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Ranjeet V. Nair & Manikrao M. Salunkhe

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**A VERSATILE AND CONVENIENT REGIOSELECTIVE
ACYLATION OF 2'-DEOXYNUCLEOSIDES AND
RIBONUCLEOSIDES BY SUPPORTED LIPASES OF
PSEUDOMONAS CEPACIA**

Ranjeet V. Nair and Manikrao M. Salunkhe*

Department of Chemistry, The Institute of Science,
15-Madam Cama Road, Mumbai 400 032, India

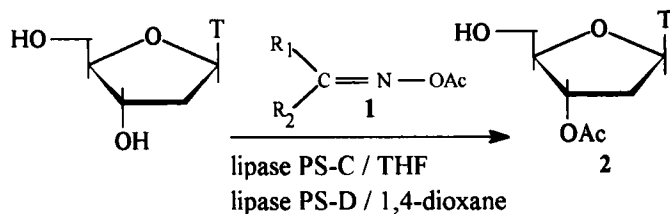
ABSTRACT : *Pseudomonas Cepacia* lipase supported on ceramic particles (lipase PS-C) and on diatomite (lipase PS-D) regioselectively acylated 2'-deoxynucleosides and ribonucleosides to 3'-*O*-acetyl- 2'-deoxynucleosides and 3'-*O*-acetyl-ribonucleosides with oxime esters in organic solvents at room temperature. This enzymatic reaction was significant because the regioselectivity was total; as any other regioisomer nor the N-acylated product were observed.

We are able to report the regioselective acylation of ribonucleosides to 3'-*O*-acyl ribonucleosides using lipase PS-C and PS-D from unprotected ribonucleosides. Lipase PS-C have been successfully employed for the

* To whom correspondence should be addressed.

synthesis of achiral half esters¹ and for the resolution of (±) - 2,3 epoxypropyl esters.² The reaction between 2'-deoxynucleosides or ribonucleosides with oxime esters did not take place in the absence of the enzyme even if strong conditions were employed. Thymidine was chosen as the substrate for the acylation reaction with different oxime esters for both PS-C and PS-D (Scheme-1). Firstly solvents for these acylation reactions were idealized. It was observed that polar solvents enhanced the reaction rates. THF was the ideal solvent for lipase PS-C concomitantly 1,4-dioxane was a better solvent for lipase PS-D. The results are compiled in Table-1. From Table-1 it can be inferred that O-acetyl benzophenone oxime (**1h**) was a better acylating agent than all other oxime esters studied for both lipase PS-C and PS-D. Reactions with different 2'-deoxynucleosides and ribonucleosides were studied using O-acetyl benzophenone oxime (**1h**) as the acylating agent (Scheme-2). The results are summarized in Table-2.

SCHEME - 1



T = Thymine

TABLE - 1

1	R ₁	R ₂	2	
			Lipase PS-C in THF (% yield)	Lipase PS-D in 1,4-dioxane (% yield)
a	CH ₃	CH ₃	74	76
b	CH ₃	C ₂ H ₅	76	75
c		(CH ₂) ₅	77	78
d	C ₆ H ₅	H	81	82
e	C ₆ H ₅	CH ₃	80	79
f	p-H ₃ C-C ₆ H ₄	CH ₃	79	77
g	p-O ₂ N-C ₆ H ₄	CH ₃	82	81
h	C ₆ H ₅	C ₆ H ₅	87	88

SCHEME - 2

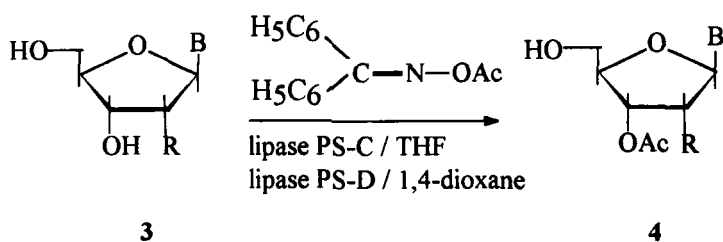


TABLE - 2

3			4		
		mp (° C)	Lipase PS-C in THF (% yield)	Lipase PS-D in 1,4-dioxane (% yield)	
a	R = H, B = Ad	218	87	86	
b	R = H, B = U	108	90	91	
c	R = H, B = G	>250	83	81	
d	R = H, B = Cy	oil	80	79	
e	R = OH, B = Ad	180-181	77	75	
f	R = OH, B = U	172-174	79	76	
g	R = OH, B = G	204	73	74	
h	R = OH, B = Cy	141-142	72	70	

The structural elucidation was accomplished by physical constant and by ^{13}C -NMR spectroscopy, the spectrum for compounds **2** and **4** (**a-h**) showed a shift on the C 3' of 4 ppm towards lower fields with respect to the same carbon atom of the starting 2'-deoxynucleosides and ribonucleosides.

EXPERIMENTAL

Products were confirmed by mp / bp and by ^{13}C -NMR spectra. Melting points and boiling points were taken in open capillaries and are uncorrected. ^{13}C -NMR were recorded on Bruker AMX 500 spectrometer using DMSO- d_6 as a solvent and TMS as an internal standard.

Enzymatic acylation of 2'-deoxynucleosides and ribonucleosides

As a typical procedure, 2'-deoxynucleosides or ribonucleosides (1 mmol) and

oxime esters (1 mmol) were added to 10 ml of THF or 1,4-dioxane. The mixture was kept for stirring at room temperature and after about half an hour PS-C and PS-D (50 mg) was added respectively. The reaction progress was monitored by TLC. After 25 hr, the reaction was quenched by filtering the enzyme through a celite pad and the filtrate was evaporated under reduced pressure. The product obtained were purified by column chromatography on silica gel (120-240) using ethyl acetate : methanol (7:3) as the eluant.

^{13}C -NMR (DMSO- d_6 / TMS_{int}) δ [ppm] of 2 and 4 (a-h)

3'-O-acetylthymidine (2): 12.58, 21.67, 36.72, 62.07, 75.38, 84.67, 85.78, 109.36, 136.19, 150.07, 163.79, 169.92.

3'-O-acetyl-2'-deoxyadenosine (4a): 21.51, 36.72, 61.84, 75.21, 84.63, 85.38, 119.56, 140.12, 149.64, 153.86, 158.31, 170.31.

3'-O-acetyl-2'-deoxyuridine (4b): 21.12, 36.61, 61.92, 75.25, 84.01, 85.12, 108.69, 136.07, 152.87, 165.53, 170.12.

3'-O-acetyl-2'-deoxyguanosine (4c): 21.58, 35.67, 61.98, 74.36, 81.57, 83.56, 119.72, 136.23, 151.17, 154.21, 157.58, 172.93.

3'-O-acetyl-2'-deoxycytidine (4d): 20.09, 36.08, 61.88, 74.18, 83.17, 84.27, 97.67, 145.08, 155.41, 162.58, 172.58.

3'-O-acetyladenosine (4e): 21.68, 62.27, 70.01, 75.73, 83.71, 84.83, 121.17, 140.19, 150.22, 152.71, 156.72, 169.94.

3'-O-acetyluridine (4f): 21.36, 62.08, 68.01, 75.56, 84.56, 85.03, 109.77, 135.97, 150.58, 163.79, 170.03.

3'-O-acetylguanosine (4g): 20.71, 62.17, 67.98, 74.08, 81.19, 83.07, 121.26, 135.07, 151.36, 154.29, 158.02, 171.37.

3'-O-acetylcytidine (4h): 21.72, 62.17, 68.11, 75.27, 82.58, 84.21, 98.39, 144.27, 156.21, 164.59, 171.28.

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