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Lipase-Catalyzed Chemo- and Enantioselective Acetylation of 2-Alkyl/aryl-3-hydroxypropiophenones

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Abstract—The chemo- and enantioselective capabilities of porcine pancreatic lipase (PPL) in tetrahydrofuran, and *Candida rugosa* lipase (CRL) in diisopropyl ether have been investigated for the acetylation of racemic 2-alkyl/aryl-3-hydroxypropiophenones, which are important precursors in the synthesis of biologically active chromanones and isoflavanones. A highly chemoselective acetylation of primary hydroxy group in preference to phenolic hydroxy group leading to the formation of enantiomerically enriched monoacetates has been observed.

Introduction

As a part of our ongoing research programme towards the design and synthesis of biologically active natural polyphenolics and their analogues, polyhydroxy aryl/alkyl and diaryl ketones, and their α-methylene hydroxymethyl derivatives were found to be important precursors.[1–4] These can be used in the synthesis of different classes of compounds, for example chalcones, dihydrochalcones, flavones, flavanones, chromanones, isoflavanones, and so on.[5–10] As a consequence, the hydroxymethylation reactions have received considerable interest in recent years. Unfortunately, almost all the chemical methods of hydroxymethylation on an active methylene group lead to the formation of a racemic mixture and thus their cyclised products, that is chromanones, isoflavanones, and so on are also racemic and difficult to resolve. Since it is well established that the enantiomers of a given bioactive compound cause different biological effects, the synthesis of optically pure compounds is becoming increasingly desirable. In this scenario, biocatalytic reactions have played a vital role in the synthesis of chiral compounds. Amongst various enzymes, lipases and proteases have found increasing use for achieving the desired selectivity in organic synthesis. This is attributed mainly to their low cost and wide tolerance towards a variety of molecules.[11,12] We have demonstrated earlier the capabilities of lipases from porcine pancreas (PPL), *Candida antarctica* (CAL), *Candida rugosa* (CRL), *Aspergillus* and *Pseudomonas* species for carrying out chemo- and stereoselective acylations/deacylations on polyols and polyphenolics.[13–18] In this communication, we report lipase-catalysed chemo- and enantioselective acetylation of 2-alkyl/aryl-3-hydroxypropiophenones using vinyl acetate as acyl donor in the presence of PPL and CRL.

Results and Discussion

We have synthesised 12 differently substituted hydroxymethyl ketones; seven aryl/alkyl ketones, namely (±)-3-hydroxy-1-(2-hydroxy-4-methoxyphenyl)-2-methylpropanone (**2a**),[19] (±)-2-hydroxymethyl-1-(2-hydroxy-4-methoxyphenyl)-butan-1-one (**2b**), (±)-2-hydroxymethyl-1-(2-hydroxy-4-methoxyphenyl)-octan-1-one (**2c**), (±)-2-hydroxymethyl-1-(2-hydroxy-4-methoxyphenyl)-dodecan-1-one (**2d**), (±)-3-hydroxy-1-(2-hydroxy-3,4-dimethoxyphenyl)-2-methylpropanone (**2e**),[19] (±)-2-hydroxymethyl-1-(2-hydroxy-3,4-dimethoxyphenyl)-butan-1-one (**2f**) and (±)-3-hydroxy-1-(4-methoxyphenyl)-2-methylpropanone (**2g**)[20] by carrying out hydroxymethylation of the corresponding ketones, that is 2-hydroxy-4-methoxypropiophenone (**1a**),[21] 2-hydroxy-4-methoxy-

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butyrophenone (**1b**),[21] 2-hydroxy-4-methoxyphenyl heptyl ketone (**1c**),[22] 2-hydroxy-4-methoxyphenyl undecyl ketone (**1d**),[22] 2-hydroxy-3,4-dimethoxypropiophenone (**1e**),[21] 2-hydroxy-3,4-dimethoxybutyrophenone (**1f**)[21] and 4-methoxypropiophenone (**1g**), respectively. The hydroxymethylation of compounds **1a**–**1g** was carried out with 1.0 equiv of formaldehyde solution (37%) in 0.5N NaOH at room temperature.[7]

The hydroxymethyl diaryl ketones, namely (±)-3-hydroxy-1-(2-hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)-propanone (**2h**),[23] (±)-1-(4-benzyloxy-2-hydroxyphenyl)-3-hydroxy-2-phenylpropanone (**2i**), (±)-1-(4-benzyloxy-2-hydroxyphenyl)-3-hydroxy-2-(4-methoxyphenyl)-propanone (**2j**) and (±)-2-hydroxymethyl-1-(2-hydroxyphenyl)-3-(3,4-methylenedioxyphenyl)-propanone (**2k**) were synthesised by the hydroxymethylation of 1-(2-hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)-ethanone (**1h**),[24] 1-(4-benzyloxy-2-hydroxyphenyl)-2-phenylethanone (**1i**),[25] 1-(4-benzyloxy-2-hydroxyphenyl)-2-(4-methoxyphenyl)-ethanone (**1j**)[25] and 1-(2-hydroxyphenyl)-3-(3,4-methylenedioxyphenyl)-propanone (**1k**),[26] respectively using ethoxymethyl chloride and anhydrous potassium carbonate in refluxing acetone[19] and the ketone (±)-1-(2,4-dihydroxyphenyl)-3-hydroxy-2-phenylpropanone (**2l**) was prepared by the debenzylation of (±)-**2i** with palladium-charcoal under hydrogen atmosphere.

All the hydroxymethyl ketones **2a**–**2l** were obtained in racemic form and their resolution was attempted by carrying out lipase-catalysed acetylation reaction using vinyl acetate as the acyl donor. Both porcine pancreatic lipase (PPL) in tetrahydrofuran (THF) and *Candida rugosa* lipase (CRL) in diisopropyl ether (DIPE) were screened. For hydroxymethylated aryl alkyl ketones (±)-**2a**–**2g**, PPL in THF was found to be a better catalyst over CRL as the reaction with CRL was much slower. However, in the case of hydroxymethylated diaryl ketones (±)-**2h**–**2l**, CRL in DIPE proved to be a better catalyst as no significant reaction occurred with PPL.

The acetylation reaction was carried by incubating the ketone with the enzyme at 40–42 °C in the presence of vinyl acetate as acylating agent. The progress of reaction was monitored through periodic checking by TLC and/or HPLC, the reaction was stopped after about 50% conversion of the ketone to its acetyl derivative by filtering off the enzyme. The acetate and the recovered, unreacted hydroxymethylated ketone were separated by column chromatography over silica gel with a gradient solvent system of petroleum ether/ethyl acetate. All the enzymatic reaction products, namely (+)-3-acetoxy-1-(2-hydroxy-4-methoxyphenyl)-2-methylpropanone (**3a**), (−)-2-acetoxymethyl-1-(2-hydroxy-4-methoxyphenyl)-butan-1-one (**3b**), (−)-2-acetoxymethyl-1-(2-hydroxy-4-methoxyphenyl)-octan-1-one (**3c**), (−)-2-acetoxymethyl-1-(2-hydroxy-4-methoxyphenyl)-dodecan-1-one (**3d**), (+)-3-acetoxy-1-(2-hydroxy-3,4-dimethoxyphenyl)-2-methylpropanone (**3e**), (+)-2-acetoxymethyl-1-(2-hydroxy-3,4-dimethoxyphenyl)-butan-1-one (**3f**), (+)-3-acetoxy-1-(4-methoxyphenyl)-2-methylpropanone (**3g**), (+)-3-acetoxy-1-(2-hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)-propanone (**3h**), (+)-3-acetoxy-1-(4-benzyloxy-2-hydroxyphenyl)-2-phenylpropanone (**3i**), (+)-3-acetoxy-1-(4-benzyloxy-2-hydroxyphenyl)-2-(4-methoxyphenyl)-propanone (**3j**), (+)-2-acetoxymethyl-1-(2-hydroxyphenyl)-3-(3,4-methylenedioxyphenyl)-propanone (**3k**) and (−)-3-acetoxy-1-(2,4-dihydroxyphenyl)-2-phenylpropanone (**3l**) were found to be the monoacetyl derivatives of their respective hydroxymethylated ketones (±)-**2a**–**2l**. However, no acetylation reaction was observed when reactions on all these substrates were carried out under identical conditions but without the addition of any lipase. All the 12 compounds **2a**–**2l** (except **2g** and **2l**) have two hydroxyl groups (one phenolic and the other alcoholic) which can undergo acetylation. The formation of monoacetates involving only the aliphatic hydroxyl group has been seen in all the compounds, this was clear as the carbinol protons in all the monoacetates **3a**–**3l** are deshielded (by δ 0.35–0.68 ppm) with respect to the corresponding protons in the respective hydroxymethylated compounds **2a**–**2l**. The presence of peak for the chelated phenolic hydroxyl group (except for **3g**) between δ12 and 13, and the absence of any resonance due to the aliphatic hydroxyl group in the ^{1}H NMR spectra of the compounds **3a**–**3l** further established the exclusive acetylation of aliphatic hydroxyl group in **2a**–**2l** by the lipase. Furthermore, the observance of dark brown colouration on spraying alcoholic $FeCl_3$ solution (2%) over the thin-layer chromatograms of the compounds **3a**–**3l** (except in that of **3g**) confirmed that the *ortho* (phenolic) hydroxy function to the nuclear carbonyl group is not acetylated in any of these compounds. This clearly indicated that, both PPL and CRL exhibit outstanding chemoselectivity for the acetylation of aliphatic hydroxyl group over the phenolic hydroxyl, to give only a monoacetate involving the primary hydroxy group, though both the phenolic and alcoholic hydroxy groups can chelate with the carbonyl group (Fig. 1). This is in confirmation with our earlier published results on two similar compounds where enzymatic acetylation took place chemoselectively at the alcoholic hydroxy group in compounds containing alcoholic hydroxy and non-chelated phenolic hydroxy groups.[15] Further the compound **2l** has an additional non-chelated phenolic hydroxy group at the C-4′ position and enzymatic acetylation is chemoselective in this case also.

