

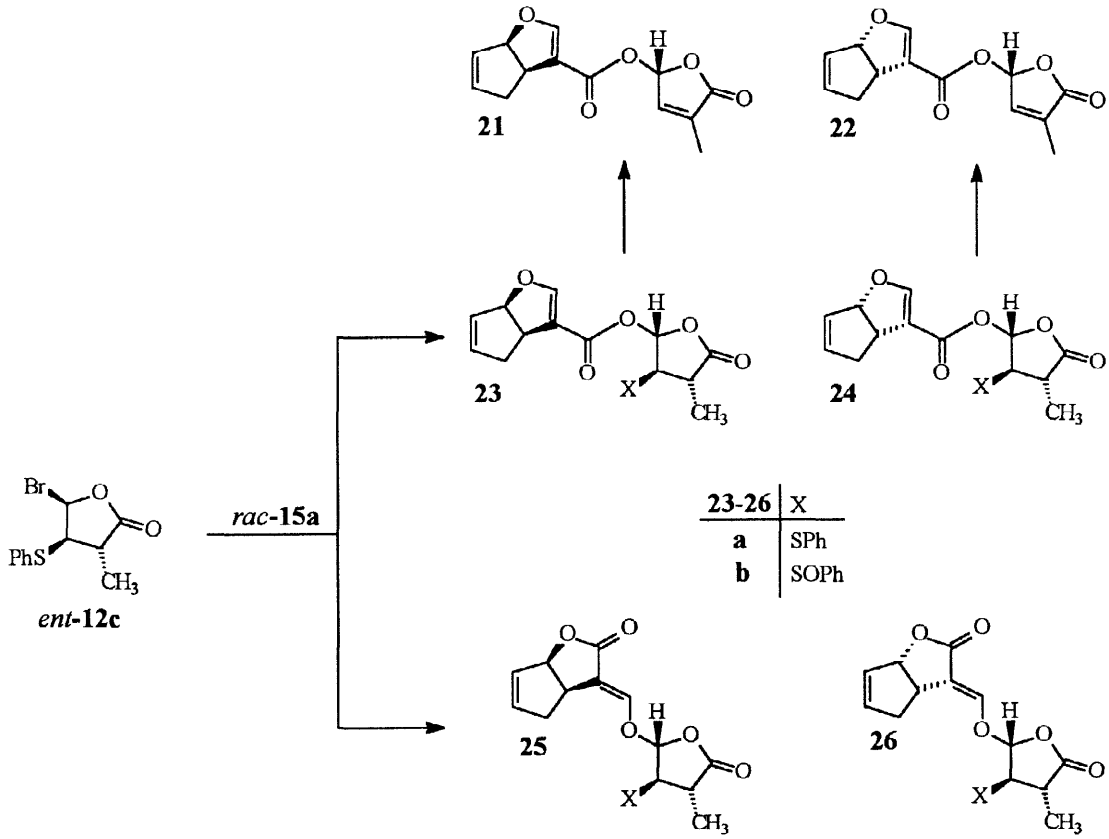
Both *rac*-**15b** and *rac*-**15c** on reaction with the anions obtained from 2,3,4,6-tetra-*O*-benzyl glucopyranose provided the four diastereoisomers **16c** - **16f**. The configuration at C-1 of the glucopyranose unit was determined measuring the $^1J(C,H)$ coupling constants (171 Hz for the α- and 163 Hz for the β-glycosides).[14] The configuration at the angular position of the bicyclic moiety of the stereoisomers was not determined. In contrast to these successful experiments, reaction of the **11** stereoisomers first with sodium hydride and then with either *rac*-**15b** or *rac*-**15c** under strict exclusion of water did not furnish the desired compounds **25a** and **26a**.



Scheme 5

Only dimers *rac*-**17** and *rac*-**18** could be isolated. We speculate that (i) base- induced water elimination from **11** (to give **20** via **19**), (ii) water attack on *rac*-**15b** and *rac*-**15c**, respectively, and (iii) reaction of the thus formed *rac*-**15a** with either *rac*-**15b** or *rac*-**15c** explains the formation of *rac*-**17** and *rac*-**18**. This assumption is corroborated by an experiment in which DBU instead of sodium hydride was used as base and *rac*-**15a** as starting material. In addition to *rac*-**17** and *rac*-**18** elimination product **20** and the thioenolether *rac*-**16a** were isolated.

As a result of this failure we turned our attention to reactions with a nucleophilic species of type **15a** and an electrophile derived from **11** (see also Scheme 1 in ref.[1]). Here, again difficulties arose. Whereas the acid-catalyzed reaction of the mixture containing **11** with (-)-menthol in the presence of acid yielded coupling products of types **7a** - **10b** (vide supra), under identical conditions no acetal formation between **11** and *rac*-**15a** could be observed. The OH group in **11** was then converted into a better leaving group. Experiments which were performed to use a tosyloxy leaving group or Schmidt's trichloroacetimidate methodology[15] met with no success.[16]



Scheme 6

A break-through was achieved by coupling reactions using *rac*-**15a** and bromide **12c**. This reaction resembles, of course, the classical Königs-Knorr glycosylation[17] with the phenylthio substituent as stereo-directing group.[18] First experiments were performed with $HgBr_2$, a promotor of medium activity.[19] A 1:1-mixture of two compounds was obtained with the correct molecular mass and NMR spectra with close similarities to those expected. A careful analysis of these spectra revealed, however, the compounds to have structures *ent*-**23a** and

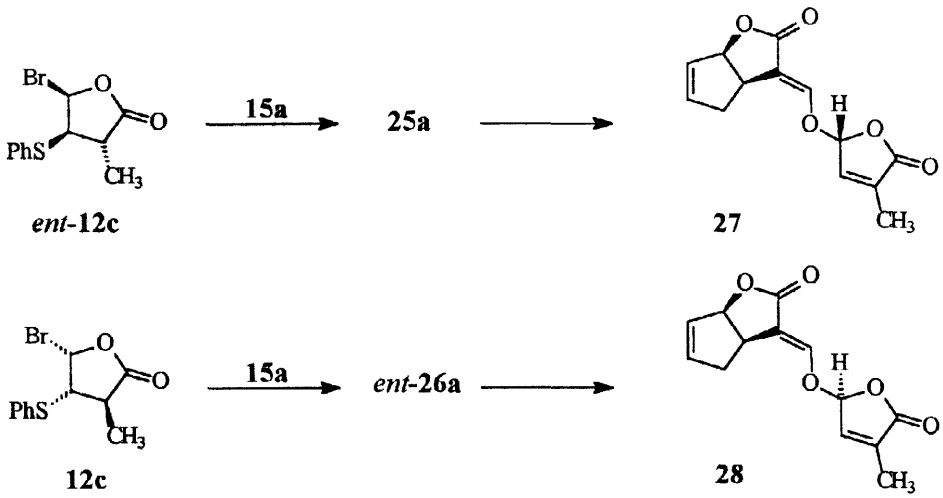
ent-**24a**, the result of (i) opening of the lactone, induced by traces of water, (ii) ester formation, (iii) hemiacetal formation, and (iv) dehydration to furnish the enol ether grouping.

With the more reactive promotors silver perchlorate / silver carbonate and silver triflate / silver carbonate[19], respectively, again only the formation of **23a** and **24a** (starting from *ent*-**12c**) was observed. When the weaker promotor mercuric cyanide / mercuric bromide was used in addition to **23a** and **24a** two further reaction products could be identified by TLC which became the main reaction products when silver carbonate was used to promote the coupling with *ent*-**12c**. The spectral data of the latter compounds (isolated in a moderate yield of 22 %, 1:1 ratio) are fully in agreement with structures **25a** and **26a**.

The two series of coupling products show characteristic differences in their NMR spectra. In the products of the rearranged series (c.f. **23a** and **24a**) the 2′-H chemical shifts are in the range of δ = 6.5 whereas in the „normal" coupling products the 2′-H chemical shift is about δ = 5.6 (for further examples, see Table 3). Another striking difference is found in the ^{13}C NMR spectra: The C-2 (lactone CO) chemical shift of the normal series is > 170 ppm whereas the ester CO in the rearranged series has a chemical shift of about 163 ppm.

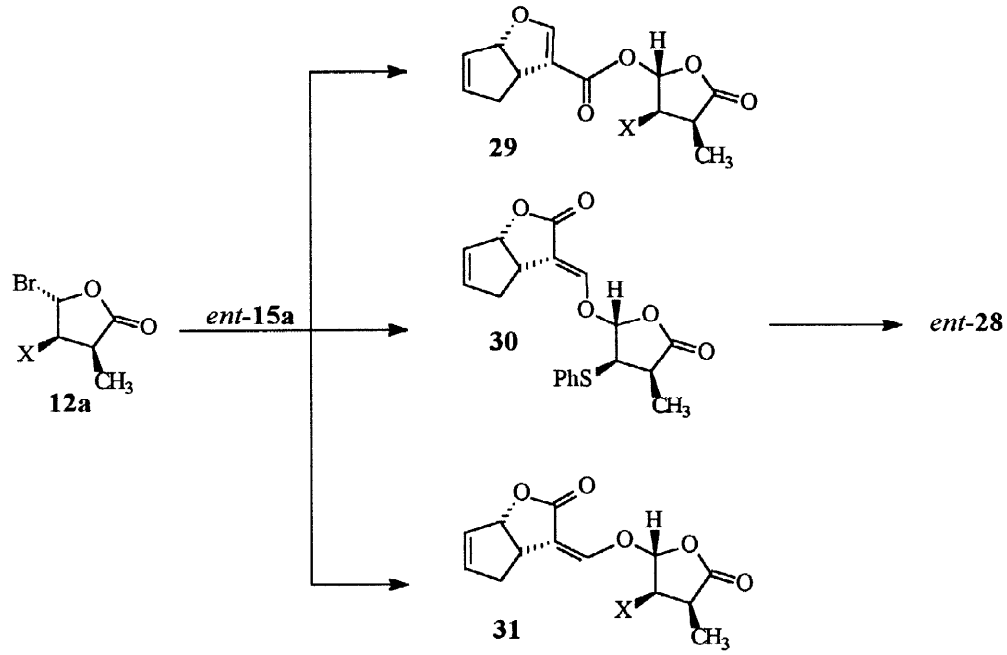
We then set out to form coupling products from single stereoisomers. Thus, *ent*-**12c** was coupled with non-racemic **15a** in the presence of silver carbonate. Here again, the promotor turned out to be quite unsuitable as far as rate and yield were concerned. A very slow reaction occurred and a mixture of compounds was formed. After 14 d **25a** was isolated in 16 % yield alongside with rearrangement product **23a**.

Because of the difficulties experienced with Ag_2CO_3 recourse was made to silver silicate.[20] Treatment of **12c** with **15a** in the presence of silver silicate yielded coupling product *ent*-**26a**[21] (30 % after 50 h).



Scheme 7

Similarly, from *ent*-**15a** and **12a** in a silver silicate-promoted reaction compound **30** and the rearrangement product **29** were obtained. In addition, the (7*Z*)-isomer of **30** was isolated and furthermore a compound the complete structure of which remained elusive although the spectral data indicated a close similarity to **30**. The (*Z*)-configuration around the enol ether double bond of **31** was deduced from the chemical shift of 7-H (δ = 6.60, see Table 3) which is in agreement with the value of a structurally related compound reported by Raphael.[22]



Scheme 8

Finally, under silver silicate promotion the coupling of **12c** with *ent*-**15a** was also performed and in this experiment again three products were obtained: *ent*-**25a**, the rearrangement product *ent*-**23a**, and the (*Z*)-isomer of *ent*-**25a**.

Conversion of the coupling products into GR28 and GR28 stereoisomers

Oxidation of **25a** with mCPBA followed by elimination[23] in the presence of Et_3N yielded stereohomogeneous GR28 (**27**) in 79 % yield (based on **25a**). On the other hand, oxidation and elimination of *ent*-**26a** provided stereoselectively 2′-*epi*-GR28 (**28**) in 50 % yield. We also submitted **30** to the two step sequence and obtained *ent*-**28** (*ent*-2′-*epi*-GR28) in 82 %. The properties of **27**, **28**, and *ent*-**28** including the chiroptical properties were identical with those of the reference samples described above.

