Bioorganic Chemistry **27,** 119–134 (1999)
Article ID bioo.1998.1117, available online at http://www.idealibrary.com on IDEAL®

Enzyme-Catalyzed Chemoselective Transesterification Reactions on Hydroxymethylated Phenolic Compounds

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Received October 30, 1998

The chemoselective capabilities of porcine pancreatic lipase (PPL) in tetrahydrofuran and *Candida rugosa* lipase (CRL) in diisopropyl ether have been investigated for selective acetylation and deacetylation of hydroxymethylated phenols and hydroxyaryl alkyl ketones and their peracetylated derivatives. Both PPL and CRL exhibited exclusive selectivity for the acetylation of alcoholic hydroxyl group over the phenolic hydroxyl group(s) of the hydroxymethylated phenols **1–5** and aryl alkyl ketones **6–9**, and for the deacetylation of ester group involving the phenolic hydroxyl group over the ester group involving alcoholic hydroxyl of the peracetates **19–24**. The preliminary results indicate that this strategy of chemoselective acetylation can also be used in the enantiomeric resolution of racemic ketones **6–9**. Single crystal X-ray diffraction studies have confirmed the structures of compounds **4, 15**, and **17**.

INTRODUCTION

In recent years, chemoenzymatic synthetic strategies have become standard techniques for the preparation of a variety of chiral and nonchiral precursors and target molecules (*1*,*2*). Among the different enzymatic methodologies, lipase-catalyzed acylations and deacylations represent an important class of enzymatic transformations in organic synthesis (*3*), wider applications of lipases are attributed to their low-cost and tolerance toward a variety of organic molecules (*4*). In recent years, we have successfully used lipases from porcine pancreas (PPL) and *Candida rugosa* (CRL) for the regioselective deacetylation of peracetates of different classes of polyphenolics (*5*) and for the regioselective and enantioselective esterifications of polyols (*6*). It has been observed that the change of enzyme may lead to complementary result. For example, use of lipases from *Aspergillus* species for the deacetylation of 2,4-diacetoxyphenyl alkyl ketones led to the formation of 2-hydroxy-4-acetoxy ketones (*7*), which is complementary to the result of deacetylation catalyzed by PPL or CRL (*5*).

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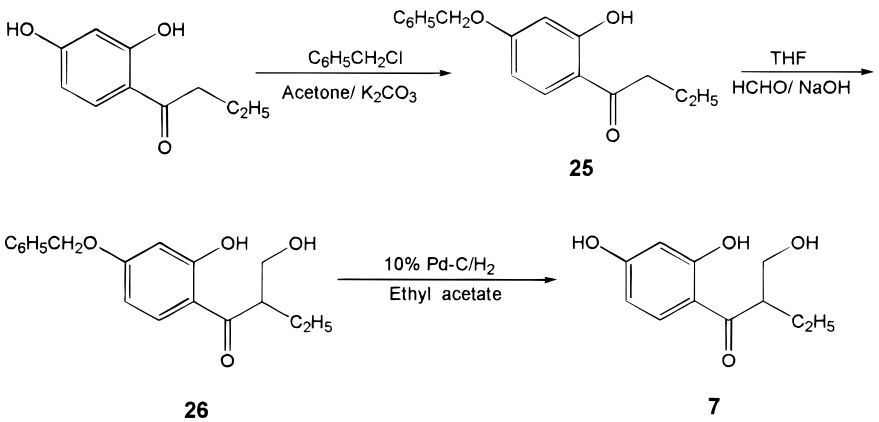
0045-2068/99 $30.00

So far, enzymes have seldom been employed for the chemoselective discrimination between the phenolic and alcoholic hydroxyl groups present in the same molecule, there is only one report in literature where such selection is achieved on 2- and 4-hydroxymethylphenols *via* enzymatic catalysis with *Aspergillus niger* lipase (*8*). We have employed PPL in tetrahydrofuran (THF) and CRL in diisopropyl ether (DIPE), relatively cheaper and more easily accessible enzymes than *Aspergillus niger* lipase for the selective acetylation of hydroxymethylated phenols and aryl alkyl ketones, novel precursors for the synthesis of phenyl alkyl carbinols (*9*), and 3-alkyl/aryl chromanones and their bioactive analogs (*10*). Further, the enzyme substrate ratio used in the present investigation is just half of that used during selective acetylation with *A. niger* lipase (*8*). The enzymatic methodology developed for chemoselective acetylation of hydroxymethylated phenols and aryl alkyl ketones has successfully been used for the enantioselective resolution of racemic hydroxymethylated aryl alkyl ketones **6–9**, which in turn can be used for the synthesis of optically pure isoflavanones and 3-alkylchromanones (*10*), which have not been synthesized in optically enriched/pure form thus far.

RESULTS AND DISCUSSION

The starting phenol, 2-hydroxymethylphenol (**1**) was procured from Aldrich Chemical Co. (U.S.A.) and other hydroxymethylated phenols; i.e., 4-hydroxymethylphenol (**2**), 4-hydroxymethyl-2-methoxyphenol (**3**), 5-hydroxymethyl-2-methoxyphenol (**4**), and 2-hydroxymethyl-6-methoxyphenol (**5**) were prepared by reduction of the corresponding aldehydes, i.e., 4-hydroxybenzaldehyde, 4-hydroxy-3-methoxybenzaldehyde, 3-hydroxy-4-methoxybenzaldehyde, and 2-hydroxy-3-methoxybenzaldehyde, respectively, with $NaBH_4$ in 80–90% yields. The diacetates of hydroxymethylated phenols **1–5**; i.e., 2-acetoxymethylphenyl acetate (**19**), 4-acetoxymethylphenyl acetate (**20**), 4-acetoxymethyl-2-methoxyphenyl acetate (**21**), 5-acetoxymethyl-2-methoxyphenyl acetate (**22**), and 2-acetoxymethyl-6-methoxyphenyl acetate (**23**) were prepared by



SCHEME 1. Preparation of 2-ethyl-3-hydroxy-1-(2′,4′-dihydroxyphenyl)propanone (**7**).

