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A New Access to Enantiopure *syn*- and *anti*-2-Methyl-1,3-diol Moieties from Chiral Nonracemic α-Bromo α′-Sulfinyl Ketones Promoted by Samarium Diiodide

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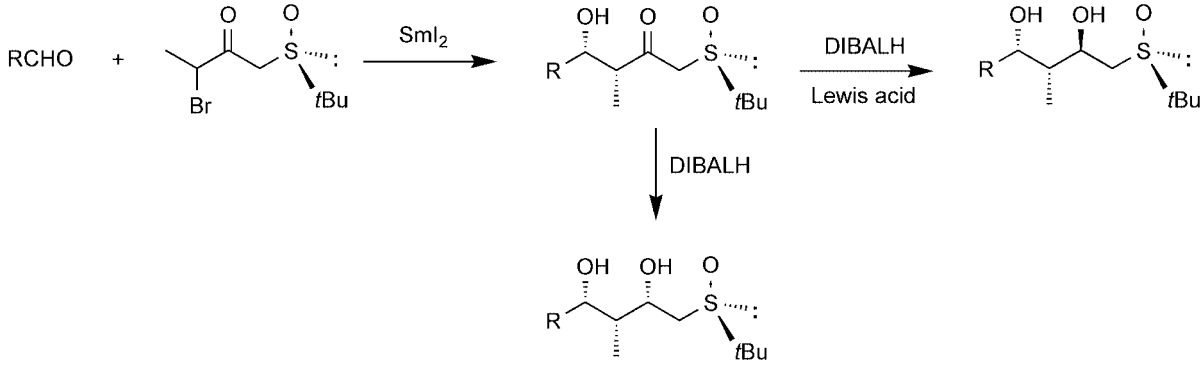
syn- and *anti*-2-Methyl-1,3-diols have been prepared by a two-step sequence that involves a SmI_2-promoted stereoselective Reformatsky addition of chiral nonracemic α-bromo α′-sulfinyl ketones to various aldehydes followed by stereoselective reduction of the Reformatsky adduct. The absolute configuration of the products was determined by comparison with literature data and by ^1H NMR NOESY experiments. The observed stereoselectivities can be explained in terms of a boat transition state. Functionalization of the aldehyde and removal or transformation of the chiral sulfoxide will allow this methodology to be applied to the total synthesis of biologically active molecules.

Introduction

Reformatsky reactions have been recognized as one of the most useful methods for the formation of carbon–carbon bonds. The scope of the Reformatsky reaction has progressed over the years and has been the subject of several reviews.[1] The reaction has a broad applicability and a great versatility in both inter- and intramolecular reactions involving a great variety of electrophiles. This reaction is also recognized as being a good alternative to base-induced aldol reactions, the advantage being that it proceeds under neutral conditions. In fact, no base or acid is required to generate the enolate or activate the electrophile, respectively.

However, in contrast to the aldol reaction, the most serious limitations attributed to Reformatsky reactions are their lower yields and diastereoselectivities.[2] The attainment of high stereoselectivity for this reaction is key to the further extension of its applicability. To date a few examples of highly diastereo- and enantioselective Reformatsky reactions have been reported.[3]

Samarium diiodide[4] has shown remarkable versatility in promoting numerous synthetic transformations with generally high chemoselectivity and high levels of stereochemical control. The samarium reagent has been used extensively and efficiently to promote intramolecular Reformatsky reactions to give medium- and large-sized carbocycles.[3g,5] Its use in intermolecular asymmetric reactions has already been reported. Fukuzawa et al.[3b] has described the SmI_2-mediated Reformatsky reaction of chiral 3-bromoacetyl-2-oxazolidinones with various aldehydes.



Scheme 1.

Recently we reported on the intermolecular diastereoselective Reformatsky reaction of chiral α-bromo α′-sulfinyl ketones and alkyl aldehydes in the presence of SmI_2. Up to 96% *syn* diastereomeric excess was obtained with linear

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aldehydes.[6] Further reduction of the Reformatsky adducts furnished *anti*- and *syn*-2-methyl-1,3-diol moieties (Scheme 1).

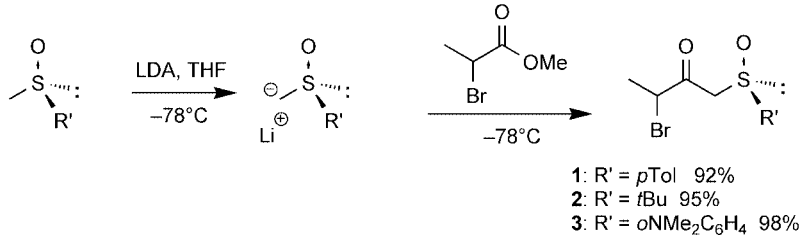
Taking into account our interest in the total synthesis of biologically active molecules, we report herein our results as well as the application of this methodology to the Reformatsky reaction with various functionalized aldehydes such as α,β-unsaturated aldehydes, protected α-hydroxy aldehydes, and protected α-keto aldehydes. The absolute configurations of the aldol adducts were confirmed by comparing the physical data obtained in this work with those of synthetic intermediates reported in the literature and by ^{1}H NMR NOESY experiments. We also propose transition-state models to rationalize the observed stereochemical outcomes.

Results and Discussion

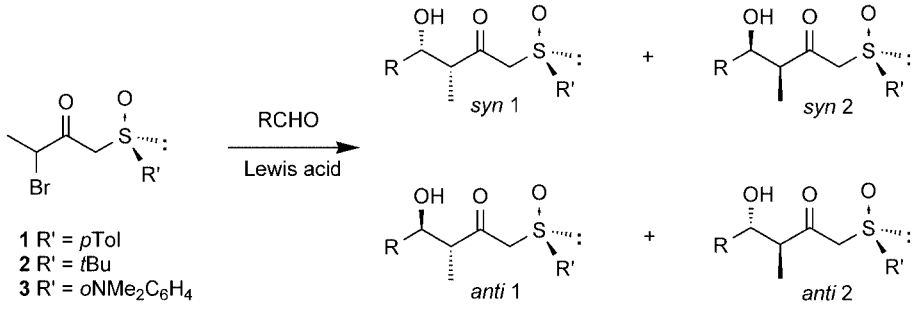
Search for the Optimum Experimental Conditions for the Reformatsky Reaction between α-Bromo α′-Sulfinyl Ketones and Benzaldehyde

Chiral α-bromo α′-sulfinyl ketones were prepared according to the procedure of Bravo and Resnati[7] (Scheme 2).

Treatment of the lithiated anion of (+)-(*R*)-methyl *p*-tolyl sulfoxide, (–)-(*R*)-methyl *tert*-butyl sulfoxide or (+)-(*R*)-methyl *o*-(dimethylamino)phenyl sulfoxide with methyl 2-bromopropionate afforded the α-bromo α′-sulfinyl ketones **1**–**3** in 92, 95 and 98% yields, respectively.

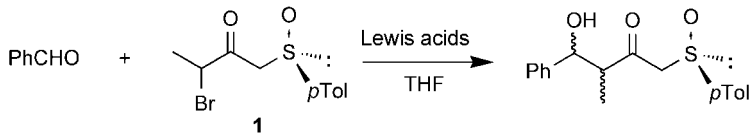


Scheme 2. Synthesis of the α-bromo α′-sulfinyl ketones **1**–**3**.



Scheme 3. Diastereoselective Reformatsky reaction between α-bromo α′-sulfinyl ketones **1**–**3** and aldehydes.

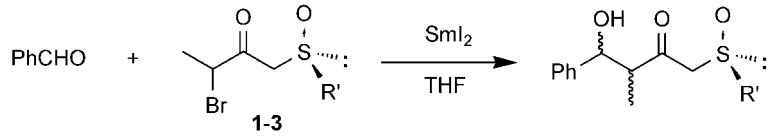
Table 1. Diastereoselective Reformatsky reaction of α-bromo α′-sulfinyl ketone **1** with benzaldehyde.[a]



Entry	Salt	*T* [°C]	*syn*/*anti*[b]	*syn*1/*syn*2[b]	Yield[c] [%]
1	GeI_2/K	room temp.	65:35	45:55	15
2	$ZnEt_2$/$RhCl(PPh_3)_3$	0	60:40	55:45	57
3	$CrCl_2$/LiI	room temp.	40:60	40:60	60
4	$CrCl_2$	–78 → –10	45:55	70:30	55
5	$CrCl_2$/LiI	–78 → –20	70:30	45:55	45
6	SmI_2	–78	70:30	85:15	47
7	SmI_2	–100	70:30	80:20	47

[a] Reaction conditions: **1** (1 equiv.), PhCHO (1.1 equiv.), SmI_2 (2 equiv.), THF, 30 min. [b] Determined by ^{1}H NMR analysis of the product. [c] Yield of the isolated mixture of diastereomers.

Table 2. Diastereoselective Reformatsky reaction of α-bromo α′-sulfinyl ketones **1**–**3** with SmI_2 and benzaldehyde.[a]



Entry	R′	*T* [°C]	*syn*/*anti*[b]	*syn*1/*syn*2[b]	*anti*1/*anti*2[b]	Yield [%][c]
1	*p*Tol	–78	70:30	85:15	50:50	47
2	*p*Tol	–100	70:30	80:20	60:40	47
3	*t*Bu	–78	75:25	90:10	70:30	45
4	*t*Bu	–100	75:25	96:4	70:30	51
5	*o*-$Me_2NC_6H_4$	–100	75:25	96:4	70:30	60

[a] Reaction conditions: **1**–**3** (1 equiv.), PhCHO (1.3 equiv.), SmI_2 (2 equiv.), THF, 30 min. [b] Determined by ^1H NMR analysis of the product. [c] Yield of the isolated mixture of diastereomers.

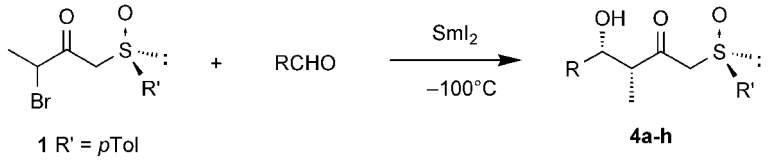
These enantiomerically pure α-bromo α′-sulfinyl ketones **1**–**3** should be good Reformatsky donors from the viewpoint of yield and stereoselectivity (Scheme 3).

Initially we studied the reaction of α-bromo α′-*p*-tolylsulfinyl ketone **1** (R′ = *p*-Tol) with benzaldehyde using different Lewis acids [GeI_2/K; $ZnEt_2$/$RhCl(PPh_3)_3$; $CrCl_2$/LiI; $CrCl_2$; SmI_2] (Table 1).

SmI_2 in THF at low temperatures (–78 to –100 °C) was found to give the best *syn* selectivity (Table 1, entries 6 and 7). Use of activated germanium,[3a] diethylzinc with a rhodium catalyst and chromium dichloride with or without lithium iodide did not improve the diastereoselectivity of the reaction (Table 1, entries 1–5).

