(*R*)-1,2,2-Triphenyl-2-(trimethylsiloxy)ethyl Propionate: *anti*-Selective and Diastereofacially Selective Aldol Addition; Diastereoselective Silylation and Alkylation

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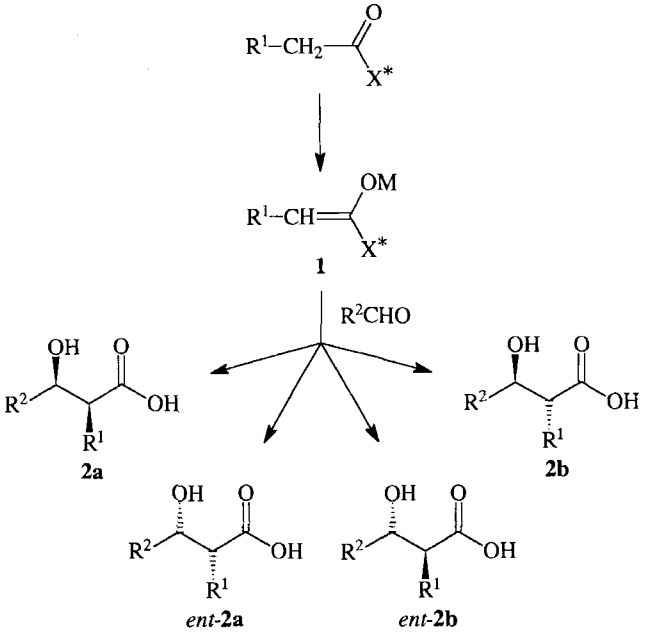
Received March 21, 1994

Key Words: Aldol reaction / Chiral enolate / Mandelic acid

The propionates (*R*)-**5** and (*R*)-**6** which are derived from the readily available chiral auxiliary reagent (*R*)-triphenylglycol (**4**) have been applied in stereoselective aldol reactions. Whereas the enolate **7** and the silyl ketene acetal **12**, both generated from the ester (*R*)-**6**, display only moderate diastereoselectivity when treated with benzaldehyde, β-hydroxyesters **8b** and **16a, b** are formed in diastereomeric ratios up to 95:5 (ratio of the main product to the sum of all other stereoisomers) when the propionate (*R*)-**5** is subsequently deprotonated, transmetalated into the zirconium enolate and allowed to react with aldehydes. Alkaline hydrolysis or reduction with $LiAlH_4$ enables the conversion of the adducts **8a** and **16a, b** into the carboxylic acid **15a** and the diols **17a, b**, respectively, which are obtained in >95% e.e. When the enolate **13** is treated with chlorotrimethylsilane, carbon silylation occurs so that the α-silyl propionate **18a** is formed diastereoselectively. On the other hand, alkylations of the enolate **13** with primary alkyl halides display only moderate diastereoselectivities. The structures of the propionate **5**, the α-silyl ester **18a**, and the alkylation product **18b** are proven unambiguously by crystal structure analyses.

The aldol addition, one of the most versatile methods for the formation of carbon-carbon bonds, has undergone a remarkable renaissance due to the recent development of numerous stereoselective variants[2]. Thus, chiral enolates **1** mainly derived from amides[3] and ketones[4] have turned out to provide both enantiomers of *syn*-carboxylic acids[5] **2a** and *ent*-**2a** in outstanding diastereomeric and enantiomeric purity. On the other hand, *anti*-selective[5] aldol additions which are able to deliver nonracemic β-hydroxycarbonyl compounds **2b** or *ent*-**2b** have been extremely rare for a long time. Only very recently, several solutions of this problem have been found which are satisfactory with respect to chemical yield and stereoselectivity[2g,h]. Thereby, the chiral information which is indispensable in order to discriminate the enantiotopic faces of an aldehyde and the diastereotopic faces of the enolate ("diastereofacial selectivity") is located either in a covalently bound auxiliary group X*[6] or in the ligands attached to the metal M[7]. In the latter approach, both stoichiometric and catalytic variants have been elaborated very recently.



Several years ago, we reported[8] on acetate aldol additions which rely on the chiral ester **3** ("HYTRA") derived from triphenylglycol (**4**). Meanwhile, HYTRA has found wide acceptance for syntheses of enantiomerically pure natural products and drugs[9]. Since both enantiomers of triphenylglycol are very readily available from the bulk chemicals (*R*)- and (*S*)-mandelic acid, we decided to study triphenylglycol-derived propionates in order to induce *anti*-selective aldol reactions. In this paper, we report on the chiral reagent 1,2,2-triphenyl-2-(trimethylsiloxy)ethyl propionate [(*R*)-**5**] which is found to provide both high *anti*:*syn* selectivity ("simple diastereoselection") as well as diastereofacial selectivity (predominant formation of **2b** compared to *ent*-**2b**[10]). A brief study of silylations and alkylations of the deprotonated ester **5** is included as well.

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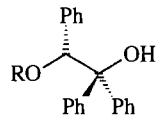
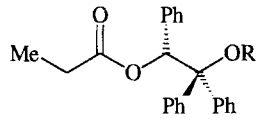


(*R*)-**3**: R = MeCO
(*R*)-**4**: R = H



(*R*)-**5**: R = $SiMe_3$
(*R*)-**6**: R = H

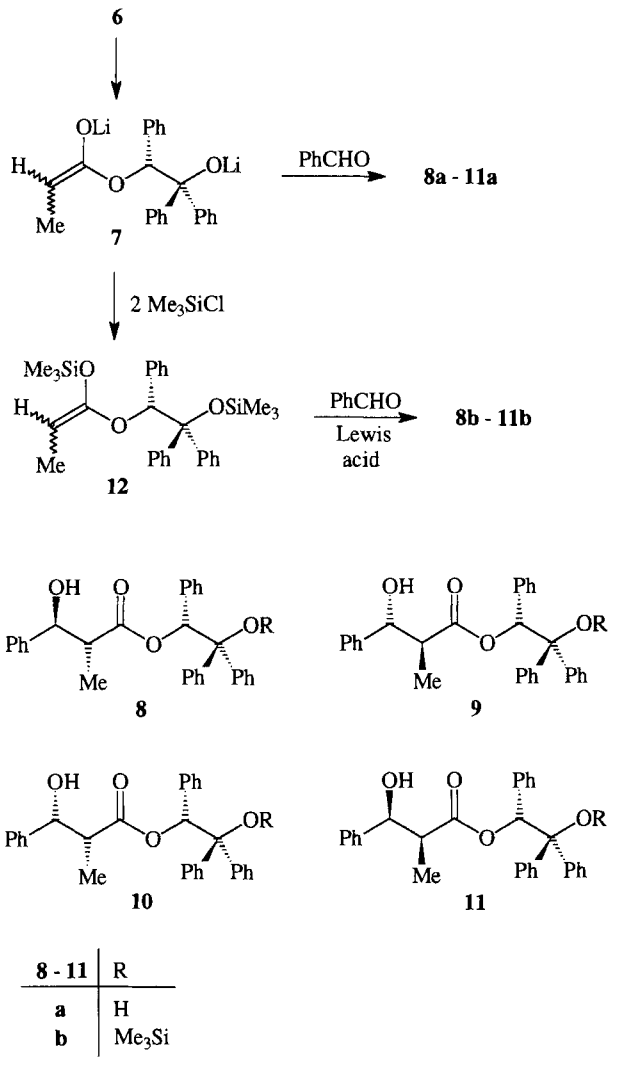
Aldol Additions of (*R*)-2-Hydroxy-1,2,2-triphenylethyl Propionate

2-Hydroxy-1,2,2-triphenylethyl propionate [(*R*)-**6**] is prepared in 96% yield by the reaction of propionyl chloride with triphenylglycol (*R*)-**4**, itself available from methyl mandelate and phenylmagnesium bromide[11]. Thereby, the secondary hydroxy group is esterified exclusively. When the ester **6** is treated with two equivalents of lithium diisopropylamide, the formation of the enolate **7** results. The subsequent addition of benzaldehyde affords the four diastereomers **8a**, **9a**, **10a**, and **11a** in both disappointing simple diastereoselection (*anti*-**8a**/**9a**: *syn*-**10a**/**11a**) and low diastereofacial selectivity for the *anti* isomers (**8a**:**9a** = 68:32) as shown in Table 1 (entry 1). A transmetalation of the lithium enolate **7** with dichlorobis(cyclopentadienyl)zirconium enhances the diastereofacial selectivity, but the *anti*-to-*syn* ratio is still unsatisfactory (entry 2). Being aware that the Mukaiyama variation of the aldol addition often brings about a significant increase of stereoselectivity[12], we investigated the Lewis acid-mediated reaction of benzaldehyde with the silyl ketene acetal **12**. The intermediate **12** is generated from **6** by treatment of the lithium enolate **7** with two equivalents of chlorotrimethylsilane. Thereby, not only the former carbonyl oxygen atom is silylated but the tertiary alkoxy group as well. When the silyl ketene acetal **12** is allowed to react with benzaldehyde, the *anti*-to-*syn* ratio (**8b**/**9b**:**10b**/**11b**) reaches 90:10, but the diastereofacial selectivity (**9b**:**8b**) does not surpass 87:13 (entry 3). It is remarkable that the major isomer **9b** formed has the *2S,3R* configuration in the carbon chain of its carboxylic moiety whereas the lithium enolate affords predominantly the *2R,3S* diastereomer. When the Mukaiyama reaction of the ketene acetal **12** is mediated by boron trifluoride–ether, the *anti*-to-*syn* ratio increases substantially. This result is paid by a decrease of diastereofacial selectivity (entries 4 and 5).

