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(*S*)-Mandelic acid enolate as a chiral benzoyl anion equivalent for the enantioselective synthesis of non-symmetrically substituted benzoins

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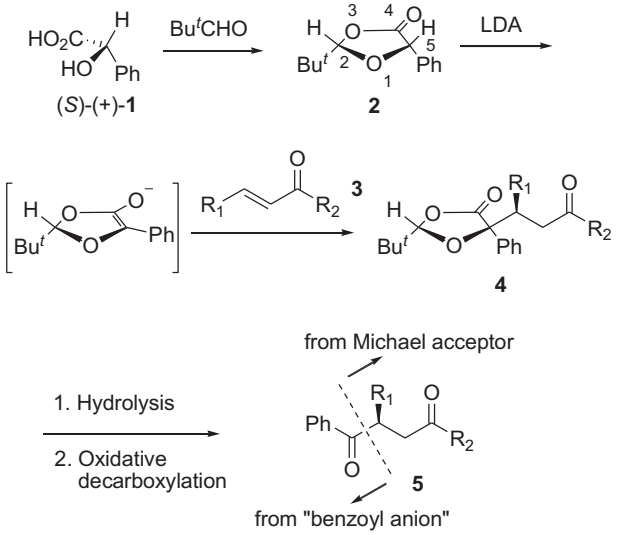
ABSTRACT

A strategy for the enantioselective synthesis of non-symmetrically substituted benzoins from (*S*)-mandelic acid and aromatic aldehydes has been developed. This strategy is based on a diastereoselective aldol reaction of the lithium enolate of the 1,3-dioxolan-4-one derived from (*S*)-mandelic acid and pivalaldehyde with aromatic aldehydes, which gives the corresponding aldols in good yields. Subsequent hydroxyl group protection as MEM ethers, basic hydrolysis of the dioxolanone ring, oxidative decarboxylation of the α-hydroxy acid moiety, and hydroxyl group deprotection provides chiral non-symmetrically substituted benzoins with high enantiomeric excesses.

1. Introduction

During the last years, we have reported several highly diastereoselective reactions of the (*S*)-mandelic acid enolate with different electrophiles and the transformation of the corresponding adducts into highly enantioenriched compounds.[1] In this context we have described the Michael reaction using α,β-unsaturated ketones as acceptors and the transformation of the resulting adducts into chiral non-racemic 2-substituted-1,4-diketones,[2] which formally involves the use of (*S*)-mandelic acid as a source of a chiral benzoyl anion (Scheme 1).

The preservation of the chiral information of (*S*)-mandelic acid is based on Seebach's principle of self-regeneration of stereocenters[3] whilst its use as an 'Umpoled' equivalent of the benzoyl anion is based on an oxidative decarboxylation of α-hydroxy acids developed in our laboratory.[4] According to this principle (Scheme 1), chiral α-hydroxy acids, such as (*S*)-mandelic acid (**1**), are transformed by acetalization with pivalaldehyde into *cis*-1,3-dioxolan-4-ones **2**, which can be isolated in enantiomerically pure form. The dioxolanone is transformed into a non-racemic enolate by deprotonation at the original sterogenic center C5 with a base such as lithium diisopropylamide (LDA) at low temperatures. Subsequent reaction of the enolate with an electrophile (an α,β-unsaturated ketone **3**, for example) proceeds under the influence of the temporary acetal stereogenic center C2, yielding a dioxolanone derivative **4** resulting from the exclusive *anti* approach of the electrophile with respect to the *tert*-butyl group. Therefore, the chirality of the starting stereocenter of (*S*)-mandelic acid is regenerated. 2-Substituted-1,4-dicarbonyl compounds **5** were obtained with very high enantiomeric excesses from compounds **4**, by



Scheme 1. Synthesis of chiral non-racemic 1,4-diketones from mandelic acid.

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hydrolysis of the dioxolanone ring and subsequent aerobic oxidative decarboxylation of the α-hydroxy acid moiety.[2]

In this paper we wish to report the use of a similar strategy (Fig. 1) for the enantioselective synthesis of non-symmetrically substituted benzoins **11** through the diastereoselective addition of the (2*S*,5*S*)-1,3-dioxolan-4-one **2** enolate to aromatic aldehydes **6** and the subsequent transformation of the resulting aldol products **7**.

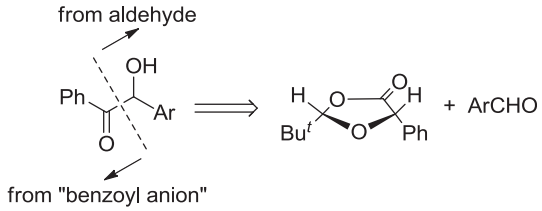
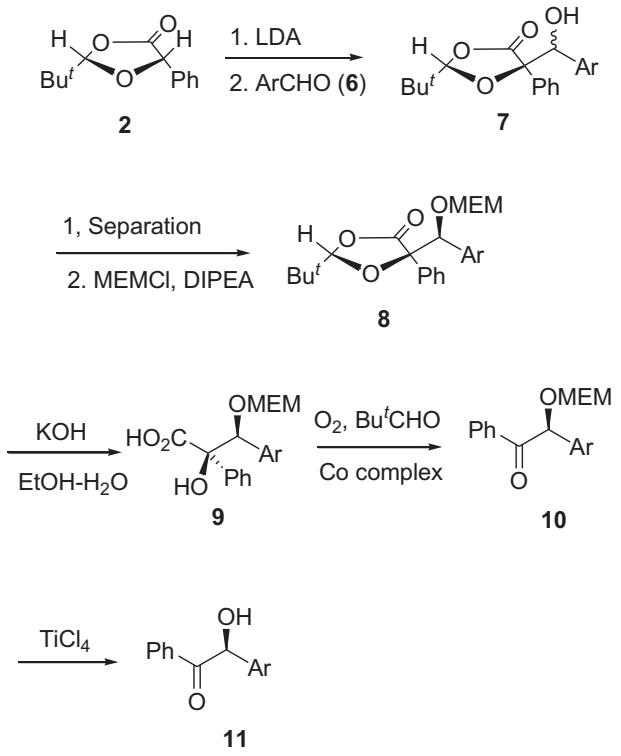


Fig. 1. Retro-synthetic analysis for benzoins.

Chiral non-symmetrically substituted benzoins are a valuable class of building blocks in organic and pharmaceutical chemistry due to their bifunctional nature and especially to the fact that they have a stereogenic center amenable to further synthetic manipulation.[5] Generally, the racemic compounds are prepared by cross-benzoin condensation from aromatic aldehydes in a reaction catalyzed by cyanide ions[6] or quaternary thiazolium salts derived ylides.[7] This condensation involves a masked acyl anion equivalent as intermediate and in fact several kinds of masked acyl anions, such as *O*-protected cyanohydrins,[8] α-(dialkylamino)nitriles,[9] cyanophosphates,[10] and dithioacetals[11] have been also used in addition reactions to carbonyl compounds to give α-hydroxy ketones. However, only few efficient enantioselective synthesis of benzoins have been described so far. Enders[12] and co-workers developed several new chiral triazolium salts as precatalysts in the synthesis of benzoins, Leeper[13] and Bach[14] introduced novel thiazolium salts as precatalysts, Davis[15] and Xu[16] showed that thiazolium and imidazolium ion-based ionic liquids also promote the benzoin condensation. Iwamoto[17] carried out the reaction in water and Degani[18] developed a microwave-assisted benzoin condensation in aqueous media. In addition, cross-benzoin condensations usually yield mixtures of all possible symmetrically and non-symmetrically substituted benzoins, and only a very few examples of synthesis of enantiopure non-symmetrically substituted benzoins have been reported so far. Muller[s]bib19b and co-workers have described the first asymmetric cross-benzoin condensation with high selectivities and enantiomeric excesses utilizing thiamine diphosphate (ThDP)-dependent enzymes by taking advantage of a new donor–acceptor concept for enzymatic cross-coupling reactions of aldehydes. Johnson[20] has reported a cross-silyl benzoin condensation catalyzed by cyanide in which the starting acylsilanes acted as good acyl anion precursors avoiding the usual problem of self-condensation. The same authors have also developed an enantioselective version using metallophosphites as catalysts.[21] A new strategy for the enantioselective synthesis of benzoins based on an oxidative kinetic resolution of racemic benzoins has been reported recently.[22]

2. Results and discussion

The synthesis of enantiomerically enriched non-symmetrically substituted benzoins is outlined in Scheme 2. The first step involves the addition of the enolate of (2*S*,5*S*)-2-*tert*-butyl-5-phenyl-1,3-dioxolan-4-one (**2**) to aromatic aldehydes **6**. According to Seebach's principle of self-regeneration of stereocenters,[3] the configuration of the starting (*S*)-mandelic acid should be regenerated during this reaction. However, the absence of stereochemical control at C5 for the addition reactions of (2*S*,5*S*)-1,3-dioxolan-4-one derived from (*S*)-lactic acid and pivalaldehyde to linear aliphatic aldehydes and benzaldehyde has been reported by Battaglia.[23]



Scheme 2. Synthesis of chiral non-symmetrically substituted benzoins.

In our case, we studied the reaction of (2*S*,5*S*)-1,3-dioxolan-4-one **2** with benzaldehyde (**6a**) in order to optimize the reaction conditions. The best results in terms of yield and diastereoselectivity were obtained in the following conditions: compound **2** was deprotonated by addition to a freshly prepared solution of LDA (1.25 equiv) in THF at −78 °C, and then benzaldehyde (**6a**) (1.25 equiv) in THF was added to the resulting enolate. Stirring for 1 h at −78 °C and quenching with aqueous NH_4Cl at −78 °C, gave product **7a** in 84% yield.[24] ^{1}H NMR analysis of the reaction mixture revealed the presence of three out of four possible diastereomers for **7a** in a 76:14:10:0 ratio (Table 1, entry 1). Flash chromatography allowed to obtain pure the two major aldols **7a**-**A** and **7a**-**B** (Fig. 2).

