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Enantioselective synthesis of 2-substituted-1,4-diketones from (*S*)-mandelic acid enolate and α,β-enones

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Abstract—An approach for the synthesis of chiral non-racemic 2-substituted-1,4-diketones from (*S*)-mandelic acid and α,β-enones has been developed. The reaction of lithium enolate of the 1,3-dioxolan-4-one derived from optically active (*S*)-mandelic acid and pivalaldehyde with α,β-unsaturated carbonyl compounds proceeds readily to give the corresponding Michael adducts in good yields and with high diastereoselectivities. The addition of HMPA (3 equiv) reverses and strongly enhances the diastereoselectivity of the reaction. A change in the reaction mechanism from a lithium catalyzed to the one where catalysis has been suppressed by coordination of HMPA to lithium is proposed to explain these results. Subsequent basic hydrolysis of the 1,3-dioxolan-4-one moiety yields the corresponding α-hydroxy acids (in hemiacetal form), which after decarboxylation with oxygen in the presence of pivalaldehyde and the Co(III)Me_2opba complex as catalyst give chiral 2-substituted 1,4-dicarbonyl compounds with very high enantiomeric excesses. In this approach, (*S*)-mandelic acid acts as an umpoled chiral equivalent of the benzoyl anion.

1. Introduction

1,4-Diketones are important and valuable precursors for the synthesis of substituted cyclopentenones,[1] such as jasmones, cuparenones, and prostaglandins, and for the synthesis of five-membered heterocyclic compounds.[2] Although a variety of synthetic methods have been developed for the preparation of 1,4-diketones,[3] the most widely used approach is the Michael addition to α,β-unsaturated ketones of either unmasked acyl anions such as acyllithium[4] and acyl-transition metal complexes,[5] or, specially, of masked acyl anions and their equivalents,[6] thiazolinium salts, alkoxyvinylcuprates, cyanohydrins, nitronate anions, and anions of 1,3-dithians.

The conjugate addition reactions often result in generation of new stereocenters, and accordingly a number of new methods to construct these stereogenic centers in a diastereo- and enantioselective fashion have been developed in the last decade.[7] In fact excellent results on the asymmetric Michael addition of enolate carbon nucleophiles to α,β-unsaturated ketones leading to 1,5-dicarbonyl compounds have been reported.[8] However, the asymmetric conjugate addition of acyl anion equivalents leading to the less accessible 1,4-dicarbonyl compounds has not been studied thoroughly.[9] During the last years, we have reported the use of different mandelic acid derivatives as umpoled masked d^1-synthons for the nucleophilic benzoylation of alkyl and aryl halides to give aryl alkyl ketones[10] and nitrobenzophenones, respectively.[11] In both syntheses, the key step is the aerobic oxidative decarboxylation of an α-hydroxy acid, which is carried out with oxygen in the presence of pivalaldehyde and a Co(III) complex as catalyst. In this paper we described a highly diastereoselective addition of (*S*)-(+)-mandelic acid enolate to α,β-enones and the transformation of the resulting adducts into chiral non-racemic 2-substituted-1,4-diketones.[12] This strategy, based on the Seebach principle of self-regeneration of stereocenters,[13] formally involves the use of (*S*)-mandelic acid as a source of the benzoyl anion and also as a source of chiral information. Similar Michael additions to ethyl crotonate[14] and cyclopentenone[15] have been reported previously.

2. Results and discussion

The synthesis of enantiomerically pure 2-substituted-1,4-diketones is outlined in Scheme 1. The first step involves the conjugate addition of (*S*)-(+)-mandelic acid enolate to α,β-enones. Although the formation of the mandelic acid

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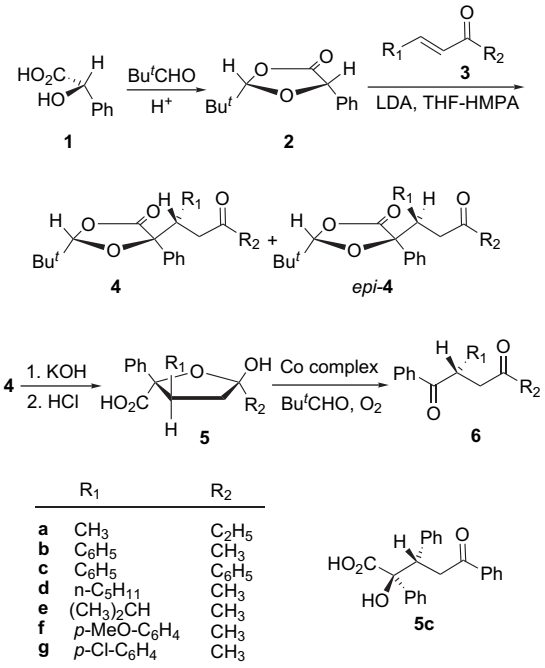
enolate leads to the loss of chirality at the stereogenic center, according to the Seebach principle of self-regeneration of stereocenters,[13] it is possible to regenerate the chiral information if (*S*)-(+)-mandelic acid (**1**) is previously transformed into (2*S*,5*S*)-*cis*-2-*tert*-butyl-5-phenyl-1,3-dioxolan-4-one (**2**) derived from pivalaldehyde.[16]



	R_1	R_2
a	CH_3	C_2H_5
b	C_6H_5	CH_3
c	C_6H_5	C_6H_5
d	n-C_5H_{11}	CH_3
e	$(CH_3)_2CH$	CH_3
f	*p*-MeO-C_6H_4	CH_3
g	*p*-Cl-C_6H_4	CH_3

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

In order to optimize the reaction conditions for the conjugate addition, we studied the reaction of 1,3-dioxolan-4-one **2** with enone **3a** (Table 1). Compound **2** was deprotonated by addition to a freshly prepared solution of LDA (1.5 equiv) in THF at −78 °C, and then enone **3a** (1 equiv) was added to the resulting enolate solution (direct addition protocol). This process provided a fair yield (49%) of a separable diastereomer mixture of **4a** and *epi*-**4a**, with moderate diastereoselectivity (**4a**:*epi*-**4a** ratio 35:65) (entry 1). In a modification of the experimental procedure we carried out the formation of enolate in the presence of the Michael acceptor since it is known that similar enolates may suffer some decomposition even at low temperatures.[17] So, LDA was added to a mixture of dioxolan-4-one **2** and enone **3a** in THF at −78 °C (inverse addition protocol). In this way, slight increases in the yield (60%) as well as in the diastereoselectivity (**4a**:*epi*-**4a** ratio 30:70) were produced (entry 2). The effect of the enolate aggregation state was also examined. In most reactions involving the participation of carbanions, the use of HMPA as an additive increases the reactivity as well as modifies the selectivity.[18] In our case, when 3 equiv of HMPA were used (entries 3 and 4) in the Michael addition of the lithium enolate of **2** to enone **3a** an improvement of the reaction yield, specially with the inverse addition protocol (85%, entry 4), together with an increase and full reversion of the diastereoselectivity were observed. Thus, only compound **4a** was obtained (de>99%). Addition of more HMPA (6 equiv) (entries 5 and 6) did neither further enhanced the yield of the reaction nor modified the diastereoselectivity, while the use of 1.5 equiv of HMPA decreased the diastereoselectivity (entry 7). The use of TMEDA[18] (entry 8) as substitutive for HMPA decreased both the yield and the diastereoselectivity. Therefore, the inverse addition protocol together with the use of HMPA (3 equiv) as additive seemed to be the optimal reaction conditions to get a good yield and a high diastereoselectivity (entry 4).