Preparation, Structure, and Aldol Reactions of (*R*)-1,2,2-Triphenyl-2-(trimethylsiloxy)ethyl Propionate

Obviously, the concept of doubly metalated enolates, which has proven to be fruitful in the case of the acetate aldol addition of **3**[8,13], fails in the corresponding reaction of the propionate **6**. Thus, we assumed that a bulky, sterically demanding *O*-protecting group would be able to effect steric discrimination rather than double metalation. As a consequence, 1,2,2-triphenyl-2-(trimethylsiloxy)ethyl propionate [(*R*)-**5**] was prepared and submitted to aldol reactions.

Since the tertiary hydroxy group of the propionate **6** cannot be silylated directly, a detour is necessary in order to obtain **5**. For this purpose, the ester **6** is first doubly metalated and subsequently treated with chlorotrimethylsilane to



8-11	R
a	H
b	Me_3Si

Table 1. Adducts **8**–**11**, formed by the addition of propionates **5** and **6** and ketene acetal **12** to benzaldehyde

Entry	Enolate precursor/ additive		Adducts **8-11**[a] *anti* : *syn* diastereomeric ratio **8/9** : **10/11**	**8** : **9**
1	**6** / –	**a**	70 : 30	68 : 32
2	**6** / Cp_2ZrCl_2	**a**	78 : 22	91 : 9
3	**12** / $TiCl_4$	**b**	90 : 10	13 : 87
4	**12** / $BF_3{\cdot}OEt_2$[b]	**b**	94 : 6	13 : 87
5	**12** / $BF_3{\cdot}OEt_2$[c]	**b**	96 : 4	15 : 85
6	**5** / –	**b**	92 : 8	52 : 48
7	**5** / $MgBr_2$	**b**	91 : 9	48 : 52
8	**5** / Cp_2ZrCl_2[d]	**b**	90 : 10	> 97 : 3
9	**5** / Cp_2ZrCl_2[e]	**b**	87 : 13	> 97 : 3
10	**5** / Cp_2ZrCl_2[f]	**b**	56 : 44	96 : 4

[a] Crude yields of adducts **8**–**11** range from 87 to 95%. – [b] **12** is added to a mixture of benzaldehyde and $BF_3 \cdot OEt_2$. – [c] $BF_3 \cdot OEt_2$ is added to a mixture of **12** and benzaldehyde. – [d] 3 equivalents of Cp_2ZrCl_2. – [e] 1 equivalent of Cp_2ZrCl_2. – [f] Zirconium enolate stirred at −30°C for ca. 12 h.

give the ketene acetal **12** as outlined above. The latter intermediate is hydrolyzed with dilute hydrochloric acid to the desired propionate **5** in 90% yield from **6**.

An X-ray structure analysis is performed with a sample of **5** which has been recrystallized from a concentrated solution in petroleum ether. The crystal structure (Figure 1) reveals a remarkably long (1.59 Å) carbon-carbon distance of the triphenylethane moiety (C4–C5). This can be explained by the accumulation of sterically demanding substituents at vicinal carbon atoms, whereby the bulkiness of the trimethylsiloxy group seems to play an important role. The dihedral angle between the carbonyl group and the methyl residue of the propionate moiety amounts to 65.4°. As a consequence, one of the diastereotopic α-carbonyl hydrogen atoms (2-H_{ReR}) is located almost antiperiplanar relative to the carbonyl group (dihedral angle: −174.6°).

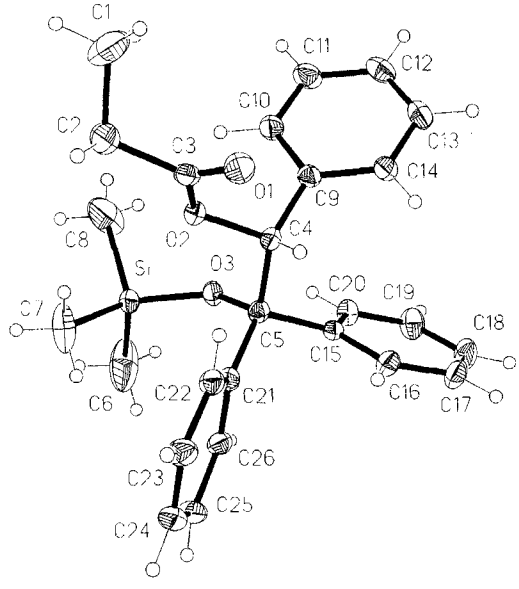
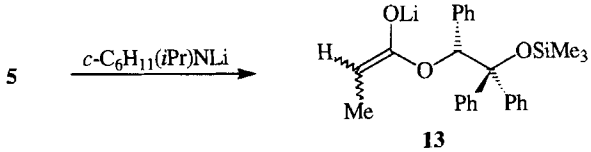


Figure 1. A view of the molecular structure of (*R*)-**5** in the crystal. Selected bond lengths [pm] and angles [°]: C(1)–C(2) 150.2(8), C(2)–C(3) 150.7(7), C(3)–O(1) 119.9(6), C(3)–O(2) 134.8(5), C(4)–O(2) 146.0(4), C(5)–O(3) 141.9(4), C(4)–C(5) 155.9(5), C(4)–C(9) 149.9(5), C(5)–C(15) 153.5(5), C(5)–C(21) 152.9(5), O(3)–Si(1) 164.3(3); Si(1)–O(3)–C(5) 138.7(2); H(2A)–C(2)–C(3)–O(1) −55.3(0.5), H(2A)–C(2)–C(3)–O(2) 125.3(0.3), H(2B)–C(2)–C(3)–O(1) −174.6(0.4), H(2B)–C(2)–C(3)–O(2) 5.9(0.4), C(1)–C(2)–C(3)–O(1) 65.4(0.6), C(4)–O(2)–C(3)–O(1) −8.1(0.6), O(2)–C(4)–C(5)–O(3) 56.4(0.3), C(9)–C(4)–C(5)–C(15) 51.6(0.4), Si(1)–O(3)–C(5)–C(4) −98.9(0.4)

When the enolate **13**, generated by treatment of the ester **5** with lithium diisopropylamide, is treated with benzaldehyde, the ratio of adducts *anti*-**8b/9b** : *syn*-**10b/11b** amounts to 92:8 (Table 1, entry 6). Unfortunately, the diastereofacial selectivity is disappointingly low and cannot be enhanced by transmetalation with magnesium bromide (entry 7). A significant improvement, however, is achieved by the in situ generation of a zirconium enolate. For this purpose, the propionate **5** is first deprotonated with lithium cyclohexylisopropylamide, and the lithium enolate **13** formed is transmetalated with three equivalents of dichlorobis(cyclopentadienyl)zirconium below −60°C. Finally, benzaldehyde is added to the yellow solution of the preformed zirconium enolate to give a 90-to-10 ratio of *anti*-**8b/9b** : *syn*-**10b/11b**. A remarkably high diastereofacial selectivity is reached in this reaction so that the ratio of **8b**:**9b** surpasses 97:3 (entry 8). A lower simple diastereoselection is found when equimolar amounts of the zirconium reagent are used for transmetallation (entry 9).



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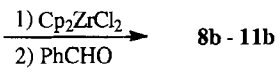
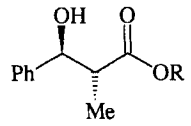
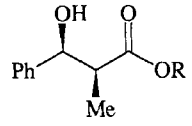


8b - 11b

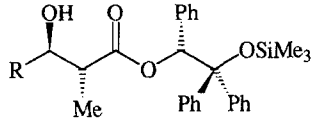


14a, b

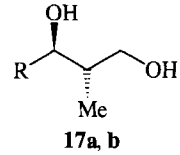


15a, b

14 - 15	R
a	H
b	Me



16a, b



17a, b

16 - 17	R
a	*i*Pr
b	*t*Bu

It seems to be plausible that the deprotonation of the propionate **5** leads to the predominant formation of the *E* (OLi) isomer of the lithium enolate **13** and that this kind of geometry is maintained after the treatment with dichlorobis(cyclopentadienyl)zirconium. When, on the other hand, the solution of the zirconium enolate is allowed to warm up to −30°C for 14 h, the simple diastereoselection vanishes almost completely in the subsequent aldol addition (entry 10). This may be interpreted in the light of the wellknown *E-anti*, *Z-syn* correlation[2] as a result of an *E-Z* interconversion of the zirconium enolate at higher temperatures. The diastereomeric ratio in the crude mixtures of **8b–11b** is determined by ^{1}H-NMR spectroscopy. Thus, the magnitude of the coupling constants of 2-H and 3-H differs in a characteristic way, and the larger value can be assigned to the *anti* diastereomers[2b]. On the other hand, the chemical shifts of 3-H are different in all of the four stereoisomers **8b**, **9b**, **10b**, and **11b**.