The stereochemical structures of these two diastereomers were elucidated by NOE experiments. Irradiation in compound **7a**-**A** of the signal at δ 0.96 corresponding to the *tert*-butyl group enhanced the signal at δ 7.47 corresponding to the *ortho*-protons of the phenyl group derived from mandelic acid. Besides, irradiation of the signal at δ 5.72 corresponding to proton H2 of the dioxolanone ring enhanced the signal at δ 5.23 corresponding to the proton geminal to the hydroxyl group. Thus, in compound **7a**-**A** the phenyl group derived from mandelic acid remains *syn* to the *tert*-butyl group. Consequently the absolute stereochemistry of the newly formed quaternary carbon was assigned to be *R* upon the consideration that the absolute configuration of the dioxolanone carbon C5 bearing the *tert*-butyl group in **2** is *S* and it keeps unaltered from **2** to **7a**-**A**. In compound **7a**-**B** irradiation of the signal at δ 0.90 corresponding to the *tert*-butyl group enhanced the signal at δ 5.22 corresponding to the proton geminal to the hydroxyl group and irradiation of the signal at δ 5.02 corresponding to proton H2 of the dioxolanone ring enhanced the signal at δ 7.38 corresponding to the *ortho*-protons of

Table 1
Aldol reaction of (2*S*,5*S*)-1,3-dioxolan-4-one (**2**) with several aromatic aldehydes **6**

Entry	Ar	6	Yield[a] (%)	Ratio[b] **A**/**B**/**C**/**D**	Ratio[c] (**A**+**C**)/(**B**+**D**)	Ratio[d] (**A**+**B**)/(**C**+**D**)
1	Ph	**6a**	84	76:14:10:0	86:14	90:10
2	4-MeC_6H_4	**6b**	86	70:22:8:0	78:22	92:8
3	4-ClC_6H_4	**6c**	60	61:22:17:0	78:22	83:17
4	4-BrC_6H_4	**6d**	71	53:19:25:3	78:22	72:28
5	4-$MeOC_6H_4$	**6e**	69	73:19:7:1	80:20	92:8
6	3,4-OCH_2O–C_6H_3	**6f**	70	68:28:4:0	72:28	96:4
7	4-$CF_3C_6H_4$	**6g**	59	33:23:40:4	73:27	56:44

[a] Combined yield of all four diastereomers.
[b] Ratio determined by ^1H NMR.
[c] See text. **A** and **C** are Seebach aldols, **B** and **D** are non-Seebach aldols.
[d] See text. Aldols **A** and **B** lead to (*S*)-benzoin, aldols **C** and **D** would lead to (*R*)-benzoin.

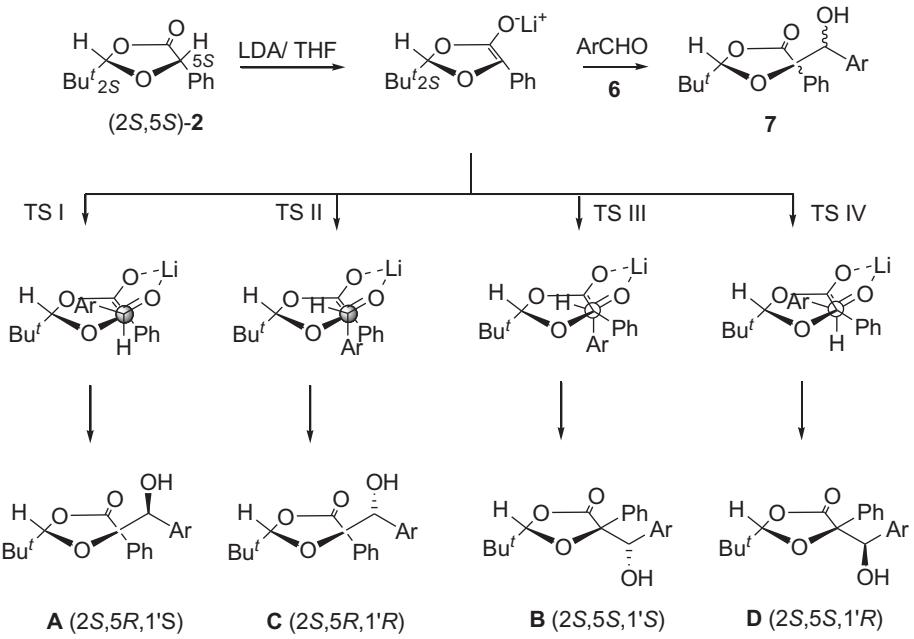


Fig. 2. Possible TS for the approach of aldehyde **6** to the enolate of compound **2**.

the phenyl group derived from mandelic acid. Therefore, in compound **7a**-**B** the phenyl group derived from mandelic acid and the *tert*-butyl group are *anti*. Consequently the absolute stereochemistry of the newly formed quaternary carbon was assigned to be *S* for aldol **7a**-**B**.

The absolute configuration of the hydroxyl-supporting carbon atom in the side chain could not be determined at this stage, but it was shown to be *S* in both major aldols, **7a**-**A** and **7a**-**B** after conversion of these compounds separately into (*S*)-(+)-benzoin and comparison of the specific rotations sign with that of an authentic commercially available sample (see further on).[25] Consequently, the stereochemistry of this hydroxyl-supporting carbon atom should be *R* in both minor diastereomers **7a**-**C** and **7a**-**D**, which would differ in the stereochemistry of the quaternary carbon of the dioxolanone ring.[26]

The optimized conditions were then applied to other substituted aromatic aldehydes (**6b**–**g**), bearing either electron-donating or electron-withdrawing groups. The reaction of **2** with aldehydes **6b**–**f** gave the corresponding aldol products **7b**–**f** in good yields and with high diastereoselectivities, in particular the high facial diastereoselectivity with respect to the aldehyde carbonyl (last column, Table 1). However, in the case of aldehyde **6g**, bearing a strong electron-withdrawing substituent, the facial diastereoselectivity was very low.

Interestingly, in the addition of compound **2** to *p*-chlorobenzaldehyde (**6c**) and also in the case of *p*-bromobenzaldehyde (**6d**), all three diastereomers could be isolated. The stereochemical structures of these three diastereomers were elucidated by NOE experiments. Compounds **7c**-**A** and **7c**-**B** showed the same stereochemical pattern as **7a**-**A** and **7a**-**B**. With regards to the third diastereomer **7a**-**C**, the NOE experiments showed that the phenyl group derived from mandelic acid remained *syn* to the *tert*-butyl group and consequently the absolute stereochemistry of the newly formed quaternary carbon was assigned to be *R* (as in **7c**-**A**), and the hydroxyl-supporting carbon atom in the side chain should be *R*.

All the diastereomers obtained in the addition reaction of **2** with the different aldehydes (**6a**–**f**) show a very good correlation between the chemical shifts of the signals corresponding to proton H2 of the dioxolanone ring and to the *tert*-butyl group, and the stereochemistry of the diastereomer compounds. So, in type A diastereomers, H2 appears at δ 5.71–5.73 ppm and the *tert*-butyl group appears at δ 0.95–0.97 ppm; in type B diastereomers, H2 appears at δ 5.01–5.02 ppm and the *tert*-butyl group appears at δ 0.90–0.94 ppm. Finally, in type C diastereomers, H2 appears at δ 4.60–4.80 ppm and the *tert*-butyl group appears at δ 0.83–0.86 ppm.

The stereochemical outcome of the reaction can be explained according to the transition states formulated by Battaglia[23] to explain the diastereoselectivity observed in a related reaction,

namely the addition of the enolate of *cis*-1,3-dioxolan-4-one derived of (*S*)-lactic acid and pivalaldehyde to aldehydes. Type **A** and **C** diastereomers could be formed through the kinetically favored transition states TS I and TS II, respectively, which result from the approach of the aldehyde to the less hindered *Re* face of the enolate, according to Seebach's principle of self-regeneration of stereocenters (Seebach products). On the other hand, type **B** and **D** diastereomers could be formed through transition states TS III and TS IV, respectively, which result from the approach to the *Si* face of the enolate (non-Seebach products). So, the facial diastereoselectivity with respect to the enolate would be (**A**+**C**)/(**B**+**D**), which indicates the extent of compliance with Seebach's principle of self-regeneration of stereocenters.

However, as the final objective of our synthesis is the preparation of enantioenriched non-symmetrically substituted benzoins, and since the quaternary stereogenic center in the dioxolanone ring is lost in further stages of our synthesis, the overall enantioselectivity of the synthetic sequence does not depend on the facial stereoselectivity with respect the enolate but with respect to the aldehyde carbonyl, that is, the ratio (**A**+**B**)/(**C**+**D**) (last column of Table 1), since **6a**-**A** and **6a**-**B** yield both the (*S*)-benzoin, while **6a**-**C** and **6a**-**D** would both lead to the (*R*)-benzoin.

With the aldol products **7** in our hands we carried out the protection of the hydroxyl group in order to avoid the retro-aldol reaction during the basic hydrolysis of the 1,3-dioxolan-4-one moiety and a possible over-oxidation[27] during the oxidative decarboxylation of the α-hydroxy acid moiety. This protection was carried out by the reaction of aldols **7** with MEM-chloride and diisopropylethylamine (DIPEA) in acetonitrile at reflux temperature to afford MEM derivatives **8**, with good yields (Table 2).[28] The structure of all MEM-protected aldols **8a**–**f** was determined by spectroscopic methods, particularly ^{1}H and ^{13}C NMR and mass spectrometry. As with aldols **7**, the ^{1}H NMR spectra signals corresponding to proton H2 and the *tert*-butyl group in compounds **8** showed characteristic chemical shifts. Thus, for type A diastereomers, H2 appeared at δ 5.71–5.73 ppm and the *tert*-butyl group appeared at δ 0.97–0.98 ppm, whilts for type B diastereomers they appeared at δ 5.01–5.04 ppm and δ 0.74–0.80 ppm, respectively.

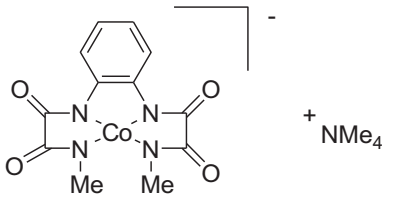


Fig. 3. Co(III) *ortho*-phenylene-bis(*N*′-methyloxamidate) complex.

