Synthesis of Substituted Tetrahydrofuran by Electrophile-Induced Cyclization of 4-Pentene-1,2,3-triols − An Example of 5-*exo versus* 5-*endo* Cyclization Governed by the Electrophile

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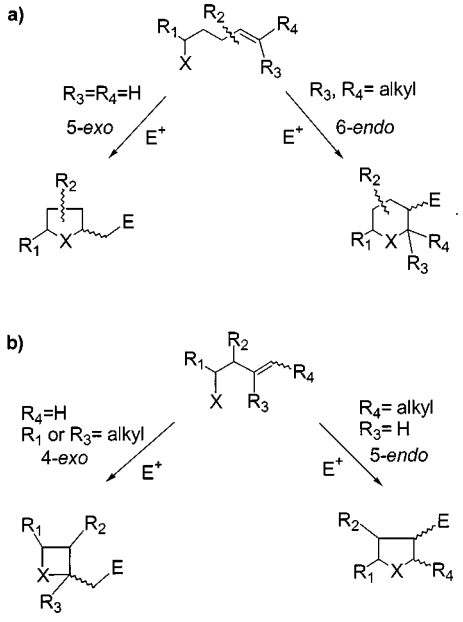
Differently protected 4-pentene-1,2,3-triols **5**–**8** were obtained from glyceraldehyde and submitted to iodine-based electrophile-induced cyclization to give tetrahydrofuran derivatives **10** and **18**, with high chemo-, regio-, and stereoselectivity, through a 5-*exo* cyclization process. However, when an electrophilic selenium reagent was treated with similar alkene triols **5**, **7**, and **8**, the product depended on the protecting group at the primary hydroxy moiety. Thus, while compounds **5a** and **5b**, unprotected at the primary hydroxy group, give compounds **26** and **27**, and **32** and **33**, respectively, through a 5-*exo* cyclization process, compounds **7** and **8**, protected at the primary hydroxy group, give the 5-*endo* cyclization products **22**–**25** and **28**–**31** in good yields. The electrophile-induced cyclization of 4-pentene-1,2,3-triols to give tetrahydrofuran derivatives can be directed towards a 5-*exo* process by the use of iodine or, when the primary hydroxy group is unprotected, selenium. When the primary hydroxy group is protected, use of selenium results in 5-*endo* cyclization.

Introduction

Cyclolactonization and cycloetherification induced by electrophilic reagents are important tools in the synthesis of complex organic molecules.[1] The conditions of cyclization are, in general, independent of the nucleophile (usually O, N, S, and C), and electrophilic reagents commonly used are, among others, mercury,[2] sulfur,[3] bromine,[4] selenium,[5] and iodine.[6] The regioselectivity in alkenol cyclizations can be explained by the Baldwin rules.[7] However, 5-*endo-trig* electrophile-induced cyclizations, which are not favored according to these rules, have been reported. The fact that these cyclizations are electrophile- rather than nucleophile-driven suggests that they are not true exceptions.[8]

In general, electrophilic cyclizations can be effected under kinetic or thermodynamic conditions.[9] Under kinetic conditions, a base is used to deprotonate the oxonium cation in the cyclic intermediate, and this makes the reaction irreversible. Under these conditions, *exo* cyclizations are usually preferred.

Concerning the regioselectivity, cyclization of alkenols has some general features. Firstly, 5-*exo* cyclization is generally preferred to 6-*endo*. The percentage of 6-*endo* products increases as substitution increases at the terminal olefinic carbon atom[10] (Scheme 1, a). Secondly, there is competition between 4-*exo* and 5-*endo* cyclization, dependent on the double bond substitution pattern (Scheme 1, b). Thus, 4-*exo* cyclizations mainly occur when the carbon atom bearing the internal nucleophile is highly substituted (tertiary[11] or quaternary[12]) or when the carbon atom of the double bond closest to it is substituted.[12b,13] On the other hand, 5-*endo* cyclizations take place when the double bond is substituted at the carbon atom furthest from the nucleophile.[11] In particular, 5-*endo* selenoetherification provides good yields.[14] Iodine electrophiles can also produce a 5-*endo* cyclization in these substrates, although reactions are slow and yields are generally lower.[11,15] In the absence of these structural factors it is not easy to predict the cyclization mode, and mixtures are usually obtained.[12b,16]



Scheme 1

The situation is more complex for polyhydroxylated alkenes (Scheme 2), since several cyclization paths may be fol-

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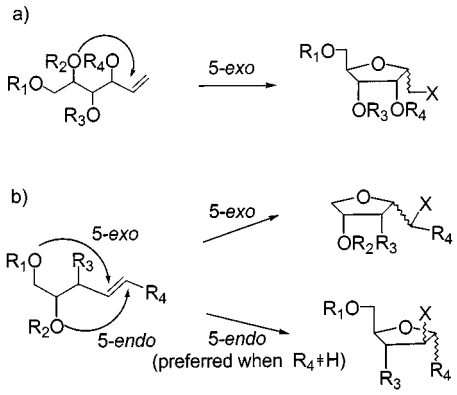
lowed. Cyclizations from tri- or tetrahydroxyhexenes with a terminal double bond (usually derived from pentoses) have been widely studied, and the preferred process is 5-*exo* (Scheme 2, a).[17]



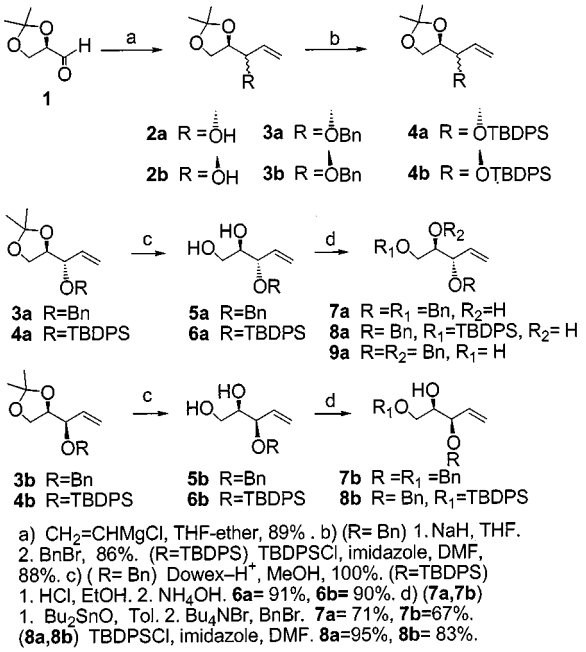
Scheme 2

However, reported electrophile-induced cyclizations in polyhydroxypentenes mainly produce 5-*endo* cyclizations (Scheme 2, b), probably because the substrates studied are polysubstituted olefins (Scheme 2, b; R^3 = H, OR; R^4 = furyl,[18] OR[19]).

Recently, we described an efficient procedure for synthesizing biologically active isonucleosides, based on the iodocyclization of pentene diols (Scheme 2, b; $R^3 = R^4$ = H).[20] Pursuing our interest in these reactions for use in the preparation of biologically active products, we report in this paper a general study of the electrophile-induced cyclization of 4-pentene-1,2,3-triols (Scheme 2, b, R^3 = OR, R^4 = H), and show that the regioselectivity of the process can be controlled through 5-*exo*-*trig*-like or 5-*endo*-*trig*-like cyclization depending on the electrophile used.

Results and Discussion

To explore the role of protecting groups in the cyclization, we prepared the differently protected pentene triols **5**−**8** from glyceraldehyde,[21a] as shown in Scheme 3. Hydroxyalkenes **2a** and **2b** were prepared as a diastereomeric mixture, following reported procedures.[21b] The free hydroxy group in the mixture of **2a** and **2b** was protected by treatment with benzyl bromide in basic medium to give compounds **3a** and **3b**, or with TBDPSCl to give compounds **4a** and **4b**. The hydrolysis of the acetal groups in **3a** and **3b**, and **4a** and **4b** led to the diols **5a** and **5b**, and **6a** and **6b**, respectively. The primary alcohol moieties in compounds **5a** and **5b** were selectively protected by treatment with Bu_2SnO and BnBr,[22] or with TBDPSCl to afford the partially protected trihydroxypentenols **7a** and **7b**, and **8a** and **8b**, respectively. In the benzylation of **5a**, compound **9a** was isolated as a minor product.



Scheme 3

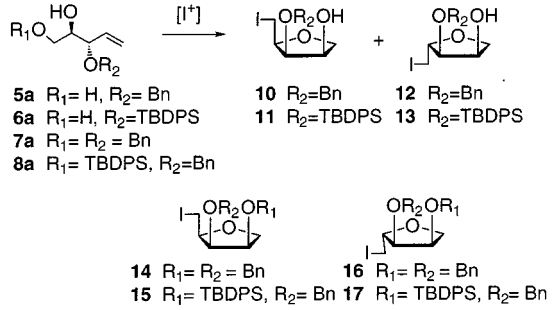
Initially, we explored the role of protecting groups in the iodine-induced cyclization of alkenetriols **5a**−**8a**. We treated the alcohol **7a** with iodine under basic conditions[8] and obtained a mixture of tetrahydrofurans **10** and **12** in an 86% yield (ratio **10/12** = 77:23) (Table 1, Entry 1; Scheme 4). These compounds were formed by 5-*exo* cyclization involving the oxygen atom bonded to C-1, with concomitant loss of the benzyl group. This consecutive cyclization/benzyl deprotection is a well-documented process.[6c,18,23] It has also been observed that ethers do not participate in the cyclization process when electrophiles with a poorly nucleophilic counter-ion are used.[17d] Because of this, we used bis(*syn*-collidine)iodonium perchlorate[24] and *N*-iodosuccinimide as electrophilic reagents, but we obtained the same mixture of products (Entries 2 and 3). This shows that benzyl ethers also participate in cyclization when there is no nucleophilic counter-ion, probably by formation of a benzyl cation.[25] When NIS was the electrophile and benzene the solvent, the reaction was very slow and gave the compounds **10** and **12**, together with their respective derivatives **14** and **16**, which are probably formed by reaction with the benzyl cation liberated during the reaction (Entry 4). Compounds **14** and **16** were inseparable and their structures were confirmed by comparing their ^{1}H and ^{13}CNMR spectra with those of products obtained by treating **9a** under conditions similar to those used for **7a**; the spectra turned out to be identical (Scheme 4). Curiously, when **7a** was treated with KH[19b] to form the alkoxide and then with I_2, there was no further reaction even after 7 d.