The conditions which have been found to effect the optimal stereoselectivity in the reaction of the enolate **13** with benzaldehyde are also applicable in the corresponding additions to 2-methylpropanal and 2,2-dimethylpropanal. It turns out that these aliphatic aldehydes display high degrees of both simple diastereoselection and diastereofacial selectivity. Thus, both adducts **16a** and **16b** are formed in >95:5 diastereoselectivity defined as the ratio of the main product to the total sum of all other stereoisomers. Here again, the diastereomeric purity is determined by ^{1}H-NMR spectroscopy.

Whereas the relative configuration of the carbon chain in the carboxylic acid moiety of the esters **8**–**11** and **14** can be assigned by the magnitude of the 2-H/3-H coupling constant, a conversion into compounds of known absolute configuration is necessary in order to determine the stereochemical outcome of this aldol reaction with respect to the diastereofacial selectivity. For this purpose, the crude mixture of adducts **8b**–**11b** (obtained according to entry 8 of Table 1) is hydrolysed with lithium hydroxide in aqueous methanol at room temperature. The carboxylic acids **14a**/**15a** obtained in this way are esterified without previous purification by treatment with diazomethane to give **14b**/**15b**. It turns out that the *anti*/*syn* ratio of the methyl esters **14b**:**15b** (86:14) is lower than that of the adducts **9a**:**9b** (*anti*:*syn* = 90:10). Obviously, partial epimerization occurs during the alkaline hydrolysis so that some of the isomeric acid **15a** forms at the expense of **14a**. The minor diastereomer **15b** is removed by column chromatography, and the main product **14b** is isolated as a pure diastereomer. Based on the comparison of the optical rotation[14], the absolute configuration of **14b** is determined to be *2R,3S*, and the optical purity is found to be 94% e.e. An independent determination of the enantiomeric excess by ^{1}H-NMR measurements in the presence of the chiral shift reagent Eu(hfc)$_3$[15] reveals 97% e.e.

The adducts **16a** and **16b** are submitted to $LiAlH_4$ reduction to deliver the diols **17a** and **17b**. Thereby, triphenylglycol (*R*)-**4** is removed by column chromatography, and the diastereomerically pure compounds **17a** and **17b** are obtained. By comparison of its optical rotation[16], the *2S,3R* configuration is assigned to the diol **17a**, and the enantiomeric excess is determined to be 95%. The latter value is confirmed by ^{19}F-NMR measurement of the diester, prepared from **17a** and Mosher's reagent[17]. In an analogous way, the absolute configuration (i.e. *2S,3S*) of **17b** is elucidated by comparison of its optical rotation ($[\alpha]_D^{25}$ = −5.1) with the reference data ($[\alpha]_D^{25}$ = −4.4[18]). Here again, the enantiomeric excess is determined independently by the preparation of the corresponding Mosher's ester[17], the ^{19}F-NMR spectra of which reveals the presence of a single diastereomer.

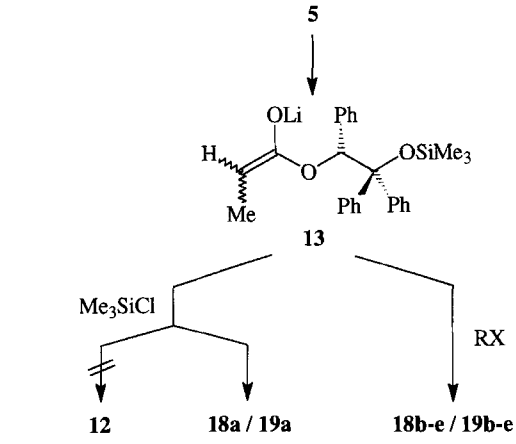
In all cases studied so far the zirconium enolate derived from silylpropionate (*R*)-**5** attacks almost exclusively the *Si* face of the aldehyde. Besides that high diastereofacial selectivity, acceptable simple diastereoselection is provided as well, so that the formation of *anti*-α-methyl-β-hydroxycarbonyl compounds **14** and *anti*-2-methyl-1,3-diols **17** results. In every case, the chiral auxiliary triphenylglycol (*R*)-**4** can be recovered and reused. Since both enantiomers of mandelic acid are bulk chemicals, (*S*)-**4** derived from (*S*)-mandelic acid is also readily available. Thus, the method disclosed opens an entry to enantiomeric acid *ent*-**14a** and diols *ent*-**17** as well. The high *anti* selectivity is quite remarkable because zirconium enolates usually are chosen in order to bring about the predominant formation of *syn* aldols[1a,3c], whereas *anti*-selective zirconium enolates are rare[19].

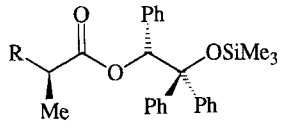
Silylation and Alkylations of (*R*)-1,2,2-Triphenyl-2-(trimethylsiloxy)ethyl Propionate

If a rationale will be given for the stereochemical outcome of the aldol reactions described above, the knowledge of the enolate geometry of **7** and **13** would be a prerequisite. The conversion of lithium enolates into the corresponding silyl enol ethers is a common[20] although not unambiguous[21] method for the assignment of either *Z* or *E* configuration to the enolate. For this purpose, the lithium compound **13** which forms upon deprotonation of the propionate **5** is allowed to react with chlorotrimethylsilane. Thereby, the formation of either *E*- or *Z*-silyl ketene acetal **12** has been anticipated. Surprisingly, an exclusive carbon silylation is observed instead of the expected oxygen silylation, so that the ketene acetal **12** does not arise at all. In contrast, α-silyl ester **18** is formed in a diastereoselective manner. Thus, the diastereomeric compounds **18a** and **19a** are obtained in a ratio of 94.5:5.5 according to the ^{1}H-NMR spectra. The main product, **18a**, is isolated as a pure stereoisomer upon recrystallization, and its configuration is determined by a crystal structure analysis (Figure 2). Obviously, the *1'R,2R* configuration has to be assigned to the predominant diastereomer **18a**.

It is not possible presently to offer a concise rationale for the high diastereoselectivity of the carbon silylation. Thus, it remains unclear whether *E* or *Z* enolate **13** is formed exclusively and reacts diastereoselectively in the subsequent silylation or whether a mixture of *E*- and *Z*-**13** affords the ester **18** in a stereoconvergent manner. In general, carbon silylations of ester enolates are rather uncommon[22] except for acetates and cyclopropanoic acid-derived esters[23]. When the preformed enolate **13** is treated with the "hard" electrophilic reagent trimethylsilyl trifluoromethanesulfonate instead of chlorotrimethylsilane, no oxygen silylation is observed either. Presumably, the very bulky alcoholic moiety of the ester **5** is directing the electrophile towards the α-carbon atom in any case. α-Silylcarbonyl compounds may serve as useful intermediates in asymmetric syntheses[24]. At a glance, it seems to be contradictory that the silyl ketene acetal **12** is formed in the silylation of the dilithium compound **7** whereas the lithium enolate **13** does not afford the same product. Therefore, one must assume that the monoanion **13** is not the intermediate in the conversion of the dianion **7** into the ketene acetal **12**.

Having in hand a procedure for the stereoselective carbon silylation of propionates, the investigation of the α-alkylation is a rather obvious idea[25]. Therefore, the lithium en-





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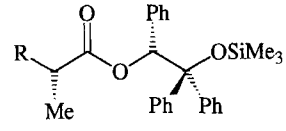
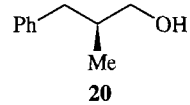


19

18, 19	R
a	Me_3Si
b	$PhCH_2$
c	$CH_2{=}CHCH_2$
d	*n*Bu
e	Et



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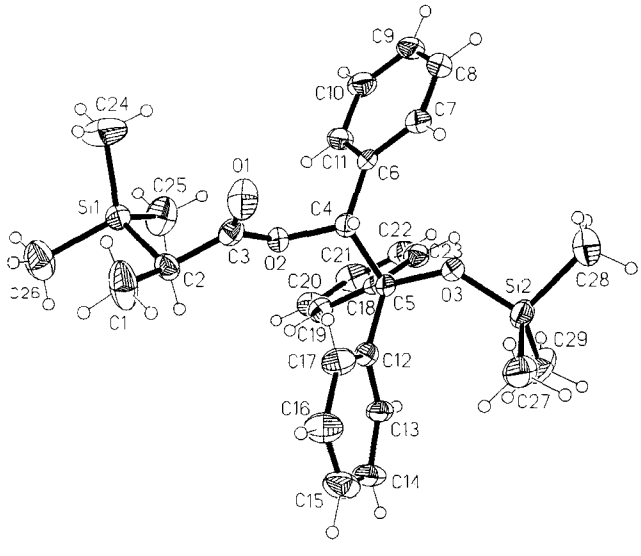

