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Nucleophilic benzoylation using lithiated methyl mandelate as a synthetic equivalent of the benzoyl carbanion. Oxidative decarboxylation of α-hydroxyacids

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Abstract—The synthesis of alkyl aryl ketones using lithiated methyl mandelate as a synthetic equivalent of the benzoyl carbanion is reported (Umpolung). The methodology involves alkylation of methyl mandelate, hydrolysis of the ester group and oxidative decarboxylation of the resulting α-hydroxyacids. The last step is carried out in a catalytic aerobic way using a Co(III) complex in the presence of pivalaldehyde under very mild and advantageous conditions. The procedure is also applied to methyl mandelates substituted on the aromatic ring.

1. Introduction

Carbon–carbon bond forming reactions are very important processes in synthetic organic chemistry. Normally, these reactions require the interaction between carbon atoms of opposite polarity, i.e. electron donor and electron acceptor carbons. In some occasions, it is convenient to invert the 'normal' reactivity of a carbon atom and therefore organic chemists have developed several protocols to achieve this inversion. These protocols are normally referred to as 'Umpolung'. Because of the importance of the carbonyl group in organic chemistry, it is not surprising that many of these 'Umpolung' methods have been aimed at temporarily reversing the characteristic reactivity of this group. Dithianes and dithiolanes,[1] TosMIC,[2] enol ethers[3] and vinyl sulfides[4] are among classical acyl anion equivalents. Other recent examples involve the use of α-aminonitriles,[5] cyanohydrins,[6] SAMP-hydrazones[7] or heterocycles.[8]

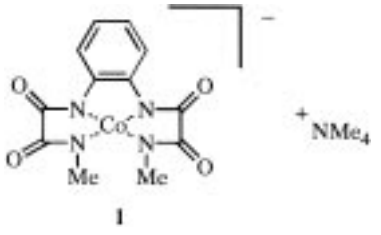

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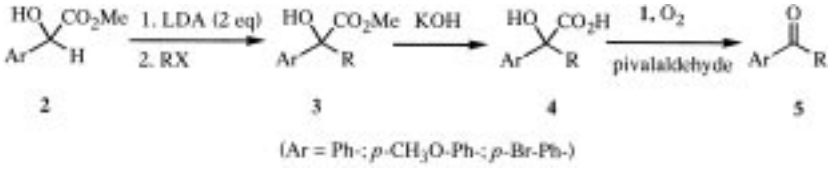
Figure 1.

In a previous communication we reported on the aerobic oxidative decarboxylation of α-hydroxyacids catalysed by a Co(III) complex **1** (Fig. 1) under very mild conditions and advanced the use of methyl mandelate as a masked d^1-synthon for nucleophilic benzoylation.[9] In this paper we describe in full our results on the application of this reaction in the synthesis of aryl alkyl ketones through Scheme 1, which involves alkylation of the methyl mandelate, hydrolysis of the ester group and oxidative decarboxylation of the resulting α-hydroxyacids.



Scheme 1.

Keywords: decarboxylation; catalysts; Umpolung; cobalt; complexes.
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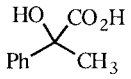
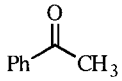
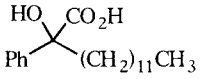
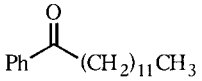
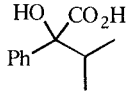
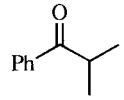
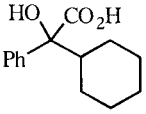
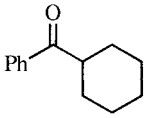
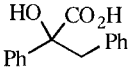
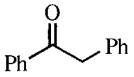
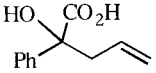
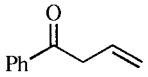
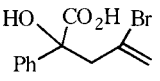
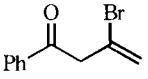
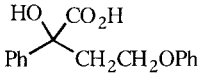
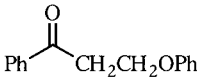
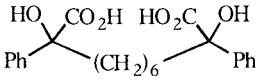
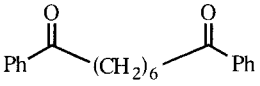
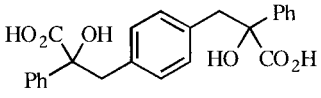
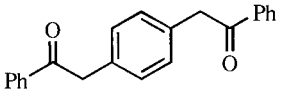
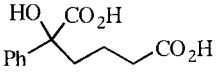
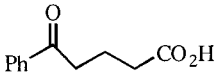
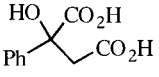
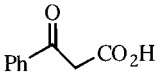
Table 1. Oxidative decarboxylation of α-alkylated mandelic acids

Entry	Hydroxyacid (**4**)	Time (h)[a]	Ketone (**5**)	Yield(%)
a		6		87
b		2		95
c		4.5		55
d		3		94
e		3		93
f		7		97
g		5.5		81
h		4		96
i		4		85
j		3		40
k		3		77
l		9.5		50

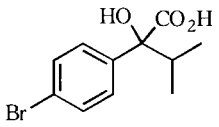
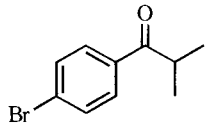
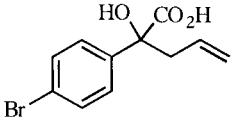
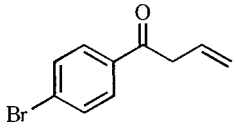
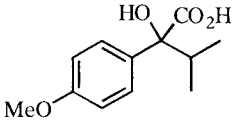
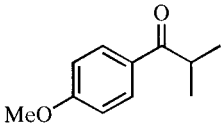
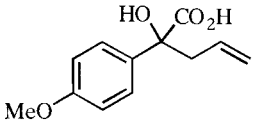
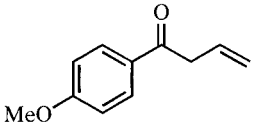
2. Results and discussion

The effective *C*-alkylation of methyl mandelate **2** has been described in the literature.[10,11] The procedure involves the use of 2 equiv. of LDA and 1 equiv. of an alkyl bromide or iodide, and gives good yields for primary and secondary halides but lower yields for tertiary halides. Following this method we prepared a range of α-alkylated methyl mandelates **3** bearing primary or secondary alkyl groups, allyl or benzyl groups, and other additional groups or functionalities such as bromide, ether or carboxyester. Also alkyl or benzyl dihalides underwent dialkylation allowing the formation of dihydroxydiesters.