However, in the cases of MEM-protected benzoins **10e**–**f**, which bear strong electron-donating substituents, the yields were lower, probably due to a benzylic oxidative cleavage. For example, when α-hydroxy acid **9e-A** was subjected to the oxidative decarboxylation three products were obtained: MEM-protected benzoin **10e** (54%), MEM-protected *p*-methoxybenzoic acid (18%) and *p*-methoxybenzaldehyde (14%). The structure of all MEM-protected benzoins **10a-f** was determined by spectroscopic methods, particularly ^{1}H and ^{13}C NMR and mass spectrometry. In the ^{1}H NMR spectra the signals corresponding to the proton geminal to the MEMO-group appeared at δ 6.03–6.09 ppm and in the ^{13}C NMR spectra the signals corresponding to the carbonyl group and the MEMO-supporting carbon appeared at δ 196.2–196.6 ppm and δ 79.1–80.0 ppm, respectively. Hydroxy acids **9a**-**A** and **9a**-**B** yielded both the same MEM-protected benzoin **10a**. The materials obtained from both hydroxy acids showed identical spectroscopic features and values of specific optical rotations $[\alpha]_D^{25}$ +11.0 (*c* 0.8, $CHCl_3$), which were also identical to those of the product obtained upon MEM protection of commercial (*S*)-(+)-benzoin. In this way, the absolute configuration of the chiral stereocenter in compound **10a** was established to be *S*. Similarly, the MEM-protected benzoins **10e** obtained separately from compounds **9e-A** and **9e-B** were shown to be identical with the same value of specific optical rotations $[\alpha]_D^{22}$ +126.1 (*c* 0.9, $CHCl_3$). On the assumption of a uniform reaction mechanism for the aldol reaction between dioxolanone **2** and aromatic aldehydes **6**, the absolute configuration for all MEM-protected benzoins **10a-f** was assigned as *S*.

Table 2
Synthesis of (*S*)-benzoins from aldols **7**

Entry		7	Hydroxyl protection		Hydrolysis		Oxidative decarboxylation		MEM cleavage		
			Product	Yield[a] (%)	Product	Yield[a] (%)	Product	Yield[a] (%)	Product	Yield[a] (%)	ee[b] (%)
1	Ph	**7a-A**	**8a-A**	70	**9a-A**	97	**10a**	62	**11a**	85	99
2	Ph	**7a-B**	**8a-B**	89	**9a-B**	86	**10a**	60	**11a**	85	99
3	4-MeC_6H_4	**7b-A**	**8b-A**	75	**9b-A**	96	**10b**	66	**11b**	90	99
4	4-ClC_6H_4	**7c-A**	**8c-A**	69	**9c-A**	80	**10c**	62	**11c**	80	99
5	4-BrC_6H_4	**7d-A**	**8d-A**	66	**9d-A**	90	**10d**	70	**11d**	91	99
6	4-$MeOC_6H_4$	**7e-A**	**8e-A**	80	**9e-A**	98	**10e**	54	**11e**	35	40
7	4-$MeOC_6H_4$	**7e-B**	**8e-B**	90	**9e-B**	89	**10e**	59	**11e**	35	40
8	3,4-OCH_2O–C_6H_3	**7f-A**	**8f-A**	75	**9f-A**	92	**10f**	39	**11f**	60	54

[a] Yields refer to isolated product.
[b] Determined by chiral HPLC.

Once the hydroxyl group was protected as MEM derivative, we carried out the basic hydrolysis of the dioxolanone moiety to obtain the corresponding α-hydroxy acids **9**. The reaction was carried out at room temperature, by treatment with 5% ethanolic KOH. In all the cases the reaction yields were equal or higher to 80% (Table 2).

The oxidative decarboxylation of the α-hydroxy acid moiety was carried out using a catalytic procedure developed in our laboratory, which employs oxygen as terminal oxidant in the presence of pivalaldehyde and of a catalytic amount of the Co(III) *ortho*-phenylene-bis(*N*′-methyloxamidate) complex (Fig. 3).[4] Under these conditions the MEM-protected benzoins **10a**–**d** were obtained with fair to good yields (Table 2).

Finally the MEM-protected benzoins were treated with $TiCl_4$ in order to remove the MEM protecting group: the reaction proceeded with good yields to provide highly enantioenriched benzoins **11a**–**d** (99% ee). However, in the cases of benzoins **11e**–**f**, bearing strong electron-donating substituents, the yields and the enantiomeric excesses were lower, due probably to the formation of a benzylic carbocation facilitated by the presence of the strong electron-donating group. In the ^{1}H NMR spectra of all benzoins **11a**–**f** the signal corresponding to the proton geminal to the hydroxyl group appeared at δ 5.84–5.94 ppm and in the ^{13}C NMR spectra the signals corresponding to the carbonyl group and the hydroxyl-supporting carbon appeared at δ 198.5–199.0 ppm and

δ 75.4–76.2 ppm, respectively. At this point, the absolute configuration of benzoin **11a** was confirmed again to be *S* by comparison of its specific optical rotation and the retention time in chiral HPLC with those of an authentic sample of enantiomerically pure (*S*)-(+)-benzoin.[25,29] Also the absolute configuration of benzoin **11c** was found to be *S* by comparison with literature data.[22]

In summary, we have developed a strategy for the enantioselective synthesis of non-symmetrically substituted benzoins. This strategy is based on a diastereoselective aldol reaction of a masked benzoyl anion equivalent with aromatic aldehydes that formally involves the use of (*S*)-mandelic acid as the source of chiral information and as source of benzoyl anion. This strategy appears as a convenient method for the synthesis of enantioenriched non-symmetrical benzoins substituted with moderate electron-donating or electron-withdrawing groups.

3. Experimental section

3.1. General procedures

All melting points are uncorrected. Column chromatography was performed on silica gel (Merck, silica gel 60, 230–400 mesh). Optical rotations were measured on a Perkin–Elmer 243 polarimeter. NMR spectra were recorded on a Bruker Avance 300 DPX spectrometer (300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR) or a Varian Unity 400 (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR) as indicated, and referenced to the residual non-deuterated solvent as internal standard. The carbon type was determined by DEPT experiments. Mass spectra were run by electron impact at 70 eV or by chemical ionization using methane as ionizing gas on a Fisons Instruments VG Autospec GC 8000 series spectrometer. Chiral HPLC analyses were performed in Hitachi chromatograph equipped with a UV diode-array detector using chiral stationary columns from Daicel. (2*S*,5*S*)-2-*tert*-Butyl-5-phenyl-1,3-dioxolan-4-one (**2**) was prepared according to the literature.[30] All new compounds were determined to be >95% pure by ^{1}H NMR spectroscopy.

3.2. General experimental procedure for the aldol addition

A solution of (2*S*,5*S*)-2-(*tert*-butyl)-5-phenyl-1,3-dioxolane-4-one (**2**) (220 mg, 1 mmol) in dry THF (0.85 mL) was added slowly to a fresh solution of LDA (1.25 mmol) in dry THF (5 mL) at −78 °C under Ar. After stirring for 45 min, a solution of the corresponding aldehyde **6** (1.25 mmol) in dry THF (0.39 mL) was added at −78 °C and the mixture was stirred for 1 h at −78 °C. The reaction was quenched with a saturated aqueous solution of NH_4Cl and was extracted with diethyl ether (3×30 mL). The combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), and evaporated and the residue was purified by flash chromatography to afford aldols **7**. Yields are included in Table 1. From the diastereomeric mixtures, the following diastereomers could be obtained in pure form by flash column chromatography (eluting with hexane–diethyl ether or hexane–dichloromethane mixtures).

*3.2.1. (2S,5R,1′S)-2-(tert-Butyl)-5-phenyl-5-(1′-phenyl-1′-hydroxymethyl)-1,3-dioxolan-4-one (**7a-A**).* Mp 112–114 °C (CH_2Cl_2); $[\alpha]_D^{25}$ −20.2 (*c* 0.7, $CHCl_3$); HRMS *m*/*z* (CI, methane) 325.3467 (M^+−H, 2.0), $C_{20}H_{21}O_4$ requires 325.3402, 220 (49.1, M^+−106); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (s, 9H), 2.46 (d, *J*=3.8 Hz, 1H, OH), 5.23 (d, *J*=3.6 Hz, 1H), 5.72 (s, 1H), 7.02 (dd, *J*=7.2, 0.8 Hz, 2H), 7.23 (m, 6H), 7.47 (dd, *J*=7.2, 3.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 35.1 (s), 81.0 (d), 85.1 (s), 111.3 (d), 125.3 (d), 127.7 (d), 127.8 (d), 127.9 (d), 128.1 (d), 128.3 (d), 135.5 (s), 137.3 (s), 173.3 (s).

*3.2.2. (2S,5S,1′S)-2-(tert-butyl)-5-phenyl-5-(1′-phenyl-1′-hydroxymethyl)-1,3-dioxolane-4-one (**7a-B**).* Mp 86–88 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +125.9 (*c* 1.5, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 326.1526 (M^+, 1.0), $C_{20}H_{22}O_4$ requires 326.1518, 220 (100.0, M^+−106); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (s, 9H), 3.00 (d, *J*=2.4 Hz, 1H, OH), 5.02 (s, 1H), 5.22 (d, *J*=2.0 Hz, 1H), 7.24 (m, 5H), 7.38 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 34.1 (s), 77.2 (d), 84.5 (s), 108.1 (d), 126.6 (d), 127.6 (d), 127.9 (d), 128.2 (d), 128.5 (d), 129.1 (d), 131.7 (s), 136.5 (s), 172.6 (s).

*3.2.3. (2S,5R,1′S)-2-(tert-butyl)-5-phenyl-5-[1′-hydroxy-1′-(4-metylphenyl)methyl]-1,3-dioxolane-4-one (**7b-A**).* $[\alpha]_D^{25}$ −20.4 (*c* 0.8, $CHCl_3$); *m*/*z* (FAB^+) 363.1572 (M^+, 100.0), $C_{21}H_{24}O_4Na$ requires 363.1572; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (s, 9H), 2.25 (s, 3H), 2.59 (br s, 1H, OH), 5.16 (br s, 1H), 5.72 (s, 1H), 6.92 (AA′ system, *J*=8.2 Hz, 4H), 7.23 (m, 3H), 7.47 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1 (q), 23.4 (q), 35.0 (s), 80.7 (d), 85.2 (s), 111.2 (d), 125.3 (d), 127.7 (d), 127.8 (d), 127.9 (d), 128.3 (d), 134.3 (s), 135.5 (s), 137.9 (s), 173.4 (s).

*3.2.4. (2S,5S,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-hydroxy-1′-(4-methylphenyl)methyl]-1,3-dioxolan-4-one (**7b-B**).* $[\alpha]_D^{25}$ +120.6 (*c* 1.4, $CHCl_3$); HRMS *m*/*z* (FAB^+) 363.1577 (M^+, 100.0), $C_{21}H_{24}O_4Na$ requires 363.1572; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (s, 9H), 2.30 (s, 3H), 2.99 (br s, 1H, OH), 5.01 (s, 1H), 5.16 (br s, 1H), 7.04 (m, 4H), 7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1 (q), 23.4 (q), 34.1 (s), 77.1 (d), 84.4 (s), 108.0 (d), 126.6 (d), 127.8 (d), 128.2 (d), 128.4 (d), 128.9 (d), 131.8 (s), 133.4 (s), 137.8 (s), 172.6 (s).