Figure 2. A view of the molecular structure of **18a** in the crystal. Selected bond lengths [pm] and angles [°]: C(1)–C(2) 153.3(7), C(2)–C(3) 148.4(7), C(2)–Si(1) 189.9(5), C(3)–O(1) 120.4(6), C(3)–O(2) 135.7(5), C(4)–O(2) 143.3(5), C(4)–C(5) 156.4(6), C(4)–C(6) 150.3(6), C(5)–C(12) 153.6(6), C(5)–C(18) 152.6(6), C(5)–O(3) 142.8(5), O(3)–Si(2) 165.1(3); C(5)–O(3)–Si(2) 135.7(2), C(3)–C(2)–Si(1) 113.2(3); H(2A)–C(2)–C(3)–O(1) –139.4(0.4), H(2A)–C(2)–C(3)–O(2) 39.9(0.4), Si(1)–C(2)–C(3)–O(1) 102.6(0.5), Si(1)–C(2)–C(3)–O(2) –78.2(0.4), C(1)–C(2)–C(3)–O(1) –23.1(0.7), O(1)–C(3)–O(2)–C(4) 14.4(0.6), O(2)–C(4)–C(5)–O(3) –177.5(0.3), C(6)–C(4)–C(5)–C(12) 177.2(0.4), C(4)–C(5)–O(3)–Si(2) 148.5(0.3)

olate **13**, which is generated by deprotonation of the propionate **5**, is treated with primary alkyl bromides and iodides to give α-branched esters **18b-e/19b–e** in 85–95% yield. The diastereomeric ratios of **18:19** listed in Table 2 are determined by ^{1}H-NMR spectroscopy of the crude mixtures. Table 2 reveals that acceptable diastereoselectivity is observed with benzyl bromide (entry 1) only, whereas allyl bromide and allyl iodide as well as butyl bromide, ethyl iodide, and ethyl bromide display moderate or poor diastereomeric ratios (entries 2–6). An excess of the alkyl halides turns out to be useful in order to bring about good chemical yields. On the other hand, the presence of additives like HMPA or DMPU is not necessary.

Table 2. Products **18b–e** and **19b–e** formed from deprotonated propionate **5** and primary alkyl halides

Entry	Alkyl halide	Products **18/19**	Diastereomeric ratio
1	$C_6H_5CH_2Br$	**b**	91 : 9
2	$CH_2{=}CH{-}CH_2Br$	**c**	85 : 15
3	$CH_2{=}CH{-}CH_2I$	**c**	85 : 15
4	$CH_3(CH_2)_3Br$	**d**	75 : 25
5	CH_3CH_2I	**e**	75 : 25
6	CH_3CH_2Br	**e**	75 : 25

The configuration of the main diastereomer **18b** obtained from the reaction with benzyl bromide is determined in two different ways. First, the crude mixture of **18b/19b** is reduced with $LiAlH_4$ to give 2-methyl-3-phenyl-1-propanol (**20**) whose absolute configuration is known[26]. Thus, a comparison of the optical rotation reveals the *S* configuration of the alcohol **20** and, as a consequence, the *1'R,2S* configuration of the main alkylation product **18b**. A second unambiguous proof for compound **18b** comes from an X-ray structure analysis which is shown in Figure 3. Despite the formal difference in the configuration of the α-carbon atom (*R* in **18a** versus *S* in **18b–e**) due to the change of priorities according to the Cahn-Ingold-Prelog nomenclature, all of the main diastereomers **18a–e** can be considered to be homochiral in as far as the electrophile replaces predominantly the *ReR* hydrogen atom of the propionate **5**, both in the silylation and in the alkylation reactions. On the other hand, the *SiR* hydrogen atom of the ester **5** has been substituted in the course of the stereoselective aldol addition outlined above. Further studies of the structures of the enolates **7** and **13** will be necessary in order to find a rationale for the stereochemical outcome of the carbon-carbon bond formation reactions performed with the versatile triphenylglycol esters. Recently, the aldol addition of the propionate **6** has been applied as a key step in a synthesis of dolastatin[27].

This work was supported by the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie*. Generous gifts of mandelic acid were provided by *BASF AG*. We thank Dr. *A. Steigel*, Mrs. *M. Beuer*, Mrs. *I. Menzel*, Mr. *K. Opdenbusch*, Mrs. *R. Boetzel*, Mr. *J. Opgenoorth*, Mr. *A. Brück*, and Mr. *S. Hellwig* for re-

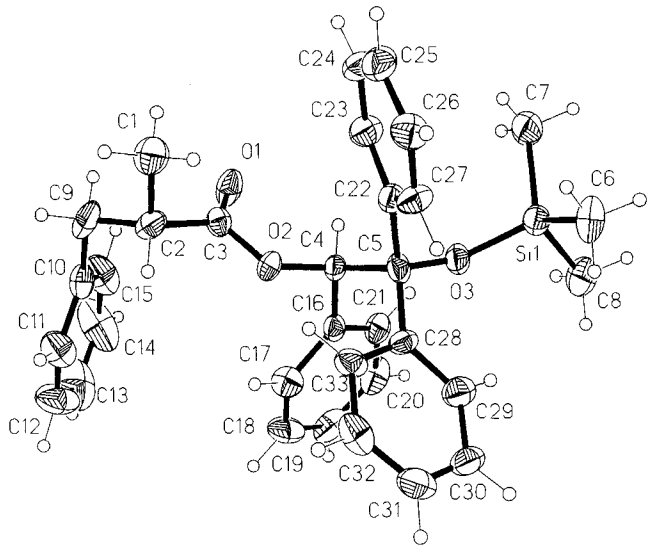

Figure 3. A view of the molecular structure of **18b** in the crystal. Selected bond lengths [pm] and angles [°]: C(1)–C(2) 156.3(16), C(2)–C(3) 149.3(14), C(2)–C(9) 153.1(12), C(3)–O(1) 120.7(13), C(3)–O(2) 135.1(10), C(4)–O(2) 142.5(10), C(4)–C(5) 156.8(10), C(4)–C(16) 149.8(14), C(5)–C(22) 155.0(14), C(5)–C(28) 152.2(14), C(5)–O(3) 141.2(11), O(3)–Si(1) 163.9(6), C(9)–C(10) 150.0(17); Si(1)–O(3)–C(5) 139.8(6), C(3)–C(2)–C(9) 112.1(9); H(2A)–C(2)–C(3)–O(1) 157.1(0.9), H(2A)–C(2)–C(3)–O(2) –23.3(0.9), C(9)–C(2)–C(3)–O(1) 35.8(1.5), C(9)–C(2)–C(3)–O(2) –144.6(0.9), C(1)–C(2)–C(3)–O(1) –85.1(1.2), C(4)–O(2)–C(3)–O(1) 0.2(1.4), O(2)–C(4)–C(5)–O(3) –171.8(0.7), C(16)–C(4)–C(5)–C(22) –177.3(0.8), Si(1)–O(3)–C(5)–C(4) 145.8(0.7), C(3)–C(2)–C(9)–C(10) 63.4(1.3)

cording the spectra. Special thanks go to Prof. *P. Williard*, Brown University, for providing diffractometer time.

Experimental

Melting points: Büchi 510. – IR: Perkin-Elmer 710 B and 1420. – Bruker WP 80 and AM 200, Varian EM 360 and VXR 300; all spectra were recorded in $CDCl_3$ with tetramethylsilane as internal standard. – MS: Varian MAT 311 A and MAT CH 5 (70 eV). – Specific rotations: Perkin Elmer 141. – TLC: DC-Alufolien Sil-G60/UV_{254} (Merck). – Preparative TLC: Kieselgel-Fertigplatten Sil-G 60/UV_{254} (Merck). – Column chromatography: Kieselgel S, mesh size 0.2–0.5 (Riedel de Haen) and MN Kieselgel 60, mesh size 0.04–0.063 mm (Macherey-Nagel). – Elemental analyses: Mikroanalytisches Laboratorium Beller (Göttingen) and Institut für Pharmazeutische Chemie, Universität Düsseldorf.

X-ray Crystallography: Data are collected by using a Siemens P4 crystallographic system (Mo-K_α radiation, λ = 0.71069 Å, graphite monochromator, ω scans). The structures are solved (direct methods) and refined by using SHELXTL program package (Siemens Analytical X-ray Insts.).

Solvents and Reagents: THF and diethyl ether are first distilled from sodium and then under N_2 from sodium/benzophenone; they can be taken from the receiving flasks, which are closed by septums, with syringes or cannulas; dichloromethane is distilled from P_2O_5 and stored over molecular sieves; diisopropylamine, cyclohexylisopropylamine and pyridine are distilled from CaH_2; *n*-butyllithium (1.6 M solution in hexane) and dichlorobis(cyclopentadienyl)zirconium are purchased from Merck. Reactions performed at temperatures lower than –20°C are monitored by introducing a thermocouple, connected with a resistance thermometer (Ebro), through a septum into the reaction mixture. General remarks concerning the handling of organolithium compounds are given in refs.[8b,11,13].