Table 1. Michael reaction of 1,3-dioxolan-4-one **2** with enone **3a**

Entry	Addition	Additive (equiv)	Yield (%)[a]	**4a**:*epi*-**4a**[b]
1	Direct	None	49	35:65
2	Inverse	None	60	30:70
3	Direct	HMPA (3)	64	97:3
4	Inverse	HMPA (3)	85	100:0
5	Direct	HMPA (6)	53	98:2
6	Inverse	HMPA (6)	82	99:1
7	Inverse	HMPA (1.5)	85	84:16
8	Inverse	TMEDA (3)	16	30:70

[a] Yields refer to isolated products.
[b] Diastereomeric ratios determined by ^{1}H NMR prior to chromatographic purification.

In order to verify the generality of the effect of HMPA as an additive in this reaction, that is, increasing of the reaction yield and specially the full reversion of the diastereoselectivity, we carried out a comparative study with two more enones (**3b** and **3c**) using the inverse addition protocol in the absence of HMPA (Table 2, entries 1, 3, and 5) and in the presence of 3 equiv of HMPA (entries 2, 4, and 6). In both cases, the results were very similar to those obtained with enone **3a**, without practically any influence of the aliphatic or aromatic nature of the substituents R_1 and R_2.

Finally the scope of the reaction using the inverse addition protocol and HMPA was studied with several different enones, bearing either aliphatic (**3d** and **3e**) or aromatic (**3f** and **3g**) substituents. In all the three cases of enones where substituents R_1 and R_2 were both aliphatic, the reaction proceeded with good yields (73–85%) and high diastereoselectivities (from 95:5 to 100:0 ratios) (entries 2, 7, and 8). In a similar way, the reaction proceeded also with good yields (76–93%) and high diastereoselectivities (from 94:6 to 99:1 ratios) with enones having R_1 aromatic and R_2 aliphatic substituents (entries 4, 9, and 10). In the case of chalcone **3c** the reaction proceeded also with good yield (70%) and full diastereoselectivity (100:0 ratio, entry 6).

Table 2. Michael reaction of 1,3-dioxolan-4-one **2** with α,β-enones **3** (inverse addition protocol)

Entry	Enone **3**	R_1	R_2	HMPA (equiv)	Yield (%)[a]	**4**:*epi*-**4**[b]
1	**3a**	CH_3	C_2H_5	0	60	30:70
2	**3a**	CH_3	C_2H_5	3	85	100:0
3	**3b**	C_6H_5	CH_3	0	34	35:65
4	**3b**	C_6H_5	CH_3	3	85	98:2
5	**3c**	C_6H_5	C_6H_5	0	58	30:70
6	**3c**	C_6H_5	C_6H_5	3	70	100:0
7	**3d**	*n*-C_5H_{11}	CH_3	3	80	95:5
8	**3e**	$(CH_3)_2CH$	CH_3	3	73	98:2
9	**3f**	*p*-$MeOC_6H_4$	CH_3	3	76	99:1
10	**3g**	*p*-ClC_6H_4	CH_3	3	93	94:6

[a] Yields refer to isolated products.
[b] Diastereomeric ratios determined by ^{1}H NMR prior to chromatographic purification.

It is important to note that under the optimized conditions (inverse addition protocol and 3 equiv of HMPA as additive) the Michael adducts were obtained practically as only one diastereomer out of the four possible ones, attending to the configuration of the two newly created stereogenic centers. The stereochemical structures of the Michael adducts **4a**–**4g** were elucidated by NOEs. These experiments showed in all of the cases the cis-relationship between the *t*-Bu group and the phenyl group from the starting 1,3-dioxolan-4-one. The absolute configuration of the newly formed quaternary carbon atom was then assigned to be *S*, upon the consideration that the absolute configuration of the carbon bearing the *t*-Bu group in **2** is *S* and it remains unaltered from **2** to **4**.[13] Furthermore, in the case of the adduct **4c** the absolute stereochemistry was unambiguously determined by single X-ray diffraction (Fig. 1).[19] According to this, the absolute configuration of the tertiary carbon atom bearing the aryl group was assigned to be *S*.

For the other adducts the assignment of the stereochemistry at the tertiary stereocenter in the side chain was established later, after hydrolysis of the 1,3-dioxolan-4-one ring and cyclization to hemiacetals **5** (see below). The configuration of this carbon was *S* in all of the cases, except in compounds **4a** and **4d** as a consequence of a change of priority when applying the Cahn–Ingold–Prelog rules. The stereochemical structures of the Michael adducts *epi*-**4a**, *epi*-**4b** and *epi*-**4c** were also elucidated by NOEs. These experiments showed again in all of the cases the cis-relationship between the *t*-Bu group and the phenyl group from the starting 1,3-dioxolan-4-one, indicating that compounds **4** and *epi*-**4** have the same configuration at the quaternary stereocenter and differ only on the stereochemistry of the tertiary stereogenic center of the side chain.

As the results in Tables 1 and 2 show, the addition of HMPA causes a dramatic change in the diastereomer distribution of the Michael products. HMPA is a highly polar aprotic solvent frequently used to accelerate organolithium reactions and, in some cases, to alter the course of the reaction. Its usefulness stems from its ability to coordinate very strongly to lithium to give separated ion pairs, in which the carbanion and lithium counterion are separated. This normally results in an increase in the nucleophilicity and reactivity of the carbanion. However, this effect is not sufficient to explain the change in the diastereomer distribution with HMPA. According to the findings by Biddle and Reich,[20] this substantial change in diastereoselectivity in the formation of the 1,4-adduct may be attributed to a change in mechanism from lithium catalyzed reaction to one where catalysis has been suppressed by the coordination of HMPA to lithium. Thus, in the absence of HMPA, the reaction is expected to proceed through an eight-membered chelated transition state (TSs C and E, Fig. 2)[21] with lithium being coordinated to the enolate and enone carbonyl oxygens with TS C being the preferred one as it minimizes any repulsion between the benzoyl group and the dioxolanone ring (Fig. 2). Addition of HMPA suppresses the lithium catalyzed mechanism and the reaction may proceed through a different, nonchelated TS D, which minimizes the *gauche* interactions between the enolate and enone substituents. Also, the lower stereoselectivity found in the absence of HMPA can be explained by a competition of these two mechanisms, chelated with contact ion pairs, and nonchelated with separated ion pairs, in low concentration but more reactive, if the reaction is governed by Curtin–Hammet kinetics.