Since the benzyl group was easily removed under the reaction conditions used, we next tried other protecting groups. When a pivaloyl group was present at the primary hydroxy group, iodine-induced cyclization resulted in a complex mixture of compounds, probably due to transes-

Table 1. Reaction of alkenols **5a−8a** with electrophilic iodine

Entry	Starting material	I^+	Conditions	Ratio of products (%)	Yield (%)
1	**7a**	I_2	$NaHCO_3$, MeCN, 0 °C, 40 min	**10/12** (77:23)	86
2	**7a**	I(*syn*-col)$_2$ClO$_4$	CH_2Cl_2, room temp., 3 h	**10/12** (43:57)	57
3	**7a**	NIS	CH_2Cl_2, −78°C to room temp., 8 d	**10/12** (80:20)	64
4	**7a**	NIS	benzene, room temp., 21 d	**10/12** (71:29)[a]	62
5	**8a**	I_2	$NaHCO_3$, MeCN, 0 °C, 18 h	**10/12** (73:27)[b]	65
6	**5a**	I_2	$NaHCO_3$, MeCN, 0 °C, 45 min	**10/12** (86:14)	91
7	**5a**	I_2	MeCN, 0 °C, 3 h	**10/12** (63:37)	38
8	**6a**	I_2	$NaHCO_3$, MeCN, 0 °C, 2 h	**11/13** (60:40)	46

[a] 36% of compounds **14** and **16** was also obtained (ratio 73:27). − [b] 21% of compounds **15** and **17** was also obtained (ratio 23:77).



Scheme 4

terification processes. When silyl derivative **8a** was treated with iodine in basic medium, the reaction was very slow and also afforded the 5-*exo* cyclization compounds **10** and **12** (Entry 5). An inseparable mixture of their derivatives **15** and **17** (Scheme 4), the result of the silylation of the free secondary hydroxy group,[20] was also found. If **8a** was previously treated with KH, or if bis(*syn*-collidine)iodonium perchlorate was used, the starting material was unaltered. In the absence of a nucleophilic counter-ion, the *tert*-butyldiphenylsilyl group is not liberated, and consequently there is no reaction.

The yield of iodoetherification was increased by treating the diol **5a** with iodine in basic medium; a mixture of compounds **10** and **12** (86:14) was obtained in a 91% yield, through a 5-*exo* cyclization (Entry 6).

The observed stereoselectivity (Entries 1, 3−7) was consistent with that reported for alkenols with an allylic alkoxy group, which turned out to be *cis* to the iodoalkyl chain.[26] It has been reported that bulky protecting groups in the allylic alcohol can invert the stereoselectivity.[27] Thus, we examined the iodine-induced cyclization of **6a**, obtaining compounds **11** and **13** as an inseparable mixture. The ratio **11/13** showed that the *trans* isomer had increased slightly, but the stereoselectivity did not invert (Entry 8). However, the yield decreased considerably.

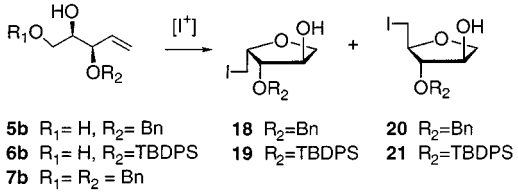
In the absence of base, treatment of **5a** with iodine resulted in a complex mixture of compounds from which compounds **10** and **12** were isolated in a 38% yield and with low stereoselectivity (Entry 7) (Scheme 4).

The diastereomer **7b** behaved similarly to **7a** when treated with iodine. Thus, treatment of **7b** with iodine in basic medium gave the 5-*exo* cyclization products **18** and **20** in an 81% yield and a ratio of **18/20** = 92:8 (Table 2, Entry 1) (Scheme 5). Treatment of the diol **5b** under the same conditions increased the yield to 95%, with no loss in stereoselectivity (Entry 2). In this case, the absence of base decreased both the yield and the selectivity (Entry 3) and necessitated longer reaction times. Treatment of **6b** under similar conditions provided compounds **19** and **21**, in an excellent yield, as an inseparable mixture. The presence of a bulky group at the allylic position also slightly increased the percentage of *trans* isomer (Entry 4), but did not invert the diastereomer ratio.

Table 2. Reaction of alkenols **5b**, **6b**, and **7b** with electrophilic iodine

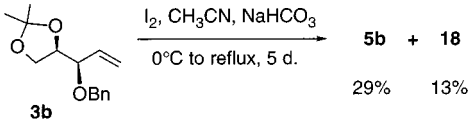
Entry[a]	Starting material	Time (min)	Ratio of products (%)	Yield (%)
1	**7b**	30	**18/20** (92:8)	81
2	**5b**	30	**18/20** (91:9)	95
3[b]	**5b**	120	**18/20** (85:15)	61
4	**6b**	20	**19/21** (84:16)	99

[a] Conditions: I_2, $NaHCO_3$, MeCN, O°C. − [b] Conditions: I_2, MeCN, 0°C.



Scheme 5

We tried to force the 4-*exo*, or possibly the 5-*endo*, processes by treating the isopropylidene derivative[28] **3b** with bis(*syn*-collidine)iodonium perchlorate, but no reaction was observed. Treating compound **3b** with iodine in basic medium, we recovered the 5-*exo* cyclization product **18** together with the diol **5b** in low yields after 5 d (Scheme 6a). In this case, the I_2 seems to behave like a Lewis acid; first it catalyses the deprotection of the acetal and then it induces the cyclization. In fact, iodine has been used as a catalyst in acetal formation.[29]



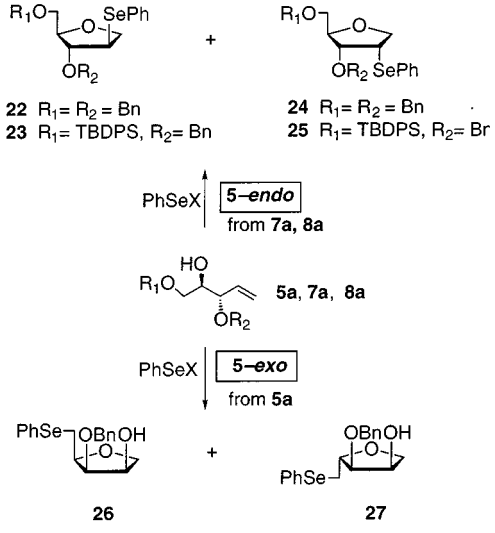
Scheme 6

Table 3. Reaction of alkenols **5a**, **7a**, and **8a** with electrophilic selenium reagents

Entry	Starting material	Selenium reagent	Conditions	Ratio of products (%)	Yield (%)
1	**5a**	NPSP	CSA, CH_2Cl_2, room temp., 1 h	**26/27** (30:70)	99
2	**5a**	PhSeOTf	NEt*i*Pr$_2$, CH_2Cl_2, 0 °C,1 h	**26/27** (10:90)	55
3	**7a**	NPSP	CSA, CH_2Cl_2, room temp., 1 h	**22/24** (50:50)	55
4	**8a**	NPSP	CSA, CH_2Cl_2, reflux, 12 h	**23/25** (56:44)	87
5	**8a**	PhSeOTf	NEt*i*Pr$_2$, CH_2Cl_2, 0 °C, 30 min	**23/25** (32:68)	42

The reaction of pentene-1,2,3-triols with iodine electrophiles described above always results in a 5-*exo* cyclization product, independently of the protecting groups on the different hydroxy moieties. The presence of a nucleophilic counter-ion assists the process and increases the yield and stereoselectivity.

It has been reported that PhSeCl gives the product of addition to terminal double bonds rather than cyclization products.[30] This problem can be solved by using a reagent with a non-nucleophilic counter-ion, such as *N*-phenylselenophthalimide (NPSP). However, this reagent is less electrophilic and usually requires the presence of acid to be active.[31] Thus, when the diol **5a** was treated with NPSP in the presence of camphorsulfonic acid (CSA), compounds **26** and **27** were obtained in a quantitative yield (ratio 30:70), through a 5-*exo* process (Table 3, Entry 1; (Scheme 7). In order to determine how selenium reagents behave in basic medium, **5a** was treated with PhSeOTf[32] in the presence of NEt$_2$*i*Pr to obtain the 5-*exo* products as well. The yield was low, however (Entry 2).



Scheme 7

In contrast, treatment of compound **7a** with NPSP/CSA afforded the 5-*endo* cyclization products **22** and **24**, in a 55% yield with zero stereoselectivity (Entry 3), through participation by the hydroxy group bonded to C-2. Small amounts of 5-*exo* and 6-*endo* cyclization products were also detected, perhaps because of the lability of the benzyl group attached to the oxygen atom at C-1.

Since we know that TBDPS is stable in the absence of a good nucleophile, we tried to make compound **8a** react with NPSP, reducing the amount of CSA to prevent deprotection. Under these conditions (Entry 4), compounds **23** and **25** were obtained in an 87% yield and a ratio of 56:44.

