Chiral Vinyl Anions for "Carbonyl Umpolung". Highly Stereoselective Addition of a Novel Enantiomerically Pure Vinyllithium Reagent to Aldehydes

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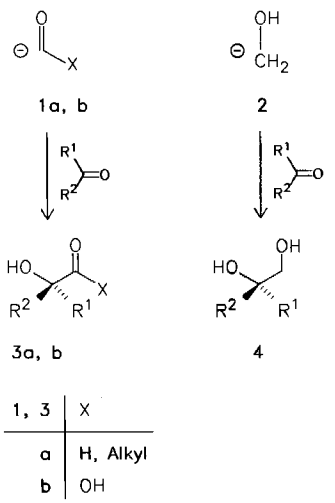
The vinyllithium reagent **13** and its enantiomer are generated by a bromine/lithium exchange reaction starting from dibromoalkenes **11** and **12**, both available from the corresponding enantiomer of alkyl lactate. When **13** is allowed to react with aldehydes or with acetophenone, a highly stereoselective addition to the *Re* face of the carbonyl compounds occurs to give predominantly the diastereomers **15**. Alkenes **25a, c**, accessible by another bromine/lithium exchange reaction of **15a, d** and subsequent protonation, can be cleaved by ozonolysis followed by reduction to afford carbinols **27a, b** in >98% ee. The sequence corresponds to a stereoselective introduction of a methanol d^1 synthon ($^{\ominus}CH_2OH$) or, as shown by other examples, of acyl and formyl d^1 synthons ($^{\ominus}$CRO and $^{\ominus}$CHO) into prochiral carbonyl compounds. As a consequence, **13** and its enantiomer may be regarded as highly stereoselective reagents for "carbonyl umpolung". A series of further vinyllithium reagents, **38a–g** and **54/55**, is treated with benzaldehyde, but none of those displays comparable enantiofacial selectivity. The prerequisites to the highly stereoselective reactions of **13** and its enantiomer are briefly discussed.

The introduction of a nucleophilic aldehyde, formic acid, or methanol synthon **1a**, **b** and **2** ("d^1 reactivity"[2]) into aldehydes or unsymmetrical ketones leads to the formation of one chiral center. There is no doubt that α-hetero-substituted carbanions, which can be considered as equivalents of the synthons **1a**, **b** and **2** are amongst the most important reagents for carbon–carbon bond formation. The plethora of methods for carbonyl-dipol inversion ("umpolung"[3]) suffers, however, from the drawback that racemic products **3a**, **b** and **4** are obtained. Enantiomerically pure acyloins **3a**, α-hydroxy carboxylic acids **3b**, and diols **4** should be available, in principle, if either *chiral* reagents incorporating d^1 reactivity or their achiral analogs combined with chiral additives are used. According to the latter conception, only moderate enantioselectivity has been obtained with most of the chiral complexing agents applied so far[4]. Proline-derived ligands, although rather promising, seem to be effective for special combinations of substrates and reagents only[5].



On the other hand, α-hetero-substituted carbanions with covalently bonded chiral auxiliary groups are rare. Some of the few examples described so far are plagued by the fact that the chiral information is not readily accessible and has to be destroyed in order to liberate the desired acyloin **3a**[6]. Other synthetic equivalents of the synthons **1a**, **b** and **2** suffer from insufficient stereoselection with respect to the enantiotopic faces of the aldehyde[7]. Synthetic chemists, being aware of this problem, have elaborated several alternatives which do not involve the direct stereoselective additon of chiral synthons **1a**, **b** and **2** to aldehydes, but, nevertheless, afford nonracemic acyloins **3a**, α-hydroxy acids **3b**, and diols **4**. Amongst these detours are the enantioselective chemical[8] or microbial[9] reduction of achiral α-oxo esters, the enantioselective catalytic hydrogenations of α-acetoxyacrylates[10], the diastereoselective additions of nucleophiles ($H^{\ominus}$ or $R^{\ominus}$) to chiral α-oxo esters[11], α-oxo amides[12], α-oxo 1,3-oxathianes[13], α-oxo aminals[14], and 4-acyl-1,3-dioxolanes[15], the oxygenation of chiral ester enolates[16] and aza enolates[17], the enantioselective protonation of α-oxy-substituted enolates[18], the alkylation of α-oxy-substituted chiral enolates[19], and the stereoselective bromolactonization of proline-derived α,β-unsaturated amides[20]. Only recently, a deprotonated chiral α-amino nitrile has been found to react in a stereoselective way with a Michael acceptor[21], and enantioselective microbial syntheses of cyanohydrins have been reported[22].

Obeying the postulate that in "asymmetric syntheses" the chiral auxiliary reagent should be available in both enantiomeric forms from easily available natural materials, we have tried to use lactic acid derived allylic ethers **5** as synthetic equivalents of d^1 synthons **1a**, **b** and **2**[23]. According to this conception, a carbon–carbon double bond is considered as a masked carbonyl, carboxyl, or hydroxymethylene group, depending on whether oxidative or reductive methods are applied after the cleavage of the double bond in the alkene **7** (for instance by ozonolysis). In order to initiate the desired nucleophilic reactivity, a vinyllithium

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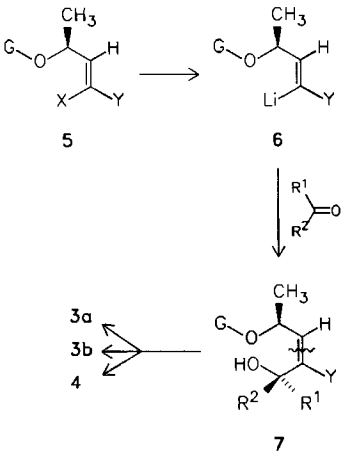
compound **6** has to be generated from the alkene **5** either by deprotonation (X = H) or by halogen/lithium exchange (X = Br, I). In the organometallic reagent **6**, the lithium is expected to be chelated by the ether oxygen atom to provide a rigid structure maximizing in this way the steric effect which should be caused by the methyl group attached to the chiral center.



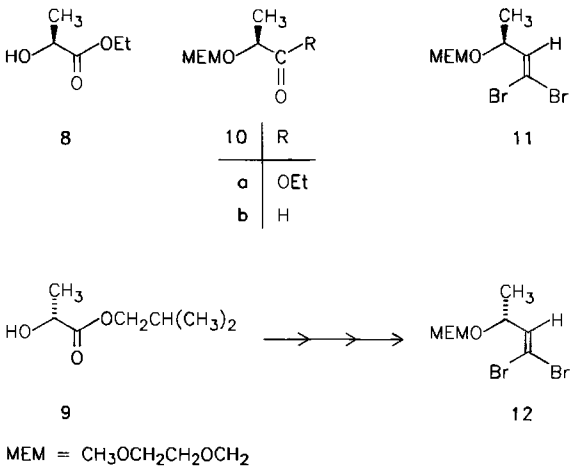
G: Protective group.

The investigation of a series of different vinyllithium compounds **6** has revealed that not only the structure of the protective group G but also the nature of the α substituent Y influences in a significant manner the diastereoselectivity in the addition to aldehydes. As a result of our search for an effective chiral vinyl anion, the lactic acid derived reagents (1*E*,3*S*)- and (1*E*,3*R*)-1-bromo-1-lithio-3-[(2-methoxyethoxy)methoxy]-1-butene (**13** and its enantiomer) have been found to be excellently suited as stereoselective synthetic equivalents of the synthons **1a**, **b** and **2**[24].

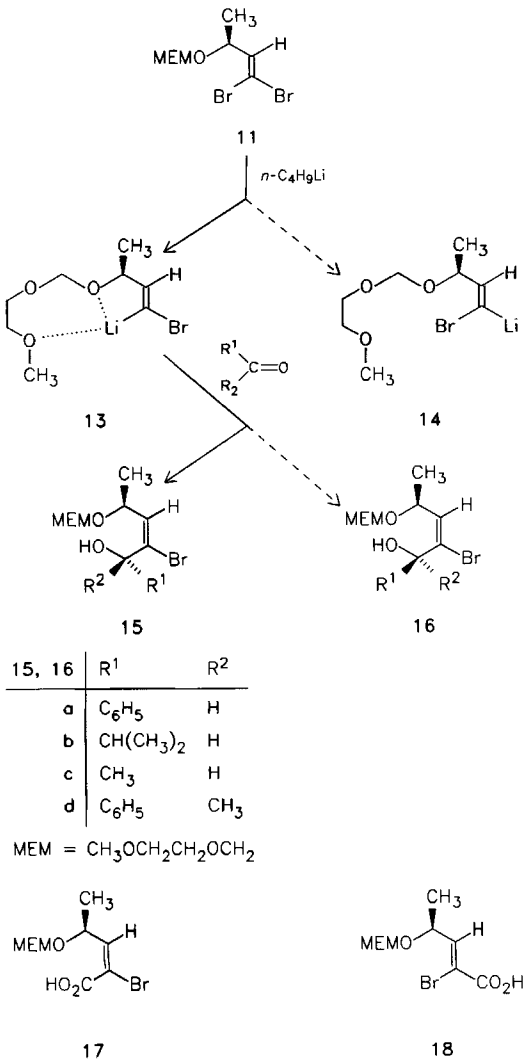
O-MEM-Protected (3*S*)- and (3*R*)-1,1-Dibromo-1-buten-2-ol (11 and 12): Preparation, Stereoselective Bromine/Lithium Exchange, and Addition to Aldehydes and Unsymmetrical Ketones

(*S*)-Dibromoalkene **11** is generated by the following three-step procedure. First, ethyl (2*S*)-lactate (**8**) is protected as (methoxyethoxy)methyl ("MEM") ether[25] **10a** which is converted into lactaldehyde **10b**[26] when submitted to reduction with DIBAH. A chain extension with carbon tetrabromide and triphenylphosphine[27] affords the alkene **11** as a colorless liquid in 150-g quantities in 67–75% overall yield. In an analogous way, **12** is available from isobutyl (2*R*)-lactate (**9**).

When dibromo alkene **11** is treated with alkyllithium reagents (e.g. *n*- or *tert*-butyllithium), in principle, both vinyllithium compounds **13** and **14** could result. It is evident that only the (*E*) reagent **13** will be able to discriminate between the enantiotopic faces of a carbonyl group, whereas the (*Z*) isomer **14** will undoubtedly behave in a stereorandom manner. Thus, the selective exchange of the (*Z*)-bromine atom in the alkene **11** for a lithium atom (to give **13**) turns out to be a "conditio sine qua non". Considering both diastereomers **13** and **14**, it is obvious that the (*E*) reagent **13** will be the thermodynamically more stable isomer, not only because of the steric demand of the bromine (compared to the lithium) atom, but also because of the chelation of the lithium atom by the MEM ether group. On the other hand, (*Z*) reagent **14** should be the major product of a kinetically controlled reaction which involves the preferred attack at the (*E*)-bromine atom, more readily accessible to the alkyllithium compound. The latter assumption is readily verified by the treatment of dibromo alkene **11** with 1.2 equivalents of *n*-butyllithium. Thereby, the isomeric vinyllithium compounds **13** and **14** are formed in a ratio of 32:68, as proven by carboxylation with carbon dioxide. The α,β-unsaturated carboxylic acids **17** and **18**, formed in this way, differ distinctly in their ^{1}H-NMR spectra. The assignment of structure **18** to the major isomer is possible by a simple calculation of increments[28] which predicts a high-field shift of 0.76 ppm of the vinylic proton signal of **17**, compared to the corresponding signal originating from the isomer **18**. Indeed, a difference of 0.64 ppm is found between the resonances of the vinylic protons of both isomers **17** and **18**.



On the other hand, the almost exclusive (up to >99:1) formation of the (*E*) reagent is possible when the bromine/lithium exchange is performed under *thermodynamically controlled conditions*. For this purpose, a slight excess of dibromo alkene **11** is allowed to react with *n*-butyllithium (0.95 equivalents) in diethyl ether at −105°C. When, after 30 min, this mixture is treated with carbon dioxide, the ratio of carboxylic acids **17**:**18** surpasses 99:1. This highly stereoselective bromine/lithium exchange[29] can be rationalized by assuming an equilibrium which does not only involve the isomers **13** and **14** but also dibromo alkene **11**. The slight excess of the latter compound enables the undesired (*Z*) isomer **14** to undergo another bromine/lithium exchange (using **11** as partner), so that, finally, the thermodynamically much more stable isomer **13** is formed as a single intermediate[30]. Thus, both carboxylic acid **17** and alkene **13** (H instead of Li) are obtained as pure isomers upon carboxylation and protonation, respectively.



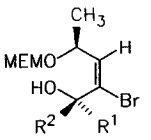
15, 16	R^1	R^2
a	C_6H_5	H
b	$CH(CH_3)_2$	H
c	CH_3	H
d	C_6H_5	CH_3

MEM = $CH_3OCH_2CH_2OCH_2$

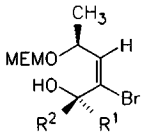
Having in hand this method which provides the exclusive exchange of the (*Z*)-bromine atom in **11**, the addition of **13** to benzaldehyde has been studied under various conditions in order to optimize the diastereoselectivity. A survey of the results is given in Table 1 in which not only the ratios of diastereomeric adducts **15a**:**16a** are listed but also the ratios of vinyllithium reagents **13**:**14**, depending on the amount of the alkyllithium compound (used for the bromine/lithium exchange), the time, the solvent, and the temperature. There is only a marginal influence on the ratio of (*E*) and (*Z*) isomers **13**:**14**, caused by the different type of the alkyllithium reagent used. However, the selectivity of the bromine/lithium exchange reaction hinges strongly on the relative amount of the alkyllithium compound and depends to a minor extent on the time available to establish an equilibrium between the vinyllithium reagents **13** and **14**. Diethyl ether proves to be the most effective solvent giving rise to the exclusive formation of **13**, whereas isopentane and tetrahydrofuran seem to be less suitable. On the other hand, the highest ratios of the diastereomeric adducts **15a**:**16a** are not obtained in diethyl ether but in tetrahydrofuran. This dilemma is easily circumvented by performing the bromine/lithium exchange in diethyl ether followed by the addition of the cosolvent tetrahydrofuran prior to the final reaction with benzaldehyde (which is also added as a solution in tetrahydrofuran). Thus, the formation of any products emerging from the (*Z*) isomer **14** is completely suppressed, and only traces of the undesired adduct **16a** may be detected by GLC but not by NMR spectroscopy. The temperature of about −105 °C is suitable both for the generation of the reagent **13** and for its addition to benzaldehyde. Compared to other bromine/lithium carbenoids[31], the vinyllithium compound **13** seems to be slightly more stable (to −90 °C). The chelation of the lithium atom may be responsible for this effect.

The conditions, which lead to a high (*E*):(*Z*) selectivity as well as high enantiofacial selectivity towards benzaldehyde have also been used in the addition of the dibromo alkene **11** to aliphatic aldehydes and acetophenone. The results are listed in Table 2.

Isobutyraldehyde, acetaldehyde, and acetophenone are attacked by the (*E*)-vinyllithium reagent **13** preferably from the *Re* face to deliver predominantly the adducts **15b**–**d**. Thus, the favored topicity is found to be *ul* (*unlike*)[32] by analogy with the stereochemical outcome of the addition to benzaldehyde. Diastereomeric ratios of **15b**–**d**:**16b**–**d** range from 10:1 (in the case of acetaldehyde) to >99:1 for acetophenone. The presence of tetrahydrofuran turns out to be a prerequisite to high enantiofacial selectivity towards isobutyraldehyde and acetaldehyde. In contrast, acetophenone is attacked by the reagent **13** in a highly stereoselective manner not only in mixtures of diethyl ether and tetrahydrofuran, but also in the absence of the latter cosolvent. Here again, the products resulting from the (*Z*) isomer **14** are not detectable in the 300-MHz ^{1}H-NMR spectra. Thus, the ratio of **13**:**14** definitely exceeds 100:1.



	R^1	R^2
19	CO_2Et	CH_3
20	CH_3	CO_2Et



	R^1	R^2
21	$C(CH_3)_3$	H
22	H	$C(CH_3)_3$

The addition of (*E*) reagent **13** to ethyl pyruvate and pivalaldehyde also occurs stereoselectively. Thus, the corresponding diastereomeric products **19**, **20** and **21**, **22** are formed in the ratios 6:1 and 50:1. Thereby, the configurations of the major products have not been determined unambiguously. Nevertheless, it seems plausible to assign the structure **21** to the adduct formed in excess in the reaction of pivalaldehyde, because the topicity is very likely the same as the one found in the addition of **11** to the aldehydes mentioned above.

Table 1. (*E*):(*Z*) selectivity of the bromine/lithium exchange reaction and ratios of diastereomers **15a**:**16a** formed in the addition of dibromo alkene **11** to benzaldehyde[a]

Conditions of the bromine lithium exchange				Conditions of the addition[b]		Distribution of products			
Reagent (equiv.)	Solvent	Temperature [°C]	Time [min]	Temperature [°C]	Time [h]	Starting material (%)	Byproducts (%)	(E):(Z)	**15a:16a**
MeLi(1.1)	THF	-95	27	-95/-70	1.1	-	5	3.5:1	≥50:1
MeLi(0.8)	DEE	-105	8	-105/-80	1.0	42	10	≥50:1	15:1
MeLi(0.9)	IP/DEE	-115	10	-115/-80	0.2	55	8	≥40:1	2.9:1
*t*BuLi(1.9)	THF	-105	24	-105/-80	1.4	-	35	≥50:1	≥40:1
*t*BuLi(1)	THF	-105	36	-105/-80	0.5	30	15	≥50:1	≥30:1
*t*BuLi(1.5)	THF	-95	11	-95/-70	0.9	15	18	2.3:1	≥40:1
*s*BuLi(1.1)	IP/THF	-105	8	-105/-80	1.0	32	14	5:1	≥50:1
*s*BuLi(0.9)	DEE	-100	38	-100/-80	1.0	18	9	≥50:1	5.8:1
*s*BuLi(0.92)	DEE	-105	30	-105/-80	1.0	26	2	99:1	≥99:1
*n*BuLi(1.1)	THF	-105	10	-105/-80	1.5	-	10	1.2:1	≥30:1
*n*BuLi(1.05)	IP/THF	-115	9	-125/-95	1.5	14	5	1:1.5	20:1
*n*BuLi(0.95)	IP	-115	23	-115/-90	1.8	18	5	6:1	1.7:1
*n*BuLi(0.91)	DEE	-105	24	-105/-80	1.6	10	10	≥50:1	10:1
*n*BuLi(0.9)	DEE	-100	2	-100/-95	0.4	40	5	≥12:1	≥10:1
*n*BuLi(0.9)	DME	-125	33	-130/-80	0.9	28	10	1.6:1	30:1
*n*BuLi(0.92)	DEE	-105	35	-105/-80	1.5	8	5	≥99:1	8.8:1
*n*BuLi(0.99)	IP	-110	35	-110/-80	1.5	1	10	11:1	50:1
*n*BuLi(0.99)	DEE	-108	48	-112/-80	1.6	1	2	99:1	≥99:1
*n*BuLi(0.9)	DEE	-108	45	-112/-45	2.5[c]	15	2	99:1	99:1

[a] MeLi: methyllithium; DEE: diethyl ether; *t*BuLi: *tert*-butyllithium; THF: tetrahydrofuran; *s*BuLi: *sec*-butyllithium; IP: isopentane; *n*BuLi: *n*-butyllithium; DME: dimethyl ether. — [b] Solvent: THF. — [c] Solvent: THF/1,4-dioxane.