All the substrates **2a**–**2l** and their corresponding acetates **3a**–**3l** were fully characterized on the basis of their spectral data. Only the ketones **2a**,[19] **2e**,[19] **2g**[20] and **2h**[23] are known earlier in literature, the remaining twenty compounds have been prepared for the first time. The ketone **2e** has been reported earlier as an oil,[19] but our sample of **2e** is a white crystalline solid, we have confirmed its structure by X-ray diffraction study (Fig. 1).[27]

All the enzymatic acetylation products **3a**–**3l** and the recovered, unreacted ketones **2a**–**2l** were found to be optically active (Table 1), thus revealing that the chemoselective acetylation is also accompanied by enantiomeric resolution of the racemic ketones **2a**–**2l**. The acetylated products **3a**–**3l**, obtained by enzymatic

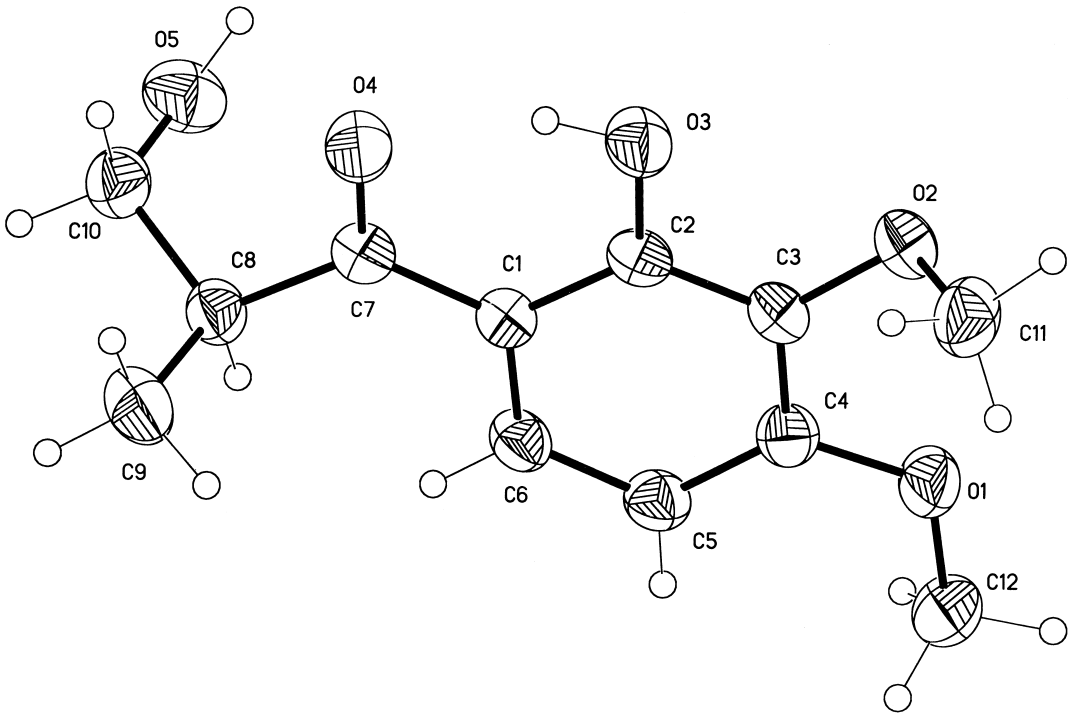


Figure 1. X-ray crystal structure of (±)-3-hydroxy-1-(2-hydroxy-3,4-dimethoxyphenyl)-2-methylpropanone (**2e**).

reaction were deacetylated by using either CRL in DIPE and *n*-butanol (for **3a**–**3g**), or by using HCl/MeOH (for **3h**–**3l**). It was ascertained in all the cases that the conversion of acetylated compounds (+)/(−)-**3a**–**3l** into hydroxy compounds (+)/(−)-**2a**–**2l** is 100%. It is interesting to note that the alcohols **2a**–**2g** are not good substrates for CRL, but their monoacetates **3a**–**3g** become better substrates for deacetylation reactions with CRL in DIPE. The optical rotations of the alcohols **2a**–**2l** obtained by deacetylation of the enzymatically acetylated compounds **3a**–**3l** were measured; as can be seen from Table 1, these were found to be of the same order (within practical limits), but having opposite sign to the rotation of the corresponding recovered, unreacted hydroxy compounds **2a**–**2l** (Scheme 1), thus showing an efficient enantiomeric resolution.

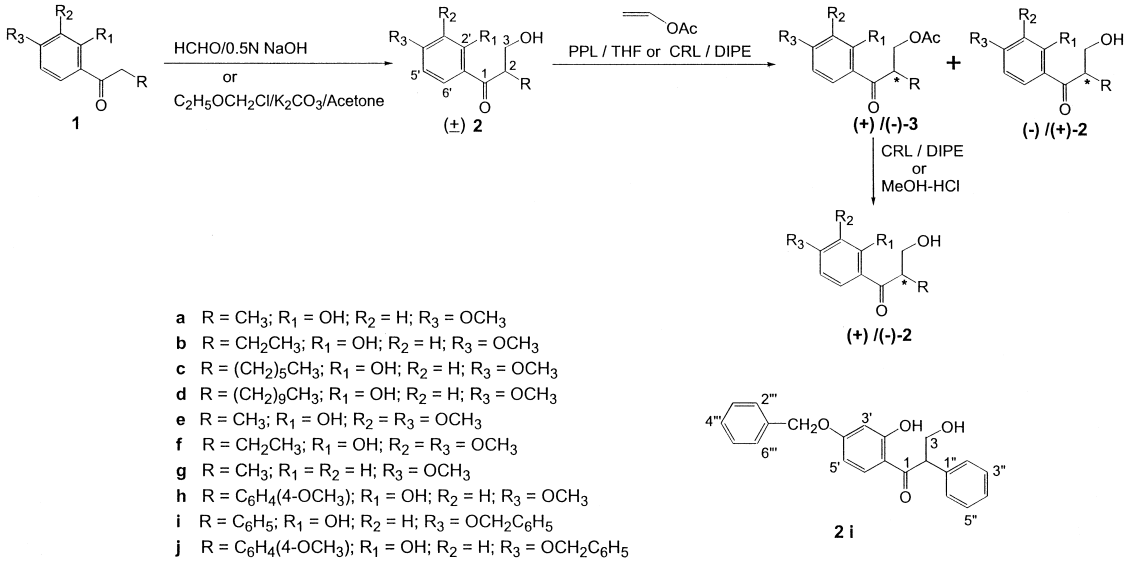
Since both, the enzymatic acetylated products **3a**–**3l** and the corresponding recovered, unreacted ketones **2a**–**2l** were found to be optically active, efforts were made to determine their enantiomeric excess (ee) values. Our initial attempts to determine the ee values of these compounds by using Chiracel OJ HPLC column were not successful. However, ee values could be determined by ^{1}H NMR (400 MHz) spectroscopy for compounds (−)-**2a** (ee 60.1) and (+)-**2c** (ee 43.0) only by using (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol (TFAE) as chiral shift reagent. Splitting of the chelated hydroxyl peak as a result of formation of diastereomeric mixture by the addition of the chiral shift reagent can be seen in Figs 2 and 3 (for **2a**) and Fig. 4 (for **2c**). All the ^{1}H NMR spectra were recorded at 223 K, and deuterated toluene was used as the solvent. Deuterated chloroform

Table 1. Enantioselective acetylation of hydroxymethylated aryl alkyl ketones **2a**–**2l** mediated by lipases in organic solvent at 40–42 °C