Oxidation of *ent*-**23a** and *ent*-**24a** furnished in each case two sulfoxides. Thermal elimination (heating in toluene) caused elimination to give *ent*-**21** and *ent*-**22**, respectively. Similarly, **21** and **22** have been prepared.

The CD spectra of these four stereoisomers as displayed in Figure 6 show again that these compounds belong to a series of GR28 structural isomers.

Stereochemical analysis of the coupling reactions and conclusions

Table 3 clearly shows that the configuration at C-4 and C-3 of bromides *ent*-**12c**, **12c**, and **12a** is transferred into the configuration at C-3′and C-4′, respectively, of coupling products **25a**, *ent*-**26a**, **30**, and *ent*-**25a**. The analysis is identical to that described for the bromides (see Table 2). The configurational assignment at C-2′ of the coupling products follows from their conversion to GR28 (**25a** → **27**), 2′-*epi*-GR28 (*ent*-**26a** → **28**), and *ent*-2′-*epi*-GR28 (**30** → *ent*-**28**). The stereochemical results imply that in each of the coupling reactions *ent*-**12c** → **25a**, **12c** → *ent*-**26a**, **12a** → **30**, and **12c** → *ent*-**25a** the phenylthio substituent did indeed exert the expected stereodirecting effect: It forced the nucleophilic attack at C-2′ to the opposite face of the ring. As

anticipated, the sequence Michael addition / nucleophilic substitution / elimination is appropriate to control the configuration at C-2′ in strigol-type compounds. The problematic point is the C-4 stereolability at the stage of **11**, which makes the method unsuitable for practical applications.

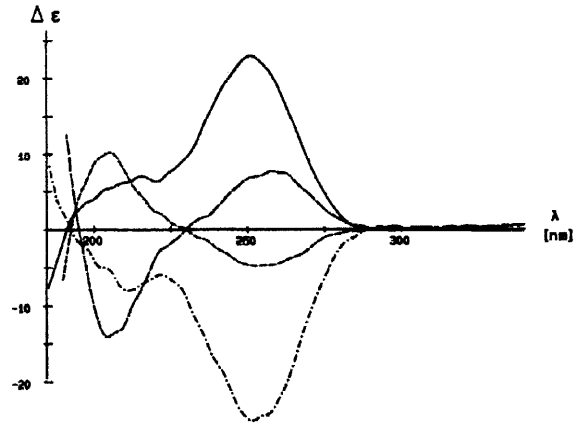


Figure 6. CD of **21**, *ent*-**21**, **22**, and *ent*-**22** (for details, see Experimental)

Table 3. Characteristic ^{1}H NMR data of the coupling products

	4′-CH_3, $J_{(4',4'\text{-}CH_3)}$	4′-H, $J_{(4',3')}$	3′-H, $J_{(3',2')}$	2′-H	7-H, $J_{(7,3a)}$
25a	1.46, d 7.3 Hz	2.59, dq 8.6 Hz	3.43, dd 4.4 Hz	5.64, d	7.29, d
ent-26a	1.46, d 7.3 Hz	2.60, dq 7.5 Hz	3.47, dd 4.1 Hz	5.61, d	7.27, d
30	1.43, d 7.3 Hz	3.26, dq 7.3 Hz	4.13, d –	5.56, s	7.22, d 2.6 Hz
***ent*-23a**	1.45, d 7.7 Hz	2.57, dq 8.8 Hz	3.39, dd 5.1 Hz	6.54, d	7.11, d 1.5 Hz
29	1.41, d 7.3 Hz	3.25, dq 7.3 Hz	4.01, dd 1.1 Hz	6.50, d	7.16, d 1.5 Hz
(*Z*)-isomer of ***ent*-25a**	1.52, d 7.3 Hz	2.63, dq 5.5 Hz	3.78, d 2.6 Hz	5.60, d	6.62, d 2.2 Hz
31	1.37, d 7.3 Hz	3.44, dq 7.3 Hz	4.30, d –	5.53, s	6.60, d 1.8 Hz

EXPERIMENTAL

Formation of 7a, 8, 9 and 10b

To a solution of **6a** (2.29 g, 9.06 mmol) and thiophenol (1.85 mL, 18.14 mmol) in CH_2Cl_2 (15 mL) triethylamine (130 µL, 0.94 mmol) was added under argon at 23°C. After stirring for 2 d at 23°C the solvent was evaporated. FC and MPLC (petrol-toluene 1:3) yielded **7a** (2.12 g, 65 %) and **9** (0.94 g, 29 %).

In a similar reaction a mixture of **6a** and **6b** (2.0559 g, 8.15 mmol) was converted into the addition products as described above. Separation furnished **7a** (619.3 mg, 21 %), a mixture of **7a** and **8** (167.6 mg, 6 %), **8** (758.1 mg, 26 %), a mixture of **8** and **9** (305.9 mg, 10 %), **9** (190.7 mg, 6 %), a mixture of **9** and **10b** (60.7 mg, 2 %), and **10b** (155.5 mg, 5 %).

(3*R*,4*R*,5*R*)-5-{(1*S*,2*S*,5*R*)-2-Isopropyl-5-methyl-cyclohexyloxy}-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (7a)

R_f (petrol-^{t}butyl methyl ether 10:1): 0.37.- M.p.: 79 - 81°C (petrol-ethyl acetate).- ^{1}H NMR ($CDCl_3$, 400 MHz, NOE): δ = 0.72 (d, 3H, menthyl-CH_3), 0.74 - 1.00 (m, 10H, (containing: 0.80 - 0.86, 2∗d, 6H, 2∗menthyl-CH_3), menthyl-H's), 1.10 - 1.18 (m, 1H, menthyl-H), 1.18 - 1.31 (m, 1H, menthyl-H), 1.34 (d, 3H, 3-CH_3), 1.55 - 1.65 (m, 1H, menthyl-H), 1.65 - 1.74 (m, 1H, menthyl-H), 1.92 - 2.03 (m, 1H, menthyl-H), 3.21 - 3.32 (dq, 1H, 3-H), 3.37 - 3.46 (dt, 1H, menthyl-1-H), 3.95 (d, 1H, 4-H), 5.40 (s, 1H, 5-H), 7.23 - 7.45 (m, 5H, arom.-H), $J_{(3,4)}$ = 7.5 Hz, $J_{(3,3\text{-}CH_3)}$ = 7.5 Hz.- IR ($CHCl_3$): 1780 cm^{-1}.- MS: m/z (%) = 362 (M^+, 1.5), 279 (1), 232 (2), 207 (1.6), 150 (100).- $[\alpha]_D^{20}$ = -6.9 (c 1.00, $CHCl_3$).- $C_{21}H_{30}O_3S$ (362.5), calcd: C 69.58 H 8.34, found: C 69.96 H 8.30.

X-ray structural analysis of 7a

7a, $C_{21}H_{30}O_3S$ (362.5), colourless prisms, monoclinic, space group $P2_1$, with a = 10.323(4) Å, b = 9.544(3) Å, c = 11.302(4) Å, ß = 108.80(4)°, V = 1054.2(10) Å^3, Z = 2, D_c = 1.142 g cm^{-3}. The structure was refined to R = 0.048 [I > 2σ(I)] and wR_2 = 0.1301 for 1754 independent reflexions collected on a Siemens P4 diffractometer (ω-scan, MoKα radiation, $2\Theta_{max}$ = 50°).[24]

(3*S*,4*R*,5*R*)-5-{(1*S*,2*S*,5*R*)-2-Isopropyl-5-methyl-cyclohexyloxy}-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (9)

R_f (petrol-^{t}butyl methyl ether 10:1): 0.29.- M.p.: 50 - 52°C (petrol-ethyl acetate).- ^{1}H NMR (400 MHz, $CDCl_3$, NOE) δ = 0.75 (d, 3H, menthyl-CH_3), 0.77 - 1.01 (m, 10H, (containing: 0.84 - 0.90, 6H, 2∗menthyl-CH_3), menthyl-H's), 1.14 - 1.23 (m, 1H, menthyl-H), 1.23 - 1.37 (m, 1H, menthyl-H), 1.40 (d, 3H, 3-CH_3), 1.57 - 1.67 (m, 1H, menthyl-H), 1.84 - 1.92 (m, 1H, menthyl-H), 2.05 - 2.14 (m, 1H, menthyl-H), 2.46 - 2.56 (dq, 1H, 3-H), 3.30 - 3.36 (dd, 1H, 4-H), 3.43 - 3.51 (dt, 1H, menthyl-1-H), 5.46 (d, 1H, 5-H), 7.26 - 7.36 (m, 3H, arom.-H), 7.40 - 7.46 (m, 2H, arom.-H), $J_{(3,3\text{-}CH_3)}$ = 7.5 Hz, $J_{(3,4)}$ = 7.5 Hz, $J_{(4,5)}$ = 4.0 Hz.- IR ($CHCl_3$): 1780 cm^{-1}.- MS: m/z (%) = 362 (M^+, 1.5), 244 (2), 207 (1.3), 150 (100).- $[\alpha]_D^{20}$ = -82.2 (c 0.99, $CHCl_3$).- $C_{21}H_{30}O_3S$ (362.5), calcd: C 69.58 H 8.34, found: C 69.57 H 8.48.

X-ray structural analysis of 9

9, $C_{21}H_{30}O_3S$ (362.5), white prisms, monoclinic, space group $P2_1$, with a = 7.487(3) Å, b = 6.865(3) Å, c = 20.619(5) Å, ß = 99.97(3)°, V = 1043.7(9) Å^3, Z = 2, D_c = 1.153 g cm^{-3}. The structure was refined to R = 0.047 [I > 2σ(I)] and wR_2 = 0.113 for 2007 independent reflexions collected on a Siemens P4 diffractometer (ω-scan, MoKα radiation, $2\Theta_{max}$ = 50°).[24]

(3*S*,4*S*,5*S*)-5-{(1*S*,2*S*,5*R*)-2-Isopropyl-5-methyl-cyclohexyloxy}-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (8)

R_f (petrol-^{t}butyl methyl ether 10:1): 0.33.- M.p.: 97 - 99°C (petrol-ethyl acetate).- ^{1}H NMR (400 MHz, $CDCl_3$, NOE): δ = 0.45 (d, 3H, menthyl-CH_3), 0.68 - 0.95 (m, 10H, (containing: 0.75 - 0.78, 3H, menthyl-CH_3, 0.83 - 0.86, 3H, menthyl-CH_3), menthyl-H's), 1.05 - 1.14 (m, 1H, menthyl-H), 1.22 - 1.30 (m, 1H, menthyl-H), 1.34 (d, 3H, 3-CH_3), 1.50 - 1.60 (m, 1H, menthyl-H), 1.64 - 1.73 (m, 1H, menthyl-H), 2.00 - 2.07 (m, 1H, menthyl-H), 3.18 - 3.30 (m, 2H, 3-H, menthyl-1-H), 3.98 (d, 1H, 4-H), 5.22 (s, 1H, 5-H), 7.27 - 7.35 (m, 3H, arom.-H), 7.38 - 7.45 (m, 2H, arom.-H), $J_{(3,4)}$ = 7.5 Hz, $J_{(3,3\text{-}CH_3)}$ = 7.5 Hz.- IR ($CHCl_3$): 1780 cm^{-1}.- MS: m/z (%) = 362 (M^+, 1.5), 207 (1.5), 150 (100).- $[\alpha]_D^{20}$= -103.8 (c 1.00, $CHCl_3$).- $C_{21}H_{30}O_3S$ (362.5), calcd: C 69.58 H 8.34, found: C 69.98 H 8.49.