*3.2.5. (2S,5R,1′S)-2-(tert-Butyl)-5-[1′-(4-chlorophenyl)-1′-hydroxymethyl]-5-phenyl-1,3-dioxolan-4-one (**7c-A**).* $[\alpha]_D^{25}$ −28.1 (*c* 0.6, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 362.1102/360.1154 (M^+, 0.7/2.2), $C_{20}H_{21}O_4Cl$ requires 362.1099/360.1128, 220 (100.0, $C_{13}H_{16}O_3$), 134 (24.3), 70 (58.4); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (s, 9H), 2.80 (br s, 1H, OH), 5.20 (br s, 1H), 5.73 (s, 1H), 6.91 (d, *J*=8.5 Hz, 2H), 7.11 (d, *J*=8.5 Hz, 2H), 7.25 (m, 3H), 7.44 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 35.1 (s), 80.2 (d), 85.1 (s), 111.4 (d), 125.2 (d), 127.7 (d), 128.0 (d), 128.2 (d), 129.1 (d), 134.0 (s), 135.1 (s), 135.8 (s), 173.2 (s).

*3.2.6. (2S,5S,1′S)-2-(tert-Butyl)-5-[1′-(4-chlorophenyl)-1′-hydroxymethyl]-5-phenyl-1,3-dioxolan-4-one (**7c-B**).* Mp 132–134 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +123.5 (*c* 0.7, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 362.1050/360.1312 (M^+, 0.6/2.1), $C_{20}H_{21}O_4Cl$ requires 362.1099/360.1128, 220 (100.0, $C_{13}H_{16}O_3$), 134 (22.8), 70 (47.9); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 9H), 3.17 (br s, 1H, OH), 5.02 (s, 1H), 5.16 (s, 1H), 7.09 (d, *J*=8.5 Hz, 2H), 7.20 (d, *J*=8.6 Hz, 2H), 7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 34.1 (s), 77.0 (d), 84.1 (s), 108.1 (d), 126.6 (d), 127.7 (d), 128.5 (d), 129.1 (d), 129.2 (d), 131.2 (s), 134.0 (s), 134.9 (s), 172.5 (s).

*3.2.7. (2S,5R,1′R)-2-(tert-Butyl)-5-[1′-(4-chlorophenyl)-1′-hydroxymethyl]-5-phenyl-1,3-dioxolan-4-one (**7c-C**).* Mp 174–176 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +21.7 (*c* 0.8, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 362.1117/360.1346 (M^+, 1.0/3.3), $C_{20}H_{21}O_4Cl$ requires 362.1099/360.1128, 220 (100.0, $C_{13}H_{16}O_3$), 134 (18.4), 70 (61.6); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 9H), 2.28 (d, *J*=2.5 Hz, 1H, OH), 4.78 (s, 1H), 5.07 (d, *J*=2.4 Hz, 1H), 7.27 (m, 4H), 7.37 (m, 3H), 7.67 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 35.3 (s), 78.9 (d), 85.1 (s), 110.6 (d), 125.7 (d), 128.3 (d), 128.4 (d), 128.6 (d), 129.1 (d), 134.6 (s), 135.1 (s), 135.4 (s), 171.3 (s).

*3.2.8. (2S,5R,1′S)-5-[1′-(4-Bromophenyl)-1′-hydroxymethyl]-2-(tert-butyl)-5-phenyl-1,3-dioxolan-4-one (**7d-A**).* Mp 58–60 °C (CH_2Cl_2); $[\alpha]_D^{25}$ −28.4 (*c* 0.6, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 276.9854/274.9928 (M^+−$C_6H_{11}O_3$, 2.9/3.1), $C_{10}H_{12}O_4Br$ requires 276.9898/274.9919, 220 (100.0, $C_{13}H_{16}O_3$), 105 (26.4, C_7H_5O), 70 (49.4, C_5H_{10}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (s, 9H), 2.69 (d, *J*=4.1 Hz, 1H, OH), 5.20 (d, *J*=3.9 Hz, 1H), 5.73 (s, 1H), 6.85 (d, *J*=8.5 Hz, 2H), 7.26 (m, 3H), 7.27 (d, *J*=8.5 Hz, 2H), 7.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q),

35.1 (s), 80.2 (d), 85.0 (s), 111.4 (d), 122.3 (s), 125.3 (d), 128.0 (d), 128.2 (d), 129.4 (d), 130.7 (d), 135.1 (s), 136.3 (s), 173.1 (s).

*3.2.9. (2S,5S,1′S)-5-[1′-(4-Bromophenyl)-1′-hydroxymethyl]-2-(tert-butyl)-5-phenyl-1,3-dioxolan-4-one (**7d-B**).* Mp 125–127 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +117.1 (*c* 0.7, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 276.9824/274.9922 ($M^+-C_6H_{11}O_3$, 6.0/6.2), $C_{10}H_{12}O_4Br$ requires 276.9898/274.9919; 220 (100.0, $C_{13}H_{16}O_3$), 105 (25.4, C_7H_5O), 70 (63.3, C_5H_{10}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 9H), 3.17 (d, *J*=2.3 Hz, 1H, OH), 5.02 (s, 1H), 5.14 (d, *J*=2.1 Hz, 1H), 7.02 (d, *J*=8.5 Hz, 2H), 7.34 (d, *J*=8.5 Hz, 2H), 7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 34.1 (s), 76.6 (d), 84.0 (s), 108.1 (d), 122.2 (s), 126.6 (d), 128.5 (d), 129.2 (d), 129.5 (d), 130.6 (d), 131.1 (s), 135.4 (s), 172.5 (s).

*3.2.10. (2S,5R,1′R)-5-[1′-(4-Bromophenyl)-1′-hydroxymethyl]-2-(tert-butyl)-5-phenyl-1,3-dioxolan-4-one (**7d-C**).* Mp 178–180 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +20.9 (*c* 0.9, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 276.9842/274.9920 ($M^+-C_6H_{11}O_3$, 6.1/6.3), $C_{10}H_{12}O_4Br$ requires 276.9898/274.9919, 220 (100.0, $C_{13}H_{16}O_3$), 105 (46.8, C_7H_5O), 70 (43.2, C_5H_{10}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 9H), 2.29 (br s, 1H, OH), 4.79 (s, 1H), 5.05 (br s, 1H), 7.19 (br d, *J*=8.5 Hz, 2H), 7.37 (m, 3H), 7.44 (br d, *J*=8.5 Hz, 2H), 7.67 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 35.3 (s), 78.9 (d), 85.0 (s), 110.6 (d), 122.8 (s), 125.7 (d), 128.4 (d), 128.7 (d), 129.4 (d), 131.2 (d), 135.0 (s), 135.9 (s), 171.3 (s).

*3.2.11. (2S,5R,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-hydroxy-1′-(4-methoxyphenyl)methyl]-1,3-dioxolan-4-one (**7e-A**).* $[\alpha]_D^{25}$ −20.7 (*c* 0.6, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 356.1618 (M^+, 0.9), $C_{21}H_{24}O_5$ requires 356.1624, 220 (33.4, $C_{13}H_{16}O_3$), 137 (100.0, $C_9H_{13}O$), 105 (16.0, C_7H_5O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (s, 9H), 2.46 (d, *J*=3.8 Hz, 1H, OH), 3.73 (s, 3H), 5.17 (d, *J*=3.8 Hz, 1H), 5.71 (s, 1H), 6.68 (d, *J*=8.9 Hz, 2H), 6.95 (d, *J*=8.9 Hz, 2H), 7.24 (m, 3H), 7.47 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 35.0 (s), 55.1 (q), 80.5 (d), 85.2 (s), 111.2 (d), 113.0 (d), 125.3 (d), 127.8 (d), 127.9 (d), 129.0 (d), 129.5 (s), 135.6 (s), 159.4 (s), 173.5 (s).

*3.2.12. (2S,5S,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-hydroxy-1′-(4-methoxyphenyl)methyl]-1,3-dioxolan-4-one (**7e-B**).* Mp 89–91 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +108.5 (*c* 0.9, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 356.1550 (M^+, 0.4), $C_{21}H_{24}O_5$ requires 356.1524, 220 (20.1, $C_{13}H_{16}O_3$), 137 ($M^+-C_{13}H_{16}O_3$, 100.0, $C_8H_9O_2$), 70 (22.9, C_5H_{10}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 9H), 3.01 (d, *J*=2.5 Hz, 1H, OH), 3.77 (s, 3H), 5.01 (s, 1H), 5.15 (d, *J*=2.5 Hz, 1H), 6.76 (d, *J*=8.9 Hz, 2H), 7.09 (d, *J*=8.7 Hz, 2H), 7.37 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 34.1 (s), 55.2 (q), 76.9 (d), 84.5 (s), 108.0 (d), 113.0 (d), 126.6 (d), 128.4 (d), 128.6 (s), 129.0 (d), 129.1 (d), 131.8 (s), 159.5 (s), 172.7 (s).

*3.2.13. (2S,5R,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-hydroxy-1′-(3,4-methylendioxyphenyl)methyl]-1,3-dioxolan-4-one (**7f-A**).* $[\alpha]_D^{25}$ −40.1 (*c* 1.1, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 370.1405 (M^+, 3.9), $C_{21}H_{22}O_6$ requires 370.1416, 220 (97.3, $C_{13}H_{16}O_3$), 151 (100.0, $C_7H_3O_4$), 93 (28.1, C_6H_5O), 70 (58.9, C_5H_{10}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (s, 9H), 2.40 (d, *J*=3.7 Hz, 1H, OH), 5.15 (d, *J*=3.7 Hz, 1H), 5.72 (s, 1H), 5.91 (d, *J*=1.4 Hz, 2H), 6.35 (dd, *J*=8.0, 1.6 Hz, 1H), 6.54 (d, *J*=8.0 Hz, 1H), 6.71 (d, *J*=1.6 Hz, 1H), 7.26 (m, 3H), 7.49 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 35.1 (s), 80.7 (d), 85.1 (s), 101.0 (t), 107.4 (d), 108.1 (d), 111.3 (d), 121.7 (d), 125.3 (d), 128.0 (d), 128.1 (d), 131.2 (s), 135.5 (s), 147.2 (s), 147.5 (s), 173.3 (s).