Substrate	Reaction condition	Reaction time	$[\alpha]_D^{25}$ Values of the acetylated compounds **3a**–**3l** obtained by enzymatic reaction	$[\alpha]_D^{25}$ Values of the recovered, unreacted hydroxy compounds **2a**–**2l**	$[\alpha]_D^{25}$ Values of the hydroxy compounds **2a**–**2l** obtained by deacetylation of the enzymatically acetylated compounds **3a**–**3l**
2a	a	22 h	+27.50	−25.00	+20.80 (b)
2b	a	48 h	−3.40	+6.80	−5.40 (b)
2c	a	7 days	−3.60	+6.00	−10.60 (b)
2d	a	20 days	−5.70	+2.00	−4.80 (b)
2e	a	52 h	+31.50	−37.40	+32.94 (b)
2f	a	68 h	+1.80	+1.40	−3.20 (b)
2g	a	10 h	+11.50	−35.00	+21.80 (b)
2h	b	10 h	+16.00	−10.00	+14.30 (c)
2i	b	25 h	+11.70	−2.80	+5.20 (c)
2j	b	22 h	+6.00	−4.20	+4.80 (c)
2k	b	9 h	+21.40	−16.50	+20.20 (c)
2l	b	48 h	−12.00	+6.20	−7.40 (c)

a, PPL in tetrahydrofuran (THF); b, CRL in diisopropyl ether (DIPE); c, methanolic-HCl.

was tried first, but no splittings were observed. On the other hand, toluene, an anisotropic solvent, induced non-equivalence and hence was useful in making the chiral separation successful. Other chiral shift reagents, namely *tris* (6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedioate)europium Eu $(fod)_3$, *tris* (6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedioate) praseodymium Pr $(fod)_3$ and *tris* dipivaloylmethane europium, Eu $(dpm)_3$, were also tried, but a clear separation of enantiomers could not be achieved. With Eu $(fod)_3$ and Eu $(dpm)_3$, a downfield shift was seen with peaks appearing as humps with no splitting; while with Pr



a R = CH_3; R_1 = OH; R_2 = H; R_3 = OCH_3
b R = CH_2CH_3; R_1 = OH; R_2 = H; R_3 = OCH_3
c R = $(CH_2)_5CH_3$; R_1 = OH; R_2 = H; R_3 = OCH_3
d R = $(CH_2)_9CH_3$; R_1 = OH; R_2 = H; R_3 = OCH_3
e R = CH_3; R_1 = OH; R_2 = R_3 = OCH_3
f R = CH_2CH_3; R_1 = OH; R_2 = R_3 = OCH_3
g R = CH_3; R_1 = R_2 = H; R_3 = OCH_3
h R = C_6H_4(4-OCH_3); R_1 = OH; R_2 = H; R_3 = OCH_3
i R = C_6H_5; R_1 = OH; R_2 = H; R_3 = $OCH_2C_6H_5$
j R = C_6H_4(4-OCH_3); R_1 = OH; R_2 = H; R_3 = $OCH_2C_6H_5$
k R = $CH_2C_6H_3$(3,4-OCH_2O-); R_1 = OH; R_2 = R_3 = H
l R = C_6H_5; R_1 = R_3 = OH; R_2 = H

Scheme 1.

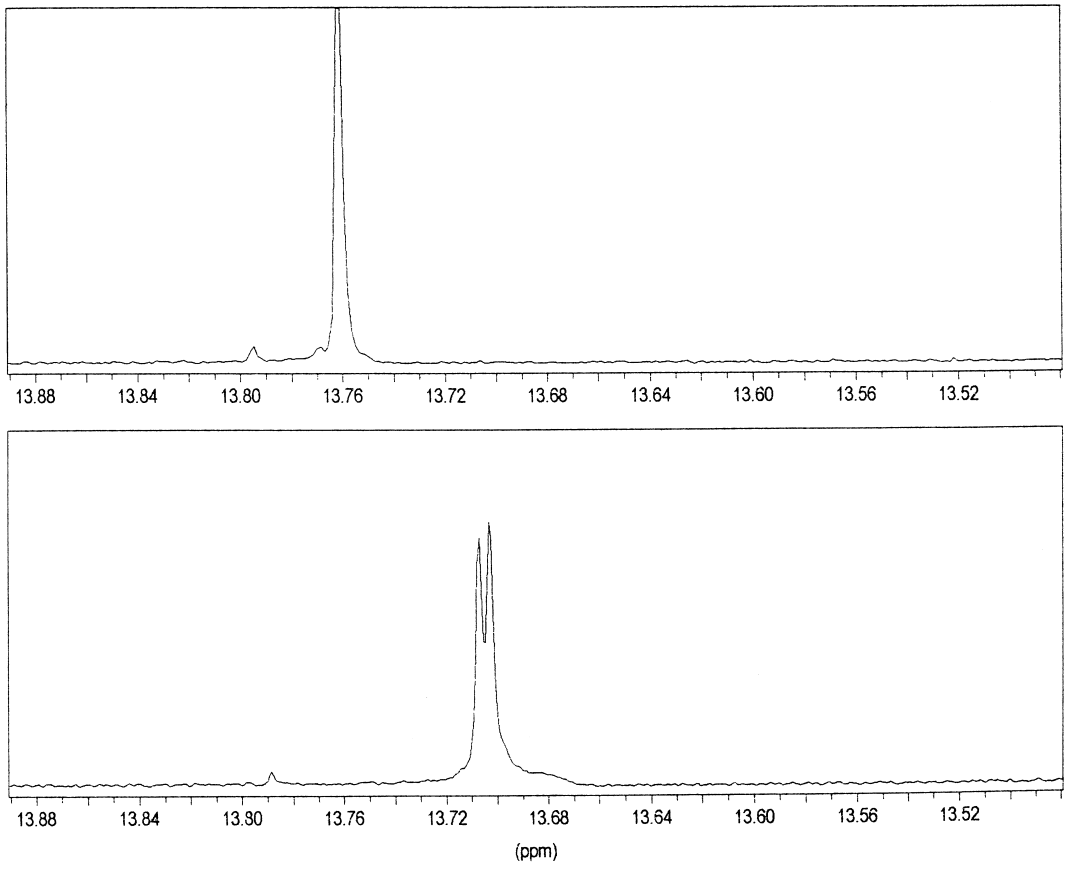


Figure 2. Compound (±)-**2a** in toluene-d_8 (top); compound (±)-**2a** with TFAE in toluene-d_8 at 223 K showing splitting of the hydroxyl group (bottom).

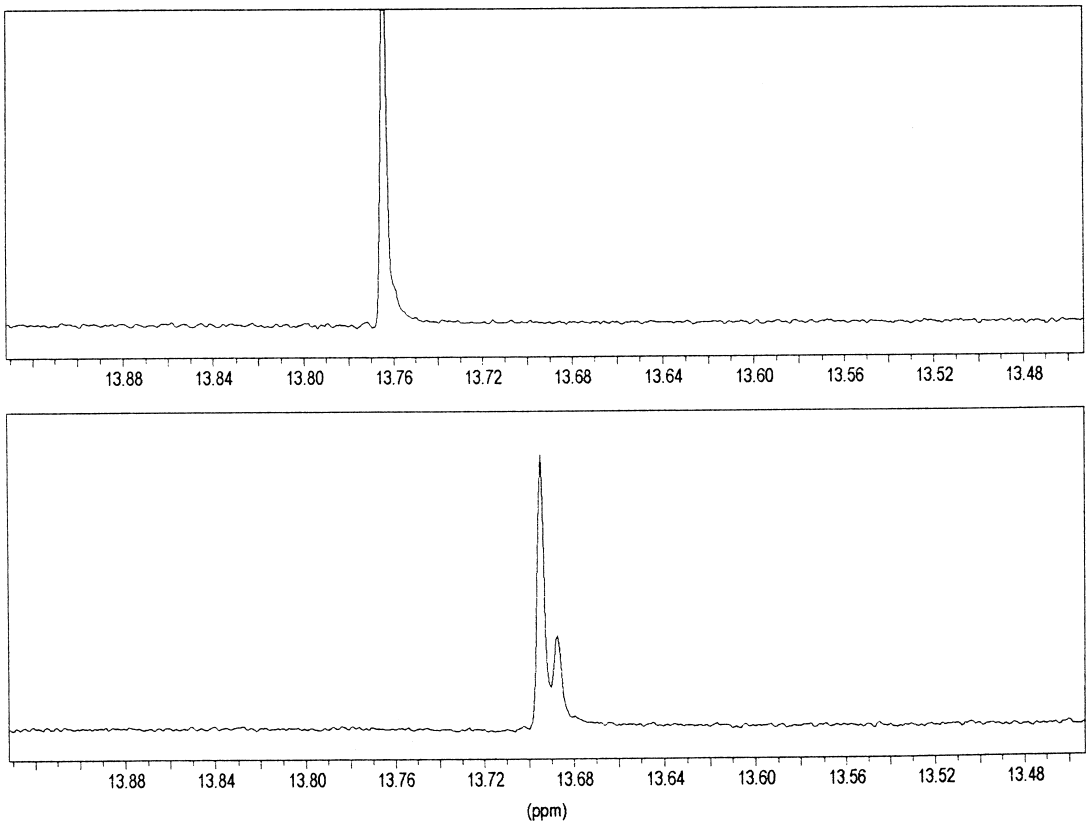


Figure 3. Compound (−)-**2a** in toluene-d_8 (top); compound (−)-**2a** with TFAE in toluene-d_8 at 223 K showing splitting of the hydroxyl group (bottom).