The α-alkylated methyl mandelates obtained in this way were transformed into the corresponding α-hydroxyacids **4** upon basic hydrolysis in almost quantitative yields.

The key step in the sequence was the final oxidative decarboxylation of these hydroxyacids to give the corresponding aryl alkyl ketones **5**. This transformation was achieved

Table 2. Oxidative decarboxylation of α-alkylated substituted mandelic acids

Entry	Hydroxyacid (**4**)	Time (h)[a]	Ketone (**5**)	Yield(%)
m		8.5		82
n		15		78
o		5.5		90
p		9		89

using a catalytic procedure developed recently 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 **1**, $(NMe_4)Co(III)Me_2opba{\cdot}2H_2O{\cdot}CH_3CN$ (Fig. 1).[12] Although the oxidative decarboxylation of α-hydroxyacids or hydroxyesters may be achieved with various oxidizing reagents, such as lead tetraacetate,[13] periodates,[14] *N*-halogenosuccinimides,[15] copper(II) bromide–lithium *tert*-butoxide[16] or by flash vacuum pyrolysis of its ethyl esters,[10] our method presents the advantages of mildness, simplicity and the use of a cheap and environmental acceptable oxidant such as molecular oxygen.

The results for the oxidative decarboxylation of α-substituted mandelic acids **4** are shown in Table 1. Good to excellent yields were obtained with substrates bearing primary or secondary alkyl groups (entries a–d). Also substrates with benzyl or allyl groups, which gave low or null yields by a recently described flash vacuum pyrolysis procedure, were decarboxylated with very good yields (entries e–g). The selective decarboxylation in the presence of a double bond or a vinyl bromide could be achieved when the reaction was carried out at 0°C (entries f, g). In a similar way an α-hydroxyacid having an additional phenolic ether group gave the expected ketone in good yield at 0°C while the same substrate gave a complex mixture at room temperature (entry h). Double oxidative decarboxylation of bis-α-hydroxyacids allowed dicarbonyl compounds to be obtained (entries i, j). The yield was dependent on the link between both hydroxyacid groups. Thus, a high yield (85%) was obtained when they were linked with a saturated alkyl chain (entry i) while the yield was lower (40%) when the link was a *p*-phenylenemethylene group (entry j). Finally, the presence of an additional carboxylic acid was tested in entries k and l. Decarboxylation of 2-hydroxy-2-phenylhexanedioic acid gave the corresponding δ-ketoacid in good yield (77%). However, oxidative decarboxylation of 2-hydroxy-2-phenylbutanedioic acid could only be optimized up to 50% yield carrying out the reaction at −45°C to give the corresponding β-ketoacid besides other unidentified by-products apparently bearing a lactone or an anhydride moiety.

Finally we have studied the extension of this methodology to other methyl mandelate esters substituted on the aromatic ring (Table 2). Thus compounds **4m–4p** were prepared from methyl *p*-bromo- and *p*-methoxymandelate, and subjected to oxidative decarboxylation with our catalytic system. The yields were comparable to those obtained with the unsubstituted mandelates. Also, in the cases where an additional double bond was present, the reaction had to be brought about at 0°C in order to avoid epoxidation and/or migration of the double bond to the conjugated position with the carbonyl group.

In summary, we present an alternative procedure for the use of methyl mandelates as masked d^1-synthons for the benzoyl group (Umpolung), in which the key step is the aerobic oxidative decarboxylation with oxygen in the presence of pivalaldehyde and a Co(III) complex **1**, under very mild conditions. Our procedure shows some advantages with regard to other described procedures and it is compatible with the presence in the molecule of other oxidizable groups.

3. Experimental section

3.1. General

All melting points are uncorrected. Column chromatography was performed on silica gel (Merck, silica gel

60, 230–400 mesh). IR spectra were recorded as liquid film in NaCl for oils and as KBr discs for solids. NMR spectra were run at 200 MHz for ^{1}H and at 50.3 MHz for ^{13}C, and referenced to the solvent as internal standard. The carbon type was determined by DEPT experiments. Mass spectra were run by electron impact at 70 eV. Complex **1** was prepared according to the literature.[12]

3.1.1. Alkylation of methyl mandelates. Methyl mandelate **2** was alkylated following procedures described in the literature.[10,11] To a solution of diisopropylamine (1.8 ml, 13.7 mmol) in dry THF (20 ml) was added dropwise 8.6 ml of a solution of 1.6 M *n*-BuLi in hexane (13.7 mmol) at 0°C under argon. After 30 min, the solution was cooled at −78°C and a solution of the methyl mandelate **2** (6.1 mmol) in THF was added. The resulting solution was stirred at −78°C during 15 min and alkyl bromide or iodide (6.1 mmol) in THF (5 ml) was added. The reaction mixture was stirred at this temperature for 15 min and then at room temperature until the reaction was complete. After this time, the reaction mixture was poured into 1 M HCl (30 ml), extracted with ether (3×30 ml), washed with 1 M HCl (2×35 ml) and brine until neutral pH, and dried with $MgSO_4$. After removal of the solvent the resulting product **3** was purified by column chromatography on silica gel.