(3*R*,4*S*,5*S*)-5-{(1*S*,2*S*,5*R*)-2-Isopropyl-5-methyl-cyclohexyloxy}-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (10b)

R_f (petrol-^{t}butyl methyl ether 10:1): 0.29.- ^{1}H NMR (400 MHz, $CDCl_3$, NOE): δ = 0.65 (d, 3H, menthyl-CH_3), 0.71 - 1.05 (m, 10H, (containing: 0.77 - 0.83, d, 3H, menthyl-CH_3, 0.85 - 0.88, d, 3H, menthyl-CH_3), menthyl-H's), 1.14 - 1.25 (m, 1H, menthyl-H), 1.25 - 1.38 (m, 1H, menthyl-H), 1.41 (d, 3H, 3-CH_3), 1.54 - 1.67 (m, 1H, menthyl-H), 1.88 - 1.99 (m, 1H, menthyl-H), 2.07 - 2.17 (m, 1H, menthyl-H), 2.40 - 2.52 (dq, 1H, 3-H), 3.29 - 3.40 (m, 2H, 4-H, menthyl-1-H), 5.33 (d, 1H, 5-H), 7.26 - 7.38 (m, 3H, arom.-H), 7.38 - 7.47 (m, 2H, arom.-H), $J_{(4,5)}$ = 4.5 Hz.- $C_{21}H_{30}O_3S$ (362.5), calcd: C 69.58 H 8.34, found: C 70.13 H 8.52.

Hydrolytic cleavage of 7a and of 8

A solution of **7a** (174.6 mg, 0.48 mmol) in 5 per cent HCl (1.7 mL) and acetone (5.2 mL) was stirred at 50°C for 15 h. The reaction mixture was neutralized with 1 mol L^{-1} NaOH, extracted with CH_2Cl_2, acidified with 5 per cent HCl and again extracted with CH_2Cl_2. The combined organic layers were dried and the solvent was evaporated. LC (petrol-ethyl acetate 3:1) provided a mixture of **11** isomers (108.4 mg, 100 %).- IR of the mixture ($CHCl_3$): 3585 (OH (free)), 3500 ((broad), OH (bridged)), 1785, 1165, 990 cm^{-1}.- MS of the mixture: m/z (%) = 224 (M^+, 40), 206 (5), 196 (20), 195 (15), 150 (100), 123 (41), 109 (68).- HRMS calcd for $C_{11}H_{12}O_3S$: 224.0507, found: 224.0505.

In a similar reaction **8** was hydrolytically cleaved.

^{1}H NMR spectra of the hydrolysis products of 7a in $CDCl_3$ at -50°C.

^{1}H NMR (400 MHz, -50°C, H,H COSY 45, $CDCl_3$): δ = 1.33 (d, 2.1H, $J_{(3,3\text{-}CH_3)}$ = 7.2 Hz, 3-CH_3^a), 1.37 (d, 0.9H, $J_{(3,3\text{-}CH_3)}$ = 7.2 Hz, 3-CH_3^b), 1.42 (d, 3H, $J_{(3,3\text{-}CH_3)}$ = 7.2 Hz, 3-CH_3^c), 2.50 - 2.59 (dq, 1H, $J_{(3,4)}$ = 9.6 Hz, 3-H^c), 2.78 - 2.87 (dq, 0.7H, $J_{(3,4)}$ = 11.6 Hz, 3-H^a), 3.32 (dd, 1H, $J_{(4,5)}$ = 6.0 Hz, 4-H^c), 3.45 (dq, 0.3H, 3-H^b), 3.58 (dd, 0.7H, $J_{(4,5)}$ = 4.4 Hz, 4-H^a), 4.09 (d, 0.3H, $J_{(4,3)}$ = 7.2 Hz, 4-H^b), 5.53 - 5.58 (m, 0.3H), 5.63 (s, 0.3H, 5-H^b), 5.67 - 5.74 (m, 1H, 5-H^c), 5.83 - 5.89 (m, 0.7H, 5-H^a), 5.97 - 6.08 (m, 1H, OH^c), 7.36 - 7.55 (m, 5*(1H+0.7H+0.3H), arom.-H).

^{1}H NMR spectra of the hydrolysis products of 7a in $CDCl_3$ in the presence of triethylamine

^{1}H NMR ($CDCl_3$, Et_3N, 400 MHz, a and b correspond to two diastereoisomers, ratio 5:1): δ = 1.32 (d, 3H, 3-CH_3^a), 1.36 (d, 3H, 3- CH_3^b), 2.54 - 2.64 (m, 1H, 3-H^b), 3.09 - 3.17 (dq, 1H, 3-H^a), 3.36 - 3.43 (dd, 1H, 4-H^b), 3.86 - 3.92 (dd, 1H, 4-H^a), 6.17 - 6.26 (s (broad), 5-H$^{a \text{ and } b}$), 7.21 - 7.49 (m, 5H, arom.-H$^{a \text{ and } b}$), a: $J_{(3,3\text{-}CH_3)}$ = 7.5 Hz, $J_{(3,4)}$ = 8.0 Hz, $J_{(4,5)}$ = 2.5 Hz, b: $J_{(3,3\text{-}CH_3)}$ = 7.5 Hz, $J_{(3,4)}$ = 10.0 Hz, $J_{(4,5)}$ = 5.0 Hz.-

128.49 (C-arom.[b]), 129.57 (C-arom.[b]), 131.75 (C-arom.[a]), 132.34 (C-arom.[b]), 133.04 (C-arom.[a]), 177.13 (C=O).

Coupling of the 11-isomers (obtained by hydrolysis of 7a) with (-)-menthol

To a mixture of the **11**-isomers (30.5 mg, 0.13 mmol), (-)-menthol (21.4 mg, 0.13 mmol) and 4 Å molecular sieves in CH_2Cl_2 (2.0 mL) a solution of p-toluenesulfonic acid (77.0 mg, 0.41 mmol) in CH_2Cl_2 (1.0 mL) was added. The reaction mixture was stirred for 4 h at 20°C, washed twice with water and dried. Solvent evaporation and MPLC (petrol-toluene 1:6) provided **7a** (13.3 mg, 27 %), **10a** (4.0 mg, 8 %), **10b** (7.9 mg, 16 %) and **7b** (2.3 mg, 5 %).

(3*R*,4*S*,5*R*)-5-{(1*S*,2*S*,5*R*)-2-Isopropyl-5-methyl-cyclohexyloxy}-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (10a)

R_f (toluene-$CHCl_3$ 20:1 (3*developed)): 0.41.- ^1H NMR (400 MHz, $CDCl_3$): δ = 0.69 - 0.98 (m, 10H, menthyl-H's, containing: 0.70 - 0.73, d, 3H, menthyl-CH_3, 0.81 - 0.84, d, 3H, menthyl-CH_3, 0.87 - 0.90, d, 3H, menthyl-CH_3), 1.15 - 1.35 (m, 8H, 5*menthyl-H's, containing: 1.19 - 1.22 (d, 3H, 3-CH_3), 1.57 - 1.67 (m, 1H, menthyl-H), 1.88 - 2.01 (m, 2H, 2*menthyl-H), 2.69 - 2.79 (dq, 1H, 3-H), 3.40 - 3.45 (dd, 1H, 4'-H), 3.45 - 3.54 (dt, 1H, menthyl-H), 5.56 - 5.58 (d, 1H, 5'-H), 7.23 - 7.31 (m, 3H, arom.-H's), 7.43 - 7.47 (m, 2H, arom.-H's), $J_{(4',5')}$ = 5.0 Hz, $J_{(3',4')}$ = 11.5 Hz, $J_{(3',3'\text{-}CH_3)}$ = 7.0 Hz.

(3*R*,4*R*,5*S*)-5-{(1*S*,2*S*,5*R*)-2-Isopropyl-5-methyl-cyclohexyloxy}-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (7b)

R_f (toluene-$CHCl_3$ 20:1 (3*developed)): 0.27.- ^1H NMR (400 MHz, $CDCl_3$): δ = 0.68 - 1.03 (m, 10H, menthyl-H's, containing: 0.73 - 0.75, d, 3H, menthyl-CH_3, 0.85 - 0.87, d, 3H, menthyl-CH_3, 0.88 - 0.90, d, 3H, menthyl-CH_3), 1.20 - 1.35 (m, 5H, menthyl-H's), 1.41 - 1.45 (d, 3H, 3'-CH_3), 1.57 - 1.65 (m, 1H, menthyl-H), 2.07 - 2.15 (m, 1H, menthyl-H), 2.24 - 2.34 (m, 1H, menthyl-H), 2.71 - 2.80 (dq, 1H, 3'-H), 3.35 - 3.42 (dt, 1H, menthyl-H), 3.97 - 4.02 (dd, 1H, 4'-H), 5.63 - 5.66 (d, 1H, 5'-H), 7.17 - 7.38 (m, 5H, arom.-H's), $J_{(4',5')}$ = 5.0 Hz, $J_{(3',4')}$ = 8.5 Hz, $J_{(3',3'\text{-}CH_3)}$ = 7.5 Hz.

Reaction of 11 and their enantiomers with triphenylphosphine and carbon tetrabromide

Carbon tetrabromide (400.7 mg, 1.21 mmol) dissolved in CH_2Cl_2 (3.0 mL) was slowly added at 20°C to a solution of **11** (108.4 mg, 0.48 mmol) and triphenylphosphine (253.3 mg, 0.97 mmol) in CH_2Cl_2 (5.5 mL) and the reaction mixture was stirred for 15 min. Solvent evaporation and LC (petrol-ethyl acetate 15:1) yielded a mixture of **12a** and **12b** (60.2 mg, 43 %) and pure **27c** (27.4 mg, 20 %). The **12a / 12b** mixture could be separated by LC (petrol-CH_2Cl_2 4:1).

In a similar fashion *ent*-**12a** and *ent*-**12b** (33.0 mg, 36 %) as well as *ent*-**12c** (26.7 mg, 29 %) could be obtained from *ent*-**11** (72.3 mg, 0.32 mmol), carbon tetrabromide (268.2 mg, 0.81 mmol) and triphenylphosphine (168.6 mg, 0.64 mmol).

(3*R*,4*R*,5*S*)-5-Bromo-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (12a)

R_f (petrol-CH_2Cl_2 1:2): 0.56.- ^1H NMR (200 MHz, $CDCl_3$): δ = 1.44 (d, 3H, 3-CH_3), 3.50 (dq, 1H, 3-H), 4.42 (d, 1H, 4-H), 6.32 (s, 1H, 5-H), 7.32 - 7.49 (m, 5H, arom.-H), $J_{(3,3\text{-}CH_3)}$ = 7.3 Hz, $J_{(3,4)}$ = 7.3 Hz.- ^{13}C NMR (100 MHz, $CDCl_3$) δ = 9.6 (3-CH_3), 35.4 (C-3), 57.2 (C-4), 82.0 (C-5), 128.1, 129.5, 132.6, 174.7 (C-2).- IR ($CHCl_3$): 1805, 1145, 1080, 1025, 965, 905 cm^{-1}.- MS: m/z (%) = 288 / 286 (M^+, 20), 207 (79), 161 (62), 151 (46), 109 (100).- HRMS calcd for $C_{11}H_{11}O_2SBr$: 285.9663, found: 285.9666.

(3*R*,4*S*,5*R*)-5-Bromo-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (12b)
R_f (petrol-CH_2Cl_2 1:2): 0.46.- ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.62 (d, 3H, 3-CH_3), 2.66 (dq, 1H, 3-H), 4.00 (dd, 1H, 4-H), 6.23 (d, 1H, 5-H), 7.35 - 7.51 (m, 5H, arom.-H), $J_{(3,3\text{-}CH_3)}$ = 7.5 Hz, $J_{(3,4)}$ = 4.6 Hz, $J_{(4,5)}$ = 2.6 Hz. - ^{13}C NMR (100 MHz, $CDCl_3$) δ = 15.5 (3-CH_3), 40.0 (C-3), 58.1 (C-4), 82.0 (C-5), 128.6, 129.4, 132.6, 174.8 (C-2).- IR ($CHCl_3$): 1805, 1150, 1050, 1010 cm^{-1}.- MS: m/z (%) = 288 / 286 (M^+, 20), 207 (67), 179 (29), 161 (41), 151 (52), 109 (98), 41 (100).- HRMS calcd for $C_{11}H_{11}O_2SBr$: 285.9663, found: 285.9659.