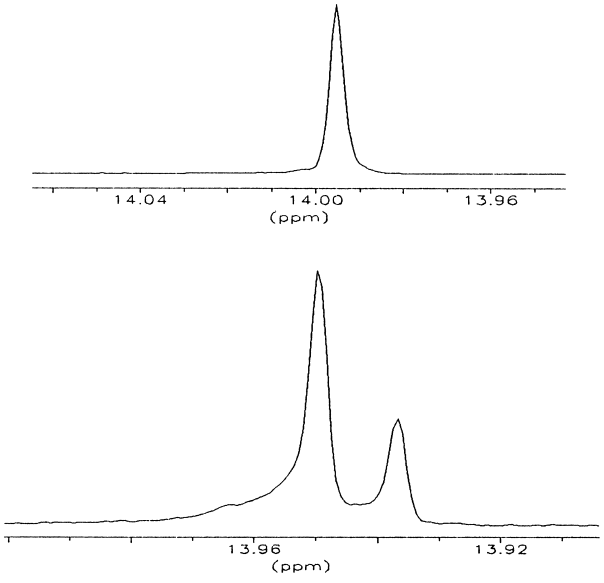


Figure 4. Compound (+)-**2c** in toluene-d_8 (top); compound (+)-**2c** with TFAE in toluene-d_8 at 223 K showing splitting of the hydroxyl group (bottom).

$(fod)_3$, a hump at lower δ value was seen without any clear separation of the peaks. When the temperature was decreased, the exchange process slowed down on the NMR time scale and produced further line broadening.

Successful chiral separation could only be achieved for the racemic (±)-**2a** and (±)-**2c** and the corresponding recovered, unreacted enantiomers in both the cases, that is the enantiomerically enriched primary alcohols (−)-**2a** and (+)-**2c**. The ee values for the acetylated products could not be determined as no splitting was observed with the acetylated enantiomer in both the cases, it may be so because no binding site (alcoholic hydroxyl) is left to bind with TFAE. The ee values were determined by comparing the chemical shift values of the chelated hydroxyl group of the sample alone in deuterated toluene and the sample plus TFAE (1:1 mole ratio) in toluene-d_8. The phenolic hydroxyl group was hydrogen bonded to the carbonyl and thus resonated downfield. Chiral splittings were observed for this hydroxyl resonance with a single peak splitting into two signals in the presence of chiral solvating agent, namely TFAE. The ee values were calculated from the integration values of these two signals. The R/S ratio could not be ascertained, since it was not feasible to assign the absolute configuration to the two enantiomers. Further work is in progress and shall be communicated in a future publication.

Conclusion

We have developed a novel, efficient and environmentally benign method for the resolution of racemic hydroxymethylated aryl alkyl ketones, this biocatalytic method for the chemo- and enantioselective acetylation of the racemic hydroxymethylated ketones may find

applications in the synthesis of optically enriched bioactive 3-alkylchromanones and isoflavanones.

Experimental

Melting points were determined on a Mettler FP62 instrument and are uncorrected. The IR spectra were recorded on a Perkin–Elmer RX/FT-IR spectrophotometer. The optical rotations were measured with Bellingham Stanley AD 220 polarimeter. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-300 spectrometer at 300 and at 75 MHz, respectively, using TMS as internal standard. The EI mass spectra were recorded with a Jeol AX 505 W mass spectrometer at 70eV. The enzymes, porcine pancreatic lipase (PPL, Type II) and *C. rugosa* (CRL, Type VII) were purchased from Sigma Chemical Co. (St. Louis, MO, USA) and used after keeping in vacuo over P_2O_5 for 24 h. Analytical TLCs were performed on precoated Merck silica gel $60F_{254}$ plates; the spots were detected either under UV light or by charring with 5% alcoholic sulphuric acid. Reactions were monitored on Shimadzu LC-10AS HPLC instrument with SPD-10A UV–vis detector and Shimpack CLC-ODS (4.6 x 150 mm) reverse phase column; solvent system used was methanol-water at the flow rate of 1 mL/min. The compound 4-methoxypropiophenone (**1g**) was procured from Aldrich Chemical Company.

General method of hydroxymethylation

Using formaldehyde and sodium hydroxide.[7] A solution of the ketone (**1a**–**1g**, 2.0 g) and formaldehyde (37%,1.0 equiv) in aqueous sodium hydroxide (0.5 N, 1.0 equiv) was stirred at room temperature. The progress of the reaction was followed by TLC. On completion, the reaction mixture was acidified with dilute hydrochloric acid and the product was extracted with diethyl ether (2×50 mL). The organic layer was combined, washed with brine (2×50 mL), dried over anhydrous sodium sulphate and the solvent evaporated. The residue so obtained was subjected to flash column chromatography over silica gel to afford the hydroxymethylated ketones **2a**–**2g**.

Using ethoxymethyl chloride.[19] To a solution of the ketone (**1h**–**1k**, 5 mmol) in anhydrous acetone (100 mL), freshly ignited potassium carbonate (3.5 g) and a solution of ethoxymethyl chloride (5.5 mmol) in anhydrous acetone (5 mL) were added and the reaction mixture was refluxed. The progress of reaction was monitored by TLC (petroleum ether/ethyl acetate, 4:1); on completion (3–4 h), the reaction mixture was filtered and the filterate concentrated under reduced pressure. The light brown residue so obtained was purified by column chromatography using a gradient system of petroleum ether and ethyl acetate as eluent to give the hydroxymethylated ketones **2h**–**2k**.

(±)-2-Hydroxymethyl-1-(2-hydroxy-4-methoxyphenyl)-butan-1-one (2b). Colourless viscous oil; yield 65%; R_f 0.35 (petroleum ether/ethyl acetate, 17:3); λ_{max} (MeOH): 230, 277 and 316 nm; ν_{max} (Nujol): 3408 (OH), 2965, 1628 (C=O), 1509, 1462, 1377, 1159 and 1030 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.96 (3H, t, C-4H), 1.74 (2H, m, C-3H), 2.30 (1H, brs, OH), 3.45–3.49 (1H, m, C-2H), 3.82 (1H, dd, $J=4.0$, 11.1 Hz, $CH_{\alpha}H_{\beta}OH$), 3.84 (3H, s, OCH_3), 3.96 (1H, dd, $J=7.0$, 11.1 Hz, $CH_{\alpha}H_{\beta}OH$), 6.45 (2H, m, C-3′H and C-5′H), 7.69 (1H, d, $J=8.8$ Hz, C-6′H) and 12.92 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 11.85 (C-4), 22.90 (C-3), 48.90 (C-2), 55.62 (OCH_3), 62.90 (CH_2OH), 101.15 (C-3′), 107.89 (C-5′), 113.72 (C-1′), 131.92 (C-6′), 166.11 and 166.45 (C-2′ and C-4′) and 208.08 (C=O); *m*/*z* EI-MS: 224 $[M]^+$ (10), 177 (4), 151 (100), 97 (8) and 57 (11).

(±)-2-Hydroxymethyl-1-(2-hydroxy-4-methoxyphenyl)-octan-1-one (2c). Colourless viscous oil; yield 52%; R_f 0.25 (petroleum ether/ethyl acetate, 19:1); λ_{max} (MeOH): 230, 277, 316 nm; ν_{max} (Nujol): 3419 (OH), 2928, 1627 (C=O), 1510, 1463, 1378, 1241, 1161, 1031, 970 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.86 (3H, t, $J=6.9$ Hz, C-8H), 1.28 (8H, brs, C-4H, C-5H, C-6H and C-7H), 1.61–1.64 (2H, m, C-3H), 2.20 (1H, brs, CH_2OH), 3.49–3.55 (1H, m, C-2H), 3.80–3.85 (4H, m, OCH_3 and $CH_{\alpha}H_{\beta}OH$), 3.94 (1H, dd, $J=7.3$, 10.5 Hz, $CH_{\alpha}H_{\beta}OH$), 6.46 (2H, m, C-3′H and C-5′H), 7.68 (1H, d, $J=8.8$ Hz, C-6′H), 12.92 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 14.04 (C-8), 22.58, 27.42, 29.40, 29.77 and 31.61 (5×CH_2), 47.48 (C-2), 55.64 (OCH_3), 63.27 (CH_2OH), 101.19 (C-3′), 107.94 (C-5′), 113.64 (C-1′), 131.86 (C-6′), 166.20 and 166.48 (C-2′ and C-4′), 208.24 (C=O); *m*/*z*, EI-MS: 280 $[M]^+$ (74), 262 (22), 196 (75), 151 (100), 124 (17), 108 (30), 95 (47), 55 (32).