3.1.2. Methyl 2-hydroxy-2-phenyltetradecanoate (3b). Mp 38–40°C; ^{1}H NMR (δ, $CDCl_3$) 7.58 (2H, dd, J=7.8, 1.2 Hz), 7.30 (3H, m), 3.76 (3H, s), 2.12 (2H, m), 1.26 (20H, m), 0.88 (3H, t, J=5.9 Hz); ^{13}C NMR (δ, $CDCl_3$) 175.9 (s), 141.9 (s), 128.2 (d), 127.6 (d), 125.5 (d), 78.4 (s), 53.2 (q), 39.7–22.7 (t, overlapped signals), 14.1 (q); MS 334 (M^+, 0.2), 276 (100), 165 (9), 105 (51), 77 (12); HRMS *m/z* found 334.2507, $C_{21}H_{34}O_3$ required 334.2508.

3.1.3. Methyl 2-hydroxy-3-methyl-2-phenylbutanoate (3c). Mp 41–43°C; ^{1}H NMR (δ, $CDCl_3$) 7.71 (2H, dd, J=8.7, 1.5 Hz), 7.30 (3H, m), 3.89 (1H, s), 3.71 (3H, s), 2.67 (1H, m, J=6.8 Hz), 1.03 (3H, d, J=6.6 Hz), 0.76 (3H, d, J=6.6 Hz); ^{13}C NMR (δ, $CDCl_3$) 176.1 (s), 141.0 (s), 127.9 (d), 127.3 (d), 125.8 (d), 80.9 (s), 53.1 (q), 35.7 (d), 17.1(q), 15.6 (q); MS *m/z* 208 (M^+, 3), 165 (17), 105 (100), 77 (45); HRMS *m/z* found 208.1099, $C_{12}H_{16}O_3$ required 208.1099.

3.1.4. Methyl 2-cyclohexyl-2-hydroxy-2-phenylacetate (3d). Mp 49–51°C; ^{1}H NMR (δ, $CDCl_3$) 7.67 (2H, d, J=7.3 Hz), 7.32 (3H, m), 3.76 (3H, s), 2.26 (1H, m), 1.13–1.84 (10H, m); ^{13}C NMR (δ, $CDCl_3$) 176.0 (s), 140.6 (s), 127.9 (d), 127.2 (d), 125.9 (d), 80.9 (s), 53.1 (q), 45.6 (s), 27.3 (t), 26.2 (t), 26.1 (t), 25.3 (t); MS *m/z* 248 (M^+, 1), 189 (100), 166 (53), 107 (36), 105 (63), 91 (14), 77 (19); HRMS *m/z* found 248.1419, $C_{15}H_{20}O_3$ required 248.1412.

3.1.5. Methyl 2-hydroxy-2,3-diphenylpropanonate (3e). Mp 80–82°C; ^{1}H NMR (δ, $CDCl_3$) 7.65 (2H, dd, J=6.7, 1.2 Hz), 7.35 (3H, m), 7.23 (5H, m), 3.72 (3H, s), 3.60 (1H, d, J=13.3 Hz), 3.19 (1H, d, J=13.5 Hz); ^{13}C NMR (δ, $CDCl_3$) 174.7 (s), 141.5 (s), 135.7 (s), 130.4 (d), 128.3 (d), 128.1 (d), 127.9 (d), 127.0 (d), 125.7 (d), 78.8 (s), 53.1 (q), 45.9 (t); MS *m/z* 256 (M^+, 1), 197 (27), 165 (55), 105 (100), 91 (24), 77 (31); HRMS *m/z* found 256.1108, $C_{16}H_{16}O_3$ required 256.1099.

3.1.6. Methyl 2-hydroxy-2-phenyl-4-pentenoate (3f). Oil; ^{1}H NMR (δ, $CDCl_3$) 7.63 (2H, dd, J=7.9, 1.3 Hz), 7.28 (3H, m), 5.85 (1H, ddt, J=17.3, 9.8, 6.5 Hz), 5.20 (1H, brd, J=17.4 Hz), 5.11 (1H, brd, J=9.9 Hz), 4.09 (1H, s), 3.65 (3H, s), 3.00 (1H, dd, J=13.9, 7.7 Hz), 2.78 (1H, dd, J=13.9, 6.6 Hz); ^{13}C NMR (δ, $CDCl_3$) 174.4 (s), 140.5 (s), 131.7 (d), 127.6 (d), 127.2 (d), 124.8 (d), 118.7 (t), 77.4 (s), 52.5 (q), 43.4 (t); MS *m/z* 207 (M^++1, 2), 206 (M^+, 0.1), 166 (13), 147 (25), 105 (66), 91 (6), 77 (76); HRMS *m/z* found 207.1026, $C_{12}H_{15}O_3$ required 207.1021.

3.1.7. Methyl 4-bromo-2-hydroxy-2-phenyl-4-pentenoate (3g). Oil; ^{1}H NMR (δ, $CDCl_3$) 7.60 (2H, dd, J=6.4, 1.8 Hz), 7.33 (3H, m), 5.73 (1H, d, J=1.3 Hz), 5.61 (1H, d, J=1.3 Hz), 3.91 (1H, s), 3.80 (3H, s), 3.48 (1H, d, J=15.7 Hz), 3.11 (1H, d, J=15.7 Hz); ^{13}C NMR (δ, $CDCl_3$) 174.4 (s), 140.8 (s), 128.3 (d), 128.1 (d), 126.1 (d), 125.4 (d), 122.0 (t), 53.4 (q), 50.3 (t); MS *m/z* 287 (M^++1, 0.1), 285 (M^++1, 0.1), 227 (5), 225 (5), 165 (71), 105 (100), 77 (37); HRMS *m/z* found 287.0127 and 285.0133, $C_{12}H_{14}BrO_3$ required 287.0106 and 285.0126.