The next step in our synthetic sequence was the cleavage of the 1,3-dioxolan-4-one moiety present in compound **4** (and also in compound *epi*-**4a** for comparison purposes), which was achieved upon basic hydrolysis with ethanolic KOH and reprotonation to give the corresponding α-hydroxy-δ-oxocarboxylic acids. Interestingly, all these compounds were obtained as cyclic hemiacetal acid **5**, and only the product resulting from the hydrolysis of **4c** was obtained as an open α-hydroxy-δ-oxocarboxylic acid **5c**. In all the cases the reaction yields were equal or higher to 90% (Table 3).

The stereochemical structures of the cyclic hemiacetal acids **5** were established by NOEs. As a representative example, irradiation in compound **5a** of the signal at δ 7.49 corresponding to the *ortho*-protons of the phenyl group enhanced the signal at δ 0.76 corresponding to the methyl group. On the other hand, irradiation in *epi*-**5a** of the signal at δ 7.70 corresponding to the *ortho*-protons of the phenyl group gave NOE with the signal at δ 2.50 corresponding to the

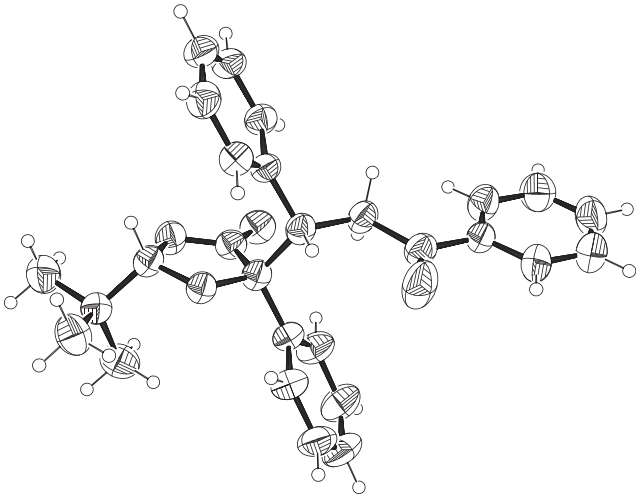


Figure 1. ORTEP drawing for compound **4c**.

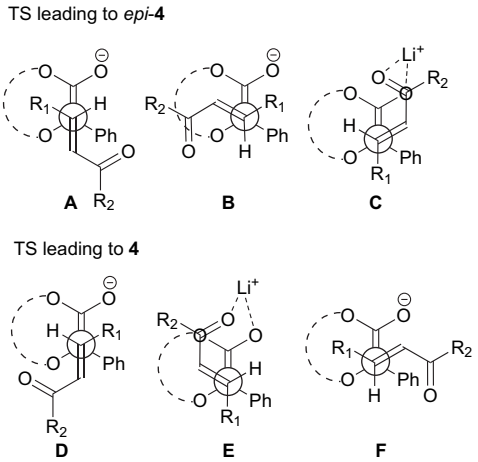


Figure 2. Possible TS for the approach of the enone to the *Re*-face of the enolate of **2**.

Table 3. Hydrolysis of the Michael adducts **4** and oxidative decarboxylation of hydroxy acids **5**

Entry	Adduct **4**	R_1	R_2	Yield **5** (%)[a,b]	Yield **6** (%)[a,c]
1	**4a**	CH_3	C_2H_5	90	75
2	*epi*-**4a**	CH_3	C_2H_5	94	78
3	**4b**	C_6H_5	CH_3	90	60
4	**4c**	C_6H_5	C_6H_5	95	82
5	**4d**	n-C_5H_{11}	CH_3	90	75
6	**4e**	$(CH_3)_2CH$	CH_3	90	82
7	**4f**	p-$MeOC_6H_4$	CH_3	90	72
8	**4g**	p-ClC_6H_4	CH_3	95	69

[a] Yields refer to isolated products.
[b] Yield from **4**.
[c] Yield from **5**.

proton on the tertiary carbon atom (Fig. 3). According to these experiments the absolute configuration of the tertiary carbon atom bearing the methyl group in the side chain was determined to be *R* in compound **5a** and *S* in compound *epi*-**5a**, upon the consideration that the absolute configuration of the quaternary carbon bearing the phenyl and carboxy groups was *S* in all the cases as explained earlier. These experiments also allowed the assignment of the absolute stereochemistry of the tertiary stereocenter of compound **4a**, that is, the *R* configuration of this stereocenter in compound **5a** was assigned to this carbon in its Michael adduct precursor **4a**. The opposite configuration *S* was therefore assigned to the adduct *epi*-**4a**.

Finally, the oxidative decarboxylation of the α-hydroxy acid moiety present in compound **5**, either in open form (**5c**) or as cyclic hemiacetal (**5a**, **5b**, **5d**–**5g**) was carried out by using a catalytic system developed in our laboratory that employs oxygen as terminal oxidant in the presence of pivalaldehyde and a catalytic amount of the Co(III)Me_2opba complex (Fig. 4).[10] Under these conditions the 1,4-diketones were obtained with fair to good yields. Much more importantly, products highly enantiomerically enriched (ee>99%) were obtained, as it was proven by ^{1}H NMR experiments using the chiral lanthanide shift reagent Eu(hfc)$_3$ under conditions previously optimized for racemic mixtures.

In summary, we have developed a strategy for the asymmetric Michael reaction of a masked benzoyl anion equivalent to α,β-enones that formally involves the use of (*S*)-mandelic acid as a source of chiral information and as a source of benzoyl anion. The preservation of the chiral information of the (*S*)-mandelic acid is based on the Seebach principle of self-regeneration of stereocenters 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. This strategy appears as a convenient method for the synthesis of highly enantioenriched chiral non-racemic 2-substituted-1,4-diketones.

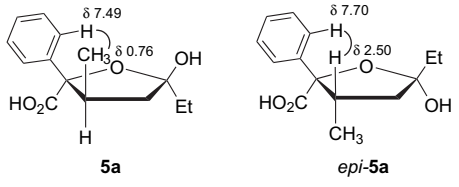


Figure 3. Significant NOE in compounds **5a** and *epi*-**5a**.

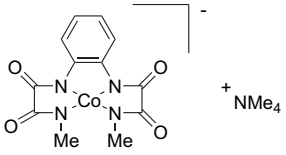


Figure 4. Co(III) *ortho*-phenylene-bis(*N*′-methyloxamidate) complex.