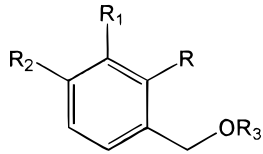
1. R=OH; R_1=R_2 =R_3= H

2. R=R_1=R_3= H; R_2=OH

3. R=R_3=H; R_1=OCH_3; R_2=OH

4. R=R_3= H; R_1= OH; R_2=OCH_3

5. R=OH; R_1=OCH_3; R_2=R_3=H



10. R=OH; R_1=R_2=H; R_3=$COCH_3$

11. R=R_1= H; R_2=OH; R_3=$COCH_3$

12. R= H; R_1=OCH_3; R_2=OH; R_3=$COCH_3$

13. R=H; R_1=OH; R_2=OCH_3; R_3=$COCH_3$

14. R=OH; R_1=OCH_3; R_2=H; R_3=$COCH_3$

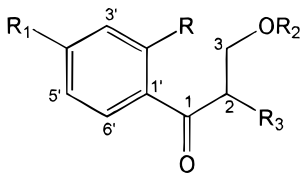
19. R=$OCOCH_3$; R_1=R_2=H; R_3=$COCH_3$

20. R=R_1=H; R_2=$OCOCH_3$; R_3=$COCH_3$

21. R=H; R_1=OCH_3; R_2=$OCOCH_3$; R_3=$COCH_3$

22. R=H; R_1=$OCOCH_3$; R_2=OCH_3; R_3=$COCH_3$

23. R=$OCOCH_3$; R_1=OCH_3; R_2=H; R_3=$COCH_3$



6. R=R_2= H; R_1= OH; R_3=CH_3

7. R=R_1=OH; R_2= H; R_3=CH_2CH_3

8. R=OH; R_1=OCH_3; R_2= H; R_3= C_6H_5

9. R=OH; R_1=R_2 = H; R_3=$CH_2C_6H_4(p)OCH_3$

15. R=H; R_1=OH; R_2=$COCH_3$; R_3=CH_3

16. R=R_1=OH; R_2=$COCH_3$; R_3=CH_2CH_3

17. R=OH; R_1=OCH_3; R_2=$COCH_3$; R_3=C_6H_5

18. R=OH; R_1=H; R_2=$COCH_3$; R_3= $CH_2C_6H_4(p)OCH_3$

24. R=H; R_1=$OCOCH_3$; R_2=$COCH_3$; R_3= CH_3

SCHEME 2

the acetic anhydride-pyridine method in the presence of catalytic amounts of dimethylaminopyridine (DMAP) in quantitative yields. The hitherto unknown diacetates **19** and **23** were identified on the basis of their spectral analysis, whereas the known hydroxymethylated phenols **2–5** and the known diacetates **20–22** were characterized by analysis of their spectral data and by comparison of their spectral and/or physical

data with those reported in literature (*11–13*). The structure of 5-hydroxymethyl-2-methoxyphenol (**4**) was also confirmed by its single crystal X-ray diffraction studies (Table 5). Though compound **22** has been synthesized earlier (*13*), its spectral data has not been reported and we herein report its complete data (*cf.* Experimental). The compound 3-hydroxy-1-(4′-hydroxyphenyl)-2-methylpropanone (**6**) was prepared by stirring a suspension of 4-hydroxypropiophenone in 37% formaldehyde and 0.5 N sodium hydroxide solution in a molar ratio of 1.0:1.1:1.1 at 28–30°C for 15 h (*14*). Further, 2-ethyl-3-hydroxy-1-(2′,4′-dihydroxyphenyl)propanone (**7**) was prepared by hydroxymethylation of 4-benzyloxy-2-hydroxybutyrophenone (**25**) (*15*) as above, followed by debenzylation of the hydroxymethylated ketone, 1-(4′-benzyloxy-2′-hydroxyphenyl)-2-ethyl-3-hydroxypropanone (**26**) by catalytic hydrogenation (Scheme 1). The hydroxypropanones, 3-hydroxy-1-(2′-hydroxy-4′-methoxyphenyl)-2-phenylpropanone (**8**) and 3-hydroxy-1-(2′-hydroxyphenyl)-2-(4″-methoxybenzyl)propanone (**9**) were prepared by reacting 2-hydroxy-4-methoxydesoxybenzoin (*16*) and 2′-hydroxy-4-methoxydihydrochalcone (*17*) with ethoxymethyl chloride in the presence of dry potassium carbonate in dry acetone in 65 and 70% yields, respectively. The diacetate, 3-acetoxy-1-(4′-acetoxyphenyl)-2-methylpropanone (**24**) was prepared as in the case of hydroxymethylated phenols in 98% yield. Attempts to prepare di/triacylated derivatives of **7, 8**, and **9** resulted in the enolization of ketonic carbonyl group and subsequent formation of the corresponding enolic peracetates as per our earlier observation in similar compounds (*18*). The hitherto unknown compounds **7, 9, 24**, and **26** were characterized on the basis of their spectral analysis and the known compounds **6** and **8** were characterized by their spectral analysis and comparison with the data reported in the literature (*14,16*).

To examine the chemoselective capabilities of PPL and CRL for the selective acetylation of two different types of hydroxyl groups, hydroxymethylated phenols **1–5** were incubated with vinyl acetate and PPL or CRL in THF and DIPE, respectively. Both the enzymes exhibited exclusive selectivity for the acetylation of aliphatic hydroxyl function over the phenolic hydroxyl, though the rate of acetylation catalyzed by CRL in DIPE was too slow with respect to PPL in THF. Thus, PPL-catalyzed acetylation of the hydroxymethylated phenols **1–5** afforded the monoacetates 2-acetoxymethylphenol (**10**), 4-acetoxymethylphenol (**11**), 4-acetoxymethyl-2-methoxyphenol (**12**), 5-acetoxymethyl-2-methoxyphenol (**13**), and 2-acetoxymethyl-6-methoxyphenol (**14**) exclusively in 95, 80, 90, 95, and 85% yields, respectively (Table 1). The results indicate that the turn over in PPL-catalyzed acetylation of hydroxymethylated phenols is almost quantitative. In addition to the selective acetylation studies on hydroxymethylated phenols, chemoselective capabilities of PPL and CRL were also investigated for the selective acetylation of hydroxymethylated aryl alkyl ketones. As in the case of acetylation of hydroxymethylated phenols, PPL and CRL exhibited 100% selectivity for the acetylation of aliphatic hydroxyl group with respect to phenolic hydroxyl group in hydroxymethylated aryl alkyl ketones. Thus, incubation of compounds **6** and **7** with PPL in THF afforded the monoacetoxy products, 3-acetoxy-1-(4′-hydroxyphenyl)-2-methylpropanone (**15**) and 3-acetoxy-2-ethyl-1-(2′,4′-dihydroxyphenyl)propanone (**16**) in 65 and 55% yields in 12 and 38 h (Table 1), respectively. It has been observed that PPL in THF catalyzes the acetylation of aliphatic hydroxyl group of **6** and **7** faster than CRL in DIPE, the rate of selective

TABLE 1

Selective Acetylation of Hydroxymethylated Phenols **1–5** and Aryl alkyl Ketones **6–9** Mediated by PPL in THF (A) and/or CRL in DIPE (B) at 42–45°C[a]