We then used this activated samarium metal in the Reformatsky reaction between the α-bromo α′-sulfinyl ketones **2** and **3**, which have a more hindered substituent on the sulfur atom, and benzaldehyde. In fact we observed a higher diastereofacial selectivity with R′ = *t*Bu and *o*-$Me_2NC_6H_4$;

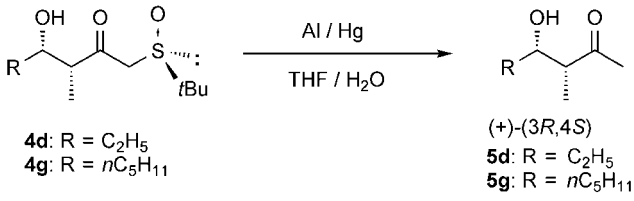
Table 3. Diastereoselective Reformatsky reaction with various aromatic and aliphatic aldehydes.[a]



Entry	R′	R	*syn*/*anti*[b]	*syn*1(**4a**–**h**)/*syn*2[b]	Yield [%][c]
1	*t*Bu	Ph	75:25	96 (**4a**):4	51 (61)[d]
2	*t*Bu	*p*-$O_2NC_6H_4$	80:20	80 (**4b**):20	86
3	*t*Bu	$(CH_3)_2CHCH_2$	90:10	90 (**4c**):10	45 (55)[d]
4	*t*Bu	C_2H_5	98:2	95 (**4d**):5	79 (85)[d]
5	*t*Bu	*n*-C_3H_7	98:2	95 (**4e**):5	85 (85)[d]
6	*t*Bu	*n*-C_7H_{15}	98:2	95 (**4f**):5	67 (77)[d]
7	*t*Bu	*n*-C_5H_{11}	98:2	92 (**4g**):8	65 (75)[d]
8	*p*Tol	*n*-C_5H_{11}	85:15	85 (**4h**):15	65

[a] Reaction conditions: **1** or **2** (1 equiv.), RCHO (1.3 equiv.), SmI_2 (2 equiv.), THF, 30 min. [b] Determined by ^1H NMR analysis of the product. [c] Yield of the isolated mixture of diastereomers. [d] Reaction conditions for yield in parentheses: **1** (2 equiv.), RCHO (1 equiv.), SmI_2 (2 equiv.), THF, 30 min.

Table 4. Correlation of configuration by reductive elimination of sulfoxide.



Entry	R	$[\alpha]_D^{exp.}$	$[\alpha]_D^{theor.}$	Configuration	yield [%]
1	C_2H_5	+45 (*c* = 1.1, $CHCl_3$)	+44 (*c* = 1.0–1.2, $CHCl_3$)	(+)-(3*R*,4*S*)	80
2	*n*-C_5H_{11}	+26.7 (*c* = 1.1, $CHCl_3$)	+26.3 (*c* = 1.0–1.2, $CHCl_3$)	(+)-(3*R*,4*S*)	90

a *syn* ratio of 96:4 was obtained compared with 80:20 for *p*-tolylsulfinyl derivatives at –100 °C (Table 2).

Reformatsky-Type Reaction with Alkyl and Aryl Aldehydes

The addition of α-bromo α′-*tert*-butylsulfinyl ketone **2** to various aromatic and aliphatic aldehydes was accomplished under the optimized reaction conditions (Table 3).

Linear aliphatic aldehydes (Table 3, entries 4–7) afforded Reformatsky adducts **4d**–**g** in moderate-to-good yields with diastereoselectivities as high as 95:5 for the *syn* product. The yields were slightly improved when excess amounts of α-bromo α′-*tert*-butylsulfinyl ketones **2** (2 equiv. instead of 1 equiv.) were employed. Isovaleraldehyde (Table 3, entry 3) also served as a viable substrate although a diminished yield was obtained. The stereoselectivity was lower with *p*-nitrobenzaldehyde than with benzaldehyde (Table 3, entries 1 and 2). In all cases the major diastereomers were easily purified by chromatography.

To confirm the strong effect of the *tert*-butyl group on the sulfinyl moiety on the diastereofacial selectivity, we carried out the condensation of α-halo α′-*p*-tolylsulfinyl ketone **1** with *n*-hexanal and found as expected a lower diastereoselectivity (*syn*/*anti*: 85:15; *syn*1/*syn*2: 85:15) (Table 3, entry 8).

The absolute stereochemistry of **4d** (R = C_2H_5) and **4g** (R = *n*-C_5H_{11}) was determined after reductive cleavage of the sulfoxide with aluminium amalgam giving the known methyl ketones **5d**[8] and **5g**[8] (Table 4).

To rationalize the observed stereochemical outcomes, we propose the transition-state models shown in Figure 1.

No attempt has been made to determine the geometry of the enolate but on the basis of the absolute configuration of the major products, the observed *syn*/*anti* selectivity of the present Reformatsky reaction can be deduced from the formation of the (*Z*)-enolate and the diastereofacial selectivity can be explained on the basis of a transition-state model in which samarium is chelated to the oxygen of the sulfoxide group, the oxygen of the enolate and the oxygen of the aldehyde.

That is to say, the reduction of **2** with the samarium salt occurs through coordination models **6** and **7** in which the samarium interacts with the carbonyl oxygen, bromine and sulfoxide oxygen atoms. Here, taking into account the non-binding interaction between the methyl and sulfinyl groups, **7** should be highly preferred over **6** to preferentially give the (*Z*)-enolate **8**. In the addition to the (*Z*)-enolate, the aldehyde approaches from the less hindered face (the sulfoxide's *tert*-butyl group is at the back) to form a boat transition state **9** in which the R group of the aldehyde is in a quasi-equatorial position.

Alternatively a coordinated chair structure **10**, in agreement with the observed stereoselectivity, would result in the R group of the aldehyde in an axial position, resulting in destabilized 1,3-diaxial interactions (Figure 2).

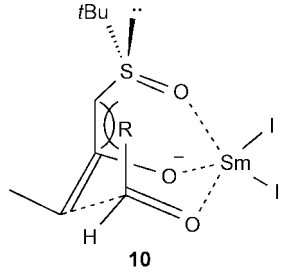


Figure 2. Chair transition state of **10**.

Boat and twist-boat transition states have been calculated[9] to lie within ±1.5 kcal/mol of the more commonly proposed chair transition states and recently, on the basis of calculated transition-state energies, Evans et al.[10] have proposed that aldol reactions with thiazolidinethiones proceed via a boat transition state.

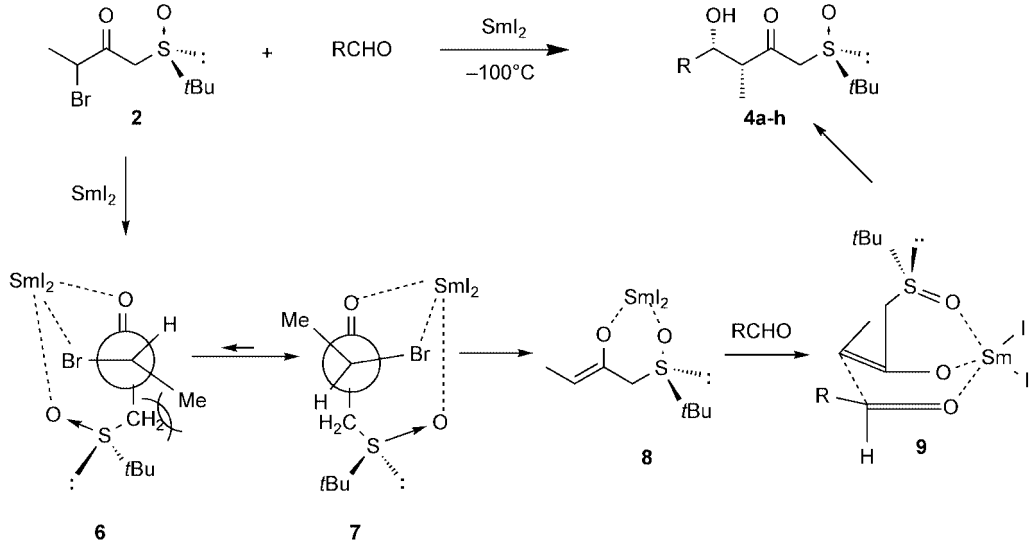


Figure 1. Proposed transition-state models for the SmI_2-mediated Reformatsky reaction of α-bromo α′-sulfinyl ketone **2** and aldehydes.

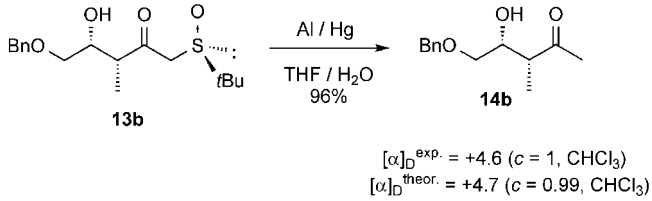
Reformatsky-Type Reaction with Functionalized Aldehydes

Taking into account our interest in total synthesis, we wanted to extend the scope of the reaction to functionalized aldehydes.

First, with α,β-unsaturated aldehydes such as acrolein and *trans*-2-hexenal, the relative *syn* selectivity was slightly lower (Table 5, entries 1 and 2). To improve the relative diastereoselectivity, additives such as Lewis acids, triphenylphosphane or TMEDA were used in the Reformatsky reaction with acrolein (Table 5, entries 3–6). Of these the use of PPh_3 slightly increased the relative diastereoselectivity (up to 85:15) but without improving the diastereofacial selectivity.

We then studied the Reformatsky reaction with protected α-hydroxylated aldehydes. Excellent diastereoselectivities were obtained with α-hydroxylated aldehydes protected with a *tert*-butyldimethylsilyl or benzyl group (Table 6, entries 1–4). However, low yields were obtained whatever the reaction time (Table 6, entries 2 and 4). Protection with MEM gave similar results (Table 6, entry 5).

The absolute configuration of **13b** (P = Bn) was determined after reductive cleavage of the sulfoxide with aluminium amalgam giving the known methyl ketone[11] **14b** (Scheme 4).

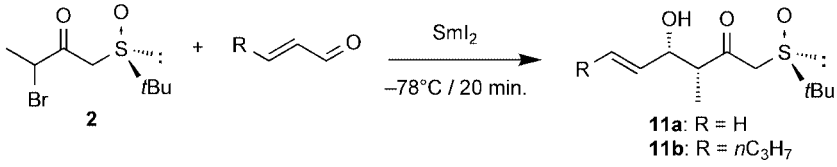


Scheme 4. Correlation of the configuration of **13b**.

Next we turned our attention to the Reformatsky reaction with α-keto aldehydes protected as dioxolane. These aldehydes were synthesized starting from dimethyl tartrate using known methodologies.

Protection of dimethyl tartrate as acetonide with dimethoxypropane in the presence of *p*-toluenesulfonic acid followed by treatment with *N*-methylmethoxyhydroxylamine and an excess of $AlMe_3$ afforded the bis-Weinreb amide[12] **16** in 72% overall yield. Amide **16** reacted with an excess of phenylmagnesium bromide in THF to afford the 1,4-diketone **17a** in 47% yield (unoptimized), whereas alkyl deriv-

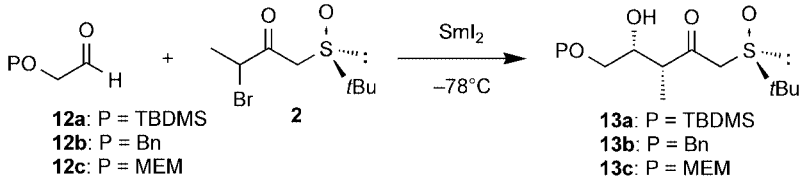
Table 5. Diastereoselective Reformatsky reaction with α,β-insaturated aldehydes with or without additives.[a]



Entry	R	Additives (equiv.)	*syn*/*anti*[a]	*syn*1/*syn*2[b]	yield [%][c]
1	H	–	70:30	84:16	59
2	n-C_3H_7	–	45:55	80:20	77
3	H	BF_3–Et_2O (3)	76:24	85:15	68
4	H	Et_2AlCl (3)	60:40	60:40	59
5	H	PPh_3 (1)	85:15	80:20	56
6	H	TMEDA (1)	67:33	82:18	27

[a] Reaction conditions: **2** (1 equiv.), RCHO (3 equiv.), SmI_2 (2 equiv.), THF, 30 min. [b] Determined by ^1H NMR analysis of the product. [c] Yield of the isolated mixture of diastereomers.