Trying to improve the stereoselectivity, we examined **8a** in basic medium, treating it with PhSeOTf[32] and NEt$_2$*i*Pr, but the yield was lower and the stereoselectivity towards the *cis* isomer increased only slightly (Entry 5).

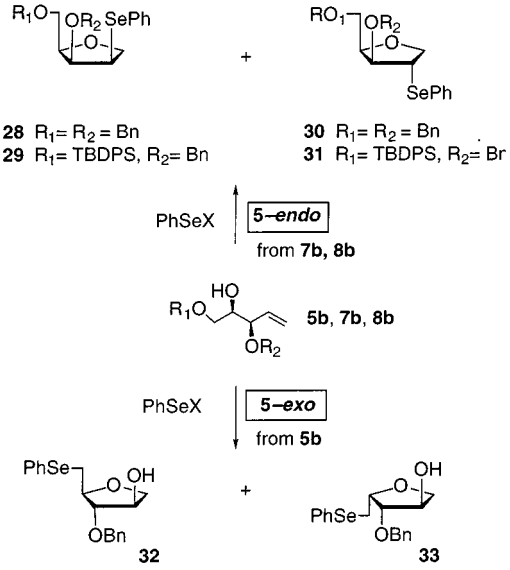
Although examples of 5-*endo* cyclization of polysubstituted alkenes[14] induced by selenium reagents have been reported, there are no examples of this cyclization in terminal olefins and no cases of competition with a 5-*exo* cyclization have been reported.

Treatment of the diastereomer **5b** under acidic (Table 4, Entry 1) or basic conditions (Entry 2) also resulted in the 5-*exo* cyclization products **32** and **33** (Scheme 8). However, if **7b** was treated with NPSP/CSA, the 5-*endo* cyclization products **28** and **30** were obtained in moderate yields and with low stereoselectivities (Entry 3). At low temperatures the yield is much smaller. When **8b** was treated with NPSP/CSA, compounds **29** and **31** were obtained in a 96% yield and with zero stereoselectivity (Entry 4). Under basic conditions (Entry 5) the yield decreased to 61%. The selectivity was inverted, although it still remained low. Compounds **28** and **30**, and **29** and **31** were obtained as inseparable mixtures, and their 5-*endo* origin was confirmed by conversion into the corresponding known glycals, through oxidation and elimination of the selenoxide (Scheme 9).[33]

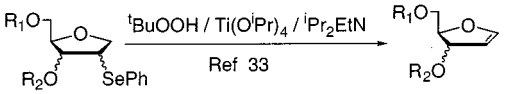
Finally, we attempted the cyclization reaction with the isopropylidene derivative **3b**. To prevent deprotection of the isopropylidene group, we initially attempted the reaction in

Table 4. Reaction of alkenols **5b**, **7b**, and **8b** with electrophilic selenium reagents

Entry	Starting material	Selenium reagent	Conditions	Ratio of products (%)	Yield (%)
1	**5b**	NPSP	CSA, CH_2Cl_2, room temp., 1 h	**32/33** (43:57)	87
2	**5b**	PhSeOTf	NEt*i*Pr$_2$, CH_2Cl_2, 0 °C, 1 h	**32/33** (34:66)	53
3	**7b**	NPSP	CSA, CH_2Cl_2, room temp., 20 min	**28/30** (36:64)	58
4	**8b**	NPSP	CSA, CH_2Cl_2, reflux, 12 h	**29/31** (50:50)	96
5	**8b**	PhSeOTf	NEt*i*Pr$_2$, CH_2Cl_2, 0 °C, 1 h	**29/31** (64:36)	61

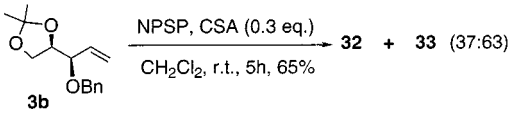


Scheme 8



Scheme 9

the absence of CSA, but it did not take place. When a catalytic amount of CSA was added, the reaction was complete in 5 h, giving a mixture of compounds **32** and **33** in a 65% yield and a ratio of 37:63, as a consequence of a 5-*exo* cyclization process (Scheme 10). Also, in this case, the isopropylidene group was hydrolyzed before cyclization.

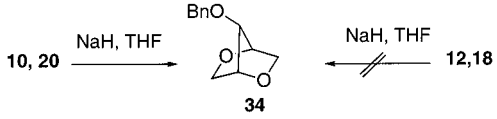


Scheme 10

Structural Elucidation

In the synthetic sequences discussed above, two new stereocenters were generated. The first one was created by addition of vinylmagnesium chloride to 2,3-*O*-isopropylideneglyceraldehyde. The configuration of this stereocenter was determined on the basis of two factors: a) comparison of the NMR-spectroscopic data for the addition products (**2a** and **2b**) with those described in the literature,[34] and b) the conversion of products of 5-*endo* selenoetherification into glycals of known configuration (Scheme 9).

The second stereocenter is generated as the consequence of the *exo* or *endo* cyclization. The mode of cyclization was deduced by DEPT experiments, focusing on the carbon atom bearing the iodine or selenium atom. The stereochemistry of the carbon atom bearing the electrophile in the 5-*endo* selenoetherification products **22** and **24**, and **28** and **30** was elucidated by NOE difference experiments. The stereochemistry of the other 5-*endo* selenoetherification products (**23** and **25**, and **29** and **31**) was assigned by comparing their ^{13}C NMR spectra to the previous ones. Finally, the stereochemistry of the stereocenter generated in the 5-*exo* cyclization was determined on the basis of two factors: a) the conversion of products **10** and **20**, by treatment with NaH in THF, into the same bicyclo compound **34** ($[\alpha]_D^{25}$ = +50.5) (Scheme 11), the enantiomer of which has been previously described[35] ($[\alpha]_D^{20}$ = −48.1), whereas compounds **12** and **18** afforded a complex mixture under the same conditions, and b) the fact that, in the ^{13}C NMR spectra, the signal of the carbon atom that bears the electrophile appears at higher fields, and the signals of the protons bonded to it at lower fields, when it is *cis* with respect to the vicinal group, as has previously been described.[12b,36]



Scheme 11

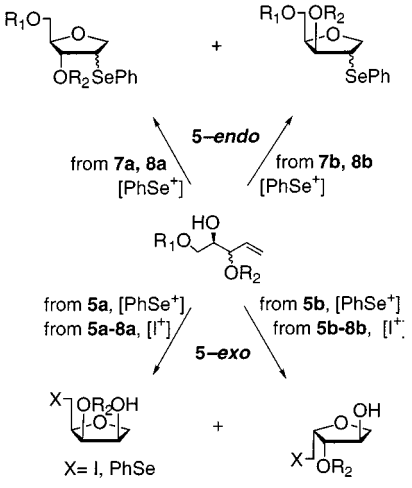
Conclusion

Pentenetriols **5**−**8** are easily obtained from glyceraldehyde and react with iodine and selenium electrophilic reagents to give a set of differently substituted tetrahydrofurans in high yields (Scheme 12). The most remarkable features of this procedure are:

− Iodine electrophilic reagents always provide the 5-*exo* cyclization products, independently of the protecting groups. The best yield is obtained in the absence of protecting group at the primary hydroxy group.

− Selenium reagents can direct the cyclization reaction towards either 5-*endo* or 5-*exo* cyclization, depending on whether the primary hydroxy group is protected or not.

− When the primary alcohol is protected, cyclization can be directed in either the 5-*exo* or the 5-*endo* direction, by using iodine or selenium reagents, respectively.



Scheme 12

Experimental Section

General Remarks: Melting points are uncorrected. Optical rotations were measured at 25°C in 10-cm cells. − ^1H NMR and ^{13}C NMR

spectra were recorded with a 300-MHz (300 and 75.4 MHz, respectively) apparatus, with $CDCl_3$ as solvent. Coupling constants are given in Hz. − Elemental analyses were determined at the Servei de Recursos Cientifics (Universitat Rovira i Virgili). − TLC was carried out on aluminium sheets precoated with silica gel 60 F_{254}. Flash column chromatography was performed using Kieselgel 60 (particle size: 40−63 microns). Radial chromatography was performed on 1-, 2-, or 4-mm plates of silica gel, depending on the amount of product. Band separation was monitored by UV. Medium pressure chromatography (MPLC) was performed using 60 A CC silica gel (6−35 microns). All chromatographic solvents were distilled at atmospheric pressure prior to use. − Dry solvents were obtained according to conventional methods.[37] Bis(*syn*-collidine)-iodonium perchlorate was prepared by Lemieux's method.[24]

General Procedure for Iodoetherification under Basic Conditions: Sodium hydrogen carbonate (9.00 mmol) was added to a solution of the alkenol (3.00 mmol) in anhydrous acetonitrile (10 mL). The mixture was cooled to 0 °C, stirred at this temperature for 5 min, and then iodine (9.00 mmol) was added. The reaction was monitored by TLC. After completion, the mixture was diluted with diethyl ether and washed with aqueous sodium thiosulfate. The aqueous phase was extracted with more diethyl ether, and the organic layers were combined and dried with magnesium sulfate. After filtration, the solvent was removed under reduced pressure. The residue thus obtained was purified by column chromatography.

General Procedure for Iodoetherification in the Absence of Base: The method followed was exactly the same as the one described above, but with the omission of sodium bicarbonate.

General Procedure for Selenoetherification under Basic Conditions: A solution of phenylselenenyl chloride (0.39 mmol) in dry dichloromethane (4 mL) was cooled in a water/ice bath. Then, silver trifluoromethanesulfonate (0.39 mmol) was added, and the mixture was stirred for 10 min. After this time, *N*-ethyldiisopropylamine (0.33 mmol) and the alkenol (0.30 mmol), dissolved in dry dichloromethane (4 mL), were added sequentially. The progress of the reaction was monitored by TLC, and when it had finished the mixture was filtered through silica gel, and the solvent was removed under vacuum. The crude product thus obtained was purified by column chromatography.