3. Experimental

3.1. General

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 Advance 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. (2*S*,5*S*)-*cis*-2-*tert*-Butyl-5-phenyl-1,3-dioxolan-4-one (**2**) was prepared according to the literature.[16] All new compounds were determined to be >95% pure by ^{1}H NMR spectroscopy.

3.2. General experimental procedure for the Michael reaction (inverse addition protocol)

A solution of freshly prepared LDA (1.25 mmol) in dry THF (1.3 mL) was slowly added to a solution of (2*S*,5*S*)-*cis*-2-*tert*-butyl-5-phenyl-1,3-dioxolan-4-one (**2**) (220 mg, 1 mmol) and α,β-unsaturated carbonyl compound **3** (1.25 mmol) in dry THF:HMPA (5 mL:0.53 mL) at −78 °C. The reaction was allowed to reach −40 °C and it was quenched with a saturated aqueous solution of NH_4Cl at this temperature, and extracted with diethyl ether (3×30 mL). 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 or hexane:dichloromethane) to afford Michael adducts **4**. Yields are included in Table 2.

3.2.1. (2*S*,5*S*,1′*R*)-2-(*tert*-Butyl)-5-(1′-methyl-3′-oxopentyl)-5-phenyl-1,3-dioxolan-4-one (4a). An oil; $[\alpha]_D^{25}$ −9 (*c* 1.1, $CHCl_3$); HRMS (EI) *m*/*z* 318.1833 (M^+, 9, $C_{19}H_{26}O_4$ requires 318.1831), 220 (62), 105 (100); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (s, 9H), 0.90 (d, *J*=7.0 Hz, 3H), 0.99 (t, *J*=7.2 Hz, 3H), 2.21 (dd, *J*=16.6, 8.9 Hz, 1H), 2.37 (dq, *J*=14.8, 7.4 Hz, 2H), 2.51 (dd, *J*=16.7, 4.3 Hz, 1H), 2.85 (m, 1H), 5.33 (s, 1H), 7.3–7.4 (m, 3H), 7.62 (dd, *J*=6.6, 1.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.6 (q), 14.5 (q), 23.3 (q), 35.2 (s), 36.6 (t), 37.5 (d), 43.9 (t), 84.1 (s), 109.5 (d), 125.8 (d), 127.9 (d), 128.0 (d), 136.2 (s), 172.6 (s), 209.1 (s).

3.2.2. (2*S*,5*S*,1′*S*)-2-(*tert*-Butyl)-5-(1′-methyl-3′-oxopentyl)-5-phenyl-1,3-dioxolan-4-one (*epi*-4a). An oil; $[\alpha]_D^{25}$

+26 (*c* 1.4, $CHCl_3$); HRMS (EI) *m/z* 318.1846 (M^+, 7.2, $C_{19}H_{26}O_4$ requires 318.1831), 220 (27.8), 105 (100); ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, *J*=7.4 Hz, 3H), 0.91 (s, 9H), 1.04 (d, *J*=6.8 Hz, 3H), 2.23 (m, 4H), 2.81 (m, 1H), 5.38 (s, 1H), 7.3–7.4 (m, 3H), 7.64 (dd, *J*=8.5, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.5 (q), 15.4 (q), 23.5 (q), 35.5 (s), 36.3 (t), 39.0 (d), 42.9 (t), 84.7 (s), 110.6 (d), 125.4 (d), 128.0 (d), 128.1 (d), 137.1 (s), 173.2 (s), 209.5 (s).

3.2.3. (2*S*,5*S*,1′*S*)-2-(*tert*-Butyl)-5-(3′-oxo-1′-phenylbutyl)-5-phenyl-1,3-dioxolan-4-one (4b). An oil; $[\alpha]_D^{25}$ −75 (*c* 0.7, $CHCl_3$); HRMS (EI) *m/z* 366.1811 (M^+, 0.3, $C_{23}H_{26}O_4$ requires 366.1831), 220 (43), 147 (31), 105 (100); ^1H NMR (300 MHz, $CDCl_3$) δ 0.73 (s, 9H), 1.95 (s, 3H), 2.76 (dd, *J*=17.2, 4.1 Hz, 1H), 3.23 (dd, *J*=17.2, 10.2 Hz, 1H), 3.88 (dd, *J*=10.2, 4.3 Hz, 1H), 4.50 (s, 1H), 7.2–7.4 (m, 8H), 7.57 (dd, *J*=8.1, 2.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.2 (q), 30.6 (q), 35.0 (s), 43.6 (t), 50.4 (d), 84.7 (s), 110.1 (d), 125.7 (d), 127.7 (d), 128.1 (d), 128.2 (d), 128.3 (d), 129.3 (d), 137.2 (s), 137.6 (s), 172.3 (s), 205.3 (s).

3.2.4. (2*S*,5*S*,1′*R*)-2-(*tert*-Butyl)-5-phenyl-5-(3′-oxo-1′-phenylbutyl)-1,3-dioxolan-4-one (*epi*-4b). Mp 136–138 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +69 (*c* 1.4, $CHCl_3$); HRMS (EI) *m/z* 366.1831 (M^+, 0.4, $C_{23}H_{26}O_4$ requires 366.1831), 220 (43), 105 (100); ^1H NMR (300 MHz, $CDCl_3$) δ 0.82 (s, 9H), 1.83 (s, 3H), 2.40 (dd, *J*=17.1, 4.4 Hz, 1H), 3.05 (dd, *J*=17.1, 10.6 Hz, 1H), 3.96 (dd, *J*=10.6, 4.4 Hz, 1H), 4.53 (s, 1H), 7.2–7.4 (m, 8H), 7.79 (dd, *J*=8.5, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 30.2 (q), 35.2 (s), 42.7 (t), 49.5 (d), 85.3 (s), 110.4 (d), 125.5 (d), 128.1 (d), 128.2 (d), 128.3 (d), 128.7 (d), 129.4 (d), 137.2 (s), 137.3 (s), 172.6 (s), 205.8 (s).

3.2.5. (2*S*,5*S*,1′*S*)-2-(*tert*-Butyl)-5-(1′,3′-diphenyl-3′-oxopropyl)-5-phenyl-1,3-dioxolan-4-one (4c). Mp 116–118 °C (CH_2Cl_2:hexane); $[\alpha]_D^{25}$ −99 (*c* 1.0, $CHCl_3$); HRMS (EI) *m/z* 428.1980 (M^+, 0.3, $C_{28}H_{28}O_4$ requires 428.1988), 209 (32), 105 (100); ^1H NMR (300 MHz, $CDCl_3$) δ 0.72 (s, 9H), 3.26 (dd, *J*=17.3, 3.8 Hz, 1H), 3.84 (dd, *J*=17.3, 10.4 Hz, 1H), 4.11 (dd, *J*=10.2, 3.8 Hz, 1H), 4.45 (s, 1H), 7.2–7.6 (m, 11H), 7.64 (dd, *J*=7.7, 1.5 Hz, 2H), 7.81 (dd, *J*=8.6, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.2 (q), 35.0 (s), 38.6 (t), 50.6 (d), 85.0 (s), 110.2 (d), 125.8 (d), 127.6 (d), 128.0 (d), 128.1 (d), 128.2 (d), 128.3 (d), 128.5 (d), 129.3 (d), 133.1 (d), 136.6 (s), 137.4 (s), 137.8 (s), 172.4 (s), 196.8 (s).