Table 6. Diastereoselective Reformatsky reaction with protected α-hydroxylated aldehydes.[a]



Entry	P	Time [min]	*syn*/*anti*[b]	*syn*1 (**13a**–**c**)/*syn*2[b]	Yield [%][c]
1	TBDMS	20	98:2	92 (**13a**):8	40
2	TBDMS	180	98:2	92 (**13a**):8	37
3	Bn	20	98:2	92 (**13b**):8	30
4	Bn	240	98:2	92 (**13b**):8	50
5	MEM	30	90:10[d]	90 (**13c**):10[d]	50

[a] Reaction conditions: **2** (1 equiv.), RCHO (3 equiv.), SmI_2 (2 equiv.), THF. [b] Determined by ^1H NMR analysis of the product. [c] Yield of the isolated mixture of diastereomers. [d] Determined after irradiations by ^1H NMR 400 MHz.

ative **17b** was obtained from **16** by treatment with *n*-heptylmagnesium bromide in THF in 78% yield. Derivatives **17a**,**b** were submitted to acetal hydrolysis in the presence of trifluoroacetic acid and water to give **18a**,**b** in excellent yields. An attempt to oxidatively cleave **18a** with either $NaIO_4$ or $Pb(OAc)_4$ did not succeed. We then protected the carbonyl functions as dioxolane to afford **19a**,**b** which were then oxidatively cleaved with $Pb(OAc)_4$ in CH_2Cl_2 to give the desired protected α-keto aldehydes **20a**,**b** in good yields.[13] These aldehydes were directly used without further purification in the Reformatsky-type reaction (Scheme 5).

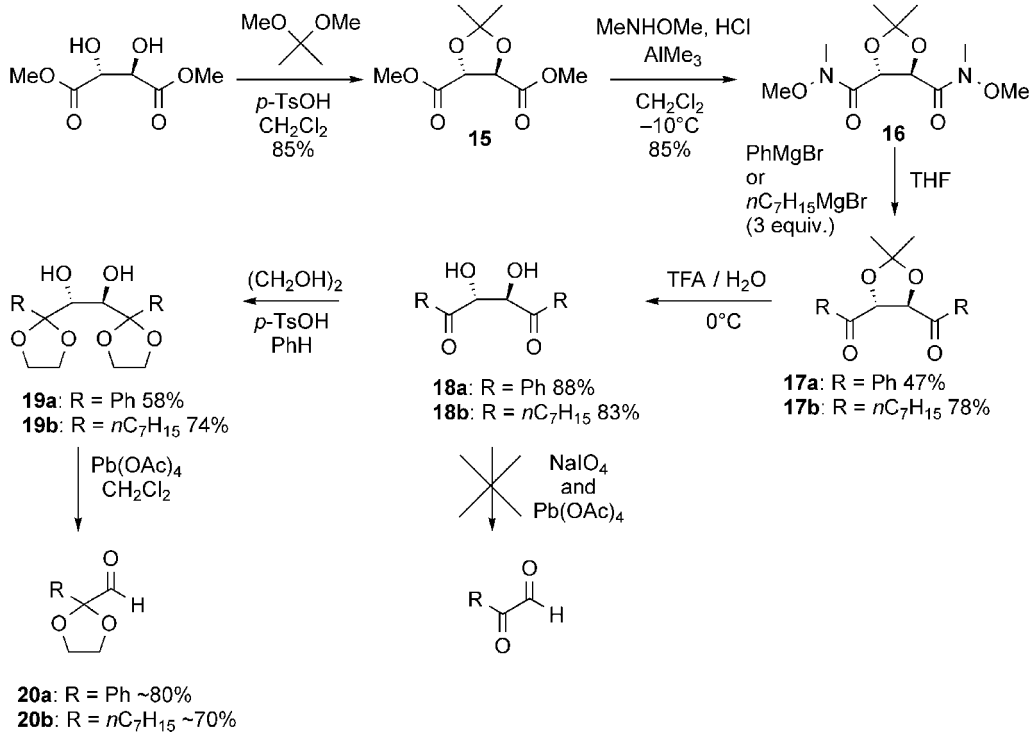
We applied our SmI_2-promoted Reformatsky-type reaction to the aldehydes **20a**,**b**. Excellent diastereoselectivity and a good yield were obtained with aldehyde **20b** (Table 7, entry 2). Surprisingly, aldehyde **20a** with a phenyl group gave high diastereofacial selectivity but poor *syn*/*anti* selectivity (Table 7, entry 1).

Synthesis of the *syn*- or *anti*-2-Methyl-1,3-diols

In order to obtain the *syn*- or *anti*-2-methyl-1,3-diol moieties we performed the well-known diastereoselective reduction of the β-keto sulfoxides[14,15] obtained in the Reformatsky reactions either with only DIBALH or with DIBALH in the presence of a Lewis acid.

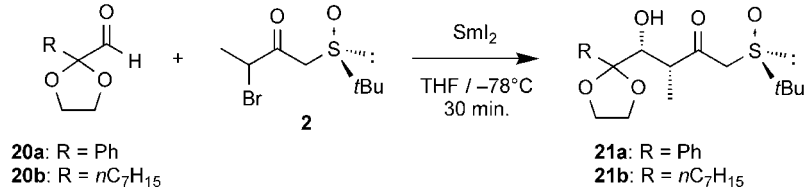
Starting from the adduct **4d** (obtained by Reformatsky condensation with propanal) the *syn*-2-methyl-1,3-diol **22** was obtained in excellent yield and diastereoselectivity in the presence of DIBALH (Table 8, entry 1).

In order to obtain the *anti*-2-methyl-1,3-diol **23** we studied the reduction of **4d** in the presence of DIBALH



Scheme 5. Synthesis of the protected α-keto aldehydes.

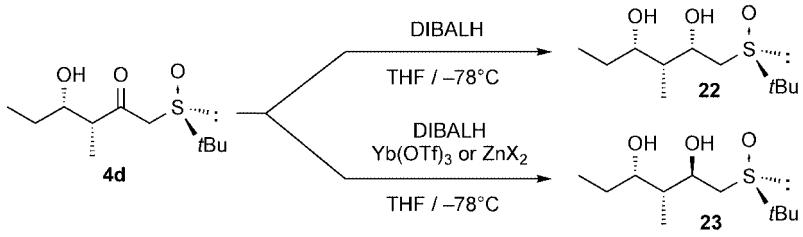
Table 7. Diastereoselective Reformatsky reaction with protected α-keto aldehydes.[a]



Entry	R	*syn*/*anti*[a]	*syn*1/*syn*2[b]	*anti*1/*anti*2[b]	Yield [%][c]
1	C_6H_5	63:37	**21a** >99:1	>99:1	67
2	*n*-C_7H_{15}	92:8	**21b** >99:1	>99:1	73

[a] Reaction conditions: **2** (1 equiv.), RCHO (1.3 equiv.), SmI_2 (2 equiv.), THF, 30 min. [b] Determined by ^1H NMR analysis of the product. [c] Yield of the isolated mixture of diastereomers.

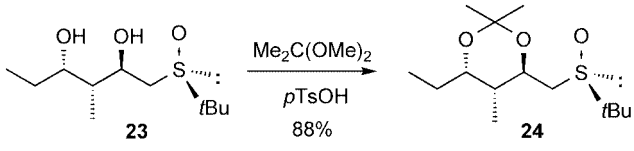
Table 8. Reduction of β-keto sulfoxide **4d**.



Entry	Reductant (equiv.)	Configuration	*de* [%][a]	Yield [%][b]
1	DIBALH (2.4)	*S* (diol *syn*)	>98	**22** 90
2	DIBALH (4)/$ZnCl_2$ (2.4)	*R* (diol *anti*)	10	**23** 85
3	DIBALH (4)/$ZnBr_2$ (2.4)	*R* (diol *anti*)	40	**23** 86
4	DIBALH (4)/ZnI_2 (2.4)	*R* (diol *anti*)	60	**23** 83
5	DIBALH (4)/$Yb(OTf)_3$ (2.4)	*R* (diol *anti*)	90	**23** 81
6	DIBALH (2.4)/$Yb(OTf)_3$ (1.2)	*R* (diol *anti*)	90	**23** 85

[a] Determined by ^{1}H NMR analysis of the product. [b] Yield of the isolated mixture of diastereomers.

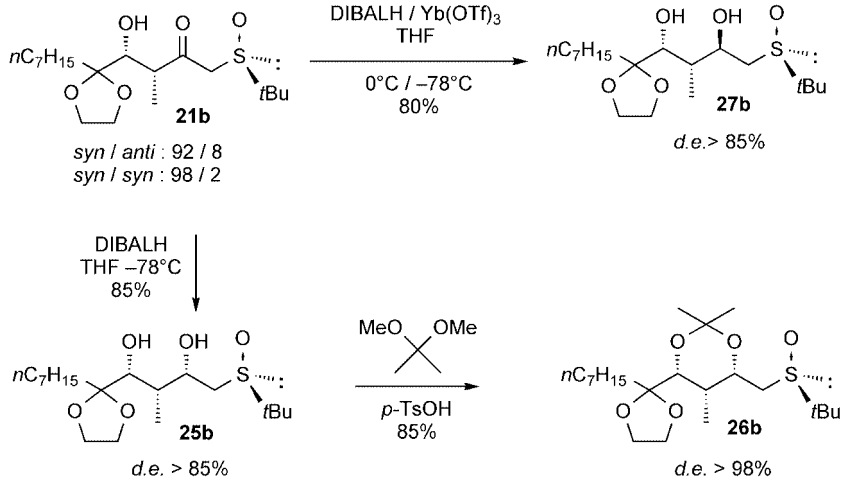
and a Lewis acid. Use of 2.4 equivalents of zinc halide with 4 equivalents of DIBALH afforded the *anti*-2-methyl-1,3-diol **23** in good yield but modest selectivity (60% *de* with ZnI_2) (Table 8, entries 2–4). The best results were obtained in the presence of $Yb(OTf)_3$ (1.2 equiv.) and DIBALH (2.4 equiv.); a 95:5 mixture of the two possible diastereomeric carbinols was obtained from which the major compound bearing the (*R*) absolute configuration at the newly created stereogenic center could be isolated after flash chromatography of the corresponding acetonide **24** (Scheme 6).



Scheme 6.

The (*S*) absolute configuration at the formed hydroxylic carbon of **22** as well as the (*R*) absolute configuration at C-2 of **23** could be deduced not only from the mechanism already published for the reduction of such β-keto sulfoxides[15] but also from the ^{1}H NMR spectra of the products. From numerous reported examples of the reduction of β-keto sulfoxides, a noticeable difference in the nonequivalence of the methylene hydrogen atoms α to the sulfoxide of the (S,R_S) and (R,R_S) epimers has been observed. For the (2*S*,3*R*,4*S*,R_S)-**22** configuration, the $\Delta\upsilon$ value for these two hydrogen atoms is larger ($\Delta\upsilon$ = 79 Hz in **22**) than that for these hydrogen atoms in (2*R*,3*R*,4*S*,R_S)-**23** ($\Delta\upsilon$ = 50 Hz in **23**).

The *anti* relative configuration of the diol in compound **24** was ascertained from the small nonequivalence of the two methyl groups of the acetonide observed in the ^{13}C NMR spectrum: δ = 24.0 and 24.9 ppm.[16] Typical values for the *syn*-diol acetonide methyl groups are δ = 20.0 and 30.2 ppm.[17] Furthermore the (2*R*,3*R*,4*S*,R_S) relative con-



Scheme 7.

figuration of **24** was confirmed by ^{1}H NMR NOESY experiments.

The efficacy of this methodology was then checked with the Reformatsky adduct **21b** in which the carbonyl functionality is protected as a dioxolane.