Substrate	Reaction condition	Time (h)	Product	Percentage yield
2-Hydroxymethylphenol (**1**)	A	120	2-Acetoxymethylphenol (**10**)(*8*)	95
4-Hydroxymethylphenol (**2**)(*11a*)	A	48	4-Acetoxymethylphenol (**11**)(*12*)	80
4-Hydroxymethyl-2-methoxyphenol (**3**)(*11b*)	A	24	4-Acetoxymethyl-2-methoxy-phenol (**12**)(*12*)	90
5-Hydroxymethyl-2-methoxyphenol (**4**)(*11b*)	A	96	5-Acetoxymethyl-2-methoxy-phenol (**13**)(*19*)	95
2-Hydroxymethyl-6-methoxyphenol (**5**)(*11c*)	A	120	2-Acetoxymethyl-6-methoxy-phenol (**14**)	85
3-Hydroxy-1-(4′-hydroxyphenyl)-2-methylpropanone (**6**)(*14*)	A/B	12/30	3-Acetoxy-1-(4′-hydroxyphenyl)-2-methylpropanone (**15**)	65
2-Ethyl-3-hydroxy-1-(2′,4′-dihydroxyphenyl)propanone (**7**)	A/B	38/72	3-Acetoxy-2-ethyl-1-(2′,4′-dihydroxyphenyl)propanone (**16**)	55
3-Hydroxy-1-(2′-hydroxy-4′-methoxyphenyl)-2-phenylpropanone (**8**)(*16*)	B	8	3-Acetoxy-1-(2′-hydroxy-4′-methoxyphenyl)-2-phenylpropanone (**17**)(*16*)	70
3-Hydroxy-1-(2′-hydroxyphenyl)-2-(4″-methoxybenzyl)propanone (**9**)	B	8	3-Acetoxy-1-(2′-hydroxyphenyl)-2-(4″-methoxybenzyl)propanone (**18**)	75

[a] All these reactions, when performed under identical conditions but without adding the lipase, did not yield any product.

acetylation of aliphatic hydroxyl function by the former is about 2.5 and 2 times faster, respectively, than the latter (Table 1). The hydroxymethylated aryl alkyl ketones **8** and **9** were poor substrates for PPL and no appreciable acetylation was observed even upon incubation for several days. However, CRL in DIPE catalyses the acetylation of compounds **8** and **9** to afford the monoacetates involving the aliphatic hydroxyl group, i.e., 3-acetoxy-1-(2′-hydroxy-4′-methoxyphenyl)-2-phenylpropanone (**17**) and 3-acetoxy-1-(2′-hydroxyphenyl)-2-(4″-methoxybenzyl)propanone (**18**) in 70 and 75% yields, respectively (Table 1). This result indicates that the substituent at C-2 position in compounds **6–9** plays an important role during their binding with PPL and CRL.

The hitherto unknown monoacetates **14, 15, 16**, and **18** were identified on the basis of their spectral analysis, while the known monoacetates **10–13** and **17** were identified on the basis of spectral analysis and their comparison with those reported in the literature (*8,12,16,19*). The formation of monoacetates involving aliphatic hydroxyl group during enzyme-catalyzed acetylation reactions has been well established as the carbinol protons in all the monoacetates (except in **16**) are deshielded (by $\Delta\delta$ 0.35–0.68 ppm) with respect to the corresponding protons in the respective hydroxylated compounds (Table 2). The presence of chelated and free phenolic hydroxyl groups at δ 12.87 and 9.99, respectively, and the absence of any resonance due to aliphatic hydroxyl group in the ^{1}H NMR spectrum of **16** in deuterated chloroform establishes the acetylation of aliphatic hydroxyl group in this compound as well. The compounds **16, 17**, and **18** gave dark brown Fe^{3+} coloration when their TLC spots were sprayed

TABLE 2

Comparison of Chemical Shift Values of Methylene Protons of the Starting Carbinols and in Their Corresponding Acetates

Carbinol	δ CH_2OH	Acetate	δ CH_2OCOCH_3	Deshielding effect (ppm)
1	4.78	**10**	5.20	0.42
2	4.54	**11**	5.08	0.54
3	4.51	**12**	5.00	0.49
4	4.49	**13**	5.05	0.56
5	4.70	**14**	5.18	0.48
6	3.59 and 3.66	**15**	4.10 and 4.34	0.51 and 0.68
7	4.33	**16**	4.23 and 4.32	
8	3.74 and 4.20	**17**	4.35 and 4.75	0.61 and 0.55
9	3.88	**18**	4.23 and 4.38	0.35 and 0.50

with 3% alcoholic $FeCl_3$ solution, thus indicating that the *ortho* (phenolic) hydroxy function to the nuclear carbonyl group is not acetylated in any of them. This is further proved by the presence of chelated hydroxyl group at δ 12.87, 12.68, and 12.31 in the ^{1}H NMR spectra of **16, 17**, and **18**, respectively. The X-ray crystallographic studies on the monoacetates **15** and **17** (Figs. 1 and 2) finally confirmed the involvement of the aliphatic hydroxyl group of **6** and **8** in ester formation during enzyme-catalyzed acetylation reaction.

In addition to the capabilities of PPL and CRL to catalyze the chemoselective

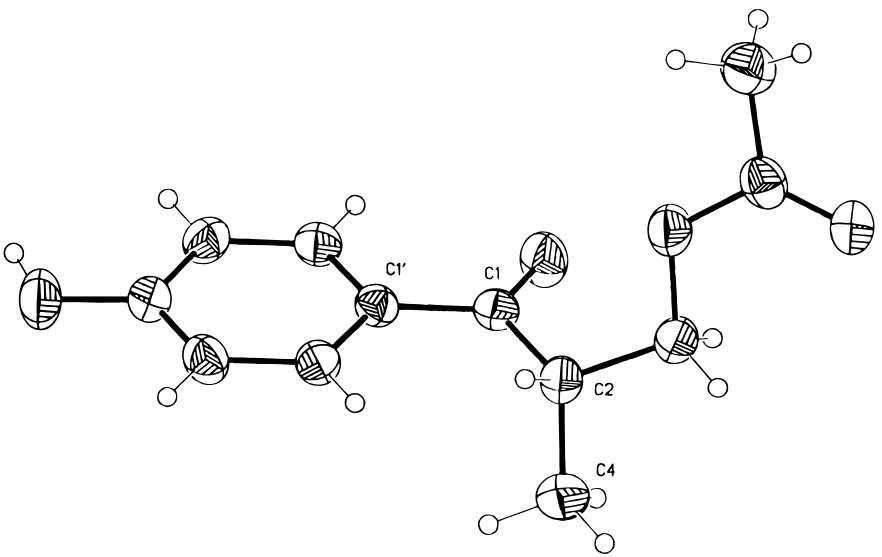


FIG. 1. Molecular structure of compound **15**. Displacement ellipsoids are shown at the 50% probability level.

