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Regioselective Esterification of Diols and Triols with Lipases in Organic Solvents#

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Abstract- Lipases from porcine pancreas (PPL) and *Candida cylindracea* (CCL) in different organic solvents allow discrimination of the primary and secondary hydroxyl groups, and also between two primary hydroxyl groups towards acylation with 2,2,2-trifluoroethyl butyrate in diols and triols with high regioselectivity.

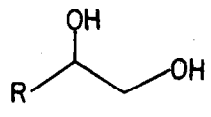
INTRODUCTION

There is an increasing demand for efficient processes in chemical transformations with high degree of stereo- and regioselectivity. For this purpose, biocatalysts have widely been utilized in recent years.[1-5] Ester formation and hydrolysis reactions are getting increasing attention in synthetic organic chemistry due to their involvement in protection-deprotection steps in the synthesis of complex molecules. Special care is, however required in order to carry out these reactions in regio- and chemoselective manner. This is where lipases come into the picture and they have extensively been used as catalysts in enantio-, regio- and chemoselective synthesis. Lipases are quite popular among the chemists because they can efficiently work in organic solvents.The other added advantages are their wide versatility, low cost, easy handling and no need of added cofactors.Thus there is an urgent demand to make lipases general and practical reagents for a variety of substrates so that the right enzyme for a given substrate could be straightway selected. As per our scrutiny of literature regarding enzyme-catalysed transesterification of aliphatic diols/triols, only one report is available on acylation of 1,2-butanediol and 1,3-butanediol with PPL and trichloroethylbutyrate (TCEB), TFEB or vinylacetate.[6] We report herein successful regioselective CCL- and PPL-catalysed esterification of eight different aliphatic diols and triols. Further the enzyme-catalysed deacylation of diacetyloxyalkanes has not been reported and our present study on selective deacetylation of diacetates of aliphatic diols in organic solvents is, perhaps the first one.

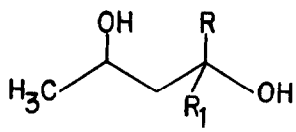
A part of this work was presented at the IUPAC-NOST International Symposium on Enzymes in Organic Synthesis held in New Delhi(India) on 6-9 January 1992.

RESULTS AND DISCUSSION

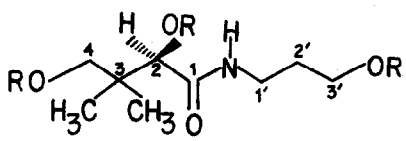
We have studied (regioselective) transesterification of 1-phenyl-1,2-ethanediol(**1**), 1,2-propanediol (**2**), 1,3-butanediol (**3**), 1,2-butanediol (**4**), 1,2-pentanediol (**5**), 1,2-hexanediol (**6**), 1,2-octanediol (**7**), N-(3'-hydroxy)propyl-3,3-dimethyl-2,4-dihydroxybutanamide (D-panthenol, **8**) and 2-methyl-2,4-pentanediol (**9**) with the acylating agent trifluoroethyl butyrate (TFEB) in different organic solvents, viz pyridine, dimethylformamide(DMF), acetonitrile, acetone, tetrahydrofuran (THF) and iso-octane by PPL and CCL. The acylating agent trifluoroethyl butyrate was preferred over trichloroethyl butyrate and other acylating agents because of its low boiling point and high reactivity, and also because the reactivity of the corresponding alcohol formed is lower because of the three fluorine atoms attached to the adjacent carbon atom.



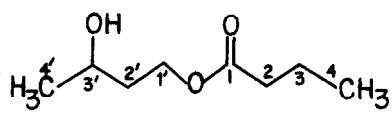
1. R=C_6H_5
2. R=CH_3
4. R=CH_3-CH_2
5. R=CH_3-CH_2-CH_2
6. R=CH_3-CH_2-CH_2-CH_2
7. R=CH_3-CH_2-CH_2-CH_2-CH_2-CH_2



3. R=R_1=H
9. R=R_1=CH_3



8. R =H
25. R=CH_3CO



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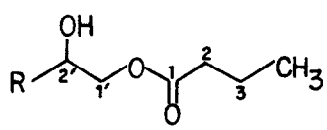