Treatment of **21b** with DIBALH afforded the corresponding *syn*-2-methyl-1,3-diol **25b** in an excellent yield and with a diastereoselectivity of up to 85%. The major diastereomer, which has the (*S*) absolute configuration at the newly created stereogenic center, was isolated after flash chromatography of the corresponding acetonide **26b** (Scheme 7). The absolute configuration (2*S*,3*R*,4*R*,R_S) of the major compound **26b** was confirmed by ^{1}H NMR spectra and ^{1}H NMR NOESY experiments.

When DIBALH with $Yb(OTf)_3$ was used to reduce the adduct **21b** compound (2*R*,3*R*,4*R*,R_S)-**27b** was obtained as the major diastereomer (*de* > 85%).

Conclusions

This new methodology constitutes an efficient access to enantiomerically pure *syn*- and *anti*-2-methyl-1,3-diols using an asymmetric Reformatsky-type reaction followed by diastereoselective reduction of the β-keto sulfoxide. Reformatsky adducts were obtained in good yields with both high *syn*/*anti* and diastereofacial selectivities. A boat transition state has been proposed to explain the observed stereoselectivities. Extension of this study to α-functionalized aldehydes as well as to substrates with a sulfinyl group has allowed the synthesis of important precursors for total synthesis.

Experimental Section

General Remarks: THF and diethyl ether were freshly distilled under nitrogen from sodium benzophenone ketyl immediately before use. All aldehydes were also freshly distilled according to the usual protocol[18] and stored under nitrogen. Diisopropylamine was distilled from calcium hydride and stored over potassium hydroxide. All other reagents and solvents were used as received from commercial sources. Moisture-sensitive reactions were conducted in oven- or flame-dried glassware under argon. Sulfoxides were prepared according to literature procedures.[19] All reactions were magnetically stirred and monitored by thin-layer chromatography using precoated silica gel (60 F_{254}) plates. Column chromatography was carried out with the indicated solvents on silica gel 60 (40–63 μm, Merck) or on unmetalled silica gel. NMR spectra were recorded at room temperature using $CDCl_3$ (δ = 7.26 ppm) as the reference (Bruker AC-200, Bruker Avance 300 and Bruker Avance 400 spectrometers, ^{1}H at 200, 300 and 400 MHz and ^{13}C at 50, 75 and 100 MHz, respectively). All chemical shifts (δ) are quoted in parts per million (ppm) and coupling constants (*J*) in Hertz. ^{13}C chemical shifts are referenced to $CDCl_3$ (δ = 77.0 ppm). Melting points were obtained on a Büchi 535 apparatus. Optical rotations were determined from a Perkin–Elmer 241 MC polarimeter operating at the sodium D line at 20 °C. IR spectra were recorded using a Perkin–Elmer Spectum One spectrometer; $\tilde{\nu}$ values are given in cm^{-1}.

General Procedure for the Preparation of α-Bromo α′-Sulfinyl Ketones 1–3: A solution of *n*BuLi (1.6 M in hexane) (5.00 mmol, 2 equiv.) was added to a solution of diisopropylamine (5.25 mmol, 2.1 equiv.) in THF (5 mL) at –78 °C. After 1 h at –78 °C, a solution of sulfoxide (5.00 mmol, 2 equiv.) in THF (5 mL) was added to the lithium diisopropylamide at –78 °C. The mixture was stirred under these conditions for 1 h. Then methyl 2-bromopropionate (2.50 mmol, 1 equiv.) in THF (5 mL) was added at –78 °C to the lithiated sulfoxide anion. The resulting solution was stirred at –78 °C for 30 min. The solution was quenched with a saturated NH_4Cl solution (10 mL) and additional water. The reaction mixture was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic extracts were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel.

(*R*$_S$)-3-Bromo-1-(*p*-totylsulfinyl)butan-2-one (1): A mixture of two diastereomers. Yellow solid (92% yield); R_f = 0.3 and 0.4 (hexane/EtOAc, 1:1). IR (neat): $\tilde{\nu}$ = 3044–2861, 1717, 1492, 1442, 1354, 1260, 1081, 1045, 1023, 1014, 971, 795 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47 and 7.42 (A_2B_2, J_{AB} = 8.1 Hz, $\Delta\nu$ = 63.9 and 41.2 Hz, 4 H, $H_{p\text{Tol}}$), 4.42 and 4.43 (q, *J* = 6.7 Hz, 1 H, C*H*Br), 4.07 and 4.13 [AB, J_{AB} = 13.8 and 13.4 Hz, $\Delta\nu$ = 102.5 and 161.9 Hz, 2 H, CH_2S(O)], 2.44 and 2.43 (s, 3 H, C$H_{3,p\text{Tol}}$), 1,70 and 1,63 (d, *J* = 6.7 Hz, 3 H, CHBrCH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.1 (*C*=O), 194.4 (*C*=O), 142.5 ($C_{p\text{Tol}}$), 142,4 ($C_{p\text{Tol}}$), 139,9 ($C_{p\text{Tol}}$), 138,8 ($C_{p\text{Tol}}$), 130,3 (*C*H$_{p\text{Tol}}$), 130,2 (*C*H$_{p\text{Tol}}$), 124,0 (*C*H$_{p\text{Tol}}$ × 2), 65.9 [*C*H$_2$S(O)], 63.5 [*C*H$_2$S(O)], 48.5 (*C*HBr), 48.4 (*C*HBr), 21.5 (*C*H$_{3,p\text{Tol}}$ × 2), 19.0 [CH(Br)*C*H$_3$], 18.9 [CH(Br)*C*H$_3$] ppm.

(*R*$_S$)-3-Bromo-1-(*tert*-butylsulfinyl)butan-2-one (2): A mixture of two diastereomers. Yellow solid (95% yield); R_f = 0.40 (EtOAc). IR (neat): $\tilde{\nu}$ = 2991–2865, 1716, 1469, 1374, 1364, 1267, 1177, 1060, 1030, 1020, 983 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.67 and 4.63 (q, *J* = 6.6 Hz, 1 H, C*H*Br), 3.85 and 3.77 [AB, J_{AB} = 13.7 and 12.5 Hz, $\Delta\nu$ = 71 and 81.5 Hz, 2 H, CH_2S(O)], 1.81 and 1.77 [d, *J* = 6.6 Hz, 3 H, CH(Br)CH_3], 1.30 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.8 (*C*=O), 196.4 (*C*=O), 55.1 [*C*H$_2$S(O)], 55.0 [*C*(*C*H$_3$)$_3$], 54.9 [*C*(CH$_3$)$_3$], 54.3 [*C*H$_2$S(O)], 48.9 (*C*HBr), 47.7 (*C*HBr), 22.8 [C(*C*H$_3$)$_3$], 22.6 [C(*C*H$_3$)$_3$], 19.5 [CH(Br)*C*H$_3$], 19.0 [CH(Br)*C*H$_3$] ppm.

(*R*$_S$)-3-Bromo-1-[*o*-(dimethylamino)phenylsulfinyl]butan-2-one (3): A mixture of two diastereomers. Yellow solid (98% yield); R_f = 0.32 and 0.45 (hexane/EtOAc, 1:1). IR (neat): $\tilde{\nu}$ = 2998–2796, 1720, 1588, 1475, 1451, 1432, 1371, 1316, 1260, 1154, 1129, 1058, 1045, 1027, 979, 940, 875, 764, 724 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.85 and 7.72 (dd, 1 H, *J* = 7.6 and 1.5 Hz, H_{Ar}), 7.48 (td, *J* = 7.6 and 1.5 Hz, 1 H, H_{Ar}), 7.32 and 7.30 (td, *J* = 7.6 and 1.2 Hz, 1 H, H_{Ar}), 7.18 and 7.20 (dd, *J* = 7.9 and 1.1 Hz, 1 H, H_{Ar}), 4.23 and 4.65 (q, *J* = 6.8 Hz, 1 H, C*H*Br), 4.24 and 4.32 (AB, J_{AB} = 13.2 and 13.0 Hz, $\Delta\nu$ = 40.3 and 152.2 Hz, 2 H, CH_2), 2.75 and 2.72 [s, 6 H, N(CH_3)$_2$], 1.69 and 1.56 (d, *J* = 6.6 Hz, 3 H, H_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.2 (*C*=O), 194.8 (*C*=O), 151.0 (C_{Ar}), 150.7 (C_{Ar}), 136.2 (C_{Ar} × 2), 132.3 (*C*H$_{Ar}$), 132.2 (*C*H$_{Ar}$), 124.9 (*C*H$_{Ar}$ × 3), 124.8 (*C*H$_{Ar}$), 120.6 (*C*H$_{Ar}$), 120.1 (*C*H$_{Ar}$), 62.1 [*C*H$_2$S(O)], 59.2 [*C*H$_2$S(O)], 48.7 (*C*HBr), 48.5 (*C*HBr), 44.8 [N(*C*H$_3$)$_2$], 19.2 [CH(Br)*C*H$_3$], 18.7 [CH(Br)*C*H$_3$] ppm.

General Procedure for the Samarium(II) Iodide Mediated Reformatsky-Type Reaction: The following is a description of a typical experimental procedure for the Reformatsky-type reaction of a chiral γ-bromo-β-keto sulfoxide with an aldehyde (only the major *syn* diastereomer is described).

A solution of SmI_2, prepared by the addition of diiodomethane (0.78 mmol, 2 equiv.) in THF (8 mL) to samarium powder (0.86 mmol, 2.2 equiv.), was stirred at room temperature for 2 h.

The solution was cooled to –78 °C and a solution of γ-bromo-β-keto sulfoxide (0.39 mmol, 1 equiv.) in THF (1.5 mL) was added dropwise. The mixture was stirred under these conditions for 10 min. A solution of aldehyde (0.51 mmol, 1.3 equiv.) in THF (1.5 mL) was then added at –78 °C. The resulting mixture was stirred at –78 °C for 30 min. The solution was quenched with a 0.1 M hydrochloric acid solution (30 mL) and brine (20 mL). The reaction mixture was extracted with diethyl ether (3×40 mL). The organic phase was washed with aqueous sodium thiosulfate (50 mL) to remove liberated iodine and brine (2×50 mL) and then dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by unmetalled silica gel chromatography.

(3*R*,4*S*,R_S)-1-(*tert*-Butylsulfinyl)-4-hydroxy-3,6-dimethylheptan-2-one (4c): Yellow oil (55% yield); R_f = 0.20 (CH_2Cl_2/EtOAc, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$, major diastereomer): δ = 4.15 (d, J = 9.2 Hz, 1 H, C*H*OH), 3.64 [AB, J_{AB} = 12.8 Hz, $\Delta\nu$ = 210.8 Hz, 2 H, CH_2S(O)], 3.20 (br. s, 1 H, O*H*), 2.83 (qd, J = 7.0, 3.0 Hz, 1 H, C*H*CH_3), 1.80–1.70 [m, 1 H, C*H*$(CH_3)_2$], 1.48–1.41 and 1.17–1.11 [m, AB part of ABXM, 2 H, CH_2CH$(CH_3)_2$], 1.27 (s, 9 H, *t*Bu), 1.09 (d, J = 6.8 Hz, 3 H, CHCH_3), 0.91 and 0.89 [d, J = 6.6 Hz, 3 H, CH(CH_3)$_2$] ppm.