General Procedure for Selenoetherification under Acidic Conditions: In a round-bottomed flask, the alkenol (1.00 mmol) was dissolved in anhydrous dichloromethane (5 mL). Then, *N*-phenylselenophthalimide (NPSP) (1.20 mmol) and camphorsulfonic acid (CSA) (0.70 mmol) were added. The reaction was monitored by TLC, and when it was complete the reaction mixture was filtered through silica gel and concentrated under reduced pressure. The crude product was purified by column chromatography.

General Method for Silylation: Imidazole (3.00 mmol) was added to a stirred solution of the alcohol (1.43 mmol) in anhydrous DMF (10 mL per gram of alcohol), and then *tert*-butyldiphenylsilyl chloride (1.57 mmol) was added under argon at 0°C. The reaction was monitored by TLC and, when it had finished, the crude silyl ether was recovered by evaporation of the solvent under vacuum. Then it was diluted with dichloromethane, the organic phase was washed with water, and the aqueous phase was extracted with more dichloromethane. The combined of organic phases were dried with magnesium sulfate, the solvent was removed in vacuo, and the product purified by column chromatography.

(2*R*,3*S*)-3-*O*-Benzyl-1,2-*O*-isopropylidene-4-pentene-1,2,3-triol (3a) and (2*R*,3*R*)-3-*O*-Benzyl-1,2-*O*-isopropylidene-4-pentene-1,2,3-triol (3b): Anhydrous THF (8 mL) was added to a 60% dispersion of NaH in mineral oil (4.06 g, 101.51 mmol), previously washed with anhydrous hexane. The flask was cooled in water/ice, and compounds **2a/b** (10.04 g, 63.44 mmol), dissolved in 20 mL of dried THF, were added dropwise and the mixture was stirred for 30 min. Then, benzyl bromide (14 mL, 117.87 mmol) was added. The reaction mixture was stirred overnight and quenched by the careful addition of a few mL of methanol. The solvent was then evaporated under reduced pressure. The crude product was purified by flash chromatography (ethyl acetate/hexane, 1:10) to recover 13.37 g of diastereoisomers **3a** (higher R_f) and **3b** (86%) as a syrup. The mixture **3a/3b** was separated using MPLC, eluting with a linear gradient [from hexane to hexane/ethyl acetate (30:1), then to hexane/ethyl acetate (20:1), and then to hexane/ethyl acetate (10:1)].

Compound 3a: $[\alpha]_D^{25} = +30.4$ ($CHCl_3$, $c = 0.68$). − ^{1}H NMR: δ = 1.38 (s, 3 H), 1.43 (s, 3 H), 3.74 (t, 1 H, $J = 6.9$), 3.87 (dd, 1 H, $J = 8.0, 5.4$), 4.06 (dd, 1 H, $J = 8.0, 5.4$), 4.13 (q, 1 H, $J = 6.0$), 4.40 (d, 1 H, $J = 11.8$), 4.65 (d, 1 H, $J = 11.8$), 5.34 (ddd, 1 H, $J = 17.2, 1.7, 0.8$), 5.41 (dt, 1 H, $J = 10.4, 0.8$), 5.83 (ddd, 1 H, $J = 17.2, 10.4, 7.6$), 7.20−7.40 (m, 5 H). − ^{13}C NMR: δ = 25.2, 26.5, 66.8, 70.4, 77.4, 80.9, 109.5, 119.9, 127.6, 127.8, 128.3, 135.0, 138.0. − $C_{15}H_{20}O_3$ (248.32): calcd. C 72.55, H 8.12; found C 72.74, H 8.23.

Compound 3b: $[\alpha]_D^{25} = -18.7$ ($CHCl_3$, $c = 0.72$). − ^{1}H NMR: δ = 1.38 (s, 3 H), 1.42 (s, 3 H), 3.74 (dd, 1 H, $J = 8.5, 6.4$), 3.83 (t, 1 H, $J = 7.4$), 3.95 (dd, 1 H, $J = 8.5, 6.6$), 4.21 (q, 1 H, $J = 6.6$), 4.69 (d, 1 H, $J = 12.3$), 4.47 (d, 1 H, $J = 12.3$), 5.34 (dt, 1 H, $J = 16.9, 1.0$), 5.36 (dt, 1 H, $J = 10.7, 1.0$), 5.72 (ddd, 1 H, $J = 16.9, 10.7, 7.3$), 7.20−7.40 (m, 5 H). − ^{13}C NMR: δ = 25.3, 26.4, 65.7, 70.1, 77.3, 80.9, 109.6, 120.2, 127.5, 127.7, 128.2, 134.1, 138.2. − $C_{15}H_{20}O_3$ (248.32): calcd. C 72.55, H 8.12; found C 72.34, H 8.20.

(2*R*,3*S*)-3-*O*-*tert*-Butyldiphenylsilyl-1,2-*O*-isopropylidene-4-pentene-1,2,3-triol (4a) and (2*R*,3*R*)-3-*O*-*tert*-Butyldiphenylsilyl-1,2-*O*-isopropylidene-4-pentene-1,2,3-triol (4b): The mixture **2a/b** (2.03 g, 12.86 mmol) was treated using the general silylation procedure over 4 h at 55 °C. After the workup, the crude product was purified by flash chromatography (hexane/ethyl acetate, 10:1) to furnish 4.51 g of the diastereoisomeric mixture **4b** (higher R_f) and **4a** (88%) as a syrup. Both isomers were isolated by MPLC, using linear gradient [hexane to hexane/ethyl acetate (30:1), to hexane/ethyl acetate (20:1)].

Compound 4a: $[\alpha]_D^{25} = -8.2$ ($CHCl_3$, $c = 1.66$). − ^{1}H NMR: δ = 1.06 (s, 9 H), 1.32 (s, 6 H), 3.81 (dd, 1 H, $J = 7.9, 6.4$), 3.97 (dd, 1 H, $J = 7.9, 6.3$), 4.05 (q, 1 H, $J = 6.1$), 4.15 (tt, 1 H, $J = 6.4, 1.2$), 4.92 (dt, 1 H, $J = 17.2, 1.2$), 4.99 (dt, 1 H, $J = 10.4, 1.2$), 5.74 (ddd, 1 H, $J = 17.2, 10.4, 7.0$), 7.30−7.80 (m, 10 H). − ^{13}C NMR: δ = 19.3, 25.2, 26.3, 26.9, 66.3, 75.6, 78.8, 109.3, 117.5, 127.4, 127.6, 129.7, 129.8, 133.7, 133.9, 136.1, 136.2, 137.3. − $C_{24}H_{32}O_3Si$ (396.60): calcd. C 72.68, H 8.13; found C 72.59, H 8.25.

Compound 4b: $[\alpha]_D^{25} = +30.7$ ($CHCl_3$, $c = 1.74$). − ^{1}H NMR: δ = 1.08 (s, 9 H), 1.26 (s, 3 H), 1.32 (s, 3 H), 3.85 (dd, 1 H, $J = 8.5, 6.2$), 3.93 (dd, 1 H, $J = 8.5, 6.6$), 4.05 (q, 1 H, $J = 6.1$), 4.30 (tt, 1 H, $J = 6.1, 1.5$), 5.12 (dt, 1 H, $J = 10.5, 1.6$), 5.16 (dt, 1 H, $J = 17.2, 1.5$), 5.84 (ddd, 1 H, $J = 17.2, 10.5, 5.9$), 7.20−7.70 (m, 10 H). − ^{13}C NMR: δ = 19.3, 24.9, 26.1, 26.9, 65.0, 74.6, 77.8, 109.4, 117.3, 127.5, 127.6, 129.7, 129.8, 133.7, 133.9, 135.7, 136.0. − $C_{24}H_{32}O_3Si$ (396.60): calcd. C 72.68, H 8.13; found C 72.73, H 8.21.

(2*R*,3*S*)-3-*O*-Benzyl-4-pentene-1,2,3-triol (5a): A solution of **3a** (7.01 g, 27.10 mmol) in dry methanol (45 mL) was prepared. Then,

Dowex 50 W/H^+ acid resin (10.50 g) was added and the suspension was stirred at room temperature for 2 h. The resin was filtered off, and the filtrate was purified by column chromatography, to obtain 5.88 g of **5a** (100%) as a syrup. − $[\alpha]_D^{25}$ = +46.6 ($CHCl_3$, *c* = 0.81). − ^{1}H NMR: δ = 2.50−3.10 (br. s, 2 H), 3.60−3.80 (m, 3 H), 3.89 (dd, 1 H, *J* = 7.7, 4.0), 4.36 (d, 1 H, *J* = 11.7), 4.63 (d, 1 H, *J* = 11.7), 5.36 (dt, 1 H, *J* = 17.3, 0.9), 5.40 (dt, 1 H, *J* = 10.4, 0.8), 5.82 (ddd, 1 H, *J* = 17.3, 10.4, 7.7), 7.35 (m, 5 H). − ^{13}C NMR: δ = 63.1, 70.6, 73.1, 82.0, 120.2, 127.8 (2 C), 128.4, 134.8, 137.7. − $C_{12}H_{16}O_3$ (208.26): calcd. C 69.21, H 7.74; found C 69.40, H 7.84.