3.2.6. (2*S*,5*S*,1′*R*)-2-(*tert*-Butyl)-5-(1′,3′-diphenyl-3′-oxopropyl)-5-phenyl-1,3-dioxolan-4-one (*epi*-4c). Mp 168–170 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +88 (*c* 0.8, $CHCl_3$); HRMS (EI) *m/z* 428.1980 (M^+, 0.5, $C_{28}H_{28}O_4$ requires 428.1988), 209 (32), 105 (100); ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (s, 9H), 2.88 (dd, *J*=17.3, 3.8 Hz, 1H), 3.70 (dd, *J*=17.3, 10.7 Hz, 1H), 4.17 (dd, *J*=10.7, 3.6 Hz, 1H), 4.59 (s, 1H), 7.2–7.5 (m, 11H), 7.69 (dd, *J*=8.6, 1.5 Hz, 2H), 7.85 (dd, *J*=8.7, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 (q), 35.3 (s), 37.6 (t), 49.8 (d), 85.6 (s), 110.4 (d), 125.5 (d), 127.8 (d), 128.0 (d), 128.3 (d), 128.37 (d), 128.42 (d), 128.6 (d), 129.5 (d), 133.0 (d), 136.7 (s), 137.3 (s), 137.4 (s), 172.7 (s), 197.2 (s).

3.2.7. (2*S*,5*S*,1′*R*)-2-(*tert*-Butyl)-5-(1′-*n*-pentyl-3′-oxobutyl)-5-phenyl-1,3-dioxolan-4-one (4d). An oil; $[\alpha]_D^{25}$ −30 (*c* 0.5, $CHCl_3$); HRMS (EI) *m/z* 360.2286 (M^+, 5.8, $C_{22}H_{32}O_4$ requires 360.2301), 247 (14), 220 (100), 141 (20), 105 (91); ^1H NMR (300 MHz, $CDCl_3$) δ 0.84 (t, *J*=6.6 Hz, 3H), 0.87 (s, 9H), 1.20 (m, 7H), 1.81 (m, 1H), 2.12 (s, 3H), 2.18 (dd, *J*=17.1, 4.7 Hz, 1H), 2.57 (dd, *J*=17.1, 6.8 Hz, 1H), 2.85 (m, 1H), 5.30 (s, 1H), 7.36 (m, 3H), 7.66 (dd, *J*=7.7, 1.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9 (q), 22.4 (t), 23.3 (q), 27.1 (t), 29.2 (t), 30.5 (q), 31.8 (t), 34.8 (s), 41.3 (d), 42.6 (t), 83.5 (s), 108.7 (d), 126.1 (d), 127.9 (d), 128.1 (d), 135.8 (s), 172.5 (s), 206.7 (s).

3.2.8. (2*S*,5*S*,1′*S*)-2-(*tert*-Butyl)-5-(1′-isopropyl-3′-oxobutyl)-5-phenyl-1,3-dioxolan-4-one (4e). Mp 78–81 °C (CH_2Cl_2); $[\alpha]_D^{25}$ −41 (*c* 0.5, $CHCl_3$); HRMS (EI) *m/z* 332.1991 (M^+, 2.3, $C_{20}H_{28}O_4$ requires 332.1988), 221 (14), 220 (100), 219 (28); ^1H NMR (300 MHz, $CDCl_3$) δ 0.51 (d, *J*=6.8 Hz, 3H), 0.80 (d, *J*=7.0 Hz, 3H), 0.83 (s, 9H), 2.07 (m, 1H), 2.12 (s, 3H), 2.26 (dd, *J*=17.0, 4.4 Hz, 1H), 2.57 (dd, *J*=17.0, 7.1 Hz, 1H), 2.84 (ddd, *J*=7.2, 4.5, 1.9 Hz, 1H), 5.28 (s, 1H), 7.32 (m, 3H), 7.67 (dd, *J*=7.9, 1.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.1 (q), 23.1 (q), 23.3 (q), 25.8 (d), 30.2 (q), 35.0 (s), 38.3 (t), 47.6 (d), 83.7 (s), 109.4 (d), 125.8 (d), 128.0 (d), 128.1 (d), 137.0 (s), 173.0 (s), 206.7 (s).

3.2.9. (2*S*,5*S*,1′*S*)-2-(*tert*-Butyl)-5-(1′-*p*-methoxyphenyl-3′-oxobutyl)-5-phenyl-1,3-dioxolan-4-one (4f). Mp 110–111 °C (CH_2Cl_2); $[\alpha]_D^{25}$ −71 (*c* 1.5, $CHCl_3$); HRMS (EI) *m/z* 396.1946 (M^+, 0.3, $C_{24}H_{28}O_5$ requires 396.1936), 177 (100), 135 (10), 105 (16), 77 (8); ^1H NMR (300 MHz, $CDCl_3$) δ 0.73 (s, 9H), 1.94 (s, 3H), 2.71 (dd, *J*=16.8, 4.4 Hz, 1H), 3.17 (dd, *J*=16.8, 10.2 Hz, 1H), 3.77 (s, 3H), 3.83 (dd, *J*=10.2, 4.4 Hz, 1H), 4.58 (s, 1H), 6.78 (d, *J*=8 Hz, 2H), 7.12 (d, *J*=8 Hz, 1H), 7.26–7.34 (m, 3H), 7.56 (dd, *J*=8.1, 1.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.2 (q), 30.5 (q), 35.0 (s), 43.7 (t), 49.6 (d), 55.1 (q), 84.7 (s), 109.9 (d), 113.6 (d), 125.7 (d), 128.0 (d), 128.1 (d), 129.4 (s), 130.3 (d), 137.2 (s), 158.9 (s), 172.2 (s), 205.4 (s).