(3*R*,4*S*,5*S*)-5-Bromo-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (12c)
R_f (petrol-ethyl acetate 3:1): 0.40.- ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.38 (d, 3H, 3-CH_3), 2.81 (m, 1H, 3-H), 3.56 (dd, 1H, 4-H), 6.57 (d, 1H, 5-H), 7.31 - 7.42 (m, 3H, arom.-H), 7.48 - 7.58 (m, 2H, arom.-H), $J_{(3,3\text{-}CH_3)}$ = 7.0 Hz, $J_{(3,4)}$ = 12.1 Hz, $J_{(4,5)}$ = 4.6 Hz.- ^{13}C NMR (50 MHz, $CDCl_3$) δ = 12.6 (3-CH_3), 38.8 (C-3), 58.4 (C-4), 87.0 (C-5), 129.2, 130.1, 132.7, 133.5, 175.0 (C-2).- IR ($CHCl_3$): 1810, 1010, 990 cm^{-1}.- MS: m/z (%) = 288 / 286 (M^+, 10), 207 (68), 151 (51), 109 (100), 97 (63).- HRMS calcd for $C_{11}H_{11}O_2SBr$: 285.9663, found: 285.9660.

(3*S*,4*S*,5*R*)-5-Brom-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (*ent*-12a)
^{1}H NMR (80 MHz, $CDCl_3$), IR, MS spectra were identical with those obtained from **12a**.- HRMS calcd for $C_{11}H_{11}O_2SBr$: 285.9663, found: 285.9668.

(3*S*,4*R*,5*S*)-5-Brom-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (*ent*-12b)
^{1}H NMR (80 MHz, $CDCl_3$), IR, MS spectra were identical with those obtained from **12b**.- HRMS calcd for $C_{11}H_{11}O_2SBr$: 285.9663, found: 285.9687.

(3*S*,4*R*,5*R*)-5-Brom-3-methyl-4-phenylsulfanyl-dihydro-furan-2-one (*ent*-12c)
^{1}H NMR (80 MHz, $CDCl_3$), IR, MS spectra were identical with those obtained from **12c**.- HRMS calcd for $C_{11}H_{11}O_2SBr$: 285.9663, found: 285.9695.

Resolution of *rac*-13
Compound ***rac*-13** was prepared as described by Larock and Hightower.[25] Resolution was performed by MPLC (cellulose triacetate, 25-40 μm, Macherey & Nagel, 60 g, ethanol-water 96:4). 617.3 mg were separated in 5 runs to give **13** (138.5 mg) and ***ent*-13** (133.6 mg). The ee was determined by HPLC analysis (cellulose triacetate, CEL-AC-40XF, Macherey & Nagel); ethanol-water 96:4, UV detection at λ = 220 nm.- **13**: $[\alpha]_D^{20}$ = -131.2 (c 1.0, CH_2Cl_2).- ***ent*-13**: $[\alpha]_D^{20}$ = +132.6 (c 0.97, CH_2Cl_2).

Conversion of 13 and *ent*-13 into GR28 (27) and its stereoisomers
The conversion of **13** and ***ent*-13**, respectively, into GR28 and its stereoisomers was preformed by known methods.[12]

(3a*R*)-3-{(*R*,*E*)-4-Methyl-5-oxo-2,5-dihydrofuran-2-yloxymethylene}-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (27)
R_f (petrol-ethyl acetate 1:1): 0.28.- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.96 - 2.03 (dd, 3H, 4'-CH_3), 2.45 - 2.50 (m, 1H, 4-H), 2.80 - 2.84 (m, 1H, 4-H*), 3.63 - 3.71 (m, 1H, 3a-H), 5.50 - 5.53 (m, 1H, 6a-H), 5.81 - 5.88, 5.98 - 6.07 (2*m, 2*1H, 6-H, 5-H), 6.12 - 6.17 (dq, 1H, 2'-H), 6.89 - 6.93 (dq, 1H, 3'-H), 7.40 - 7.45 (d, 1H, =CHO), $J_{(3a,4)}$ = 2.5 Hz, $J_{(3a,4*)}$ = 9.0 Hz, $J_{(3a,\text{=}CHO)}$ = 2.5 Hz, $J_{(4,4*)}$ = 17.5 Hz, $J_{(2',3')}$ = $J_{(2',4'\text{-}CH_3)}$ = $J_{(3',4'\text{-}CH_3)}$ = 1.5 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT): δ = 11.0 (4'-CH_3), 37.6 (C-3a), 38.7 (C-4), 88.0 (C-6a),

100.7 (C-2'), 113.9 (C-3), 128.9 (C-6), 136.2 (C-4'), 137.4 (C-5), 141.1 (C-3'), 150.7 (=CHO), 170.4 (C-2), 171.5 (C-5').- IR ($CHCl_3$): 1785, 1750, 1680 cm^{-1}.- CD (c 1.083 mmol L^{-1}, acetonitrile): λ_{max} ($\Delta\varepsilon$): 200 (-18.1), 227 (+20.3), 263 nm (-2.0).- $[\alpha]_D^{20}$ = +130.9 (c 0.573, $CHCl_3$).- MS: m/z (%) = 248 (M^+, 1), 151 (12), 97 (100), 69 (11), 41 (33).- HRMS calcd for $C_{13}H_{12}O_5$: 248.0685, found: 248.0677.

(3a*R*)-3-{(*S*,*E*)-4-Methyl-5-oxo-2,5-dihydrofuran-2-yloxymethylene}-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydrocyclopenta[*b*]furan-2-one (28)

R_f (petrol-ethyl acetate 1:1): 0.20.- M.p.: 142 - 143°C (petrol-ethyl acetate). The ^1H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100.6 MHz, $CDCl_3$), IR, MS spectra were superimposible with those of **27**.- CD (c 0.893 mmol L^{-1}, acetonitrile): λ_{max} ($\Delta\varepsilon$): 196 (-11.6), 222 (-10.0), 253 nm (+2.8).- $[\alpha]_D^{20}$ = +28.6 (c 0.594, $CHCl_3$).- HRMS calcd for $C_{13}H_{12}O_5$: 248.0685, found: 248.0679.

***ent*-GR28 (*ent*-27)**

CD (c 1.014 mmol L^{-1}, acetonitrile): λ_{max} ($\Delta\varepsilon$): 198 (+12.0), 228 (-12.3), 261 nm (+1.4).- $[\alpha]_D^{20}$ = -135.5 (c 0.627, $CHCl_3$).

***ent*-2'-*epi*-GR28 (*ent*-28)**

CD (c 1.082 mmol L^{-1}, acetonitrile): λ_{max} ($\Delta\varepsilon$): 197 (+8.1), 218 (+6.9), 223 (+7.2), 255 nm (-2.1).- $[\alpha]_D^{20}$ = -28.0 (c 0.608, $CHCl_3$).

Reaction of *rac*-15a and 11-isomers with p-toluenesulfonic acid

No product formation could be observed by TLC within 4 d when the same reaction conditions as described above were applied to the coupling of **11** (11.2 mg, 0.05 mmol) and ***rac*-15a** (7.7 mg, 0.05 mmol).

2-Oxo-(3a*r*,6a*c*)-3a,6a-dihydro-4*H*-cyclopenta[*b*]furan-3-(*E*)-ylidenemethyl toluene-4-sulfonate (*rac*-15b)

Triethylamine (1.5 mL, 10.82 mmol) and p-toluenesulfonyl chloride (560.5 mg, 2.94 mmol) were added to a solution of ***rac*-15a** (399.2 mg, 2.62 mmol) in THF (25 mL) at -30°C. Quenching with sat. aq. $NaHCO_3$, usual work-up (CH_2Cl_2), and LC (petrol-ethyl acetate 3:1) yielded ***rac*-15b** (737.5 mg, 92 %).- M.p.: 114 - 115°C (petrol-ethyl acetate).- ^1H NMR ($CDCl_3$, 80 MHz): δ = 2.06 - 2.42 (m, 1H, 4-H), 2.45 (s, 3H, CH_3), 2.63 - 3.09 (m, 1H, 4-H*), 3.46 - 3.80 (m, 1H, 3a-H), 5.36 - 5.60 (m, 1H, 6a-H), 5.70 - 5.90 (m, 1H, 6-H), 5.90 - 6.10 (m, 1H, 5-H), 7.26 - 7.50 (m, 2H, arom-H), 7.50 - 7.63 (d, 1H, =CHO), 7.69 - 7.94 (m, 1H, arom-H), $J_{(3a,=CHO)}$ = 2.5 Hz.- IR ($CHCl_3$): 1750, 1680, 1600 1390, 1180, 1060, 1040 cm^{-1}.- MS: m/z (%) = 306 (M^+, 0.6), 242 (1.4), 155 (41), 134 (59), 91 (100), 65 (25).- $C_{15}H_{14}O_5S$ (306.3), calcd: C 58.81 H 4.61, found: C 58.86 H 4.58.

2-Oxo-(3a*r*,6a*c*)-3a,6a-dihydro-4*H*-cyclopenta[*b*]furan-3-(*E*)-ylidenemethyl trifluoromethanesulfonate (*rac*-15c)

Trifluoromethanesulfonic acid (15.0 g) and phosphorus pentoxide (15.0 g) were refluxed for 5 h. Then the trifluoromethanesulfonic anhydride was distilled at 120°C (bath temperature). At 0°C, to a mixture of ***rac*-15a** (62.2 mg, 0.41 mmol) and 2,6-di-^{t}butyl-4-methylpyridine (130.4 mg, 0.65 mmol), and CH_2Cl_2 (1.5 mL), trifluoromethanesulfonic anhydride (97 µL, 0.59 mmol) was slowly added. The reaction mixture was stirred for 45 min at 0°C. Solvent evaporation and LC (petrol-ethyl acetate 5:1) gave ***rac*-15c** (85.2 mg, 73 %).- ^1H NMR (80 MHz, $CDCl_3$): δ = 2.28 - 2.72 (m, 1H, 4-H), 2.81 - 3.27 (m, 1H, 4-H*), 3.64 - 3.99 (m, 1H, 3a-H), 5.50 -

5.74 (m, 1H, 6a-H), 5.81 - 6.00 (m, 1H, 6-H), 6.00 - 6.20 (m, 1H, 5-H), 7.60 - 7.73 (dd (2 long range couplings), 1H, =CHO).- IR ($CHCl_3$): 1760, 1690, 1440, 1240, 1140, 1030, 825 cm^{-1}.

3-(*E*)-Phenylsulfanylmethylene-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (*rac*-16a)
Thiophenol (15.0 µL, 0.15 mmol) was added at 0°C to a solution of *rac*-**15b** (21.9 mg, 0.07 mmol) in pyridine (2.0 mL). The reaction mixture was stirred at 0°C for 12 h, then it was warmed to 20°C. After stirring of a total of 21 h usual work-up (ethyl acetate) and LC (petrol-ethyl acetate 15:1) gave *rac*-**16a** (16.0 mg, 91 %).- ^{1}H NMR (80 MHz, $CDCl_3$): δ = 2.37 - 3.05 (m, 2H, CH_2-4), 3.50 - 3.84 (m, 1H, 3a-H), 5.45 - 5.70 (m, 1H, 6a-H), 5.80 - 5.99, 5.99 - 6.18 (2*m, 2*1H, 6-H, 5-H), 7.27 - 7.57 (m, 5H, arom.-H), 7.66 (d, 1H, =CHO), $J_{(3a,=CHO)}$ = 2.5 Hz.- IR ($CHCl_3$): 1730, 1610, 1580, 1340, 1310, 1190 cm^{-1}.- MS: m/z (%) = 244 (M^+, 100), 215 (28), 151 (46), 150 (46), 135 (41).- HRMS calcd for $C_{14}H_{12}O_2S$: 244.0558, found: 244.0570.

Reaction of *rac*-15c with sodium methoxide
A solution of *rac*-**15a** (32.7 mg, 0.22 mmol) and 2,6-di-^{t}butyl-4-methylpyridine (53.4 mg, 0.26 mmol) in CH_2Cl_2 (2.0 mL) was cooled to 0°C. Slowly trifluoromethanesulfonic anhydride (38.8 µL, 0.24 mmol) was added. After 30 min and after 2.5 h two portions of 0.64 mol L^{-1} solution of sodium methoxide in methanol, each 0.4 mL (0.26 mmol sodium methoxide) were added. The reaction mixture was stirred for 3 h. Usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 4:1) provided *rac*-**16b** (10.4 mg, 29 %).