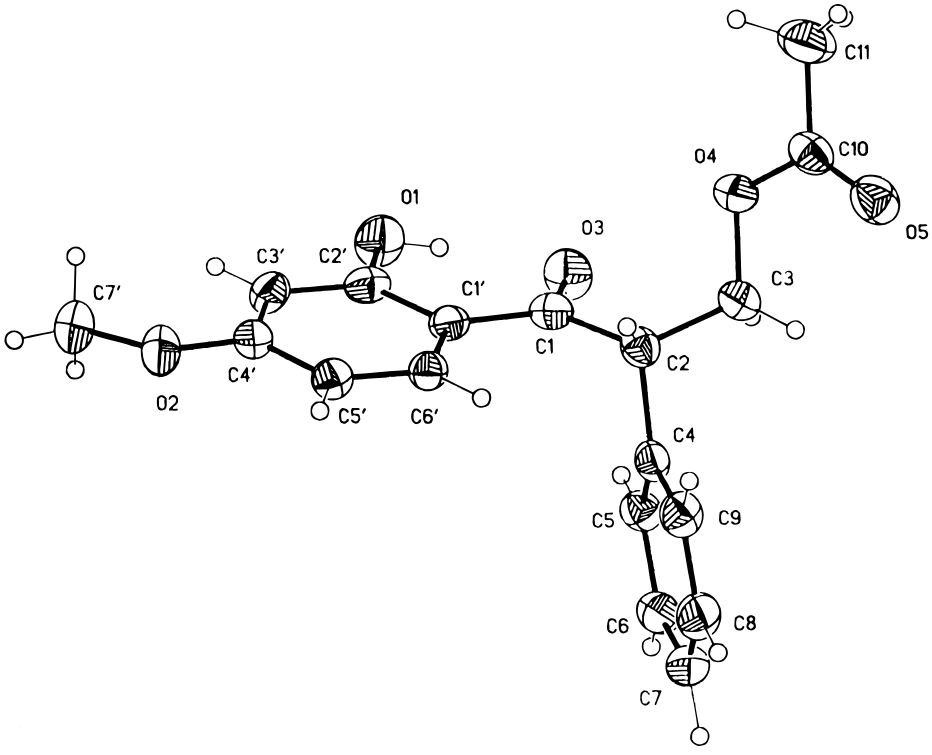


FIG. 2. Molecular structure of compound **17**. Displacement ellipsoids are shown at the 50% probability level.

acetylation of aliphatic hydroxyl groups of hydroxymethylated phenols and aryl alkyl ketones, we tried to extend these studies to enantiomeric resolution of racemic ketones **6–9**. The racemic hydroxymethylated aryl alkyl ketones **6** and **7**, and **8** and **9** were incubated with PPL in THF and CRL in DIPE, respectively, and the reactions were stopped by filtering off the enzyme after about 45% conversion of the dihydroxy ketone to monoacetate. The monoacetates and the unreacted dihydroxy ketones were separated on silica gel column with a gradient solvent system of petrol:ethyl acetate and their optical rotations measured. The monoacetates and the unreacted dihydroxy compounds were found to be optically active in each case (Table 3). The monoacetates were deacetylated enzymatically and the rotations of the dihydroxy compounds thus obtained were measured, the rotations of these compounds were found to be of the same order and had opposite sign to the rotation of the corresponding unreacted dihydroxy compound (Table 3). These observation revealed that the chemoselective acetylation is also accompanied by enantiomeric resolution of the racemic ketones **6–9**. The evaluation of enantiomeric excess (*ee*) of the monoacetates in each case is in progress by ^{1}H NMR spectral studies using diamagnetic anthryl chiral shift reagent and on chiral HPLC columns.

Together with enzyme-catalyzed acetylation, deacetylation reactions of peracetates

TABLE 3

Optical Rotations of Products Obtained after Enzymatic Acetylation of Compounds **6–9**[a] and Deacetylation of the Monoacetoxy Products[b]

Substrate (*racemic*)	Enzyme/ solvent	$[\alpha]^{25}_{D}$ Values of the compounds obtained by incubation with enzymes: Monoacetoxy-propanones	Unreacted Dihydroxy-propanones	Dihydroxypropanones obtained by the CRL-catalyzed deacetylation of the monoacetoxypropanones in DIPE (containing *n*-butanol)[c]
6	PPL/THF	+23.7	−26.2	+29.9
7	PPL/THF	+3.7	+6.6	−10.8
8	CRL/DIPE	−46.0	+16.0	−12.7
9	CRL/DIPE	+30.8	−25.6	+29.5

[a] All the enzyme-assisted reactions carried out for enantiomeric resolution studies were stopped by filtering off the enzyme after about 45% conversion (as seen on HPLC) of the starting racemic substrate to the product.

[b] All these acetylation and deacetylation reactions, when performed under identical conditions but without adding the lipase, did not yield any product.

[c] The specific rotations of the unreacted dihydroxypropanones are less than those of the corresponding dihydroxypropanones obtained by enzymatic deacetylation of the monoacetates, except in the case of compound **8**. This may be due to partial racemization of the unreacted dihydroxypropanones taking place during their separation from the monoacetoxypropanones on silica gel column, the deacetylated products of monoacetates did not require purification as they were found to be sufficiently pure on TLC/HPLC examination. Such partial racemization on silica gel due to its acidic nature is known in literature (*24*).

of hydroxymethylated phenols **19–23** and hydroxymethylated aryl alkyl ketone **24** catalysed by PPL in THF and CRL in DIPE were also studied. It has been found that the incubation of compounds **19–23** with CRL in DIPE catalyzes the deacetylation of ester group involving the phenolic hydroxyl function and afforded the monoacetates **10, 11, 12, 13**, and **14** (Table 4), respectively. None of the diacetates was a substrate for PPL in THF. In general, the deacetylation reactions on peracetates **19–23** catalyzed by CRL in DIPE were slow than the acetylation reactions on corresponding dihydroxy compounds **1–5** (Tables 1 and 4). In contrast to the selective deacetylation reactions on **19–23** which were catalysed by CRL in DIPE, the deacetylation reaction on 3-acetoxy-1-(4′-acetoxyphenyl)-2-methylpropanone (**24**) was catalyzed by PPL in THF affording the monoacetate **15** in 60% yield due to the selective deacetylation of ester function involving phenolic hydroxyl group over alcoholic hydroxyl (Table 4). The incubation of compound **24** with CRL in DIPE led to the formation of an inseparable mixture.

The enzymatic method developed for the chemoselective acetylation of hydroxymethylated phenols and aryl alkyl ketones may find applications in the efficient synthesis of phenyl alkyl carbinols, known for their chloretic properties, and for the synthesis of bioactive analogs of naturally occurring 3-alkylchromanones and isoflavanones, respectively. It has been demonstrated that this strategy of selective esterification also leads to enantiomeric resolution of racemic aryl alkyl ketones which in turn can be used for the synthesis of optically pure isoflavanones. Further, in the

TABLE 4

Selective Deacetylation of Peracetates of Hydroxymethylated Phenols **19–23** and Aryl alkyl Ketone **24** Mediated by PPL in THF (A) and CRL in DIPE (B) at 42–45°C[a]

Substrate	Reaction condition	Time (days)	Product	Percentage yield
2-Acetoxymethylphenyl acetate (**19**)	B	15	2-Acetoxymethylphenol (**10**)(*8*)	40
4-Acetoxymethylphenyl acetate (**20**)(*11a*, *12*)	B	2	4-Acetoxymethylphenol (**11**)(*12*)	60
4-Acetoxymethyl-2-methoxyphenyl acetate (**21**)(*12*)	B	12	4-Acetoxymethyl-2-methoxyphenol (**12**)(*12*)	50
5-Acetoxymethyl-2-methoxyphenyl acetate (**22**)(*13*)	B	10	5-Acetoxymethyl-2-methoxyphenol (**13**)(*19*)	55
2-Acetoxymethyl-6-methoxyphenyl acetate (**23**)	B	10	2-Acetoxymethyl-6-methoxyphenol (**14**)	50
3-Acetoxy-1-(4′-acetoxyphenyl)-2-methylpropanone (**24**)	A	3	3-Acetoxy-1-(4′-hydroxyphenyl)-2-methylpropanone (**15**)	60

[a] All these reactions, when performed under identical conditions but without adding the lipase, did not yield any product.

course of this enzyme-assisted selective acetylation studies, 10 new compounds, *i.e.*, **7, 9, 14, 15, 16, 18, 19, 23, 24**, and **26** have been obtained.