(+)-(3*R*,4*S*,R_S)-1-(*tert*-Butylsulfinyl)-4-hydroxy-3-methylhexan-2-one (4d): Yellow oil (85% yield); R_f = 0.10 (CH_2Cl_2/EtOAc, 1:1). $[\alpha]_D^{20}$ = +190 (c = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3405, 2980–2871, 1706, 1462, 1364, 1357, 1140, 1077, 1038, 1028, 1007, 962, 935 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.04–3.94 (m, 1 H, C*H*OH), 3.65 [AB, J_{AB} = 12.8 Hz, $\Delta\nu$ = 173.3 Hz, 2 H, CH_2S(O)], 3.18 (d, J = 5.3 Hz, 1 H, O*H*), 2.89 (qd, J = 7.0, 3.0 Hz, 1 H, C*H*CH_3), 1.60–1.40 (m, 2 H, C$H_2$$CH_3$), 1.30 (s, 9 H, *t*Bu), 1.12 (d, J = 7.0 Hz, 3 H, CHCH_3), 0.98 (t, J = 7.3 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.0 (*C*=O), 72.5 (*C*HOH), 56.2 [*C*H_2S(O)], 54.4 [*C*$(CH_3)_3$], 53.5 (*C*HCH_3), 26.4 (*C*$H_2$$CH_3$), 22.8 [C(*C*$H_3$)$_3$], 10.7 (CH*C*$H_3$), 8.9 ($CH_2$*C*$H_3$) ppm. $C_{11}H_{22}O_3S$ (234.36): C 56.38, H 9.46; found C 55.89, H 9.51.

(+)-(3*R*,4*S*,R_S)-1-(*tert*-Butylsulfinyl)-4-hydroxy-3-methylheptan-2-one (4e): Yellow oil (85% yield); R_f = 0.2 (CH_2Cl_2/EtOAc, 1:1). $[\alpha]_D^{20}$ = +175 (c = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3391, 2960–2873, 1713, 1463, 1368, 1258, 1178, 1144, 1028, 968 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.11–4.01 (m, 1 H, C*H*OH), 3.64 [AB, J_{AB} = 12.8 Hz, $\Delta\nu$ = 158.4 Hz, 2 H, CH_2S(O)], 3.25 (d, J = 5.3 Hz, 1 H, O*H*), 2.84 (qd, J = 7.0, 3.0 Hz, 1 H, C*H*CH_3), 1.56–1.30 (m, 4 H, CH_2C$H_2$$CH_3$), 1.27 (s, 9 H, *t*Bu), 1.09 (d, J = 7.0 Hz, 3 H, CHCH_3), 0.91 (t, J = 7.3 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.8 (*C*=O), 70.7 (*C*HOH), 56.2 [*C*H_2S(O)], 54.3 [*C*$(CH_3)_3$], 53.7 (*C*HCH_3), 35.6 (*C*H_2CHOH), 22.7 [C(*C*H_3)$_3$], 19.4 (*C*$H_2$$CH_3$), 13.9 (CH*C*$H_3$), 9.0 [$(CH_2)_2$*C*$H_3$] ppm. $C_{12}H_{24}O_3S$ (248.39): C 58.03, H 9.74; found C 58.17, H 9.93.

(+)-(3*R*,4*S*,R_S)-1-(*tert*-Butylsulfinyl)-4-hydroxy-3-methylundecan-2-one (4f): Yellow oil (77% yield); R_f = 0.25 (CH_2Cl_2/EtOAc, 1:1). $[\alpha]_D^{20}$ = +130 (c = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3370, 2956–2856, 1701, 1465, 1366, 1248, 1232, 1178, 1144, 1113, 1016, 997, 958 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.11–4.03 (m, 1 H, C*H*OH), 3.64 [AB, J_{AB} = 12.6 Hz, $\Delta\nu$ = 166.5 Hz, 2 H, CH_2S(O)], 3.18 (d, J = 5.3 Hz, 1 H, O*H*), 2.86 (qd, J = 7.0, 3.0 Hz, 1 H, C*H*CH_3), 1.56–1.20 [m, 12 H, $(CH_2)_6CH_3$], 1.29 (s, 9 H, *t*Bu), 1.11 (d, J = 7.0 Hz, 3 H, CHCH_3), 0.87 (t, J = 6.6 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.9 (*C*=O), 71.0 (*C*HOH), 56.2 [*C*H_2S(O)], 54.4 [*C*$(CH_3)_3$], 53.7 (*C*HCH_3), 33.5 (*C*H_2), 31.8 (*C*H_2), 29.5 (*C*H_2), 29.2 (*C*H_2), 26.3 (*C*H_2), 22.8 [C(*C*H_3)$_3$], 22.6 (*C*H_2), 14.1 (CH*C*H_3), 8.9 [$(CH_2)_6$*C*H_3] ppm. $C_{16}H_{32}O_3S$ (304.49): C 63.11, H 10.59; found C 63.25, H 10.71.

(+)-(3*R*,4*S*,R_S)-1-(*tert*-Butylsulfinyl)-4-hydroxy-3-methylnonan-2-one (4g): Yellow oil (75% yield); R_f = 0.2 (CH_2Cl_2/EtOAc, 7:3). $[\alpha]_D^{20}$ = +145 (c = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3382, 2957–2861, 1713, 1463, 1368, 1256, 1178, 1143, 1032, 935 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.13–4.02 (m, 1 H, C*H*OH), 3.65 [AB, J_{AB} = 12.6 Hz, $\Delta\nu$ = 112.7 Hz, 2 H, CH_2S(O)], 3.25 (d, J = 5.1 Hz, 1 H, O*H*), 2.86 (qd, J = 7.0, 3.0 Hz, 1 H, C*H*CH_3), 1.55–1.35 [m, 8 H, $(CH_2)_4CH_3$], 1.29 (s, 9 H, *t*Bu), 1.11 (d, J = 6.7 Hz, 3 H, CHCH_3), 0.88 (t, J = 6.5 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.9 (*C*=O), 71.0 (*C*HOH), 56.2 [*C*H_2S(O)], 54.3 [*C*$(CH_3)_3$], 53.7 (*C*HCH_3), 33.4 (*C*H_2CHOH), 31.7 (*C*H_2), 25.9 (*C*H_2), 22.7 [C(*C*H_3)$_3$], 22.6 (*C*H_2), 14.0 (CH*C*H_3), 8.9 [$(CH_2)_4$*C*H_3] ppm. $C_{14}H_{28}O_3S$ (276.44): C 60.83, H 10.21; found C 60.91, H 10.30.

(3*R*,4*S*,R_S)-4-Hydroxy-3-methyl-1-(*p*-tolylsulfinyl)nonan-2-one (4h): White solid (65% yield); R_f = 0.33 (CH_2Cl_2/EtOAc, 7:3). IR (neat): $\tilde{\nu}$ = 3371, 3010–2857, 1693, 1455, 1252, 1106, 1083, 1035, 1003, 931, 803 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45 (A_2B_2, J_{AB} = 8.1 Hz, $\Delta\nu$ = 61.6 Hz, 4 H, C$H_{p\text{Tol}}$), 4.07–4.00 (m, 1 H, C*H*OH), 3.95 [AB, J_{AB} = 13.7 Hz, $\Delta\nu$ = 88.8 Hz, 2 H, CH_2S(O)], 2.83 (d, J = 4.7 Hz, 1 H, O*H*), 2.68 (qd, J = 7.0, 3.0 Hz, 1 H, C*H*CH_3), 2.43 (s, 3 H, C$H_{3,p\text{Tol}}$), 1.53–1.20 [m, 8 H, $(CH_2)_4CH_3$], 1.02 (d, J = 7.0 Hz, 3 H, CHCH_3), 0.88 (t, J = 6.8 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.5 (*C*=O), 142.3 ($C_{p\text{Tol}}$), 139.5 ($C_{p\text{Tol}}$), 130.2 (*C*H$_{p\text{Tol}}$), 124.0 (*C*H$_{p\text{Tol}}$), 71.0 (*C*HOH), 67.3 [*C*H_2S(O)], 53.1 (*C*HCH$_3$), 33.6 (*C*H_2CHOH), 31.7 (*C*H_2), 25.8 (*C*H_2), 22.6 (*C*H_2), 21.4 (*C*$H_{3,p\text{Tol}}$), 14.0 (CH*C*H_3), 8.7 [$(CH_2)_4$*C*H_3] ppm. $C_{17}H_{26}O_3S$ (310.46): C 65.77, H 8.44; found C 66.17, H 8.38.

(+)-(3*R*,4*R*,R_S)-5-(*tert*-Butyldimethylsilyloxy)-1-(*tert*-butylsulfinyl)-4-hydroxy-3-methylpentan-2-one (13a): Pale yellow oil (40% yield); R_f = 0.25 (CH_2Cl_2/EtOAc, 7:3). $[\alpha]_D^{20}$ = +92.8 (c = 0.5, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3352, 2956–2858, 1713, 1472, 1463, 1365, 1255, 1122, 1040, 1008, 838, 778 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.17 (td, J = 6.4, 4.0 Hz, 1 H, C*H*OH), 3.67 [AB, J_{AB} = 13.0 Hz, $\Delta\nu$ = 86.3 Hz, 2 H, CH_2S(O)], 3.61 (AB part of ABX, J_{AB} = 10.2, J_{AX} = 6.4, J_{BX} = 6.4 Hz, $\Delta\nu$ = 16.1 Hz, 2 H, CH_2CHOH), 3.00 (qd, J = 7.0, 4.0 Hz, 1 H, C*H*CH_3), 1.30 [s, 9 H, S(O)*t*Bu], 1.11 (d, J = 7.0 Hz, 3 H, CHCH_3), 0.90 (s, 9 H,Si*t*Bu), 0.08 [s, 6 H, Si(CH_3)$_2$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.7 (*C*=O), 70.7 (*C*HOH), 63.8 (*C*H_2CHOH), 56.6 [*C*H_2S(O)], 54.3 [S(O)*C*$(CH_3)_3$], 50.3 (*C*HCH$_3$), 25.9 [Si-C(*C*H_3)$_3$], 22.8 [S(O)C(*C*H_3)$_3$], 18.2 [Si-*C*$(CH_3)_3$], 9.2 (CH*C*H_3), –5.4 (Si-*C*H_3), –5.5 (Si-*C*H_3) ppm.

(+)-(3*R*,4*R*,R_S)-5-Benzyloxy-1-(*tert*-butylsulfinyl)-4-hydroxy-3-methylpentan-2-one (13b): White solid (50% yield); R_f = 0.20 (EtOAc); m.p. 48 °C. $[\alpha]_D^{20}$ = +121 (c = 0.5, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3351, 3089–2869, 1711, 1455, 1367, 1256, 1177, 1102, 1029, 1012, 741, 700 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 5 H, C_6H_5), 4,54 (AB, J_{AB} = 11.9 Hz, $\Delta\nu$ = 12.9 Hz, 2 H, CH_2Ar), 4.34 (td, J = 5.9, 4.1 Hz, 1 H, C*H*OH), 3.64 [AB, J_{AB} = 13.0 Hz, $\Delta\nu$ = 109.0 Hz, 2 H, CH_2S(O)], 3.53 (AB part of ABX, J_{AB} = 9.5, J_{AX} = 6.3, J_{BX} = 5,8 Hz, $\Delta\nu$ = 16.7 Hz, 2 H, CH_2CHOH), 3.01 (qd, J = 6.8, 4.1 Hz, 1 H, C*H*CH_3), 2.87 (s, 1 H, O*H*), 1.28 (s, 9 H, *t*Bu), 1.15 (d, J = 7.5 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.7 (*C*=O), 137.8 ($C_{IV\text{-}Ar}$), 128.4 ($C_{III\text{-}Ar}$), 127.9 ($C_{III\text{-}Ar}$), 127.8 ($C_{III\text{-}Ar}$), 73.5 (*C*H$_2$-O), 71.1 (*C*H$_2$-O), 69.6 (*C*HOH), 56.5 [*C*H_2S(O)], 54.3 [*C*$(CH_3)_3$], 50.9 (*C*HCH$_3$), 22.8 [C(*C*H_3)$_3$], 9.5 (CH*C*H_3) ppm. $C_{17}H_{26}O_4S$ (326.46): C 62.55, H 8.03; found C 62.75, H 8.09.