Table 2. Ratios of diastereomers **15b–d**:**16b–d** formed by the addition of dibromo alkene **11** to aliphatic aldehydes and acetophenone[a]

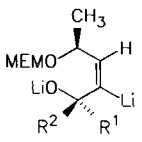
Conditions of the bromine lithium exchange				Conditions of the addition		Distribution of products		
Reagent (equiv.)	Solvent	Temperature [°C]	Time [min]	Cosolvent	Temperature [°C]	Starting material (%)	Byproducts (%)	Products
				Isobutyraldehyde				**15b:16b**
*n*BuLi(0.95)	DEE	-105	45	THF	-105/-80	5	5	16 : 1
*n*BuLi(0.95)	DEE	-105	45	-	-105/-80	9	15	1.7 : 1
				Acetaldehyde				**15c:16c**
*n*BuLi(0.94)	DEE	-105	38	THF	-105/-60	5	7	10 : 1
*n*BuLi(0.94)	DEE	-105	35	-	-95/-50	8	17	1.4 : 1
				Acetophenone				**15d:16d**
*n*BuLi(0.93)	DEE	-105	32	-	-100/-60	7	25	>90 : 1
*n*BuLi(0.93)	IP	-110	48	-	-110/-60	16	11	6.5 : 1
*n*BuLi(0.97)	DEE	-105	45	THF	-105/-90	4	9	>90 : 1

[a] See footnote of Table 1 for abbreviations.

Assignment of the Structures 15 and 16 and Synthesis of Diols 27a, b

When the crude mixtures of the adducts **15a**/**16a** and **15d**/**16d**, both formed in a ratio of >100:1 under optimized conditions, are subjected to another bromine/lithium exchange, the dilithium compounds **23a**/**24a** and **23d**/**24d** are formed in situ. Subsequently, the protonation delivers the alkenes **25a**/**26a** and **25c**/**26c** without any detectable (*E*):(*Z*)

isomerization. Finally, the ozonolysis, followed by reduction with lithium aluminium hydride, affords the (*S*)-diols **27a** and **27b** in >98% enantiomeric excess (e.e.) according to their optical rotations[33,34]. The chemical yields amount to 74% (relative to **15a**/**16a**) and 73% (relative to **15d**/**16d**). The cleavage of the double bond of the alkenes **25**/**26** also provides the chiral auxiliary information. For this purpose, the MEM-protected (*S*)-**28**, emerging from ozonolysis and subsequent reduction, may be converted by Swern oxidation[35] into the MEM-protected (*S*)-lactaldehyde **10b**. Thus, the chiral auxiliary reagent may by recovered.



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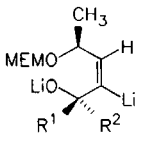
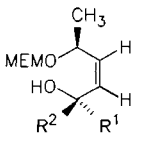


24

23, 24	R^1	R^2
a	C_6H_5	H
b	$CH(CH_3)_2$	H
c	CH_3	H
d	C_6H_5	H



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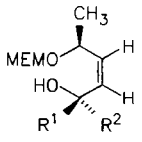
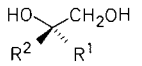


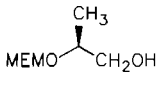
26

25, 26	R^1	R^2
a	C_6H_5	H
b	CH_3	H
c	C_6H_5	CH_3



27

	R^1	R^2
a	C_6H_5	H
b	C_6H_5	CH_3



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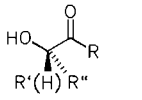

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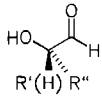

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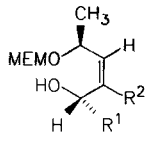

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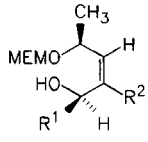
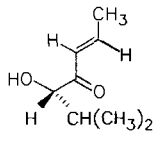


32

31, 32	R^1	R^2
a	C_6H_5	CH_3
b	C_6H_5	SCH_3
c	$CH(CH_3)_2$	SCH_3



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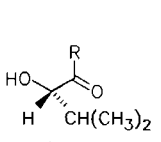
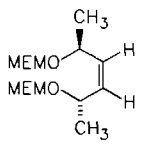


34

	R
a	$(CH_2)_2CH_3$
b	NH_2



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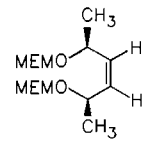


36

When, on the other hand, a mixture of dilithium compounds **23a**/**24a** is treated with methyl iodide, diastereomeric olefins **31a**/**32a** result (in a ratio of >100:1). Alkenes of type **31** and **25**/**26** have recently been shown to be converted into *O*-protected α-hydroxy ketones[36a] of type **29** and α-hydroxy aldehydes[36b] of type **30** in high enantiomeric purity upon *O* protection and subsequent cleavage of the carbon–carbon double bond by ozonolysis. Thus, it has been shown that this methodology is also suitably applied to the stereoselective addition of an acetaldehyde d^1 synthon or a formyl d^1 synthon to prochiral carbonyl compounds. Furthermore, the structures of the diastereomers **15a** and **16a** have been proven by the following reaction sequence: A mixture of the dilithium compounds **23a**/**24a** has been treated with dimethyl disulfide to afford the vinylic sulfides **31b**/**32b** in a ratio of >100:1. As the configurations of the isomers **31b** and **32b**, which differ significantly in their ^{1}H-NMR spectra, have been determined independently[23], the assignment of the structure **15a** to the major product, formed by the addition of **11** to benzaldehyde, is confirmed.

In a similar way, the major product, emerging from the reaction of **11** with isobutyraldehyde, is shown to have the configuration **15b**. For this purpose, the crude mixture of the adducts **15b**/**16b** (ratio 16:1) is converted by treatment with *tert*-butyllithium into the dilithium compounds **23b**/**24b** which are transformed into the vinyl thioethers **31c**/**32c** upon reaction with dimethyl disulfide. The mercury(II) chloride mediated hydrolysis of the mixture of the vinylic sulfides **31c**/**32c** leads to the formation of (*S*)-hydroxy enone **33** whose catalytic hydrogenation affords the (*S*)-hydroxy ketone **34a**[37]. The latter compound has been prepared independently[37] by the addition of propylmagnesium bromide to (*S*)-amide **34b**[38]. The comparison of the optical rotations of both samples unambiguously proves the structures of the main products **15b** and **31c**.

The structure **15c** has been assigned to the major product formed in the addition of **11** to acetaldehyde in the following manner: The crude mixture **15c**/**16c** (ratio 10:1) is subjected to a bromine/lithium exchange to afford the dilithium compounds **23c**/**24c** which are converted in situ into the (*Z*)-alkenes **25b**/**26b** by protonation. Finally, the protection of the hydroxyl group with MEM chloride delivers the olefins **35** and **36**. The major product, isolated in 94% diastereomeric excess (according to ^{1}H NMR and GC) turns out to have an optical rotation $[\alpha]_D^{20} = -119.5$. As the compound **36** is achiral, the structure **35** has to be assigned to the obviously chiral major product. Thus, **15c** has been proven to have been formed in favor of **16c**.

Reaction of Benzaldehyde with Further Chiral Vinyllithium Reagents Related to 13

High degrees of stereoselectivity in "asymmetric syntheses" call for a rationalization of both the sense and the extent of the stereochemical outcome. In order to elucidate the prerequisites which enable the chiral carbenoid **13** to add to prochiral carbonyl compounds in a highly stereoselective manner (see above), a series of vinyllithium reagents **38a–g**, obviously related to **13**, have been subjected to reaction with benzaldehyde. The model compounds **38a–g** differ from the parent system **13** with respect to the vinylic α-substituent as well as to the hydroxy protecting group.

For this purpose, (*Z*)-vinyllithium compounds **38a–e** are generated by an iodine/lithium exchange of the racemic vinyl iodides **37a–e**. An additional deprotonation of the hydroxy

groups occurs when the alcohols **37c** and **37e** are chosen as starting materials. On the other hand, the lithiated (*E*)-vinylic anions **38f** and **38g** are available by metalation of the corresponding enantiomerically pure vinyl thioether **37f** and vinyl sulfone **37g**, respectively. The ratios of diastereomeric adducts **25a/26a**, **31b/32b**, and **39**–**48** formed by the reaction with benzaldehyde have been determined by ^{1}H-NMR spectroscopy. The results, obtained under various conditions, are listed in Table 3. The structures of the major diastereomeric adducts have not been assigned, except for the pairs **25a/26a** and **31b/32b**.

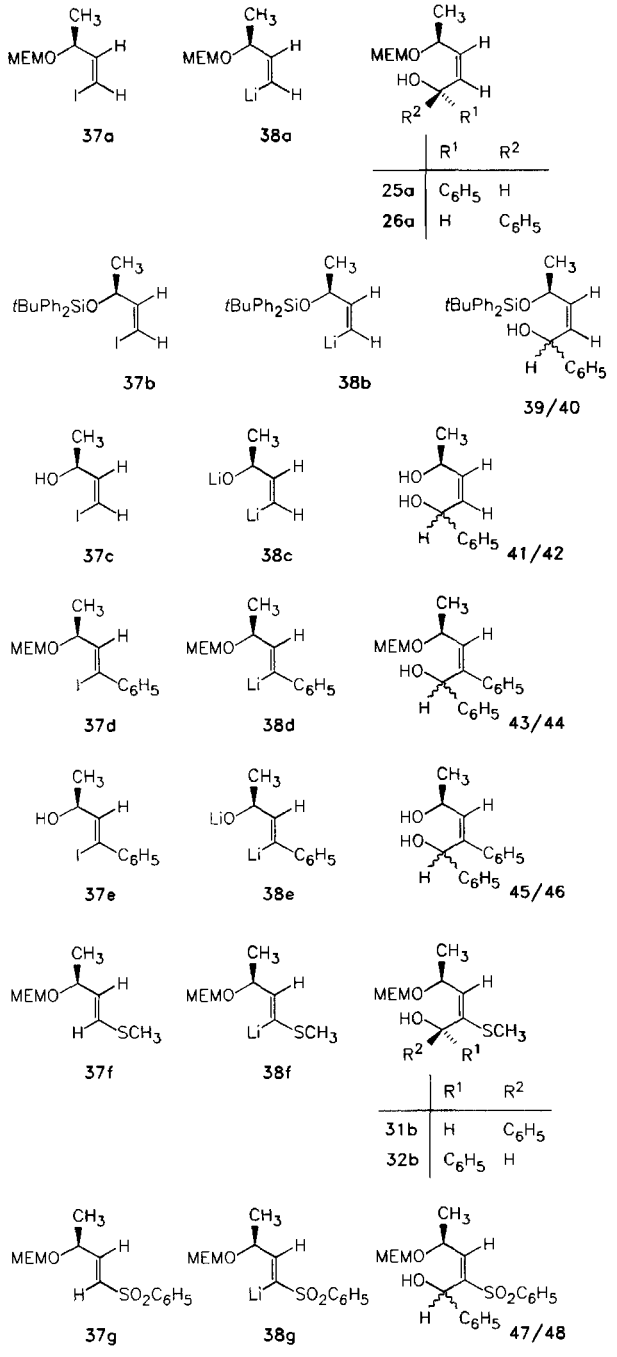


Table 3. Ratios of diastereomers **25a/26a**, **31b/32b** and **39**–**48** formed by the addition of vinyllithium reagents **38a**–**g** to benzaldehyde in THF[a]

Anion	Reagent[b] (equiv.)	Temperature [°C]	Adducts	Yield (%)	Diastereomeric ratio
38a	*t*BuLi (2)	-78	**25a:26a**	64	1 :1.4
38a	*t*BuLi (2)	-95	**25a:26a**	71	1 :1.2
38b	*t*BuLi (2)	-95	**39/40**	61	1.6 :1
38c	*n*BuLi (3)	-78	**41/42**	76	1.18:1
38c	*n*BuLi/ *t*BuLi (2)	-78	**41/42**	76	1.68:1
38d	*t*BuLi (2)	-90	**43/44**	85	1.4 :1
38d	*t*BuLi (2)	-105	**43/44**	90	5.5 :1
38e	*t*BuLi/ LDA (2) $MgBr_2$	-105	**45/46**	89	1.5 :1
38f	LDA	-78	**31b:32b**	90	25 :1[c]
38g	LDA/$MgBr_2$	-95	**47/48**	82	1.1 :1

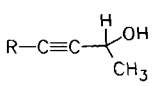
[a] See footnote of Table 1 for abbreviations. — [b] LDA: lithium diisopropylamide. — [c] See ref.[23].

The vinyllithium reagents **38a**–**c**, **e** have been found to be unable to cause a significant enantiofacial differentation towards benzaldehyde. A higher selectivity emerges from the corresponding reaction of the phenyl-substituted vinyllithium reagent **38d**. Furthermore, the ratio of diastereomeric adducts **31b**:**32b** surpasses 95:5 when the lithiated vinyl sulfide **38f** is treated with benzaldehyde[23,39]. In contrast, the deprotonated vinyl sulfone **38g** is unable to display any enantiofacial selectivity towards benzaldehyde.

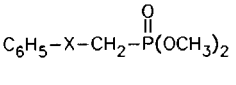
The allylic alcohols **37c** and **37e** are prepared by hydroalumination of racemic alkynes **49a,b** with lithium aluminum hydride followed by treatment with iodine. The subsequent protection of the hydroxy group affords the ethers **37a**, **37b**, and **37d**. On the other hand, vinyl sulfide **37f** and vinyl sulfone **37b** are both available in enantiomerically pure form by a Wittig-Horner reaction of the MEM-protected lactaldehyde **10b** with dimethyl (phenylthiomethyl)phosphonate (**50a**) and dimethyl (phenylsulfonylmethyl)phosphonate (**50b**), respectively.

The stereochemical outcome of the addition of the vinyllithium reagents **38a**–**g** is not easily understood. Nevertheless, some rough generalizations may be deduced from the results listed in Table 3. Obviously, the combination of the MEM protecting group with an α substituent other than hydrogen is a prerequisite to any significant enantiofacial differentiation. Thus, not only the α-unsubstituted derivatives **38a**–**c** are unselective but also the phenyl-substituted vinyllithium reagent **38e**, which lacks the MEM protecting group (cf. Table 3). The key role played by the MEM group may be interpreted in a plausible manner by assuming a chelation of the lithium atom by oxygen atoms of the protecting group (see below). The insufficient selectivity of the

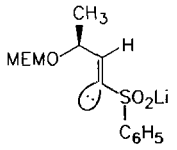
deprotonated sulfone **38g** is surprising, especially when compared to that of the lithiated vinyl sulfide **38f**. A key to a rationalization may come from recent X-ray structure analyses of lithiated alkyl sulfones, indicating that these reagents have to be regarded as carbanions with an adjacent SO–Li bond (i.e. without a C–Li bond)[40]. Assuming that metalated vinyl sulfones behave in a similar way, the structure **51** seems to be more adequate than that of the vinyllithium compound **38g**. Obviously, there is no possibility of forming an intramolecular chelate including the MEM group and the lithium atom in **51**.



49	R
a	H
b	C_6H_5

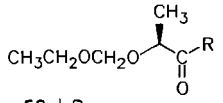


50	X
a	S
b	SO_2

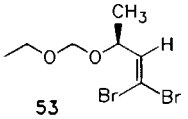


51

In order to evaluate the role which is played by the MEM group in the highly stereoselective addition of α-bromo-substituted vinyllithium reagent **13**, dibromo alkene **53** has been prepared by protecting ethyl (2*S*)-lactate (**8**) with chloromethyl ethyl ether to give **52a**, followed by reduction to the aldehyde **52b** and subsequent olefination. Obviously, the (ethoxymethoxy)-substituted alkene **53** differs from the MEM-protected reagent **11** only in as far as the ultimate oxygen atom of the MEM group in the latter compound has been replaced by a hydrogen atom in the former.



52	R
a	OC_2H_5
b	H



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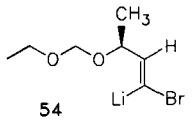

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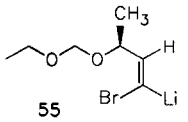

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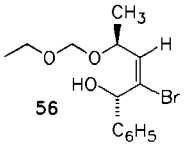

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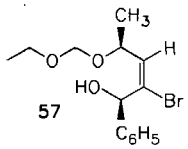

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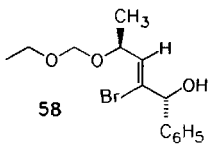

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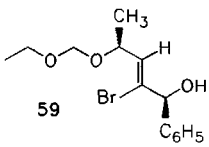
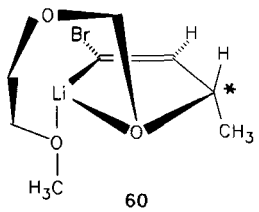


59

A mixture of four diastereomers **56**–**59** is formed when **53** is lithiated and subsequently treated with benzaldehyde under those conditions which have been found to lead not only to the exclusive formation of (*Z*)-isomeric vinyllithium reagent **13** but also to enable the latter to attack the *Re* face of the aldehyde in a highly stereoselective manner. However, the ratio of products **56**:**57**:**58**:**59**, determined by the ^{1}H-NMR spectra to be 75:12:6.5:6.5, clearly indicates that dibromo alkene **53** is unable to undergo a highly stereoselective bromine/lithium exchange reaction. Thus, (*E*)- and (*Z*)-vinyllithium compounds **54** and **55** are obviously formed in a ratio of 87:13 only[41]. Furthermore, the stereoselectivity in the addition of the (*E*) compound **54** to benzaldehyde is also found to be moderate (**56**:**57** = 75:12).