X-RAY CRYSTALLOGRAPHY

The molecular structures of the compounds **4, 15**, and **17** were confirmed by single crystal X-ray diffraction studies. Some of the crystallographic data are summarized in Table 5. All bond lengths and angles are unexceptional. In the molecular structure of hydroxymethylated phenol **4**, the carbinol oxygen atom is twisted out of the plane of the phenyl ring to give a C6-C1-C7-O1 torsion angle of 80.2(2)°; in contrast the methoxy group is almost coplanar with the phenyl group and has a C8-O3-C4-C3 torsion angle of 176.5(1)°. Intermolecular H-bonding interactions are responsible for the integrity of the solid state.

The structures of compounds **15** and **17** are illustrated in Figs. 1 and 2, respectively. Both molecules deviate considerably from planarity as illustrated by torsion angles C1′-C1-C2-C4 of 83.4(2)° and 77.9(2)°, respectively. Both structures are stabilized by hydrogen bonding; in compound **15**, intermolecular H-bonding occurs between the hydrogen of phenolic hydroxyl group and the acetyl oxygen of an adjacent molecule, while in **17** there is intramolecular H-bonding between the phenolic hydroxyl group and the ketonic carbonyl group.

EXPERIMENTAL

Melting points were determined on a Mettler FP62 instrument and are uncorrected. The IR spectra were recorded on a Perkin–Elmer model 435 spectrophotometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded either on Bruker AC-250, Bruker AC-300, or Bruker AC-400 spectrometer at 250, 300, and 400 MHz, and at 62.8, 75.0, and 100.0 MHz, respectively, using TMS as internal standard. The chemical shift

TABLE 5

Crystal Data and Structure Refinement for Compounds **4, 15**, and **17**.

Compounds	**4**	**15**	**17**
Formula	$C_8H_{10}O_3$	$C_{12}H_{14}O_4$	$C_{18}H_{18}O_5$
M	154.16	222.23	314.32
Crystal system	Orthorhombic	Monoclinic	Monoclinic
Space Group	Pbca	P2(1)/c	P2(1)
a/A	14.9898(10)	10.8613(3)	8.2127(3)
b/A	6.0337(4)	9.0667(2)	9.0559(4)
c/A	16.5351(11)	11.9286(3)	10.5774(5)
α/°	90	90.00	90.00
β/°	90	101.059(2)	99.036(1)
γ/°	90	90.00	90.00
V/A^3	1495.5(2)	1152.87(5)	776.91(6)
T/K	180(2)	210(2)	200(2)
Z	8	4	2
λ/A	0.71073	0.71073	0.71073
ρ(calcd.)/Mg/m^3	1.369	1.280	1.344
μ/mm^{-1}	0.105	0.096	0.098
hkl ranges	−19, 19; −5, 7; −21, 20	−13, 13; −12, 12; −10, 15	−10, 10; −10, 11; −7, 13
Number of data collected	8208	6673	4724
Independent reflections	1807	2693	3254
Transmission coefficients	0.9834, 0.9495	0.9051, 0.6049	0.9844, 0.9768
R(F) [I>2σ(I)]	0.045	0.049	0.033
wR(F^2) (all data)	0.124	0.135	0.079
Goodness of fit on F^2	1.055	0.929	0.918
Peak diff. & hole/eA^{-3}	0.479, −0.415	0.192, −0.229	0.130, −0.176
Data, restraints, parameters	1807, 0, 106	2693, 0, 151	3254, 1, 211

values are on δ scale and the coupling constants (J) are in Hz. The EI mass spectra were recorded on a Jeol JMSDX 303 or on a Jeol AX 505 W instrument at 70 eV. The enzymes, porcine pancreatic lipase (PPL, Type II) and *Candida rugosa* lipase (CRL, Type VII) were purchased from Sigma Chemical Co. (U.S.A.) and used after keeping *in vacuo* over P_2O_5 for 24 h. The organic solvents (THF and DIPE) used were distilled and dried over molecular sieves (4 A), while *n*-butanol was dried and distilled over ignited potassium carbonate. Analytical TLCs were performed on precoated Merck silica gel 60 F_{254} plates; the developing agent was alcoholic $FeCl_3$ solution (3%). Reactions were monitored at λ_{254} nm on a Shimadzu LC-10AS HPLC instrument with SPD-10A UV-VIS detector and Shimpack CLC-ODS (4.6 × 150 mm) reverse phase column, solvent system used was methanol–water (3:2) at the flow rate of 0.50 ml/min.

The hydroxymethylated phenols **2–5** were prepared by the reduction of their respective aldehydes with $NaBH_4$ in methanol at ice temperature in 80–90% yields, 2-hydroxymethylphenol (**1**) was purchased from Aldrich Chemical Co. (U.S.A.). The peracetates of hydroxymethylated phenols, *i.e.*, the compounds **19–24**, were prepared in quantitative yields by stirring a solution of the corresponding phenolic compounds

1–6 in acetic anhydride-pyridine in the presence of catalytic amount of dimethylaminopyridine either at room temperature (28–30°C) or at 40–45°C.

*General Method of Enzymatic Acetylation of Hydroxymethylated Phenolic Compounds **1–9***

The hydroxymethylated phenolic compounds (**1–9**, 2 mmol) were dissolved in dry tetrahydrofuran or diisopropyl ether (25–30 ml), vinyl acetate (4 mmol), and porcine pancreatic lipase or *C. rugosa* lipase (200 mg) were added to the solution. The suspension was stirred at 42–45°C and progress of the reaction was monitored by TLC and/or HPLC. After completion, the reaction was quenched by filtering off the enzyme, solvent removed under reduced pressure, and the crude product was purified by column/preparative thin layer chromatography and/or by crystallization to afford the pure monoacetates **10–18** involving the aliphatic hydroxyl group. The hitherto unknown monoacetates **14, 15, 16**, and **18** obtained were fully characterized on the basis of their spectral analysis. The known monoacetates **10** (*8*), **11** (*12*), **12** (*12*), **13** (*19*), and **17** (*16*) were identified on the basis of their spectral analysis and their comparison with those reported in the literature.