(R)-2-Hydroxy-1,2,2-triphenylethyl Propionate (**6**): A solution of (*R*)-triphenylglycol (**4**)[8,11] (40.0 g, 138 mmol) in 400 ml of dichloromethane and 16 ml (200 mmol) of dry pyridine is stirred under nitrogen at 0°C in a 1000-ml flask which is equipped with a dropping funnel and a magnetic stirrer. A solution of propionyl chloride (16 ml, 176 mmol) in 100 ml of dichloromethane is added dropwise within 30 min, whereby the hydrochloride precipitates gradually. The ice bath is removed, and the suspension is stirred for another 12 h at room temp. Water (200 ml) is added in order to dissolve the hydrochloride. The mixture is concentrated in a rotary evaporator, and the precipitate formed is collected in a suction filter and washed several times carefully with a total amount of about 800 ml of water. Air is sucked through the colorless solid for 2 h in order to remove most of the adherent water. Finally, the product is dissolved in 750 ml of toluene, and the solution is concentrated to a volume of 250–300 ml by distillation at atmospheric pressure in order to remove remaining water. The toluene solution is finally treated with hexane, and the precipitate is filtered and dried in vacuo to yield 46.7 g (96%) of colorless **6**, m.p. 208–209°C, R_f = 0.35 (hexane/ethyl acetate, 6:1), $[\alpha]_D^{25}$ = 199.8 (*c* = 1.5 in chloroform). – ^1H NMR (300 MHz): δ = 0.99 (t, *J* = 7.57 Hz, 3H, 3-H), 2.24 (q, *J* = 7.57 Hz, 2H, 2-H), 2.81 [s, 1H, C(O*H*)Ph_2], 6.69 [s, 1H, OC*H*(Ph)], 7.0–7.6 (m, 15H, aromatic H). – IR (KBr): $\tilde{\nu}$ = 3530 cm^{-1}, 2960, 1720, 1600, 1580, 1495, 1450, 1270 1180. – MS (70 eV), *m/z* (%): 273 (1) [$(C_6H_5)_2C(OH)CH(C_6H_5)^+$], 184 (15), 183 (100) [$(C_6H_5)_2C(OH)^+$], 165 (5) [fluorenyl cation], 106 (5) [$C_6H_5COH^+$], 105 (44) [$C_6H_5CO^+$], 77 (19) [$C_6H_5^+$], 57 (14) [$CH_3CH_2CO^+$]. – $C_{23}H_{22}O_3$ (346.4): calcd. C 79.74, H 6.23; found C 79.91, H 6.45.

(R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl Propionate (**5**): A solution of diisopropylamine (15.1 ml, 106 mmol) in 150 ml of THF is stirred under N_2 in a 250-ml two-necked flask equipped with a magnetic stirrer, closed with a septum and connected to a vacuum line. At –78°C, 68.7 ml (110 mmol) of a 1.6 M solution of *n*-butyllithium in *n*-hexane is added by means of a syringe with vigorous stirring. The dry ice/acetone bath is replaced by an ice bath, and stirring is continued for 30 min to give a pale solution of lithium diisopropylamide. A 500-ml two-necked flask equipped with a magnetic stirrer, a septum, and a connection to the vacuum line is charged with 17.32 g (50 mmol) of **6** and 180 ml of THF. The suspension is cooled to –78°C with stirring while the temperature is monitored with a thermocouple. The solution of lithium diisopropylamide is added by means of a cannula to the suspension of **6**. Thereby, the 500-ml flask is slightly evacuated and a gentle nitrogen overpressure is maintained in the 250-ml flask by connecting it to the vacuum line. Stirring is continued for 2 h at –35°C, and a clear yellowish solution forms. After the mixture has been cooled to –78°C, a solution of chlorotrimethylsilane (20 ml; 158 mmol) in 20 ml of THF is added slowly by means of a syringe. Stirring is continued for 24 h at 0°C and for another 2 h at room temp. The mixture is concentrated in a rotary evaporator and 0.5 N HCl (100 ml) is added to the remaining solution (about 200 ml). The emulsion is stirred vigorously for 1 h at room temp., the layers are separated, and the aqueous layer is extracted three times with a total volume of 100 ml of dichloromethane. The combined organic layers are dried with $MgSO_4$, and the solvents are removed in a rotary evaporator. The remaining solid is dissolved in petroleum ether (b.p. 30–50°C), the resulting solution is filtered and concentrated. The crude product is recrystallized from petroleum ether to give 18.8 g (90%) of colorless, crystalline **5**, b.p. 80–81°C, R_f = 0.77 (*n*-hexane/ethyl acetate, 4:1), $[\alpha]_D^{25}$ = 39.3 (*c* = 1.15 in

chloroform). – ^{1}H NMR (300 MHz): δ = −0.13 [s, 9H, $(CH_3)_3Si$], 1.04 (t, *J* = 7.5 Hz, 3H, 3-H), 2.27 (q, *J* = 7.5 Hz, 2H, 2-H), 6.60 [s, 1H, $OCH(C_6H_5)$], 6.80–7.30 (m, 15H, aromatic H). – IR (KBr): $\tilde{\nu}$ = 3100 cm^{-1}, 2960, 1740, 1500, 1450, 1340, 1250, 1190, 1140. – MS (70 eV), *m/z* (%): 418 (< 1) [M^+], 256 (10) [$(C_6H_5)_3C_2H^+$], 255 (40), 254 (100), 165 (1) [fluorenyl cation], 131 (5), 105 (2) [$C_6H_5CO^+$], 73 (70) [$(CH_3)_3Si^+$], 57 (6) [$CH_3CH_2CO^+$]. – $C_{26}H_{30}O_3Si$ (418.6): calcd. C 74.60, H 7.22; found C 74.68, H 7.21. – Crystal data for **5**[28]: orthorhombic space group $P2(1)2(1)2(1)$; *a* = 9.846(2), *b* = 10.190(1), *c* = 24.103(7) Å; *V* = 2418.2(6) $Å^3$; *Z* = 4; d_{calcd} = 1.150 g cm^{-3}; μ(Mo-$K_α$) = 0.120 mm^{-1}; *F*(000) = 896; intensity data $0 \leq h \leq 11$, $0 \leq k \leq 11$, $0 \leq l \leq 26$; 271 parameters refined by using 2057 non-equivalent reflections ($2\theta_{max}$ = 45.0°); *R* = 0.046 (*wR* = 0.052, GOF = 1.47) over 1854 reflections with $F > 2\sigma(F)$.

(R)-1-(Trimethylsilyloxy)-1-[1,2,2-triphenyl-2-(trimethylsilyloxy)ethoxy]-1-propene (**12**): A suspension of **6** (0.87 g, 2.5 mmol) in 10 ml of THF is stirred under N_2 in a 100-ml two-necked flask equipped with a magnetic stirrer, a connection to a vacuum line, a septum, and a thermocouple. At −50°C, a solution of 5.5 mmol of lithium diisopropylamide in THF (10 ml), prepared as described above, is added by means of a cannula. Stirring is continued for 2 h at −35°C whereby a clear yellowish solutions forms. A solution of chlorotrimethylsilane (1.02 ml, 8.0 mmol) in THF (5 ml) is added dropwise at −78°C. The mixture is stirred for 1 h at the same temp., for 24 h at 0°C, and for another 2 h at room temp. The solvents are removed by condensing them under reduced pressure (oil pump) in a trap cooled with liquid nitrogen. The crude oily ketene acetal **12** is used without purification. – ^{1}H NMR (300 MHz): δ = −0.14 [s, 9H, $(CH_3)_3Si$], −0.05 [s, 9H, $(CH_3)_3Si$], 1.38 (t, *J* = 6.6 Hz, 3H, 3-H), 3.42 (q, *J* = 6.6 Hz, 1H, 2-H), 5.98 (s, 1H, $OCHC_6H_5$), 6.70–7.41 (m, 15H, aromatic H). The minor diastereomer differs in δ = 3.48 (q, *J* = 6.6 Hz), 5.59 (s).

(1R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl (2S,3R)- and (2R,3S)-3-Hydroxy-2-methyl-3-phenylpropanoate (**9b** and **8b**): A solution of crude **12** (2.5 mmol) in 20 ml of dichloromethane is stirred under N_2 at −78°C. Benzaldehyde (0.25 ml, 2.5 mmol) and $BF_3 \cdot OEt_2$ (0.32 ml, 2.5 mmol) are injected subsequently by means of syringes, and stirring is continued for 1 h at −78°C. After water (20 ml) and a saturated aqueous solution of NH_4Cl (20 ml) have been added, the mixture is allowed to reach room temp. The organic layer is separated, and the aqueous phase is extracted three times with a total volume of 80 ml of ethyl acetate. The combined organic layers are washed with 1 N HCl (5 ml) and brine (10 ml) and dried with $MgSO_4$. The solvent is removed in a rotary evaporator, and the oily residue is dried in vacuo to give 1.1 g (89%) of a yellowish solid mixture of **9b** and **8b** besides minor amounts of the *syn* diastereomers **10b** and **11b**.

9b (main diastereomer): ^{1}H NMR (300 MHz): δ = −0.14 [s, 9H, $(CH_3)_3Si$], 0.85 [d, *J* = 7.14 Hz, 3H, $CH(CH_3)$], 2.70 [s, 1H, CH(O*H*)], 2.75 [m, 1H, $CH(CH_3)$], 4.61 [d, *J* = 8.37, 1H, C*H*(OH)], 6.61 [s, 1H, $OCH(C_6H_5)$], 6.70–7.40 (m, 20H, aromatic H).