3.1.8. Methyl 2-hydroxy-4-phenoxy-2-phenylbutanoate (3h). Mp 74–76°C; ^{1}H NMR (δ, $CDCl_3$) 7.66 (2H, dd, J=8.4, 1.7 Hz), 7.32 (5H, m), 6.95 (1H, t, J=8.0 Hz), 6.87 (2H, d, J=8.4 Hz), 4.23 (1H, m), 4.14 (1H, s), 4.12 (1H, m), 3.79 (3H, s), 2.95 (1H, m), 2.46 (1H, m); ^{13}C NMR (δ, $CDCl_3$) 175.3 (s), 158.4 (s), 141.6 (s), 129.4 (d), 128.3 (d), 127.8 (d), 125.3 (d), 120.8 (d), 114.3 (d), 99.5 (s), 63.4 (t), 53.2 (q), 38.5 (t); MS *m/z* 286 (M^+, 23), 228 (15), 227 (87), 193 (64), 161 (39), 133 (58), 105 (100), 77 (53); HRMS *m/z* found 286.1206, $C_{17}H_{18}O_4$ required 286.1205.

3.1.9. Dimethyl 2,9-dihydroxy-2,9-diphenyldecanedioate (3i). Mp 86–88°C; ^{1}H NMR (δ, $CDCl_3$) 7.57 (4H, dd, J=8.4, 1.7 Hz), 7.29 (6H, m), 3.75 (6H, s), 2.11 (2H, m), 1.95 (2H, m), 1.25 (8H, m); ^{13}C NMR (δ, $CDCl_3$) 175.8 (s), 141.8 (s), 128.1 (d), 127.6 (d), 125.4 (d), 78.4 (s), 53.1 (q), 39.6 (t), 29.4 (t), 23.5 (t); MS *m/z* 355 (M^+-CO_2Me, 25), 337 (74), 305 (66), 277 (30), 259 (25), 133 (90), 105 (100), 77 (21); HRMS *m/z* found 355.1908, $C_{22}H_{27}O_4$ required 355.1909.

3.1.10. *p*-Bis(2-hydroxy-2-methoxycarbonyl-2-phenylethyl)-benzene (3j). Mp 212–214°C; ^{1}H NMR (δ, $CDCl_3$) 7.65 (4H, dd, J=8.0, 1.3 Hz), 7.34 (6H, m), 7.10 (4H, s), 3.71 (6H, s), 3.54 (2H, d, J=13.6 Hz), 3.15 (2H, d, J=13.6 Hz); ^{13}C NMR (δ, $CDCl_3$) 141.9 (s), 134.8 (s), 130.7 (d),128.8 (d), 128.4 (d), 126.2 (d), 79.3 (C_d), 53.6 (2q), 46.1 (t); MS *m/z* 434 (M^+, 0.2), 357 (4), 329 (6), 270 (11), 252 (100), 193 (41), 165 (21), 105 (91), 77 (21); HRMS *m/z* found 434.1712, $C_{26}H_{26}O_6$ required 434.1729.

3.1.11. Ethyl 5-hydroxy-5-methoxycarbonyl-5-phenylpentanoate (3k). Mp 82–84°C; ^{1}H NMR (δ, $CDCl_3$) 7.60 (2H, m), 7.30 (3H, m), 4.08 (2H, q, J=7.3 Hz), 3.74 (3H, s), 2.28 (2H, t, J=7.3 Hz), 2.11 (2H, m), 1.66 (2H, m), 1.20 (3H, t, J= 7.3 Hz); ^{13}C NMR (δ, $CDCl_3$) 175.3 (s), 158.3 (s), 141.6 (q), 129.3 (d), 128.3 (d), 127.8 (d), 125.3 (d), 120.8 (d), 114.8 (d), 76.2 (s), 63.4 (t), 53.2 ($-OCH_3$), 38.4 (q); MS *m/z* 221 (M^+-CO_2Me, 2), 175 (11), 128 (100), 107 (33), 105 (9), 86 (100); HRMS *m/z* found 221.1179, $C_{13}H_{17}O_3$ required 221.1178.

3.1.12. Dimethyl 2-hydroxy2-phenylbutanedioate (3l). Mp 61–63°C; ^{1}H NMR (δ, $CDCl_3$) 7.60 (2H, m), 7.35 (3H, m), 4.40 (1H, s), 3.80 (3H, s), 3.75 (3H, s), 3.50 (1H, d, J=16 Hz), 2.95 (1H, d, J=16 Hz); ^{13}C NMR (δ, $CDCl_3$) 174.1 (s), 171.4 (s), 140.0 (s), 128.4 (d), 128.1 (d), 124.9 (d), 67.8 (s), 53.2 (q), 51.9 (q), 44.2 (t); MS m/z 239 (M^++1, 0.1), 179 (100), 147 (18), 105 (100), 77 (24); HRMS m/z found 239.0915, $C_{12}H_{15}O_5$ required 239.1909.

3.1.13. Methyl 2-(4′-bromophenyl)-2-hydroxy-3-methylbutanoate (3m). Mp 94–96°C; ^{1}H NMR (δ, $CDCl_3$) 7.52 (2H, d, J=8.6 Hz), 7.43 (2H, d, J=8.5 Hz), 3.75 (3H, s), 2.54 (1H, m, J=6.5, 0.8 Hz), 0.94 (3H, dd, J=6.4, 0.8 Hz), 0.67 (3H, dd, J=6.4, 0.8 Hz); ^{13}C NMR (δ, $CDCl_3$) 175.6 (s), 140.1 (s), 131.1 (d), 127.8 (d), 121.6 (d), 80.6 (s), 53.3 (q), 35.8 (d), 17.0 (q), 15.5 (q); MS m/z 288 (M^+, 3), 286 (M^+, 3), 245 (22), 243 (22), 229 (97), 227 (100), 185 (91), 183 (92), 105 (38); HRMS m/z found 288.0182 and 286.0206, $C_{12}H_{15}BrO_3$ required 288.0184 and 286.0205.