*General Method of Enzymatic Deacetylation of Peracetates of Hydroxymethylated Phenols **19–23**and Aryl Alkyl Ketone **24***

The peracetates (**19–24**, 2 mmol) were dissolved in dry tetrahydrofuran or diisopropyl ether (25–30 ml) containing *n*-butanol (4 mol eq.), porcine pancreatic lipase, or *C. rugosa* lipase (200 mg) was added to the solution. The suspension was stirred at 42–45°C and progress of the reaction was monitored by TLC and/or HPLC. After completion, the reaction was quenched by filtering off the enzyme, solvent removed under reduced pressure, and the crude product was purified by column/preparative thin layer chromatography and/or by crystallization to afford the pure monoacetates **10–15**, which were fully characterized as mentioned in the preceding paragraph.

2-Ethyl-3-hydroxy-1-(2′, 4′-dihydroxyphenyl)propanone (7)

To a solution of 1-(4′-benzyloxy-2′-hydroxyphenyl)-2-ethyl-3-hydroxypropanone (**26**, 1.20 g, 4 mmol) in ethyl acetate (40 ml), Pd-C (10%)was added and the reaction mixture was stirred under hydrogen at atmospheric pressure at 25–30°C for 2 h, TLC examination of the reaction showed 100% conversion to the product. The catalyst was filtered off, solvent removed, and the residue was kept under high vaccum to remove the traces of toluene formed during debenzylation to afford pure **7** as a colorless oil (0.82g), 98% yield; R_f 0.30 (petrol:ethyl acetate, 3:2); IR (thin film): 3254, 2967, 2361, 1632, 1514, 1455, 1385, 1314, 1233, 1146, and 1036 cm^{-1}; ^1H NMR (300 MHz, CD_3 OD) δ: 1.61(t, J = 7.5 Hz, 3H, CH_3), 2.38(m, 2H, CH_2-CH_3), 4.33(m, 2H, CH_2-OH), 4.48(m, 1H, C-2H), 5.50(brs, 1H, CH_2-O*H*), 7.08(d, J = 1.8 Hz, 1H, C-3′H), 7.20(d, J = 9.0 Hz, 1H, C-5′H), 8.67(d, J = 9.0 Hz, 1H, C-6′H), 11.50(brs, 1H, phenolic OH), and 13.83(s, 1H, chelated OH); ^{13}C NMR (75 MHz, CD_3OD) δ: 12.00(CH_3), 23.76(CH_2CH_3), 50.51(C-2), 64.28(C-3), 103.78 and 108.25(C-3′ and C-5′), 115.03(C-1′), 133.92(C-6′), 166.37 and 166.67(C-2′ and C-4′) and 208.54(CO); EIMS, m/z (% rel. int.): 210[M^+](10), 192(10), 180(4), 163(6), 149(14), 137(100), 121(23), 98(6), 81(9) and 77(3).

*3-Hydroxy-1-(2′-hydroxyphenyl)-2-(4″-methoxybenzyl)propanone (**9**)*

A solution of 2′-hydroxy-4-methoxydihydrochalcone (*17*) (1.28g, 5 mmol) in dry acetone (100 ml) and anhydrous potassium carbonate (3.5 g, 25 mmol) was treated with a solution of ethoxymethyl chloride (*20*) (0.75 ml, 5.5 mmol) in dry acetone (8 ml). The resulting mixture was refluxed at 60–70°C for 2.5 h. The reaction mixture was filtered and the filterate concentrated at reduced pressure. The light brown residue was purified by column chromatography on silica gel to afford compound **9** as a light yellow colored oil (0.72 g), 50% yield; R_f 0.35 (petrol:ethyl acetate, 4:1); IR (thin film): 3435, 2934, 2837, 1633, 1512, 1487, 1446, 1290, 1246, 1179 and 1035 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.10 and 2.92(2m, 1H each, 2H, PhCH_α and PhCH_β), 3.02(m, 1H, C-2H), 3.76(s, 3H, OCH_3), 3.84(brm, 1H, OH), 3.88(m, 2H, C-3H), 6.80(d, J = 8.8Hz, 2H, C-3″H and C-5″H), 6.88(m, 1H, C-5′H), 6.98(dd, J = 1.1 and 8.4Hz, 1H, C-3′H), 7.11(d, J = 8.8 Hz, 2H, C-2″H, and C-6″H), 7.48(m, 1H, C-4′H), 7.73(dd, J = 1.8 and 8.1Hz, 1H, C-6′H) and 12.31(s, 1H, chelated OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 34.31(CH_2), 49.59(C-2), 55.13(OCH_3), 62.39(C-3), 113.92(C-3′, C-3″ and C-5″), 118.68 and 118.95(C-1′ and C-5′), 129.82 and 130.04(C-4′, C-1″, C-2″ and C-6″), 136.72(C-6′), 158.22(C-4″), 162.99(C-2′), and 209.27(C-1); EIMS, *m*/*z* (% rel. int.): 286[M^+](35), 255(92), 147(52), 121(100), 97(55), 91(58), and 65(98).

*2-Acetoxymethyl-6-methoxyphenol (**14**)*

The column chromatographic purification of the crude product on silica gel afforded compound **14** as a colorless viscous oil in 85% yield; R_f = 0.40 (petrol:ethyl acetate, 4:1); IR (thin film): 3437, 2941, 2844, 2361, 1734, 1620, 1597, 1484, 1443, 1382, 1362, 1275, 1084, and 1027 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.06(s, 3H, $OCOCH_3$), 3.84(s, 3H, OCH_3), 5.18(s, 2H, CH_2OCOCH_3), 6.82(m, 2H, C-3H and C-5H), and 6.90(m, 1H, C-4H); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 20.73(CH_3), 55.91(CH_2), 61.33(OCH_3), 110.90(C-4), 119.41 and 121.68(C-3 and C-5), 121.17(C-2), 144.15 and 146.65 (C-1 and C-6) and 171.14(CO); EIMS, *m*/*z* (% rel. int.): 196[M^+] (20), 153(3), 136(100), 122(7), 118(7), 107(33), 106(33), 93(16), 80(12), and 77(10).

*3-Acetoxy-1-(4′-hydroxyphenyl)-2-methylpropanone (**15**)*

The column chromatographic purification of the crude product on silica gel afforded compound **15** as a colorless solid that was crystallized from petrol:chloroform as white shining powder in 60% yield. Mp 136°C; R_f 0.30 (petrol:ethyl acetate, 4:1); IR (thin film): 3305, 2979, 2818, 1714, 1667, 1601, 1514, 1442, 1371, 1219, 1174, 1153 and 1039 cm^{-1}; ^1H NMR (250 MHz, DMSO-d_6) δ: 1.17(d, J = 6.8 Hz, 3H, CH_3), 1.92(s, 3H, $OCOCH_3$), 3.88(m, 1H, C-2H), 4.10(dd, J = 6.2 and 10.6 Hz, 1H, C-3 H_α), 4.34(dd, J = 7.9 and 10.6Hz, 1H, C-3H_β), 6.94(d, J = 8.9 Hz, 2H, C-3′H and C-5′H), 7.94(d, J = 8.9 Hz, 2H, C-2′H and C-6′H) and 9.25(brs, 1H, phenolic OH); ^{13}C NMR(62.8 MHz, $CDCl_3$) δ: 15.03(CH_3), 20.58(COCH_3), 39.95(C-2), 66.61(C-3), 116.14(C-3′ and C-5′), 129.26(C-1′), 131.64(C-2′ and C-6′), 162.91(C-4′), 170.83(CO) and 199.85(C-1); EIMS, *m*/*z* (% rel. int.): 222[M^+] (3), 180(17), 122(15), 121(100), 93(17), 77(3), and 71(3).