*3.2.14. (2S,5S,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-hydroxy-1′-(3,4-methylendioxyphenyl)methyl]-1,3-dioxolan-4-one (**7f-B**).* $[\alpha]_D^{25}$ +114.5 (*c* 0.6, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 370.1414 (M^+, 15.3), $C_{21}H_{22}O_6$ requires 370.1416, 220 (100.0, $C_{13}H_{16}O_3$), 151 (80.3), 105 (29.7, C_7H_5O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (s, 9H), 3.03 (d, *J*=2.5 Hz, 1H, OH), 5.02 (s, 1H), 5.11 (d, *J*=2.4 Hz, 1H), 5.90 (s, 2H), 6.67 (m, 3H), 7.38 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 34.1 (s), 77.0 (d), 84.5 (s), 100.9 (t), 107.4 (d), 108.1 (d), 108.6 (d), 121.5 (d), 126.6 (d), 128.5 (d), 129.1 (d), 130.4 (s), 131.7 (s), 147.0 (s), 147.4 (s), 172.6 (s).

*3.2.15. (2S,5R,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-hydroxy-1′-(4-trifluoromethylphenyl)methyl]-1,3-dioxolan-4-one (**7g-A**).* HRMS *m*/*z* (EI, 70 eV) 263.0665 ($M^+-C_6H_{11}O_3$, 12.6), $C_{15}H_{10}OF_3$ requires 263.0684, 220 (100.0, $C_{13}H_{16}O_3$), 105 (61.4, C_7H_5O), 70 (77.2, C_5H_{10}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (s, 9H), 2.65 (d, *J*=4.1 Hz, 1H, OH), 5.31 (d, *J*=4.1 Hz, 1H), 5.75 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 35.1 (s), 80.2 (d), 85.0 (s), 111.5 (d), 173.0 (s).

*3.2.16. (2S,5S,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-hydroxy-1′-(4-trifluoromethylphenyl)methyl]-1,3-dioxolan-4-one (**7g-B**).* HRMS *m*/*z* (EI, 70 eV) 263.0670 ($M^+-C_6H_{11}O_3$, 10.8), $C_{15}H_{10}OF_3$ requires 263.0684, 220 (100.0, $C_{13}H_{16}O_3$), 105 (53.8, C_7H_5O), 70 (64.9, C_5H_{10}); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (s, 9H), 3.18 (d, *J*=2.4 Hz, 1H, OH), 5.03 (s, 1H), 5.26 (d, *J*=2.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 34.1 (s), 76.6 (d), 84.1 (s), 108.2 (d), 172.4 (s).

3.3. General procedure for the protection of the hydroxyl group

A solution of compound **7** (0.5 mmol) and diisopropylethylamine (0.43 mL, 2.4 mmol) in dry CH_3CN (1.6 mL) under argon was treated with 0.18 mL (1.6 mmol) of MEMCl. The mixture was stirred and heated at reflux for 1–2 h. The reaction was quenched with water and extracted with CH_2Cl_2 (3×20 mL). The combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), and evaporated and the residue was purified by flash chromatography (silica gel, hexane–diethyl ether), to afford adducts **8**. Yields are included in Table 2.

*3.3.1. (2S,5R,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-phenyl-1′-(2-methoxyethoxymethoxy)methyl]-1,3-dioxolan-4-one (**8a-A**).* $[\alpha]_D^{25}$ +103.3 (*c* 1.0, $CHCl_3$); HRMS *m*/*z* (CI, methane) 415.2121 (M^++1, 8.1), $C_{24}H_{31}O_6$ requires 415.2121, 309 (20.3), 195 (21.0), 167 (66.2), 105 (14.2, C_7H_5O), 89 (100.0, C_7H_5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (s, 9H), 3.39 (s, 3H), 3.56 (m, 3H), 3.90 (m, 1H), 4.63 (d, *J*=7.0 Hz, 2H), 5.21 (s, 1H), 5.73 (s, 1H), 6.96 (dd, *J*=8.4, 1.6 Hz, 2H), 7.0–7.2 (m, 6H), 7.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 35.0 (s), 59.0 (q), 67.4 (t), 71.7 (t), 83.4 (d), 84.9 (s), 92.9 (t), 110.9 (d), 125.4 (d), 127.4 (d), 127.8 (d), 128.0 (d), 128.2 (d), 129.0 (d), 134.0 (s), 135.3 (s), 173.1 (s).

*3.3.2. (2S,5S,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-phenyl-1′-(2-methoxyethoxymethoxy)methyl]-1,3-dioxolan-4-one (**8a-B**).* $[\alpha]_D^{25}$ +134.4 (*c* 1.2, $CHCl_3$); HRMS *m*/*z* (CI, methane) 413.1915 (M^+−H, 1.5), $C_{24}H_{29}O_6$ requires 413.1964, 223 (8.4), 195 (29.3, $C_{14}H_{11}O$), 167 (93.7), 89 (100.0); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.74 (s, 9H), 2.70 (m, 1H), 3.06 (m, 2H), 3.20 (m, 1H), 3.27 (s, 3H), 4.45 (d, *J*=7.2 Hz, 2H), 5.01 (s, 1H), 5.27 (s, 1H), 7.2–7.4 (m, 8H), 7.66 (dd, *J*=8.1 Hz, 1.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 33.9 (s), 58.9 (q), 66.6 (t), 71.4 (t), 80.4 (d), 85.8 (s), 93.3 (t), 108.1 (d), 126.3 (d), 127.9 (d), 128.4 (d), 128.5 (d), 128.6 (d), 129.4 (d), 133.8 (s), 135.4 (s), 171.3 (s).

*3.3.3. (2S,5R,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-(4-methylphenyl)-1′-(2-methoxyethoxymethoxy)methyl]-1,3-dioxolan-4-one (**8b-A**).* $[\alpha]_D^{25}$ +105.2 (*c* 0.8, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 401.1929 ($M^+-C_2H_3$, 0.3), $C_{23}H_{29}O_6$ requires 401.1964, 209 (11.0, $C_{12}H_{17}O_3$), 105 (15.7, C_7H_5O), 89 (100.0, $C_4H_9O_2$), 59 (38.8, C_3H_7O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (s, 9H), 2.24 (s, 3H), 3.39 (s, 3H), 3.59 (m, 3H), 3.88 (m, 1H), 4.61 (d, *J*=7.0 Hz, 2H), 5.18 (s, 1H), 5.72 (s, 1H), 6.84 (d,

J=8.3 Hz, 2H), 6.91 (d, J=8.2 Hz, 2H), 7.23 (m, 3H), 7.47 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1 (q), 23.5 (q), 34.9 (s), 58.9 (q), 67.3 (t), 71.7 (t), 83.2 (d), 84.9 (s), 92.6 (t), 110.7 (d), 125.4 (d), 127.8 (d), 127.9 (d), 128.2 (d), 128.9 (d), 130.8 (s), 135.4 (s), 137.8 (s), 173.2 (s).

*3.3.4. (2S,5R,1′S)-2-(tert-Butyl)-5-[1′-(4-chlorophenyl)-1′-(2-methoxyethoxymethoxy)methyl]-5-phenyl-1,3-dioxolan-4-one (**8c-A**).* $[\alpha]_D^{25}$ +94.0 (*c* 0.7, $CHCl_3$); HRMS *m/z* (EI, 70 eV) 423.1325/421.1413 ($M^+-C_2H_3$, 0.3/1.0), $C_{22}H_{26}O_6Cl$ requires 423.1388/421.1418, 105 (17.9, C_7H_5O), 89 (100.0, $C_4H_9O_2$), 59 (41.3, C_3H_7O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (s, 9H), 3.39 (s, 3H), 3.5–3.9 (m, 4H), 4.61 (d, J=7.0 Hz, 2H), 5.19 (s, 1H), 5.72 (s, 1H), 6.88 (d, J=8.5 Hz, 2H), 7.09 (d, J=8.5 Hz, 2H), 7.23 (m, 3H), 7.44 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 35.0 (s), 59.0 (q), 67.5 (t), 71.6 (t), 82.6 (d), 84.6 (s), 92.9 (t), 110.9 (d), 125.3 (d), 127.7 (d), 128.0 (d), 128.2 (d), 130.2 (d), 132.6 (s), 134.1 (s), 135.0 (s), 172.8 (s).

*3.3.5. (2S,5R,1′S)-5-[1′-(4-Bromophenyl)-1′-(2-methoxyethoxymethoxy)methyl]-2-(tert-butyl)-5-phenyl-1,3-dioxolan-4-one (**8d-A**).* $[\alpha]_D^{25}$ +87.6 (*c* 0.6, $CHCl_3$); HRMS *m/z* (EI, 70 eV) 309.1483/308.1507 ($M^+-C_4H_9O_3$–Br, 3.2/3.4, $C_{20}H_{20}O_3$ requires 309.1446/308.1413), 89 (100.0); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (s, 9H), 3.40 (s, 3H), 3.58 (m, 3H), 3.89 (m, 1H), 4.62 (d, J=7.0 Hz, 2H), 5.18 (s, 1H), 5.71 (s, 1H), 6.81 (d, J=8.5 Hz, 2H), 7.25 (m, 5H), 7.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 35.0 (s), 59.0 (q), 67.5 (t), 71.6 (t), 82.7 (d), 84.6 (s), 92.9 (t), 110.9 (d), 122.4 (s), 125.3 (d), 128.0 (d), 128.2 (d), 130.5 (d), 130.7 (d), 133.2 (s), 135.0 (s), 172.8 (s).

*3.3.6. (2S,5R,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-(4-methoxyphenyl)-1′-(2-methoxyethoxymethoxy)methyl]-1,3-dioxolan-4-one (**8e-A**).* Mp 69–71 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +112.1 (*c* 0.6, $CHCl_3$); HRMS *m/z* (EI, 70 eV) 339.1597 ($M^+-C_4H_9O_3$, 1.2), $C_{21}H_{23}O_4$ requires 339.1596), 225 ($M^+-C_{13}H_{15}O_3$, 15.2, $C_{12}H_{17}O_4$, 105 (13.6, C_7H_5O), 89 (100.0, C_7H_5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (s, 9H), 3.40 (s, 3H), 3.5–3.7 (m, 3H), 3.73 (s, 3H), 3.90 (m, 1H), 4.60 (d, J=7.0 Hz, 2H), 5.16 (s, 1H), 5.72 (s, 1H), 6.65 (d, J=8.7 Hz, 2H), 6.90 (d, J=8.7 Hz, 2H), 7.23 (m, 3H), 7.46 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 35.0 (s), 55.0 (q), 58.9 (q), 67.3 (t), 71.7 (t), 82.9 (d), 84.9 (s), 92.5 (t), 110.8 (d), 112.9 (d), 125.4 (d), 125.9 (s), 127.8 (d), 127.9 (d), 130.2 (d), 135.5 (s), 159.4 (s), 173.2 (s).