3.2.10. (2*S*,5*S*,1′*S*)-2-(*tert*-Butyl)-5-(1′-*p*-chlorophenyl-3′-oxobutyl)-5-phenyl-1,3-dioxolan-4-one (4g). An oil; $[\alpha]_D^{25}$ −70 (*c* 0.9, $CHCl_3$); HRMS (EI) *m/z* 400.1441 (M^+, 0.3, $C_{23}H_{25}ClO_4$ requires 400.1441), 220 (20), 181 (13), 105 (100); ^1H NMR (300 MHz, $CDCl_3$) δ 0.76 (s, 9H), 1.97 (s, 3H), 2.75 (dd, *J*=16.8, 4.2 Hz, 1H), 3.17 (dd, *J*=16.8, 10.2 Hz, 1H), 3.86 (dd, *J*=10.2, 4.2 Hz, 1H), 4.72 (s, 1H), 7.11 (d, *J*=8.7 Hz, 2H), 7.21 (d, *J*=8.7 Hz, 1H), 7.27–7.31 (m, 3H), 7.53 (dd, *J*=7.7, 1.95 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.2 (q), 30.5 (q), 35.2 (s), 43.6 (t), 49.8 (d), 84.4 (s), 110.2 (d), 125.6 (d), 128.1 (d), 128.3 (d), 128.4 (d), 130.6 (6), 133.4 (s), 136.1 (s), 136.9 (s), 172.0 (s), 204.9 (s).

3.3. General experimental procedure for the basic hydrolysis of the Michael adducts 4

The Michael adducts **4** (0.28 mmol) were treated with a 5% KOH solution in ethanol (0.63 mL, 0.56 mmol) at room temperature until complete reaction of the starting material (TLC) is achieved. The solution was poured into ice and

acidified with 1 M HCl until pH 2. The aqueous mixture was extracted with EtOAc (3×30 mL), and the organic layers were washed with brine until neutrality, dried, filtered, and concentrated under reduced pressure to give compound **5**. Yields are included in Table 3.

3.3.1. (2*S*,3*R*,5*R*)-5-Ethyl-5-hydroxy-3-methyl-2-phenyltetrahydrofuran-2-carboxylic acid (5a). An oil; $[\alpha]_D^{27}$ +89 (*c* 1.0, $CHCl_3$); HRMS (CI) *m/z* 233.1153 (M^++1−H_2O, 100, $C_{14}H_{17}O_3$ requires 233.1178), 215 (93), 188 (32); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76 (d, *J*=6.8 Hz, 3H), 1.15 (t, *J*=7.6 Hz, 3H), 1.62 (q, *J*=6.8 Hz, 1H), 2.14 (q, *J*=7.6 Hz, 2H), 2.50 (m, 2H), 7.3–7.4 (m, 3H), 7.49 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.6 (q), 17.0 (q), 25.4 (t), 35.4 (d), 42.8 (t), 88.7 (s), 113.8 (s), 125.7 (d), 128.17 (d), 128.22 (d), 131.2 (s), 173.6 (s).

3.3.2. (2*S*,3*S*,5*S*)-5-Ethyl-5-hydroxy-3-methyl-2-phenyltetrahydrofuran-2-carboxylic acid (*epi*-5a). An oil; $[\alpha]_D^{25}$ +91 (*c* 0.8, $CHCl_3$); HRMS (EI) *m/z* 232.1090 (M^+-H_2O, 0.6, $C_{14}H_{16}O_3$ requires 232.1100), 105 (100); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (t, *J*=7.5 Hz, 3H), 1.18 (d, *J*=7.0 Hz, 3H), 1.78 (dd, *J*=12.1, 4.5 Hz, 1H), 1.86 (br s, 1H, OH), 2.11 (q, *J*=7.5 Hz, 2H), 2.41 (dd, *J*=12.4, 10.2 Hz, 1H), 2.50 (m, 1H), 7.3–7.5 (m, 3H), 7.70 (dd, *J*=8.1, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.5 (q), 14.8 (q), 25.5 (t), 39.0 (d), 41.3 (t), 89.1 (s), 113.4 (s), 126.1 (d), 128.4 (d), 128.8 (d), 132.2 (s), 171.8 (s).

3.3.3. (2*S*,3*S*,5*R*)-5-Hydroxy-3-methyl-2,3-diphenyltetrahydrofuran-2-carboxylic acid (5b). An oil; $[\alpha]_D^{25}$ +104 (*c* 1.3, $CHCl_3$); HRMS (EI) *m/z* 281.1176 (M^++1−H_2O, 100, $C_{18}H_{17}O_3$ requires 281.1178), 264 (45), 263 (93), 253 (57), 236 (30), 193 (39), 176 (34), 105 (22); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00 (s, 3H), 2.31 (dd, *J*=13.2, 4.3 Hz, 1H), 2.93 (dd, *J*=13.2, 8.6 Hz, 1H), 3.63 (dd, *J*=8.7, 4.4 Hz, 1H), 7.0–7.2 (m, 8H), 7.33 (dd, *J*=7.9, 1.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.4 (q), 46.7 (t), 47.5 (d), 90.5 (s), 111.3 (s), 126.0 (d), 127.1 (d), 127.7 (d), 127.9 (d), 128.2 (d), 128.3 (d), 130.7 (s), 139.1 (s), 173.0 (s).

3.3.4. (2*S*,3*S*)-2-Hydroxy-5-oxo-2,3,5-triphenylpentanoic acid (5c). Mp 128–130 °C (EtOAc); $[\alpha]_D^{25}$ −58 (*c* 0.7, CH_3OH); HRMS (EI) *m/z* 342.1261 (M^+-H_2O, 7, $C_{23}H_{18}O_3$ requires 342.1256), 296 (67), 105 (100); ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.16 (dd, *J*=16.8, 2.5 Hz, 1H), 3.85 (dd, *J*=17.0, 11.1 Hz, 1H), 4.24 (dd, *J*=0.9, 2.5 Hz, 1H), 6.9–7.6 (m, 13H), 7.87 (d, *J*=8.0 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 41.5 (t), 48.9 (d), 81.3 (s), 126.1 (d), 126.2 (d), 126.9 (d), 127.3 (d), 127.6 (d), 128.2 (d), 129.1 (d), 130.2 (d), 133.5 (d), 137.0 (s), 140.1 (s), 142.2 (s), 176.1 (s), 198.5 (s).

3.3.5. (2*S*,3*R*,5*R*)-5-Hydroxy-5-methyl-3-*n*-pentyl-2-phenyltetrahydrofuran-2-carboxylic acid (5d). An oil; $[\alpha]_D^{25}$ +74 (*c* 1.4, $CHCl_3$); HRMS (EI) *m/z* 247.1709 (M^+-CO_2H, 3, $C_{16}H_{23}O_2$ requires 247.1698), 230 (67), 173 (85), 160 (42), 105 (100); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, *J*=7.2 Hz, 3H), 1.00 (m, 1H), 1.14 (m, 7H), 1.76 (dd, *J*=12.6, 3.7 Hz, 1H), 1.89 (s, 3H), 2.36 (ddt, *J*=7.8, 7.7, 3.5 Hz, 1H), 2.49 (dd, *J*=12.6, 8.0 Hz, 1H), 7.38 (tt, *J*=8.7, 1.4 Hz, 1H), 7.44 (m, 2H), 7.53 (dd, *J*=8.6, 1.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9 (q), 18.5 (q), 22.5 (t), 26.4 (t), 30.7 (t), 31.5 (t), 41.2 (d), 42.6 (t), 88.9 (s), 111.3 (s), 125.7 (d), 128.1 (d), 128.2 (d), 131.3 (s), 173.5 (s).