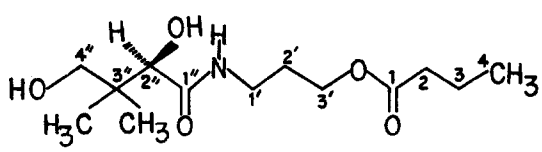

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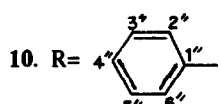


10. R=
11. R=CH_3
13. R=CH_3-CH_2
14. R=CH_3-CH_2-CH_2
15. R=CH_3-CH_2-CH_2-CH_2
16. R=CH_3-CH_2-CH_2-CH_2-CH_2-CH_2

The comparative study in different organic solvents revealed that PPL suspended in acetone is best suited for maximum conversion of the substrates **1-7**. In the case of D-panthenol (**8**), 100% conversion was obtained in DMF. However the regioselectivity of the lipase from porcine pancreas remains the same in the different solvents. The reaction proceeds with high regioselectivity (approaching 100%) in the diols **1-7** where the acylation takes place at the primary hydroxyl group giving the prevalent and

exclusive products 2-phenyl-2-hydroxyethyl butyrate (**10**), 2-hydroxypropyl butyrate (**11**), 3-hydroxybutyl butyrate (**12**), 2-hydroxybutyl butyrate (**13**), 2-hydroxypentyl butyrate (**14**), 2-hydroxyhexyl butyrate (**15**) and 2-hydroxyoctyl butyrate (**16**), respectively. This conclusion that the esterification takes place at the primary hydroxyl group in the diols **1-7** was drawn by comparing the ^{1}H-NMR spectra of the parent diols with the corresponding enzyme-catalysed transesterified products **10-16**. The H-1' and H-2' appeared around δ 4.18 and 4.97, respectively in our chemically prepared diacetates **19-24**, these protons appeared around δ 3.50 and 3.80 in the corresponding parent diols **2-7**. It was found that the signal for H-1' in the enzyme-catalysed reaction product monoesters **10-16** appeared around δ 4.20 as compared to the H-1 in the parent diols (around δ 3.50, thus showing a downfield shift of around 0.70 ppm) and no significant shift in the multiplet for the H-2' occurs, thus clearly showing that lipase-mediated transesterification takes place at the primary hydroxyl group. The fact that the acylation of the primary hydroxyl group takes place regioselectively is further confirmed by our attempted transesterification of 2-methyl-2,4-pentanediol (**9**) under similar conditions where no esterification occurred due to the absence of any primary hydroxyl group. No appreciable enantioselectivity was observed in these reactions either with PPL or CCL.

In the case of N-(3'-hydroxy)propyl-3,3-dimethyl-2,4-dihydroxybutanamide (D-panthenol, **8**) which has two primary hydroxyl groups and one secondary hydroxyl group, only the primary hydroxyl group at the far end position of the asymmetric carbon atom gets acylated and N-(3'-butanoyloxy)propyl-3,3-dimethyl-2,4-dihydroxybutanamide (**17**) is obtained in 99% yield. The exclusive esterification at the C-3' primary hydroxy group in **8** was established by comparing the ^{1}H-NMR spectra of D-panthenol (**8**) and the transesterified product (**17**), where it was observed that the two-proton triplet for the C-3' protons shifts downfield by 0.53 ppm in the product ester **17** and no shift in the singlets for the C-4" andC-2" protons occurs. The esterification of the hydroxyl group at the far end of the asymmetric carbon is in conformity with the two-active site model proposed earlier by Bhalerao *et al.*[7] for CCL, these workers have shown that the substrate fits into the cavity of the enzyme in such a way that the group further away from the asymmetric centre in the substrate interacts with the required serine residue of the lipase. The present result can be further explained with the help of our model for PPL (Fig. 1), taking clue from the CCL model proposed by Hult and Norin.[8]

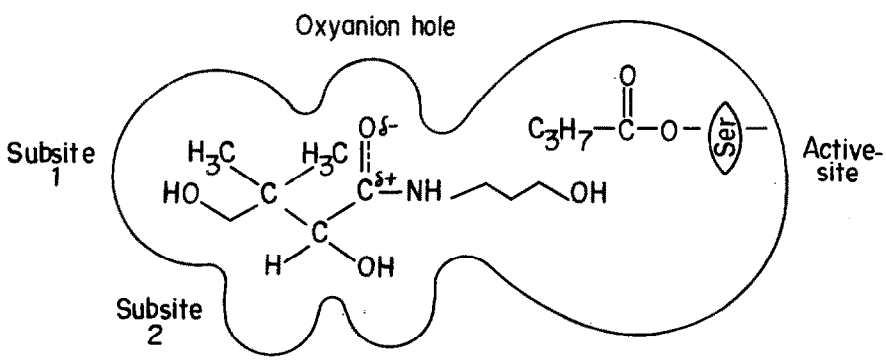
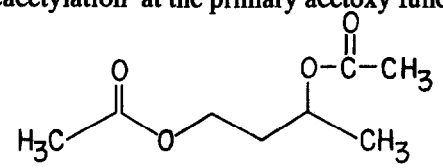