(*E*)-3-Methoxymethylene-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (*rac*-16b)
The data were identical to those reported in the preceding paper.- Analogously, the non-racemic enantiomers **16b** and *ent*-**16b** were prepared. **16b**: CD (c 2.198 mmol L^{-1}, acetonitrile): λ_{max} (Δε): 197 (-7.1), 245 nm (+4.9).- $[\alpha]_D^{20}$ = +69.5 (c 0.676, $CHCl_3$). *Ent*-**16b**: CD (c 1.933 mmol L^{-1}, acetonitrile): λ_{max} (Δε): 198 (+5.9), 203 (+4.6), 240 nm (-4.7).- $[\alpha]_D^{20}$ = -64.9 (c 0.693, $CHCl_3$).

Reaction of 11-isomers and *rac*-15b with sodium hydride
A solution of **11** (20.8 mg, 0.09 mmol) dissolved in THF (1.0 mL) was added to sodium hydride (55-60 per cent dispersion in oil, 4.8 mg, 0.11 mmol) at 20°C. After 15 min the reaction mixture was cooled to 0°C and *rac*-**15b** (28.8 mg, 0.09 mmol) in THF (1.0 mL) was added. The reaction mixture was stirred at 0°C for 5 h and at 20°C for 4 d. The resulting precipitate was dissolved with 5 per cent HCl. Usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 6:1 (1 % acetic acid)) gave a mixture of *rac*-**17** and *rac*-**18** (12.2 mg, 91 %). Separation into two pure fractions was achieved by MPLC (petrol-ethyl acetate 3:1).

(3a*RS*,3'a*RS*)- and meso-(3a*r*,6a*c*,3'a*r*,6'a*c*)-3,3a,4,6a,3',3'a,4',6'a-Octahydro-3,3'-{(*E*,*E*)-2-oxapropane-1,3-diylidene}-bis-cyclopenta[*b*]furan-2-one (*rac*-17 and *rac*-18)
Stereoisomer 1: R_f (petrol-ethyl acetate 1:1): 0.33.- M.p.: 163 - 164°C (petrol-ethyl acetate).- ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.54 - 2.63 (m, 2H, 2*4-H), 2.87 - 2.98 (m, 2H, 2*4-H*), 3.75 - 3.83 (m, 2H, 2*3a-H), 5.55 - 5.63 (m, 2H, 2*6a-H), 5.87 - 5.94 (m, 2H, 2*6-H), 6.03 - 6.10 (m, 2H, 2*5-H), 7.50 - 7.54 (d, 2H, 2*=CHO), $J_{(3a,4)}$ = 2.5 Hz, $J_{(3a,4')}$ = 9.0 Hz, $J_{(3a,6a)}$ = 8.0 Hz, $J_{(3a,=CHO)}$ = 2.5 Hz, $J_{(4,4')}$ = 17.5 Hz.- IR ($CHCl_3$): 1750, 1710, 1650, 1170, 1150 cm^{-1}.- MS: m/z (%) = 286 (M^+,15), 152 (18), 135 (100), 134 (65), 107 (69), 91 (45), 77 (36), 65 (59), 39 (44).- $C_{16}H_{14}O_5$ (286.3), calcd: C 67.13 H 4.93, found: C 67.02 H 4.99.
Stereoisomer 2: R_f (petrol-ethyl acetate 1:1): 0.26.- M.p.: 246 - 248°C (decomposition, petrol-CH_2Cl_2).- ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.48 - 2.59 (m, 2H, 2*4-H), all other spectral features and IR and MS spectra are superimposible with those obtained from stereoisomer 1.- $C_{16}H_{14}O_5$ (286.3), calcd: C 67.13 H 4.93, found: C 67.27 H 5.02.

Reaction of 11-isomers and *rac*-15c with sodium hydride

To a mixture of **11** (26.0 mg, 0.12 mmol), and sodium hydride (55-60 per cent dispersion in oil, 8 mg, 0.2 mmol) in THF (8.0 mL), which was stirred at -10°C for 30 min, a solution of *rac*-**15c** (32.1 mg, 0.11 mmol) in THF (2.0 mL) was added and the reaction mixture was stirred for 2 h at -10°C. Quenching with sat. aq. $NaHCO_3$, usual work-up (CH_2Cl_2), and LC (petrol-ethyl acetate 3:1) gave **11** (9.8 mg, 38 %) and a mixture of *rac*-**17** and *rac*-**18** (8.0 mg, 50 %).

Formation of *rac*-17 and *rac*-18 from *rac*-15b, *rac*-15a, and triethylamine

A solution of *rac*-**15b** (19.0 mg, 0.06 mmol) and *rac*-**15a** (10.0 mg, 0.07 mmol) in THF (1.5 mL) was stirred at 20°C. TLC did not show any reaction within 24 h. Then triethylamine (26 µL, 0.19 mmol) was added and the reaction mixture was stirred for further 29 h. Solvent evaporation and LC (petrol-ethyl acetate 5:1) yielded a mixture of *rac*-**17** and *rac*-**18** (18.3 mg, 100 %).

Reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose and *rac*-15b with sodium hydride

Sodium hydride (55-60 per cent dispersion in oil, 9 mg, 0.2 mmol) was added at 20°C during 1 h in two portions to a solution of *rac*-**15b** (20.7 mg, 0.07 mmol) and 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (36.9 mg, 0.07 mmol) in THF (4.0 mL). After 2 h excess sodium hydride was destroyed with 5 per cent HCl. Usual work-up (ethyl acetate) and LC (petrol-ethyl acetate 6:1) gave a mixture of **16c**, **16d**, **16e** and **16f** (33.1 mg, 72 %). 33.6 mg of such a mixture were separated by MPLC (petrol-toluene-$CHCl_3$ 1:1:20) to give **16c** and **16d** (17.1 mg), and two fractions of 4.9 mg and 2.6 mg (**16e** and **16f**, respectively).

(3a*R*)- and (3a*S*)-3-{(*E*)-2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyloxymethylene}-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (16c and 16d)

R_f (petrol-$CHCl_3$ 1:20 (3*developed)): 0.14.- ^{1}H NMR (400 MHz, $CDCl_3$, of a 3 (a) : 7 (b) - mixture): δ = 2.37 - 2.45 (m, 0.3H, 4'-H (a)), 2.60 - 2.69 (m, 0.7H, 4'-H (b)), 2.73 - 2.82 (m, 0.7H, 4'-H* (b)), 2.82 - 2.93 (m, 0.3H, 4'-H* (a)), 3.56 - 3.83 (m, 6H, 2-H, 3-H, 4-H, 5-H, CH_2-6), 3.86 - 3.96 (m, 1H, 3a'-H), 4.41 - 4.52 (2*2d, 2H, benzyl-H), 4.56 - 4.65 (2*2d, 2H, benzyl-H), 4.73 - 4.79 (d, 1H, benzyl-H), 4.79 - 4.89 (2*2d, 2H, benzyl-H), 4.92 - 4.98 (2d, 1H, benzyl-H), 5.07 (d, 0.3H, 1-H (a)), 5.11 (d, 0.7H, 1-H (b)), 5.48 - 5.56 (m, 1H, 6a'-H), 5.81 - 5.88, 5.97 - 6.04 (2*m, 2*1H, 6'-H, 5'-H), 7.10 - 7.18 (m, 2H, arom.-H), 7.23 - 7.40 (m, 19H, =CHO, arom.-H), $J_{(1,2)}$ = 3.5 Hz, $J_{(3a',4')}$ = 2.5 Hz, $J_{(3a',4'*)}$ = 9.0 Hz, $J_{(4',4'*)}$ = 17.5 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT, characteristic signals): δ = 37.63 and 37.76 (C-3a'), 38.44 and 39.22 (C-4'), 67.95 (C-6), 72.30 and 72.58 (C-5), 87.80 (C-6a'), 100.53 and 100.72 (C-1), 153.10 and 153.20 (=CHO), 172.21 (C-2').- IR ($CHCl_3$): 1740, 1680, 1270 cm^{-1}.- $C_{42}H_{42}O_8$ (674.8), (mixture of **16c** and **16d**) calcd: C 74.76 H 6.27, found: C 74.18 H 6.44.

(3a*R*)- and (3a*S*)-3-{(*E*)-2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyloxymethylene}-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (16e and 16f)

Stereoisomer 1: R_f (petrol-$CHCl_3$ 1:20 (3*developed)): 0.11.- M.p.: 112 - 115°C (petrol-ethyl acetate).- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43 - 2.51 (m, 1H, 4'-H), 2.75 - 2.84 (m, 1H, 4'-H*), 3.48 - 3.54 (ddd, 1H, 3a'-H), 3.60 - 3.80 (m, 6H, 2-H, 3-H, 4-H, 5-H, CH_2-6), 4.47 - 4.55 (2d, 2H, benzyl-H), 4.58 - 4.65 (d, 1H, benzyl-H), 4.72 - 4.90 (6d, 6H, 1-H, benzyl-H), 5.50 - 5.55 (m, 1H, 6a'-H), 5.83 - 5.87, 5.94 - 5.99 (2*m, 2*1H, 6'-H, 5'-H), 7.10 - 7.15 (m, 2H, arom.-H), 7.23 - 7.36 (m, 18H, arom.-H), 7.53 (d, 1H, =CHO), $J_{(3a',4')}$ = 2.5 Hz, $J_{(3a',4'*)}$ = 9.0 Hz, $J_{(3a',6a')}$ = 7.5 Hz, $J_{(3a',=CHO)}$ = 2.5 Hz, $J_{(4',4'*)}$ = 17.5 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 37.55 (C-3a'), 39.17 (C-4'), 68.16 (C-6), 73.84 (C-5), 75.25, 75.29, 75.88 and 75.99 (benzyl-C), 81.62 and 84.51 (C-2, C-3, C-4), 87.81 (C-6a'), 104.48 (C-1), 127.98, 128.03, 128.12, 128.19, 128.66, 128.75

and 129.05 (C-3', C-6' or C-5', arom.-C), 137.30, 137.91, 137.95, 138.07 and 138.45 (C-5' or C-6', arom.-C), 153.19 (=CHO), 172.20 (C-2').- IR ($CHCl_3$): 1740, 1680, 1070 cm^{-1}.- $[\alpha]_D^{25}$= +52.6 (c 1.01, $CHCl_3$).- $C_{42}H_{42}O_8$ (674.8), calcd: C 74.76 H 6.27, found: C 74.54 H 6.37.

Stereoisomer 2: R_f (petrol-$CHCl_3$ 1:20 (3*developed)): 0.07.- M.p.: 115 - 118°C (petrol-ethyl acetate).- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.57 - 2.66 (m, 1H, 4'-H), 2.74 - 2.84 (m, 1H, 4'-H*), 3.47 - 3.52 (m, 1H, 3a'-H), 3.57 - 3.77 (m, 6H, 2-H, 3-H, 4-H, 5-H, CH_2-6), 4.46 - 4.62 (3d, 3H, benzyl-H), 4.73 - 4.92 (6d, 6H, 1-H, benzyl-H), 5.49 - 5.54 (m, 1H, 6a'-H), 5.82 - 5.88, 6.00 - 6.04 (2*m, 2*1H, 6'-H, 5'-H), 7.11 - 7.17 (m, 2H, arom.-H), 7.23 - 7.37 (m, 18H, arom.-H), 7.54 (d, 1H, =CHO), $J_{(3a',4')}$ = 2.5 Hz, $J_{(3a',4'*)}$ = 9.0 Hz, $J_{(3a',=CHO)}$ = 2.5 Hz, $J_{(4',4'*)}$ 18.0 Hz, $J_{(4',5')}$ = 2.5 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 37.65 (C-3a'), 38.76 (C-4'), 68.17 (C-6), 73.78 (C-5), 75.28 and 75.92 (benzyl-C), 81.58 and 84.48 (C-2, C-3, C-4), 87.83 (C-6a'), 104.16 (C-1), 127.96, 128.01, 128.11, 128.14, 128.23, 128.67, 128.73 and 128.93 (C-3', C-6' or C-5', arom.-C), 137.47, 137.99, 138.09 and 138.53 (C-5' or C-6', arom.-C), 153.04 (=CHO), 172.13 (C-2').- IR ($CHCl_3$): 1740, 1680, 1070 cm^{-1}.- $[\alpha]_D^{25}$= -67.6 (c 0.98, $CHCl_3$).- $C_{42}H_{42}O_8$ (674.8), calcd: C 74.76 H 6.27, found: C 74.39 H 6.44.

Reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose and *rac*-15c with sodium hydride

To ***rac*-15a** (18.3 mg, 0.12 mmol) a solution of 2,6-di-^{t}butyl-4-methylpyridine (29.9 mg, 0.15 mmol) in CH_2Cl_2 (0.5 mL) and trifluoromethanesulfonic anhydride (22 µL, 0.13 mmol) were added at 0°C. 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose (53.1 mg, 0.10 mmol) dissolved in THF (5.5 mL) and sodium hydride (55-60 per cent dispersion in oil, 13 mg, 0.3 mmol) were added after 30 min. A further portion of sodium hydride (9 mg, 0.2 mmol) was added after 90 min and the reaction mixture was stirred for 1 h. Destroying the excess of sodium hydride with 5 per cent HCl, usual work-up (ethyl acetate) and LC (petrol-ethyl acetate 6:1) provided a mixture of **16c**, **16d**, **16e** and **16f** (33.6 mg, 50 %).

Reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose and *rac*-15b with DBU

DBU (11 µL, 0.07 mmol) was added to a solution of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (37.2 mg, 0.07 mmol) and ***rac*-15b** (21.1 mg, 0.069 mmol) in CH_2Cl_2 (2.0 mL) at 20°C. The reaction mixture was stirred for 24 h, washed three times with water, dried and the solvent was evaporated. LC (petrol-ethyl acetate 6:1) yielded a mixture of **16c**, **16d**, **16e** and **16f** (22.0 mg, 47 %).

Reaction of 11-isomers with *rac*-15b and DBU

11 (20.1 mg, 0.09 mmol), ***rac*-15b** (27.5 mg, 0.09 mmol) and DBU (17 µL, 0.11 mmol) were stirred at 40 - 45°C in CH_2Cl_2 (2.0 mL) for 4 d. Washing with water (three times), drying, solvent evaporation, and LC (petrol-ethyl acetate 6:1) gave a 1:1-mixture of ***rac*-16a** and **20** (11.4 mg, 29 % respectively), as well as a mixture of ***rac*-17** and ***rac*-18** (8.0 mg, 62 %).

3-Methyl-4-phenylsulfanyl-5*H*-furan-2-one (20)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86 - 1.90 (t, 3H, 3-CH_3), 4.34 - 4.40 (q, 2H, CH_2-5), 7.29 - 7.68 (m, 5H, arom.-H), $J_{(5,3\text{-}CH_3)}$ = 2.0 Hz.- IR ($CHCl_3$): 1750, 1630, 1300, 1020 cm^{-1}.- MS: m/z (%) = 206 (M^+, 100), 97 (57), 69 (30), 51 (28), 41 (36).- HRMS calcd for $C_{11}H_{10}O_2S$: 206.0402, found: 206.0409.

Mercuric bromide-promoted coupling of *rac*-15a with 12c and *ent*-12c, respectivly.

***Rac*-15a** (37.7 mg, 0.25 mmol) was stirred with mercuric bromide (89.4 mg, 0.25 mmol) and 4 Å molecular sieves in CH_2Cl_2 (4.0 mL) for 1 h at 20°C. **12c** (78.6 mg, 0.25 mmol) dissolved in CH_2Cl_2 (6.0 mL) was added and the reaction mixture was stirred for 72 h. The reaction mixture was filtered through Celite®, washed with

10 per cent aq. KI and $NaHCO_3$, dried, and the solvent was evaporated. LC (petrol-ethyl acetate 10:1) furnished **12a** and **12c** (28.8 mg, 37 %) as well as a mixture of *ent*-**23a** and *ent*-**24a** (stereoisomers *ent*-1 and *ent*-2) (25.9 mg, 29 %), which could be separated by MPLC (petrol-toluene-^{t}butyl methyl ether 10:100:1). The more polar fraction contained approximately 25 % of **20**.
In a similar reaction *ent*-**12c** (39.3 mg, 0.14 mmol), *rac*-**15a** (17.7 mg, 0.12 mmol) and mercuric bromide (41.5 mg, 0.12 mmol) yielded **23a** and **24a** (stereoisomers 1 and 2) (17.2 mg, 41 %).

(3a*R*,6a*c*)- and (3a*S*,6a*c*) Dihydro-4*H*-cyclopenta[*b*]furan-3-carboxylic acid (2*R*,3*R*,4*R*)-4-methyl-5-oxo-3-phenylsulfanyl-tetrahydro-furan-2-yl ester (*ent*-23a and *ent*-24a)
Stereoisomer *ent*-1: R_f (petrol-toluene-^{t}butyl methyl ether 10:100:1 (3∗developed)): 0.21.- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (d, 3H, 4'-CH_3), 2.40 - 2.48 (m, 1H, 4-H), 2.50 - 2.59 (dq, 1H, 4'-H), 2.63 - 2.73 (m, 1H, 4-H*), 3.34 - 3.39 (dd, 1H, 3'-H), 3.70 - 3.77 (m, 1H, 3a-H), 5.74 - 5.78 (m, 1H, 6-H), 5.81 - 5.85 (m, 1H, 6a-H), 6.04 - 6.08 (m, 1H, 5-H), 6.51 (d, 1H, 2'-H), 7.02 (d, 1H, 2-H), 7.27 - 7.36 (m, 3H, arom.-H), 7.40 - 7.50 (m, 2H, arom.-H), $J_{(2,3a)}$ = 1.5 Hz, $J_{(3a,4)}$ = 2.5 Hz, $J_{(3a,4*)}$ = 8.0 Hz, $J_{(3a,6a)}$ = 9.5 Hz, $J_{(4,4*)}$ = 18.0 Hz, $J_{(2',3')}$ = 5.0 Hz, $J_{(3',4')}$ = 9.0 Hz, $J_{(4',4'\text{-}CH_3)}$ = 7.5 Hz.- IR ($CHCl_3$): 1795, 1720, 1620, 1610, 1140, 1105, 975 cm^{-1}.- MS: m/z (%) = 358 (M^+, 0.8), 206 (80), 178 (43), 135 (100), 107 (36), 77 (28), 41 (22).- HRMS calcd for $C_{19}H_{18}O_5S$: 358.0875, found: 358.0855.
Stereoisomer *ent*-2: R_f (petrol-toluene-^{t}butyl methyl ether 10:100:1 (3∗developed)): 0.19.- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (d, 3H, 4'-CH_3), 2.45 - 2.53 (m, 1H, 4-H), 2.53 - 2.60 (m, 1H, 4'-H), 2.66 - 2.75 (m, 1H, 4-H*), 3.35 - 3.42 (dd, 1H, 3'-H), 3.66 - 3.74 (m, 1H, 3a-H), 5.77 - 5.87 (m, 2H, 6-H, 6a-H), 6.07 - 6.13 (m, 1H, 5-H), 6.52 (d, 1H, 2'-H), 7.08 (d, 1H, 2-H), 7.28 - 7.35 (m, 3H, arom.-H), 7.39 - 7.50 (m, 2H, arom.-H), $J_{(2,3a)}$ = 1.5 Hz, $J_{(3a,4)}$ = 2.5 Hz, $J_{(3a,4*)}$ = 12.0 Hz, $J_{(4,4*)}$ = 18.0 Hz, $J_{(2',3')}$ = 5.0 Hz, $J_{(3',4')}$ = 8.5 Hz, $J_{(3',4'\text{-}CH_3)}$ = 7.5 Hz, signals from **20**: δ = 1.86 - 1.88 (t), 4.34 - 4.37 (q).- IR ($CHCl_3$): 1795, (shoulder at 1740), 1720, 1620, 1610, 1140, 1105, 975 cm^{-1}.- MS: m/z (%) = 358 (M^+, 1), 206 (100), 178 (41), 135 (96), 107 (36), 77 (30), 41 (30).- HRMS calcd for $C_{19}H_{18}O_5S$: 358.0875, found: 358.0854.
Stereoisomer 1: R_f-value, ^{1}H NMR (400 MHz, $CDCl_3$), IR, MS spectra were identical with those obtained from *ent*-**23a** and *ent* **24a** (stereoisomer *ent* 1).- HRMS calcd for $C_{19}H_{18}O_5S$: 358.0875, found: 358.0881.
Stereoisomer 2: R_f-value, ^{1}H NMR (400 MHz, $CDCl_3$), IR, MS spectra were identical with those obtained from *ent* **23a** and *ent* **24a** (stereoisomer *ent* 2). ^{1}H NMR revealed the presence of **20**.- HRMS calcd for $C_{19}H_{18}O_5S$: 358.0875, found: 358.0873.

Coupling of *rac*-15a and *ent*-12c with silver carbonate
A mixture of *rac*-**15a** (13.7 mg, 0.09 mmol), silver carbonate (56.2 mg, 0.20 mmol) and 4 Å molecular sieves in toluene (1.0 mL) was stirred for 1 h at -10°C. *Ent*-**12c** (23.9 mg, 0.08 mmol) dissolved in CH_2Cl_2 (1.0 mL) was added. After being stirred at -10°C for 6 d the reaction mixture was filtered and washed with aq. $NaHCO_3$ and water. Drying, solvent evaporation, and LC (petrol-ethyl acetate 10:1) furnished **21 / 22** (stereoisomeric series *ent*-1 and *ent*-2) (2.8 mg, 9 %) as well as a mixture of **25a** and **26a** (6.4 mg, 22 %). For spectral data see below.

Coupling of *ent*-12a and *ent*-12c with *rac*-15a and silver triflate
A solution of *ent*-**12a** and *ent*-**12c** (27.2 mg, 0.10 mmol) dissolved in CH_2Cl_2 (3.0 mL) was added to a -20°C cold mixture of *rac*-**15a** (12.8 mg, 0.08 mmol), silver carbonate (466.8 mg, 1.69 mmol), silver triflate (24.0 mg, 0.09 mmol), 4 Å molecular sieves, and CH_2Cl_2 (3.0 mL). The reaction mixture was stirred for 3.5 h at -20°C, filtered, washed with sat. aq. $NaHCO_3$ and water, dried, and then the solvent was evaporated. LC

(petrol-ethyl acetate 15:1) provided a mixture of **23a** / **24a** (stereoisomeric series *ent*-1 and *ent*-2) (6.1 mg, 20 %).

Coupling of *ent*-12a and *ent*-12c with *rac*-15a and silver perchlorate

Compounds *ent*-**12a** and *ent*-**12c** (36.1 mg, 0.13 mmol) dissolved in CH_2Cl_2 (1.0 mL) were added at -10°C to a mixture of silver carbonate (83.4 mg, 0.30 mmol), *rac*-**15a** (19.0 mg, 0.13 mmol), silver perchlorate (7.8 mg, 0.04 mmol), 4 Å molecular sieves, and toluene (2.0 mL). The reaction mixture was stirred at -10°C for 20.5 h. Filtration, washing the filtrates with $NaHCO_3$ and water, drying, and solvent evaporation, followed by LC (petrol-ethyl acetate 15:1) yielded a mixture of **23a** / **24a** (stereoisomeric series *ent*-1 and *ent*-2) (7.9 mg, 18 %).

Coupling of 12c and *rac*-15a with mercuric cyanate and mercuric bromide

12c (16.1 mg, 0.06 mmol), *rac*-**15a** (8.7 mg, 0.06 mmol), mercuric cyanate (22.8 mg, 0.09 mmol), mercuric bromide (10.2 mg, 0.03 mmol) and 4 Å molecular sieves in CH_2Cl_2 (1.5 mL) were stirred for 75 h at 20°C. The reaction mixture was filtered and the solutes washed with 10 per cent aq. NaI. Usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 10:1) gave a mixture of **23a** and **24a** (stereoisomeric series 1 and 2) (7.2 mg).