3.1.14. Methyl 2-(4′-bromophenyl)-2-hydroxy-4-pentenoate (3n). Mp 37–39°C; ^{1}H NMR (δ, $CDCl_3$) 7.45 (4H, s), 5.74 (1H, ddd, J=17.8, 10.0, 6.8 Hz), 5.12 (1H, d, J=17.8 Hz), 5.10 (1H, d, J=10.0 Hz), 3.73 (3H, s), 2.90 (1H, ddd, J=13.8, 6.5, 1.2 Hz), 2.69 (1H, ddd, J=13.8, 6.7, 0.9 Hz); ^{13}C NMR (δ, $CDCl_3$) 174.3 (s), 140.1 (s), 131.6 (d), 131.1 (d), 127.3 (d), 121.8 (s), 119.4 (t), 77.7 (s), 53.1 (q), 44.0 (t); MS m/z 286 (M^+, 0.2), 284 (M^+, 0.2), 269 (1), 267 (1), 245 (70), 243 (70), 185 (98), 183 (100), 157 (28), 155 (28); HRMS m/z found 286.0054 and 284.0053, $C_{12}H_{13}BrO_3$ required 286.0028 and 284.0048.

3.1.15. Methyl 2-hydroxy-2-(4′-methoxyphenyl)-3-methylbutanoate (3o). Mp 70–73°C; ^{1}H NMR (δ, $CDCl_3$) 7.52 (2H, d, J=8.6 Hz), 6.85 (2H, d, J=8.6 Hz), 3.78 (3H, s), 3.75 (3H, s), 2.55 (1H, m, J=6.6 Hz), 0.94 (3H, d, J=6.6 Hz), 0.69 (3H, d, J=6.6 Hz); ^{13}C NMR (δ, $CDCl_3$) 175.7 (s), 158.2 (d), 132.4 (s), 126.4 (d), 112.7 (d), 80.0 (s), 54.5 (q), 52.5 (q), 35.0 (t), 16.5 (q), 15.0 (q); MS m/z 238 (M^+, 13), 195 (61), 179 (71), 135 (100), 77 (17); HRMS m/z found 238.1205, $C_{13}H_{18}O_4$ required 238.1205.

3.1.16. Methyl 2-hydroxy-2-(4′-methoxyphenyl)-4-pentenoate (3p). Oil; ^{1}H NMR (δ, $CDCl_3$) 7.49 (2H, dd, J=8.8, 2.9 Hz), 6.87 (2H, dd, J=8.8, 2.9 Hz), 5.77 (1H, ddt, J=17.5, 9.4, 7.1 Hz, H_4), 5.14 (1H, dd, J=17.5, 1.6 Hz), 5.12 (1H, dd, J=9.4, 1.9 Hz), 3.78 (3H, s), 3.74 (3H, s), 2.93 (1H, dd, J=14.1, 7.5 Hz), 2.72 (1H, ddd, J=13.9, 6.6, 1.3 Hz); ^{13}C NMR (δ, $CDCl_3$) 175.3 (s), 159.1 (s), 133.3 (d), 132.4 (d), 126.8 (d), 119.3 (t), 113.6 (d), 77.7 (d), 55.2 (q), 53.1 (q), 44.1 (t); MS m/z 236 (M^+, 1), 219 (1), 195 (100), 177 (17), 135 (71), 107 (8), 92 (19), 77 (24); HRMS m/z found 236.1038, $C_{13}H_{16}O_4$ required 236.1048.

3.1.17. Hydrolysis of α-alkylated methyl mandelates. The α-alkylated methyl mandelate **3** (1 mmol) was treated with 5% ethanolic KOH (2.5 ml, 2 mmol) at room temperature until complete reaction of the starting material (TLC). The solution was poured into ice and acidified with 1 M HCl until pH≈2. The aqueous mixture was extracted with EtOAc (3×60 ml), the organic layers were washed with brine until neutrality, dried, filtered and concentrated under vacuum to give the α-alkylated mandelic acid **4**.

3.1.18. 2-Hydroxy-2-phenyltetradecanoic acid (4b). Mp 98–100°C; ^{1}H NMR (δ, DMSO) 7.60 (2H, dd, J=7.8, 1.4 Hz), 7.31 (3H, m), 2.16 (2H, m), 1.22 (20H, m), 0.86 (3H, t, J=6.3 Hz).

3.1.19. 2-Hydroxy-3-methyl-2-phenylbutanoic acid (4c). Mp 142–144°C; ^{1}H NMR (δ, DMSO) 7.63 (2H, dd, J=7.2, 1.6 Hz), 7.33 (3H, m), 2.63 (1H, m, J=6.5 Hz), 1.03 (3H, d, J=6.6 Hz), 0.69 (3H, d, J=6.6 Hz).

3.1.20. 2-Cyclohexyl-2-hydroxy-2-phenylacetic acid (4d). Mp 169–171°C; ^{1}H NMR (δ, DMSO) 7.52 (2H, d, J=7.6 Hz), 7.47 (3H, m), 3.23 (1H, m), 1.90–1.06 (10H, m).

3.1.21. 2-Hydroxy-2,3-diphenylpropanoic acid (4e). Mp 164–166°C; ^{1}H NMR (δ, DMSO) 7.75 (2H, dd, J=7.8, 1.5 Hz), 7.30 (8H, m), 3.60 (1H, d, J=13.6 Hz), 3.2 (1H, d, J=13.6 Hz).