*3-Acetoxy-2-ethyl-1-(2′, 4′-dihydroxyphenyl)propanone (**16**)*

The column chromatographic purification of the crude product on silica gel afforded compound **16** as a light brownish oil in 55% yield; R_f 0.60 (petrol:ethyl acetate, 3:2); IR (thin film): 3337, 2969, 2879, 2361, 1714, 1630, 1512, 1447, 1376, 1231 and 1042 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ: 0.91(t, J = 7.5 Hz, 3H, CH_3), 1.62(m, 1H, CH_αH$_\beta$CH$_3$), 1.71(m, 1H, CH$_\alpha$$H_\beta$CH$_3$), 1.92(s, 3H, OCOC$H_3$), 3.77(dt, J = 2.4 and 8.0 Hz, 1H, C-2H), 4.23(dd, J = 5.1 and 10.8 Hz, 1H, C-3H$_\alpha$), 4.32(dd, J = 8.7 and 10.5 Hz, 1H, C-3H$_\beta$) 6.29(d, J = 2.4 Hz, 1H, C-3′H), 6.39(dd, J = 2.4 and 9.0 Hz, 1H, C-5′H), 7.78(d, J = 9.0 Hz, 1H, C-6′H) and 12.83(s, 1H, chelated OH); ^1H NMR (300 MHz, $CDCl_3$) δ: 0.92(t, J = 7.5 Hz, 3H, CH_3), 1.62(m, 1H, CH_αH$_\beta$CH$_3$), 1.76(m, 1H, CH$_\alpha$$H_\beta$CH$_3$), 1.96(s, 3H, OCOC$H_3$), 3.65(m, 1H, C-2H), 4.24(dd, J = 6.0 and 12.0 Hz, 1H, C-3H$_\alpha$), 4.34(dd, J = 8.0 and 9.0 Hz, 1H, C-3H$_\beta$), 6.42(m, 2H, C-3′H and C-5′H), 7.63(d, J = 8.4 Hz, 1H, C-6′H), 9.99(brs, 1H, phenolic OH), and 12.87(s, 1H, chelated OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 11.52(CH_3), 20.83 and 23.08(CH_2 and COCH_3), 45.67(C-2), 64.99(C-3), 103.59 and 108.30 (C-3′ and C-5′), 113.85 (C-1′), 132.27(C-6′), 164.23 and 165.79(C-2′ and C-4′) and 171.48(COCH$_3$); EIMS, m/z (% rel. int.): 252[M^+](4), 192(18), 177(3), 163(7), 149(4), 137(100), 121(19), 84(6), and 81(6).

*3-Acetoxy-1-(2′-hydroxyphenyl)-2-(4″-methoxybenzyl)propanone (**18**)*

The column chromatographic purification of the crude product on silica gel afforded compound **18** as a colorless oil in 75% yield; R_f 0.50 (petrol:ethyl acetate, 4:1); IR (thin film): 2956, 2934, 2837, 1743, 1635, 1613, 1581, 1514, 1488, 1446, 1375, 1247, 1179, 1158, and 1036 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 1.92(s, 3H, OCOCH_3), 2.81(dd, J = 14.0 and 7.4Hz, 1H, PhCH_αH$_\beta$), 3.05(dd, J = 14.0 and 7.0Hz, 1H, PhCH$_\alpha$$H_\beta$), 3.75(s, 3H, OC$H_3$), 4.01(m, 1H, C-1H), 4.23(dd, J = 10.5 and 4.5Hz, 1H, C-3H$_\alpha$), 4.38(dd, J = 10.9 and 8.8Hz, 1H, C-3H$_\beta$), 6.78(d, J = 8.8Hz, 2H, C-3″H and C-5″H), 6.85(dtd, J = 1.1, 1.0 and 1.4Hz, 1H, C-5′H), 6.97(dd, J = 1.1 and 8.4Hz, 1H, C-3′H), 7.05(d, J = 8.8Hz, 2H, C-2″H and C-5″H), 7.45(dtd, J = 1.7, 1.4 and 1.4Hz, 1H, C-4′H), 7.68(dd, J = 8.0 and 1.4Hz, 1H, C-6′H), and 12.31(s, 1H, chelated OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.61(COCH_3), 34.60(ArCH_2), 46.51(C-2), 55.11(OCH_3), 64.38(C-3), 113.94(C-3″ and C-5″), 118.57, 118.87 and 119.28(C-1′, C-3′ and C-5′), 129.55(C-1″), 129.73 and 129.79(C-4′, C-2″ and C-6″), 136.64(C-6′), 158.28(C-4″), 162.85(C-2′), 171.00(CO) and 206.48(C-1); EIMS, m/z (% rel. int.): 328[M^+](9), 268(58), 255(17), 237(8), 148(13), 147(33), 121(100), 93(11), and 77(10).

*2-Acetoxymethylphenyl acetate (**19**)*

The column chromatographic purification of the crude product on silica gel column afforded compound **19** as a colorless oil in 92% yield; R_f 0.35 (petrol:ethyl acetate, 19:1); IR (KBr): 1739, 1600, 1492, 1458, 1370, 1232, 1178, 1110 and 1027 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$)δ: 2.04 and 2.28(2s, 3H each, 2 × OCOCH_3), 5.07(s, 2H, CH_2OCOCH_3), and 7.08, 7.32, 7.23 and 7.42(4dd, J = 1.3 and 8.0 Hz, 1.3 and 7.5 Hz, 1.8 and 7.7 Hz, and 1.7 and 7.3 Hz, respectively, 1H each, 4H, C-3H, C-4H, C-5H and C-6H); ^{13}C NMR (62.5 MHz, $CDCl_3$)δ: 20.57(2 × OCOCH_3), 61.14(CH_2), 122.49 and 125.94(C-3 and C-6), 127.90(C-2), 129.40 and 130.18(C-4 and C-5),

148.94(C-1), and 169.01 and 170.35(2 × CO); EIMS *m/z* (% rel. int.): 208[M]$^+$(9), 166(61), 149(17), 124(7), 106(100), 97(8), 78(28), 71(9), 57(16), and 43(32).