*3.3.7. (2S,5S,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-(4-methoxyphenyl)-1′-(2-ethoxyethoxymethoxy)methyl]-1,3-dioxolan-4-one (**8e-B**).* $[\alpha]_D^{25}$ +138.9 (*c* 0.8, $CHCl_3$); HRMS *m/z* (CI, methane) 443.2059 (M^+-H, 0.3), $C_{25}H_{31}O_7$ requires 443.2070, 339 (71.4, $C_{21}H_{23}O_4$), 197 (81.2), 89 (100.0); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79 (s, 9H), 2.68 (m, 1H), 3.0–3.3 (m, 3H), 3.27 (s, 3H), 3.79 (s, 3H), 4.44 (d, J=7.2 Hz, 2H), 5.01 (s, 1H), 5.21 (s, 1H), 6.82 (d, J=8.9 Hz, 2H), 7.33 (d, J=8.9 Hz, 2H), 7.35 (m, 3H), 7.65 (dd, J=8.4, 1.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4 (q), 33.9 (s), 55.2 (q), 58.9 (q), 66.5 (t), 71.4 (t), 80.0 (d), 85.9 (s), 93.0 (t), 108.0 (d), 113.2 (d), 126.2 (d), 127.2 (d), 127.4 (s), 128.5 (d), 130.7 (d), 133.9 (s), 159.6 (s), 171.3 (s).

*3.3.8. (2S,5R,1′S)-2-(tert-Butyl)-5-phenyl-5-[1′-(3,4-methylendioxyphenyl)-1′-(2-methoxyethoxymethoxy)methyl]-1,3-dioxolan-4-one (**8f-A**).* $[\alpha]_D^{25}$ +76.7 (*c* 0.9, $CHCl_3$); HRMS *m/z* (CI, methane) 457.1866 (M^+-H, 0.6), $C_{25}H_{29}O_8$ requires 457.1862, 353 (17.1, $C_{18}H_{25}O_7$), 239 (21.9), 211 (100.0); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (s, 9H), 3.41 (s, 3H), 3.59 (m, 3H), 3.90 (m, 1H), 4.60 (d, J=7.0 Hz, 2H), 5.12 (s, 1H), 5.71 (s, 1H), 5.90 (d, J=1.5 Hz, 2H), 6.29 (dd, J=8.1, 1.7 Hz, 1H), 6.49 (d, J=7.9 Hz, 1H), 6.68 (d, J=1.5 Hz, 1H), 7.24 (m, 3H), 7.48 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 35.0 (s), 59.0 (q), 67.4 (t), 71.7 (t), 82.9 (d), 84.9 (s), 92.5 (t), 100.9 (t), 107.2 (d), 108.8 (d), 110.8 (d), 123.2 (d), 125.3 (d), 127.6 (s), 127.8 (d), 128.0 (d), 135.3 (s), 147.1 (s), 147.4 (s), 173.1 (s).

3.4. General procedure for the hydrolysis of compounds 8

Compound **8** (0.28 mmol) was treated with a 5% KOH solution in ethanol at room temperature until complete reaction of the starting material (TLC) was achieved. The solution was poured into ice and acidified with 1 M HCl until pH 2. The aqueous mixture was extracted with EtOAc and the organic layers were washed with brine until neutrality, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give α-hydroxy acids **9**. Yields are included in Table 2.

*3.4.1. (2R,3S)-2,3-Diphenyl-2-hydroxy-3-(2-methoxyethoxymethyoxy)propanoic acid (**9a-A**).* $[\alpha]_D^{25}$ +14.5 (*c* 0.7, CH_3OH); HRMS *m/z* (CI, methane) 347.1487 (M^++1, 1.9), $C_{19}H_{23}O6$ requires 347.1495, 241 (19.5), 225 (12.2), 195 (16.0, C_4H_{11}), 105 (30.2, C_7H_5O), 89 (100.0, C_7H_5); ^{1}H NMR (300 MHz, DMSO) δ 3.18 (s, 3H), 3.2–3.5 (m, 3H), 3.66 (m, 1H), 4.52 (d, J=6.6 Hz, 2H), 5.31 (s, 1H), 7.12 (m, 8H), 7.48 (d, J=8.3, 1.7 Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 58.3 (q), 66.8 (t), 71.3 (t), 80.8 (s), 82.3 (d), 93.1 (t), 126.5 (d), 127.1 (d), 127.2 (d), 127.3 (d), 127.5 (d), 127.7 (d), 129.6 (d), 136.9 (s), 175.1 (s).

*3.4.2. (2S,3S)-2,3-Diphenyl-2-hydroxy-3-(2-methoxyethoxymethoxy)propanoic acid (**9a-B**).* $[\alpha]_D^{25}$ +61.9 (*c* 0.6, CH_3OH); HRMS *m/z* (EI, 70 eV) 346.1424 (M^+, 0.3), $C_{19}H_{22}O_6$ requires 346.1416, 105 (31.0, C_7H_5O), 89 (100.0, $C_4H_9O_2$); ^{1}H NMR (300 MHz, DMSO) δ 2.9–3.3 (m, 4H), 3.14 (s, 3H), 4.28 (d, J=7.0 Hz, 2H), 5.33 (s, 1H), 7.2–7.4 (m, 8H), 7.71 (br d, J=7.2 Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 58.4 (q), 66.5 (t), 71.2 (t), 81.0 (s), 81.1 (d), 92.6 (t), 126.8 (d), 127.3 (d), 127.5 (d), 127.6 (d), 128.0 (d), 129.9 (d), 137.6 (s), 141.5 (s), 173.8 (s).

*3.4.3. (2R,3S)-2-Phenyl-2-hydroxy-3-(4-methylphenyl)-3-(2-methoxyethoxymethoxy)propanoic acid (**9b-A**).* $[\alpha]_D^{25}$ +25.9 (*c* 0.5, CH_3OH); HRMS *m/z* (EI, 70 eV) 296.1438 ($M^+-CO_2-H_2O-H_2$), 0.1, $C_{19}H_{20}O_3$ requires 296.1413, 209 (17.4, $C_{12}H_{17}O_3$), 105 (20.7, C_7H_5O), 89 (100.0, $C_4H_9O_2$), 59 (58.9, C_3H_7O); ^{1}H NMR (300 MHz, DMSO) δ 2.15 (s, 3H), 3.20 (s, 3H), 3.36 (m, 3H), 3.71 (m, 1H), 4.49 (d, J=6.8 Hz, 2H), 5.29 (s, 1H), 6.87 (d, J=7.9 Hz, 2H), 6.98 (d, J=8.0 Hz, 2H), 7.16 (m, 3H), 7.49 (dd, J=7.9, 1.1 Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 21.0 (q), 58.3 (q), 66.8 (t), 71.3 (t), 80.8 (s), 81.9 (d), 92.8 (t), 126.5 (d), 127.3 (d), 127.7 (d), 127.9 (d), 129.7 (d), 133.6 (s), 136.5 (s), 136.6 (s), 175.1 (s).

*3.4.4. (2R,3S)-3-(4-Chlorophenyl)-2-phenyl-2-hydroxy-3-(2-methoxyethoxymethoxy)propanoic acid (**9c-A**).* $[\alpha]_D^{25}$ +5.7 (*c* 0.4, CH_3OH); HRMS *m/z* (EI, 70 eV) 365.0617/363.0679 (M^+-CH_5, 0.1/0.2), $C_{18}H_{16}O_6Cl$ requires 365.0606/363.0635, 105 (28.9, C_7H_5O), 89 (100.0, $C_4H_9O_2$), 59 (62.1, C_3H_7O); ^{1}H NMR (300 MHz, DMSO) δ 3.18 (s, 3H), 3.31 (m, 3H), 3.65 (m, 1H), 4.53 (d, J=6.2 Hz, 2H), 5.29 (br s, 1H), 7.12 (m, 7H), 7.51 (d, J=7.7 Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 58.3 (q), 66.7 (t), 71.3 (t), 80.7 (s), 81.9 (d), 93.5 (t), 126.5 (d), 127.1 (d), 127.2 (d), 127.6 (d), 131.3 (d), 132.0 (s), 135.9 (s), 136.7 (s), 174.6 (s).

*3.4.5. (2R,3S)-3-(4-Bromophenyl)-2-phenyl-2-hydroxy-3-(2-methoxyethoxymethoxy)propanoic acid (**9d-A**).* Mp 125–127 °C (EtOAc); $[\alpha]_D^{25}$ +5.3 (*c* 0.5, CH_3OH); HRMS *m/z* (CI, methane) 427.0589/425.0668 (M^++1, 0.3/0.3), $C_{19}H_{22}O_6Br$ requires 427.0579/425.0600, 323/321 (3.4/3.7, $C_{11}H_{14}O_6Br$), 305/303 (3.6/3.9, $C_{15}H_{12}O_2Br$), 277/275 (4.5/4.8, $C_{14}H_{12}OBr$), 187/185 (6.2/6.5, C_7H_6OBr), 165 (7.0, $C_7H_{17}O_4$), 89 (100.0, $C_4H_9O_2$), 59 (45.1, C_3H_7O); ^{1}H NMR (300 MHz, DMSO) δ 3.18 (s, 3H), 3.35 (m, 3H), 3.64 (m, 1H), 4.54 (d, J=6.8 Hz, 2H), 5.29 (s, 1H), 7.02 (d, J=8.5 Hz, 2H), 7.17 (m,

3H), 7.26 (d, *J*=8.4 Hz, 2H), 7.49 (dd, *J*=7.9, 1.1 Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 58.3 (q), 66.8 (t), 71.3 (t), 80.6 (s), 81.9 (d), 93.4 (t), 120.9 (s), 126.4 (d), 127.5 (d), 127.8 (d), 130.1 (d), 131.7 (d), 136.6 (s), 139.9 (s), 174.8 (s).

