Carbohydrate Research, 145 (1986) C5–C7
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Preliminary communication

A new synthesis of lipid Y by the use of chemoselective debenzylation as a key step*

KIYOSHI IKEDA, SHINICHI NAKAMOTO, TOSHIO TAKAHASHI, and KAZUO ACHIWA**
Shizuoka College of Pharmacy, 2-2-1 Oshika, Shizuoka 422 (Japan)

(Received September 27th, 1985; accepted for publication October 11th, 1985)

Improved methods for chemoselective protection and deprotection of 2-amino-2-deoxy-D-glucose derivatives remain important, especially in the field of lipid A syntheses[1–3]. We describe here a chemoselective debenzylation of the glycosidic benzyl group of a 2-amino-2-deoxy-D-glucose derivative that carries another benzyl group protecting a 3-hydroxytetradecanoyl substituent at O-3, and the application of this strategy in an efficient synthesis (Scheme 1) of lipid Y (1, ref. 3), the lipid A component of *Salmonella minnesota*[4].

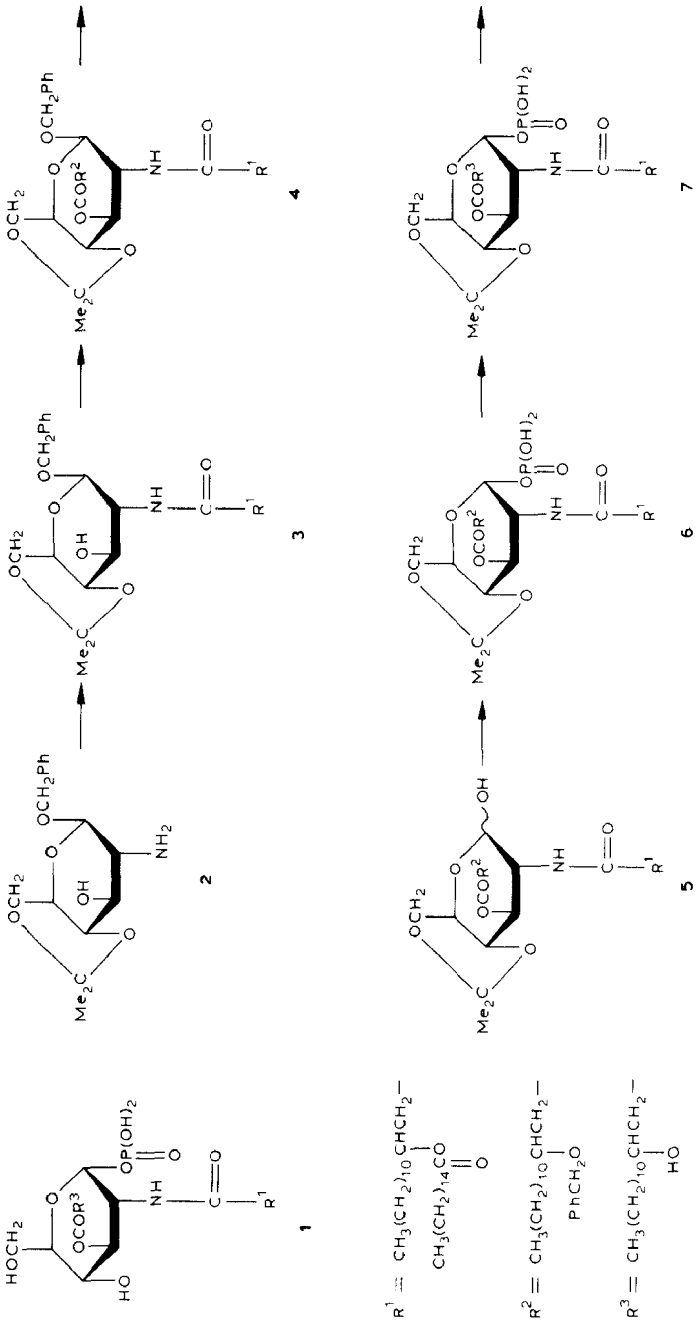
Benzyl 2-amino-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside[1] (2) was *N*-acylated with optically pure (*R*)-3-(hexadecanoyloxy)tetradecanoic acid–*N*,*N*'-dicyclohexylcarbodiimide in CH_2Cl_2 at room temperature for 20 h to afford 3† [97%, m.p. 72–74°, $[\alpha]_D^{20}$ −41.1° (*c* 1.13, $CHCl_3$)]. The 3-hydroxyl group was then acylated with (*R*)-3-benzyloxytetradecanoic acid–*N*,*N*'-dicyclohexylcarbodiimide–*N*,*N*-dimethylaminopyridine in CH_2Cl_2 at room temperature for 20 h to afford 4† [79%, viscous oil, $[\alpha]_D^{20}$ −21.2° (*c* 1.80, $CHCl_3$)]. Selective hydrogenolysis of the glycosidic benzyl group was effected with 10% Pd-on-carbon at 1 bar 1:1 in THF–EtOH to afford the free aldose derivative 5† (64%, viscous oil) as a 3:1 α,β anomeric mixture (^{1}H-n.m.r.). N.m.r. and t.l.c. analyses of this debenzylated product indicated high chemoselectivity. [However, a related experiment indicated that the benzyl group protecting a 2-(3-benzyloxy)tetradecanamido substituent was removed, under the same conditions, as readily as the glycosidic benzyl group.] Anomerization to the α from the β anomer could be accelerated by dissolving the mixture in 3:1 THF–AcOH at room temperature. The glycosidic hydroxyl group was phosphorylated by treatment initially with BuLi in THF at −70°, and then with dibenzylphosphorochloridate at the same temperature[5]. The mixture was immediately subjected to hydrogenolysis with 10% Pd-on-carbon to afford 6† [48%, viscous oil, $[\alpha]_D^{22}$ +17.4° (*c* 0.76, $CHCl_3$)], after purification with a column of silica gel (5:1 $CHCl_3$–CH_3OH). Hydrogenolytic deprotection of the remaining benzyl group was effected with 30% $Pd(OH)_2$-on-carbon in 1:1 THF–MeOH to afford 7† [63%, m.p. 89–92° $[\alpha]_D^{24}$ +15.0° (*c*