3.3.6. (2*S*,3*S*,5*R*)-5-Hydroxy-3-isopropyl-5-methyl-2-phenyltetrahydrofuran-2-carboxylic acid (5e). Mp 105–107 °C ($CHCl_3$); $[\alpha]_D^{25}$ +123 (*c* 0.6, $CHCl_3$); HRMS (EI) *m/z* 228.1157 (M^+-2H_2O, 0.4, $C_{15}H_{16}O_2$ requires 228.1150), 202 (42), 160 (34), 159 (100), 131 (13), 115 (17), 105 (94), 77 (60), 51 (19); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.60 (d, *J*=6.8 Hz, 3H), 0.78 (d, *J*=6.9 Hz, 3H), 1.80 (m, 1H), 1.91 (s, 3H), 1.97 (dd, *J*=12.9, 4.6 Hz, 1H), 2.29 (dd, *J*=12.9, 8.6 Hz, 1H), 2.47 (m, 1H), 7.46 (m, 3H), 7.52 (dd, *J*=8.5, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.7 (q), 18.3 (q), 21.6 (q), 26.5 (d), 36.2 (t), 45.5 (d), 89.3 (s), 111.2 (s), 126.0 (d), 128.1 (d), 128.2 (d), 131.1 (s), 173.5 (s).

3.3.7. (2*S*,3*S*,5*R*)-5-Hydroxy-5-methyl-3-*p*-methoxyphenyl-2-phenyltetrahydrofuran-2-carboxylic acid (5f). An oil; $[\alpha]_D^{25}$ +124 (*c* 1.1, $CHCl_3$); HRMS (EI) *m/z* 310.1197 (M^+-H_2O, 11, $C_{19}H_{18}O_4$ requires 310.1205), 266 (5), 223 (7), 176 (100), 134 (12), 105 (80), 77 (19); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00 (s, 3H), 2.26 (dd, *J*=13.2, 4.2 Hz, 1H), 2.92 (dd, *J*=13.2, 8.7 Hz, 1H), 3.60 (dd, *J*=8.7, 4.2 Hz, 1H), 3.67 (s, 3H), 6.62 (d, *J*=9.0 Hz, 2H), 6.99 (d, *J*=9.0 Hz, 1H), 7.11–7.22 (m, 3H), 7.33 (dd, *J*=8.1, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3 (q), 46.7 (d), 46.8 (t), 55.0 (q), 90.4 (s), 111.2 (s), 113.6 (d), 125.9 (d), 127.7 (d), 127.8 (d), 129.3 (d), 130.9 (s), 131.1 (s), 158.4 (s), 173.1 (s).

3.3.8. (2*S*,3*S*,5*R*)-3-*p*-Chlorophenyl-5-hydroxy-5-methyl-2-phenyltetrahydrofuran-2-carboxylic acid (5g). An oil; $[\alpha]_D^{25}$ +99 (*c* 1.1, $CHCl_3$); HRMS (EI) *m/z* 314.0710 (M^+-H_2O, 0.3, $C_{18}H_{15}O_3Cl$ requires 314.0709), 270 (9), 176 (42), 105 (100), 77 (26); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00 (s, 3H), 2.24 (dd, *J*=13.5, 4.2 Hz, 1H), 2.94 (dd, *J*=13.5, 8.7 Hz, 1H), 3.61 (dd, *J*=8.7, 4.2 Hz, 1H), 7.00 (d, *J*=8.7 Hz), 7.06 (d, *J*=8.7 Hz, 1H), 7.15–7.23 (m, 3H), 7.31 (dd, *J*=7.5, 1.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3 (q), 46.8 (t), 46.9 (d), 90.3 (s), 111.2 (s), 125. 8 (d), 127.9 (d), 128.1 (d), 128.4 (d), 129.5 (d), 130.4 (s), 132.9 (s), 137.7 (s), 172.7 (s).

3.4. General experimental procedure for the catalytic aerobic decarboxylation of compound 5

A solution of compound **5** (0.11 mmol) in 0.2 mL of acetonitrile was added to a stirred mixture of Co(III)Me_2opba complex (6.5×10^{-3} mmol) and pivalaldehyde (0.33 mmol) in 0.2 mL of acetonitrile under a dioxygen atmosphere. The mixture was stirred at room temperature until consumption of the starting material as indicated by TLC. The reaction product **6** was purified by flash column chromatography.

3.4.1. (*R*)-2-Methyl-1-phenyl-1,4-hexanedione (6a). An oil; $[\alpha]_D^{25}$ +16 (*c* 0.6, $CHCl_3$); HRMS (EI) *m/z* 204.1159 (M^+, 5, $C_{13}H_{16}O_2$ requires 204.1150), 175 (51), 105 (100); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (t, *J*=7.4 Hz, 3H), 1.16 (d, *J*=7.4 Hz, 3H), 2.47 (q, *J*=7.4 Hz, 2H), 2.54 (dd, *J*=17.9, 5.1 Hz, 1H), 3.12 (dd, *J*=17.9, 8.7 Hz, 1H), 3.97

(m, 1H), 7.45 (m, 2H), 7.53 (m, 1H), 7.96 (dd, *J*=8.4, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.6 (q), 17.8 (q), 36.0 (t), 36.1 (d), 45.6 (t), 128.4 (d), 128.6 (d), 133.0 (d), 135.9 (s), 203.5 (s), 210.0 (s).

3.4.2. (*S*)-2-Methyl-1-phenyl-1,4-hexanedione (*epi*-6a). An oil; $[\alpha]_D^{25}$ −15 (*c* 1.3, $CHCl_3$); ^{1}H and ^{13}C NMR spectra identical to those of compound **6a**.

3.4.3. (*S*)-1,2-Diphenyl-1,4-pentanedione (6b). An oil; $[\alpha]_D^{25}$ +263 (*c* 1.1, $CHCl_3$). HRMS (EI) *m*/*z* 252.1155 (M^+, 7.3, $C_{17}H_{16}O_2$ requires 252.1150), 234 (2), 105 (100), 77 (24); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.19 (s, 3H), 2.76 (dd, *J*=18.1, 4.0 Hz, 1H), 3.62 (dd, *J*=17.9, 10.0 Hz, 1H), 5.11 (dd, *J*=10.2, 4.0 Hz, 1H), 7.2–7.4 (m, 7H), 7.47 (tt, *J*=6.4, 1.3 Hz, 1H), 7.96 (dd, *J*=8.7, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.7 (q), 48.1 (t), 48.8 (d), 127.3 (d), 128.1 (d), 128.4 (d), 128.9 (d), 129.2 (d), 132.9 (d), 136.3 (s), 138.6 (s), 198.9 (s), 206.8 (s).