(2*R*,3*R*)-3-*O*-Benzyl-4-pentene-1,2,3-triol (5b): This compound was prepared according to the same procedure as for **5a**, starting from compound **3b** (4.01 g, 16.14 mmol), dry methanol (25 mL), and Dowex 50 W/H^+ acid resin (6.40 g). After purification, **5b** (3.36 g, 100%) was recovered. − $[\alpha]_D^{25}$ = −40.6 ($CHCl_3$, *c* = 0.47). − ^{1}H NMR: δ = 2.80 (br. s, 1 H), 3.00 (br. s, 1 H), 3.50−3.80 (m, 3 H), 3.84 (t, 1 H, *J* = 7.7), 4.34 (d, 1 H, *J* = 11.5), 4.65 (d, 1 H, *J* = 11.5), 5.37 (ddd, 1 H, *J* = 16.8, 1.6, 0.8), 5.39 (ddd, 1 H, *J* = 11.0, 1.6, 0.6), 5.77 (ddd, 1 H, *J* = 16.8, 11.0, 7.7), 7.20−7.40 (m, 5 H). − ^{13}C NMR: δ = 62.9, 70.4, 73.8, 81.3, 120.7, 127.9, 128.0, 128.5, 134.5, 137.5. − $C_{12}H_{16}O_3$ (208.26): calcd. C 69.21, H 7.74; found C 69.05, H 7.80.

(2*R*,3*S*)-3-*O*-*tert*-Butyldiphenylsilyl-4-pentene-1,2,3-triol (6a): A solution of dilute hydrochloric acid in ethanol (65 mL, 1 mL of concentrated HCl per 100 mL of ethanol) was added to compound **4a** (265 mg, 0.67 mmol). The reaction was complete after 3 h. The excess of acid was neutralized by adding 1 mL of aqueous NH_3, and the solvent was removed in vacuo. The product was purified by column chromatography (hexane/ethyl acetate, 2:1), and diol **6a** (216 mg, 91%) was obtained as a syrup. − $[\alpha]_D^{25}$ = −4.84 ($CHCl_3$, *c* = 2.65). − ^{1}H NMR: δ = 1.08 (s, 9 H), 2.35 (br. s, 1 H), 2.53 (br. s, 1 H), 3.60−3.70 (m, 3 H), 4.19 (ddt, 1 H, *J* = 7.1, 3.9, 1.2), 4.94 (dt, 1 H, *J* = 17.2, 1.2), 5.04 (dt, 1 H, *J* = 10.4, 1.3), 5.79 (ddd, 1 H, *J* = 17.2, 10.4, 7.1), 7.30−7.80 (m, 10 H). − ^{13}C NMR: δ = 19.2, 26.9, 63.0, 74.5, 76.7, 118.0, 127.6, 127.8, 129.9, 130.1, 133.3, 133.2, 135.9, 136.1, 136.5. − $C_{21}H_{28}O_3Si$ (356.54): calcd. C 70.74, H 7.92; found C 70.84, H 8.06.

(2*R*,3*R*)-3-*O*-*tert*-Butyldiphenylsilyl-4-pentene-1,2,3-triol (6b): The procedure used was identical to the one above, starting from compound **4b** (249 mg, 0.63 mmol) and a dilute solution of HCl in ethanol (65 mL). After the workup and flash chromatography (hexane/ethyl acetate, 2:1), diol **6b** (202 mg, 90%) was recovered. − $[\alpha]_D^{25}$ = +15.7 ($CHCl_3$, *c* = 2.64). − ^{1}H NMR: δ = 1.08 (s, 9 H), 2.04 (br. s, 1 H), 2.61 (br. s, 1 H), 3.50 (dd, 1 H, *J* = 12.0, 6.9), 3.60−3.70 (m, 2 H), 4.19 (ddt, 1 H, *J* = 7.3, 5.8, 1.3), 4.96 (dt, 1 H, *J* = 17.3, 1.3), 5.02 (dt, 1 H, *J* = 10.4, 1.3), 5.80 (ddd, 1 H, *J* = 17.3, 10.4, 7.3), 7.30−7.80 (m, 10 H). − ^{13}C NMR: δ = 19.2, 26.9, 62.7, 74.7, 75.8, 117.8, 127.5, 127.7, 129.8, 129.9, 133.3, 135.8, 136.0, 136.6. − $C_{21}H_{28}O_3Si$ (356.54): calcd. C 70.74, H 7.92; found C 70.86, H 8.09.

(2*R*,3*S*)-1,3-Di-*O*-benzyl-4-pentene-1,2,3-triol (7a) and (2*R*,3*S*)-2,3-Di-*O*-benzyl-4-pentene-1,2,3-triol (9a): To a solution of diol **5a** (612 mg, 2.94 mmol) in toluene (75 mL) were added 4-Å molecular sieves (6.00 g) and dibutyltin oxide (951 mg, 3.82 mmol). The mixture was heated at 110 °C for 2 d, removing water with a Dean-Stark apparatus. Then, BnBr (600 μL, 5.05 mmol) and tetrabutylammonium bromide (1.06 g, 2.94 mmol) were added, and the mixture was stirred at 70°C for two more days. The solvent was removed under vacuum, the molecular sieves were filtered off and the residue was purified by MPLC using a linear gradient [hexane to hexane/ethyl acetate (2:1)], to afford compounds **7a** and **9a** (731 mg). This mixture was separated by radial chromatography (hexane with 1% of methanol). Finally, compounds **7a** (625 mg, 71%) and **9a** (106 mg, 12%) were isolated as syrups.

Compound 7a: $[\alpha]_D^{25}$ = +26.5 ($CHCl_3$, *c* = 1.60). − ^{1}H NMR: δ = 2.41 (d, 1 H, *J* = 4.5), 3.56 (dd, 1 H, *J* = 9.8, 6.0), 3.62 (dd, 1 H, *J* = 9.8, 4.0), 3.86 (tt, 1 H, *J* = 6.7, 0.8), 3.91 (br. s, 1 H), 4.37 (d, 1 H, *J* = 11.7), 4.54 (s, 2 H), 4.62 (d, 1 H, *J* = 11.7), 5.34 (ddd, 1 H, *J* = 17.3, 1.8, 0.9), 5.40 (ddd, 1 H, *J* = 10.4, 1.8, 0.7), 5.86 (ddd, 1 H, *J* = 17.3, 10.4, 7.6), 7.20−7.40 (m, 10 H). − ^{13}C NMR: δ = 70.2, 70.6, 72.2, 73.3, 80.7, 120.1, 127.6, 127.7, 127.8, 127.8, 128.4, 128.4, 135.0, 138.0, 138.1. − $C_{19}H_{22}O_3$ (298.38): calcd. C 76.41, H 7.43; found C 76.37, H 7.51.

Compound 9a: $[\alpha]_D^{25}$ = +45.6 ($CHCl_3$, *c* = 1.72). − ^{1}H NMR: δ = 2.20−2.40 (br. s, 1 H), 3.55 (dd, 1 H, *J* = 5.6, 10.0), 3.70−3.80 (br. s, 2 H), 3.98 (dd, 1 H, *J* = 7.5, 5.6), 4.40 (d, 1 H, *J* = 11.8), 4.59 (d, 1 H, *J* = 11.6), 4.66 (d, 1 H, *J* = 11.8), 4.69 (d, 1 H, *J* = 11.6), 5.37 (ddd, 1 H, *J* = 17.0, 1.8, 0.8), 5.39 (ddd, 1 H, *J* = 10.7, 1.8, 0.8), 5.87 (ddd, 1 H, *J* = 17.0, 10.7, 7.5), 7.20−7.40 (m, 10 H). − ^{13}C NMR: δ = 61.8, 70.5, 72.6, 80.7, 81.0, 119.5, 127.7, 127.8, 128.0 (2 C), 128.5 (2 C), 135.6, 138.1, 138.1. − $C_{19}H_{22}O_3$ (298.38): calcd. C 76.41, H 7.43; found C 76.32, H 7.55.

(2*R*,3*R*)-1,3-Di-*O*-benzyl-4-pentene-1,2,3-triol (7b): The procedure followed was the same as that for the synthesis of **7a**, using diol **5b** (383 mg, 1.84 mmol), toluene (45 mL), 4-Å molecular sieves (4.00 g), dibutyltin oxide (595 mg, 2.39 mmol), benzyl bromide (370 μL, 3.12 mmol), and tetrabutylammonium bromide (664 mg, 1.84 mmol). Purification was carried out in an MPLC apparatus, using a linear gradient [hexane to hexane/ethyl acetate (3:1)], to obtain 368 mg of **7b** (67%) as a syrup. − $[\alpha]_D^{25}$ = −28.6 ($CHCl_3$, *c* = 1.74). − ^{1}H NMR: δ = 2.64−2.92 (br. s, 1 H), 3.48 (dd, 1 H, *J* = 10.0, 5.7), 3.58 (dd, 1 H, *J* = 10.0, 3.9), 3.78 (td, 1 H, *J* = 6.1, 3.8), 3.92 (t, 1 H, *J* = 7.2), 4.36 (d, 1 H, *J* = 11.4), 4.49 (d, 1 H, *J* = 12.0), 4.55 (d, 1 H, *J* = 12.0), 4.63 (d, 1 H, *J* = 11.4), 5.34 (ddd, 1 H, *J* = 9.8, 1.5, 0.8), 5.34 (ddd, 1 H, *J* = 17.9, 1.5, 0.8), 5.78 (ddd, 1 H, *J* = 17.9, 9.8, 7.9), 7.30 (m, 10 H). − ^{13}C NMR: δ = 70.3, 70.4, 72.8, 73.4, 80.7, 119.9, 127.7, 127.7, 127.8, 127.8, 127.9, 128.4, 128.4, 134.9, 138.0. − $C_{19}H_{22}O_3$ (298.38): calcd. C 76.41, H 7.43; found C 76.19, H 7.52.

