

## SELECTIVE LIPASE-CATALYZED ACYLATION OF 4,6-O-BENZYLIDENE-D-GLUCOPYRANOSIDES TO SYNTHETICALLY USEFUL ESTERS

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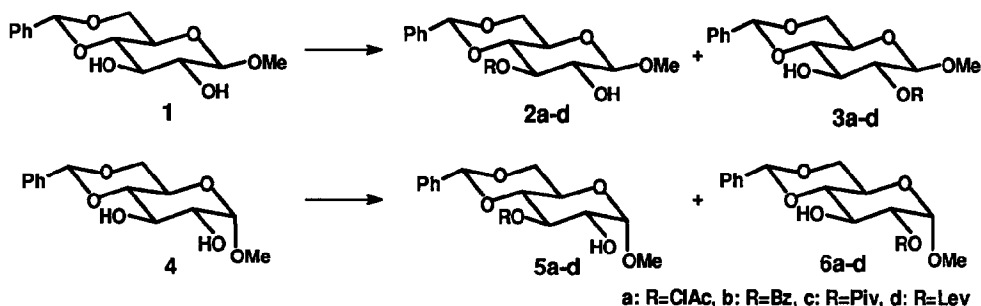
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**Abstract:** Simple and regioselective lipase-catalyzed acylation of compounds **1** and **4** with synthetically useful esters such as benzoates, chloroacetates, pivaloates and levulinates is described.

Selective acylation of different hydroxyls is of great importance and widespread application in carbohydrate chemistry.<sup>1</sup> In previous works, we<sup>2</sup> and others,<sup>3</sup> have reported the efficient lipase-catalyzed acetylation of 4,6-*O*-benzylidene- $\beta$ -D-glycopyranosides, compounds that are particularly suitable for the preparation of other *O*-substituted derivatives as well as for the synthesis of oligosaccharides. Here we report on the extension of this procedure to other acylating agents such as chloroacetates, pivaloates, benzoates and levulinates, esters that are of common use,<sup>4</sup> and can be removed under mild or chemoselective conditions.

The enzyme used was lipase P (from *Pseudomonas cepacia*) adsorbed on celite, and the substrates were methyl 4,6-*O*-benzylidene- $\beta$ - or  $\alpha$ -D-glucopyranosides. As acylating agents the trifluoroethyl or vinyl chloroacetate, benzoate, pivaloate and levulinate<sup>5</sup> have been tested, and compared for their reactivities and selectivities.



In a typical procedure, a suspension of 250 mg of lipase P on celite in 5 ml of the acylating agent/THF mixture containing 100 mg of the sugar was shaken according to the conditions reported in Table 1. Usual work up and, in some cases, flash-chromatography purification afforded the products.<sup>6</sup>

The results are shown in Table 1. The conversion was good for almost all the reactions and, as already observed with acetate donors,<sup>2</sup> the  $\alpha$ -glucoside reacted slower and was acylated at the position 2 with good regioselectivity. The more reactive  $\beta$  isomer was acylated with good selectivity by chloroacetate and vinyl pivaloate, while less satisfactory results were obtained with benzoates and levulinates. As acylating agents both

**Table 1. Lipase Catalyzed Acylation of Methyl 4,6-O-Benzylidene  $\alpha$ - and  $\beta$ -D-Glucopyranosides**

Substrate	Acylating agent/THF ratio (v:v)	Reaction time(h)	Temp.(°C)	Conversion <sup>a</sup>	Products(ratio) <sup>a</sup>
1	trifluoroethyl chloroacetate (3:2)	5	45	94%	2a/3a (97:3)
"	trifluoroethyl benzoate (3:2)	60	80	95%	2b/3b (77:23)
"	trifluoroethyl pivaloate (3:2)	60	60	10%<	-
"	trifluoroethyl levulinate (3:2)	18	80	quantitative	2d/3d (78:22)
"	vinyl chloroacetate (3:2)	0.5	45	quantitative	2a/3a (93:7)
"	vinyl benzoate (3:2)	60	80	96%	2b/3b (73:27)
"	vinyl pivaloate (3:2)	60	60	99%	2c (100)
4	trifluoroethyl chloroacetate (4:1)	18	45	93%	5a/6a (6:94)
"	trifluoroethyl benzoate (4:1)	60	80	98%	5b/6b (2:98)
"	trifluoroethyl pivaloate (4:1)	60	60	10%<	-
"	trifluoroethyl levulinate (4:1)	18	80	98%	5d/6d (18:82)
"	vinyl chloroacetate (4:1)	5	45	quantitative	5a/6a (5:95)
"	vinyl benzoate (4:1)	60	80	97%	5b/6b (3:97)
"	vinyl pivaloate (4:1)	40	60	97%	6c (100)

a. Obtained by HPLC analysis: WHATMAN Partisil 10 (SiO<sub>2</sub>) column, eluent hexane-isopropanol 98:2 for 10 min then to 80:20 in 20 min, 1 ml/min, UV detector,  $\lambda$  260 nm.

the trifluoroethyl and the vinyl esters worked well with the exception of trifluoroethyl pivaloate probably because of solubility problems.

In conclusion, the esterification of the methyl 4,6-O-benzylidene- $\beta$ - or  $\alpha$ -D-glucopyranosides can be simply and efficiently effected using lipase P with synthetically useful acylating agents which have never been used previously. Work is in progress to further extend the scope of the methodology to other carbohydrate derivatives.

#### Acknowledgements

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#### References and notes

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- The trifluoroethyl esters have been prepared with conventional procedures; the vinyl esters have been obtained according to A. S. Mondal, R. Van Der Meer, A. L. German and D. Heikens, *Tetrahedron*, **1974**, *30*, 4205.
- Selected <sup>1</sup>H-NMR data (CDCl<sub>3</sub> sol.): **2a**  $\delta$  5.30 (t,  $J_{2,3}=J_{3,4}=9.3$  Hz, H-3); **2b**  $\delta$  5.47 (t,  $J_{2,3}=J_{3,4}=9.0$  Hz, H-3); **2c**  $\delta$  5.15 (t,  $J_{2,3}=J_{3,4}=9.4$  Hz, H-3); **2d**  $\delta$  5.22 (t,  $J_{2,3}=J_{3,4}=9.5$  Hz, H-3); **3b**  $\delta$  5.18 (t,  $J_{1,2}=J_{2,3}=8.7$  Hz, H-2); **3d**  $\delta$  4.91 (t,  $J_{1,2}=J_{2,3}=8.7$  Hz, H-2); **6a**  $\delta$  4.86 (dd,  $J_{1,2}=3.9$  Hz,  $J_{2,3}=9.8$  Hz, H-2); **6b**  $\delta$  5.04 (dd,  $J_{1,2}=3.9$  Hz,  $J_{2,3}=9.8$  Hz, H-2); **6c**  $\delta$  4.73 (dd,  $J_{1,2}=3.6$  Hz,  $J_{2,3}=9.5$  Hz, H-2); **6d**  $\delta$  4.84 (dd,  $J_{1,2}=3.6$  Hz,  $J_{2,3}=9.2$  Hz, H-2).