Fig. 1

The model suggests that the lipase from porcine pancreas possesses two active sites, one having two hydrophobic binding sites and one oxyanion hole. The larger hydrocarbon chain ($HOCH_2$-$C(CH_3)_2$-) can be visualised to be bound to the hydrophobic binding site 1, the smaller hydrocarbon chain (H atom in this case) can be visualised as being bound at the other hydrophobic binding site 2. The carbonyl group fits into the oxyanion hole, thereby leaving the primary hydroxyl group at the far end of the chiral centre in proximity to the second active site carrying the acylated serine residue, hence transesterification occurs at the C-3' position. Our finding can become a general and efficient method for discrimination between chemically similar hydroxyl groups by biocatalysts and thus should find importance in the synthesis of polyfunctional compounds which can serve as building blocks for liquid crystals, pheromones and enantiomerically pure epoxides.

We have prepared the peracetates of the compounds **1-8** and lipase- catalysed deacetylation reactions on the diacetates **(18-24)** and the triacetate **25** were attempted in different organic solvents with PPL and CCL. The deacetylation reaction took place only on the diacetates **18, 21, 22** and **23**, to give the monoacetates **26, 27, 28** and **29**, respectively, but the rate of reaction decreased with increase in chain length. The deacetylation reaction in all these four cases took place only at the secondary acetoxy linkage, but the reaction was faster with 1,2-diacetoxybutane and was slowest with 1,2-diacetoxyhexane. Our observed regioselective hydrolysis at the secondary acetoxy group in compounds **18** and **21-23** may be due to the lipase -mediated predominant deacetylation at this position. Else, the observed formation of compounds **26-29** from **18** and **21-23** could be due to the migration of the acetyl group from the secondary acetoxy function to the free primary hydroxy group, formed by the otherwise lipase- mediated deacetylation at the primary acetoxy function in the compounds **18** and **21-23.**



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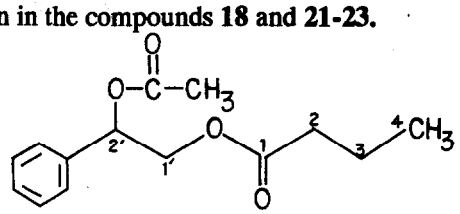

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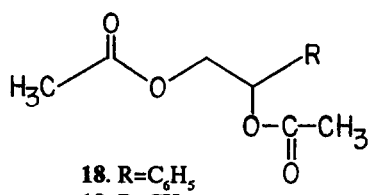
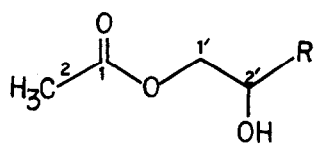
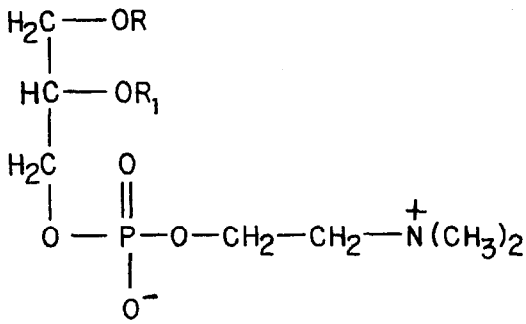


18. R=C_6H_5
19. R=CH_3
21. R=CH_3-CH_2
22. R=CH_3-CH_2-CH_2
23. R=CH_3-CH_2-CH_2-CH_2
24. R=CH_3-CH_2-CH_2-CH_2-CH_2-CH_2



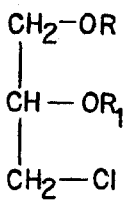
26. R=C_6H_5
27. R=CH_3-CH_2
28. R=CH_3-CH_2-CH_2
29. R=CH_3-CH_2-CH_2-CH_2