(2*R*,3*S*)-3-*O*-Benzyl-1-*O*-*tert*-butyldiphenylsilyl-4-pentene-1,2,3-triol (8a): The diol **5a** (264 mg, 1.27 mmol) was treated under the general conditions for silylation. TLC monitoring showed that the starting material was consumed in 50 min. The crude silyl ether was recovered as usual and purified by column chromatography (hexane/ethyl acetate, 10:1), to afford 537 mg of **8a** (95%) as a syrup. − $[\alpha]_D^{25}$ = +4.9 ($CHCl_3$, *c* = 1.75). − ^{1}H NMR: δ = 1.01 (s, 9 H), 2.42 (d, 1 H, *J* = 4.3 Hz), 3.06−3.80 (m, 3 H), 3.90 (dd, 1 H, *J* = 7.7, 5.4), 4.33 (d, 1 H, *J* = 11.8), 4.60 (d, 1 H, *J* = 11.8), 5.32 (ddd, 1 H, *J* = 17.2, 1.8, 0.9), 5.37 (ddd, 1 H, *J* = 10.4, 1.8, 0.6), 5.85 (ddd, 1 H, *J* = 17.2, 10.4, 7.7), 7.10−7.70 (m, 15 H). − ^{13}C NMR: δ = 19.1, 26.7, 64.3, 70.3, 73.4, 80.7, 119.8, 127.6, 127.8 (2 C), 128.4, 129.8 (2 C), 133.2, 135.2, 135.6 (2 C), 136.0, 138.2. − $C_{28}H_{34}O_3Si$ (446.66): calcd. C 75.29, H 7.67; found C 75.42, H 7.53.

(2*R*,3*R*)-3-*O*-Benzyl-1-*O*-*tert*-butyldiphenylsilyl-4-pentene-1,2,3-triol (8b): Diol **5b** (255 mg, 1.22 mmol) was treated under the general conditions for silylation. After flash chromatography, 452 mg of the silyl ether **8b** (83%) was obtained as a syrup. − $[\alpha]_D^{25}$ = −19.6 ($CHCl_3$, *c* = 1.70). − ^{1}H NMR: δ = 1.04 (s, 9 H), 2.64 (d, 1 H, *J* = 4.5), 3.60−3.80 (m, 2 H), 3.77 (dd, 1 H, *J* = 11.4, 6.3), 4.01 (ddt, 1 H, *J* = 7.9, 5.1, 0.8), 4.37 (d, 1 H, *J* = 11.6), 4.65 (d, 1 H, *J* = 11.6), 5.32 (ddd, 1 H, *J* = 10.4, 1.8, 0.8), 5.33 (ddd, 1 H, *J* =

17.3, 1.8, 0.8), 5.81 (ddd, 1 H, J = 17.3, 10.4, 7.9), 7.20−7.70 (m, 15 H). − ^{13}C NMR: δ = 19.1, 26.7, 64.1, 70.4, 74.1, 80.3, 119.5, 127.8, 127.9 (2 C), 128.4, 129.8 (2 C), 133.3, 133.4, 135.2, 135.6, 135.7, 138.2. − $C_{28}H_{34}O_3Si$ (446.66): calcd. C 75.29, H 7.67; found C 75.24, H 7.87.

Reaction of 5a with Iodine under Basic Conditions. − Synthesis of (2*S*,3*R*,4*R*)-3-Benzyloxy-2-iodomethyltetrahydrofuran-4-ol (10) and (2*R*,3*R*,4*R*)-3-Benzyloxy-2-iodomethyltetrahydrofuran-4-ol (12): Diol **5a** (5.01 g, 24.04 mmol) was treated under the general basic conditions for iodoetherification. The reaction was completed in 45 min. After the workup, the residue was purified by column chromatography (hexane/ethyl acetate, 2:1) to afford 7.34 g of diastereoisomers **10** and **12** (ratio 86:14, 91% yield) as a syrup. The two isomers were separated by MPLC (hexane/chloroform, 1:1).

Compound 10: Higher R_f value. − m.p. = 70−71°C. − $[\alpha]_D^{25}$ = −35.8 ($CHCl_3$, c = 0.56). − ^{1}H NMR: δ = 2.56 (d, 1 H, J = 6.9), 3.32 (dd, 1 H, J = 9.9, 7.2), 3.38 (dd, 1 H, J = 6.5, 9.9), 3.83 (dd, 1 H, J = 4.3), 3.89 (dd, 1 H, J = 9.8, 5.3), 4.11 (t, 1 H, J = 5.4), 4.19 (q, 1 H, J = 6.0), 4.36 (ddt, 1 H, J = 6.9, 4.1, 5.3), 4.70 (d, 1 H, J = 11.2), 4.77 (d, 1 H, J = 11.2), 7.20−7.40 (m, 5 H). − ^{13}C NMR: δ = 3.0, 71.1, 72.9, 74.8, 79.2, 80.9, 128.0, 128.4, 128.7, 136.9. − $C_{12}H_{15}O_3I$ (334.15): calcd. C 43.13, H 4.52; found C 43.01, H 4.62.

Compound 12: $[\alpha]_D^{25}$ = −39.9 ($CHCl_3$, c = 1.80). − ^{1}H NMR: δ = 2.62 (d, 1 H, J = 4.5), 3.22 (dd, 1 H, J = 10.7, 3.9), 3.35 (dd, 1 H, J = 10.7, 4.6), 3.7−3.8 (m, 2 H), 3.84 (dd, 1 H, J = 9.8, 3.3), 4.09 (dd, 1 H, J = 9.8, 4.5), 4.24 (quint, 1 H, J = 4.1), 4.66 (s, 2 H), 7.3−7.5 (m, 5 H). − ^{13}C NMR: δ = 8.0, 69.9, 72.9, 73.5, 79.0, 83.1, 128.1, 128.5, 128.7, 137.0. − $C_{12}H_{15}O_3I$ (334.15): calcd. C 43.13, H 4.52; found C 43.22, H 4.63.

Reaction of 6a with Iodine under Basic Conditions. − Synthesis of (2*S*,3*R*,4*R*)-3-*tert*-butyldiphenylsilyloxy-2-iodomethyltetrahydrofuran-4-ol (11) and (2*R*,3*R*,4*R*)-3-*tert*-butyldiphenylsilyloxy-2-iodomethyltetrahydrofuran-4-ol (13): Diol **6a** (173 mg, 0.48 mmol) was treated with iodine under the general basic conditions. The reaction mixture was stirred for 2 h. After workup, the residue was purified by flash chromatography (hexane/ethyl acetate, 5:1) to afford 108 mg (46%) of diastereoisomers **11** and **13** in a ratio of 60:40 as an inseparable mixture.

Compound 11: ^{1}H NMR: δ = 1.14 (s, 9 H), 2.63 (br. s, 1 H), 3.30 (dd, 1 H, J = 10.8, 3.3), 3.41 (t, 1 H, J = 10.8), 3.80−4.00 (m, 3 H), 4.00 (br. s, 1 H), 4.28 (dd, 1 H, J = 6.9, 5.1), 7.30−7.80 (m, 10 H). ^{13}C NMR (aliphatic C): δ = 6.2, 19.1, 26.9, 71.0, 71.7, 74.5, 80.1.

Compound 13: ^{1}H NMR: δ = 1.12 (s, 9 H), 2.54 (dd, 1 H, J = 11.0, 5.4), 2.64 (br. s, 1 H), 2.98 (dd, 1 H, J = 11.0, 3.3), 3.64 (dt, 1 H, J = 5.4, 3.0), 3.80−4.01 (m, 4 H), 4.06 (br. s, 1 H), 7.30−7.80 (m, 10 H). − ^{13}C NMR (aliphatic C): δ = 7.9, 19.1, 26.9, 71.5, 72.8, 77.2, 81.0.

Reaction of 5b with Iodine under Basic Conditions. − Synthesis of (2*R*,3*S*,4*R*)-3-Benzyloxy-2-iodomethyltetrahydrofuran-4-ol (18) and (2*S*,3*S*,4*R*)-3-Benzyloxy-2-iodomethyltetrahydrofuran-4-ol (20): Compound **5b** (2.37 g, 11.37 mmol) was treated with iodine under basic conditions. The reaction was stirred for 30 min. After flash chromatography (hexane/ethyl acetate, 2:1), 3.61 g of diastereoisomers **18** and **20** (ratio 91:9) were recovered (95%) as a syrup. The two isomers were separated by MPLC, eluting with linear gradient [hexane to hexane/ethyl acetate (10:1) to hexane/ethyl acetate (5:1) to hexane/ethyl acetate (3:1)].

Compound 18: $[\alpha]_D^{25}$ = +81.5 ($CHCl_3$, c = 1.35). − ^{1}H NMR: δ = 2.10 (br. s, 1 H), 3.28 (dd, 1 H, J = 9.3, 5.9), 3.35 (t, 1 H, J = 9.0), 3.82 (d, 1 H, J = 9.8), 4.00 (d, 1 H, J = 3.5), 4.19 (dd, 1 H, J = 9.8, 3.8), 4.39 (br. s, 1 H), 4.42 (ddd, 1 H, J = 9.0, 5.9, 3.5), 4.62 (d, 1 H, J = 11.4), 4.67 (d, 1 H, J = 11.4), 7.20−7.40 (m, 5 H). − ^{13}C NMR: δ = 1.0, 72.9, 74.6, 74.6, 81.1, 83.7, 127.9, 128.1, 128.5, 137.5. − $C_{12}H_{15}O_3I$ (334.15): calcd. C 43.13, H 4.52; found C 43.25, H 4.58.

Compound 20: Higher R_f value. − $[\alpha]_D^{25}$ = +7.8 ($CHCl_3$, c = 1.46). − ^{1}H NMR: δ = 2.10 (br. s, 1 H), 3.30 (dd, 1 H, J = 10.1, 5.4), 3.39 (dd, 1 H, J = 10.1, 7.0), 3.84 (dt, 1 H, J = 1.2, 3.0), 3.90−4.00 (m, 2 H), 4.02 (dd, 1 H, J = 10.0, 3.4), 4.33 (br. s, 1 H), 4.64 (s, 2 H), 7.20−7.40 (m, 5 H). − ^{13}C NMR: δ = 7.1, 71.9, 74.7, 76.1, 83.6, 88.6, 127.9, 128.1, 128.6, 137.6. − $C_{12}H_{15}O_3I$ (334.15): calcd. C 43.13, H 4.52; found C 43.26, H 4.62.