8b (minor diastereomer): Physical and spectroscopic data: see below.

10b and **11b** (minor diastereomers): ^{1}H NMR differs in δ = 5.01 (m, 1H, 3-H).

(1R)-2-Hydroxy-1,2,2-triphenylethyl (2R,3S)- and (2S,3R)-3-Hydroxy-2-methyl-3-phenylpropanoate (**8a** and **9a**): Propionate **6** (0.87 g, 2.5 mmol) is deprotonated with 5.5 mmol of lithium diisopropylamide as described in the procedure for the preparation of **12**. At −78°C, a solution of Cp_2ZrCl_2 (0.76 g, 2.6 mmol) in 15 ml of THF is added slowly. The mixture is allowed to reach −60°C within 1 h. Benzaldehyde (0.27 ml, 2.7 mmol) is added at −78°C and stirring is continued for 1 h. After the successive addition of 1 N HCl (15 ml), saturated aqueous NH_4Cl (10 ml), and water (40 ml) the ice/acetone bath is removed. The mixture is stirred for 1 h and extracted several times with a total volume of 200 ml of ethyl acetate. The combined organic layers are washed with 1 N HCl (10 ml) and brine, dried with $MgSO_4$, concentrated in a rotary evaporator and dried *in vacuo* to yield 1.1 g (84%) of a mixture of **8a** and **9a** besides minor amounts of the *syn* isomers **10a** and **11a** (see Table 1).

8a (main diastereomer): ^{1}H NMR (300 MHz): δ = 0.87 [d, *J* = 7.2 Hz, 3H, $CH(CH_3)$], 2.62 [d, *J* = 5.0 Hz, 1H, CH(O*H*)], 2.80 (m_c, 1H, 2-H), 2.89 [s, 1H, $C(C_6H_5)_2OH$], 4.61 (dd, *J* = 8.06 Hz, 4.54 Hz, 1H, 3-H), 6.71 [s, 1H, $OCH(C_6H_5)$], 6.90–7.60 (m, 20H, aromatic H).

9a (minor diastereomer): ^{1}H NMR differs in: δ = 4.58 (dd, 8.0 Hz, 4.0 Hz, 1 H, 3-H).

10a and **11a** (minor diastereomers): ^{1}H NMR differs in: δ = 4.87 and 4.92 (m_c, 1H, 3-H).

General Procedure for the Stereoselective Addition of Propionate **5** *to Aldehydes via the Zirconium Enolate:* A solution of cyclohexylisopropylamine (0.36 ml, 2.1 mmol) in THF (10 ml) is stirred under N_2 in a 100-ml two-necked flask equipped with a magnetic stirrer, a septum, and a connection to a vacuum line. At −78°C, a 1.6 M solution of *n*-butyllithium in hexane (1.35 ml, 2.1 mmol) is added by means of a syringe, and stirring is continued for 30 min in an ice bath. A precooled (−105°C) mixture of propionate **5** (0.84 g, 2.0 mmol) and THF (10 ml) is added dropwise by means of a cannula to the solution of lithium cyclohexylisopropylamide which is stirred at −105°C. Stirring is continued for 90 min and the temp. is allowed to reach −78°C. The mixture is cooled to −105°C, and a precooled (−78°C) solution of Cp_2ZrCl_2 (1.84 g, 6.3 mmol) in THF (26 ml) is added slowly through a cannula. The temp. is raised to −60°C whereby the previously pale solution turns bright yellow. The mixture is subsequently cooled to −105°C, and a cold solution (−105°C) of the corresponding aldehyde (3.0 mmol) in 10 ml of THF is added dropwise. After stirring for 1 h the mixture is allowed to reach −78°C, and stirring is continued for 1–3 h at the same temp. Subsequently, a solution of 1 N HCl (15 ml), a saturated aqueous solution of NH_4Cl (10 ml), and water (40 ml) are added. The cooling bath is removed, the mixture is stirred for another 1 h, and extracted several times with a total volume of 200 ml of ethyl acetate. The combined organic layers are washed with 1 N HCl (10 ml) and with brine and dried with $MgSO_4$. The solvent is removed in a rotary evaporator, the residue is dried in vacuo, and the crude product is purified by preparative TLC. According to this general procedure are obtained:

(1R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl (2R,3S)-3-Hydroxy-2-methyl-3-phenyl-propanoate (**8b**): Prepared by reaction of **5** with benzaldehyde (0.3 ml, 3.0 mmol); yield 0.94 g (90%); R_f = 0.5 (*n*-hexane/ethyl acetate, 4:1). – ^{1}H NMR (300 MHz): δ = −0.13 [s, 9H, $Si(CH_3)_3$], 0.88 [d, *J* = 7.3 Hz, 3H, $CH(CH_3)$], 2.79 (m, 1H, 2-H), 2.94 [d, *J* = 4.8 Hz, 1H, CH(O*H*)], 4.66 [dd, *J* = 8.15 Hz, 4.80 Hz, 1H, C*H*(OH)], 6.59 [s, 1H, $OCH(C_6H_5)$], 6.90–7.33 (m, 20H, aromatic H). Minor amounts of the *syn* isomers **10b** and **11b** are detected in the ^{1}H-NMR spectra, whereas diastereomer **9b** is not found. δ = 5.02 (m_c). – IR (KBr): $\tilde{\nu}$ = 3530 cm^{-1}, 3100, 2970, 1740, 1500, 1460, 1450, 1380, 1255, 1160, 1140. – MS (70 eV), *m/z* (%): 257 (10), 256 (35), 255 (100) [$(C_6H_5)_2COSi(CH_3)_3^+$], 239 (4), 183 (3), 107 (6), 105 (4) [$C_6H_5CO^+$], 73 (42) [$Si(CH_3)_3^+$]. – $C_{33}H_{36}OSi$ (524.7): calcd. C 75.54, H 6.92; found C 75.45, H 6.93.

(1R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl (2R,3R)-2,4-Dimethyl-3-hydroxypentanoate (**16a**): Prepared by reaction of **5** with 2-methylpropanal (0.27 ml, 3.0 mmol); yield 0.80 g (82%), R_f = 0.61 (*n*-hexane/ethyl acetate, 4:1). – ^{1}H NMR (300 MHz): δ = −0.15 [s, 9H, $Si(CH_3)_3$], 0.77 [d, *J* = 6.6 Hz, 3H, $(CH_3)_2CH$], 0.90 [d, *J* = 6.8 Hz, 3H, $(CH_3)_2CH$], 1.08 [d, *J* = 7.3 Hz, 3H, $CH(CH_3)$], 1.62 [m_c, 1H, $(CH_3)_2CH$], 2.51 [d, *J* = 8.4 Hz, 1H, CH(OH)], 2.63 (dq, J_d = 5.5 Hz, J_q = 7.3 Hz, 1H, 2-H), 3.19 (m_c, 1H, 3-H), 6.60 [s, 1H, $OCH(C_6H_5)$], 6.77–7.30 (m, 15H, aromatic H). – Minor amounts of diastereomers are detected in the ^{1}H-NMR spectra: δ = 0.81 [d, *J* = 6.45, 3H, $(CH_3)_2CH$], 0.84 [d, *J* = 6.0 Hz, 3H, $(CH_3)_2CH$]. – IR (CCl_4): $\tilde{\nu}$ = 3530 cm^{-1}, 3100, 2975, 1725, 1450, 1255, 1165. – MS (70 eV), *m/z* (%): 345 (11), 257 (9), 256 (36), 255 (100) $[(C_6H_5)_2COSi(CH_3)_3^+]$, 239 (5), 105 (6) $[C_6H_5CO^+]$, 73 (94) $[Si(CH_3)_3^+]$. – $C_{30}H_{38}O_4Si$ (490.7): calcd. C 73.43, H 7.81; found C 73.49, H 7.83.

(1R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl (2R,3S)-3-Hydroxy-2,4,4-trimethylpentanoate (**16b**): Prepared by reaction of **5** with 2,2-dimethylpropanal (0.33 ml, 3.0 mmol); yield 0.76 g (75%); R_f = 0.47 (*n*-hexane/ethyl acetate, 4:1). – ^{1}H NMR (300 MHz): δ = −0.13 [s, 9H, $Si(CH_3)_3$], 0.84 [s, 9H, $C(CH_3)_3$], 1.17 [d, *J* = 7.3 Hz, 3H, $CH(CH_3)$], 2.67 (dq, J_d = 1.9, J_q = 7.3 Hz, 1H, 2-H), 3.11 (dd, *J* = 9.8/1.9 Hz, 1H, 3-H), 3.75 [d, *J* = 9.8 Hz, 1H, CH(OH)], 6.55 [s, 1H, $OCH(C_6H_5)$], 6.78–7.31 (m, 15H, aromatic H). Diastereomers cannot be detected in the ^{1}H-NMR spectra. – IR (CCl_4): $\tilde{\nu}$ = 3510 cm^{-1}, 3075, 2960, 1720, 1255, 1160. – MS (70 eV), *m/z* (%): 345 (16), 257 (9), 256 (36), 255 (100) $[(C_6H_5)_2COSi(CH_3)_3^+]$, 239 (6), 86 (4), 84 (6), 75 (8), 74 (8), 73 (20) $[Si(CH_3)_3^+]$. – $C_{31}H_{40}O_4Si$ (504.7): calcd. C 73.77, H 7.99; found C 74.02, H 8.09.