In order to confirm that deacetylation takes place at the secondary hydroxyl and no acetyl group transfer from C-2 to C-1 takes place during the deacetylation of the diacetates **18** and **21-23**, we have studied the deacetylation of the mixed ester **30**, obtained by acetylation of **10** prepared earlier. The PPL-mediated deacylation of **30** in THF at 42-45°C produced exclusively the monobutyrate **10**, which was characterized from its ^{1}H NMR spectrum. The acyl migration is ruled out as in that case, we would have obtained the monoacetate **26** or the mixture of **26** and **10**, and not exclusively the monobutyrate **10**. Earlier Regen *et al*[9] have carried out similar studies on the hydrolysis of bis [12-(methacryloyloxy)dodecanoyl]-L-α-phosphatidylcholine (**31**) and dipalmitoyl-L-α-phosphatidylcholine (**32**) with phospholipase A_2 from crude rattle snake venom (*Crotalus adamanteus*), these reactions yielded 1-[12-(methacryloyloxy)dodecanoyl]-2-hydroxy-L-α-phosphatidylcholine (**33**) and 1-palmitoyl-2-hydroxy-L-α-phosphatidylcholine (**34**), respectively. In order to confirm that no significant acyl migration from C-1 to C-2 occurred during the deacylation of the secondary ester group, they have converted **33** and **34** to 1-[12-(methacryloyloxy) dodecanoyl]-2-palmitoyl-L-α-phosphatidylcholine (**35**) and 1-palmitoyl-2-[12-(methacryloyloxy)dodecanoyl]-L-α-phosphatidylcholine (**36**), respectively and have carried out the phospholipase A_2 catalysed deacylation on both of them. The free acid formed in case of **35** was identified as palmitic acid, whereas the deacylation of **36** yielded 12-methacryloyloxydodecanoic acid as the free acid, thus showing that in the 1,2-diacyloxypropane derivatives **31** and **32**, the lipase deacylates the secondary acyloxy group in a regioselective fashion. These results are in agreement with those obtained by us and further confirm that the product esters **26-29** are obtained directly by the lipase-mediated deacetylation of the peracetates **18**, **21**,**22** and **23** at the secondary acetoxy position, and are not those obtained by acetyl migration, from C-2 to C-1 position in the otherwise initial product persumably obtained by the deacetylation at the primary acetoxy function.

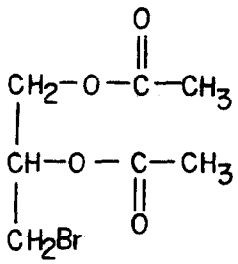


31. $R=R_1=CO(CH_2)_{11}OCOC(CH_3)=CH_2$
32. $R=R_1=CO(CH_2)_{14}CH_3$
33. $R=CO(CH_2)_{11}OCOC(CH_3)=CH_2$; $R_1=H$
34. $R=CO(CH_2)_{14}CH_3$; $R_1=H$
35. $R=CO(CH_2)_{11}OCOC(CH_3)=CH_2$; $R_1=CO(CH_2)_{14}CH_3$
36. $R=CO(CH_2)_{14}CH_3$; $R_1=CO(CH_2)_{11}OCOC(CH_3)=CH_2$

Further, Iriuchijima *et al*[10] have earlier reported hydrolytic studies in aqueous buffer on 1,2-diacetoxy-3-chloropropane (**37**), 1,2-diacetoxy-3-bromopropane (**38**) and 1,2-diacetoxy ethylbenzene (**18**) using lipoprotein lipase. They, however have not reported the details of the hydrolysis products of **38** and **18**, but have reported the formation of the mixture of two monohydroxy compounds, **39** and **40** in the rattio 4:1 from **37**. So they have observed 80% regioselectivity of hydrolysis at the secondary acetoxy group. Ours is the first study on the deacylation of polyol peracetates in organic medium with 100% regioselectivity at the secondary acetoxy. We have observed that the optimal chain length required for carrying out regioselective deacylation of 1,2-diacetoxyalkanes is 4 and with increase or decrease in the chain length, the reaction rate decreases. In the case of diacetate **18** of the phenyl substituted diol **1**, the rate of reaction was faster, from this it could be inferred that presence of aromatic ring helps the deacylation reaction to move in a forward direction.