(±)-2-Hydroxymethyl-1-(2-hydroxy-4-methoxyphenyl)-dodecan-1-one (2d). Colourless viscous oil; yield 67%; R_f 0.35 (petroleum ether/ethyl acetate, 19:1); λ_{max} (MeOH): 230, 279, 318 nm; ν_{max} (Nujol): 3413 (OH), 2925, 1628 (C=O), 1509, 1464, 1443, 1378, 1247, 1209, 1161, 1032, 838 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.87 (3H, t, $J=6.5$ Hz, C-12H), 1.23 (16H, brs, C-4H, C-5H, C-6H, C-7H, C-8H, C-9H, C-10H and C-11H), 1.64–1.70 (2H, m, C-3H), 2.31 (1H, brs, OH), 3.51–3.59 (1H, m, C-2H), 3.79–3.84 (4H, m, OCH_3 and $CH_{\alpha}H_{\beta}OH$), 3.91–3.97 (1H, dd, $J=7.4$, 10.5 Hz, $CH_{\alpha}H_{\beta}OH$), 6.42–6.47 (2H, m, C-3′H and C-5′H), 7.68 (1H, d, $J=8.8$ Hz, C-6′H), 12.93 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 14.39 (C-12), 21.00, 24.36, 28.83, 29.01, 29.17, 33.23 (9×CH_2), 48.20 (C-2), 55.03 (OCH_3), 64.45 (CH_2OH), 100.13 (C-3′), 106.47 (C-5′), 113.14 (C-1′), 132.51 (C-6′), 165.55 and 165.86 (C-2′ and C-4′), 207.60 (C=O); *m*/*z*, EI-MS: 336 $[M]^+$ (16), 318 (8), 238 (15), 196 (60), 178 (80), 167 (20), 151 (100), 150 (21), 123 (11), 108 (46), 95 (88), 55 (70).

(±)-3-Hydroxy-1-(2-hydroxy-3,4-dimethoxyphenyl)-2-methylpropanone (2e). White crystalline solid; mp 70 °C; yield 60.0%; R_f 0.30 (petroleum ether/ethyl acetate, 3:1); λ_{max} (MeOH): 218, 284 and 355 nm; ν_{max} (Nujol): 3516 (OH), 2925, 1625 (C=O), 1506, 1450, 1378, 1269, 1154 and 1071 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.27 (3H, d, $J=7.1$ Hz, CH_3), 2.32 (1H, brs, OH), 3.61–3.68 (1H, m, C-2H), 3.77–3.81 (1H, m, C-3H$_{\alpha}$), 3.90 and 3.95 (6H, 2s, 3H each, 2×OCH_3), 3.86–3.99 (1H, m,

C-3H$_\beta$), 6.53 (1H, d, J=9.1 Hz, C-5′H), 7.59 (1H, d, J=9.1 Hz, C-6′H) and 12.64 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 15.10 (CH_3), 40.92 (C-2), 56.18 and 60.67 (2×OCH_3), 64.63 (C-3), 103.19 (C-5′), 114.36 (C-1′), 126.61 (C-6′), 136.83 (C-3′), 157.86 and 158.78 (C-2′ and C-4′) and 208.71 (C=O); m/z, EI-MS: 240 $[M]^+$ (18), 222 (12), 181 (100), 137 (10), 120 (20), 95 (13) and 55 (12).

(±)-2-Hydroxymethyl-1-(2-hydroxy-3,4-dimethoxyphenyl)-butan-1-one (2f). Colourless viscous oil; yield 64%; R_f 0.40 (petroleum ether/ethyl acetate, 3:1); λ_{max} (MeOH): 221, 287 and 355 nm; ν_{max} (Nujol): 3429 (OH), 2934, 1628 (C=O), 1506, 1447, 1379, 1274, 1138, 1068 and 1007 cm^{-1}; δ_H (400 MHz, $CDCl_3$): 0.95 (3H, t, J=7.7 Hz, CH_2CH_3), 1.24 (1H, brs, OH), 1.65–1.80 (2H, m, CH_2CH_3), 3.40–3.60 (1H, m, C-2H), 3.82 (1H, dd, J=4.0, 12.0 Hz, $CH_\alpha H_\beta OH$), 3.87 and 3.92 (6H, 2s, 3H each, 2×OCH_3), 3.95 (1H, dd, J=12.0, 15.0 Hz, $CH_\alpha H_\beta OH$), 6.50 (1H, d, J=9.1 Hz, C-5′H), 7.56 (1H, d, J=9.1 Hz, C-6′H) and 12.71 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 11.74 (CH_2CH_3), 22.82 (CH_2CH_3), 48.87 (C-2), 56.02 and 60.55 (2×OCH_3), 62.79 (CH_2OH), 102.95 (C-5′), 114.98 (C-1′), 126.61 (C-6′), 136.56 (C-3′), 157.66 and 158.68 (C-2′ and C-4′) and 208.68 (C=O); m/z, EI-MS: 254 $[M]^+$ (15), 236 (8), 195 (13), 181 (100), 152 (10), 120 (8), 86 (44), 69 (19) and 55 (8).

(±)-1-(4-Benzyloxy-2-hydroxyphenyl)-3-hydroxy-2-phenylpropanone (2i). Colourless viscous oil; yield 58%; R_f 0.52 (petroleum ether/ethyl acetate, 4:1); ν_{max} ($CHCl_3$): 3441 (OH), 2934, 1627 (C=O), 1580, 1455, 1303, 1250, 1147, 1035 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.50 (1H, brs, OH), 3.84 (1H, dd, J=4.5, 12.0 Hz, C-3H$_\alpha$), 4.25 (1H, dd, J=7.5, 12.0 Hz, C-3H$_\beta$), 4.74 (1H, dd, J=4.5 and 9.0 Hz, C-2H), 5.04 (2H, s, OCH_2Ph), 6.40 (1H, dd, J=3.0 and 7.5 Hz, C-5′H), 6.49 (1H, d, J=3.0 Hz, C-3′H), 7.22–7.24 (10H, m, C-2″H, C-3″H, C-4″H, C-5″H, C-6″H and $CH_2C_6H_5$), 7.64 (1H, d, J=9.0Hz, C-6′H), 12.70 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 56.0 (C-2), 65.0 (C-3), 71.0 (OCH_2Ph), 102.5 (C-3′), 109.0 (C-5′), 114.0 (C-4″), 128.0 (C-2″, C-6″, C-2‴ and C-6‴), 128.7 (C-4‴), 129.0 (C-1‴), 129.3 (C-3″, C-5″, C-3‴ and C-5‴), 129.7 (C-1″), 136.0 (C-6′), 137.0 (C-1′), 165.6 (C-2′), 166.4 (C-4′), 204.0 (C=O).

(±)-1-(4-Benzyloxy-2-hydroxyphenyl)-3-hydroxy-2-(4-methoxyphenyl)- propanone (2j). Thick brownish oil; yield 66%; R_f 0.50 (petroleum ether/ethyl acetate, 4:1); ν_{max} ($CHCl_3$): 3441 (OH), 3032, 1627 (C=O), 1612, 1580, 1455, 1369, 1303, 1250, 1183, 1071 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.95 (1H, brs, OH), 3.65 (3H, s, OCH_3), 3.83 (1H, dd, J=4.5, 12.0 Hz, C-3H$_\alpha$), 4.23 (1H, dd,J=9.0, 12.0 Hz, C-3H$_\beta$), 4.67 (1H, dd, J=4.5 and 9.0 Hz, C-2H), 5.10 (2H, s, $OCH_2C_6H_5$), 6.42 (1H, dd, J=3.4 and 8.4 Hz, C-3′H), 6.51 (1H, d, J=3.4 Hz, C-5′H), 6.87 (2H, d, J=9.0 Hz, C-3″H and C-5″H), 7.24 (2H, d, J=9.0 Hz, C-2″H and C-6″H), 7.34–7.38 (5H, m, $OCH_2C_6H_5$), 7.70 (1H, d, J=9.0Hz, C-6′H), 12.85 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 55.5 (C-2), 57.0 (OCH_3), 65.5 (C-3), 71.0 ($OCH_2C_6H_5$), 102.5 (C-3′), 109.0 (C-5′), 114.1 and 115.4 (C-2‴, C-6‴ and C-3″, C-5″), 128.2 (C-2″ and C-6″), 129.0 (C-1‴), 129.2 (C-4‴), 129.3 (C-3‴ and C-5‴), 130.0 (C-1″), 133.0 (C-6′), 136.5 (C-1′), 159.8 (C-2′), 165.9 (C-4′), 167.0 (C-4″), 205.0 (C=O).