3.4.4. (*S*)-1,2,4-Triphenyl-1,4-butanedione (6c). Mp 153–155 °C (CH_2Cl_2); $[\alpha]_D^{25}$ +50 (*c* 1.1, $CHCl_3$); HRMS (EI) *m*/*z* 314.1311 (M^+, 10, $C_{22}H_{18}O_2$ requires 314.1307), 209 (12), 111 (17), 105 (100), 97 (29), 77 (31); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.31 (dd, *J*=18.1, 3.8 Hz, 1H), 4.22 (dd, *J*=18.0, 10.0 Hz, 1H), 5.33 (dd, *J*=10.0, 3.7 Hz, 1H), 7.23 (tt, *J*=7.2, 2.3 Hz, 1H), 7.3–7.5 (m, 8H), 7.49 (tt, *J*=7.4, 2.1 Hz, 1H), 7.56 (tt, *J*=7.3, 1.2 Hz, 1H), 7.99 (dd, *J*=7.1, 1.5 Hz, 2H), 8.03 (dd, *J*=7.2, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.9 (t), 48.7 (d), 127.4 (d), 128.1 (d), 128.2 (d), 128.5 (d), 128.6 (d), 128.9 (d), 129.2 (d), 132.9 (d), 133.3 (d), 136.3 (s), 136.4 (s), 138.6 (s), 198.1 (s), 198.9 (s).

3.4.5. (*R*)-2-Pentyl-1-phenyl-1,4-pentanedione (6d). An oil; $[\alpha]_D^{25}$ +57 (*c* 0.5, $CHCl_3$); HRMS (EI) *m*/*z* 246.1638 (M^+, 1.2, $C_{16}H_{22}O_2$ requires 246.1620), 176 (26), 133 (15), 105 (100), 77 (77); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81 (t, *J*=6.6 Hz, 3H), 1.21 (m, 6H), 1.41 (m, 1H), 1.63 (m, 1H), 2.13 (s, 3H), 2.58 (dd, *J*=18.0, 4.1 Hz, 1H), 3.14 (dd, *J*=18.1, 9.4 Hz, 1H), 3.90 (m, 1H), 7.45 (br t, *J*=7.7 Hz, 2H), 7.54 (tt, *J*=7.1, 1.5 Hz, 1H), 7.97 (dd, *J*=8.7, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9 (q), 22.4 (t), 26.8 (t), 30.1 (q), 31.7 (t), 32.3 (t), 41.3 (d), 45.1 (t), 128.4 (d), 128.6 (d), 132.9 (d), 136.8 (s), 203.4 (s), 207.4 (s).

3.4.6. (*S*)-2-Isopropyl-1-phenyl-1,4-pentanedione (6e). An oil; $[\alpha]_D^{25}$ +110 (*c* 0.7, $CHCl_3$); HRMS (EI) *m*/*z* 218.1292 (M^+, 2, $C_{14}H_{18}O_2$ requires 218.1307), 161 (17), 133 (5), 105 (100), 77 (33), 51 (9); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (d, *J*=6.8 Hz, 3H), 1.04 (d, *J*=6.9 Hz, 3H), 2.02 (m, 1H), 2.15 (s, 3H), 2.52 (dd, *J*=18.0, 3.3 Hz, 1H), 3.18 (dd, *J*=18.0, 10.5 Hz, 1H), 3.82 (ddd, *J*=10.2, 4.8, 3.3 Hz, 1H), 7.44 (dt, *J*=7.5, 1.2 Hz, 2H), 7.52 (tt, *J*=7.2, 1.5 Hz, 1H), 7.96 (dd, *J*=8.7, 1.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.5 (q), 21.2 (q), 29.7 (d), 30.1 (q), 41.1 (t), 47.0 (d), 128.4 (d), 128.5 (d), 132.7 (d), 137.4 (s), 203.1 (s), 207.7 (s).

3.4.7. (*S*)-2-*p*-Methoxyphenyl-1-phenyl-1,4-pentanedione (6f). An oil; $[\alpha]_D^{25}$ +39 (*c* 1.8, $CHCl_3$); HRMS (EI) *m*/*z* 282.1244 (M^+, 66, $C_{18}H_{18}O_3$ requires 282.1255), 264 (19), 177 (100), 135 (21), 105 (88), 91 (11), 77 (51); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18 (s, 3H), 2.73 (dd, *J*=17.7, 4.2 Hz, 1H), 3.57 (dd, *J*=17.7, 9.9 Hz, 1H), 3.73 (s, 3H), 5.06 (dd, *J*=9.9, 4.2 Hz, 1H), 6.80 (d, *J*=8.7 Hz, 2H), 7.17 (d, *J*=8.7 Hz, 1H), 7.36 (d, *J*=7.2 Hz, 2H), 7.46 (tt, *J*=7.2, 1.5 Hz, 1H), 7.95 (dd, *J*=7.2, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.0 (q), 47.8 (d), 48.0 (t), 55.1 (q), 114.5 (d), 128.4 (d), 128.8 (d), 129.1 (d), 130.4 (s), 132.8 (d), 136.2 (s), 158.7 (s), 199.9 (s), 207.0 (s).

3.4.8. (*S*)-2-*p*-Chlorophenyl-1-phenyl-1,4-pentanedione (6g). An oil; $[\alpha]_D^{25}$ +13 (*c* 0.6, $CHCl_3$); HRMS (EI) *m*/*z* 286.0760 (M^+, 4, $C_{17}H_{15}ClO_2$ requires 286.0760), 268 (1), 165 (1), 138 (3), 105 (100), 77 (25); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.19 (s, 3H), 2.74 (dd, *J*=18.0, 4.2 Hz, 1H), 3.57 (dd, *J*=18.0, 9.8 Hz, 1H), 5.09 (dd, *J*=9.8, 4.2 Hz, 1H), 7.20 (d, *J*=8.6 Hz, 2H), 7.25 (d, *J*=8.6 Hz, 1H), 7.38 (d, *J*=7.5 Hz, 2H), 7.50 (tt, *J*=7.2, 1.5 Hz, 1H), 7.93 (dd, *J*=7.5, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.0 (q), 47.8 (t), 47.9 (d), 128.5 (d), 128.8 (d), 129.3 (d), 129.4 (d), 133.1 (d), 133.2 (s), 136.0 (s), 137.0 (s), 198.5 (s), 206.5 (s).

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