37. R=R$_1$=COCH$_3$
39. R=COCH$_3$, R$_1$=H
40. R=H, R$_1$=COCH$_3$



38

All our reactions discussed above on different compounds, when performed under the same conditions, but without adding the enzyme did not indicate any esterification or deacetylation. Thus it is found that transesterification for recognising the primary and secondary hydroxyl groups in the same molecule by enzyme is more general. Since partially protected polyols are important starting materials for the synthesis of various important compounds, our results on regioselective protection of hydroxyl groups should find utility in the rapidly growing field of 'synthetic modifications' on polyols and carbohydrates of importance in medicine, industry and biology. Thus, the linear esters of 1,3-dihydroxybutyrate exhibit antimicrobial activity against *Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Trichophyton mentagnophytes, Candida albicans* and *Aspergillus niger*[11] and derivatives of 1-(2,4-dichloro)phenyl-1,2-butanediol, 1,2-octanediol and 1,2-hexanediol esters are used as fungicides in agriculture against *Puccinia recondita*.[12] In addition, the monoacetate and the monobutyrate of propylene glycol and the monoacetate of glycerol are found to be extremely valuable biosurfactants with numerous applications in the food, cosmetics and pharmaceutical preparations.[13,14] We have prepared the twelve esters - eight butanoates (**10-17**) and four acetates (**26-29**) in a regiocontrolled manner for the first time and have fully characterised them from their spectral data.

EXPERIMENTAL

The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker AC 250 MHz spectrometer, the chemical shifts are expressed in δ values and J values are expressed in Hz. The IR spectra were recorded on a Shimadzu model 435 spectrophotometer using nujol film. Mass spectra were recorded on a Varian Mat 311A instrument. Analytical and preparative TLC were carried out on silica gel-GF_{254} E.Merck and the spots were detected by reaction with iodine, alternatively by spraying with 50% aqueous H_2SO_4 and heating at 110°C. Column chromatography was performed with silica gel G (60-80 mesh). Porcine pancreatic lipase (PPL, Type II) and *Candida cylindracea* lipase (CCL, Type VII) were obtained from Sigma Chemical Company. Both the enzymes were kept under vacuum over P_2O_5 for 3-4 hr prior to their use. Acetone was dried and distilled just prior to use from fused potassium carbonate.

General procedure of lipase-catalysed transesterification in organic solvents. To a stirred solution of the diol (5 mmol) in the dry organic solvent (50 ml) containing TFEB(6 mmol), PPL (500 mg) was added and the suspension was stirred at 42°-45°C. The reaction was monitored by TLC and quenched by filtering off the enzyme. Solvent was removed *in vacuo* and the product esters were isolated by column/preparative thin layer chromatography. All the esters were obtained as colourless oily materials and have been fully identified on the basis of their spectral data.

2-Phenyl-2-hydroxyethyl butyrate(**10**), 68%; ^{1}H-NMR($CDCl_3$) : 0.95(3H, t, J= 7 , H-4), 1.63 (2H,m, H-3), 2.31(2H, t, J= 7, H-2),2.63 (1H, br s, OH), 4.19 (1H, d, J= 6 , H-2'), 4.91(2H, m,H-1') and 7.46 (5H,m, aromatic protons); IR : 3400, 1720, 1490, 1445, 1370 and 1235 cm^{-1}; ^{13}C-NMR($CDCl_3$): 13.61(C-4), 18.39(C-3), 36.36 (C-2), 68.12 (C-1'), 76.41(C-2'), 126.17 (C-3" & C-5"), 128.19 (C-4"), 128.57 (C-2" & C-6"), 139.97 (C-1") and 173.29 (C-1); CIMS, m/z(%): 209.4 $[M+1]^+$(10), 191$[M-H_2O]^+$(100) and 71 $[C_3H_7CO]^+$ (10).

2-Hydroxypropyl butyrate (**11**), 75%; ^{1}H-NMR($CDCl_3$): 0.95(3H, t, J= 7 , H-4), 1.25 (3H, d, J = 7, H-3'), 1.65(2H,m, H-3), 2.35 (2H, t, J=7 , H-2), 4.00-4.12 (3H, m, H-1' & H-2') and 4.35 (1H, br s, OH); IR :3420, 1720, 1460 and 1375 cm^{-1}; ^{13}C-NMR($CDCl_3$):13.63 (C-4), 18.45 (C-3'), 19.2 (C-3), 36.44 (C-2), 66.19(C-1'), 71.79 (C-2') and 173.79 (C-1); CIMS, m/z (%): 147 $[M+1]^+$(100), 129 $[M-H_2O]^+$ (32), 89$[C_3H_7COOH]^+$(4) and 71 $[C_3H_7CO]^+$(6).