(±)-2-Hydroxymethyl-1-(2-hydroxyphenyl)-3-(3,4-methylenedioxyphenyl)- propanone (2k). Thick brownish oil; yield 45%; R_f 0.42 (petroleum ether/ethyl acetate, 4:1); ν_{max} ($CHCl_3$): 2923, 1633 (C=O), 1609, 1579, 1488, 1358, 1289, 1245, 1157, 1039, 960 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.40 (1H, brs, OH), 2.90 and 3.00 (1H each, 2m, C-3H$_\alpha$ and C-3H$_\beta$), 3.86–3.89 (3H, m, C-2H and CH_2OH), 5.90 (2H, s, OCH_2O), 6.68 (3H, m, C-2″H, C-3′H and C-6″H), 6.88 (1H, m, C-5′H), 6.98 (1H, d, J=7.5 Hz, C-5″H), 7.46 (1H, m, C-4′H), 7.73 (1H, d, J=9.0 Hz, C-6′H), 12.25 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 31.0 (C-2), 51.0 (C-3), 64.0 (CH_2OH), 102.0 (OCH_2O), 109.0 (C-3′), 110.0 (C-2″), 119.6 (C-6″), 120.0 (C-5″), 120.5 (C-1″), 123.0 (C-4′), 131.0 (C-6′), 133.0 (C-5′), 137.9 (C-1′), 147.5 and 148.5 (C-3″, C-4″),164.0 (C-2′), 201.0 (C=O); m/z, EI-MS: 300 $[M]^+$ (50), 282 (15), 269 (60), 162 (10), 161 (9), 135 (100), 121 (98), 89 (15), 77 (22), 65 (25).

(±)-1-(2,4-Dihydroxyphenyl)-3-hydroxy-2-phenylpropanone (2l). To a solution of 1-(4-benzyloxy-2-hydroxyphenyl)-3-hydroxy-2-phenylpropanone (**2i**, 500 mg) in ethyl acetate (15 mL), Pd-C (10%, 50 mg) was added and the reaction mixture was stirred under hydrogen at atmospheric pressure at 25–30 °C, progress of the reaction was monitored by TLC (petroleum ether/ethyl acetate, 3:2). After completion (3 h), the catalyst was filtered off, solvent removed under vacuum to afford **2l** as a white solid (320 mg, 86% yield); mp 90–91 °C; R_f 0.32 (petroleum ether/ethyl acetate, 3:2); ν_{max} ($CHCl_3$): 3423, 2939, 1620, 1491, 1439, 1329, 1256, 1160, 1051, 940, 821 and 753 cm^{-1}; δ_H (300 MHz, CD_3OD): 3.30 (1H, brs, OH), 3.72 (1H, dd, J=6.0 Hz and 10.5 Hz, C-3H$_\alpha$), 4.30 (1H, dd, J=8.0, 10.5 Hz, C-3H$_\beta$), 4.77 (1H, dd, J=6.0 and 8.0 Hz, C-2H), 6.23 (1H, d, J=3.0 Hz, C-3′H), 6.28 (1H, dd, J=3.0 and 9.0 Hz, C-5′H), 7.24–7.32 (5H, m, C-2″H, C-3″H, C-4″H, C-5″H and C-6″H), 7.78 (1H, d, J=9.0 Hz, C-6′H), 12.70 (1H, s, chelated OH); δ_C (75.5 MHz, CD_3OD): 56.5 (C-2), 65.0 (C-3), 103.5 (C-5′), 109.0 (C-3′), 114.0 (C-4″), 129.4 (C-3″ and C-5″), 129.7 (C-1″), 130.2 (C-2″ and C-6″), 134.2 (C-6′), 138.6 (C-1′), 166.5 (C-4′), 167.5 (C-2′) and 204.0 (C=O).

General method of lipase-catalysed acetylation of hydroxymethylated aryl alkyl ketones

To a solution of the hydroxymethylated ketone (±)-**2a**–**2l** (2.0 mmol) in anhydrous THF/DIPE (20 mL) was added vinyl acetate (4.4 mmol) as the acylating agent and the lipase (half the weight of the ketone). The reaction mixture was incubated at 40 °C and the progress of the reaction was monitored periodically by HPLC/TLC examination. After 50% conversion, the reaction was quenched by filtering off the enzyme and the filterate concentrated under vacuo; the thick oil so obtained was column chromatographed over silica gel using a gradient system of petroleum ether/ethyl acetate as eluent to afford the corresponding acetates and the unreacted hydroxy compounds.

(+)-3-Acetoxy-1-(2-hydroxy-4-methoxyphenyl)-2-methylpropanone (3a). Colourless viscous oil; yield 48%; R_f 0.40 (petroleum ether/ethyl acetate, 17:3); λ_{max} (MeOH): 217, 234, 281, 318 nm; ν_{max} (Nujol): 2937, 1745 ($OCOCH_3$), 1632 (C=O), 1510, 1463, 1376, 1220, 1163, 1124, 1036, 983 cm^{-1}; δ_H (300 MHz, $CHCl_3$): 1.25 (3H, d, $J=6.9$ Hz, CH_3), 1.99 (3H, s, $OCOCH_3$), 3.75–3.85 (4H, m, OCH_3 and C-2H), 4.17 (1H, dd, $J=5.8$, 10.8 Hz, C-3H$_\alpha$), 4.40 (1H, dd, $J=8.2$, 10.8 Hz, C-3H$_\beta$), 6.45–6.48 (2H, m, C-3′H and C-5′H), 7.69 (1H, d, $J=8.6$ Hz, C-6′H), 12.82 (1H, s, chelated OH); δ_C (100.6 MHz, $CDCl_3$): 15.10 (CH_3), 20.86 ($OCOCH_3$), 39.21 (C-2), 55.65 (OCH_3), 65.72 (C-3), 101.15 and 107.92 (C-3′ and C-5′), 112.87 (C-1′), 131.49 (C-6′), 166.15 and 166.39 (C-2′ and C-4′), 170.95 ($OCOCH_3$), 205.27 (C=O); *m/z* EI-MS: 252 $[M]^+$ (42), 238 (7), 210 (22), 192 (80), 177 (33), 151 (100), 108 (35), 95 (40), 71 (71), 57 (65), 43 (85).

(−)-2-Acetoxymethyl-1-(2-hydroxy-4-methoxyphenyl)-butan-1-one (3b). Colourless viscous oil; yield 66%; R_f 0.45 (petroleum ether/ethyl acetate, 11:2); λ_{max} (MeOH): 214, 230, 278, 317 nm; ν_{max} (Nujol): 2929, 2853, 1747 ($OCOCH_3$), 1631 (C=O), 1510, 1462, 1376, 1220, 1162, 1124, 1038 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.93 (3H, t, $J=7.5$ Hz, C-4H), 1.56–1.70 (1H, m, C-3H$_\alpha$), 1.73–1.88 (1H, m, C-3H$_\beta$), 1.96 (3H, s, $OCOCH_3$), 3.64–3.75 (1H, m, C-2H), 3.85 (3H, s, OCH_3), 4.27 (1H, dd, $J=5.4$, 10.7 Hz, CH$_\alpha$H$_\beta$OAc), 4.36 (1H, dd, $J=8.7$, 10.7 Hz, CH$_\alpha$H$_\beta$OAc), 6.45–6.48 (2H, m, C-3′H and C-5′H), 7.69 (1H, d, $J=8.6$ Hz, C-6′H), 12.95 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 11.12 (C-4), 20.36 (C-3), 22.65 ($COCH_3$), 45.36 (C-2), 55.18 (OCH_3), 64.40 (CH_2OAc), 101.44 and 107.39 (C-3′ and C-5′), 113.58 (C-1′), 131.23 (C-6′), 165.62 and 166.00 (C-2′ and C-4′), 174.85 ($OCOCH_3$), 204.89 (C=O); *m/z*, EI-MS: 266 $[M]^+$ (70), 206 (80), 177 (54), 151 (100), 122 (12), 108 (41), 65 (17), 52 (26), 43 (85).

(−)-2-Acetoxymethyl-1-(2-hydroxy-4-methoxyphenyl)-octan-1-one (3c). Colourless viscous oil; yield 70%; R_f 0.35 (petroleum ether/ethyl acetate, 19:1); λ_{max} (MeOH): 214, 230, 278 nm; ν_{max} (Nujol): 2929, 2857, 1745 ($OCOCH_3$), 1632 (C=O), 1509, 1464, 1444, 1376, 1238, 1162, 1125, 1033, 982 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.85 (3H, t, $J=6.8$ Hz, C-8H), 1.24–1.26 (8H, m, C-4H, C-5H, C-6H and C-7H), 1.53–1.58 (1H, m, C-3H$_\alpha$), 1.74–1.78 (1H, m, C-3H$_\beta$), 1.95 (3H, s, $OCOCH_3$), 3.68–3.78 (1H, m, C-2H), 3.85 (3H, s, OCH_3), 4.23–4.37 (2H, m, CH_2OAc), 6.45–6.48 (2H, m, C-3′H and C-5′H), 7.68 (1H, d, $J=8.6$ Hz, C-6′H), 12.98 (1H, s, chelated OH); δ_C (100 MHz, $CDCl_3$): 13.87 (C-8), 20.71 ($OCOCH_3$), 22.40, 26.98, 29.20, 29.76 and 31.37 (5×CH_2), 44.22 (C-2), 55.49 (OCH_3), 65.01 (CH_2OAc), 100.93 (C-3′), 107.73 (C-5′), 113.79 (C-1′), 131.43 (C-6′), 165.88 and 166.25 (C-2′ and C-4′), 170.81 ($OCOCH_3$), 205.32 (C=O); *m/z*, EI-MS: 322 $[M]^+$ (20), 284 (5), 262 (42), 178 (80), 177 (37), 151 (100), 150 (18), 149 (14), 123 (7), 111 (12), 108 (22), 95 (27), 74 (4), 73 (37), 57 (55).