It has been found that the "ultimate" oxygen atom of the MEM protecting group is not only a prerequisite to the exclusive formation of (*E*)-configurated vinyllithium reagent **13**, but also indispensable to provide high enantiofacial selectivity towards aldehydes. As a consequence, one may assume that the lithium atom in the reagent **13** is chelated by both the allylic and the ultimate oxygen atom. A model which takes account of these results is presented in **60** and **61**. It seems plausible that the methyl group at the asymmetric carbon atom C* forces the methylene bridge to occupy the *trans* position, favoring in this way the formation of **60** and avoiding the gauche interaction which would inevitably occur in **61**. Nevertheless, we hesitate to propose an (undoubtedly highly speculative) transition-state model which would be suitable to explain the stereochemical outcome found in the addition of **13** to aldehydes. Calculations aimed to elucidate the pathway of lowest energy taken during the addition of vinyllithium to a carbonyl group are under way in this laboratory.



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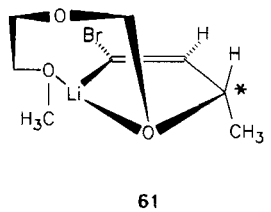

61

This work was supported by the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie*. Generous gifts of (*R*)-lactate were provided by the *BASF AG*. We would like to thank Dr. *A. Steigel*, Dr. *H. Haddad*, Mrs. *I. Menzel*, and Mr. *J. Keul* for recording the spectra.

Experimental

General: Melting points: Kofler-Heiztischmikroskop (Reichert), Büchi/Tottoli melting-point apparatus. – IR: Perkin-Elmer 221 and 297, Beckman Acculab 8. – NMR: Bruker WH 90 and WH 250, Varian VXR 300; all spectra were recorded in $CDCl_3$ as

solvent and with tetramethylsilane as internal standard. – MS: Varian MAT CH-5 (70 eV), – GLC/MS: Hewlett-Packard 5890/MS 5970 (70 eV), capillary column UV-1 (10 m); initial temperatures: injection 80°C, oven 80°C; program: 12°C/min up to 200°C. – Specific rotations: Perkin-Elmer 141. – TLC: Polygram-Sil-G/UV_{254}-Fertigfolien (Macherey-Nagel). – Preparative TLC: Kieselgel-Fertigplatten Sil-G-200/UV_{254} (Merck). – Column chromatography: Kieselgel 60, mesh size 0.2–0.5 mm (Merck). – GC: Carlo-Erba FTV 4100, capillary column SE 52 (25 m). Elemental analyses: Mikroanalytisches Laboratorium Beller (Göttingen) and Institut für Pharmazeutische Chemie, Univ. Düsseldorf.

Solvent and Reagents: The solvents tetrahydrofuran (THF), diethyl ether, 2-methylbutane, *n*-pentane, *n*-hexane, and benzene are distilled first from sodium and then under nitrogen from $LiAlH_4$; they can be taken from the receiving flasks, which are closed by septums, with syringes or cannulas. Dichloromethane is distilled under nitrogen from Na/Pb alloy and stored over molecular sieves (3 Å). Diisopropylamine and all the aldehydes are distilled before used in organometallic reactions. Dimethyl ether is passed successively through an aqueous KOH solution, a cylinder filled with granulated KOH, a freezing trap cooled to –20°C, and finally again through a cylinder containing solid, granulated KOH. Diisobutylaluminum hydride (DIBAH) is purchased either as a 2 M solution in *n*-hexane or neat. In the latter case, a 2 M solution is prepared by dilution with *n*-hexane. The organolithium compounds *n*-, *sec*-, and *tert*-butyllithium are purchased as solutions in *n*-hexane, cyclohexane/isopentane, and *n*-pentane, respectively.

General Remarks Concerning the Handling of Organolithium Compounds: The flasks, stopcocks, and syringes are dried at 160°C and subsequently stored in a dessiccator over phosphorus pentoxide. Solid and nonvolatile liquid compounds are placed into the reaction flasks which are connected with a combined nitrogen/vacuum line. Nitrogen is passed through a cylinder filled with BST catalyst (BASF), a bubbler filled with paraffin oil, and finally through a U tube filled with Sicapent (Merck). An excess pressure of about 7 Torr is kept in the nitrogen line and in all flasks by allowing the nitrogen to pass finally through a mercury valve. The combined nitrogen/vacuum line enables the reaction flasks to be evacuated and filled with nitrogen, a procedure which is usually repeated three times. The flasks are closed with rubber septums which allow liquid reagents and solutions to be added with syringes or cannulas. When two flasks are connected with a cannula with 1–2 mm inside diameter, solutions can be transferred through the cannula from one flask to the other by evaporating slightly (and carefully) the latter. Reactions performed at temperatures lower than –78°C are monitored by introducing a thermocouple, connected with a resistance thermometer (Ebro), through a septum into the reaction mixture.

(2S)-2-[(2-Methoxyethoxy)methoxy]propanal (**10b**): A solution of crude **10a**[26] (5.98 g, 2.90 mol, available from **8** in 98% yield) in 2 l of dichloromethane is prepared in a 6-l four-necked flask equipped with a pressure-equalizing dropping funnel (1 l) closed with a septum, an overhead stirrer (KPG), an inlet thermometer, and a stopcock maintaining the connection to the combined nitrogen/vacuum line. The stirred mixture is cooled to –78°C by an acetone/dry ice bath. A 2 M solution of DIBAH in *n*-hexane (1675 ml, 3.35 mol) is introduced into the dropping funnel through a cannula. The solution of DIBAH is added in such a way to the vigorously stirred reaction mixture that the temperature reaches –56 to –61°C. For this purpose, it is recommended to add first 200 ml of the solution of DIBAH in one portion, followed by dropwise addition (within about 25 min) of the remaining solution. Stirring is continued at –60 to –63°C for 2 h and subsequently at –78°C for 3 h. A satd. aqueous solution of NH_4Cl (600 ml) is added at –78°C through the dropping funnel. Thereafter, 1000 ml of a 6% hydrochloric acid is added, and the cooling bath is removed. The precipitation of aluminum hydroxide may cause a rapid rise of the temperature. In this case, the mixture should be dipped again into the cooling bath. After having reached room temperature, the vigorously stirred mixture is adjusted to pH = 4–5 by addition of 4% hydrochloric acid in order to dissolve the precipitate. The mixture is poured into a separatory funnel, the organic layer is separated, and the aqueous layer extracted successively with 500 ml of diethyl ether and six times with a total amount of 2.5 l of chloroform. The combined organic layers are washed twice with a total amount of 400 ml of water. The combined aqueous layers are extracted with three 200-ml portions of diethyl ether, the ether solutions are washed once with 10 ml of 3.5% hydrochloric acid and twice with 50-ml portions of water. All organic layers are combined and dried with $MgSO_4$. The major part of the solvent is removed in a rotary evaporator, and the remaining solvent is distilled through a short Vigreux column at 40°C/1 Torr. The residue (462 g, 98%) is purified by distillation through a 30-cm Vigreux column to yield 419 g (89%) of colorless **10b**; bp 40°C/0.01 Torr (ref.[26] 53–54°C/0.6 Torr). – $[\alpha]_D^{20} = -16.4$ (c = 1, 95% aqueous ethanol; measured 1 min after dissolution); $[\alpha]_D^{20} = -28.9$ (c = 1, 95% aqueous ethanol; measured 20 h after dissolution) {ref.[26] $[\alpha]_D^{23} = -29.3$ (c = 1, absolute ethanol)}. – ^1H NMR (250 MHz):δ = 1.31 (d, J = 7.5 Hz, 3H, 3-H), 3.37 (s, 3H, OCH_3), 3.52–3.84 (m, 4H, OCH_2CH_2O), 4.09 (dq, J_q = 7.5 Hz, J_d = 1 Hz, 1H, 2-H), 4.82 (s, 2H, OCH_2O), 9.65 (d, J = 1 Hz, 1H).

(2S)-2-(Ethoxymethoxy)propanal (**52b**): Prepared from 44.2 g (0.25 mol) of **52a** according to the procedure for **10b**; yield 27.6 g (84%) of **52b**, bp 49°C/20 Torr. – $[\alpha]_D^{20} = -65.5$, $[\alpha]_{578}^{20} = -67.5$, $[\alpha]_{546}^{20} = -76.4$, $[\alpha]_{436}^{20} = -125.9$, $[\alpha]_{365}^{20} = -188.2$ (c = 1.4, 95% aqueous ethanol, 1 min after dissolution; significant mutarotation is not observed). – IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 2940, 2890, 1735, 1390, 1185, 1155, 1115, 1100, 1040. – ^1H NMR (MHz): δ = 1.20 (t, J = 7 Hz, 3H, OCH_2CH_3), 1.30 (t, J = 7 Hz, 3H, 3-H), 3.44 to 3.89 (m, 2H, OCH_2CH_3), 4.02 (qd, J_q = 7 Hz, J_d = 1 Hz, 2-H), 4.76 (s, 2H, OCH_2O), 9.59 (d, J = 1 Hz, 1-H). – MS: m/z (%) = 103 (17) [$M^+ - C_2H_5$], 87 (7) [$M^+ - OC_2H_5$], 59 (100) [$C_3H_7O^+$], 58 (10), 57 (15), 45 (43) [$C_2H_5O^+$].

$C_6H_{12}O_3$ (132.2) Calcd. C 54.53 H 9.15
Found C 54.67 H 9.16

(3S)-1,1-Dibromo-3-[(2-methoxyethoxy)methoxy]-1-butene (**11**): A mixture of zinc dust (170 g, 2.60 mol), triphenylphosphine (656 g, 2.50 mol) and 2.5 l of dichloromethane is stirred at 0°C (ice bath) under nitrogen in a 6-l four-necked flask, equipped with a pressure-equalizing dropping funnel (1 l), an overhead stirrer (KPG), an inlet thermometer, and a connection to the combined nitrogen/vacuum line. A solution of tetrabromomethane (829 g, 2.50 mol) in 400 ml of dichloromethane is added rapidly under vigorous stirring. A first portion of 100 ml of the solution of tetrabromomethane is added within 20 s, whereby the mixture reaches 25°C. The remaining part of the solution is added in such a way that the temperature of the reaction mixture, cooled by an ice bath, is 21–23°C. The ice bath is replaced by a water bath in order to keep the reaction mixture at 21°C for 5 h, and stirring is continued for 24 h. Thereby, the color of the mixture, initially yellowish, turns to chocolate-brown. Thereafter, the vigorously stirred mixture is cooled to 0°C, and a solution of **10b** (108 g, 0.66 mol) in 100 ml of dichloromethane is added, whereby the temperature is not allowed to exceed 8°C. Stirring is continued at 0°C for 15 min and subsequently at room temperature for 4 h. The mixture is poured into a bucket filled with

20 l of pentane and filtered. The pasty residue is dissolved in a minimum amount of dichloromethane, diluted with the fivefold volume of pentane, and filtered. The combined filtrates are concentrated in a rotary evaporator, and the oily residue is subjected to refraction through a 30-cm Vigreux column. A forerun containing small amounts of tetrabromomethane is taken off generously. The main fraction consists of 182 g (87%) of pure **11**; bp 65°C/0.005 Torr, 52–53°C/0.001 Torr. – $[\alpha]_D^{20} = -64.8$, $[\alpha]_{578}^{20} = -67.7$, $[\alpha]_{546}^{20} = -76.2$, $[\alpha]_{436}^{20} = -126.3$, $[\alpha]_{365}^{20} = -189.6$ (c = 1.2, 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 1.28 (d, J = 6.5 Hz, 3H, 4-H), 3.40 (s, 3H, OCH_3), 3.54–3.58 (m, 2H, OCH_2CH_2O), 3.62–3.78 (m, 2H, OCH_2CH_2), 4.45 (dq, J_d = 8 Hz, J_q = 6.5 Hz, 1H, 3-H), 4.71 (pseudo q, 2H, OCH_2O), 6.42 (d, J = 8 Hz, 1H, 2-H). – ^{13}C NMR (75 MHz): δ = 19.72 (C-4), 59.02 (OCH_3), 67.04 (OCH_2CH_2), 71.69 (OCH_2CH_2), 72.84 (C-4), 90.36 (C-1), 93.52 (OCH_2O), 140.30 (C-2). – MS: m/z (%) = 211, 213, 215 (3) [$M^+ - C_4H_9O_3$], 161, 163 (3) [$M^+ - C_3H_{10}O_2Br$], 131, 133 (12) [$M^+ - C_4H_{10}BrO_3$], 105 (5) [$C_4H_9O_3^+$], 89 (64) [$C_4H_9O_2^+$], 73 (18) [$C_4H_9O^+$], 59 (100) [$C_3H_7O^+$].

$C_8H_{14}Br_2O_3$ (318.0) Calcd. C 30.22 H 4.44 Br 50.25
Found C 30.14 H 4.42 Br 50.39

(3R)-1,1-Dibromo-3-[(2-methoxyethoxy)methoxy]-1-butene (**12**): Available from the enantiomer of **10b** by means of the same procedure. – $[\alpha]_{589}^{20} = +63.8$, $[\alpha]_{578}^{20} = +66.6$, $[\alpha]_{546}^{20} = +74.7$, $[\alpha]_{436}^{20} = 124.3$, $[\alpha]_{365}^{20} = -186.0$ (c = 2.3, 95% aqueous ethanol).

(3S)-1,1-Dibromo-3-(ethoxymethoxy)-1-butene (**53**): Available according to an analogous procedure starting from zinc dust (36 g, 0.55 mol), triphenylphosphine (139 g, 0.53 mol), tetrabromomethane (173 g, 0.52 mol), and **52b** (17 g, 0.13 mol) which are allowed to react in 1 l of dichloromethane. Distillation of the crude product affords 29 g (78%) of **53**; bp 27–28°C/0.006 Torr. – $[\alpha]_D^{20} = -65.7$, $[\alpha]_{578}^{20} = -68.3$, $[\alpha]_{546}^{20} = -76.7$, $[\alpha]_{436}^{20} = -126.9$, $[\alpha]_{365}^{20} = -189.0$ (c = 1.5, 95% aqueous ethanol). – IR (neat): $\tilde{\nu}$ = 2970 cm^{-1}, 2930, 2880, 1605, 1440, 1386, 1370, 1185, 1150, 1090, 1030, 855, 780. – ^{1}H NMR (300 MHz): δ = 1.23 (t, J = 7 Hz, 3H, CH_2CH_3), 1.28 (d, J = 6.5 Hz, 3H, 4-H), 3.60 (m_c, 2H, CH_2CH_3), 4.44 (dq, J_d = 8.2 Hz, J_q = 6.5 Hz, 1H, 3-H), 4.67 (pseudo q, 2H, OCH_2O), 6.40 (d, J = 8.2 Hz, 1H, 2-H). – ^{13}C NMR (75 MHz): δ = 15.14 (CH_2CH_3), 19.78 (C-4), 63.45 (CH_3), 72.62 (C-3), 90.33 (C-1), 93.11 (OCH_2O), 140.42 (C-2). – MS: m/z (%) = 275, 273, 271 (3, 7, 3) [$M^+ - CH_3$], 245, 243, 241 (2, 4, 2) [$M^+ - C_2H_5O$], 215, 213, 211 (32, 58, 27) [$M^+ - C_4H_9O$], 165, 163 (5) [$M^+ - C_2H_4BrO$], 151, 149 (5) [$M^+ - C_3H_6BrO$], 59 (100) [$C_3H_7O^+$], 53 (18), 51 (21).

$C_7H_{12}Br_2O_2$ (288.0) Calcd. C 29.20 H 4.20
Found C 29.61 H 4.31

(2E,4S)- and (2Z,4S)-2-Bromo-4-[(2-methoxyethoxy)methoxy]-2-pentenoic Acid (**17** and **18**) ("nonstereoselective bromine/lithium exchange"): A mixture of **11** (3.18 g, 10.0 mmol) and 150 ml of THF is stirred under nitrogen at −110°C in a 250-ml two-necked flask equipped with a stirring bar, a septum, and a connection to the combined nitrogen/vacuum line. Within 50 s, 7.50 ml (12.0 mmol) of a 1.6 M solution of *n*-butyllithium in *n*-hexane is added, and stirring is continued at −100°C for 10 min. Thereafter, the solution is poured into a 1-l nitrogen-rinsed beaker containing a rapidly prepared mixture of 200 ml of THF and 100 g of freshly broken dry ice. When the mixture has reached room temperature, 100 ml of 2 N hydrochloric acid is added, and THF is removed in a rotary evaporator (water bath: 30°C). The residue is extracted four times with a total amount of 200 ml of diethyl ether. The combined organic layers are washed with 2 N hydrochloric acid and subsequently extracted with four 30-ml portions of a dild. aqueous solution of K_2CO_3. The combined alkaline extracts are washed twice with a total amount of 60 ml of chloroform, acidified, and finally extracted five times with diethyl ether. The combined organic layers are washed with 2 N hydrochloric acid and dried with Na_2SO_4. The solvent is removed first in a rotary evaporator and subsequently by an oil pump at 0.1 Torr to give 2.31 g (85%) of the crude mixture of **17** and **18** as a viscous oil which solidifies on standing at ca. 4°C in a refrigerator.

17 (minor isomer): ^{1}H NMR (250 MHz): 1.33 (d, J = 6 Hz, 3H, 5-H), 3.42 (s, 3H, OCH_3), 3.58–3.76 (m, 4H, OCH_2CH_2O), 5.00–5.12 (m, 1H, 4-H), 4.74 (s, 2H, OCH_2O), 6.73 (d, J = 9 Hz, 1H, 3-H), 10.69 (m, 1H, OH).

18 (major isomer): ^{1}H NMR (250 MHz) differs from that of **17** in: δ = 1.35 (d, J = 6 Hz, 3H, 5-H), 4.64–4.80 (m, 1H, 4-H), 7.37 (d, J = 9 Hz, 1H, 3-H).