Coupling of *ent*-12c and 15a in the presence of silver carbonate

A mixture of **13** (26.6 mg, 0.17 mmol) silver carbonate (89.4 mg, 0.32 mmol) und 4 Å molecular sieves in dry toluene (1.8 mL) was stirred at -10°C under argon for 1 h. A solution of *ent*-**12c** (46.6 mg, 0.18 mmol) in dry CH_2Cl_2 (1.8 mL) was added and the mixture was stirred at 20°C for 14 d. Dilution with CH_2Cl_2, filtration (Celite®), and MPLC (petrol-ethyl acetate 6:1) provided a mixture of **23a** and **20** (5.8 mg), and **25a** (8.5 mg, 16 %).

(3a*S*)-3-(*E*)-[4-Methyl-5-oxo-3-phenylsulfanyl-tetrahydro-furan-2-yloxy-methylene]-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (25a)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (d, 3H, 4'-CH_3), 2.13 - 2.22 (m, 1H, 4-H), 2.59 (dq, 1H, 4'-H), 2.63 - 2.72 (m, 1H, 4-H*), 3.43 (dd, 1H, 3'-H), 3.57 - 3.64 (m, 1H, 3a-H), 5.47 - 5.57 (m, 1H, 6a-H), 5.64 (d, 1H, 2'-H), 5.81 - 5.88 (m, 1H, 6-H), 5.95 - 6.05 (m, 1H, 5-H), 7.29 (d, 1H, 7-H), 7.31 - 7.38 (m, 3H, arom.-H), 7.43 - 7.50 (m, 2H, arom.-H), $J_{(4',4'\text{-}CH_3)}$ = 7.3 Hz, $J_{(2',3')}$ = 4.4 Hz, $J_{(3',4')}$ = 8.6 Hz.- $C_{19}H_{18}O_5S$ (358.4), MS: m/z (%) = 358 (M^+, 0.8), 207 (100), 161 (63), 151 (70), 109 (65), 41 (58).

Coupling of 15a with 12c (silver silicate promotor)

A mixture of **15a** (14.1 mg, 0.09 mmol) and silver silicate (184.7 mg) in THF (1.5 mL) was stirred at -20°C under argon for 15 min. A solution of **12c** (42.8 mg, 0.15 mmol) in THF (0.5 mL) was slowly added. The mixture was stirred at -20°C for 50 h. Dilution with CH_2Cl_2, filtration (Celite®), and LC (petrol-ethyl acetate 6:1) provided a mixture of *ent*-**24a** and **20** (2.3 mg), and *ent*-**26a** (10.0 mg, 30 %).

(3a*S*)-3-(*E*)-[4-Methyl-5-oxo-3-phenylsulfanyl-tetrahydro-furan-2-yloxy-methylene]-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (*ent*-26a), slightly impure

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (d, 3H, 4'-CH_3), 2.38 - 2.46 (m, 1H, 4-H), 2.60 (dq, 1H, 4'-H), 2.70 - 2.80 (m, 1H, 4-H*), 3.47 (dd, 1H, 3'-H), 3.68 - 3.76 (m, 1H, 3a-H), 5.47 - 5.57 (m, 1H, 6a-H), 5.61 (d, 1H, 2'-H), 5.81 - 5.89 (m, 1H, 6-H), 5.98 - 6.09 (m, 1H, 5-H), 7.27 (d, 1H, 7-H), 7.31 - 7.40 (m, 3H, arom.-H), 7.41 - 7.48 (m, 2H, arom.-H), $J_{(4',4'\text{-}CH_3)}$ = 7.3 Hz, $J_{(2',3')}$ = 4.1 Hz, $J_{(3',4')}$ = 7.5 Hz.- IR ($CHCl_3$): 1800, 1744,

1682, 1154, 981 cm^{-1}.- $C_{19}H_{18}O_5S$ (358.4), MS: m/z (%) = 358 (M^+, 1), 207 (100), 161 (56), 151 (60), 109 (58), 97 (58), 41 (59).

Reaction of *ent*-15a and 12a in the presence of silver silicate

The reaction was performed as described for the coupling of **15a** with **12c**.

(2*S*,3*R*,4*R*)-4-Methyl-5-oxo-3-phenylsulfanyl-tetrahydro-furan-2-yl (3a*R*,6a*c*)-dihydro-4*H*-cyclopenta[*b*]furan-3-carboxylate (29)

R_f (petrol-ethyl acetate 1:1) = 0.51.- ^1H NMR (200 MHz, $CDCl_3$): δ = 1.41 (d, 3H, $J_{(4',4'\text{-}CH_3)}$ = 7.3 Hz, 4'-CH_3), 2.39 - 2.54 (dddd, 1H, $J_{(4,4^*)}$ = 18.0 Hz, $J_{(4,3a)}$ = 2.2 Hz, J = 4.4 Hz, 2.2 Hz, 4-H), 2.63 - 2.80 (ddddd, 1H, $J_{(4^*,3a)}$ = 8.8 Hz, 2.2 Hz, 2.2 Hz, ≈ 1 Hz, 4*-H), 3.17 - 3.34 (dq, 1H, $J_{(4',3')}$ = 7.3 Hz, 4'-H), 3.67 - 3.79 (dddd, 1H, $J_{(3a,6a)}$ = 7.7 Hz, 1.8 Hz, 1.8 Hz, 3a-H), 4.01 (dd, 1H, $J_{(3',2')}$ = 1.1 Hz, 3'-H), 5.75 - 5.88 (m, 2H, 6-H, 6a-H), 6.05 - 6.12 (m, 1H, 5-H), 6.50 (d, 1H, 2'-H), 7.16 (d, 1H, $J_{(7,3a)}$ = 1.5 Hz, 7-H), 7.25 - 7.50 (m, 5H, arom.-H).- ^{13}C NMR (50 MHz, APT, $CDCl_3$): δ = 11.18 (-) (4'-CH_3), 37.11 (-) (C-4'), 39.36 (+) (C-4), 41.99 (-) (C-3a), 53.10 (-) (C-3'), 96.55 (-) (C-2' or C-6a), 96.79 (-) (C-6a or C-2'), 111.76 (+) (C-3), 128.38 (-) (C-6 or p-C-arom.), 128.74 (-) (p-C-arom. or C-6), 130.03 (-) (m-C-arom.), 132.33 (+) (i-C-arom.), 132.76 (-) (o-C-arom.), 137.44 (-) (C-5), 158.53 (-) (C-7), 162.71 (+) (C-2), 176.69 (+) (C-5').- FAB MS: 381.3 $[M+Na]^+$, 359.3 $[M+H]^+$.- CD (c 27.90 μmol L^{-1}, acetonitrile): λ_{max} (Δε) = 261 nm (-34.3).- HRMS calcd for $C_{19}H_{19}O_5S$ $[M+H]^+$: 359.0953, found: 359.0947.

(3a*S*)-3-(*E*)-[(2*R*,3*R*,4*R*)-4-Methyl-5-oxo-3-phenylsulfanyl-tetrahydro-furan-2-yloxy-methylene]-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (30)

R_f (petrol-ethyl acetate 1:1) = 0.40.- ^1H NMR (200 MHz, $CDCl_3$): δ =1.43 (d, 3H, $J_{(4',4'\text{-}CH_3)}$ = 7.3 Hz, 4'-CH_3), 2.30 - 2.46 (dddd, 1H, $J_{(4,4^*)}$ = 17.6 Hz, $J_{(4,3a)}$ = 2.6 Hz, J = 5.1 Hz, 2.6 Hz, 4-H), 2.70 - 2.88 (m, 1H, 4*-H), 3.17 - 3.34 (dq, 1H, $J_{(4',3')}$ = 7.3 Hz, 4'-H), 3.52 - 3.66 (m, 1H, $J_{(3a,4^*)}$ = 8.8 Hz, 3a-H), 4.13 (d, 1H, 3'-H), 5.46 - 5.56 (dm, 1H, $J_{(6a,3a)}$ = 7.7 Hz, 6a-H), 5.56 (s, 1H, 2'-H), 5.80 - 5.90 (ddd, 1H, $J_{(6,5)}$ = 5.5 Hz, J = 4.4 Hz, 2.2 Hz, 6-H), 5.98 - 6.06 (m, 1H, 5-H), 7.22 (d, 1H, $J_{(7,3a)}$ = 2.6 Hz, 7-H), 7.30 - 7.50 (m, 5H, arom.-H).- ^{13}C NMR (50 MHz, APT, $CDCl_3$): δ = 10.96 (-) (4'-CH_3), 36.66 (-) (C-3a or C-4'), 37.75 (-) (C-4' or C-3a), 38.99 (+) (C-4), 52.83 (-) (C-3'), 88.10 (-) (C-6a), 105.36 (-) (C-2'), 114.19 (+) (C-3), 129.16 (-) (p-C-arom.), 129.20 (-) (C-6), 130.36 (-) (m-C-arom.), 131.75 (+) (i-C-arom.), 132.78 (-) (o-C-arom.), 137.53 (-) (C-5), 151.27 (-) (C-7), 171.60 (+) (C-2), 175.95 (+) (C-5').- FAB MS: 381.2 $[M+Na]^+$, 359.3 $[M+H]^+$.- CD (c 27.90 μmol L^{-1}, acetonitrile): λ_{max} (Δε) = 226 nm (-14.8).- HRMS calcd for $C_{19}H_{19}O_5S$ $[M+H]^+$: 359.0953, found: 359.0953.

(3a*S*)-3-(*Z*)-[(2*R*,3*R*,4*R*)-4-Methyl-5-oxo-3-phenylsulfanyl-tetrahydro-furan-2-yloxy-methylene]-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (31)

R_f (petrol-ethyl acetate 1:1) = 0.34.- ^1H NMR (200 MHz, $CDCl_3$): δ = 1.37 (d, 3H, $J_{(4',4'\text{-}CH_3)}$ = 7.3 Hz, 4'-CH_3), 2.22 - 2.37 (dddd, 1H, $J_{(4,4^*)}$ = 17.2 Hz, $J_{(4,3a)}$ = 2.6 Hz, J = 5.1 Hz, 2.6 Hz, 4-H), 2.80 - 2.97 (m, 1H, 4*-H), 3.36 - 3.54 (dq, 1H, $J_{(4',3')}$ = 7.3 Hz, 4'-H), 3.55 - 3.67 (dddd, 1H, $J_{(3a,4^*)}$ = 8.4 Hz, 3a-H), 4.30 (d, 1H, 3'-H), 5.44 - 5.51 (dm, 1H, $J_{(6a,3a)}$ = 7.7 Hz, 6a-H), 5.53 (s, 1H, 2'-H), 5.82 - 5.90 (ddd, 1H, $J_{(6,5)}$ = 5.5 Hz, J = 4.4 Hz, 2.2 Hz, 6-H), 5.99 - 6.06 (m, 1H, 5-H), 6.60 (d, 1H, $J_{(7,3a)}$ = 1.8 Hz, 7-H), 7.25 - 7.53 (m, 5H, arom.-H).-^{13}C NMR (50 MHz, APT, $CDCl_3$): δ = 10.66 (-) (4'-CH_3), 36.59 (-) (C-3a or C-4'), 38.43 (-) (C-4' or C-3a), 42.08 (+) (C-4), 52.39 (-) (C-3'), 87.62 (-) (C-6a), 104.62 (-) (C-2'), 113.38 (+) (C-3), 128.63 (-) (C-6 or p-C-arom.), 129.67 (-) (p-C-arom. or C-6), 130.18 (-) (m-C-arom.), 132.16 (-) (o-C-arom.), 132.27 (+) (i-C-arom.), 136.99 (-) (C-5), 150.06 (-) (C-7), 168.44 (+) (C-2), 176.59 (+) (C-5').- FAB MS: 381.3

$[M+Na]^+$, 359.3 $[M+H]^+$.- CD (c 27.90 µmol L^{-1}, acetonitrile): λ_{max} ($\Delta\varepsilon$) = 215 (+3.8), 234 (-2.9), 254 nm (-14.4).- HRMS calcd for $C_{19}H_{19}O_5S$ $[M+H]^+$: 359.0953, found: 359.0953

Coupling of *ent*-15a with 12c in the presence of silver silicate
The reaction was performed as described for the coupling of **15a** with **12c**.