*3.4.6. (2R,3S)-2-Phenyl-2-hydroxy-3-(4-methoxyphenyl)-3-(2-methoxyethoxymethoxy)propanoic acid (**9e-A**).* Mp 77–79 °C (EtOAc); $[\alpha]_D^{25}$ +30.3 (*c* 0.5, CH_3OH); HRMS *m*/*z* (EI, 70 eV) 254.0903 ($M^+-C_4H_9O_3-OH$, 2.4), $C_{16}H_{14}O_3$ requires 254.0943, 226 ($M^+-C_4H_9O_3-CO_2H$, 28.3, $C_{15}H_{14}O_2$), 121 (49.4), 89 (100.0, C_7H_5); ^{1}H NMR (300 MHz, DMSO) δ 3.21 (s, 3H), 3.37 (m, 3H), 3.62 (s, 3H), 3.72 (m, 1H), 4.48 (d, *J*=6.8 Hz, 2H), 5.28 (s, 1H), 6.63 (d, *J*=8.7 Hz, 2H), 7.03 (d, *J*=8.7 Hz, 2H), 7.15 (m, 3H), 7.49 (dd, *J*=8.3, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 55.1 (q), 58.3 (q), 66.8 (t), 71.4 (t), 80.8 (s), 81.6 (d), 92.7 (t), 112.7 (d), 126.5 (d), 127.3 (d), 127.7 (d), 128.5 (s), 128.6 (s), 130.9 (d), 158.7 (s), 175.1 (s).

*3.4.7. (2S,3S)-2-Phenyl-2-hydroxy-3-(4-methoxyphenyl)-3-(2-methoxyethoxymethoxy)propanoic acid (**9e-B**).* $[\alpha]_D^{25}$ +68.9 (*c* 0.7, CH_3OH); HRMS *m*/*z* (EI, 70 eV) 314.1509 ($M^+-CO_2-H_2O$, 0.3), $C_{19}H_{22}O_4$ requires 314.1518, 225 (100.0, $C_{15}H_{13}O_2$); ^{1}H NMR (300 MHz, DMSO) δ 2.9–3.5 (m, 4H), 3.15 (s, 3H), 3.73 (s, 3H), 4.25 (d, *J*=6.8 Hz, 2H), 5.28 (s, 1H), 6.83 (br d, *J*=8.6 Hz, 2H), 7.2–7.4 (m, 3H), 7.32 (d, *J*=8.6 Hz, 2H), 7.71 (br d, *J*=7.1 Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 55.3 (q), 58.3 (q), 66.5 (t), 71.3 (t), 80.6 (d), 81.1 (s), 92.2 (t), 113.1 (d), 126.8 (d), 127.2 (d), 127.6 (d), 128.8 (s), 129.4 (s), 131.1 (d), 159.1 (s), 173.8 (s).

*3.4.8. (2R,3S)-2-Phenyl-2-hydroxy-3-(3,4-methylendioxyphenyl)-3-(2-methoxyethoxymethoxy)propanoic acid (**9f-A**).* $[\alpha]_D^{25}$ +11.4 (*c* 0.8, CH_3OH); HRMS *m*/*z* (EI, 70 eV) 372.1198 (M^+-H_2O, 1.0), $C_{20}H_{20}O_7$ requires 372.1209, 239 (36.0, $C_{12}H_{15}O_5$), 89 (100.0, $C_4H_9O_2$); ^{1}H NMR (300 MHz, DMSO) δ 3.22 (s, 3H), 3.39 (m, 3H), 3.71 (m, 1H), 4.50 (d, *J*=6.8 Hz, 2H), 5.26 (s, 1H), 5.89 (s, 2H), 6.44 (dd, *J*=7.9, 1.3 Hz, 1H), 6.56 (d, *J*=8.1 Hz, 1H), 6.82 (d, *J*=1.3 Hz, 1H), 7.18 (m, 3H), 7.50 (dd, *J*=8.5, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 58.4 (q), 66.9 (t), 71.4 (t), 80.8 (s), 81.7 (d), 92.7 (t), 101.0 (t), 107.0 (d), 109.8 (d), 123.6 (d), 126.5 (d), 127.4 (d), 127.8 (d), 130.4 (s), 139.7 (s), 146.6 (s), 146.7 (s), 175.0 (s).

3.5. General procedure for the oxidative decarboxylation

To a stirred solution of α-hydroxy acid **9** (0.13 mmol) in acetonitrile (0.5 mL) were added 3.3 mg of Co(III)Me$_2$opba complex (6.5×10^{-3} mmol) and pivalaldehyde (0.39 mmol) and the mixture was stirred for 5 min under air and then under oxygen atmosphere at room temperature until consumption of the starting material as indicated by TLC. The reaction was quenched with water and extracted with diethyl ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated and the residue was purified by flash chromatography (silica gel, hexane–diethyl ether) to afford ketone **10**. Yields are included in Table 2.

*3.5.1. (2S)-1,2-Diphenyl-2-(2-methoxyethoxymethoxy)ethanone (**10a-A**, **10a-B**).* Mp 77–79 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +111.0 (*c* 0.8, $CHCl_3$); HRMS *m*/*z* (CI, methane) 301.1433 (M^++1, 0.1), $C_{18}H_{21}O_4$ requires 301.1439, 225 (29.5, $C_{15}H_{13}O_2$), 195 (100.0, $C_{10}H_{11}O_4$), 105 (16.3, C_7H_5O), 89 (70.8, C_7H_5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.34 (s, 3H), 3.48 (br t, *J*=4.6 Hz, 2H), 3.70 (m, 2H), 4.85 (d, *J*=7.1 Hz, 2H), 6.09 (s, 1H), 7.2–7.5 (m, 8H), 7.96 (dd, *J*=8.8, 1.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 59.0 (q), 67.4 (t), 71.6 (t), 80.0 (d), 94.0 (t), 128.1 (d), 128.5 (d), 128.7 (d), 128.9 (d), 129.0 (d), 133.2 (d), 135.1 (s), 135.8 (s), 196.5 (s).

*3.5.2. (2S)-1-Phenyl-2-(4-methylphenyl)-2-(2-methoxyethoxymethoxy)ethanone (**10b-A**).* $[\alpha]_D^{25}$ +134.0 (*c* 1.4, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 314.1522 (M^+, 0.1), $C_{19}H_{22}O_4$ requires 314.1518, 209 (44.2, $C_{12}H_{17}O_3$), 105 (28.9, C_7H_5O), 89 (100.0, $C_4H_9O_2$), 59 (52.5, C_3H_7O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.29 (s, 3H), 3.34 (s, 3H), 3.48 (t, *J*=4.5 Hz, 2H), 3.71 (m, 2H), 4.83 (d, *J*=7.0 Hz, 2H), 6.07 (s, 1H), 7.14 (d, *J*=7.9 Hz, 2H), 7.37 (d, *J*=7.9 Hz, 2H), 7.38 (m, 2H), 7.48 (tt, *J*=7.4, 1.3 Hz, 1H), 7.95 (dd, *J*=8.7, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1 (q), 58.9 (q), 67.3 (t), 71.6 (t), 79.6 (d), 93.8 (t), 128.1 (d), 128.4 (d), 128.9 (d), 129.6 (d), 132.8 (s), 133.1 (d), 135.1 (s), 138.5 (s), 196.4 (s).

*3.5.3. (2S)-2-(4-Chlorophenyl)-1-phenyl-2-(2-methoxyethoxymethoxy)ethanone (**10c-A**).* $[\alpha]_D^{25}$ +89.8 (*c* 1.5, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 336.0976/334.1011 (M^+, 0.1/0.3), $C_{18}H_{19}O_4Cl$ requires 336.0942/334.0972, 229 (20.2, $C_{13}H_9O_4$), 105 (45.1, C_7H_5O), 89 (100.0, $C_4H_9O_2$), 59 (59.1, C_3H_7O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.33 (s, 3H), 3.47 (t, *J*=4.5 Hz, 2H), 3.68 (m, 2H), 4.84 (d, *J*=7.0 Hz, 2H), 6.05 (s, 1H), 7.31 (d, *J*=8.5 Hz, 2H), 7.41 (d, *J*=8.4 Hz, 2H), 7.3–7.5 (m, 2H), 7.51 (tt, *J*=7.5, 1.3 Hz, 1H), 7.94 (dd, *J*=8.7, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 58.9 (q), 67.5 (t), 71.6 (t), 79.2 (d), 94.0 (t), 128.5 (d), 129.0 (d), 129.1 (d), 129.3 (d), 133.4 (d), 134.4 (s), 134.6 (s), 134.9 (s), 196.6 (s).

*3.5.4. (2S)-2-(4-Bromophenyl)-1-phenyl-2-(2-methoxyethoxymethoxy)ethanone (**10d-A**).* Mp 75–77 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +77.1 (*c* 0.5, $CHCl_3$); HRMS *m*/*z* (CI, methane) 302.9875/300.9856 (M^++1$-C_6H_5$, 13.5/14.0), $C_{15}H_{10}O_2Br$ requires 302.9844/300.9864, 274/272 ($M^+-COC_6H_5$, 35.4/37.0, $C_{11}H_{13}O_3Br$), 194 ($M^+-COC_6H_5-Br$, 41.2, $C_{14}H_{10}O$), 105 (17.4, C_7H_5O), 89 (100.0, $C_4H_9O_2$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.34 (s, 3H), 3.47 (t, *J*=4.7 Hz, 2H), 3.69 (m, 2H), 4.84 (d, *J*=7.1 Hz, 2H), 6.03 (s.1H), 7.3–7.6 (m, 7H), 7.94 (dd, *J*=8.7, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 59.0 (q), 67.6 (t), 71.6 (t), 79.3 (d), 94.1 (t), 122.9 (s), 128.6 (d), 129.0 (d), 129.6 (d), 132.1 (d), 133.4 (d), 134.9 (s), 135.0 (s), 196.2 (s).

*3.5.5. (2S)-1-Phenyl-2-(4-methoxyphenyl)-2-(2-methoxyethoxymethoxy)ethanone (**10e-A**, **10e-B**).* $[\alpha]_D^{25}$ +126.6 (*c* 0.9, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 330.1475 (M^+, 2.0), $C_{19}H_{22}O_5$ requires 330.1467, 225 (50.4), 135 (20.6), 105 (19.1, C_7H_5O), 89 (100.0, $C_4H_9O_2$), 77 (11.4, C_6H_5), 59 (63.3, C_3H_7O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.35 (s, 3H), 3.50 (t, *J*=4.5 Hz, 2H), 3.6–3.8 (m, 2H), 3.76 (s, 3H), 4.83 (d, *J*=7.1 Hz, 2H), 6.07 (s, 1H), 6.86 (d, *J*=8.6 Hz, 2H), 7.39 (m, 4H), 7.49 (tt, *J*=7.4, 1.3 Hz, 1H), 7.95 (dd, *J*=8.6, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.2 (q), 58.9 (q), 67.3 (t), 71.6 (t), 79.1 (d), 93.6 (t), 114.4 (d), 127.7 (s), 128.5 (d), 128.9 (d), 129.7 (d), 133.1 (d), 135.2 (s), 159.9 (s), 196.4 (s).