Methyl (2R,3S)-3-Hydroxy-2-methyl-3-phenylpropionate (**14b**): The crude ester **8b** (0.94 g, 1.8 mmol) is dissolved in methanol (80 ml) and water (20 ml), and the solution is stirred in an ice bath. A solution of LiOH · H_2O (0.84 g, 20 mmol) in 20 ml of water is added, and stirring is continued for 30 min at 0°C and subsequently for 3 d at room temp. After the addition of 50 ml of water the mixture is extracted several times with diethyl ether (200 ml) in order to remove **4**. The aqueous layer is carefully acidified with 1 N HCl with stirring in an ice bath (pH 3), saturated with sodium chloride and extracted several times with ethyl acetate. The combined organic layers are dried with $MgSO_4$, and the solvent is evaporated under reduced pressure. The crude mixture of **14a/15a** (0.38 g, 90%) is dissolved in 60 ml of diethyl ether/water (10:1), and the obtained soluton is treated with an ethereal solution of diazomethane until the yellow color persists. After stirring overnight at room temp. the mixture is washed with brine (10 ml), dried with $MgSO_4$, and concentrated in vacuo. The crude product is purified by column chromatography (*n*-hexane/ethyl acetate, 4:1) in order to remove minor amounts of *syn* diastereomer **15b** and to yield 0.36 g (90%) of *anti* carboxylic ester **14b**; $[\alpha]_D^{25}$ = −53.8 (*c* = 1.34 in chloroform) {ref.[14]: $[\alpha]_D^{23}$ = −57.1 (*c* = 0.12 in chloroform)}. – ^{1}H NMR (300 MHz): δ = 1.00 [d, *J* = 7.3 Hz, 3H, $CH(CH_3)$], 2.81 (dq, J_d = 8.5, J_q = 7.3 Hz, 1H, 2-H), 3.03 [s, 1H, CH(OH)], 3.73 (s, 3H, OCH_3), 4.74 (d, *J* = 8.5 Hz, 1H, 3-H), 7.26-7.36 (m, 5H, aromatic H).

(2S,3R)-2,4-Dimethyl-1,3-pentanediol (**17a**): A solution of the crude adduct **16a** (0.80 g, 1.6 mmol) in diethyl ether (80 ml) is added slowly to a suspension of $LiAlH_4$ (1.15 g, 30 mmol) in 50 ml of diethyl ether which is stirred under N_2 at room temp. After stirring for 24 h, water and 1 N HCl are added carefully. The layers are separated, and the aqueous phase is extracted several times with a total amount of 400 ml of diethyl ether. The combined organic layers are dried with $MgSO_4$ and concentrated in a rotary evaporator. The residue is purified by column chromatography (*n*-hexane/ethyl acetate, 1:1). Thereby triphenylglycol (**4**) is removed, and 0.14 g of the diol **17a** (63% yield, relative to propionate **5**) is isolated as a colorless oil; R_f = 0.38 (*n*-hexane/ethyl acetate, 1:1); $[\alpha]_D^{25}$ = 19.0 (*c* = 1.30 in chloroform) {ref.[16]: $[\alpha]_D^{25}$ = 20.75 (*c* = 0.66 in chloroform)}. – ^{1}H NMR (200 MHz): δ = 0.84 [d, *J* = 6.95 Hz, 3H, $CH(CH_3)_2$], 0.88 [d, *J* = 6.7 Hz, 3H, $CH(CH_3)_2$], 0.94 [d, *J* = 6.9 Hz, 3H, $CH(CH_3)$], 1.69–1.90 (m, 2H, 2-H and 4-H), 3.30 [dq, *J* = 3.8/8.07 Hz, 1H, CH(OH)], 3.75 (br. s, 1H, OH), 4.15 (br. s, 1H, OH), 3.62 and 3.74 (AB part of an ABX system, J_{AB} = 10.8, J_{AX} = 7.2, J_{BX} = 3.5 Hz, 2H, CH_2OH).

(2S,3S)-2,4,4-Trimethyl-1,3-pentanediol (**17b**) is prepared according to the procedure described above by reduction of **16b** (0.76 g, 1.5 mmol) with 1.15 g (30 mmol) of $LiAlH_4$. The crude product is purified by column chromatography (*n*-hexane/ethyl acetate, 3:2) to yield 0.18 g (68%, relative to propionate **5**) of diol **17b**; R_f = 0.45 (*n*-hexane/ethyl acetate, 3:2); $[\alpha]_D^{25}$ = −5.1 (*c* = 1.78 in chloroform) {ref.[18]: $[\alpha]_D^{25}$ = −4.4 (*c* = 0.87 in chloroform)}. – ^{1}H NMR (200 MHz): δ = 0.95 [s, 9H, $C(CH_3)_3$], 1.05 [d, *J* = 6.9 Hz, 3H, $CH(CH_3)_3$], 1.91 (m, 1H, 2-H), 2.82 (br. s, 2H, OH), 3.24 (d, *J* = 4.8 Hz, 1H, 3-H), 3.62 and 3.80 (AB part of an ABX system, 2H, CH_2OH).

(1R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl (2R)-2-(Trimethylsilyl)propanoate (**18a**): A mixture of **5** (0.84 g, 2 mmol) and 10 ml of THF is cooled to −105°C and added slowly by means of a cannula to a solution of 2.1 mmol of lithium diisopropylamide (prepared as described above) in THF, which is stirred at −105°C under N_2 in a 100-ml two-necked flask equipped with a magnetic stirrer, a connection to a vacuum line, a septum, and a thermocouple. Stirring is continued for 1 h at −78°C in order to complete enolate formation. A solution of chlorotrimethylsilane (0.38 ml, 3.0 mmol) in 10 ml of THF is added dropwise by means of a cannula at the same temp. After stirring for 1 h at −78°C the dry ice-acetone bath is replaced by an ice-bath, and stirring is continued overnight. The mixture is treated with water (20 ml) and with a saturated aqueous solution of NH_4Cl (20 ml). The layers are separated, and the aqueous phase is extracted three times with a total amount of 70 ml of dichloromethane. The combined organic layers are washed with 1 N HCl (5 ml) and brine (10 ml), dried with $MgSO_4$ and concentrated in a rotary evaporator. The crude product is dried in vacuo and recrystallized from petroleum ether to deliver 1.1 g (93%) of colorless, crystalline **18a**, m.p. 96–99°C, R_f = 0.83 (*n*-hexane/ethyl acetate, 4:1), $[\alpha]_D^{25}$ = 7.6 (*c* = 1.32 in chloroform). – ^{1}H NMR (300 MHz): δ = −0.18 [s, 9H, $Si(CH_3)_3$], −0.12 [s, 9H, $Si(CH_3)_3$], 1.14 (d, *J* = 7.15 Hz, 3H, 3-H), 1.94 (q, *J* = 7.15 Hz, 1H, 2-H), 6.66 [s, 1H, $OCH(C_6H_5)$], 6.70–7.40 (m, 15H, aromatic H). – ^{29}Si NMR (39 MHz): δ = 6.80 [s, $OSi(CH_3)_3$], 12.92 [s, $CSi(CH_3)_3$]. – IR (KBr): $\tilde{\nu}$ = 3050 cm^{-1}, 2980, 1730, 1500, 1455, 1325, 1270, 1180, 1150, 1110. – MS (70 eV), *m/z* (%): 257 (6), 256 (23), 255 (100), 179 (6), 129 (9) $[CH_3CHSi(CH_3)_3CO^+]$, 73 (74) $[Si(CH_3)_3^+]$. – $C_{29}H_{38}O_3Si_2$ (490.8): calcd. C 70.97, H 7.80; found C 71.08, H 7.74. – Crystal data for **18a**[28]: orthorhombic space group *P*2(1)2(1)2(1); *a* = 10.951(2), *b* = 14.522(3), *c* = 18.619(4) Å; *V* = 2960.9(15) Å^3; *Z* = 4; d_{calcd} = 1.101 g cm^{-3}; μ(Mo-K_α) = 0.145 mm^{-1}; *F*(000) = 1056; intensity data $0 \le h \le 11$, $-1 \le k \le 15$, $-1 \le l \le 20$; 307 parameters refined by using 2226 non-equivalent reflections ($2\theta_{max}$ = 45.0°); *R* = 0.044 (*wR* = 0.047, GOF = 1.21) over 1970 reflections with $F > 2\sigma(F)$.