3.1.22. 2-Hydroxy-2-phenyl-4-pentenoic acid (4f). Mp 106–108°C; ^{1}H NMR (δ, DMSO) 7.61 (2H, dd, J=7.8, 1.2 Hz), 7.40 (3H, m), 5.85 (1H, ddt, J=19.2, 10.6, 7.2 Hz), 5.30 (1H, d, J=19.2 Hz), 5.2 (1H, d, J=10.6 Hz), 3.00 (1H, dd, J=14.5, 7.2 Hz), 2.98 (1H, dd, J=14.3, 7.4 Hz).

3.1.23. 4-Bromo-2-hydroxy-2-phenyl-4-pentenoic acid (4g). Mp 72–74°C; ^{1}H NMR (δ, DMSO) 7.62 (2H, dd, J=7.8, 1.9 Hz), 7.33 (3H, m), 5.74 (1H, d, J=1.5 Hz), 5.62 (1H, d, J=1.5 Hz), 3.51 (1H, d, J=15.4 Hz), 3.15 (1H, d, J=15.4 Hz).

3.1.24. 2-Hydroxy-4-phenoxy-2-phenylbutanoic acid (4h). Mp 109–112°C; ^{1}H NMR (δ, DMSO) 7.66 (2H, dd, J=7.9, 1.9 Hz), 7.35 (5H, m), 6.93 (1H, t, J=7.5 Hz), 6.80 (2H, d, J=7.3 Hz), 4.60 (1H, s, —OH), 4.15 (2H, t, J=5.1 Hz), 2.86 (1H, dt, J=14.7, 5.9 Hz), 2.53 (1H, dt, J=14.6, 5.0 Hz).

3.1.25. 2,9-Dihydroxy-2,9-diphenyldecanedioic acid (4i). Mp 176–177°C; ^{1}H NMR (δ, DMSO) 7.51 (4H, d, J=7.2 Hz), 7.27 (6H, m), 3.34 (1H, s, —OH), 2.02 (4H, m), 1.82 (4H, m), 1.18 (4H, m).

3.1.26. *p*-Bis(2-carboxy-2-hydroxy-2-phenylethyl)benzene (4j). Mp >250°C; ^{1}H NMR (δ, DMSO) 7.54 (4H, d, J= 7.7 Hz), 7.27 (6H, m), 3.35 (2H, d, J=13.6 Hz), 3.05 (2H, d, J=13.6 Hz).

3.1.27. 2-Hydroxy-2-phenylhexanedioic acid (4k). Mp 131–132°C; ^{1}H NMR (δ, DMSO) 7.50 (2H, dd, J=6.6, 1.4 Hz), 7.32 (3H, m), 6.70 (1H, s, —OH), 2.17 (2H, t, J= 7.5 Hz), 1.97 (2H, m), 1.44 (2H, q, J=7.6 Hz).

3.1.28. 2-Hydroxy-2-phenylbutanedioic acid (4l). Mp 200–201°C; ^{1}H NMR (δ, DMSO) 7.55 (2H, d, J=7.1 Hz), 7.32 (3H, m), 3.33 (1H, d, J=16.0 Hz), 2.65 (1H, d, J=16.0 Hz).

3.1.29. 2-(4′-Bromophenyl)-2-hydroxy-3-methylbutanoic acid (4m). Mp 143–146°C; ^{1}H NMR (δ, DMSO) 7.52 (4H,

m), 2.57 (1H, m, J=6.7, 2.6 Hz), 2.04 (1H, d, J=2.7 Hz), 1.01 (3H, dd, J=6.5, 2.6 Hz), 0.68 (3H, dd, J=6.6, 2.5 Hz).

3.1.30. 2-(4′-Bromophenyl)-2-hydroxy-4-pentenoic acid (4n). Mp 94–96°C; ^{1}H NMR (δ, DMSO) 7.48 (4H, m), 5.66 (1H, m), 5.03 (1H, d, J=14.4 Hz), 4.98 (1H, d, J=9.8 Hz), 2.80 (1H, dd, J=13.9, 6.9 Hz), 2.64 (1H, dd, J=13.9, 6.6 Hz).

3.1.31. 2-Hydroxy-2-(4′-methoxyphenyl)-3-methylbutanoic acid (4o). Mp 146–148°C; ^{1}H NMR (δ, DMSO) 7.60 (2H, d, J=18.1 Hz), 6.89 (2H, d, J=7.9 Hz), 3.77 (3H, s), 2.62 (1H, m, J=6.6 Hz), 1.01 (3H, d, J=6.6 Hz), 0.67 (3H, d, J=6.6 Hz).

3.1.32. 2-Hydroxy-2-(4′-methoxyphenyl)-4-pentenoic acid (4p). Mp 80–82°C; ^{1}H NMR (δ, DMSO) 7.51 (2H, d, J=8.8 Hz), 6.87 (2H, d, J=8.8 Hz), 5.73 (1H, m), 5.19 (1H, d, J= 18.7 Hz), 5.17 (1H, d, J=9.3 Hz), 3.78 (3H, s), 2.97 (1H, dd, J=14.1, 7.3 Hz), 2.75 (1H, dd, J=14.0, 7.0 Hz).

3.1.33. Catalytic aerobic decarboxylation of α-hydroxyacids 4. A solution of α-hydroxyacid **4** (0.11 mmol) in 0.2 ml of acetonitrile was added to a stirred mixture of Co(III) complex **1** (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 the indicated temperature until consumption of the starting α-hydroxyacid as indicated by TLC. The reaction products **5** were purified by flash column chromatography.