(2*S*,3*S*,4*R*)-4-Methyl-5-oxo-3-phenylsulfanyl-tetrahydro-furan-2-yl (3a*R*,6a*c*)-dihydro-4*H*-cyclopenta[*b*]furan-3-carboxylate (*ent*-23a)
R_f (petrol-ethyl acetate 2:1) = 0.43.- ^1H NMR (200 MHz, $CDCl_3$): δ = 1.45 (d, 3H, $J_{(4',4'\text{-}CH_3)}$ = 7.7 Hz, 4′-CH_3), 2.39 - 2.54 (m, 1H, $J_{(4,4^*)}$ = 18.0 Hz, $J_{(4,3a)}$ = 2.2 Hz, 4-H), 2.50 - 2.64 (m, 1H, $J_{(4',3')}$ = 8.8 Hz, $J_{(4',4'\text{-}CH_3)}$ = 7.7 Hz, 4′-H), 2.63 - 2.82 (m, 1H, $J_{(4^*,4)}$ = 17.6 Hz, 4*-H), 3.39 (dd, 1H, $J_{(3',2')}$ = 5.1 Hz, 3′-H), 3.70 - 3.85 (m, 1H, 3a-H), 5.77 - 5.91 (m, 2H, J = 2.2 Hz, 6-H, $J_{(6a,3a)}$ = 8.8 Hz, 6a-H), 6.06 - 6.14 (m, 1H, 5-H), 6.54 (d, 1H, 2′-H), 7.11 (d, 1H, $J_{(7,3a)}$ = 1.5 Hz, 7-H), 7.34 - 7.42 (m, 3H, arom.-H), 7.48 - 7.56 (m, 2H, arom.-H).

(3a*S*)-3-(*E*)-[(2*S*,3*S*,4*R*)-4-Methyl-5-oxo-3-phenylsulfanyl-tetrahydro-furan-2-yloxy-methylene]-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one (*ent*-25a)
R_f (petrol-ethyl acetate 2:1) = 0.31.- ^1H NMR (200 MHz, $CDCl_3$): δ = 1.49 (d, 3H, $J_{(4',4'\text{-}CH_3)}$ = 7.3 Hz, 4′-CH_3), 2.11 - 2.27 (dddd, 1H, $J_{(4,4^*)}$ = 17.6 Hz, $J_{(4,3a)}$ = 2.6 Hz, J = 5.1 Hz, 2.6 Hz, 4-H), 2.54 - 2.79 (m, 2H, 4′-H, 4*-H), 3.46 (dd, 1H, $J_{(3',4')}$ = 8.8 Hz, $J_{(3',2')}$ = 4.4 Hz, 3′-H), 3.56 - 3.70 (dddd, 1H, $J_{(3a,4^*)}$ = 8.8 Hz, 3a-H), 5.48 - 5.58 (dm, 1H, $J_{(6a,3a)}$ = 7.7 Hz, 6a-H), 5.67 (d, 1H, 2′-H), 5.82 - 5.92 (ddd, 1H, $J_{(6,5)}$ = 5.5 Hz, J = 4.4 Hz, 2.2 Hz, 6-H), 5.96 - 6.06 (m, 1H, 5-H), 7.32 (d, 1H, $J_{(7,3a)}$ = 2.6 Hz, 7-H), 7.34 - 7.45 (m, 3H, arom.-H), 7.45 - 7.56 (m, 2H, arom.-H).

(3a*S*)-3-(*Z*)-[(2*S*,3*S*,4*R*)-4-Methyl-5-oxo-3-phenylsulfanyl-tetrahydro-furan-2-yloxy-methylene]-(3a*r*,6a*c*)-3,3a,4,6a-tetrahydro-cyclopenta[*b*]furan-2-one ((*Z*)-isomer of *ent*-25a)
R_f (petrol-ethyl acetate 2:1) = 0.22.- ^1H NMR (200 MHz, $CDCl_3$): δ = 1.52 (d, 3H, $J_{(4',4'\text{-}CH_3)}$ = 7.3 Hz, 4′-CH_3), 2.31 - 2.47 (dddd, 1H, $J_{(4,4^*)}$ = 17.2 Hz, $J_{(4,3a)}$ = 2.6 Hz, J = 5.1 Hz, 2.6 Hz, 4-H), 2.55 - 2.71 (dq, 1H, $J_{(4',3')}$ = 5.8 Hz, 4′-H), 2.81 - 2.99 (m, 1H, $J_{(4^*,3a)}$ = 8.4 Hz, 4*-H), 3.54 - 3.67 (m, 1H, 3a-H), 3.78 (dd, 1H, $J_{(3',2')}$ = 2.6 Hz, 3′-H), 5.44 - 5.54 (dm, 1H, $J_{(6a,3a)}$ = 8.1 Hz, 6a-H), 5.60 (d, 1H, 2′-H), 5.82 - 5.93 (ddd, 1H, $J_{(6,5)}$ = 5.9 Hz, J = 4.4 Hz, 2.2 Hz, 6-H), 5.99 - 6.10 (m, 1H, 5-H), 6.62 (d, 1H, $J_{(7,3a)}$ = 2.2 Hz, 7-H), 7.30 - 7.42 (m, 3H, arom.-H), 7.42 - 7.54 (m, 2H, arom.-H).

GR28 (27) from 25a
To a solution of **25a** (8.5 mg, 0.02 mmol) in CH_2Cl_2 (0.6 mL) at -20°C a solution of m-CPBA (55 per cent, 7.2 mg, 0.02 mmol) in CH_2Cl_2 (0.6 mL) was added dropwise. After stirring for 30 min the solvent was removed in a stream of argon. LC (petrol-ethyl acetate 3:1) provided 7.1 mg of the sulfoxide(s). The latter were dissolved in dry CH_2Cl_2 (0.5 mL), and triethylamine (3 µL, 0.03 mmol) was added. Stirring for 6 h, solvent removal in a stream of argon, and LC (petrol-ethyl acetate 2:1) furnished **27** (4.8 mg, 79 %), identical with a reference sample (R_f value, ^1H NMR and MS).- $[\alpha]_D^{25}$ = +138.0 (c 0.99, $CHCl_3$).

2'-*epi*-GR28 (28) from *ent*-26a
Ent-**26a** (7.7 mg, 0.02 mmol) was converted to **28** (3.4 mg, 50 %) as described above. The **28** sample was identical with a reference sample (R_f value, ^1H NMR and MS).- $[\alpha]_D^{25}$ = +29.4 (c 0.99, $CHCl_3$).

***Ent*-2'-*epi*-GR28 (*ent*-28) from 30**

30 (9.0 mg, 0.0251 mmol) was converted to ***ent*-28** (5.1 mg, 82 %) as described above. The sample was identical with the reference sample (R_f value, ^{1}H NMR).

Oxidation of 23a / 24a

A solution of m-CPBA (55 per cent, 6.4 mg, 0.03 mmol) in CH_2Cl_2 (0.6 mL) was added at -20°C to **23a / 24a** (stereoisomer 1) (10.6 mg, 0.03 mmol) dissolved in CH_2Cl_2 (0.6 mL). Solvent evaporation after 30 min and LC (petrol-ethyl acetate 4:1) provided a mixture of diastereoisomeric sulfoxides **23b / 24b** (stereoisomeric series 1) (11.1 mg, 100 %).

Oxidation of **23a / 24a** (stereoisomer 2) (12.6 mg, 0.04 mmol) yielded **23b / 24b** (stereoisomeric series 2) (9.4 mg, 72 %).

Oxidation of **23a / 24a** (stereoisomer *ent*-1) (14.5 mg, 0.04 mmol) yielded **23b / 24b** (stereoisomeric series *ent*-1) (12.7 mg, 83 %).

Oxidation of **23a / 24a** (stereoisomer *ent*-2) (15.5 mg, 0.04 mmol) yielded **23b / 24b** (stereoisomeric series *ent*-2) (15.0 mg, 93 %).

Thermolysis of 23b / 24b

23b / 24b (stereoisomeric series 1) (11.6 mg, 0.04 mmol) were heated to 110°C in toluene (1.2 mL) for 30 min. Solvent evaporation and LC (petrol-ethyl acetate 8:1) gave a compound which was either **21** or **22** (stereoisomeric series 1) (6.4 mg, 83 %).

Thermolysis of **23b / 24b** (stereoisomeric series 2) (9.4 mg, 0.03 mmol) gave **21 / 22** (stereoisomeric series 2) (3.8 mg, 61 %).

Thermolysis of **23b / 24b** (stereoisomeric series *ent*-1) (12.7 mg, 0.03 mmol) gave **21 / 22** (stereoisomeric series *ent*-1) (6.2 mg, 74 %).

Thermolysis of **23b / 24b** (stereoisomeric series *ent*-2) (15.0 mg, 0.04 mmol) gave **21 / 22** (stereoisomeric series *ent*-2) (7.0 mg, 71 %).

(3a*R*,6ac) / (3a*S*,6ac)-Dihydro-4*H*-cyclopenta[*b*]furan-(2*R*)-3-carboxylic acid-4-methyl-5-oxo-2,5-dihydro-furan-2-yl ester (21 / 22)

Stereoisomeric series 1: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.96 - 1.98 (dd, 3H, 4'-CH_3), 2.52 - 2.60 (m, 1H, 4-H), 2.69 - 2.78 (m, 1H, 4-H*), 3.74 - 3.81 (m, 1H, 3a-H), 5.76 - 5.80 (m, 1H, 6-H), 5.82 - 5.87 (m, 1H, 6a-H), 6.07 - 6.11 (m, 1H, 5-H), 6.87 - 6.90 (dq, 1H, 2'-H), 6.95 - 6.97 (dq, 1H, 3'-H), 7.23 (d, 1H, 2-H), $J_{(2,3a)}$ = 1.5 Hz, $J_{(3a,4)}$ = 2.5 Hz, $J_{(3a,4*)}$ = 7.5 Hz, $J_{(3a,6a)}$ = 9.0 Hz, $J_{(4,4*)}$ = 18.0 Hz, $J_{(2',4'\text{-}CH_3)}$ = $J_{(2',3')}$ = $J_{(3',4'\text{-}CH_3)}$ = 1.5 Hz.- IR ($CHCl_3$): 1785, 1720, 1620, 1610, 1140, 1095, 1045, 1010, 965 cm^{-1}.- MS: m/z (%) = 248 (M^+, 4), 151 (25), 135 (17), 133 (17), 97 (100), 77 (17).- CD (c 1.870 mmol L^{-1}, acetonitrile): λ_{max} (Δε) = 256.2 (-24.5), 251.4 (-25.2), 211.2 nm (-8.0).- HRMS calcd for $C_{13}H_{12}O_5$: 248.0685, found: 248.0681.

Stereoisomeric series 2: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.49 - 2.57 (m, 1H, 4-H), 3.76 - 3.83 (m, 1H, 3a-H), further signals, IR MS spectra are superimposible with those obtained from **21 / 22** (stereoisomeric series 1).- CD (c 1.607 mmol L^{-1}, acetonitrile): λ_{max} (Δε) = 257.8 (+7.67), 204.2 nm (-14.13).- HRMS calcd for $C_{13}H_{12}O_5$: 248.0685, found: 248.0686.

Stereoisomerioc series *ent*-1: ^{1}H NMR (400 MHz, $CDCl_3$), IR, MS: these spectra are superimposible with those obtained from **21 / 22** (stereoisomeric series 1). CD (c 2.063 mmol L^{-1}, acetonitrile): λ_{max} (Δε) = 251.0 (+22.98), 215.4 nm (+6.99).- HRMS calcd for $C_{13}H_{12}O_5$: 248.0685, found: 248.0697.

Stereoisomeric series *ent*-2: ^{1}H NMR (400 MHz, $CDCl_3$), IR, MS: these spectra are superimposible with those obtained from **21 / 22** (stereoisomeric series 2). CD (c 2.962 mmol L^{-1}, acetonitrile): λ_{max} ($\Delta\varepsilon$) = 256.4 (-4.71), 252.6 (-4.79), 205.0 nm (+10.21).- HRMS calcd for $C_{13}H_{12}O_5$: 248.0685, calcd: 248.0701.

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