General Procedure for the Alkylation of Propionate **5**: A solution of lithium diisopropylamide (2.1 mmol) in 10 ml of THF prepared as described above is stirred at −105°C in a 100-ml two necked

flask equipped with a magnetic stirrer, a connection to a vacuum line, a septum, and a thermocouple. A solution of propionate **5** (0.84 g, 2 mmol) in 10 ml of THF is added through a cannula, and stirring is continued for 90 min at −78°C. The mixture is cooled to −105°C, and a solution of the alkyl halide (15 mmol) in THF (10 ml) is added. Finally, the temp. of the stirred mixture is allowed to reach 25°C overnight. After water (20 ml) and a saturated solution of NH_4Cl (20 ml) have been added, the layers are separated, and the aqueous phase is extracted three times with 30-ml portions of dichloromethane. The combined organic layers are washed with 1 N HCl (5 ml) and brine (5 ml) and dried with $MgSO_4$. The solvent is removed in a rotary evaporator, the residue is dried in vacuo and purified by column chromatography. According to this procedure are obtained:

(1R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl (2S)-2-Methyl-3-phenylpropanoate (**18b**): Prepared by reaction of **5** with benzyl bromide (1.8 ml, 15 mmol); yield 0.91 g (90%); R_f = 0.7 (toluene); $[\alpha]_D^{25}$ = 48.0 (*c* = 0.86 in chloroform). − ^{1}H NMR (300 MHz): δ = −0.15 [s, 9H, $Si(CH_3)_3$], 1.01 [d, *J* = 7.0 Hz, 3H, $CH(CH_3)$], 2.67 (m_c, 1H, 2-H), 2.30−3.00 (m, 2H, 3-H), 6.58 [s, 1H, $OCH(C_6H_5)$], 6.70−7.40 (m, 20H, aromatic H). − IR (KBr): ṽ = 3100 cm^{-1}, 3080, 2980, 1740, 1450, 1265, 1130. − MS (70 eV), *m/z* (%): 257 (6), 256 (28), 255 (100) $[(C_6H_5)_2COSi(CH_3)_3^+]$, 91 (8) $[C_7H_7^+]$, 73 (29) $[Si(CH_3)_3]$. − $C_{33}H_{36}O_3Si$ (508.7): calcd. C 77.91, H 7.13; found C 77.88, H 7.12. − Crystal data for **18b**[28]: monoclinic space group $P2_1$; *a* = 9.396(2), *b* = 15.038(3), *c* = 10.939(2) Å, β = 107.64(3)°; *V* = 1473.1(5) $Å^3$; *Z* = 2; d_{calcd} = 1.147 g cm^{-3}; μ(Mo-K_α) = 0.110 mm^{-1}; *F*(000) = 544; intensity data $-1 < h < 10$, $-1 < k < 16$, $-12 < l < 11$; 333 parameters refined by using 2445 non-equivalent reflections ($2\theta_{max}$ = 47°); *R* = 0.049 (*wR* = 0.048, GOF = 1.08) over 1351 reflections with $F > 4\sigma(F)$.

(1R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl (2S)- and (2R)-2-Methyl-4-pentenoate (**18c** and **19c**): Prepared by reaction of **5** with allyl bromide (1.3 ml, 15 mmol); yield 0.81 g (88%), R_f = 0.71 (toluene); $[\alpha]_D^{25}$ = 25.6 (*c* = 1.25 in chloroform). − ^{1}H NMR (300 MHz): δ = −0.15 [s, 9H, $Si(CH_3)_3$], 1.02 [d, *J* = 6.9 Hz, 3H, $CH(CH_3)$], 2.45 (m_c, 1H, 2-H), 2.00−2.40 (m, 2H, 3-H), 4.90 (m_c, 2H, 5-H), 5.55 (m_c, 1H, 4-H), 6.59 [s, 1H, $OCH(C_6H_5)$], 6.90−7.33 (m, 15H, aromatic H). − ^{1}H NMR of the minor diastereomer **19c** differs in: δ = 1.00 (d, *J* = 6.8 Hz). − IR (neat): ṽ = 3080 cm^{-1}, 2980, 1745, 1645, 1450, 1255, 1110. − MS (70 eV), *m/z* (%): 257 (12), 256 (36), 255 (100) $[(C_6H_5)_2COSi(CH_3)_3^+]$, 239 (6), 171 (5), 165 (3) [fluorenyl cation], 105 (2) $[C_7H_5O^+]$, 75 (4) $[(C_2H_7OSi^+]$, 74 (5), 73 (60) $[Si(CH_3)_3^+]$, 69 (9) $[CH_2{=}CHCH_2CHCH_3^+]$, 41 (7) $[C_3H_5^+]$. − $C_{29}H_{34}O_3Si$ (458.7): calcd. C 75.94, H 7.47; found C 76.09, H 7.72.

(1R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl (2S)- and (2R)-2-Methylhexanoate (**18d** and **19d**): Prepared by reaction of **5** with 1-bromobutane (1.7 ml, 15 mmol); yield 0.80 g (2%); R_f = 0.76 (toluene); $[\alpha]_D^{25}$ = 15.9 (*c* = 1.07 in chloroform). − ^{1}H NMR (300 MHz): δ = −0.15 [s, 9H, $Si(CH_3)_3$], 0.77 (t, *J* = 6.9 Hz, 3H, 6-H), 1.02 [d, *J* = 7.3 Hz, 3H, $CH(CH_3)$], 1.00−1.60 (m, 6H, 3,4,5-H), 2.38 (m_c, 1H, 2-H), 6.59 [s, 1H, $OCH(C_6H_5)$], 6.70−7.40 (m, 15H, aromatic H). − ^{1}H NMR of the minor diastereomer **19d** differs in: δ = 0.79 (t, *J* = 6.2 Hz), 0.98 (d; *J* = 7 Hz). − IR (neat): ṽ = 3085 cm^{-1}, 2970, 1740, 1500, 1450, 1255, 1145, 1110. − MS (70 eV), *m/z* (%): 257 (10), 256 (46), 255 (100) $[(C_6H_5)_2COSi(CH_3)_3^+]$, 239 (5), 187 (5), 165 (2) [fluorenyl cation], 105 (2) $[C_7H_5O^+]$, 85 (5), 75 (4), 74 (4), 73 (44) $[Si(CH_3)_3^+]$, 43 (11) $[C_3H_7^+]$. − $C_{30}H_{38}O_3Si$ (474.7): calcd. C 75.90, H 8.07; found C 76.15, H 8.13.

(1R)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethyl (2S)- and (2R)-2-Methylbutanoate (**18e** and **19e**): Prepared by reaction of **5** with iodoethane (1.2 ml, 15 mmol); yield 0.85 g (95%); R_f = 0.74 (toluene); $[\alpha]_D^{25}$ = 10.5 (*c* = 1.1 in chloroform). − ^{1}H NMR (300 MHz): δ = −0.14 [s, 9H, $Si(CH_3)_3$], 0.72 (t, *J* = 7.30 Hz, 3H, 4-H), 1.02 [d, *J* = 7.0 Hz, 3H, $CH(CH_3)$], 1.30−1.65 (m, 2H, 3-H), 2.32 (m_c, 1H, 2-H), 6.59 [s, 1H, $OCH(C_6H_5)$], 6.80−7.40 (m, 15H, aromatic H). − ^{1}H NMR of the minor diastereomer **19e** differs in: δ = 0.77 (t, *J* = 6.4 Hz), 0.98 (d, *J* = 7.0 Hz). − IR (neat): ṽ = 3050 cm^{-1}, 2980, 1745, 1460, 1255, 1150, 1110, 1080. − MS (70 eV), *m/z* (%): 257 (11), 256 (47), 255 (100) $[(C_6H_5)_2COSi(CH_3)_3^+]$, 240 (3), 239 (6), 165 (2) [fluorenyl cation], 159 (6), 105 (2) $[C_7H_5O^+]$, 75 (6), 74 (4), 73 (71) $[Si(CH_3)_3]$, 57 (16) $[CH_3CH_2CHCH_3^+]$. − $C_{28}H_{34}O_3Si$ (446.7): calcd. C 75.29, H 7.67; found C 75.18 H 7.59.

(2S)-2-Methyl-3-phenyl-1-propanol (**20**): A solution of crude **18b/19b** (0.6 g, 1.2 mmol) in 10 ml of THF is added slowly to a suspension of $LiAlH_4$ (0.8 g, 20 mmol) in THF (50 ml) which is stirred at room temp. under N_2. After stirring for another 24 h at 25°C, water and 1 N HCl are added cautiously. The layers are separated, and the aqueous phase is extracted several times with chloroform (200 ml) and ethyl acetate (150 ml). The combined organic layers are dried with $MgSO_4$. The solvents are removed in a rotary evaporator, and the oily crude product is purified by column chromatography (*n*-hexane/ethyl acetate, 2:1) to deliver 0.16 g (90%) of colorless **20**; R_f = 0.49 (*n*-hexane/ethyl acetate, 2:1); $[\alpha]_D^{25}$ = −8.8 (*c* = 3.41 in benzene) {ref.[26]: $[\alpha]_D^{25}$ = −11.08 (*c* = 4.6 in benzene)}. − ^{1}H NMR (300 MHz): δ = 0.88 [d, *J* = 7.3 Hz, 3H, $CH(CH_3)$], 2.79 (m_c, 1H, 2-H), 2.94 (d, *J* = 4.8 Hz, 1H, OH), 4.66 (dd, *J* = 8.15/4.8 Hz, 2H, 1-H), 6.59 (s, 2H, 3-H).

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[1] Part of the Dissertation of H. Sacha, Universität Düsseldorf, **1993**.

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