*For Part I of the series: Lipid A and Related Compounds, see ref. 1.

**To whom correspondence should be addressed.

†Satisfactory analytical and spectral data were obtained for these compounds.

0008-6215/86/$03.50


1
2
3
4
5
6
7
$R^1 = CH_3(CH_2)_{10}CHCH_2-$
$CH_3(CH_2)_{14}CO$
$R^2 = CH_3(CH_2)_{10}CHCH_2-$
$PhCH_2O$
$R^3 = CH_3(CH_2)_{10}CHCH_2-$
HO

0.44, $CHCl_3$)]. The *O*-isopropylidene group was removed by heating in 90% AcOH for 15 min at 85°, and successive acidic precipitation (0.1M HCl at 0°), and lyophilization from 1,4-dioxane afforded **1**† [90%, m.p. 85–90°, $[\alpha]_D^{25}$ +11.6° (*c* 0.38, $CHCl_3$) (lit.[3] $[\alpha]_D^{13}$ +10.0° (*c* 0.53, $CHCl_3$))].

REFERENCES

1 T. Takahashi, C. Shimizu, S. Nakamoto, K. Ikeda, and K. Achiwa, *Chem. Pharm. Bull.*, 33 (1985) 1760–1762.

2 M. Imoto, H. Yoshimura, N. Sakaguchi, S. Kusumoto, and T. Shiba, *Tetrahedron Lett.*, 26 (1985) 1545–1548, and references therein.

3 S. Kusumoto, M. Yamamoto, and T. Shiba, *Tetrahedron Lett.*, 25 (1984) 3727–3730.

4 (a) U. Seydel, B. Lindner, H.-W. Wollenweber, and E. T. Rietschel, *Eur. J. Biochem.*, 145 (1984) 505–509; (b) K. Takayama, N. Qureshi, P. Mascagni, L. Anderson, and C. R. H. Raetz, *J. Biol. Chem.*, 258 (1983) 14245–14252.

5 M. Inage, H. Chaki, S. Kusumoto, and T. Shiba, *Chem. Lett.*, (1982) 1281–1284.