Reaction of 6b with Iodine under Basic Conditions. − Synthesis of (2*R*,3*S*,4*R*)-3-*tert*-Butyldiphenylsilyloxy-2-iodomethyltetrahydrofuran-4-ol (19) and (2*S*,3*S*,4*R*)-3-*tert*-Butyldiphenylsilyloxy-2-iodomethyltetrahydrofuran-4-ol (21): Diol **6b** (220 mg, 0.62 mmol) was treated according to the general procedure for basic iodoetherification. The reaction mixture was stirred for 20 min. After the workup, the residue was purified by flash chromatography (hexane/ethyl acetate, 5:1), to afford 295 mg (99%) of diastereoisomers **19** and **21** in a ratio of 84:16 as an inseparable mixture. Spectroscopic data obtained from the spectra of the mixture.

Compound 19: ^{1}H NMR: δ = 1.09 (s, 9 H), 1.60 (br. s, 1 H), 2.35−3.30 (m, 2 H), 3.61 (dd, 1 H, J = 9.9, 1.6), 4.01 (dt, 1 H, J = 4.5, 1.6), 4.19 (dd, 1 H, J = 9.9, 4.5), 4.15−4.25 (m, 2 H), 7.30−7.80 (m, 10 H). − ^{13}C NMR: δ = 1.9, 19.3, 26.8, 73.4, 77.4, 79.0, 82.0, 127.9, 128.0, 130.1, 130.3, 132.4, 133.7, 135.7, 135.9.

Compound 21: ^{1}H NMR: δ = 1.08 (s, 9 H), 1.74 (br. s, 1 H), 2.86 (dd, 1 H, J = 10.5, 6.8), 2.97 (dd, 1 H, J = 10.5, 5.4), 3.88 (br. s, 1 H), 3.97 (dt, 1 H, J = 2.7, 1.2), 4.06 (dd, 1 H, J = 9.9, 3.9), 4.15−4.25 (m, 2 H), 7.30−7.80 (m, 10 H). − ^{13}C NMR: δ = 6.5, 18.9, 26.7, 74.0, 78.5, 82.4, 86.3, 128.0, 135.2, 135.7, 135.9.

Selenoetherification of 7a under Acidic Conditions. − Synthesis of (2*R*,3*R*,4*R*)-3-Benzyloxy-2-benzyloxymethyl-4-(phenylselenenyl)-tetrahydrofuran (22) and (2*R*,3*R*,4*S*)-3-benzyloxy-2-benzyloxymethyl-4-(phenylselenenyl)tetrahydrofuran (24): Alkenol **7a** (216 mg, 0.72 mmol) was treated under the conditions described for selenoetherification under acidic conditions. The reaction mixture was stirred at room temperature for 1 h. After workup, the crude product was purified by MPLC, eluting with linear gradient [hexane to hexane/ethyl acetate (1:3) to hexane/ethyl acetate (1:1)] to afford 181 mg of 5-*endo* products **22** and **24** (ratio 1:1, 55% yield). Products **22** and **24** were separated by MPLC, eluting with linear gradient [hexane to hexane/ethyl acetate (30:1) to hexane/ethyl acetate (20:1) to hexane/ethyl acetate (10:1)].

Compound 22: Higher R_f value. − $[\alpha]_D^{25}$ = +2.0 ($CHCl_3$, c = 0.90). − ^{1}H NMR: δ = 3.58 (dd, 1 H, J = 10.3, 5.2), 3.62 (dd, 1 H, J = 10.3, 5.7), 3.76 (ddd, 1 H, J = 6.0, 3.8, 2.3), 3.98 (dd, 1 H, J = 10.1, 3.8), 3.99 (dd, 1 H, J = 3.8, 2.3), 4.06 (td, 1 H, J = 5.6, 3.8), 4.25 (dd, 1 H, J = 10.1, 6.0), 4.34 (d, 1 H, J = 11.8), 4.45 (d, 1 H, J = 11.8), 4.56 (s, 2 H), 7.10−7.60 (m, 15 H). − ^{13}C NMR: δ = 45.6, 70.4, 71.7, 72.8, 73.3, 83.9, 85.8, 127.7, 127.8 (2 C), 127.9, 128.3, 128.4 (2 C), 129.0, 129.3, 134.5, 137.6, 138.1. − $C_{25}H_{26}O_3Se$ (453.44): calcd. C 66.22, H 5.78; found C 66.43, H 5.85.

Compound 24: $[\alpha]_D^{25}$ = +2.1 ($CHCl_3$, c = 0.50). − ^{1}H NMR: δ = 3.46 (dd, 1 H, J = 10.5, 4.8), 3.49 (dd, 1 H, J = 10.5, 4.2), 3.76

(ddd, 1 H, J = 9.2, 7.0, 6.0), 4.03 (t, 1 H, J = 9.0), 4.13 (dd, 1 H, J = 6.0, 3.1), 4.19 (td, 1 H, J = 4.6, 3.1), 4.25 (dd, 1 H, J = 9.2, 7.0), 4.49 (d, 1 H, J = 12.0), 4.54 (d, 1 H, J = 12.0), 4.58 (d, 1 H, J = 11.7), 4.64 (d, 1 H, J = 11.7), 7.10−7.60 (m, 15 H). − ^{13}C NMR: δ = 45.1, 70.3, 72.0, 73.4, 73.9, 81.0, 82.8, 127.3, 127.7, 127.8, 127.9, 128.0, 128.4 (2 C), 129.2, 129.5, 133.6, 137.6, 138.0. − $C_{25}H_{26}O_3Se$ (453.44): calcd. C 66.22, H 5.78; found C 66.41, H 5.93.

Selenoetherification of 8a under Acidic Conditions. − Synthesis of (2*R*,3*R*,4*R*)-3-Benzyloxy-2-(*tert*-butyldiphenylsilyloxy)-4-(phenylselenenyl)tetrahydrofuran (23) and (2*R*,3*R*,4*S*)-3-Benzyloxy-2-(*tert*-butyldiphenylsilyloxy)-4-(phenylselenenyl)tetrahydrofuran (25): Compound **8a** (330 mg, 0.74 mmol) was treated according to the general procedure for selenoetherification under acidic conditions, reducing the amount of CSA (35 mg, 0.15 mmol). The reaction mixture was refluxed for 12 h. The residue was purified by MPLC, eluting with linear gradient [hexane to hexane/ethyl acetate (5:10) to hexane/ethyl acetate (3:1)], to obtain 388 mg of a mixture of **23** and **25** (87%, ratio 56:44) as an inseparable mixture. The spectral data given are for this mixture. − ^{1}H NMR: δ = 1.02 (s, 9 H), 1.09 (s, 9 H), 3.61 (dd, 1 H, J = 10.7, 5.4), 3.67 (dd, 1 H, J = 10.7, 3.8), 3.70−3.80 (m, 4 H), 3.90−4.30 (m, 8 H), 4.37 (d, 1 H, J = 11.8), 4.44 (d, 1 H, J = 11.8), 4.62 (s, 2 H), 7.00−7.80 (m, 40 H). − ^{13}C NMR: δ = 19.0, 26.7, 26.8, 29.6, 45.4, 45.6, 64.3, 64.5, 71.8, 71.9, 72.9, 73.9, 81.4, 84.0, 85.3, 85.7, 127.3, 127.7 (2 C), 127.8, 127.9 (2 C), 128.4, 128.5, 129.2, 129.3, 129.8, 129.9, 133.2, 133.3, 133.7, 134.4, 134.7, 135.6, 135.7, 135.8 (2 C), 137.8, 137.9.

Selenoetherification of 5a under Acidic Conditions. − Synthesis of (2*S*,3*R*,4*R*)-3-Benzyloxy-2-(phenylselenenylmethyl)tetrahydrofuran-4-ol (26) and (2*R*,3*R*,4*R*)-3-Benzyloxy-2-(phenylselenenylmethyl)-tetrahydrofuran-4-ol (27): Compound **5a** (75 mg, 0.36 mmol) was treated under acidic conditions for selenoetherification. The reaction mixture was stirred for 30 min. After the usual workup, the crude product was purified by MPLC, eluting with a linear gradient [hexane to hexane/ethyl acetate (1:4)], to afford 130 mg (99%) of an inseparable mixture of **26** and **27** (ratio 70:30). Spectroscopic data obtained from the spectra of the mixture.

Compound 26: ^{1}H NMR: δ = 2.92 (br. s, 1 H), 3.18 (m, 2 H), 3.70−3.80 (m, 1 H), 3.80−3.90 (m, 1 H), 4.10−4.20 (m, 2 H), 4.31 (br. s, 1 H), 4.64 (d, 1 H, J = 11.2), 4.69 (d, 1 H, J = 11.2), 7.30−7.80 (m, 10 H). − ^{13}C NMR: δ = 27.4, 70.8, 72.9, 74.1, 79.3, 79.4, 123.5, 128.2, 128.6, 129.0, 132.4, 134.2.

Compound 27: ^{1}H NMR: δ 2.70 (br. s, 1 H), 3.04 (dd, 1 H, J = 13, 5.2), 3.14 (dd, 1 H, J = 13.0, 5.2), 3.78 (dd, 1 H, J = 9.8, 3.9), 3.86 (t, 1 H, J = 5.8), 4.06 (dd, 1 H, J = 9.8, 5.1), 4.13 (q, 1 H, J = 5.7), 4.31 (br. s, 1 H), 4.53 (s, 2 H), 4.65 (d, 1 H, J = 11.7), 7.20−7.90 (m, 10 H). − ^{13}C NMR: δ = 30.7, 69.8, 72.6, 73.3, 79.5, 82.2, 127.0, 128.0, 128.3, 128.6, 129.1, 132.4, 137.0.