3.1.34. Dodecyl phenyl ketone (5b). Mp 39–41°C; IR ν 2924, 2853, 1688 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.94 (2H, dd, J=8.4, 1.6 Hz), 7.47 (3H, m), 2.94 (2H, t, J=7.3 Hz), 1.24 (20H, s), 0.86 (3H, t, J=6.2 Hz); ^{13}C NMR (δ, $CDCl_3$) 200.5 (s), 137.0 (s), 132.8 ($C_{4'}$), 128.5 (d), 128.0 (d), 38.6 (t), 31.8 (t), 29.6 (t), 29.4 (t), 29.3 (t), 24.3 (t), 22.6 (t), 14.1 (q); MS m/z 274 (M^+, 14), 120 (100), 105 (60), 77 (21), 55 (4); HRMS m/z found 274.2291, $C_{19}H_{30}O$ required 274.2297.

3.1.35. Isopropyl phenyl ketone (5c). Oil; IR ν 2800, 1680 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.94 (2H, dd, J=8.2, 1.3 Hz), 7.49 (3H, m), 3.55 (1H, m, J=6.9 Hz), 1.18 (6H, d, J=6.8 Hz); ^{13}C NMR (δ, $CDCl_3$) 136.7 (s), 133.3 (d), 129.1 (d), 128.8 (d), 35.8 (d), 19.7 (q); MS m/z 148 (M^+, 10), 105 (100), 77 (25); HRMS m/z found 148.0891, $C_{10}H_{12}O$ required 148.0888.

3.1.36. Cyclohexyl phenyl ketone (5d). Mp 55°C; IR ν 2925, 1638 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.94 (2H, dd, J=8.2, 1.5 Hz), 7.41 (3H, m), 3.26 (1H, m), 1.90–1.24 (10H, m); ^{13}C NMR (δ, $CDCl_3$) 136.1 (s), 132.7 (d), 128.5 (d), 128.2 (d), 45.6 (d), 29.4 (t), 25.9 (t), 25.8 (t); MS m/z 188 (M^+, 15), 105 (100), 77 (65); HRMS m/z found 188.1189, $C_{13}H_{16}O$ required 188.1201.

3.1.37. Deoxybenzoin (5e). Mp 48–51°C; IR ν 1685 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 8.01 (2H, dd, J=6.5, 1.1 Hz), 7.48 (3H, m), 7.28 (5H, m), 4.28 (2H, s); ^{13}C NMR (δ, $CDCl_3$) 197.7 (s), 136.2 (s), 134.3 (s), 133.2 (d), 129.6 (d), 128.7 (d), 126.9 (d), 45.6 (t); MS m/z 197 (M^++1, 10), 196 (M^+, 27), 105 (100), 91 (21), 77 (60), 52 (15); HRMS m/z found 196.0894, $C_{14}H_{12}O$ required 196.0888.

3.1.38. Allyl phenyl ketone (5f). Oil; IR ν 2925, 1680, 1635 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.95 (2H, dd, J=7.0, 1.7 Hz), 7.44 (3H, m), 6.00 (1H, ddt, J=18.2, 10.0, 6.9 Hz), 5.22 (1H, dd, J=18.2, 1.5 Hz), 5.20 (1H, dd, J=10.0, 1.5 Hz), 3.75 (2H, dd, J=6.9, 1.4 Hz); ^{13}C NMR (δ, $CDCl_3$) 197.9 (s), 136.3 (s), 133.0 (d), 130.8 (d), 128.4 (d), 128.1 (d), 118.5 (t), 43.2 (t); MS m/z 146 (M^+, 8), 105 (100), 77 (48), 51 (14); HRMS m/z found 146.0726, $C_{10}H_{10}O_4$ required 146.0732.

3.1.39. 3-Bromo-1-phenyl-3-buten-1-one (5g). Oil; IR ν 1688, 1598 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.97 (2H, m), 7.46 (3H, m), 5.75 (1H, d, J=1.8 Hz), 5.69 (1H, d, J=1.8 Hz), 4.12 (2H, s); ^{13}C NMR (δ, $CDCl_3$) 136.1 (s), 133.6 (d), 128.7 (d), 128.4 (d), 124.8 (s), 121.5 (t), 50.3 (t); MS m/z 226 (M^+, 11), 224 (M^+, 13), 149 (15), 147 (74); HRMS m/z found 225.9827 and 223.9819, $C_{10}H_9BrO$ required 225.9816 and 223.9837.

3.1.40. 3-Phenoxy-1-phenyl-1-propanone (5h). Mp 57–59°C; IR ν 2935, 1680, 1248, 1210 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 8.00 (2H, d, J=6.9 Hz), 7.47 (3H, m), 7.27 (2H, m), 6.94 (3H, m), 4.42 (2H, t, J=6.5 Hz), 3.46 (2H, t, J=6.6 Hz); ^{13}C NMR (δ, $CDCl_3$) 158.6 (s), 136.8 (s), 133.3 (d), 129.4 (d), 128.6 (d), 128.1 (d), 120.9 (d), 114.5 (d), 63.1 (t), 38.1 (t); MS m/z 226 (M^+, 30), 133 (48), 105 (100), 77 (45); HRMS m/z found 226.0997, $C_{15}H_{14}O_2$ required 226.0994.

3.1.41. 1,8-Diphenyl-1,8-octanedione (5i). Mp 82–84°C; IR ν 2932, 1684, 1446 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.94 (4H, dd, J=8.0, 1.1 Hz), 7.45 (6H, m), 2.95 (4H, t, J=7.1 Hz), 1.74 (4H, m), 1.43 (4H, m); ^{13}C NMR (δ, $CDCl_3$) 200.0 (s), 137.0 (s), 132.7 (d), 128.5 (d), 127.9 (d), 38.4 (t), 29.1 (t), 24.1 (t); MS m/z 294 (M^+, 3), 276 (33), 252 (12), 189 (5), 175 (78), 133 (17), 120 (84), 105 (100); HRMS m/z found 294.1623, $C_{20}H_{22}O_2$ required 194.1620.