(3*R*,4*R*,R_S)-1-(*tert*-Butylsulfinyl)-4-hydroxy-5-(methoxyethoxymethyl)-3-methylpentan-2-one (13c): Pale yellow oil (50% yield); R_f = 0.13 (EtOAc/MeOH, 95:5). IR (neat): $\tilde{\nu}$ = 3351, 3089–2869, 1711, 1455, 1367, 1256, 1177, 1102, 1029, 1012, 741, 700 cm^{-1}. ^{1}H NMR

(300 MHz, $CDCl_3$): δ = 4,74 (s, 2 H, O-CH_2-O), 4.26 (m, 1 H, C*H*OH), 3.75–3.54 (m, 6 H, O-CH_2CH_2-O and O-CH_2CHOH), 3.68 [AB, J_{AB} = 13.2 Hz, $\Delta\nu$ = 88.8 Hz, 2 H, CH_2S(O)], 3.39 (s, 3 H, OCH_3), 3.00 (qd, J = 7.0, 4.1 Hz, 1 H, C*H*CH$_3$), 1.30 (s, 9 H, *t*Bu), 1.18 (d, J = 7.0 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.6 (*C*=O), 96.1 (O-*C*H_2-O), 71.8 (*C*H_2-O), 70.0 (*C*HOH), 69.9 (*C*H_2-O), 67.3 (*C*H_2-O), 59.0 (O-*C*H_3), 56.9 [*C*H_2S(O)], 54.4 [*C*(CH$_3$)$_3$], 50.7 (*C*HCH$_3$), 22.8 [C(*C*H$_3$)$_3$], 9.9 (CH*C*H$_3$) ppm.

1-(*tert*-Butylsulfinyl)-4-hydroxy-3-methyl-4-(2-phenyl-[1,3]dioxolan-2-yl)butan-2-one (21a): A mixture of two diastereomers *syn* (**A**) and *anti* (**B**)]. White solid (67% yield); R_f = 0.18 (AcOEt). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.33 (m, 5 H, C*H*^{Ar} **A** and **B**), 4.29 (d, J = 6.0 Hz, 1 H, C*H*OH **A**), 4.16–4.02 and 3.86–3.77 (m, 4 H, OCH_2CH_2O **A** and **B**), 3.93 (d, J = 4.2 Hz, 1 H, C*H*OH **B**), 3.64 [AB, J_{AB} = 18.6 Hz, $\Delta\nu$ = 27.6 Hz, 2 H, CH_2S(O) **B**], 3.55 [s, 2 H, CH_2S(O) **A**], 2.96 (qd, J = 7.2 and 4.2 Hz, 1 H, C*H*CH$_3$ **B**), 2.85 (q^t, J = 7.2 Hz, 1 H, C*H*CH$_3$ **A**), 2.03 (s, 1 H, O*H*), 1.29 (s, 9 H, *t*Bu **B**), 1.26 (s, 9 H, *t*Bu **A**), 1.22 (d, J = 7.2 Hz, 3 H, CHCH_3 **A**), 1.21 (d, J = 7.2 Hz, 3 H, CHCH_3 **B**) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.5 (*C*=O **B**), 204.1 (*C*=O **A**), 139.3 ($C_{IV\text{-}Ar}$ **A**), 139.0 ($C_{IV\text{-}Ar}$ **B**), 128.7 ($C_{III\text{-}Ar}$ **A**), 128.6 ($C_{III\text{-}Ar}$ **B**), 128.3 ($C_{III\text{-}Ar}$ **A**), 128.2 ($C_{III\text{-}Ar}$ **B**), 126.5 ($C_{III\text{-}Ar}$ **A**), 126.4 ($C_{III\text{-}Ar}$ **B**), 110.0 [*C*(OCH$_2$-)$_2$ **A** and **B**], 78.8 (*C*HOH **B**), 75.0 (*C*HOH **A**), 65.5 and 64.5 (O-*C*H_2*C*H_2-O **A**), 65.1 and 65.0 (O-*C*H_2*C*H_2-O **B**), 59.0 [*C*H_2S(O) **B**], 57.3 [*C*H_2S(O) **A**], 54.1 [*C*(CH$_3$)$_3$ **A**], 53.8 [*C*(CH$_3$)$_3$ **B**], 48.6 (*C*HCH$_3$ **A**), 46.3 (*C*HCH$_3$ **B**), 22.9 [C(*C*H$_3$)$_3$ **B**], 22.8 [C(*C*H$_3$)$_3$ **A**], 14.7 (CH*C*H$_3$ **B**), 11.5 (CH*C*H$_3$ **A**) ppm. $C_{18}H_{26}O_5S$ (354.47): C 60.99, H 7.39; found C 60.67, H 7.25.

(3*R*,4*R*,R_S)-1-(*tert*-Butylsulfinyl)-5,5-ethylenedioxy-4-hydroxy-3-methyldodecan-2-one (21b): Pale yellow oil (73% yield); R_f = 0.16 (CH_2Cl_2/AcOEt, 4:1). IR (neat): $\tilde{\nu}$ = 3391, 2931–2820, 1713, 1463, 1368, 1251, 1176, 1117, 1040, 849 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.02–3.86 (m, 4 H, O-CH_2-CH_2-O), 3.93 (d, J = 10.4 Hz, 1 H, C*H*OH), 3.58 [AB, J_{AB} = 21.4 Hz, $\Delta\nu$ = 16.3 Hz, 2 H, CH_2S(O)], 2.89 (q^t, J = 10.4 Hz, 1 H, C*H*CH$_3$), 2.24 (br. s, 1 H, O*H*) 1.87–1.54 [m, 2 H, CH_2(CH$_2$)$_5$CH$_3$], 1.43–1.13 [m, 10 H, CH$_2$(CH_2)$_5$CH$_3$], 1.29 (s, 9 H, *t*Bu), 1.27 (d, J = 10.4 Hz, 3 H, CHCH_3), 0.88 [t, J = 9.9 Hz, 3 H, CH$_2$(CH$_2$)$_5$CH_3] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.1 (*C*=O), 111.5 [*C*(OCH$_2$)$_2$], 74.4 (*C*HOH), 65.5 (O-*C*H$_2$CH$_2$-O), 65.3 (O-CH$_2$*C*H$_2$-O), 57.6 [*C*H$_2$S(O)], 54.1 [*C*(CH$_3$)$_3$], 48.7 (*C*HCH$_3$), 33.7 (*C*H$_2$), 31.8 (*C*H$_2$), 29.8 (*C*H$_2$), 29.3 (*C*H$_2$), 22.8 [C(*C*H$_3$)$_3$], 22.9 (*C*H$_2$), 22.6 (*C*H$_2$), 14.1 (CH*C*H$_3$), 12.6 [(CH$_2$)$_6$*C*H$_3$] ppm.

General Procedure for the Reductive Elimination of the Reformatsky-Type Reaction Product: The following is a description of a typical experimental procedure for sulfoxide reductive cleavage.

Small fractions of aluminium amalgam made from aluminium foils (35.00 mmol, 100 equiv.) were added to a solution of the Reformatsky-type reaction product (0.35 mmol, 1 equiv.) dissolved in THF (27 mL) and water (3 mL), the temperature being maintained between 15 and 20 °C. The mixture was stirred under these conditions for 1 h, filtered through Celite, washed with diethyl ether, dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by unmetalled silica gel chromatography.

(+)-(3*R*,4*S*)-4-Hydroxy-3-methylhexan-2-one (5d): Colorless liquid (80% yield); R_f = 0.30 (hexane/EtOAc, 8:2). $[\alpha]_D^{20}$ = +45 (c = 1.1, $CHCl_3$) {ref.[8] $[\alpha]_D^{20}$ = +44 (c = 1.0–1.2, $CHCl_3$)}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.88–3.81 (m, 1 H, C*H*OH), 2.65 (br. s, 1 H, O*H*), 2.58 (qd, J = 7.2, 3.0 Hz, 1 H, C*H*CH$_3$), 2.20 (s, 3 H, COCH_3), 1.59–1.31 (m, 2 H, CH_2CH$_3$), 1.13 (d, J = 7.2 Hz, 3 H, CHCH_3), 0.94 (t, J = 7.5 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 213.8 (*C*=O), 72.4 (*C*HOH), 50.4 (*C*HCH$_3$), 29.1 (CO*C*H$_3$), 26.9 (*C*H$_2$CH$_3$), 10.4 (*C*H$_3$), 9.5 (*C*H$_3$) ppm.

(+)-[3*R*,4*S*]-4-Hydroxy-3-methylnonan-2-one (5g): Colorless liquid (90% yield); R_f = 0.20 (hexane/EtOAc, 8:2). $[\alpha]_D^{20}$ = +26.3 (c = 1.1, $CHCl_3$), {ref.[8] $[\alpha]_D^{20}$ = +26.7 (c = 1.0–1.2, $CHCl_3$)}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.98–3.90 (m, 1 H, C*H*OH), 2.56 (qd, J = 7.3, 3.0 Hz, 1 H, C*H*CH$_3$), 2.19 (s, 3 H, COCH_3), 2.13–2.03 (m, 1 H, O*H*), 1.55–1.23 [m, 8 H, (CH_2)$_4$CH$_3$], 1.14 (d, J = 7.3 Hz, 3 H, CHCH_3), 0.88 (t, J = 6.6 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 213.1 (*C*=O), 71.0 (*C*HOH), 51.0 (*C*HCH$_3$), 34.2 (*C*H$_2$), 32.0 (*C*H$_2$), 29.4 (CO*C*H$_3$), 25.9 (*C*H$_2$), 22.6 (*C*H$_2$), 14.3 (CH*C*H$_3$), 10.0 [(CH$_2$)$_4$*C*H$_3$] ppm.

(+)-[3*R*,4*R*]-5-Benzyloxy-4-hydroxy-3-methylpentan-2-one (14b): Colorless liquid (96% yield); R_f = 0.43 (CH_2Cl_2/Et_2O, 7:3). $[\alpha]_D^{20}$ = +4.6 (c = 1.0, $CHCl_3$), {ref.[11] $[\alpha]_D^{20}$ = +4.7 (c = 0.99, $CHCl_3$).} IR (neat): $\tilde{\nu}$ = 3345, 3089–2966, 1705, 1455, 1360, 1094, 1028, 741, 699 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.26 (m, 5 H, H_{Ar}), 4.54 (s, 2 H, CH_2C$_6$H$_5$), 4.12 (dt, J = 6.4, 5.0 Hz, 1 H, C*H*OH), 3.47 (AB part of ABX, J_{AB} = 9.4, J_{AX} = 5.0, J_{BX} = 6.4 Hz, $\Delta\nu$ = 15.3 Hz, 2 H, CH_2CHOH), 2.76 (qd, J = 7.2, 5.0 Hz, 1 H, C*H*CH$_3$), 2.70 (br. s, 1 H, O*H*), 2.19 (s, 3 H, COCH_3), 1.16 (d, J = 7.3 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 212.3 (*C*=O), 137.8 (C_{Ar}), 128.4 (C_{Ar}), 127.8 (C_{Ar}×2), 73.4 (*C*H$_2$-O), 71.6 (*C*H$_2$-O), 70.3 (*C*HOH), 48.6 (*C*HCH$_3$), 29.3 (CO*C*H$_3$), 11.1 (CH*C*H$_3$) ppm.

General Procedure for the Diastereoselective Reduction of the Reformatsky-Type Reaction Adduct: The following is a description of a typical experimental procedure for the diastereoselective reduction of the Reformatsky adduct with DIBALH.

A solution of the β-keto sulfoxide (0.307 mmol, 1 equiv.) in THF (6 mL) was cooled to –78 °C and a solution of DIBALH (0.737 mmol, 2.4 equiv.) in hexane was added dropwise. The mixture was stirred under these conditions for 30 min. The solvent was removed in vacuo and the residue was dissolved in ethyl acetate (10 mL) and a saturated disodium L-tartrate solution (10 mL). The mixture was stirred overnight and extracted with ethyl acetate (3×10 mL). The organic phases were dried with magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by unmetalled silica gel chromatography (EtOAc/MeOH, 98:2).