(1E,3S)-1-Bromo-3-[(2-methoxyethoxy)methoxy]-1-butene (**13**, H instead of Li) ("stereoselective bromine/lithium exchange"): A solution of **11** (3.18 g, 10.0 mmol) in 50 ml of diethyl ether is stirred under nitrogen at −108°C. Within 5 min 5.90 ml (9.44 mmol) of a 1.6 M solution of *n*-butyllithium in *n*-hexane is added with a syringe whereby the temperature of the reaction mixture, monitored by a thermocouple, is not allowed to exceed −105°C. A fine white precipitate forms gradually upon continued stirring at −105° to −100°C for 45 min. The mixture is cooled to −112°C, and 2.00 ml (50.0 mmol) of methanol is injected followed by the addition of 50 ml of a satd. aqueous solution of NH_4Cl. After having reached room temperature, the mixture is extracted twice with 50-ml portions of diethyl ether. The combined organic layers are washed with 10 ml of a satd. aqueous solution of NH_4Cl and 10 ml of brine, dried with $MgSO_4$, and concentrated in a rotary evaporator. The residue is distilled in vacuo to yield 2.19 g (92%) of **13** (H instead of Li); bp 50–52°C/0.05 Torr $[\alpha]_D^{20} = -127.9$ (c = 1.6, 95% aqueous ethanol). – IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 2940, 2890, 1140, 1100, 1035. – ^{1}H NMR (250 MHz): δ = 1.28 (d, J = 6.5 Hz, 3H, 4-H), 3.40 (s, 3H, OCH_3), 3.53–3.80 (m, 4H, OCH_2CH_2O), 4.23 (dq, J_d = 8 Hz, J_q = 6.5 Hz, 1H, 3-H), 4.67–4.72 (dd, J = 7.5 Hz, J = 8 Hz, 2H, OCH_2O), 6.12 (pseudo q, 1H, 2-H), 6.32 (dd, J = 7.5 Hz, J = 1 Hz, 1H, 1-H). – MS: m/z (%) = 135, 133 (30) [$M^+ - C_4H_9O_3$], 89 (41) [$C_4H_9O_2^+$], 83 (20) [$C_5H_7O^+$], 73 (12) [$C_4H_9O^+$], 59 (100) [$C_3H_7O^+$], 53 (49) [$C_4H_5^+$], 45 (73) [$C_2H_5O^+$].

$C_8H_{15}BrO_3$ (239.1) Calcd. C 40.19 H 6.32
Found C 40.44 H 6.36

When the stereoselective bromine/lithium exchange of **11** described above is followed by the addition of 2 ml of CH_3OD instead of CH_3OH, the deuterated product **13** (D instead of Li) results. The ^{1}H-NMR spectrum (250 MHz) of the latter compound differs from that of **13** (H instead of Li) in: δ = 6.12 (br. d, J = 8 Hz, 1H, 2-H), no signal at δ = 6.32.

17: Obtained as single isomer when the vinyllithium reagent **13**, generated by the stereoselective bromine/lithium exchange described above, is treated with CO_2. Traces of the isomeric acid **18** are not detected in the ^{1}H-NMR spectrum.

General Procedure 1 (G. P. 1) *for the Stereoselective Addition of Lithiated* **11** *to Aldehydes or Ketones in Diethyl Ether/THF:* A solution of **11** (31.8 g, 100 mmol) in 500 ml of diethyl ether is stirred at −108°C under nitrogen in a 1-l four-necked flask equipped with an overhead stirrer (KPG), a pressure-equalizing dropping funnel which is closed by a septum, a thermocouple introduced through a septum, and a connection to the combined nitrogen/vacuum line. A 1.6 M solution (59.0 ml, 95 mmol) of *n*-butyllithium in *n*-hexane is added through the dropping funnel within 10 min. Thereby, the flask is plunged into a bath of liquid nitrogen in order to prevent

the temperature from exceeding −105°C. A fine white precipitate forms during a further 15-min period of vigorous stirring, and another 2.50 ml (4 mmol) of a 1.6 M solution of *n*-butyllithium in *n*-hexane is added within 10 min. Stirring is continued at −105 to −100°C für 15 min. The mixture is diluted with 20 ml of THF at −112°C, stirring is continued for 1 min, and 120 mmol of the corresponding carbonyl compound is added. Thereby, the latter is dissolved in 100 ml of THF, and the precooled solution (−105°C) is added through a cannula within 2 min in such a way that the temperature of the reaction mxiture does not exceed −108°C. Stirring is continued at −112°C for 30 min, and the temperature is allowed to reach −78°C within 100 min. A satd. aqueous solution of NH_4Cl (50 ml) is added, and the cooling bath is removed. Having reached room temperature, the mixture is poured into a separatory funnel. The organic layer is separated, the aqueous phase treated with another 100-ml portion of a satd. aqueous solution of NH_4Cl, and subsequently extracted five times with a total amount of 500 ml of diethyl ether. The combined organic layers are washed successively with 100 ml of a satd. aqueous solution of NH_4Cl and brine, dried with $MgSO_4$, and concentrated in a rotary evaporator. The oily residue is exposed to vacuum (0.01 Torr) at room temperature for several hours and finally purified by short-path distillation in vacuo. According to this general procedure are obtained:

(1S,2E,4S)-2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-penten-1-ol (**15a**): Prepared by reaction of **11** (31.8 g, 100 mmol) with benzaldehyde (12.7 g, 120 mmol); yield 32.1 g (93%) of distilled product, bp 132−134°C/0.001 Torr; R_f = 0.44 [silica gel; diethyl ether/pentane (2:1)]. − $[\alpha]_D^{20}$ = −202.7, $[\alpha]_{578}^{20}$ = 211.7, $[\alpha]_{546}^{20}$ = −240.9, $[\alpha]_{436}^{20}$ = −424.4, $[\alpha]_{365}^{20}$ = −689.4 (*c* = 1.2, 95% aqueous ethanol). IR (neat): $\tilde{\nu}$ = 3420 cm^{-1}, 2930, 2890, 1450, 1180, 1130, 1100, 1030, 700. − ^1H NMR (250 MHz): δ = 1.32 (d, *J* = 7 Hz, 3H, 5-H), 3.36 (s, 3H, OCH_3), 3.40 (br. d, *J* = 6Hz, OH), 3.51−3.55 (m, 2H, OCH_2CH_2O), 3.67−3.72 (m, 2H, OCH_2CH_2O), 4.76 (pseudo q, 2H, OCH_2O), 4.94 (dq, J_d = 9 Hz, J_q = 7 Hz, 1H, 4-H), 5.66 (d, *J* = 6 Hz, 1H, 1-H), 6.05 (d, *J* = 9 Hz, 1H, 3-H), 7.26−7.50 (m, 5H, aromatic H). − ^{13}C NMR (75 MHz): δ = 21.31 (C-5), 58.93 (OCH_3), 66.82 (OCH_2CH_2O), 69.19 (C-4), 71.57 (OCH_2CH_2O), 73.45 (C-1), 92.97 (OCH_2O), 125.81 (C-*o*), 127.77 (C-*p*), 128.23 (C-*m*), 130.60 (C-2), 136.25 (C-3), 140.44 (C-*i*). − MS: *m/z* (%) = 240, 238 (34) [$M^+ - C_4H_{10}O_3$], 159 (75) [$M^+ - C_4H_{10}BrO_3$], 143 (34) [$M^+ - C_5H_{14}BrO_3$], 131 (44) [$C_9H_7O^+$], 129 (265), 116 (47) [$C_9H_8^+$], 115 (24), 107 (23), 105 (29), [$C_4H_9O_3^+$], 91 (26), 89 (56) [$C_4H_9O_2^+$], 79 (22) [$C_6H_7^+$], 77 (33) [$C_6H_5^+$], 59 (100) [$C_3H_7O^+$].

$C_{15}H_{21}BrO_4$ (345.2) Calcd. C 52.19 H 6.13
Found C 52.26 H 6.23

Traces of the diastereomer **16a** are neither detected by ^1H NMR (see below for the corresponding data) nor by GC.

(3S,4E,6S)- and (3R,4E,6S)-4-Bromo-6-[(2-methoxyethoxy)methoxy]-2-methyl-4-hepten-3-ol (**15b** and **16b**): Prepared by reaction of **11** (3.18 g, 10 mmol) with 2-methylpropanal (0.8 g, 12 mmol); yield 2.94 g (96%) of a 16:1 mixture of **15b**:**16b** purified by a short-path distillation (receiving flask cooled by liquid nitrogen); bp 80°C (bath)/0.005 Torr. Further purification of 300 mg of the distilled product by preparative TLC (silica gel; diethyl ether; R_f = 0.6) affords 260 mg (87%) of a mixture of diastereomers **15b**/**16b** (18:1). − IR (neat): $\tilde{\nu}$ = 3450 cm^{-1}, 3010, 2970, 2940, 2900, 1145, 1105, 1035.

15b (major diastereomer): ^1H NMR (250 MHz): δ = 0.93 (d, *J* = 6.5 Hz, 3H) and 1.05 (d, *J* = 6.5 Hz, 3H) [$CH(CH_3)_2$], 1.28 (d, *J* = 6.5 Hz, 3H, 7-H), 1.85−2.04 (m, 1H, 2-H), 2.50 (br. d, *J* = 7 Hz, OH), 3.40 (s, 3H, OCH_3), 3.51−3.76 (m, 4H, OCH_2CH_2O), 3.97−4.03 (m, 1H, 3-H), 4.68−43.85 (m, 3H, OCH_2O and 6-H), 5.98 (d, *J* = 9 Hz, 1H, 5-H). − GLC/MS (t_r = 8.86 min): *m/z* (%) = 163, 161 (16) [$M^+ - C_6H_{13}O_4$], 125 (9) [$C_8H_{13}O^+$], 89 (67) [$C_4H_9O_2^+$], 83 (14) [$C_5H_7O^+$], 59 (100) [$C_3H_7O^+$], 55 (21) [$C_3H_3O^+$].

16b (minor diastereomer): ^1H NMR (250 MHz): Differs from that of **15b** in: δ = 0.77 (d, *J* = 6.5 Hz, 3H) and 1.10 (d, *J* = 6.5 Hz, 3H) [$CH(CH_3)_2$], 1.27 (d, *J* = 6.5 Hz, 3H, 7-H), 3.41 (s, 3H, OCH_3), 5.92 (d, *J* = 10 Hz, 1H, 5-H). − GLC/MS (t_r = 9.1 min): the intensities of the major peaks are slightly different from those of **15b**.

$C_{12}H_{23}BrO_4$ (311.2) Calcd. C 46.31 H 7.45
Found C 46.64 H 7.62

(2S,3E,5S)- and (2R,3E,5S)-3-Bromo-5-[(2-methoxyethoxy)methoxy]-3-hexen-2-ol (**15c** and **16c**): Synthesized by reaction of **11** (16.9 g, 53 mmol) with acetaldehyde (3.00 g, 68 mmol); yield 12.9 g (86%) of distilled colorless oil consisting of a mixture of **15c** and **16c** (10:1), bp 96−97°C/0.01 Torr. When 200 mg of this mixture is subjected to preparative TLC (silica gel; diethyl ether; R_f = 0.65), the diastereomeric ratio of the purified product (161 mg, 81%) is increased to 97:3. − $[\alpha]_D^{20}$ = −141.9, $[\alpha]_{578}^{20}$ = −148.5, $[\alpha]_{546}^{20}$ = −168.0, $[\alpha]_{436}^{20}$ = −284.5, $[\alpha]_{365}^{20}$ = −437.9 (*c* = 3.2, 95% aqueous ethanol). − IR (neat): $\tilde{\nu}$ = 3440 cm^{-1}, 2980, 2930, 2885, 1450, 1370, 1180, 1145, 1105, 1030, 865. − MS: *m/z* (%) = 179, 177 (5) [$M^+ - C_4H_9O_3$], 97 (25) [$C_6H_9O^+$], 89 (49) [$C_4H_9O_2^+$], 59 (100) [$C_3H_7O^+$].
15c (major diastereomer): ^1H NMR (250 MHz): δ = 1.29 (d, *J* = 6.5 Hz, 3H) and 1.38 (d, *J* = 6 Hz, 3H) (1-H and 6-H), 2.50 (br. d, *J* = 7 Hz, 1H, OH), 3.40 (s, 3H, OCH_3), 3.52−3.76 (m, 4H, OCH_2CH_2O), 4.60−4.85 (m, 2H, 2-H and 5-H), 4.70 (pseudo q, 2H, OCH_2O), 5.84 (d, *J* = 9 Hz, 1H, 4-H). − ^{13}C NMR (75 MHz): δ = 21.21, 21.31 (C-1 and C-6), 59.00 (OCH_3), 66.80 (OCH_2CH_2O), 67.74, 68.48 (C-2 and C-5), 71.65 (OCH_2CH_2), 93.28 (OCH_2O), 133.74, 134.08 (C-3 and C-4).

16c (minor diastereomer): ^1H NMR (250 MHz): Differs from that of **15c** in: δ = 1.25 (d, *J* = 6.5 Hz, 3H) and 1.31 (d, *J* = 6 Hz, 3H) (1-H and 6-H), 4.74 (pseudo q, 2H, OCH_2O). − ^{13}C NMR (75 MHz): Differs from that of **15c** in: δ = 21.38, 21.15 (C-1 and C-6), 58.90 (OCH_3), 66.75 (OCH_2OCH_2O), 64.95, 68.38 (C-2 and C-5), 71.67 (OCH_2CH_2O), 92.72 (OCH_2O).

$C_{10}H_{19}BrO_4$ (283.2) Calcd. C 42.42 H 6.76 Br 28.22
Found C 42.41 H 6.71 Br 28.37

(2S,3E,5S)-3-Bromo-5-[(2-methoxyethoxy)methoxy]-2-phenyl-3-hexen-2-ol (**15d**): Prepared by reaction of **11** (11.1 g, 35 mmol) with acetophenone (3.48 g, 29 mmol); yield 9.68 g (93%) of distilled product, bp 115−125°C/0.001 Torr. − $[\alpha]_D^{20}$ = −35.8, $[\alpha]_{578}^{20}$ = −37.3, $[\alpha]_{546}^{20}$ = −41.4, $[\alpha]_{365}^{20}$ = −73.5 (*c* = 1.5, 95% aqueous ethanol). − IR (neat): $\tilde{\nu}$ = 3430 cm^{-1}, 2895, 2940, 2890, 1450, 1375, 1200, 1180, 1130, 1105, 1070, 1035, 850, 790, 770, 705. − ^1H NMR (300 MHz): δ = 0.98 (d, *J* = 6.3 Hz, 3H, 6-H), 1.85 (s, 3H, 1-H), 3.40 (s, 3H, OCH_3), 3.57−3.61 (m, 2H, OCH_2CH_2O), 3.68−3.72 (m, 2H, OCH_2CH_2O), 4.32 (br. s, 1H, OH), 4.73 (pseudo q, 2H, OCH_2O), 4.82 (dq, J_d = 9.8 Hz, J_q = 6 Hz, 1H, 4-H), 5.95, (d, *J* = 9 Hz, 1H, 3-H), 7.23−7.38 (m, 3H, aromatic H), 7.50−7.53 (m, 2H, aromatic H). − ^{13}C NMR (75 MHz): δ = 20.36 (C-6), 32.53 (C-1), 58.94 (OCH_3), 66.70 (OCH_2CH_2O), 69.48 (C-5), 71.51 (OCH_2CH_2O), 78.38 (C-2), 93.05 (OCH_2O), 125.17 (C-*o*), 127.31 (C-*p*), 127.31 (C-*m*), 134.51 (C-3), 136.39 (C-4), 146.28 (C-*i*); assignment of signals according to a DEPT-NMR experiment. − MS: *m/z* (%) = 271, 269 (2) [$M^+ - C_4H_9O_2$], 239, 237 (5) [$M^+ - C_4H_9O_4$], 173 (15) [$M^+ - C_4H_{10}BrO_3$], 143 (15) [$M^+ - C_5H_{12}BrO_4$], 130 (13) [$C_{10}H_{10}^+$], 89 (48) [$C_4H_9O_2^+$], 77 (16) [$C_6H_5^+$], 59 (100) [$C_3H_7O^+$].

$C_{16}H_{23}BrO_4$ (359.3) Calcd. C 53.49 H 6.45 Br 22.24
Found C 54.26 H 6.48 Br 22.00

Ethyl (2S,3E,5S)- and (2R,3E,5S)-3-Bromo-2-hydroxy-5-[(2-methoxyethoxy)methoxy]-2-methyl-3-hexenoate (**19** and **20**): Prepared by reaction of **11** (3.18 g, 10 mmol) with ethyl 2-oxopropanoate (1.39 g, 12 mmol); yield 2.10 g (59%) of a crude mixture of **19**/**20**. The diastereomeric ratio is determined to be 6:1 according to the ^{1}H-NMR spectrum. When 200 mg of the crude product is subjected to preparative TLC [silica gel; diethyl ether/hexane (3:1); R_f = 0.5] the diastereomeric excess is increased to 67% d.e. – IR (neat): $\tilde{\nu}$ = 3420 cm^{-1}, 2985, 2940, 2890, 1450, 1370, 1295, 1245, 1200, 1180, 1135, 1105, 1030, 865.

Major diastereomer: ^{1}H NMR (250 MHz): δ = 1.25 (d, *J* = 6 Hz, 3H, 6-H), 1.33 (t, *J* = 6 Hz, 3H, OCH_2CH_3), 1.72 [s, 3H, $C(OH)CH_3$], 3.40 (s, 3H, OCH_3), 3.53–3.78 (m, 4H, OCH_2CH_2O), 4.18–4.32 (m, 2H, OCH_2CH_3), 4.64 (pseudo q, 2H, OCH_2O), 4.88–4.99 (m, 1H, 5-H), 6.20 (d, *J* = 10 Hz, 1H, 4-H). – GLC/MS (t_r = 11.5 min): *m/z* (%) = 283, 281 (1) [$M^+ - C_3H_5O_2$], 251, 249 (2) [$M^+ - C_4H_9O_3$], 177, 175 (25) [$M^+ - C_7H_{17}O_5$], 96 (30) [$C_6H_8O^+$], 59 (100) [$C_3H_7O^+$].