3-Hydroxybutyl butyrate (**12**), 60%; ^{1}H-NMR($CDCl_3$): 0.95 (3H, t, J=7 , H-4), 1.24(3H, d, J=7 , H-4'), 1.67 (4H, m, H-3 & H-2'), 2.16 (2H, t, J= 7 , H-2), 2.66 (1H, br s, OH), 3.84 (1H, m, H-3') and 4.22 (2H, m, H-1'); IR : 3400, 1720, 1450 and 1380 cm^{-1}; ^{13}C-NMR($CDCl_3$): 13.65 (C-4), 18.57 (C-3), 23.52 (C-4'), 36.3(C-2'), 38.2 (C-2), 61.62 (C-1'), 64.91 (C-3') and 173.98 (C-1); CIMS, m/z (%): 161 $[M+1]^+$ (51.7), 143 $[M-H_2O]^+$ (100), 89 $[CH_3CH(OH)C_2H_4O]^+$(60) and 71 $[C_3H_7CO]^+$ (100).

2-Hydroxybutyl butyrate (**13**), 70%; ^{1}H-NMR($CDCl_3$) 0.92 (6H, m, H-4 and H-4'), 1.59 (4H, m, H-3' and H-3), 2.26 (2H, t, J=7, H-2), 2.55 (1H, br s, OH), 3.64 (1H, m, H-2') and 4.04-4.12(2H, m, H-1'); IR : 3400, 1730, 1458 and 1370 cm^{-1}; ^{13}C-NMR($CDCl_3$):9.74(C-4'), 13.66 (C-4), 18.49(C-3'), 23.77(C-3), 36.39 (C-2), 68.20 (C-1'), 76.5(C-2') and 173.96 (C-1); CIMS, m/z, (%) : 161.4 $[M+1]^+$ (100), 143.4 $[M-H_2O]^+$ (25), 89 $[C_2H_5CH(OH)CH_2O]^+$ (15) and 71 $[C_3H_7CO]^+$ (17).

2-Hydroxypentyl butyrate (**14**), 65%; ^{1}H-NMR($CDCl_3$): 0.95 (6H, m, H-4 and H-5'), 1.48 (6H, m, H-3, H-3' and H-4'), 2.21 (1H, br s, OH), 2.38(2H, t, J=7, H-2), 3.62 (1H, m, H-2') and 4.25 (2H, m, H-1'); IR : 3400, 1720, 1450, 1380, 1250 and 1170 cm^{-1}; ^{13}C-NMR($CDCl_3$): 13.64 (C-5'), 13.69 (C-4), 18.46 (C-4'), 29.69 (C-3), 36.12 (C-3'), 36.45 (C-2), 64.95 (C-1'), 76.41 (C-2') and 173.87 (C-1); CIMS, m/z, (%) : 175 $[M+1]^+$(100), 157 $[M- H_2O]^+$(14), 102 $[C_3H_7CH(OH)CH_2O]^+$(5) and 71 $[C_3H_7CO]^+$(10).

2-Hydroxyhexyl butyrate(**15**), 65%; ^{1}H-NMR($CDCl_3$) : 0.95(6H, t, J= 7, H-4 and H-6'), 1.35 (6H, m, H-3, H-4' and H-5'), 1.62 (2H, m, H-3'), 2.09 (1H, br s, OH), 2.34 (2H, t, J= 7, H-2), 3.63 (1H, m, H-2') and 4.14 (2H, m, H-1'); IR : 3450, 1740, 1450 and 1370 cm^{-1}; ^{13}C-NMR($CDCl_3$): 13.64 (C-6'), 13.69 (C-4), 18.45 (C-5'), 22.52 (C-4'), 22.64(C-3), 36.12 (C-3'), 36.46 (C-2), 64.94 (C-1'), 75.46 (C-2')and 173.87 (C-1); EIMS, m/z, (%) : 188 $[M]^+$(92), 170 $[M-H_2O]^+$(100), 116 $[C_4H_9CH(OH)CH_2O]^+$(4), 101 $[C_4H_9CH(OH)CH_2]^+$(21), 87 $[C_3H_7COO]^+$ (36) and 71 $[C_3H_7CO]^+$(85).