Selenoetherification of 7b under Acidic Conditions. − Synthesis of (2*R*,3*S*,4*R*)-3-Benzyloxy-2-benzyloxymethyl-4-(phenylselenenyl)tetrahydrofuran (28) and (2*R*,3*S*,4*S*)-3-Benzyloxy-2-benzyloxymethyl-4-(phenylselenenyl)tetrahydrofuran (30): Compound **7b** (193 mg, 0.65 mmol) was treated with NPSP under acidic conditions, and dichloromethane was replaced by dichloroethane. The reaction mixture was heated to reflux. After 20 min, the mixture was filtered and the solvent was removed. The crude product was purified by MPLC, eluting with linear gradient [from hexane to hexane/ethyl acetate (1:4) to hexane/ethyl acetate (1:2)] to afford, in order of elution, 108 mg (37%) of **28** and 62 mg (21%) of compound **30** as syrups.

Compound 28: $[\alpha]_D^{25}$ = −13.4 ($CHCl_3$, c = 1.16). − ^{1}H NMR: δ = 3.69 (dd, 1 H, J = 9.8, 6.8), 3.72 (dd, 1 H, J = 9.8, 5.8), 3.79 (ddd, 1 H, J = 9.2, 7.8, 5.0), 4.05 (t, 1 H, J = 8.8), 4.16 (q, 1 H, J = 5.6), 4.18 (dd, 1 H, J = 8.8, 7.8), 4.26 (t, 1 H, J = 4.5), 4.50 (d, 1 H, J = 11.7), 4.58 (d, 1 H, J = 11.7), 4.61 (d, 1 H, J = 11.4), 4.80 (d, 1 H, J = 11.4), 7.20−7.60 (m, 15 H). − ^{13}C NMR: δ = 46.5, 68.7, 72.9, 73.5, 74.5, 80.2, 80.7, 127.3, 127.7, 127.9, 127.9, 128.1, 128.4 (2 C), 129.2, 129.8, 133.5, 137.7, 138.0. − $C_{25}H_{26}O_3Se$ (453.44): calcd. C 66.22, H 5.78; found C 66.32, H 5.69.

Compound 30: Higher R_f values. − $[\alpha]_D^{25}$ = −42.3 ($CHCl_3$, c = 1.70). − ^{1}H NMR: δ = 3.69 (dd, 1 H, J = 10.2, 5.2), 3.73 (dd, 1 H, J = 10.2, 6.4), 3.78 (ddd, 1 H, J = 8.0, 4.6, 1.5), 3.79 (dd, 1 H, J = 11.0, 4.6), 4.00 (dd, 1 H, J = 4.1, 1.5), 4.15 (d, 1 H, J = 12.3), 4.30 (td, 1 H, J = 5.8, 4.1), 4.40 (d, 1 H, J = 12.3), 4.44 (dd, 1 H, J = 11.0, 8.0), 4.50 (d, 1 H, J = 11.8), 4.62 (d, 1 H, J = 11.8), 7.00−7.70 (m, 15 H). − ^{13}C NMR: δ = 45.0, 68.8, 71.2, 72.0, 73.4, 79.7, 84.4, 127.6 (2 C), 127.8, 127.9, 128.2, 128.4 (2 C), 128.7, 129.4, 134.9, 137.7, 138.2. − $C_{25}H_{26}O_3Se$ (453.44): calcd. C 66.22, H 5.78; found C 66.43, H 6.05.

Selenoetherification of 8b under Acidic Conditions. − Synthesis of (2*R*,3*S*,4*R*)-3-Benzyloxy-2-(*tert*-butyldiphenylsilyloxymethyl)-4-(phenylselenenyl)tetrahydrofuran (29) and (2*R*,3*S*,4*S*)-3-Benzyloxy-2-(*tert*-butyldiphenylsilyloxymethyl)-4-(phenylselenenyl)tetrahydrofuran (31): Compound **8b** (197 mg, 0.44 mmol) was treated according to the general procedure for selenoetherification under acidic conditions, reducing the amount of CSA to 20 mg (0.09 mmol). The mixture was refluxed for 12 h. After workup, the mixture was purified by flash chromatography (hexane/ethyl acetate, 10:1) to afford 254 mg of compounds **29** and **31** (global yield: 96%, ratio 1:1) as an inseparable mixture. The spectral data given are for this mixture. − ^{1}H NMR: δ = 1.04 (s, 9 H), 1.07 (s, 9 H), 3.70−4.50 (m, 16 H), 4.78 (d, 1 H, J = 11.1), 4.85 (d, 1 H, J = 11.1), 7.00−7.80 (m, 40 H). − ^{13}C NMR: δ = 19.0 (2 C), 26.7, 26.8, 44.9, 46.5, 62.0, 62.1, 71.7, 72.0, 72.0, 73.1, 80.4, 81.0, 82.6, 84.2, 127.3, 127.6, 127.7 (2 C), 127.8, 128.0, 128.1, 128.4 (2 C), 128.5, 129.2, 129.4, 129.6, 129.7, 129.8, 130.0, 133.2, 133.5, 134.9, 135.7 (2 C), 137.0, 138.0.

Selenoetherification of 5b under Acidic Conditions. − Synthesis of (2*R*,3*S*,4*R*)-3-benzyloxy-2-(phenylselenenylmethyl)tetrahydrofuran-4-ol (32) and (2*S*,3*S*,4*R*)-3-Benzyloxy-2-(phenylselenenylmethyl)-tetrahydrofuran-4-ol (33): Compound **5b** (63 mg, 0.30 mmol) was treated with NPSP under acidic conditions. The reaction mixture was stirred at room temperature for 1 h. After purification by MPLC, eluting with linear gradient [hexane to hexane/ethyl acetate (1:4)], 96 mg (87%) of **32** and **33** (ratio 43:57) were isolated as an inseparable mixture. For analytical purposes, a pure sample of compound **32** was obtained after successive purification by radial chromatography (hexane/ethyl acetate, 5:1).

Compound 32: $[\alpha]_D^{25}$ = −4.3 ($CHCl_3$, c = 1.36). − ^{1}H NMR: δ = 2.40 (br. s, 1 H), 3.12 (dd, 1 H, J = 12.9, 4.8), 3.27 (dd, 1 H, J = 12.9, 6.3), 3.70 (m, 2 H), 3.81 (d, 1 H, J = 3.2), 4.11 (ddd, 1 H, J = 6.3, 4.8, 3.2), 4.27 (br. s, 1 H), 4.52 (d, 1 H, J = 11.1), 4.59 (d, 1 H, J = 11.8), 7.20−7.60 (m, 10 H). − ^{13}C NMR: δ = 31.1, 71.9, 74.5, 76.1, 83.4, 88.6, 127.3, 127.8, 128.0, 128.6, 129.3, 130.0, 132.8, 137.5. − $C_{18}H_{20}O_3Se$ (363.31): calcd. C 59.51, H 5.55; found C 59.45, H 5.68.

Compound 33: Spectral data obtained from the spectra of the mixture of diastereomers. − ^{1}H NMR: δ = 2.30 (br. s, 1 H), 3.10−3.20 (m, 2 H), 3.69 (dd, 1 H, J = 10.0, 1.8), 3.93 (dd, 1 H, J = 4.0, 1.0), 4.15 (dd, 1 H, J = 10.0, 4.4), 4.20−4.40 (m, 2 H), 4.50 (d, 1 H, J = 11.8), 4.62 (d, 1 H, J = 11.8), 7.10−7.60 (m, 10 H). − ^{13}C

NMR: δ = 25.5, 72.3, 73.9, 74.7, 80.1, 84.1, 126.9, 127.7, 127.9, 128.5, 129.1, 130.2, 132.4, 137.8.

Reaction of 10 with Sodium Hydride. − Synthesis of (1*R*,4*R*)-7-Benzyloxy-2,5-dioxabicyclo[2.2.1]heptane (34): In a two-necked flask, 60% sodium hydride (14 mg, 0.35 mmol) was washed with anhydrous hexane. Then THF (8 mL) was added, and the flask was cooled with ice/water/salt. Compound **10** (107 mg, 0.32 mmol), dissolved in 8 mL of THF, was added dropwise. The reaction mixture was stirred for 10 min, and TLC monitoring showed that the starting material had been completely consumed and a that product with nearly the same R_f had appeared. The reaction was quenched by carefully adding a few drops of methanol and removing the solvent in vacuo. The product was filtered through silica gel and purified by radial chromatography to obtain 59 mg of **34** (89%). − $[\alpha]_D^{25}$ = +50.5 ($CHCl_3$, *c* = 1.35). − ^{1}H NMR: δ = 3.90 (d, 1 H, *J* = 8.4), 3.94 (d, 1 H, *J* = 8.4), 3.99 (d, 1 H, *J* = 8.1), 4.10 (dt, 1 H, *J* = 8.1, 0.5), 4.12 (d, 1 H, *J* = 2.4), 4.18 (dd, 1 H, *J* = 1.0, 2.6), 4.29 (br. s, 1 H), 4.58 (d, 1 H, *J* = 11.7), 4.68 (d, 1 H, *J* = 11.7), 7.20−7.40 (m, 5 H). − ^{13}C NMR: δ = 72.1, 72.8, 73.8, 75.8, 75.8, 79.6, 127.9, 128.1, 128.6, 137.5. − $C_{12}H_{14}O_3$ (206.24): calcd. C 69.89, H 6.84; found C 70.03, H 6.95.

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