Minor diastereomer: ^{1}H NMR (250 MHz): Differs from that of the major diastereomer in: δ = 1.26 (d, *J* = 6 Hz, 3H, 6-H), 1.32 (t, *J* = 6 Hz, 3H, OCH_2CH_3), 1.65 [s, 3H, $C(OH)CH_3$], 4.85 (pseudo q, 2H, OCH_2O), 5.22–5.34 (m, 1H, 5-H), 6.08 (d, *J* = 10 Hz, 1H, 4-H). – GLC/MS (t_r = 9.9 min): Differs from that of the major diastereomer slightly with respect to the intensity of the peaks.

$C_{13}H_{23}BrO_6$ (355.2) Calcd. C 43.96 H 6.53
Found C 44.28 H 6.48

(3S,4E,6S)- and (4R,4E,6S)-4-Bromo-2,2-dimethyl-6-[(2-methoxyethoxy)methoxy]-4-hepten-3-ol (**21** and **22**): Prepared by reaction of **11** (6.36 g, 20 mmol) with 2,2-dimethylpropanal (2.07 g, 24 mmol); yield 2.99 g (92%) of product purified by short-path distillation, bp 93–95/0.01 Torr. – $[\alpha]_D^{20}$ = –89.2, $[\alpha]_{578}^{20}$ = –93.0, $[\alpha]_{546}^{20}$ = –105.1, $[\alpha]_{436}^{20}$ = –178.5, $[\alpha]_{365}^{20}$ = –275.7 (*c* = 1.5, 95% aqueous ethanol); the ratio of **21**:**22** is determined to be >50:1 by ^{1}H-NMR spectroscopy and GC. – IR (neat): $\tilde{\nu}$ = 3465 cm^{-1}, 2980, 2940, 2890, 1485, 1470, 1460, 1370, 1200, 1180, 1135, 1105, 1090, 1040, 980, 870, 855, 795.

21: (major diastereomer): ^{1}H NMR (250 MHz): δ = 1.04 [s, 9H, $C(CH_3)_3$] 1.42 (d, *J* = 6.5 Hz, 3H, 7-H), 3.37 (s, OH), 3.405 (s, 3H, OCH_3), 3.54–3.82 (3 m, 4H, OCH_2CH_2O), 4.18 (s, 1H, 3-H), 4.72–4.92 (m, 3H, 6-H, OCH_2O), 6.23 (d, 9.5 Hz, 1H, 5-H). – GLC/MS (t_r = 11.73 min): *m/z* (%) = 240, 238 (1) [$M^+ - C_5H_{10}O$], 221, 219 (1) [$M^+ - C_4H_9O_3$], 205, 203 (1) [$M^+ - C_4H_9O_4$], 193, 191 (2) [$M^+ - C_5H_{11}O_4$], 164, 162 (45) [$C_6H_{11}Br^+$], 135, 133 (5) [$C_4H_7Br^+$], 89 (70) [$C_4H_9O_2^+$], 83 (19) [$C_6H_{11}^+$], 59 (100) [$C_3H_7O^+$], 57 (95) [$C_4H_9^+$], 55 (17) [$C_4H_7^+$], 45 (30) [$C_2H_5O^+$], 43 (30) [$C_2H_3O^+$, $C_3H_7^+$].

22 (minor diastereomer): ^{1}H NMR (250 MHz): Differs from that of **21** in: δ = 1.00 [s, 9H, $C(CH_3)_3$], 1.41 (d, *J* = 6.5 Hz, 3H, 7-H), 3.40 (s, 3H, OCH_3), 5.98 (d, 9.5 Hz, 1H, 5-H). – GLC/MS (t_r = 12.01 min): Differs slightly from that of **21** with respect to the relative intensity of the peaks.

$C_{13}H_{25}BrO_4$ (325.2) Calcd. C 48.01 H 7.75 Br 24.57
Found C 48.00 H 7.78 Br 24.42

General Procedure 2 (G.P.2) *for the Addition of Lithiated* **11** *to Aldehydes in Diethyl Ether* (without THF): A suspension of the vinyllithium compound **13**/**14** is generated from the dibromo alkene **11** (6.36 g, 20.0 mmol) in diethyl ether according to G.P.1. A solution of the carbonyl compound (20.0 mmol) in 20 ml of diethyl ether is added through a cannula within 2 min at –108°C. Stirring is continued at –112°C for 30 min, and the precipitate dissolves gradually. Thereafter, the temperature is allowed to reach –78°C within 100 min. The mixture is poured into a satd. aqueous solution of NH_4Cl, and the products are isolated as described in G.P.1. According to this general procedure are obtained:

15a *and (1R,2E,4S)-2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-penten-1-ol* (**16a**): Obtained in a ratio of 8.8:1 (according to the ^{1}H-NMR spectra). The mixture of the isomers **15a**/**16a** (crude yield 6.25 g, 91%) can be isolated by preparative TLC [silica gel; diethyl ether/pentane (2:1)].

15a (major diastereomer): R_f = 0.44. Physical and spectroscopic data: See above.

16a: (minor diastereomer): R_f = 0.31. – The spectroscopic data differ from those of **15a** in: ^{1}H NMR (250 MHz): δ = 1.36 (d, *J* = 7 Hz, 3H, 5-H), 3.38 (s, 3H, OCH_3), 3.53–3.61 (m, 2H, OCH_2CH_2O), 3.66–3.73 (m, 2H, OCH_2CH_2O), 4.86–5.04 (m, 1H, 4-H), 5.86 (s, 1H, 1-H), 6.01 (d, *J* = 9 Hz, 1H, 3H), 7.26–7.50 (m, 5H, aromatic H). – ^{13}C NMR (75 MHz): δ = 21.15 (C-5), 58.85 (OCH_3), 66.73 (OCH_2CH_2O), 68.64 (C-4), 71.67 (OCH_2CH_2O), 70.17 (C-1), 93.15 (OCH_2O), 126.22 (C-*o*), 127.48 (C-*p*), 128.17 (C-*m*) 133.27 (C-2), 135.1 (C-3), 140.3 (C-*i*).

15d *and (2R,3E,5S)-3-Bromo-5-[(2-methoxyethoxy)methoxy]-2-phenyl-3-hexen-2-ol* (**16d**): Prepared in a ratio of 90:1 (according to the ^{1}H- and ^{13}C-NMR spectra). The mixture of the isomers **15d**/**16d** (crude yield 4.80 g, 67%) can be isolated by preparative TLC (silica gel; diethyl ether).

15d (major diastereomer): R_f =0.75. Physical and spectroscopic data: See above.

16d (minor diastereomer): R_f = 0.81. – The spectroscopic data differ from those of **15d** in: ^{1}H NMR (300 MHz): 1.22 (d, *J* = 6.3 Hz, 3H, 6-H), 1.91 (s, 3H, 1-H), 3.23 (s, 3H, OCH_3), 3.47–3.61 (m, 2H, OCH_2CH_2O), 3.56–3.63 (m, 2H, OCH_2CH_2O), 4.72 (pseudo q, 2H, OCH_2O), 5.13 (dq, J_d = 9.8 Hz, J_q = 6 Hz, 1H, 4-H), 6.01 (d, *J* = 9 Hz, 1H, 3-H). – ^{13}C NMR (75 MHz): δ = 21.07 (C-6), 28.57 (C-1), 58.78 (OCH_3), 66.61 (OCH_2CH_2O), 68.9 (C-5), 71.57 (OCH_2CH_2O), 79.33 (C-2), 92.62 (OCH_2O), 125.74 (C-*o*), 127.75 (C-*p*), 128.29 (C-*m*), 133.85 (C-3), 136.22 (C-4), 145.16 (C-*i*).

The physical and the spectroscopic data of the products **15b**/**16b**, **15c**/**16c**, and **21**/**22**, available also according to G.P.2, are outlined above. The diastereomeric ratios, obtained by this procedure are listed in Table 2.

General Procedure 3 (G.P.3) *for the Conversion of Vinyl Bromides* **15**/**16** *into (Z)-Alkenes* **25**/**26**: A solution of 32.1 mmol of the vinyl bromide **15** (or of a diastereomeric mixture of **15** and **16**) in 200 ml of THF or diethyl ether is stirred under nitrogen at –109°C in a 500-ml two-necked flask equipped with a stirring bar and a connection to the combined nitrogen/vacuum line. A thermocouple is introduced through a septum. A 1.7 M solution of *tert*-butyllithium (65 ml, 110 mmol) in *n*-pentane is added to the vigorously stirred reaction mixture drop by drop in such a way that the temperature does not exceed –95°C. Subsequently, the mixture is allowed to reach –30°C within 1h. Thereafter, the solution is cooled to –78°C, and methanol (10 ml, 247 mmol) is injected slowly. Finally, 100 ml of a satd. aqueous solution of NH_4Cl is added, and the mixture is poured into a separatory funnel containing 400 ml of diethyl ether. The organic layer is separated, and the aqueous phase is extracted thrice with a total amount of 300 ml of diethyl ether. The combined organic layers are washed successively with 100 ml of a satd. aqueous solution of NH_4Cl and with 100 ml of brine and then dried with $MgSO_4$ and concentrated in a rotary evaporator. The residue is purified by distillation under reduced pressure. According to this general procedure are obtained:

(1R,2Z,4S)-4-[(2-Methoxyethoxy)methoxy]-1-phenyl-2-penten-1-ol (**25a**): Yield 8.01 g (94%) from **15a** (11.1 g, 32.1 mmol), bp 91–93°C/0.05 Torr. – $[\alpha]_{589}^{20}$ = –231,3, $[\alpha]_{578}^{20}$ = –241.3,

$[\alpha]_{546}^{20}$ = −275.9, $[\alpha]_{436}^{20}$ = −493, $[\alpha]_{365}^{20}$ = −815.2 (*c* = 1, 95% aqueous ethanol). − IR (neat): $\tilde{\nu}$ = 3440, 2980, 2930, 2890, 1450, 1130, 1100, 1030, 915, 855, 760, 700. − ^{1}H NMR (250 MHz): δ = 1.27 (d, *J* = 7 Hz, 3H, 5-H), 2.50 (s, 1H, OH), 3.40 (s, 3H, OCH_3), 3.51−3.79 (2 m, 4H, OCH_2CH_2O), 4.75−4.86 (pseudo q, 2H, OCH_2O), 4.75−4.97 (m, 1H, 4-H), 5.37−5.83 (m, 2H, 1-H, 2-H, 3-H), 7.25−7.49 (m, aromatic H). − GLC/MS (t_r = 13.5 min): *m/z* (%) = 161 (15) ($M^+ - C_4H_9O_3$), 160 (75) [$M^+ - C_4H_{10}O_3$], 159 (26), 145 (56) [$M^+ - C_5H_{12}O_3$, $M^+ - C_4H_9O_4$], 144 (8), 143 (11), 131 (20) [$C_9H_7O^+$], 129 (17), 117 (15), 115 (17), 105 (100) [$C_4H_9O_3^+$], 91 (26), 89 (25) [$C_4H_9O_2^+$], 79 (16), 77 (56) [$C_6H_5^+$], 59 (73) [$C_3H_7O^+$], 55 (17) 45 (43) [$C_2H_5O^+$], 43 (31) [$C_3H_7^+$].

$C_{15}H_{22}O_4$ (266.34) Calcd. C 67.65 H 8.33
Found C 67.79 H 8.22

(2S,3Z,5S)- and (2R,3Z,5S)-5-[(2-Methoxyethoxy)methoxy]-3-hexen-2-ol (**25b** *and* **26b**): Yield 5.30 g (92%) from **15c**/**16c** (7.93 g, 28 mmol; ratio 10:1), bp 68°C/0.01 Torr. − $[\alpha]_D^{20}$ = −76.7, $[\alpha]_{578}^{20}$ = −79.9, $[\alpha]_{546}^{20}$ = −89.9, $[\alpha]_{436}^{20}$ = −148.5, $[\alpha]_{365}^{20}$ = −221.6 (*c* = 1.2, 95% aqueous ethanol). − IR (neat): $\tilde{\nu}$ = 3440 cm^{-1}, 2975, 2930, 2885, 1370, 1180, 1150, 1100, 1040, 975, 935, 770, 735. − ^{1}H NMR (300 MHz): δ = 1.27, 1.277 (2 d, *J* = 6.4 Hz, 6H, 1-H, 6-H), 2.22 (d, *J* = 3 Hz, 1H, OH), 3.394 (s, 3H, OCH_3), 3.54−3.79 (2 m, 4H, OCH_2CH_2O), 4.60−4.80 (2 m, 2H, 2-H, 5-H), 4.64−4.71 (pseudo q, 2H, OCH_2O), 5.28−5.35, 5.52−5.59 (2 m, 2H, 3-H, 4-H). − GLC/MS (t_r = 7.5 min): *m/z* (%) = 129 (1) [$M^+ - C_3H_7O_2$], 115 (1) [$M^+ - C_4H_9O_2$], 113 (1), 105 (1) [$C_4H_9O_3^+$], 99 (13), 98 (16) [$C_6H_{11}O^+$], 89 (28) [$C_4H_9O_2^+$], 83 (19) [$C_6H_9O_2^+$], 83 (19) [$C_6H_{11}^+$], 59 (66) [$C_3H_7O^+$], 45 (19) [$C_2H_5O^+$], 44 (5), 43 (100) [$C_3H_7^+$, $C_2H_3O^+$].

$C_{10}H_{20}O_4$ (204.3) Calcd. C 58.80 H 9.87
Found C 58.11 H 9.65

(2R,3Z,5S)-5-[(2-Methoxyethoxy)methoxy]-2-phenyl-3-hexen-2-ol (**25c**): Yield 2.63 g (94%) from **15d** (3.59 g, 10. mmol), bp 100°C (bath)/0.001 Torr (receiving flask cooled with liquid nitrogen). − $[\alpha]_D^{20}$ = 4.0, $[\alpha]_{578}^{20}$ = 5.3, $[\alpha]_{546}^{20}$ = 7.3, $[\alpha]_{436}^{20}$ = 26.4, $[\alpha]_{365}^{20}$ = 72.9 (*c* = 0.4, 95% aqueous ethanol). − IR (neat): $\tilde{\nu}$ = 3455 cm^{-1}, 3015, 2980, 2940, 2895, 1450, 1375, 1200, 1180, 1160, 1130, 1100, 1040, 760, 705. − ^{1}H NMR (60 MHz) δ = 1.33 (d, *J* = 6.5 Hz, 3H, 5-H), 2.01 (s, 3H, 2-H), 3.86 (s, 3H, OCH_3), 3.90−4.30 (m, 4H, OCH_2CH_2O), 4.53 (br. s, 1H, OH), 4.85−6.13 (m, 5H, 3-H, 4-H), GLC/MS (t_r = 12.6 min): *m/z* (%) = 190 (1) [$M^+ - C_4H_{10}O_2$], 189 (7) [$M^+ - C_3H_7O_3$], 175 (4) [$M^+ - C_4H_9O_3$], 159 (27) [$M^+ - C_4H_9O_4$], 144 (9) [$M^+ - C_9H_{12}O$], 132 (7), 131 (7) [$C_{10}H_{11}^+$], 105 (16) [$C_4H_9O_3^+$], 89 (35) [$C_4H_9O_2^+$], 77 (12) [$C_6H_5^+$], 59 (73) [$C_3H_7O^+$], 45 (20) [$C_2H_5O^+$], 43 (100) [$C_2H_3O^+$, $C_3H_7^+$].

$C_{16}H_{24}O_4$ (280.4) Calcd. C 68.55 H 8.63
Found C 68.35 H 8.69

25a *from* **11** *and Benzaldehyde* ("one-pot procedure"): A solution of **11** (9.54 g, 30 mmol) in diethyl ether (150 ml) is treated successively with *n*-butyllithium (1.6 M solution in *n*-hexane, 18.4 ml, 29.5 mmol) and benzaldehyde (3.82 g, 36.0 mmol), dissolved in THF (30 ml), according to G.P.1. After stirring at −78°C for 3 h, the reaction mixture is cooled to −95°C, and 42 ml (70 mmol) of a 1.7M solution of *tert*-butyllithium in *n*-pentane is added slowly. The temperature is allowed to reach −30°C within 1 h. The protonation according to G.P.3 and subsequent isolation afford 6.65 g (83%) of **25a** which is found to be identical with a sample of **25a** obtained by G.P.3.

(1S,2Z,4S)-4-[(2-Methoxyethoxy)methoxy]-2-methyl-1-phenyl-2-penten-1-ol (**31a**): A solution of **15a** (3.45 g, 10 mmol) in 65 ml of diethyl ether is stirred at −109°C under nitrogen. A 1.7 M solution of *tert*-butyllihtium (20 ml, 34 mmol) is added in such a way, that the temperature does not exceed −95°C. After stirring at −30°C for 1 h, the mixture is cooled to −90°C and treated with 3.10 ml (50 mmol) of iodomethane within 10 min. The solution is allowed to reach room temperature within 1 h, and stirring is continued for another 30 min at the same temperature. A satd. aqueous solution of NH_4Cl (50 ml) is added. The organic layer is separated and the aqueous phase extracted several times with 50-ml portions of diethyl ether. The combined organic layers are washed with 50 ml of a satd. solution of aqueous NH_4Cl and 50 ml of brine and thereafter dried with $MgSO_4$. The solvent is removed in a rotary evaporator and the residue purified by destillation under reduced pressure to yield 2.36 g (84%) of **31a**, bp 121−124°C/0.01 Torr. − $[\alpha]_D^{20}$ = −246.9, $[\alpha]_{578}^{20}$ = −258.0, $[\alpha]_{546}^{20}$ = −293.6, $[\alpha]_{436}^{20}$ = −521.7, $[\alpha]_{365}^{20}$ = −860.0 (*c* = 0.9, 95% aqueous ethanol). − IR (neat): $\tilde{\nu}$ = 3450 cm^{-1}, 3015, 2985, 2940, 2900, 1455, 1180, 1135, 1100, 1030, 705. − ^{1}H NMR (250 MHz): δ = 1.28 (d, *J* = 6.5 Hz, 3H, 5-H), 1.63 (d, *J* = 1.5 Hz, 3H, 2'-H), 2.70 (br. s, OH), 3.37 (s, 3H, OCH_3), 3.50−3.80 (m, 4H, OCH_2CH_2O), 4.70−4.83 (pseudo q, 2H, OCH_2O), 4.93 (qd, J_q = 9.5 Hz, J_d = 6.5 Hz, 1H, 4-H), 5.29 (dd, J_1 = 9.5 Hz, J_2 = 1.5 Hz, 1H, 3-H), 5.59 (br. s, 1H, 1-H), 7.23−7.44 (m, 5H, aromatic H). − GLC/MS (t_r = 13.6 min): *m/z* (%) = 186 (1) [$M^+ - C_6H_6O$], 176 (1), 175 (12) [$M^+ - C_4H_9O_3$], 174 (56) [$M^+ - C_4H_{10}O_3$], 173 (14), 159 (53) [$M^+ - C_4H_9O_4$], 145 (11) [$M^+ - C_5H_{11}O_4$], 105 (67) [$C_4H_9O_3^+$], 89 (25) [$C_4H_9O_2^+$], 79 (21) [$C_6H_7^+$], 77 (39) [$C_6H_5^+$], 59 (100) [$C_3H_7O^+$], 45 (44) [$C_2H_5O^+$].