3.1.42. *p*-Bis(phenacyl)benzene (5j). Mp 187–189°C; IR ν 2925, 1686 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 8.02 (4H, m), 7.48 (10H, m), 4.27 (4H, s); ^{13}C NMR (δ, $CDCl_3$) 197.6 (s), 137.0 (d), 133.2 (d), 129.7 (d), 128.6 (d), 45.0 (t); MS m/z 314 (M^+, 8), 223 (9), 105 (100), 77 (40); HRMS m/z found 314.1321, $C_{22}H_{18}O_2$ required 314.1307.

3.1.43. 5-Oxo-5-phenylpentanoic acid (5k). Oil; IR ν 2927, 2873, 2856, 1731, 1685 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.95 (2H, dd, J=6.7, 1.3 Hz), 7.47 (3H, m), 3.06 (2H, t, J=7.1 Hz), 2.49 (2H, t, J=7.1 Hz), 2.07 (2H, q, J=7.0 Hz); ^{13}C NMR (δ, $CDCl_3$) 199.3 (s), 178.8 (s), 136.7 (s), 133.1 (d), 128.6 (d), 128.0 (d), 37.3 (t), 33.0 (t), 29.6 (t); MS m/z 192 (M^+, 64), 120 (56), 105 (100), 77 (86), 52 (48); HRMS m/z found 192.0787, $C_{11}H_{12}O_3$ required 192.0786.

3.1.44. 3-Oxo-3-phenylpropanoic acid (5l). Oil; IR ν 2963, 2927, 2855, 1684, 1642 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 10.50 (1H, s), 7.94 (2H, d, J=7.4 Hz), 7.41 (3H, m), 3.50 (2H, s); ^{13}C NMR (δ, $CDCl_3$) 134.2 (s), 133.6 (d), 128.9 (d), 128.2 (d), 46.1 (t); MS m/z 164 (M^+, 4), 120 (59), 105 (100), 79 (82); HRMS m/z found 164.0473, $C_9H_8O_3$ required 164.0471.

3.1.45. 4-Bromophenyl isopropyl ketone (5m). Oil; IR ν 2965, 2927, 1687, ^{1}H NMR (δ, $CDCl_3$) 7.81 (2H, d, J=7.0 Hz), 7.60 (2H, d, J=7.2 Hz), 3.49 (1H, m, J=6.4 Hz), 1.23 (6H, d, J=6.4 Hz); ^{13}C NMR (δ, $CDCl_3$) 203.3 (s), 134.8 (s), 131.8 (d), 129.8 (d), 127.8 (d), 35.3 (d), 19.0 (q); MS m/z 228 (M^+, 11), 226 (M^+, 12), 185 (63), 183 (66), 157 (24), 155 (26), 76 (89), 74 (51); HRMS m/z 227.9979 and 226.0002, $C_{10}H_{11}BrO$ required 227.9973 and 225.9993.

3.1.46. Allyl 4-bromophenyl ketone (5n). Oil; IR ν 2900, 1726, 1584 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.81 (2H, d, J=8.6 Hz), 7.58 (2H, d, J=8.6 Hz), 6.04 (1H, ddt, J=17.3, 10.3, 6.7 Hz), 5.22 (1H, dd, J=17.3, 1.4 Hz), 5.18 (1H, dd, J=10.0, 1.4 Hz), 3.70 (2H, dd, J=6.5, 1.3 Hz); ^{13}C NMR (δ, $CDCl_3$) 196.6 (s), 135.0 (s), 131.7 (d), 130.4 (d), 129.6 (d), 128.2 (d), 118.8 (t), 43.2 (t); MS m/z 226 (M^+, 7), 224 (M^+, 8), 185 (98), 183 (100), 157 (26), 155 (26), 76 (12), 74 (4), 57 (8); HRMS m/z found 225.9812 and 223.9840, $C_{10}H_9BrO$ required 225.9816 and 223.9837.

3.1.47. Isopropyl 4-methoxyphenyl ketone (5o). Oil; IR ν 1706 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.93 (2H, d, J=8.7 Hz), 6.91 (2H, d, J=8.8 Hz), 3.84 (3H, s), 3.49 (1H, m, J= 6.8 Hz), 1.18 (6H, d, J=6.7 Hz); ^{13}C NMR (δ, $CDCl_3$) 203.1 (s), 165.2 (s), 130.5 (d), 129.1 (s), 113.7 (d), 55.4 (q), 34.9 (d), 19.3 (q); MS m/z 178 (M^+, 9), 135 (100), 107 (4); HRMS m/z found 178.0998, $C_{11}H_{14}O_2$ required 178.0994.

3.1.48. Allyl 4-methoxyphenyl ketone (5p). Oil; IR ν 2900, 1674, 1600, 1259 cm^{-1}; ^{1}H NMR (δ, $CDCl_3$) 7.93 (2H, d, J=8.9 Hz), 6.91 (2H, d, J=8.8 Hz), 6.05 (1H, ddt, J=17.2, 10.8, 6.6 Hz), 5.20 (1H, dd, J=17.2, 1.3 Hz), 5.18 (1H, d, J=10.7 Hz), 3.84 (3H, s), 3.69 (2H, d, J=6.6 Hz); ^{13}C NMR (δ, $CDCl_3$) 196.5 (s), 163.4 (s), 131.3 (d), 130.4 (d), 129.5 (d), 118.3 (t), 113.6 (d), 55.3 (q), 43.1 (t); MS m/z 176.0841 (M^+, 4), 135 (100), 107 (6), 77 (13), 64 (5); HRMS m/z found 176.0841, $C_{11}H_{12}O$ required 176.0837.

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