*3.5.6. (2S)-1-Phenyl-2-(3,4-methylendioxyphenyl)-2-(2-methoxyethoxymethoxy)ethanone (**10f-A**).* $[\alpha]_D^{25}$ +115.7 (*c* 1.5, $CHCl_3$); HRMS *m*/*z* (EI, 70 eV) 344.1244 (M^+, 0.6), $C_{19}H_{20}O_6$ requires 344.1260, 239 (75.7, $C_{12}H_{15}O_5$), 89 (100.0); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.35 (s, 3H), 3.50 (t, *J*=4.5 Hz, 2H), 3.71 (m, 2H), 4.83 (d, *J*=7.4 Hz, 2H), 5.92 (d, *J*=1.3 Hz, 2H), 6.03 (s, 1H), 6.75 (d, *J*=8.5 Hz, 1H), 6.93 (m, 2H), 7.40 (m, 2H), 7.50 (tt, *J*=7.4, 1.3 Hz, 1H), 7.96 (dd, *J*=8.1, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 59.0 (q), 67.4 (t), 71.7 (t), 79.2 (d), 93.6 (t), 101.3 (t), 108.4 (d), 108.6 (d), 122.4 (d), 128.5 (d), 128.9 (d), 129.5 (s), 133.2 (d), 135.2 (s), 148.0 (s), 148.2 (s), 196.3 (s).

3.6. General procedure for the deprotection of the hydroxyl group

To a solution of ketone **10** (0.11 mmol) in dry CH_2Cl_2 (0.64 mL) cooled at −20 °C was added dropwise a 1 M solution of $TiCl_4$ in CH_2Cl_2 (0.22 mL, 0.22 mmol) under argon. The reaction was stirred for 5 min and then quenched with 9.3% aqueous NH_4OH solution (0.22 mL) at 0 °C until pH 7. Water was added and the mixture was

extracted with CH_2Cl_2 (3×20 mL). The combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), and evaporated and the residue was purified by flash chromatography (silica gel, hexane–diethyl ether). Yields and enantiomeric excess of benzoins **11** are included in Table 2.

*3.6.1. (2S)-1,2-Diphenyl-2-hydroxyethanone (**11a**).* Mp 134–136 °C (acetone); $[\alpha]_D^{23}$ +109.5 (*c* 1.3, acetone), commercially available (*S*)-(+)-benzoin:[25] $[\alpha]_D^{19}$ +115 (*c* 1.5, acetone); HRMS *m*/*z* (EI, 70 eV) 212, 0813 (M^+, 0.6), $C_{14}H_{12}O_2$ requires 212.0837, 107 (54.8), 105 (100.0, C_7H_5O), 79 (30.2, C_6H_7), 77 (53.4, C_6H_5), 51 (13.7); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.53 (d, *J*=6.1 Hz, 1H, OH), 5.93 (d, *J*=6.2 Hz, 1H), 7.31 (m, 5H), 7.38 (t, *J*=7.8 Hz, 2H), 7.48 (tt, *J*=7.5, 1.1 Hz, 1H), 7.90 (dd, *J*=8.7, 1.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 76.2 (d), 127.7 (d), 128.5 (d), 128.6 (d), 129.0 (d), 129.1 (d), 133.4 (s), 133.9 (d), 139.0 (s), 198.9 (s); enantiomeric excess (99%) was determined by HPLC (Chiralpak AD-H), hexane–*i*-PrOH 90:10, 1 mL/min, major enantiomer (*S*) t_R=26.6 min, minor enantiomer (*R*) t_R=21.0 min.[29]

*3.6.2. (2S)-1-Phenyl-2-hydroxy-2-(4-methylphenyl) ethanone (**11b**).* Mp 113–115 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +103.9 (*c* 1.0, acetone); HRMS *m*/*z* (EI, 70 eV) 226.0989 (M^+, 6.1), $C_{15}H_{14}O_2$ requires 226.0994, 121 (100.0, C_8H_9O), 105 (19.9, C_7H_5O), 93 (26.3, C_7H_9), 77 (32.4, C_6H_5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3H), 4.47 (d, *J*=6.1 Hz, 1H, OH), 5.90 (d, *J*=6.0 Hz, 1H), 7.10 (d, *J*=8.2 Hz, 2H), 7.20 (d, *J*=8.2 Hz, 2H), 7.37 (t, *J*=7.7 Hz, 2H), 7.50 (t, *J*=7.6 Hz, 1H), 7.89 (d, *J*=7.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1 (q), 76.0 (d), 127.7 (d), 128.6 (d), 129.1 (d), 129.8 (d), 133.5 (s), 133.8 (d), 136.1 (s), 138.4 (s), 199.0 (s); enantiomeric excess (99%) was determined by HPLC (Chiralcel OD-H), hexane–*i*-PrOH 90:10, 1 mL/min, major enantiomer (*S*) t_R=9.8 min, minor enantiomer (*R*) t_R=14.0 min.

*3.6.3. (2S)-2-(4-Chlorophenyl)-1-phenyl-2-hydroxyethanone (**11c**).* $[\alpha]_D^{25}$ +68.9 (*c* 0.6, acetone); HRMS *m*/*z* (EI, 70 eV) 248.0456/246.0426 (M^+, 0.4/1.3), $C_{14}H_{11}O_2Cl$ requires 248.0418/246.0448, 143/141 (8.1/24.4, C_7H_6OCl), 105 (100.0, C_7H_5O), 77 (38.1, C_6H_5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.55 (br s, 1H, OH), 5.93 (br s, 1H), 7.28 (m, 4H), 7.41 (br t, *J*=7.5 Hz, 2H), 7.55 (tt, *J*=7.5, 1.3 Hz, 1H), 7.89 (dd, *J*=8.5, 1.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.4 (d), 128.8 (d), 129.0 (d), 129.1 (d), 129.3 (d), 133.2 (s), 134.1 (d), 134.5 (s), 137.5 (s), 198.6 (s); enantiomeric excess (99%) was determined by HPLC (Chiralpak AS-H), hexane–*i*-PrOH 85:15, 1 mL/min, major enantiomer (*S*) t_R=7.8 min, minor enantiomer (*R*) t_R=10.9 min.[22]

*3.6.4. (2S)-2-(4-Bromophenyl)-1-phenyl-2-hydroxyethanone (**11d**).* Mp 95–97 °C (Acetone); $[\alpha]_D^{25}$ +60.4 (*c* 0.5, acetone); HRMS *m*/*z* (EI, 70 eV) 291.9953/289.9931 (M^+, 0.3/0.4), $C_{14}H_{11}O_2Br$ requires 291.9922/289.9942, 187/185 (16.1/17.3, C_7H_6OBr), 105 (100.0, C_7H_5O), 77 (33.4, C_6H_5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.57 (d, *J*=5.8 Hz, 1H, OH), 5.94 (d, *J*=5.6 Hz, 1H), 7.23 (dd, *J*=6.5, 1.8 Hz, 2H), 7.46 (m, 4H), 7.55 (br t, *J*=7.5 Hz, 1H), 7.90 (dd, *J*=8.5, 1.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.4 (d), 122.7 (s), 128.8 (d), 129.1 (d), 129.4 (d), 132.3 (d), 133.2 (s), 134.1 (d), 138.0 (s), 198.5 (s); enantiomeric excess (99%) was determined by HPLC (Chiralpak AS-H), hexane–*i*-PrOH 80:20, 1 mL/min, major enantiomer (*S*) t_R=9.5 min, minor enantiomer (*R*) t_R=16.1 min.

*3.6.5. (2S)-1-Phenyl-2-hydroxy-2-(4-methoxyphenyl)ethanone (**11e**).* $[\alpha]_D^{25}$ +47.8 (*c* 0.8, acetone), lit.[21] $[\alpha]_D^{25}$ +111 (*c* 1.1, acetone); HRMS *m*/*z* (EI, 70 eV) 242.0933 (M^+, 11.3), $C_{15}H_{14}O_3$ requires 242.0943, 137 (100.0, $C_8H_9O_2$), 135 (84.3, $C_8H_7O_2$), 105 (7.7), 77 (14.5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (s, 3H), 4.47 (br s, 1H, OH), 5.89 (br s, 1H), 6.82 (d, *J*=8.7 Hz, 2H), 7.23 (d, *J*=8.7 Hz, 2H), 7.37 (br t, *J*=7.2 Hz, 2H), 7.47 (tt, *J*=7.3, 1.3 Hz, 1H), 7.89 (dd, *J*=8.4, 1.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.2 (q), 75.7 (d), 114.5 (d), 128.6 (d), 129.0 (d), 129.1 (d), 131.2 (s), 133.5 (s), 133.8 (d), 159.7 (s), 199.0 (s); enantiomeric excess (40%) was determined by HPLC (Chiralcel OD-H), hexane–*i*-PrOH 90:10, 1 mL/min, major enantiomer (*S*) t_R=14.2 min, minor enantiomer (*R*) t_R=19.3 min.

*3.6.6. (2S)-1-Phenyl-2-hydroxy-2-(3,4-methylendioxyphenyl)ethanone (**11f**).* HRMS *m*/*z* (EI, 70 eV) 256.0701 (M^+, 6.8), $C_{15}H_{12}O_4$ requires 256.0736, 162 (33.0), 151 (100.0, $C_8H_7O_3$), 149 (46.2), 93 (31.3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.47 (d, *J*=6.0 Hz, OH), 5.84 (d, *J*=6.0 Hz, 1H), 5.89 (d, *J*=1.2 Hz, 2H), 6.73 (m, 2H), 6.83 (dd, *J*=8.0, 1.6 Hz, 1H), 7.39 (t, *J*=7.4 Hz, 2H), 7.52 (br t, *J*=7.4 Hz, 1H), 7.89 (dd, *J*=8.6, 1.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.8 (d), 101.3 (t), 107.8 (d), 108.8 (d), 121.9 (d), 128.7 (d), 129.1 (d), 132.9 (s), 133.4 (s), 133.9 (d), 147.9 (s), 148.2 (s), 198.8 (s); enantiomeric excess (54%) was determined by HPLC (Chiralpak AD-H), hexane–*i*-PrOH 90:10, 1 mL/min, major enantiomer (*S*) t_R=45.5 min, minor enantiomer (*R*) t_R=40.9 min.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.12.012.

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