(−)-2-Acetoxymethyl-1-(2-hydroxy-4-methoxyphenyl)-dodecan-1-one (3d). Colourless viscous oil; yield 50%; R_f 0.45 (petroleum ether/ethyl acetate, 19:1); λ_{max} (MeOH): 213, 228, 277 nm; ν_{max} (Nujol): 2927, 2854, 1745 ($OCOCH_3$), 1628 (C=O), 1509, 1464, 1444, 1376, 1241, 1163, 1126, 1033, 980 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.87 (3H, t, $J=6.4$ Hz, C-12H), 1.22 (16H, brs, C-4H, C-5H, C-6H, C-7H, C-8H, C-9H, C-10H and C-11H), 1.49–1.57 (1H, m, C-3H$_\alpha$), 1.69–1.78 (1H, m, C-3H$_\beta$), 1.95 (3H, s, $OCOCH_3$), 3.68–3.78 (1H, m, C-2H), 3.85 (3H, s, OCH_3), 4.23–4.37 (2H, m, CH_2OAc), 6.45–6.48 (2H, m, C-3′H and C-5′H), 7.68 (1H, d, $J=8.7$ Hz, C-6′H), 12.98 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 14.12 (C-12), 19.84 ($OCOCH_3$), 20.83, 22.69, 27.17, 28.73, 29.32, 29.54, 29.67, 29.91, 31.89 (9×CH_2), 44.37 (C-2), 55.62 (OCH_3), 65.12 (CH_2OAc), 101.08 (C-3′), 107.86 (C-5′), 113.95 (C-1′), 131.59 (C-6′), 166.05 and 166.40 (C-2′ and C-4′), 170.92 ($OCOCH_3$), 205.48 (C=O); *m/z*, EI-MS: 378 $[M]^+$ (2), 318 (10), 178 (40), 151 (100), 95 (5), 43 (4).

(+)-3-Acetoxy-1-(2-hydroxy-3,4-dimethoxyphenyl)-2-methylpropanone (3e). Colourless viscous oil; yield 56%; R_f 0.45 (petroleum ether/ethyl acetate, 3:1); λ_{max} (MeOH): 221, 286 nm; ν_{max} (Nujol): 2935, 1744 ($OCOCH_3$), 1631 (C=O), 1507, 1462, 1423, 1376, 1270, 1183, 1067, 1035 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.26 (3H, d, $J=7.0$ Hz, CH_3), 2.00 (3H, s, $OCOCH_3$), 3.76–3.86 (1H, m, C-2H), 3.90 and 3.99 (6H, 2s, 3H each, 2×OCH_3), 4.17 (1H, dd, $J=5.8$, 10.8 Hz, C-3H$_\alpha$), 4.41 (1H, dd, $J=8.1$, 10.8 Hz, C-3H$_\beta$), 6.54 (1H, d, $J=9.1$ Hz, C-5′H), 7.58 (1H, d, $J=9.1$ Hz, C-6′H), 12.63 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 14.95 (CH_3), 20.73 ($COCH_3$), 39.33 (C-2), 56.10 and 60.57 (2×OCH_3), 65.62 (C-3), 102.67 (C-5′), 114.22 (C-1′), 126.23 (C-6′), 136.72 (C-3′), 157.74 and 158.72 (C-2′ and C-4′), 170.79 ($OCOCH_3$), 205.92 (C=O); *m/z,* EI-MS: 282 $[M]^+$ (50), 240 (3), 222 (80), 207 (51), 181 (100), 166 (45), 148 (55), 120 (47), 95 (26), 55 (21), 43 (95).

(+)-2-Acetoxymethyl-1-(2-hydroxy-3,4-dimethoxyphenyl)-butan-1-one (3f). Colourless viscous oil; yield 62%; R_f 0.35 (petroleum ether/ethyl acetate, 4:1); λ_{max} (MeOH): 219, 286 nm; ν_{max} (Nujol): 2934, 1744 ($OCOCH_3$), 1630 (C=O), 1506, 1448, 1423, 1377, 1276, 1120, 1067, 1041 cm^{-1}; δ_H (250 MHz, $CDCl_3$): 0.86 (3H, t, $J=8.4$ Hz, C-4H), 1.56–1.62 (1H, m, C-3H$_\alpha$), 1.64–1.70 (1H, m, C-3H$_\beta$), 1.95 (3H, s, $OCOCH_3$), 3.65–3.71 (1H, m, C-2H), 3.89 and 4.23 (6H, 2s, 3H each, 2×OCH_3), 4.25–4.39 (2H, m, CH_2OAc), 6.50 (1H, d, $J=9.0$ Hz, C-5′H), 7.55 (1H, d, $J=9.0$ Hz, C-6′H), 12.73 (1H, s, chelated OH); δ_C (62.5 MHz, $CDCl_3$): 11.44 (C-4), 20.71 (C-3), 23.01 ($COCH_3$), 45.77 (C-2), 56.02 and 60.55 (2×OCH_3), 64.66 (CH_2OAc), 102.88 (C-5′), 115.24 (C-1′), 126.30 (C-6′), 136.55 (C-3′), 158.66 and 157.60 (C-2′ and C-4′), 170.82 ($OCOCH_3$), 205.90 (C=O); *m/z,* EI-MS: 296 $[M]^+$ (55), 236 (95), 221 (32), 207 (34), 181 (100), 166 (18), 86 (78), 74 (31), 73 (30), 69 (64), 55 (42).

(+)-3-Acetoxy-1-(4-methoxyphenyl)-2-methylpropanone (3g). Colourless viscous oil; yield 77%; R_f 0.40 (petroleum ether/ethyl acetate, 9:1); λ_{max} (MeOH): 220, 276 nm; ν_{max} (Nujol): 2938, 2846, 1744 ($OCOCH_3$), 1625 (C=O), 1601, 1574, 1511, 1462, 1421, 1375, 1309, 1238, 1175, 1035, 975 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.22 (3H, d, $J=7.0$ Hz, CH_3), 1.96 (3H, s, $OCOCH_3$), 3.76–3.85

(1H, m, C-2H), 3.88 (3H, s, OCH_3), 4.17 (1H, dd, $J=5.9$, 10.7 Hz, C-3H$_\alpha$), 4.42 (1H, dd, $J=7.9$, 10.7 Hz, C-3H$_\beta$), 6.96 (2H, d, $J=8.5$ Hz, C-3′H and C-5′H), 7.96 (2H, d, $J=8.5$ Hz, C-2′H and C-6′H); δ_C (75.5 MHz, $CDCl_3$): 14.78 (CH_3), 20.84 ($OCO\mathit{C}H_3$), 39.56 (C-2), 55.51 (OCH_3), 66.14 (C-3), 113.92 (C-3′ and C-5′), 129.20 (C-1′), 130.70 (C-2′ and C-6′), 164.00 (C-4′), 171.00 ($O\mathit{C}OCH_3$), 200.00 (C=O); *m/z*, EI-MS: 236 $[M]^+$ (20), 194 (17), 176 (53), 135 (100), 121 (10), 107 (44), 92 (73), 77 (82), 64 (30), 43 (85).

(+)-3-Acetoxy-1-(2-hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)-propanone (3h). Colourless oil; ν_{max} ($CHCl_3$): 2956, 1739 ($OCOCH_3$), 1628 (C=O), 1579, 1459, 1304, 1249, 1218, 1180, 1151, 1133 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.00 (3H, s, $OCOCH_3$), 3.75 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 4.34 (1H, dd, $J=6.0$ and 10.5, C-3H$_\alpha$), 4.73 (1H, dd, $J=9.0$, 10.5 Hz, C-3H$_\beta$), 4.83 (1H, dd, $J=6.0$ and 9.0 Hz, C-2H), 6.36 (1H, dd, $J=3.0$ and 9.0 Hz, C-5′H), 6.39 (1H, d, $J=3.0$ Hz, C-3′H), 6.84 (2H, d, $J=8.4$ Hz, C-3″H and C-5″H), 7.24 (2H, d, $J=8.4$ Hz, C-2″H and C-6″H), 7.64 (1H, d, $J=9.0$ Hz, C-6′H), 12.70 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 22.5 ($OCO\mathit{C}H_3$), 52.0 (C-2), 56.0 (OCH_3), 56.5 (OCH_3), 66.0 (C-3), 102.0 (C-3′), 109.0 (C-1″), 114.0 (C-5′), 116.0 (C-3″ and C-5″), 128.5 (C-6′), 130.5 (C-2″ and C-6″), 133.0 (C-1′), 161.0 (C-2′), 167.0 (C-4′ and C-4″), 172.0 (OCO), 202.5 (C=O).