(+)-(2*S*,3*R*,4*S*,R_S)-1-(*tert*-Butylsulfinyl)-3-methylhexane-2,4-diol (22): Orange oil. (90% yield); R_f = 0.65 (EtOAc/MeOH, 90:10). $[\alpha]_D^{20}$ = +35.5 (c = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3480, 2972–2879, 1463, 1399, 1368, 1285, 1180, 1142, 1113, 1050, 1015, 970, 805 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.69 (m, 1 H, O*H*), 4.39 (m, 1 H, C*H*OH), 3.80 (m, 1 H, C*H*OH), 3.65 (m, 1 H, O*H*), 2.55 [AB part of ABX, J_{AB} = 12.4, J_{AX} = 10.2, J_{BX} = 2.3 Hz, $\Delta\nu$ = 79.2 Hz, 2 H, CH_2S(O)], 1.73–1.35 (m, 3 H, C*H*CH$_3$ and CH_2CH$_3$), 1.42 (s, 9 H, *t*Bu), 0.95 (d, J = 7.1 Hz, 3 H, CHCH_3), 0.93 (t, J = 7.3 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 76.6 (*C*HOH), 69.8 (*C*HOH), 59.7 [*C*(CH$_3$)$_3$], 50.4 [*C*H$_2$S(O)], 41.2 (*C*HCH$_3$), 27.8 (*C*H$_2$CH$_3$), 23.2 [C(*C*H$_3$)$_3$], 10.4 [CH*C*H$_3$], 5.5 [CH$_2$*C*H$_3$] ppm.

(+)-(2*S*,3*R*,4*R*,R_S)-1-(*tert*-Butylsulfinyl)-5,5-ethylenedioxy-3-methyldodecane-2,4-diol (25b): Pale yellow oil (85% yield); R_f = 0.20 (EtOAc/MeOH, 95:5). $[\alpha]_D^{20}$ = +79.4 (c = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3383, 2955–2854, 1463, 1377, 1177, 1034 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.42 (dt, J = 12.4, 2.1 Hz, 1 H, CH$_2$C*H*OH), 4.08–3.92 (m, 4 H, O-CH_2CH_2-O), 3.88 (d, J = 2.1 Hz, 1 H, C*H*OH), 3.64 (br. s, 1 H, O*H*), 2.62 (br. s, 1 H, O*H*), 2.59 (AB part of ABX, J_{AB} = 12.4, J_{AX} = 10.4, J_{BX} = 2.1 Hz, $\Delta\nu$

= 83.0 Hz, 2 H, CH_2CHOH), 1.96–1.87 (m, 1 H, CHCH$_3$), 1.77–1.52 [m, 2 H, CH_2(CH$_2$)$_5$CH$_3$], 1.43–1.10 [m, 10 H, CH$_2$(CH_2)$_5$-CH$_3$], 1.27 (s, 9 H, *t*Bu), 1.07 (d, J = 7.0 Hz, 3 H, CHCH_3), 0.89 [t, J = 7.0 Hz, 3 H, (CH$_2$)$_6$CH_3] ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 112.1 [C(OCH$_2$)$_2$], 77.0 (CHOH), 69.9 (CH$_2$$C$HOH), 66.2 (O-$CH_2CH_2$-O), 65.6 (O-CH$_2$$CH_2$-O), 52.7 [$C$(CH$_3$)$_3$], 50.6 [$CH_2$S(O)], 38.6 ($CHCH_3$), 34.7 ($CH_2$), 32.8 ($CH_2$), 29.9 ($CH_2$), 29.2 ($CH_2$), 23.0 ($CH_2$), 22.9 [C($CH_3$)$_3$], 22.6 ($CH_2$), 14.1 (CH$CH_3$), 7.2 [(CH$_2$)$_6$$CH_3$] ppm.

Typical Experimental Procedure for the Diastereoselective Reduction of the Reformatsky Adduct with DIBALH in the Presence of Yb(OTf)$_3$: A solution of the β-keto sulfoxide (0.306 mmol, 1 equiv.) in THF (4 mL) was added to a solution of Yb(OTf)$_3$ (0.368 mmol, 1.2 equiv.) in THF (4 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C and then cooled to –78 °C. A solution of DIBALH (0.735 mmol, 2.4 equiv.) in hexane was then added dropwise. The mixture was stirred at –78 °C for 30 min. The solvent was removed in vacuo and the residue was dissolved in ethyl acetate (10 mL) and a saturated disodium L-tartrate solution (10 mL). The mixture was stirred overnight and extracted with ethyl acetate (3 × 10 mL). The organic phases were dried with magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by unmetalled silica gel chromatography (AcOEt/MeOH, 98:2).

(+)-(2*R*,3*R*,4*S*,R_S)-1-(*tert*-Butylsulfinyl)-3-methylhexane-2,4-diol (23): Orange solid (85% yield); R_f = 0.40 (EtOAc/MeOH, 90:10). $[a]_D^{20}$ = +30.0 (c = 1, CHCl$_3$). IR (neat): $\tilde{\nu}$ = 3434, 3256, 2977–2878, 1462, 1366, 1253, 1176, 1130, 1053, 1038, 1022, 1003, 981, 964, 938 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 4.88 (m, 1 H, OH), 4.34 (m, 1 H, CHOH), 3.81 (m, 1 H, CHOH), 3.19 (m, 1 H, OH), 2.68 [AB part of ABX, J_{AB} = 12.8, J_{AX} = 9.1, J_{BX} = 2.6 Hz, $\Delta\nu$ = 49.8 Hz, 2 H, CH_2S(O)], 1.77–1.33 (m, 3 H, CHCH$_3$ and CH_2CH$_3$), 1.26 (s, 9 H, *t*Bu), 0.98 (d, J = 7.0 Hz, 3 H, CHCH_3), 0.95 (t, J = 7.3 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 73.4 (CHOH), 73.1 (CHOH), 53.9 [C(CH$_3$)$_3$], 47.0 [CH$_2$S(O)], 42.2 (CHCH$_3$), 26.8 (CH$_2$CH$_3$), 22.5 [C(CH$_3$)$_3$], 10.8 (CH$_3$), 10.7 (CH$_3$) ppm. $C_{11}H_{24}O_3S$ (236.38): C 55.90, H 10.23; found C 55.80, H 10.21.

(2*R*,3*R*,4*R*,R_S)-1-(*tert*-Butylsulfinyl)-5,5-ethylenedioxy-3-methyldodecane-2,4-diol (27b): Pale yellow solid (80% yield); R_f = 0.12 (pure EtOAc). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 5.08 (br. s, 1 H, OH), 4.37–4.28 (m, 1 H, CH$_2$CHOH), 4.10–3.92 (m, 4 H, O-CH_2CH_2-O), 3.94–3.92 (m, 1 H, CHOH), 3.13 (br. s, 1 H, OH), 2.76 (AB part of ABX, J_{AB} = 13.0, J_{AX} = 10.0, J_{BX} = 1.9 Hz, $\Delta\nu$ = 57.9 Hz, 2 H, CH_2CHOH), 2.02–1.94 (m, 1 H, CHCH$_3$), 1.77–1.50 [m, 2 H, CH_2(CH$_2$)$_5$CH$_3$], 1.42–1.10 [m, 10 H, CH$_2$(CH_2)$_5$CH$_3$], 1.27 (s, 9 H, *t*Bu), 1.10 (d, J = 7.2 Hz, 3 H, CHCH_3), 0.87 [t, J = 6.6 Hz, 3 H, (CH$_2$)$_6$CH_3] ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 112.3 [C(OCH$_2$)$_2$], 73.3 (CHOH), 73.0 (CHOH), 66.3 (O-CH$_2$CH$_2$-O), 65.5 (O-CH$_2$$CH_2$-O), 54.0 [$C$(CH$_3$)$_3$], 47.4 [$CH_2$S(O)], 39.2 ($CHCH_3$), 34.8 ($CH_2$), 31.8 ($CH_2$), 29.9 ($CH_2$), 29.3 ($CH_2$), 23.0 ($CH_2$), 22.7 [C($CH_3$)$_3$], 22.6 ($CH_2$), 14.1 (CH$CH_3$), 10.0 [(CH$_2$)$_6$-$CH_3$] ppm.

General Procedure for the Acetonide Protection of the 1,3-Diol: The following is a description of a typical experimental procedure for the acetonide protection of a *syn*- or *anti*-1,3-diol.

A catalytic quantity of *p*TsOH (0.09 mmol, 0.1 equiv.) was added to a solution of the 1,3-diol (0.90 mmol, 1 equiv.) in 2,2-dimethoxypropane (2 mL). The mixture was stirred for 45 min at room temperature, diluted with Et$_2$O (4 mL) and washed with a saturated solution of NaHCO$_3$ (5 mL). The organic phase was dried with magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography.

(+)-(2*R*,3*R*,4*S*,R_S)-1-(*tert*-Butylsulfinyl)-2,4-(isopropylidenedioxy)-3-methylhexane (24): Pale yellow oil (88% yield); R_f = 0.25 (pure EtOAc). $[a]_D^{20}$ = +109.0 (c = 1, CHCl$_3$). IR (neat): $\tilde{\nu}$ = 2966–2877, 1462, 1380, 1226, 1177, 1151, 1041, 993 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.84–3.75 (m, 2 H, CHOH × 2), 2.75 [AB part of ABX, J_{AB} = 13.2, J_{AX} = 6.6, J_{BX} = 5.4 Hz, $\Delta\nu$ = 45.2 Hz, 2 H, CH_2S(O)], 2.05 (q^{t}d, J = 6.6, 4.8 Hz, 1 H, CHCH$_3$), 1.53–1.34 (m, 2 H, CH_2CH$_3$), 1.39 [s, 3 H, C(CH_3)$_2$], 1.37 [s, 3 H, C(CH_3)$_2$], 1.28 (s, 9 H, *t*Bu), 0.98 (d, J = 6.6 Hz, 3 H, CHCH_3), 0.95 (t, J = 7.2 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 101.1 [C-(CH$_3$)$_2$], 71.2 (CHOR′), 70.7 (CHOR′), 53.3 [C(CH$_3$)$_3$], 52.2 [CH$_2$S(O)], 38.9 (CHCH$_3$), 24.9 [C(CH$_3$)$_2$], 24.0 [C(CH$_3$)$_2$], 23.4 (CH$_2$CH$_3$), 22.8 [C(CH$_3$)$_3$], 11.9 (CH$_3$), 10.5 (CH$_3$) ppm.

(+)-(2*S*,3*R*,4*R*,R_S)-1-(*tert*-Butylsulfinyl)-5,5-ethylenedioxy-2,4-(isopropylidenedioxy)-3-methyldodecane (26b): Obtained as the product of the protection of the *syn*-1,3-diol **25b** with an acetonide. White solid (85% yield); R_f = 0.30 (pure EtOAc); m.p. 63–64 °C. $[a]_D^{20}$ = +95.2 (c = 1, CHCl$_3$). IR (neat): $\tilde{\nu}$ = 2981–2853, 1465, 1389, 1379, 1261, 1205, 1158, 1136, 1067, 1030, 1012, 957, 941, 905 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 4.44 [dt, J = 10.4, 2.1 Hz, 1 H, CHCH$_2$S(O)], 4.09–3.84 (m, 4 H, O-CH_2CH_2-O), 3.99 (d, J = 2.1 Hz, 1 H, CHOR′), 2.47 [AB part of ABX, J_{AB} = 12.4, J_{AX} = 10.4, J_{BX} = 2.1 Hz, $\Delta\nu$ = 83.0 Hz, 2 H, CH_2S(O)], 1.67–1.53 (m, 1 H, CHCH$_3$), 1.48 [s, 3 H, C(CH_3)$_2$], 1.43 [s, 3 H, C(CH_3)$_2$], 1.45–1.18 [m, 12 H, (CH_2)$_6$CH$_3$], 1.26 (s, 9 H, *t*Bu), 1.04 (d, J = 6.8 Hz, 3 H, CHCH_3), 0.89 (t, J = 6.4 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 110.8 [C(OCH$_2$)$_2$], 99.6 [C(CH$_3$)$_2$], 77.5 (CHOR′), 67.9 [CHCH$_2$S(O)], 66.6 (O-CH$_2$CH$_2$-O), 65.8 (O-CH$_2$$CH_2$-O), 52.6 [$C$(CH$_3$)$_3$], 49.7 [$CH_2$S(O)], 35.1 ($CH_2$), 33.6 ($CHCH_3$), 31.8 ($CH_2$), 29.9 ($CH_2$), 29.8 [C($CH_3$)$_2$], 29.3 ($CH_2$), 22.8 [C($CH_3$)$_3$], 22.7 ($CH_2$), 22.6 ($CH_2$), 19.4 [C($CH_3$)$_2$], 14.1 (CH$CH_3$), 6.6 (CH$_2$$CH_3$) ppm.