The diastereomer **31b** is neither detected in a 250-MHz NMR spectrum nor by GC.

$C_{16}H_{24}O_4$ (280.4) Calcd. C 68.55 H 8.63
Found C 68.61 H 8.64

(1S)-1-Phenyl-1,2-ethanediol (**27a**): A stream of ozone (ca. 40 mmol) in oxygen is passed through a solution of **25a** (5.32 g, 20 mmol) in 200 ml of diethyl ether at −85°C until the blue color persists. Subsequent stirring at −78°C leads to a colorless solution, which is successively treated with a stream of oxygen and nitrogen. Thereafter, the solution of the ozonide is added through a separatory funnel to a mixture of $LiAlH_4$ (1.52 g, 40 mmol) and diethyl ether (100 ml) and stirred at −78°C in a 500-ml three-necked flask under nitrogen. The mixture is allowed to reach room temperature, another 760-mg portion (20 mmol) of $LiAlH_4$ is added, and stirring is continued at room temperature for 10 h. Water is added drop by drop in order to destroy the excess of $LiAlH_4$. The precipitate is filtered, washed several times with diethyl ether, and dissolved in 3% hydrochlorid acid. The acid is extracted several times with diethyl ether. The extracts are washed twice with brine and subsequently combined with the filtrates. Ethyl acetate (200 ml) is added, and the combined organic solutions are washed with a total amount of 100 ml of brine, dried with $MgSO_4$ and concentrated in a rotary evaporator (50°C bath/2 Torr). The residue is subjected to short-path distillation in vacuo.

The first fraction, collected at 45°C/0.01 Torr, consists of 3.01 g (92%) of **28** which is shown to be identical with an authentic sample (see below) according to its physical and spectroscopic data. − $[\alpha]_D^{20}$ = 11.6 (*c* = 4.5, in 95% aqueous ethanol).

The second fraction, collected in a liquid-nitrogen-cooled receiving flask (70°C/0.001 Torr), consists of 2.28 g (83%) of **27a**. When 200 mg of this product is subjected to preparative TLC (silica gel without fluorescence indicator; diethyl ether; R_f = 0.6) 140 mg (70%) of **27a** is obtained as colorless solid, mp 61−64°C (ref.[33] 59−63°C, ref.[42] 64−65°C). − $[\alpha]_D^{20}$ = +40.8 (*c* = 2.5, 95% aqueous ethanol) {enantiomer of **27a**: ref.[33] $[\alpha]_D^{20}$ = −39.7 (*c* = 4.5, 95% aqueous ethanol); ref.[42] $[\alpha]_D^{20}$ = −41.2 (*c* = 8.4, 95% aqueous ethanol)}. ^{1}H NMR (250 MHz): δ = 2.25 (s, 1H, OH), 2.68 (s, 1H, OH), 3.62−3.80 (m, 2H, 2-H), 4.81−4.85 (pseudo q, 1H, 1-H), 7.30−7.39 (m, 5H, aromatic H).

(2S)-2-Phenyl-1,2-propanediol (**27b**): Prepared from 1.40 g (5 mmol) of **25c** by ozonolysis and subsequent reduction with $LiAlH_4$ as described above for **27a**. By means of this procedure, 0.55 g (73%) of **27b** is obtained, bp 70°C (bath)/0.001 Torr (receiving flask cooled with liquid nitrogen), mp 45–47°C (ref.[34] 47.5–48.5°C). – $[\alpha]_D^{20} = +8.81$ ($c = 2.3$, diethyl ether) {ref.[34] $[\alpha]_D^{20} = 8.94$ ($c = 7$, diethyl ether)}. – ^{1}H NMR (250 MHz): δ = 1.48 (s, 3H, 3-H), 2.74 (s, OH), 3.18 (s, OH), 3.53–3.73 (pseudo q, 2H, 1-H), 7.22–7.43 (m, 5H, aromatic H).

(2S)-2-[(2-Methoxyethoxy)methoxy]propanol (**28**) (authentic sample): Prepared from **10a** by reduction with $LiAlH_4$ according to ref.[43] in 92% yield, bp 45°C/0.01 Torr. – $[\alpha]_D^{20} = 11.7$ (c = 4.5, 95% aqueous ethanol). – IR (neat): $\tilde{\nu}$ = 3460 cm^{-1}, 2970, 2935, 2880, 1450, 1200, 1175, 1135, 1100, 1035, 980, 850. – ^{1}H NMR (250 MHz): δ = 1.17 (d, J = 6.5 Hz, 3H, 3-H), 3.12 (s, 1H, OH), 3.40 (s, 3H, OCH_3), 3.43, 3.83 (m, 7H, OCH_2CH_2O, 1-H, 2-H), 4.81 (s, 2H, OCH_2O). – GLC/MS (t_r = 5.3 min): m/z (%) = 133 (1) [$M^+ - CH_3O$], 105 (2) [$M^+ - C_3H_7O$], 103 (5) [$M^+ - C_2H_5O_2$], 89 (44) [$C_4H_9O_2^+$], 59 (100) [$C_3H_7O^+$], 58 (12) [$C_3H_6O^+$], 45 (18) [$C_2H_5O^+$], 43 (10) [$C_3H_7^+$].

$C_7H_{16}O_4$ (164.2) Calcd. C 51.20 H 9.82
Found C 51.86 H 9.76

(3S,4E,6S)-6-[(2-Methoxyethoxy)methoxy]-2-methyl-4-(methylthio)-4-hepten-3-ol (**31c**): A mixture of the vinyl bromides **15b**/**16b** (16:1) (2.00 g, 6.4 mmol) is stirred in 100 ml of diethyl ether at −95°C under nitrogen. Within 10 min, 14.0 ml (23.8 mmol) of a 1.7 M solution of *tert*-butyllithium in *n*-pentane is added, and stirring is continued at −50°C for 1 h. The mixture is cooled to −95°C, and 2.80 g (30 mmol) of dimethyl disulfide is injected. The temperature is allowed to reach 0°C, and stirring is continued for 16 h. Thereafter, 10 ml of water and 50 ml of a satd. aqueous solution of NH_4Cl are added. The mixture is poured into a separatory funnel, the organic layer is separated, and the aqueous phase extracted several times with 50-ml portions of diethyl ether. The combined organic layers are washed successively with 100 ml of a satd. aqueous solution of NH_4Cl and brine, and then dried with $MgSO_4$. The solvent is removed, and 300 mg of the oily residue (1.44 g, 81%) is subjected to preparative TLC (silica gel; diethyl ether; R_f = 0.6) to give exclusively the isomer **31c** (195 mg, 65%). – IR (neat): $\tilde{\nu}$ = 3450 cm^{-1}, 2960, 2920, 2880, 1455, 160, 1240, 1105, 1030, 930, 850, 730, 690. – ^{1}H NMR (250 MHz): δ = 0.91 (d, J = 6.5 Hz, 3H) and 1.05 (d, J = 6.5 Hz, 3H) [$CH(CH_3)_2$], 1.29 (d, J = 6.5 Hz, 3H, 7-H), 1.83–1.99 (m, 1H, 2-H), 2.24 (s, 3H, SCH_3), 2.50 (d, J = 3 Hz, OH), 3.40 (s, 3H, OCH_3), 3.54–3.78 (m, 4H, OCH_2CH_2O), 4.05 (dd, J_1 = 9 Hz, J_2 = 3 Hz, 1H, 3-H), 4.70–4.775 (pseudo q, 2H, OCH_2O and dq, J_d = 9 Hz, J_q = 6.5 Hz, 1H, 6-H), 5.07 (d, J = 9 Hz, 1H, 5-H). – MS: m/z (%) = 278 (19) [M^+], 260 (25) [$M^+ - H_2O$], 189 (41) [$M^+ - C_4H_9O_2$], 173 (44) [$M^+ - C_4H_9O_3$].

$C_{13}H_{26}O_4S$ (278.4) Calcd. C 56.08 H 9.41
Found C 55.97 H 9.29

31c *and (3R,4E,6S)-[(2-Methoxyethoxy)methoxy]-2-methyl-4-(methylthio)-4-hepten-3-ol* (**32c**): Obtained in a ratio of 1.7:1 according to the same procedure from **15b**/**16b** (1.7:1).

31c (major diastereomer): ^{1}H NMR (250 MHz): See above.

32c (minor diastereomer): ^{1}H NMR (250 MHz): Differs from that of **31c** in: δ = 0.90 (d, J = 6 Hz, 3H) and 1.08 (d, J = 7 Hz, 3H) [$CH(CH_3)_2$], 1.27 (d, J = 7 Hz, 3H, 7-H), 1.85–2.03 (m, 1H, 2-H), 3.29 (d, J = 3 Hz, OH), 4.32 (dd, J_1 = 10 Hz, J_2 = 3 Hz, 1H, 3-H), 4.67–4.8 (m, 1H, 6-H), 5.0 (d, J = 9.5 Hz, 1H, 5-H).

(3S)-3-Hydroxy-2-methylheptan-4-one (**34a**) *from* **31c**/**32c**: A mixture of the vinyl sulfides **31c**/**32c** (2:1) (1.39 g, 5.0 mmol) is dissolved in 50 ml of acetonitrile and 15 ml of water containing mercury(II) chloride (2.72 g, 10 mmol) and subsequently heated under reflux for 2 h. The precipitate is removed by filtration of the mixture, cooled to room temperature, and washed several times with 100-ml portions of diethyl ether. The combined solutions are filtered once again, the organic layer is separated, and the aqueous layer is extracted twice with a total amount of 200 ml of diethyl ether. The combined organic solutions are washed once with a satd. aqueous solution of $NaHCO_3$ and thrice with brine and thereafter dried with Na_2SO_4. The solvent is removed in a rotary evaporator and the residue treated at 40°C/1 Torr for 2 h. The crude product **33** (0.27 g, 38%) is used without purification in the following step. – $[\alpha]_D^{20} = 15.4$ (c = 1.1; chloroform). – IR (neat): $\tilde{\nu}$ = 3420 cm^{-1}, 1720. – ^{1}H NMR (90 MHz): δ = 0.70 (d, J = 7 Hz, 3H) and 1.09 (d, J = 7 Hz, 3H) [$CH(CH_3)_2$], 1.93 (dd, J_1 = 7 Hz, J_2 = 2 Hz, 3H, 7-H), 1.93–2.29 (m, 1H, 2-H), 3.53 (d, J = 6 Hz, OH), 4.22 (m, 1H, 3-H), 6.24 (d, J = 16 Hz, 1H, 5-H), 7.02 (m, 1H, 6-H).

A solution of 0.12 g (0.85 mmol) of **33** in 10 ml of ethanol is treated with 5 mg of Pd/C and subsequently hydrogenated at room temperature in an atmospheric-pressure apparatus. The catalyst is removed by filtration and washed with chloroform. After evaporation of the solvent in a rotary evaporator, 0.08 g (69%) of crude, yellowish **34a** is obtained. When subjected to preparative TLC, the product decomposes. – $[\alpha]_D^{20} = +4.4$ (c = 0.45, ethanol). – IR (neat): $\tilde{\nu}$ = 3410 cm^{-1}, 1705. – ^{1}H NMR (250 MHz): δ = 0.71 (d, J = 7.5 Hz, 3H) and 0.95 (t, J = 7 Hz, 3H) [$CH(CH_3)_2$], 1.11 (d, J = 7 Hz, 3H, 1-H), 1.60–1.75 (m, 2H, 6-H), 2.18 (sept d, J_{sept} = 7 Hz, J_d = 3 Hz, 1H, 2-H), 2.41–2.48 (m, 2H, 5-H), 3.41 (br. s, 1H, OH), 4.08 (d, J = 3 Hz, 1H, 3-H).

34a *from* **34b**: A solution of propylmagnesium bromide in 10 ml of diethyl ether is prepared from 1.02 g (42 mmol) of magnesium turnings and 5.20 g (42 mmol) of propyl bromide. Amide **34b** (0.70 g, 6 mmol) {$[\alpha]_{589}^{20} = -64$ (c = 1, methanol)}[38] is dissolved in diethyl ether (15 ml) and added to the Grignard solution. The mixture is heated to reflux for 4 h, hydrolyzed by the addition of a satd. aqueous solution of NH_4Cl, and extracted thrice with diethyl ether. The combined organic layers are dried with $MgSO_4$ and concentrated under reduced pressure to yield 0.40 g (46%) of crude **34**, identical with respect to the spectroscopic data and the sense of its optical rotation with a sample prepared from **31c**/**32c**. – $[\alpha]_{578}^{20} = +7.4$ (c = 0.68, ethanol).

(2S,3Z,5S)-2,5-Bis-[(2-methoxyethoxy)methoxy]-3-hexene (**35**) *and (2R,3Z,5S)-2,5-Bis-[(2-methoxyethoxy)methoxy]-3-hexene* (**36**): A mixture of diastereomeric alkenes **15c**/**16c** (10:1) (2.04 g, 10 mmol) is dissolved under nitrogen in 100 ml of dichloromethane. When cooled to −20°C, ethyldiisopropylamine (7.76 g, 20 mmol) is added and, after stirring for 10 min, (2-methoxyethoxy)methyl chloride (MEM chloride) (4.98 g, 20 mmol) is added. Stirring is continued at 0°C for 2 h. Thereafter, another portion of 3.88 g (10 mmol) of ethyldiisopropylamine, and, after stirring for 10 min, a further portion of 2.50 g (10 mmol) of MEM chloride is added. Stirring is continued at 0°C for 24 h, 50 ml of water is added, and the mixture is stirred at 0°C for another 2 h. The mixture is poured into a separatory funnel, containing 500 ml of diethyl ether, and washed successively with 5% hydrochloric acid, water, a dild. aqueous solution of $Na_2S_2O_3$, and brine. The organic layer is dried with $MgSO_4$ and the solvent removed in a rotary evaporator. The residue is subjected to high vacuum (20°C/0.01 Torr) for 1 h. Thereafter, the residue is distilled into a receiving flask which is cooled with liquid nitrogen (50°C/0.001 Torr) to yield 2.76 g (94%) of **35**/**36**. The ratio of the diastereomers **35**/**36** is determined to be 91:9 according to the ^{1}H-NMR spectra. – $[\alpha]_{589}^{20} = -110.5$, $[\alpha]_{578}^{20} =$

-114.7, $[\alpha]_{546}^{20} = -129.8$, $[\alpha]_{436}^{20} = -216.7$, $[\alpha]_{365}^{20} = -327.3$ (c = 2.1, chloroform). – When 200 mg of this product **35**/**36** is subjected to preparative TLC [silica gel; diethyl ether/hexane (1:1); R_f = 0.57], an enrichment of the major diastereomer occurs so that the product thus obtained consists of a 97:3 mixture of **35** and **36**. – $[\alpha]_{589}^{20} = -119.5$, $[\alpha]_{578}^{20} = -124.6$, $[\alpha]_{546}^{20} = -141.1$, $[\alpha]_{436}^{20} = -234.8$, $[\alpha]_{365}^{20} = -353.7$ (c = 1.2, chloroform). – IR (neat): $\tilde{\nu}$ = 2985 cm^{-1}, 2940, 2890, 2825, 1470, 1455, 1375, 1200, 1180, 1150, 1135, 1110, 1080, 1035, 985, 855.

35 (major diastereomer): ^1H NMR (300 MHz): δ = 1.265 (d, J = 6.4 Hz, 6H, 1-H, 6-H), 3.398 (s, 6H, OCH_3), 3.53–3.79 (2 m, 4H, OCH_2CH_2O), 4.52–4.63 (m, 2H, 2-H, 5-H), 4.63–4.68 (pseudo q, 4H, OCH_2O), 5.36–5.44 (6 lines, AB system, J_{AB} = 10 Hz, J_{HH} = 6.3 Hz, $J_{allylic}$ = 2 Hz, 2H, 3-H, 4-H). – GLC/MS (t_r = 11.36 min): m/z (%) = 129 (1) [$C_7H_{13}O_2^+$], 127 (1) [$C_7H_{11}O_2^+$], 113 [$C_6H_{11}O_2^+$], 98 (3) [$C_6H_{11}O^+$], 89 (73) [$C_4H_9O_2^+$], 83 (10) [$C_6H_{11}^+$], 82 (13), 59 (100) [$C_3H_7O^+$], 45 (14) [$C_2H_5O^+$], 43 (15) [$C_3H_7^+$, $C_2H_3O^+$].

36 (minor diastereomer): ^1H NMR (300 MHz): Differs from that of **35** in: δ = 1.22 (d, J = 6.4 Hz, 6H, 1-H, 6-H), 3.391 (s, 6H, OCH_3). – GLC/MS (t_r = 11.27 min): Differs from that of **35** with respect to the relative intensities of the major peaks.

$C_{14}H_{28}O_6$ (292.4) Calcd. C 57.51 H 9.65
Found C 57.65 H 9.65

(2R,3Z)-4-Iodo-3-buten-2-ol* (**37c**): Available from 3-butyn-2-ol according to ref.[44].