2-Hydroxyoctyl butyrate (**16**), 60%; ^{1}H-NMR($CDCl_3$): 0.89(6H,t, J=7, H-4 and H-8'), 1.23 (8H, m, H-4', H-5', H-6' and H-7'), 1.46 (2H, m, H-3), 1.62 (2H, m, H-3'), 2.05 (1H, br s, OH), 2.39 (2H, t, J=7, H-2), 3.65 (1H, m, H-2') and 4.18 (2H, m, H-1'); IR : 3400, 1730, 1450 and 1370 cm^{-1}; ^{13}C-NMR($CDCl_3$): 13.64 (C-8'), 14.0 (C-4), 18.49 (C-7'), 18.58 (C-6'), 22.57 (C-5'), 25.29 (C-4'), 25.34 (C-3), 36.16 (C-3'), 36.49 (C-2), 68.55(C-1'), 76.59 (C-2') and 173.74 (C-1); CIMS, m/z (%): 217$[M+1]^+$ (100), 199 $[M-H_2O]^+$(41), 129 $[C_6H_{13}CH(OH)CH_2]^+$(8), 111$[C_6H_{13}CH=CH]^+$ (10) and 71$[C_3H_7CO]^+$ (12).

N-(3'-butanoyloxy)propyl-3,3-dimethyl-2,4-dihydroxybutanamide(**17**), 99%; ^{1}H-NMR($CDCl_3$): 0.95 (9H, m, 3X-CH_3), 1.62 (2H, m, H-3), 1.84 (2H, m, H-2'), 2.18 (2H, br s, 2XOH), 2.33 (3H, m, H-2 and NH), 3.33 (2H, t, J=9 , H-1'), 3.51 (2H, s, H-4"), 4.03 (1H, s, H-2") and 4.15 (2H, t, J=9 , H-3'); IR : 3350, 1720, 1640, 1520, 1450 and 1360 cm^{-1}; ^{13}C-NMR($CDCl_3$):13.67 (C-4), 18.45 (CH_3), 20.29 (CH_3), 21.39 (C-3), 36.01 (C-2'), 36.18 (C-2), 39.36 (C-1'), 40.2 (C-3"), 61.80 (C-4"), 71.27 (C-3'), 76.41 (C-2") and 173.35 (C-1 and C-1"); CIMS, m/z,(%) : 276 $[M+1]^+$ (45), 258 $[M-H_2O]^+$(100), 203 $[C_3H_7CO]^+$ (10), 146 (45) and 115 (6).

General procedure of lipase-catalysed deacylation in organic solvents. The eight acetates **18-25** were prepared by acetic anhydride-pyridine method either at room temperature or by heating below 100° in 80-85% yield, all the acetates were identified by comparison of their physical and spectral data with those reported in the literature. To a stirred solution of 1,2-diacetyloxyalkane (10 mmol) in di-isopropyl ether (25 ml) containing n-butanol (50 mmol), PPL (500 mg) was added and the suspension was stirred at 45°C, the progress of reaction was monitored by TLC. After 48 hr, the reaction was quenched by filtering off the enzyme, the solvent removed to dryness *in vacuo* and the product isolated by preparative thin layer chromatography. The esters were obtained as colourless oily materials and were fully identified on the basis of their spectral data.

2-Phenyl-2-hydroxyethyl acetate (**26**), 75%; IR : 3330, 1730, 1460, 1320 cm^{-1}; ^1H NMR ($CDCl_3$): 2.03 (3H, s, H-2),2.88 (1H, br s,OH), 4.28 (1H, m, H-2'), 4.83 (2H, m, H-1') and 7.56 (5H, br s, aromatic protons); ^{13}C NMR ($CDCl_3$) : 29.26 (C-2), 65.96 (C-1'), 76.62 (C-2'),126.12 (C-3" & C- 5"),126.63 (C-4"),128.56 (C-2" & C-6"), 139.97 (C-1") and 171.1 (>C=O); CIMS, m/z (%) : 181 $[M+1]^+$(5), 163 $[M-H_2O]^+$ (100), 120 $[M - COCH_3]^+$ (30), 107 $[M - CH_3COOCH_2]^+$ (70) and 77 $[C_6H_5]^+$ (22).