Synthesis of Glyoxal-Derived Aldehydes: The following is a description of a typical experimental procedure for the synthesis of the aldehydes **20a** and **20b**.

(+)-(9*R*,10*R*)-9,10-(Isopropylidenedioxy)octadecane-8,11-dione (17b): A solution of heptyl bromide (4.43 mL, 28.20 mmol, 4.1 equiv.) in Et$_2$O (25 mL) was slowly added to magnesium turnings (669 mg, 27.51 mmol, 4.0 equiv.) recovered by Et$_2$O (2 mL). At the end of the addition, the mixture was refluxed for 30 min and then allowed to cool to room temperature. The mixture was added dropwise to a solution of the bis-Weinreb amide **16**[20] (1.90 g, 6.88 mmol, 1 equiv.) in THF (55 mL) cooled to –10 °C. After 15 min at –10 °C, the reaction was quenched with saturated NH$_4$Cl and the mixture acidified with 10% HCl and extracted with EtOAc (3 × 40 mL). The combined organic extracts were washed with brine, dried with magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc, 9:1, R_f = 0.45) to give pure **17b** in 78% yield (1.91 g, 5.38 mmol). Colorless liquid. $[a]_D^{20}$ = +4.7 (c = 1, CHCl$_3$). IR (neat): $\tilde{\nu}$ = 2990–2857, 1727, 1463, 1404, 1375, 1260, 1211, 1153, 1081, 862 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 4.55 (s, 2 H, CHOR′), 2.73–2.56 [AB part of ABMN, 2nd order, 4 H, CH_2(CH$_2$)$_5$CH$_3$], 1.67–1.52 (m, 4 H, CH$_2$), 1.43 [s, 6 H, C(CH_3)$_2$], 1.34–1.24 [m, 16 H, (CH_2)$_4$CH$_3$], 0.88 [t, J = 7.2 Hz, 6 H, (CH$_2$)$_6$CH_3] ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 208.7 (C=O), 112.4 [C(CH$_3$)$_2$], 81.5 (CHOR′), 39.1 (CH$_2$), 31.6 (CH$_2$), 29.1 (CH$_2$), 29.0 (CH$_2$), 26.2 [C(CH$_3$)$_2$], 23.1 (CH$_2$), 22.6 (CH$_2$), 14.0 (CH$_3$) ppm. $C_{21}H_{38}O_4$ (354.53): C 71.15, H 10.80; found C 71.15, H 10.62.

(–)-(2*R*,3*R*)-2,3-(Isopropylidenedioxy)-1,4-diphenylbutane-1,4-dione (17a): Obtained by the addition of 4 equiv. of PhMgBr to the bis-

Weinreb amide **16**. White solid (47% yield, unoptimized); R_f = 0.20 (cyclohexane/CH_2Cl_2, 1:1); m.p. 51 °C. $[\alpha]_D^{20}$ = –78.7 (*c* = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3058–2932, 1679, 1597, 1580, 1449, 1376, 1319, 1281, 1242, 1206, 1143, 1091, 1003, 831, 773, 703, 685, 657 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 7.2 Hz, 4 H, C*H*$_{Ar}$), 7.61 (t, *J* = 7.2 Hz, 2 H, C*H*$_{Ar}$), 7.49 (t, *J* = 7.2 Hz, 4 H, C*H*$_{Ar}$), 4.85 (s, 2 H, C*H*OR′), 1.44 [s, 6 H, C(C*H*$_3$)$_2$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.3 (*C*=O), 134.8 (*C*$_{Ar}$), 133.8 (*C*H$_{Ar}$), 129.5 (*C*H$_{Ar}$), 128.6 (*C*H$_{Ar}$), 113.3 [*C*(CH$_3$)$_2$], 79.0 (*C*HOR′), 26.7 [C(*C*H$_3$)$_2$] ppm.

(–)-(9*R*,10*R*)-9,10-Dihydroxyoctadecane-8,11-dione (18b): A mixture of trifluoroacetic acid/water (9:1, v/v) (13 mL) was added to **17b** (2.50 g, 7.06 mmol, 1 equiv.) cooled to 0 °C. After storage of the mixture at this temperature for 2 h, the aqueous acid was removed under reduced pressure and the residue was triturated with Et_2O (5 mL). The supernatant liquid was removed by means of a Pasteur pipette. The remaining solid was washed with diethyl ether (3 × 3 mL), leaving a crystalline solid, the major portion of the hydrolysis product **18b**. The ethereal supernatant liquid and the washings were combined, concentrated under reduced pressure, and the residue thus obtained triturated and washed with diethyl ether in a similar manner to that used for the initial residue to afford a second crystalline portion of the hydrolysis product **18b**. The two portions were combined to obtain pure **18b** in 83% yield (1.84 g, 5.85 mmol). White solid; R_f = 0.30 (hexane/EtOAc, 8:2); m.p. 98–100 °C. $[\alpha]_D^{20}$ = –72 (*c* = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3434, 2953–2850, 1717, 1690, 1469, 1399, 1376, 1276, 1158, 1124, 1103, 1082, 1049 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.56 (d, *J* = 6.5 Hz, 2 H, C*H*OH), 3.68 (d, *J* = 6.5 Hz, 2 H, CHO*H*), 2.73–2.51 [AB part of ABMN, 2nd order, 4 H, C*H*$_2$(CH$_2$)$_5$CH$_3$], 1.75–1.64 (m, 4 H, CH$_2$), 1.40–1.25 [m, 16 H, (C*H*$_2$)$_4$CH$_3$], 0.88 [t, *J* = 6.9 Hz, 6 H, (CH$_2$)$_6$C*H*$_3$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.8 (*C*=O), 77.0 (*C*HOH), 38.0 (*C*H$_2$), 31.6 (*C*H$_2$), 29.1 (*C*H$_2$), 29.0 (*C*H$_2$), 23.4 (*C*H$_2$), 22.6 (*C*H$_2$), 14.0 (*C*H$_3$) ppm. $C_{18}H_{34}O_4$ (314.47): C 68.75, H 10.90; found C 68.67, H 10.87.

(–)-(2*R*,3*R*)-2,3-Dihydroxy-1,4-diphenylbutane-1,4-dione (18a): Obtained by the hydrolysis of the acetonide function of **17a**. White solid (88% yield); R_f = 0.40 (CH_2Cl_2/EtOAc, 9:1); m.p. 148–150 °C. $[\alpha]_D^{20}$ = –191.5 (*c* = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3452, 1677, 1595, 1452, 1397, 1310, 1244, 1115, 1080, 966, 793, 746, 692, 666 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.00 (br. d, *J* = 7.0 Hz, 4 H, C*H*$_{Ar}$), 7.72 (t, *J* = 7.3 Hz, 2 H, C*H*$_{Ar}$), 7.49 (t, *J* = 7.2 Hz, 4 H, C*H*$_{Ar}$), 5.39 (d, *J* = 7.5 Hz, 2 H, C*H*OH), 3.93 (d, *J* = 7.5 Hz, 2 H, CHO*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.6 (*C*=O), 134.2 (*C*H$_{Ar}$), 133.8 (*C*$_{Ar}$), 129.2 (*C*H$_{Ar}$), 128.3 (*C*H$_{Ar}$), 74.7 (*C*HOH) ppm. $C_{16}H_{14}O_4$ (270.28): C 71.10, H 5.22; found C 70.82, H 5.34.

(–)-(1*R*,2*R*)-1,2-Bis(2-heptyl-1,3-dioxolan-2-yl)ethane-1,2-diol (19b): A solution of the diketone **18b** (1.26 g, 4.02 mmol, 1 equiv.), *p*TsOH (77 mg, 0.40 mmol, 0.1 equiv.) and ethylene glycol (0.68 mL, 12.06 mmol, 3 equiv.) in benzene (40 mL) was refluxed for 16 h in a Dean–Stark trap. Benzene was then removed by evaporation and the crude product was diluted in AcOEt (40 mL), washed with saturated $NaHCO_3$ (20 mL) and water (20 mL), dried with magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/EtOAc, 1:1, R_f = 0.40) to obtain pure **19b** in 74% yield (1.20 g, 2.98 mmol). White solid; m.p. 47 °C. $[\alpha]_D^{20}$ = –3.8 (*c* = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3436, 2956–2853, 1468, 1395, 1379, 1215, 1161, 1105, 1031, 951, 891, 790, 726, 686 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.13–3.99 (m, 8 H, O-C*H*$_2$C*H*$_2$-O), 3.86 (s, 2 H, C*H*OH), 2.03 (s, 2 H, CHO*H*), 1.87–1.57 [m, 4 H, C*H*$_2$(CH$_2$)$_5$CH$_3$], 1.48–1.20 [m, 20 H, (C*H*$_2$)$_5$CH$_3$], 0.90 [t, *J* = 6.6 Hz, 6 H, (CH$_2$)$_6$C*H*$_3$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.4 [*C*(OCH$_2$)$_2$], 71.0 (*C*HOH), 65.9 (O-*C*H$_2$CH$_2$-O), 65.7 (O-CH$_2$*C*H$_2$-O), 34.4 (*C*H$_2$), 31.8 (*C*H$_2$), 29.8 (*C*H$_2$), 29.3 (*C*H$_2$), 23.0 (*C*H$_2$), 22.6 (*C*H$_2$), 14.1 (*C*H$_3$) ppm.

(–)-(1*R*,2*R*)-1,2-Bis(2-phenyl-1,3-dioxolan-2-yl)ethane-1,2-diol (19a): Obtained by ethylene ketal protection of the dione **18a**. White solid (58% yield, unoptimized); R_f = 0.13 (CH_2Cl_2/Et_2O, 4:1); m.p. 196 °C. $[\alpha]_D^{20}$ = –18.1 (*c* = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3524, 3062–2886, 1447, 1217, 1169, 1130, 1074, 1040, 1024, 997, 941, 877, 771, 701 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.41–7.27 (m, 10 H, C*H*$_{Ar}$), 4.18–3.72 (m, 8 H, O-C*H*$_2$C*H*$_2$-O), 4.04 (s, 2 H, C*H*OH), 3.30 (s, 2 H, CHO*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.1 (*C*$_{Ar}$), 128.6 (*C*H$_{Ar}$), 128.1 (*C*H$_{Ar}$), 126.3 (*C*H$_{Ar}$), 110.7 [*C*(OCH$_2$)$_2$], 72.0 (*C*HOH), 65.5 (O-*C*H$_2$CH$_2$-O), 64.7 (O-CH$_2$*C*H$_2$-O) ppm. $C_{20}H_{22}O_6$ (358.39): C 67.03, H 6.19; found C 67.15, H 6.04.

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