(1Z,3R)-1-Iodo-3-[(2-methoxyethoxy)methoxy]-1-butene* (**37a**): A solution of **37c** (1.98 g, 10 mmol) in 100 ml of dichloromethane is stirred at –20°C under nitrogen in a 250-ml two necked flask, which is protected against the action of light with aluminum foil. Ethyldiisopropylamine (7.76 g, 20 mmol) and, after stirring for 10 min, 4.98 g (20 mmol) of MEM chloride are added. After the mixture has been stirred at –5°C for 36 h, 50 ml of water is added, and stirring is continued at 0°C for 2 h. The mixture is transferred to a separatory funnel, containing 400 ml of diethyl ether, and washed successively with water, 5% hydrochloric acid, a dild. aqueous solution of $Na_2S_2O_3$, and brine. The organic layer is dried with $MgSO_4$ and concentrated in a rotary evaporator. The residue is distilled under reduced pressure to yield 3.22 g (76%) of **37a**, bp 55–57°C/0.03 Torr. – IR (neat): $\tilde{\nu}$ = 2975 cm^{-1}, 2935, 2885, 1270, 1110, 1090, 1030, 980, 935, 845, 715. – ^1H NMR (90 MHz): δ = 1.26 (d, J = 6.5 Hz, 3H, 4-H), 3.38 (s, 3H, OCH_3), 3.47–3.77 (2 m, 4H, OCH_2CH_2O), 4.33–4.61 (dq, J_d = J_q = 6.5 Hz, 1H, 3-H), 4.69 (s, 2H, OCH_2O), 6.08–6.40 (m, 2H, 1-H, 2-H). – GLC/MS (t_r = 7.9 min): m/z (%) = 211 (2) [$M^+ - C_3H_7O_2$], 210 (4) [$M^+ - C_3H_8O_2$], 197 (2) [$M^+ - C_4H_9O_2$], 181 (51) [$M^+ - C_4H_9O_3$], 127 (3) [I^+], 89 (52) [$C_4H_9O_2^+$], 83 (33) [$C_5H_7O^+$], 73 (10) [$C_4H_9O^+$], 59 (100) [$C_3H_7O^+$], 55 (10) [$C_4H_7^+$], 54 (34) [$C_4H_6^+$], 53 (40) [$C_4H_5^+$], 45 (63) [$C_2H_5O^+$], 43 (19) [$C_3H_7^+$].

$C_8H_{15}IO_3$ (286.1) Calcd. C 33.58 H 5.28
Found C 33.40 H 5.11

(1Z,3R)-3-(tert-Butyldiphenylsilyloxy)-1-iodo-1-butene* (**37b**): A solution of **37c** (1.98 g, 10 mmol) in 20 ml of dimethylformamide is stirred at –20°C under nitrogen in a 100-ml two-necked flask, which is protected against the action of light with aluminum foil. Imidazol (1.70 g, 25 mmol) and *tert*-butyldiphenylsilyl chloride (3.60 g, 13 mmol) are added to the vigorously stirred solution. Stirring is continued at –10°C for 40 h. After 10 ml of water has been added, the mixture is stirred for another 20 min, poured into a separatory funnel, containing ice and water, and extacted twice with a total amount of 200 ml of dichloromethane. The combined organic layers are washed five times with water (20-ml portions), 50 ml of a dild. aqueous solution of $Na_2S_2O_3$, and 50 ml of brine. The organic solution is dried with $MgSO_4$ and concentrated in a rotary evaporator. Traces of solvents are finally removed at 40°C/0.001 Torr for 2 h. In order to avoid decomposition, the crude product **37b** (4.35 g, quant.) is used in the following step without further purification. – IR (neat): $\tilde{\nu}$ = 2960 cm^{-1}, 2930, 2860, 1425, 1270, 1110, 1090, 1060, 820, 740, 700. – ^1H NMR (250 MHz): δ = 1.05 [s, 9H, $C(CH_3)_3$], 1.15 (d, J = 6.5 Hz, 3H, 4-H), 4.47–4.58 (m, 1H, 3-H), 5.99 (dd, J_1 = 8 Hz, J_2 = 1H, 1H, 1-H), 6.30 (dd, J_1 = 8 Hz, J_2 = 7.5 Hz, 1H, 2-H), 7.28–7.40 (m, 3H, aromatic H), 7.62–7.70 (m, 2H, aromatic H). – GLC/MS (t_r = 16.7 min): m/z (%) = 381 (6) [$M^+ - C_4H_7$], 380 (22) [$M^+ - C_4H_8$], 379 (100) [$M^+ - C_4H_9$], 309 (36) [$M^+ - I$], 301 (12) [$M^+ - C_{10}H_{15}$], 249 (10) [$M^+ - C_4H_{10}I$], 209 (17), 199 (55) [$C_4H_8IO^+$, $C_{12}H_{11}OSi^+$], 181 (23) [$C_4H_6I^+$, $C_{12}H_9Si^+$], 105 (15), 77 (21) [$C_6H_5^+$], 57 (8) [$C_4H_9^+$], 53 (14) [$C_4H_5^+$], 45 (16) [$C_2H_5O^+$], 43 (27) [$C_3H_7^+$].

$C_{20}H_{25}IOSi$ (436.4) Calcd. C 55.05 H 5.77
Found C 55.75 H 5.98

(2R,3Z)-4-Iodo-4-phenyl-3-buten-2-ol* (**37e**): Available from 4-phenyl-3-butyn-2-ol according to ref.[44].

(1Z,3R)-1-Iodo-3-[(2-methoxyethoxy)methoxy]-1-phenyl-butene* (**37d**): Vinyl iodide **37e** (5.50 g, 20 mmol) is treated with ethyldiisopropylamine (11.6 g, 30 mmol) and MEM chloride (7.47 g, 30 mmol) in the same way as described for **37a**. The crude product is distilled under reduced pressure to yield 5.95 g (82%) of **37d**, bp 112–117°C/0.001 Torr. The product should be kept in a freezer at –28°C. – ^1H NMR (250 MHz): δ = 1.37 (d, J = 6.5 Hz, 3H, 4-H), 3.42 (s, 3H, OCH_3), 3.57–3.62 (m, 2H, OCH_2CH_2O), 3.68–3.92 (m, 2H, OCH_2CH_2O), 4.61 (dq, J_d = 7.5 Hz, J_q = 6.5 Hz, 1H, 3-H), 4.77–4.85 (pseudo q, 2H, OCH_2O), 5.97 (d, J = 7.5 Hz, 1H, 2-H), 7.27–7.37 (m, 3H, aromatic H), 7.45–7.51 (m, 2H, aromatic H). – IR (neat): $\tilde{\nu}$ = 2980 cm^{-1}, 2935, 2885, 1135, 1110, 1080, 1030, 760, 695. – GLC/MS (t_r = 13.9 min): m/z (%) = 286 (2) [$M^+ - C_3H_8O_2$], 273 (7) [$M^+ - C_4H_9O_2$], 257 (6) [$M^+ - C_4H_9O_3$], 159 (12) [$M^+ - C_3H_8IO_2$], 131 (23) [$M^+ - C_4H_8IO_3$], 130 (26) [$M^+ - C_4H_9IO_3$], 129 (22), 128 (13), 115 (20) [$C_9H_7^+$], 89 (51) [$C_4H_9O_2^+$], 77 (6) [$C_6H_5^+$], 59 (100) [$C_3H_7O^+$], 51 (6) [$C_4H_3^+$], 45 (24) [$C_2H_5O^+$], 44 (5), 43 (22) [$C_3H_7^+$, $C_2H_3O^+$].

$C_{14}H_{19}IO_3$ (362.2) Calcd. C 46.43 H 5.29
Found C 47.10 H 5.41

(1E,3S)-3-[(2-Methoxyethoxy)methoxy]-1-(methylthio)-1-butene (**37f**): Available from **10b** according to ref.[23].

(1E,3S)-3-[(2-Methoxyethoxy)methoxy]-1-butenyl Phenyl Sulfone (**37g**) *via Dimethyl (Phenylsulfonemethyl)phosphonate* (**50b**): A solution of **50a** (6.97 g, 30 mmol), available from (phenylthio)methyl chloride and trimethyl phosphite[45], in 30 ml of dichloromethane is stirred at 0°C, and 85% 3-chloroperbenzoic acid (15.3 g, 75 mmol), dissolved in 150 ml of dichloromethane, is added within 50 min. The mixture is kept at 0°C for 40 h and the precipitate is separated by filtration and washed with 200 ml of ice-cold dichloromethane. The combined filtrates are washed successively twice with a 10% aqueous solution of $NaHSO_3$, twice with a satd. aqueous solution of NH_4Cl, and with water and dried with $MgSO_4$. The solvent is removed in a rotary evaporator and the residue subjected to vacuum (0.001 Torr) at 50°C for 30 min. The crude product **50b** (7.47 g, 94%), which is contaminated with methyl phenyl sulfone (originating from an impurity of thioanisol), is used in the following step without further purification. – ^1H NMR (250 MHz): δ = 3.69 (d, J = 9.5 Hz, 3H, OCH_3), 3.75 (d, J = 16.5 Hz, 2H, CH_2), 7.44–7.64 (m, 3H, aromatic H), 7.83–7.94 (m, 2H, aromatic H). – GLC/MS (t_r = 3.3 min): m/z (%) = 201 (3), 200 (29) [$M^+ - C_2H_8O_2$], 199 (13%), 155 (23) [$M^+ - C_2H_6O_3P$], 125 [$C_3H_{10}O_3P^+$], 109 (23) [$C_2H_6O_3P^+$], 104 (81) [$C_3H_4O_2S^+$], 94 (49)

$[CH_3O_3P^+]$, 91 (96) $[C_2H_6O_2P^+]$, 79 (41) $[CH_3O_2S^+]$, 77 (100) $[C_6H_5^+]$, 51 (57) $[C_4H_3^+]$.

A solution of crude **50b** (8.14 g, 24.60 mmol) in 70 ml of THF is stirred under nitrogen in a 250-ml two-necked flask at −95°C. A 1.6 M solution of *n*-butyllithium in *n*-hexane (14.4 ml, 23.04 mmol) is added dropwise within 15 min, and stirring is continued at −105°C for 1 h. Aldehyde **10b** (3.82 g, 23.55 mmol), dissolved in 10 ml of THF, is injected within 5 min, whereby the temperature is kept at −105°C by dipping the flask into a liquid-nitrogen bath for a short period. Stirring is continued at −105°C for 30 min, at −78°C for 5 min, and finally at room temperature for 60 h. A satd. aqueous solution of NH_4Cl (70 ml) is added to the mixture which is transferred to a separatory funnel containing 400 ml of diethyl ether. The organic layer is separated, washed thrice with water and brine, dried with $MgSO_4$, and concentrated in a rotary evaporator. In order to remove methyl phenyl sulfone, the crude product is evaporated at 60°C/0.001 Torr for 3 h, cooling the receiving flask in a bath of liquid nitrogen. The residue is purified by chromatography in a water-cooled column on 300 g silica gel. The obtained product is first eluated with dichloromethane and thereafter with diethyl ether/dichloromethane (1:1) to yield 6.30 g (92% relative to *n*-butyllithium) of **37g**, the (*E*):(*Z*) ratio of which is determined to be 40:1 according to the ^{1}H-NMR spectrum. − $[\alpha]_{589}^{20} = -49.4$, $[\alpha]_{578}^{20} = -51.3$, $[\alpha]_{546}^{20} = -58.4$, $[\alpha]_{436}^{20} = -101.5$, $[\alpha]_{365}^{20} = -163.1$ (*c* = 1.4, 95% aqueous ethanol). − IR (neat): $\tilde{\nu}$ = 3060 cm^{-1}, 2980, 2935, 2890, 2820, 1445, 1320, 1305, 1145, 1100, 1085, 1035, 970, 930 845, 820, 755, 725, 715, 690.

37g (major product): ^{1}H NMR (250 MHz): δ = 1.24 (d, *J* = 7.5 Hz, 3H, 4-H), 3.27 (s, 3H, OCH_3), 3.40−3.70 (m, 4H, OCH_2CH_2O), 4.32−4.43 (m, 1H, 3-H), 4.57−4.67 (pseudo q, 2H, OCH_2O), 6.44−6.51 (m, 1H, 1-H), 6.81−6.90 (m, 1H, 2-H), 7.60−7.68 (m, 3H, aromatic H), 7.87−7.93 (m, 2H, aromatic H). − GLC/MS (t_r = 16.1 min): *m/z* (%) = 227 (1) $[M^+ - C_4H_9O]$, 225 (1) $[M^+ - C_3H_7O_2]$, 212 (1), 211 (2) $[M^+ - C_4H_9O_2]$, 196 (23) $[M^+ - C_4H_8O_3]$, 195 (15) $[M^+ - C_4H_9O_3]$, 129 (12), 125 (82) $[M^+ - C_7H_9SO_3]$, 97 (16), 89 (37) $[C_4H_9O_2^+]$, 83 (10) $[C_5H_7O^+]$, 77 (23) $[C_6H_5^+]$, 59 (100) $[C_3H_7O^+]$, 51 (16) $[C_4H_3^+]$, 45 (62), $[C_2H_3O^+]$.

(*Z*) isomer (minor product): ^{1}H NMR (250 MHz): Differs from that of **37g** in: δ = 1.31 (d, *J* = 7.5 Hz, 3H, 4-H), 4.63−4.70 (pseudo q, 2H, OCH_2O), 5.93−6.50 (m, 2H, 2-H, 1-H). − GLC/MS (t_r = 15.1 min): Differs from that of **37g** with respect to the intensities of several peaks.

$C_{14}H_{20}SO_5$ (300.4) Calcd. C 55.98 H 6.71
Found C 55.89 H 6.65

(1R,2Z,4S*)- and (1R*,2Z,4R*)-4-[(2-Methoxyethoxy)methoxy]-1-phenyl-2-penten-1-ol* (**25a** and **26a**) *from* **37a**: A solution of 0.86 g (3.0 mmol) of vinyl iodide **37a** in 10 ml of THF is added with a syringe to a mixture of 4.00 ml (6.4 mmol) of a 1.6 M solution of *tert*-butyllithium in *n*-pentane and 50 ml of THF and stirred at −95°C under nitrogen. Thereby the temperature should not exceed −95°C. Stirring is continued for 20 min, and 0.61 ml (9.0 mmol) of benzaldehyde is injected. After the mixture has been stirred at the same temperature for another 20 min, 1.2 ml of a 5 M solution of acetic acid in THF is added. The mixture is transferred to a separatory funnel containing 400 ml of diethyl ether. The organic layer is washed several times with 50 ml portions of water and brine and dried with $MgSO_4$. The solvent is removed in a rotary evaporator, and the oily residue is exposed to vacuum (0.01 Torr) at 50°C to yield 0.78 g (99%) of a crude mixture of **25a**/**26a** which is purified by preparative TLC [silica gel; diethyl ether/hexane (1:1); R_f = 0.15]. The product, thus isolated in 65% yield, is shown to consist of **25a**/**26a** according to the ^{1}H-NMR spectrum (see above for the corresponding data). The ratio **25a**/**26a** is found to be 1:1.2. In an analogous way are also prepared:

(1R,2Z,3S*)- and (1R*,2Z,3R*)-4-(tert-Butyldiphenylsilyloxy)-1-phenyl-2-penten-1-ol* (**39** and **40**) (mixture of diastereomers): Obtained by treatment of **37b** (0.7 g, 1.6 mmol) with *tert*-butyllithium (1.7 M solution in *n*-pentane, 2.8 ml, 4.5 mmol) and subsequent reaction with benzaldehyde (0.2 g, 2.0 mmol). The diastereomeric mixture of **39**/**40** is isolated in 61% yield (0.4 g) after preparative TLC [silica gel; diethyl ether/hexane (1:1); R_f = 0.70]; ratio of diastereomers 1.6:1. − IR (neat): $\tilde{\nu}$ = 3680 cm^{-1}, 3610, 3440, 3020, 2970, 2940, 2900, 2870, 1430, 1110, 830, 700. − MS: *m/z* (%) = 255 (6) $[M^+ - C_{11}H_{13}O]$, 254 (23) $[M^+ - C_{11}H_{14}O_2]$, 253 (100) $[M^+ - C_{11}H_{15}O_2]$, 200 (12), 199 (66) $[C_{12}H_{11}OSi^+]$, 197 (11), 181 (17) $[C_{12}H_9Si^+]$, 175 (83) $[C_{10}H_{11}OSi^+]$, 77 (25) $[C_6H_5^+]$, 45 (15) $[C_2H_5O^+]$.

Major diastereomer: ^{1}H NMR (250 MHz): δ = 0.91 (d, *J* = 6.5 Hz, 3H, 5-H), 1.02 [s, 9H, $C(CH_3)_3$], 2.00 (s, 1H, OH), 3.83−3.95 (m, 1H, 4-H), 4.92−6.62 (4 m, 3H, 1-H, 2-H, 3-H), 7.25−7.75 (m, 5H, aromatic H).

Minor diastereomer: ^{1}H NMR (250 MHz): Differs in: δ = 1.14 (d, *J* = 6.5 Hz, 3H, 5-H), 1.07 [s, 9H, $C(CH_3)_3$], 4.27−4.36 (m, 1H, 4-H).

$C_{27}H_{32}O_2Si$ (416.6) Calcd. C 77.84 H 7.74
Found C 77.27 H 7.91

(1R,2Z,4S*)- and (1R*,2Z,4R*)-4-[(2-Methoxyethoxy)methoxy]-1,2-diphenyl-2-penten-1-ol* (**43** and **44**) (mixture of diastereomers): Prepared by treatment of **37d** (1.08 g, 3.0 mmol) with *tert*-butyllithium (1.6 M solution in *n*-pentane, 4.0 ml, 6.4 mmol) (−105°C, 10 min) and subsequent reaction with benzaldehyde (0.35 g, 3.3 mmol) (−105°C, 2 h). The diastereomeric mixture of **43**/**44** is isolated in 84% yield (0.86 g) after preparative TLC [silica gel; diethyl ether/hexane (1:1); R_f =0.3]; ratio of diastereomers 5.5:1. − MS: *m/z* (%) = 237 (23) $[M^+ - C_4H_9O_3]$, 236 (100) $[M^+ - C_4H_{10}O_3]$, 235 (27), 221 (37) $[M^+ - C_4H_9O_4]$, 193 (23) $[M^+ - C_6H_{13}O_4]$, 131 (18) $[C_{10}H_{11}^+]$, 130 (18) $[C_{10}H_{10}^+]$, 129 (30) $[C_{10}H_9^+]$, 115 (38) $[C_9H_7^+]$, 105 (95) $[C_4H_9O_3^+]$, 91 (25) $[C_7H_7^+]$, 89 (25) $[C_4H_9O_2^+]$, 77 (39) $[C_6H_5^+]$, 59 (83) $[C_3H_7O^+]$, 45 (27) $[C_2H_5O^+]$, 43 (51) $[C_3H_7^+, C_2H_3O^+]$.