*5-Acetoxymethyl-2-methoxyphenyl acetate (**22**)*

The column chromatographic purification of the crude product on silica gel afforded compound **22** as a colorless oil in 90% yield; R_f 0.30 (petrol:ethyl acetate, 19:1); IR (thin film): 2941, 1767, 1739, 1620, 1516, 1444, 1370, 1271, 1227, 1203, 1126, and 1025 cm^{-1}; ^{1}H NMR(250 MHz, $CDCl_3$) δ: 2.06 and 2.30(2s, 3H each, 2 × $OCOCH_3$), 3.81(s, 3H, OCH_3), 5.02(s, 2H, CH_2OCOCH_3), 6.94(d, J = 9.5 Hz, 1H, C-5H), 7.08(d, J = 1.8 Hz, 1H, C-2H) and 7.19(dd, J = 9.5 and 1.8 Hz, 1H, C-4H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ: 20.50 and 20.88(2 × $OCOCH_3$), 55.85(CH_2), 65.42(OCH_3), 121.16, 123.13 and 127.10(C-2, C-4 and C-5), 128.48(C-3), 139.57(C-1), 151.05(C-6), and 168.82 and 170.73(2 × CO); EIMS, *m/z* (% rel. int.): 238[M]$^+$(17), 196(100), 179(7), 154(84), 137(55), 136(18), 122(17), 93(8), 65(6), and 43(28).

*2-Acetoxymethyl-6-methoxyphenyl acetate (**23**)*

The column chromatographic purification of the crude product on silica gel afforded compound **23** as a light yellow viscous oil in 85% yield; R_f 0.30 (petrol:ethyl acetate, 19:1); IR (thin film): 2942, 2843, 1769, 1739, 1614, 1589, 1483, 1368, 1282, 1227, 1176, 1085, and 1028 cm^{-1} ^{1}H NMR (250 MHz, $CDCl_3$) δ: 2.04 and 2.31(2s, 3H each, 2 × $OCOCH_3$), 3.80(s, 3H, OCH_3), 5.06(s, 2H, CH_2OCOCH_3), 6.95(dd, J = 8.2 and 1.4 Hz, 1H, C-3H), 7.00(dd, J = 7.78 and 1.48 Hz, 1H, C-5H) and 7.18(t, J = 10.00 Hz, 1H, C-4H); ^{13}C NMR (62.5 MHz, $CDCl_3$)δ: 20.24 and 20.64(2 × $OCOCH_3$), 55.86(CH_2), 61.15(OCH_3), 112.40, 121.49 and 126.40(C-3, C-4 and C-5), 129.29(C-2), 138.34(C-1), 151.22(C-6), and 168.47 and 170.48(2 × CO); EIMS, *m/z*(% rel. int.): 238[M$^+$](9), 196(28), 136(100), 135(26), 107(17), 93(4), 65(5), and 43(18).

*3-Acetoxy-1-(4′-acetoxyphenyl)-2-methylpropanone (**24**)*

The column chromatographic purification of the crude product on silica gel afforded compound **24** as a thick oil in 92% yield; R_f 0.50 (petrol:ethyl acetate, 19:1); IR (thin film): 2979, 1764, 1742, 1683, 1599, 1504, 1370, 1196, 1167 and 1039 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.25(d, J = 7.0 Hz, 3H, CH_3), 2.01 and 2.36(2s, 3H each, 2 × $OCOCH_3$), 3.87(m, 1H, C-2H), 4.20(dd, J = 10.8 and 5.6 Hz, 1H, C-3 H_α), 4.45(dd, J = 10.8 and 8.0 Hz, 1H, C-3 H_β), 7.24(d, J = 10.0 Hz, 2H, C-3′H and C-5′H) and 8.03(d, J = 10.0 Hz, 2H, C-2′H and C-6′H); ^{13}C NMR (75 MHz, $CDCl_3$)δ: 14.23 (CH_3), 20.35 and 20.69(2 × $COCH_3$), 39.59(C-2), 65.52(C-3), 121.65(C-3′ and C-5′), 129.66(C-2′ and C-6′), 133.41(C-1′), 154.26(C-4′), and 168.40 and 170.42 (2 × $COCH_3$); EIMS, *m/z* (% rel. int.): 264[M$^+$](1), 222(18), 180(10), 163(40), 121(100), and 93(10).

*1-(4′-Benzyloxy-2′-hydroxyphenyl)-2-ethyl-3-hydroxypropanone (**26**)*

To a solution of 4-benzyloxy-2-hydroxybutyrophenone (*15*) (2.70 g, 10 mmol) in 37% formaldehyde (11 mmol) and tetrahydrofuran (2 ml), 0.5 N sodium hydroxide solution (22 mmol) was added and the reaction mixture stirred at 25–30°C for 5 h, it was acidified to pH 4 with dilute hydrochloric acid and extracted with ether (2 ×

50 ml). The organic layer was separated, washed with brine (2 × 50 ml), dried, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel eluting with petrol:ethyl acetate (23:2) and finally by crystallization from petrol:chloroform mixture to afford **26** as a white fluffy solid (1.65 g), 55% yield; Mp 76°C; R_f 0.50 (petrol:ethyl acetate, 17:1); IR (KBr): 3432, 2929, 2871, 1635, 1581, 1515, 1401, 1272, 1243, 1158, 1074, and 1005 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.93(t, J = 7.4Hz, 3H, CH_3), 1.68(m, 2H, CH_2), 2.46(brs, 1H, aliphatic OH), 3.45(m, 1H, C-2H), 3.78(dd, J = 10.9 and 3.9 Hz, 1H, C-3H_α), 3.93(dd, J = 10.8 and 7.1Hz, 1H, C-3H_β), 5.06(s, 2H, C$H_2C_6H_5$), 6.49(brs, 1H, C-3′H), 6.51(d, J = 8.5Hz, 1H, C-5′H), 7.38(m, 5H, C_6H_5) and 7.68(d, J = 8.5Hz, 1H, C-6′H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 11.82(CH_3), 22.84(CH_2), 48.91(C-2), 62.67(C-3), 70.24(C$H_2C_6H_5$), 102.12(C-3′), 108.32(C-5′), 113.90(C-1′), 127.51, 128.31, 128.69, 129.19 and 135.82 (aromatic carbons), 131.80(C-6′), and 165.45 and 165.94(C-2′ and C-4′); EIMS, *m*/*z* (% rel. int): 300[M^+](9), 282(6), 270(18), 227(20), 91(100) and 65(7).

*X-Ray Crystallography of Compounds **4, 15**, and **17***

All data were collected using a Siemens SMART CCD area-detector diffractometer. A full hemisphere of reciprocal space was scanned by a combination of three sets of exposures; each set had a different ϕ angle for the crystal and each exposure of 10 s covered 0.3° in ω. The crystal to detector distance was 5.01 cm. Crystal decay was monitored by repeating the initial frames at the end of the data collection and analyzing the duplicate refractions, and was found to be negligible in all cases. A multiscan absorption correction was applied using SADABS(*21*).

The structures were solved by direct methods using SHELXTL-PC (*22*) and refined by full matrix least-squares on F^2 for all data using SHELXL-97 (*23*). Hydrogen atoms were added at calculated positions and refined using a riding model. Anisotropic temperature factors were used for all non-H atoms; H-atoms were given isotropic temperature factors equal to 1.2 times (or 1.5 for methyl hydrogens) the equivalent isotropic displacement parameter of the atom to which they are attached.

ACKNOWLEDGMENT

We thank the Council of Scientific and Industrial Research (CSIR, New Delhi, India) for financial assistance.

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