(+)-3-Acetoxy-1-(2-hydroxy-4-benzyloxyphenyl)-2-phenyl-propanone (3i). Colourless oil; ν_{max} ($CHCl_3$): 3031, 1739 ($OCOCH_3$), 1628 (C=O), 1575, 1454, 1368, 1232, 1215, 1147, 1075, 1023 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.00 (3H, s, $OCOCH_3$), 4.38 (1H, dd, $J=6.0$ and 12.0, C-3H$_\alpha$), 4.77 (1H, dd, $J=9.0$, 12.0 Hz, C-3H$_\beta$), 4.88 (1H, dd, $J=6.0$ and 9.0 Hz, C-2H), 5.06 (2H, s, $OC\mathit{H}_2C_6H_5$), 6.44 (1H, dd, $J=3.0$ and 9.0 Hz, C-5′H), 6.49 (1H, d, $J=3.0$ Hz, C-3′H), 7.34–7.37 (10H, m, C-2″H, C-3″H, C-4″H, C-5″H, C-6″H, $OCH_2C_6\mathit{H}_5$), 7.66 (1H, d, $J=9.0$ Hz, C-6′H), 12.70 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 21.5 ($OCO\mathit{C}H_3$), 52.5 (C-2), 66.0 (C-3), 71.0 ($O\mathit{C}H_2C_6H_5$), 103.0 (C-3′), 109.0 (C-5′), 114.0 (C-1″), 128.3 (C-3″ and C-5″), 128.8 (C-4″) 129.0 (C-2″ and C-6″), 129.2 (C-1‴), 129.5 (C-3‴ and C-5‴), 130.1 (C-2‴ and C-6‴), 132.8 (C-4‴), 136.4 (C-6′), 136.6 (C-1′), 166.0 (C-2′), 167.0 (C-4′), 172.0 (OCO), 201.0 (C=O).

(+)-3-Acetoxy-1-(4-benzyloxy-2-hydroxyphenyl)-2-(4-methoxyphenyl)- propanone (3j). Thick brown oil; ν_{max} ($CHCl_3$): 2956, 1739 ($OCOCH_3$), 1628 (C=O), 1511, 1459, 1368, 1249, 1180, 1151 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.00 (3H, s, $OCOCH_3$), 3.75 (3H, s, OCH_3), 4.34 (1H, dd, $J=6.0$ and 12.0, C-3H$_\alpha$), 4.72 (1H, dd, $J=9.0$, 12.0 Hz, C-3H$_\beta$), 4.82 (1H, dd, $J=6.0$ and 9.0 Hz, C-2H), 5.06 (2H, s, $OC\mathit{H}_2C_6H_5$), 6.34 (1H, dd, $J=3.0$ and 9.0 Hz, C-5′H), 6.47 (1H, d, $J=3.0$ Hz, C-3′H), 6.85 (2H, d, $J=9.0$ Hz, C-3″H and C-5″H), 7.23 (2H, d, $J=9.0$ Hz, C-2″H and C-6″H), 7.36–7.38 (5H, m, $OCH_2C_6\mathit{H}_5$), 7.65 (1H, d, $J=9.0$ Hz, C-6′H), 12.70 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 21.5 ($OCO\mathit{C}H_3$), 51.5 (C-2), 56.0 (OCH_3), 66.0 (C-3), 71.0 ($O\mathit{C}H_2Ph$), 102.5 (C-5′), 108.5 (C-3′), 113.0 (C-1″ and C-1‴), 115.0 (C-3″ and C-5″), 127.5 (C-2‴ and C-6‴), 128.0 (C-4‴), 128.5 (C-3‴ and C-5‴), 130.0 (C-2″ and C-6″), 132.5 (C-6′), 137.0 (C-1′), 159.5 (C-4″), 166.5 (C-2′), 168.5 (C-4′), 171.0 (OCO), 201.0 (C=O).

(+)-2-Acetoxymethyl-1-(2-hydroxyphenyl)-3-(3,4-methylenedioxyphenyl)- propanone (3k). Brown coloured oil; ν_{max} ($CHCl_3$): 2922, 1741 ($OCOCH_3$),1635 (C=O), 1489, 1245, 1207, 1100, 1039 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.92 (3H, s, $OCOCH_3$), 2.78 (1H, dd, $J=7.5$, 13.5 Hz, C-3H$_\alpha$), 3.02 (1H, dd, $J=7.5$, 13.5 Hz, C-3H$_\beta$), 4.08 (1H, m, C-2H), 4.24 (1H, dd, $J=6.0$, 12.0 Hz, CH_αH$_\beta$OAc), 4.38 (1H, dd, $J=7.5$, 12.0 Hz, CH$_\alpha\mathit{H}_\beta$OAc), 5.86 (2H, s, OCH_2O), 6.58 (1H, dd, $J=3.0$ and 9.0 Hz, C-3′H), 6.63 (1H, d, $J=2.5$ Hz, C-2″H), 6.66 (1H, d,$J=9.0$ Hz, C-5″H), 6.86 (1H, m, C-5′H), 6.96 (1H, dd, $J=2.5$ and 9.0 Hz, C-6″H), 7.45 (1H, m, C-4′H), 7.70 (1H, dd, $J=3.0$, 9.0 Hz, C-6′H), 12.30 (1H, s, chelated OH); δ_C (75.5 MHz, $CDCl_3$): 22.0 ($OCO\mathit{C}H_3$), 36.0 (C-3), 47.5 (C-2), 65.0 ($\mathit{C}H_2OAc$), 101.0 (OCH_2O), 109.0 (C-3′), 110.0 (C-2″), 119.0 (C-6″), 119.5 (C-5″), 120.0 (C-1″), 123.0 (C-4′), 130.5 (C-6′), 132.5 (C-5′), 137.5 (C-1′), 146.5 (C-4″), 148.0 (C-3″), 164.0 (C-2′), 171.0 (OCO), 201.0 (C=O); *m/z*, EI-MS: 342 $[M]^+$ (10), 282 (30), 162 (3), 161 (10), 135 (65), 121 (100), 905 (7), 93 (10), 77 (30), 43 (30).

(−)-3-Acetoxy-1-(2,4-dihydroxyphenyl)-2-phenylpropanone (3l). White solid; mp 115–116 °C; yield 58%; ν_{max}: 2956, 1739, 1628, 1579, 1459, 1368, 1304, 1218, 1151, 1133 and 945 cm^{-1}; δ_H (300 MHz, CD_3OD): 1.96 (3H, s, $OCOCH_3$), 4.30 (1H, dd, $J=4.5$, 12.0 Hz, CH_αH$_\beta$OAc), 4.72 (1H, dd, $J=9.0$, 12.0 Hz, CH$_\alpha\mathit{H}_\beta$OAc), 4.97 (1H, dd, $J=4.5$ and 9.0 Hz, C-2H), 6.24 (1H, d, $J=2.5$ Hz, C-3′H), 6.28 (1H, dd, $J=3.0$ and 8.0 Hz, C-5′H), 7.25–7.32 (5H, m, C-2″H, C-3″H, C-4″H, C-5″H and C-6″H), 7.71 (1H, d, $J=9.0$ Hz, C-6′H), 12.60 (1H, s, chelated OH); δ_C (75.5 MHz, CD_3OD): 21.0 ($OCO\mathit{C}H_3$), 52.5 (C-3), 66.0 (C-2), 104.0 (C-3′), 109.5 (C-5′), 113.5 (C-6′), 129.0-134.0 (C-2″, C-3″, C-4″, C-5″ and C-6″),134.0 (C-1″),137.5 (C-1′), 166.5 (C-4′), 167.0 (C-2′), 172.5 (OCO) and 201.0 (C=O).

General procedure for the enzymatic deacetylation of the acetates 3a–3g

To a solution of the acetylated ketones **3a**–**3g** (100 mg) in diisopropyl ether (10–15 mL) containing *n*-butanol (5 mmol), *C. rugosa* lipase (100 mg) was added and the reaction mixture was stirred at 40–42 °C. On completion of deacetylation (checked upto 100% in all cases by TLC/HPLC), the reaction mixture was filtered and the filterate concentrated in vacuo to get the deacetylated hydroxymethylated ketones **2a**–**2g**.

General procedure for the chemical hydrolysis of acetates 3h–3l

To a solution of the acetylated ketones **3h**–**3l** (50 mg) in analytical grade MeOH (3.0 mL), 2–3 drops of analytical grade HCl were added and the mixture was stirred till deacetylation was complete (4–5 h) at 28–30 °C. The reaction was quenched with water, and extracted with dichloromethane (4×10 mL). The organic phases were

combined and washed with brine and dried. Evaporation of the solvent afforded the crude product, which was purified by column chromatography over silica gel using petroleum ether/ethyl acetate mixture as eluent to give the desired alcohols **2h**–**2l**.

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