Major diastereomer: ^{1}H NMR (250 MHz): δ = 1.12 (d, *J* = 6.5 Hz, 3H, 5-H), 3.89 (d, *J* = 3.5 Hz, OH), 3.38 (s, 3H, OCH_3), 3.53−3.60 (m, 2H, OCH_2CH_2O), 3.68−3.78 (m, 2H, OCH_2CH_2O), 4.73−4.87 (pseudo q, 2H, OCH_2O), 4.74−4.91 (m, 1H, 4-H), 5.63 (d, *J* = 10 Hz, 1H, 3-H), 5.82 (d, *J* = 3.5 Hz, 1H, 1-H), 7.12−7.43 (m, 10H, aromatic H). Minor diastereomer: ^{1}H NMR (250 MHz): Differs in δ = 1.42 (d, *J* = 6.5 Hz, 3H, 5-H), 1.82 (s, 1H, OH), 3.35 (s, 3H, OCH_3), 4.73−4.87 (m, 3H, OCH_2O, 4-H), 5.67 (d, *J* = 10 Hz, 1H, 3-H), 6.17 (s, 1H, 1-H).

$C_{21}H_{26}O_4$ (342.4) Calcd. C 73.66 H 7.65
Found C 73.81 H 7.72

(1R,2Z,4S*)- and (1R*,2Z,4R*)-1-Phenyl-2-pentene-1,4-diol* (**41** and **42**): A mixture of 0.99 g (5.00 mmol) of **37c** and 100 ml of THF is stirred in a 250-ml two-necked flask at −95°C under nitrogen. Within 15 min, 3.20 ml (5.00 mmol) of a 1.6 M solution of *n*-butyllithium in *n*-hexane is added with a syringe. Stirring is continued at −78°C for 30 min and at −40°C for 10 min. Thereafter, 6.20 ml (11.8 mmol) of a 1.9 M solution of *tert*-butyllithium in *n*-pentane is added whereby the temperature is not allowed to exceed −95°C. After stirring for 5 min, a solution of 0.66 ml (6.50 mmol) of benzaldehyde in 5 ml of THF is added slowly. The mixture is stirred at −95°C for 30 min and at −78°C for 20 min, treated with 20 ml of a satd. aqueous solution of NH_4Cl and allowed to reach room temperature. Thereafter, the solution is poured into a separatory funnel containing 50 ml of water and extracted twice

with a total amount of 200 ml of a 1:1 mixture of diethyl ether and ethyl acetate. The combined organic layers are washed five times with 50-ml portions of brine, dried with $MgSO_4$, and concentrated in a rotary evaporator. The residue is distilled under reduced pressure to give 0.66 g (74%) of diastereomeric mixture of **41/42** as a colorless oil which solidifies spontaneously, bp 108°C/0.005 Torr, mp 54–56°C: ratio of diastereomers 1.68:1. – IR (neat): $\tilde{\nu}$ = 3410 cm^{-1}, 3010, 2985, 1460, 1035, 710.

Major diastereomer: ^1H NMR (250 MHz): δ = 1.17 (d, J = 6.2 Hz, 3H, 5-H), 4.67–4.78 (m, 1H, 4-H), 5.44–5.62 (m, 3H, 1-H, 2-H, 3-H), 7.18–7.31 (m, 5H, aromatic H). – GLC/MS (t_r = 8.3 min): m/z (%) = 161 (3) [M^+ – HO], 160 (24) [M^+ – H_2O], 118 (13), 117 (100) [M^+ – $C_2H_5O_2$], 116 (12), 115 (53), [M^+ – $C_2H_7O_2$], 91 (19) [$C_7H_7^+$], 77 (3) [$C_6H_5^+$], 43 (96) [$C_3H_7^+$, $C_2H_3O^+$].

Minor diastereomer: ^1H NMR (250 MHz): Differs in: δ = 1.25 (d, J = 6.2 Hz, 3H, 5-H), 7.18–7.39 (m, 5H, aromatic H). – GLC/MS (t_r = 6.5 min): Differs from that of the main diastereomer with respect to the relative intensity of peaks.

$C_{11}H_{14}O_2$ (178.2) Calcd. C 74.13 H 7.92
Found C 74.27 H 7.91

(1R,2Z,4S*)- and (1R*,2Z,4R*)-1,2-Diphenyl-2-pentene-1,4-diol* (**45** and **46**): A solution of 3.0 mmol of lithium diisopropylamide in THF is generated by the addition of 1.90 ml (30 mmol) of a 1.6 M solution of *n*-butyllithium in *n*-hexane to 0.46 ml (3.2 mmol) of diisopropylamine, dissolved in 25 ml of THF, at –78°C under nitrogen and subsequent stirring at –20°C for 15 min. The mixture is cooled to –78°C, and 0.82 g (3.0 mmol) of vinyl iodide **37e**, dissolved in 10 ml of THF, is added dropwise with a syringe. Thereafter, the mixture is allowed to reach room temperature, and the solvent is evaporated by using the combined nitrogen/vacuum line at 0.001 Torr in order to remove diisopropylamine. The pasty residue is dissolved in 100 ml of THF, the solution is cooled and transferred through a cannula to a second flask, which contains 4.30 ml (6.8 mmol) of a 1.6 M solution of *tert*-butyllithium in *n*-pentane diluted with 100 ml of THF. The solution of *tert*-butyllithium is precooled to –105°C, and the temperature is not allowed to exceed –95°C during the additon. Stirring is continued for 10 min, and benzaldehyde (0.60 g, 60 mmol) is added at –105°C. The mixture is stirred at the same temperature for 2 h, and 2 ml of a 5 M solution of acetic acid in THF is injected. After having reached room temperature, the mixture is poured into a separatory funnel containing 300 ml of diethyl ether, washed twice with water and brine, and dried with $MgSO_4$. The solvent is removed in a rotary evaporator, and the residue is purified by preparative TLC [silica gel; ethyl acetate/chloroform/hexane (7:3:3); R_f = 0.45], which does not bring about an enrichement of one of the diastereomers. The diastereomers ratio of the product **45/46** thus obtained in 89% yield (0.47 g) is 1.5:1. – MS: m/z (%) = 237 (10) [M^+ – HO], 236 (57) [M^+ – H_2O], 221 (16) [M^+ – H_3O_2], 194 (17), 193 (76) [M^+ – C_2H_5O], 191 (11), 178 (30) [M^+ – C_6H_4], 165 (12), 129 (14) [$C_{10}H_9^+$], 128 (11), 115 (100) [$C_9H_7^+$], 105 (32) [$C_7H_5O^+$], 91 (27) [$C_7H_7^+$], 77 (22) [$C_6H_5^+$], 51 (16) [$C_4H_3^+$], 43 (58) [$C_2H_3O^+$, $C_3H_7^+$].

Major diastereomer: ^1H NMR (250 MHz): δ = 1.40 (d, J = 6.5 Hz 3H, 5-H), 3.05 (s, 2H, OH), 4.93 (qd, J_d = J_q = 6.5 Hz, 1H, 4-H), 5.83 (d, J = 8.5 Hz, 1H, 3-H), 6.03 (s, 1H, 1-H). 7.18–7.43 (m, 10H, aromatic H).

Minor diastereomer: ^1H NMR (250 MHz): Differs in: δ = 1.30 (d, J = 6.5 Hz, 3H, 5-H), 4.78 (qd, J_d = J_q = 6.5 Hz, 1H, 4-H), 5.87 (s, 1H, 1-H).

$C_{17}H_{18}O_2$ (254.3) Calcd. C 80.28 H 7.13
Found C 79.91 H 7.29

(1R,2E,4S*)- and (1R*,2E,4R*)-2-(Benzenesulfonyl)-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-penten-1-ol* (**47** and **48**): A mixture of 0.90 g (3 mmol) of sulfone **37g** and 50 ml of THF is combined with a solution of 3 mmol of lithium diisopropylamide in 25 ml of THF as outlined in the procedure for the preparation of **45/46**. Thereafter, the mixture is cooled to –95°C, treated with 0.50 g (5 mmol) of benzaldehyde, and stirred at –78°C for 12 h. A 5 M solution (2 ml) of acetic acid in THF is added to the mixture which is poured into a separatory funnel containing 300 ml of diethyl ether. The organic layer is washed twice with a total amount of 100 ml of water, 50 ml of a satd. aqueous solution of $NaHCO_3$, and 50 ml of brine and dried with $MgSO_4$. The solvent is removed in a rotary evaporator, and the residue is exposed to high vacuum (0.001 Torr) at 60°C for 2 h to give a crude diastereomeric mixture of **47/48** in 94% yield (1.15 g). The diastereomers, whose ratio is determined to be 1.05:1, may be separated by preparative TLC (silica gel; diethyl ether). – IR (neat): $\tilde{\nu}$ = 3520 cm^{-1}, 3440, 3035, 3015, 2940, 2900, 1450, 1320, 1310, 1160, 1140, 1105, 1085, 1040, 910, 700, 690.

Major diastereomer: R_f = 0.5. – ^1H NMR (90 MHz): δ = 0.91 (d, J = 6.5 Hz, 3H, 5-H), 3.22 (s, 3H, OCH_3), 3.29–3.59 (m, 4H, OCH_2CH_2O), 3.87–4.07 (s, 1H, OH), 4.33–4.67 (m, 1H, 4-H), 4.50–4.61 (pseudo q, 2H, OCH_2O), 5.63 (d, J = 3.5 Hz, 1H, 1-H), 6.84 (d, J = 9 Hz, 1H, 3-H), 7.11 (s, 5H, aromatic H), 7.02–7.74 (m, 5H, aromatic H). – GLC/MS (t_r = 23 min): m/z (%) = 301 (4) [M^+ – $C_4H_9O_3$], 300 (25) [M^+ – $C_4H_{10}O_3$], 232 (18), 217 (20), 188 (77), 159 (25) [$C_{11}H_9O^+$], 158 (76), 145 (17) [$C_{10}H_7O^+$], 143 (15) [$C_{11}H_9^+$], 141 (10) [$C_6H_5SO_2^+$], 131 (13) [$C_9H_7O^+$], 130 (32), 129 (44), 116 (62), 115 (100) [$C_9H_7^+$], 105 (42) [$C_4H_9O_3^+$, $C_7H_5O^+$], 91 (14) [$C_7H_7^+$], 89 (19) [$C_4H_9O_2^+$], 77 (75) [$C_6H_5^+$], 51 (34) [$C_4H_3^+$], 43 (79).

Minor diastereomer: R_f = 0.6. – ^1H NMR (90 MHz): Differs in: δ = 1.21 (d, J = 6.5 Hz, 3H, 5-H), 3.25 (s, 3H, OCH_3), 3.33–3.59 (m, 4H, OCH_2CH_2O), 4.31–4.48 (pseudo q, 2H, OCH_2O), 5.72 (d, J = 3.5 Hz, 1H, 1-H), 6.94 (d, J = 9 Hz, 1H, 3-H), 7.06 (s, 5H, aromatic H), 7.11–7.67 (m, 5H, aromatic H). – GLC/MS (t_r = 22.6 min): Differs form that of the major isomer with respect to the relativ intensity of several peaks.

$C_{21}H_{26}O_6S$ (406.5) Calcd. C 62.05 H 6.45
Found C 63.33 H 7.02

(1S,2E,4S)-, (1R,2E,4S)-, (1S,2Z,4S)-, and (1R,2Z,4S)-2-Bromo-4-(ethoxymethoxy)-1-phenyl-2-buten-1-ol (**56**, **57**, **58**, and **59**): Prepared from **53** (864 mg, 3.0 mmol) according to G. P. 1. By preparative TLC [silica gel; diethyl ether/hexane (2:3)], the mixture of the (*Z*) isomers **58/59** [R_f = 0.42; yield 94 mg (9.9%)] is separated from the mixture of the (*E*) isomers **56/57** [R_f = 0.51; yield 605 mg (64%)].

(*Z*) isomers **58/59**: GLC/MS (t_r = 11.35 min): m/z (%) = 240, 238 (14) [M^+ – $C_3H_8O_2$], 209 (5) [M^+ – $C_4H_9O_3$], 198 (11), 159 (44) [M^+ – $C_3H_8BrO_2$], 131 (36) [$C_9H_7O^+$], 116 (94) [$C_9H_8^+$], 107 (38) [$C_7H_7O^+$], 91 (32), 79 (42), 77 (61) [$C_6H_5^+$], 59 (100) [$C_3H_7O^+$], 53 (36), 51 (23), 43 (39) [$C_3H_7^+$].

Major diastereomer: ^1H NMR (300 MHz): δ = 1.21 (t, J = 7 Hz, 3H, OCH_2CH_3), 1.305 (d, J = 6.5 Hz, 3H, 5-H), 2.70 (d, J = 6.5 Hz, 1H, OH), 3.50–3.65 (m, 2H, CH_2CH_3), 4.675 (s, 2H, OCH_2O), 4.61–4.72 (m, 1H, 4-H), 5.27 (d, J = 6.5 Hz, 1H, 1-H), 6.19 (dd, J_1 = 8 Hz, J_2 = 1 Hz, 1H, 3-H), 7.30–7.48 (m, 5H, aromatic H).

Minor diastereomer: ^1H NMR (300 MHz): Differs in: δ = 1.213 (t, J = 7 Hz, 3H, OCH_2CH_3), 1.315 (d, J = 6.5 Hz, 3H, 5-H), 2.711 (d, J = 6.5 Hz, 1H, OH), 5.278 (d, J = 6.5 Hz, 1H, 1-H), 6.226 (dd, J_1 = 8 Hz, J_2 = 1H, 1H, 3-H).

(*E*) isomers **56**/**57**: IR (neat): $\tilde{\nu}$ = 3430 cm^{-1}, 2980, 2930, 2880, 1450, 1185, 1140, 1090, 1030, 700. – GLC/MS (t_r = 11.11 min): *m/z* (%) = 240, 238 (21, 20) [$M^+ - C_3H_8O_2$], 160 (14), 159 (100) [$M^+ - C_3H_8BrO_2$], 158 (47) [$M^+ - C_6H_5Br$], 144 (41) [$M^+ - C_4H_{11}BrO_2$], 131 (36) [$C_9H_7O^+$], 129 (22), 116 (28), 115 (41) [$C_9H_7^+$], 105 (25) [$C_7H_5O^+$], 91 (26), 79 (30), 77 (62) [$C_6H_5^+$], 59 (64) [$C_3H_7O^+$], 53 (39), 51 (24), 43 (43) [$C_3H_7^+$].

Major diastereomer: ^{1}H NMR (300 MHz): δ = 1.205 (t, *J* = 7 Hz, 3H, OCH_2CH_3), 1.305 (d, *J* = 6.5 Hz, 3H, 5-H), 3.39 (d, *J* = 6.5 Hz, 1H, OH), 3.50–3.70 (m, 2H, CH_2CH_3), 4.724 (pseudo q, 2H, OCH_2O), 4.83–4.92 (m, 1H, 4-H), 5.66 (d, *J* = 6.5 Hz, 1H, 1-H), 6.04 (d, *J* = 9.5 Hz, 1H, 3-H), 7.29–7.48 (m, 5H, aromatic H).

Minor diastereomer: ^{1}H NMR (300 MHz): Differs in: δ = 1.24 (t, *J* = 7 Hz, 3H, OCH_2CH_3), 1.355 (d, *J* = 6.5 Hz, 3H, 5-H), 4.72 (pseudo q, 2H, OCH_2O), 5.81 (d, *J* = 5 Hz, 1H, 1-H), 6.03 (d, *J* = 9.5 Hz, 1H, 3-H).

$C_{14}H_{19}BrO_3$ (315.2) Calcd. C 53.35 H 6.07
Found C 53.22 H 5.67

CAS Registry Numbers

10a: 86163-00-0 / **10b**: 86163-01-1 / **11**: 114091-68-8 / **12**: 132204-93-4 / **13** (H): 132204-94-5 / **14** (H): 132204-95-6 / **15a**: 114091-69-9 / **15b**: 114124-11-7 / **15c**: 114091-70-2 / **15d**: 114091-71-3 / **16a**: 114091-72-4 / **16b**: 114091-73-5 / **16c**: 114091-74-6 / **16d**: 114124-12-8 / **17**: 132204-96-7 / **18**: 132204-97-8 / **19**: 132204-98-9 / **20**: 132204-99-0 / **21**: 132205-00-6 / **22**: 132205-01-7 / **25a**: 114091-76-8 / **25b**: 132204-92-3 / **25c**: 132232-96-3 / **26b**: 132205-02-8 / **27a**: 25779-13-9 / **27b**: 2406-22-6 / **28**: 114614-81-2 / **31a**: 132232-69-0 / **31c**: 114091-77-9 / **32c**: 114091-79-1 / **33**: 132205-03-9 / **34a**: 116297-05-3 / **34b**: 132205-27-7 / **35**: 132295-70-6 / **36**: 132205-04-0 / **37a**: 132205-05-1 / **37b**: 132205-06-2 / **37c**: 132295-71-7 / **37d**: 132205-17-5 / **37e**: 132295-72-8 / **37g** (isomer 1): 132205-21-1 / **37g** (isomer 2): 132205-22-2 / **39**: 132205-07-3 / **40**: 132205-108-4 / **41**: 132205-09-5 / **42**: 132205-10-8 / **43**: 132205-11-9 / **44**: 132205-12-0 / **45**: 132205-13-1 / **46**: 132205-14-2 / **47**: 132205-15-3 / **48**: 132205-16-4 / **50a**: 70369-42-5 / **50b**: 132205-18-6 / **52a**: 132205-19-7 / **52b**: 132204-91-2 / **53**: 132205-20-0 / **56**: 132205-23-3 / **57**: 132205-24-4 / **58**: 132205-25-5 / **59**: 132205-26-6 / benzaldehyde: 100-52-7 / 2-methylpropanal: 78-84-2 / acetaldehyde: 75-07-0 / acetophenone: 98-86-2 / ethyl 2-oxopropanoate: 617-35-6 / 2,2-dimethylpropanal: 630-19-3

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[316/90]