2-Hydroxybutyl acetate (**27**), 45%; IR : 3400, 1725, 1460 and 1370 cm^{-1}; ^1H NMR ($CDCl_3$) : 0.92 (3H, t, J=7, H-4'), 1.46 (2H, m, H-3'), 2.07 (3H, s, H-2), 3.66 (1H, m, H-2') and 4.43 (2H, m, H-1'); ^{13}C NMR ($CDCl_3$) : 13.97 (C-4'), 18.60 (C-3'), 29.71 (C-2), 64.92(C-2'), 75.49 (C-1') and 174.59 (C-1); CIMS, m/z (%) : 133 $[M+1]^+$ (6), 115 $[M-H_2O]^+$ (20), 89 $[C_2H_5CH(OH)CH_2O]^+$ (10), 84 $[CH_3COOCH_2]^+$ (30) and 74 $[C_2H_5CH(OH)CH_2]^+$ (30).

2-Hydroxypentyl acetate (**28**), 20%; IR : 3350, 1730, 1500 and 1450 cm^{-1}; ^1H NMR ($CDCl_3$) : 0.92 (3H, t, J=7, H-5'), 1.32 (4H, m, H-3' & H-4'), 1.93 (3H, s, H-2), 3.52 (1H, m, H-2') and 4.13 (2H, m, H-1').

2-Hydroxyhexyl acetate (**29**), 12%; IR : 3400, 1720, 1450 and 1360 ; ^1H NMR ($CDCl_3$) : 0.92 (3H, t, J=7, H-6'), 1.41 (6H, m, H-3', H-4' & H-5') , 2.07 (3H, s, H-2), 2.49(1H, br s, OH), 3.56 (1H, m, H-2') and 3.98 (2H, m, H-1').

2-Phenyl-2-acetoxy ethyl butyrate (**30**). Acetylation of **10** with acetic anhydride/pyridine afforded **30**, which was purified by column chromatography; ^1H NMR (CCl_4) : 0.95 (3H, t, J=7, H-4), 1.63 (2H, m, H-3), 2.20 (2H, m, H-2), 2.10 (3H, s, CH_3-COO), 4.18 (2H, m, H-1'), 5.80 (1H, m, H-2'), 7.16 (5H, m, aromatic protons).

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References

1. Whitesides, G.M.; Wong, C.H. *Angew. Chem. Int. Ed. Engl.*, 1985, **24**, 617.
2. Jones, J.B. *Tetrahedon*, 1986, **42**, 3351.
3. Klibanov, A.M. *Chemtech*, 1986, **16**, 354.
4. Hennen, W.J.; Smeers, H.M.; Wang, Y.F.; Wong, C.H. *J. Org. Chem.*, 1988, **53**, 4939.
5. Chen, C.S.; Sih, C.J. *Angew. Chem. Int. Ed. Engl.*, 1989, **28**, 695.
6. Ramaswamy, S.; Morgan, B.; Ochischilager, A.C. *Tetrahedron Lett.*, 1990, **31**, 3405.
7. Bhalerao, U.T.; Dasaradhi, L.; Neelakantan, P.; Fadnavis, N.W. *J. Chem. Soc., Chem. Commun.*, 1991, 1197.
8. Hult, K. ; Norin, T. *Pure Appl. Chem.*, 1992, **64**, 1129.
9. Regen, S.L.; Singh A.; Oehme, G.; Singh, M. *J. Am. Chem. Soc.*, 1982, **104**, 791.
10. Iriuchijima, S.; Kojima, N. *Agric. Biol. Chem.*, 1982, **46**, 1153
11 Rehn, D.; Siegert, W.; Nolte, H. *Pharm. Acta. Helv.*, 1984, **59**, 162; *Chem. Abstr.*, 1984, **101**, 51626.
12. Zierke, T.; Ziepperer, B.; Sauter, H.; Ammermann, E. ; Lorenz, G. *European Patent; Chem. Abstr.*, 1991, **115**, 207976.
13. Toshiaki, N.; Tetsuya, M. *Japanese Patent; Chem. Abstr.*, 1976, **84**, 149559.
14. Ader, U.; Andersch, P.; Berger, M.; Goergens, U.; Seemayer, R. ; Schneider , M. *Pure Appl. Chem.*, 1992, **64**, 1165.