Synthesis of Enantiomerically Pure Heterocycles: Access to Hydroxylated Piperidines from a Sugar Lactone

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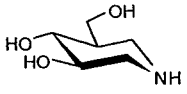
A protected hydroxylated piperidine **7** and its bicyclo- and substituted diastereoisomers **12** and **13**, respectively, have been synthesized from α-D-isosaccharino-1,4-lactone (**3**), in two very short sequences.

The importance of azasugars has increased in the last decade due mostly to their activity against glycosidases.[1,2] Very recently, a new type of these analogues has been synthesised with "a nitrogen atom in place of the anomeric carbon" and they were demonstrated to have a good activity.[3] Unfortunately, the large number of steps involved in each synthesis has caused poor overall yields. Isofagomine (**1**) has been prepared[3a] in a 10 step synthesis (6%) from levoglucosan, whereas its C-4 epimer has been obtained[3b] in only a 2 steps shorter synthesis. *N*-Alkyl-5-hydroxypiperidines **2** have been found to inhibit glycolipid biosynthesis.[3c] The position of the hydroxyl group on C-4 has been demonstrated to induce various activities against glycosidases.[3b] Therefore, it could be interesting to test the activity of a 4-deoxy derivative. We present here a short synthesis of such a piperidine, which is an *N*-benzyl-4-deoxy-analogue of **2** (namely compound **7**), and a synthesis leading to two substituted derivatives **12** and **13**. An optically pure lactone, readily available from lactose, has been chosen as their common starting material.



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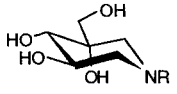
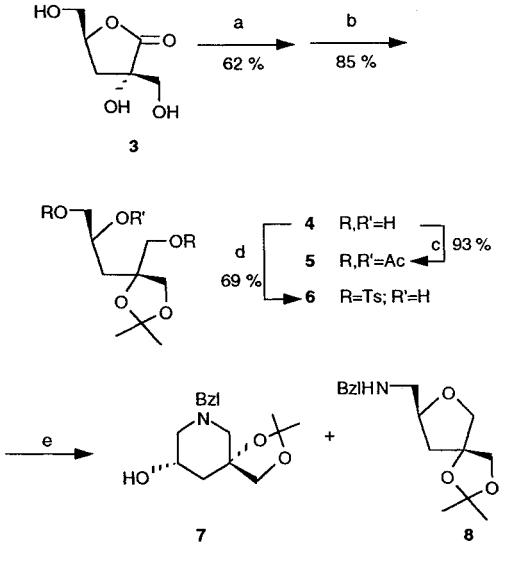


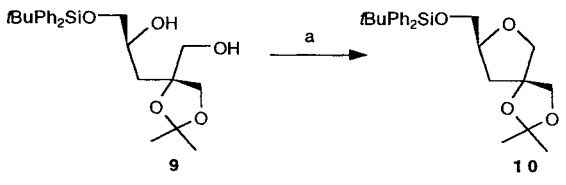
2 R=n-Bu; n-Octyl

The α-D-isosaccharino-1,4-lactone **3** has already been used in different syntheses of biologically active molecules, in our laboratory[4] and by others.[5] It was protected as the 2,2[1]-*O*-isopropylidene derivative according to a well-established procedure, and then reduced with sodium borohydride to give the triol **4** (Scheme 1). It was identified as its corresponding triacetate **5**. The protected pentitol **4** was activated selectively by using 2.4 equivalents of *p*-toluenesulfonyl chloride in a mixture of chloroform/pyridine (2:1) as solvent, leading to the unstable ditosylate **6** (69%). This compound was warmed at 120°C for 48 hours in the presence of benzylamine to give the expected piperidine **7** (53%), and a minor product identified as the tetrahydrofuran **8**. The chemical shifts and coupling constants (^{1}H NMR data, 400 MHz, $CDCl_3$) recorded for the major product were in agreement with the structure of compound **7**. In particular, the retention of the isopropylidene protecting group (δ = 1.32 and 1.40), of the OH-5 (δ = 3.10) and appearance of the *N*-benzyl group (δ = 7.20–7.35) support the structure **7**. The second compound was characterized by comparison with its analogue **10** (Scheme 2). Compound **10** was prepared from the diol **9**[4] in one step, by selective tosylation of the primary hydroxyl group and heating. The resemblance of the NMR spectral data of the two products provided good evidence for the structure of compound **8**.



a)Me_2CO, H^+; b)2.0 eq $NaBH_4$, MeOH; c) Ac_2O, pyr; d) 2.4 eq TsCl, $CHCl_3$/pyr: 2/1; e) NH_2Bzl, 120°C, 48h.

Scheme 1

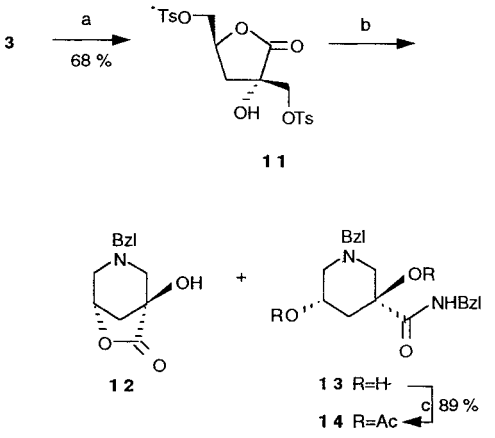


a) TsCl, pyr, rt; then 85-90°C

Scheme 2

By using a two-step sequence from lactone **3** (Scheme 3), we obtained two analogues of the piperidine **7**. Tosylation of the diol **3** with 3.0 equivalents of *p*-toluenesulfonyl chloride led to the ditosylate **11** in good yield (68%). Proof of the ditosylation of both primary hydroxyl groups was deduced from the NMR spectral data obtained for compound **11**. As expected in this case, we noticed, when comparing the ^{13}C NMR data (DMSO-d_6) for compounds **3** and **11**, the downfield chemical shift of

C-2[1] and C-5 (from 63.10 and 62.75 to 73.17 and 70.62 for **3** and **11**, respectively) whereas the signal corresponding to the C-2 quaternary center showed no significant variation. The ditosylate **11** was then heated at 120°C overnight in the presence of benzylamine. Purification of the crude mixture on silica gel (2:1 ethyl acetate/cyclohexane) gave the two protected piperidines **12** and **13**. Their ^{1}H NMR spectral data showed the disappearance of the tosyl groups and the presence of an *N*-benzyl group (multiplet around $\delta = 7.25$, and AB doublet for each proton of the NCH_2 group). Chemical shifts and coupling constants for all other signals, together with the ^{13}C NMR data and elemental analyses, were in agreement with those expected for the piperidines **12** and **13**. In particular, the ^{13}C NMR spectrum for the first compound to be eluted ($R_f \sim 0.5$) showed one signal at $\delta = 168$, corresponding to the carbonyl of a lactone. Therefore, nucleophilic displacement of both tosyl groups by the primary amine led to the piperidinic ring and gave, as expected,[6] the bicyclic derivative **12** (15%). The configuration of the (1*S*,5*S*)-diastereoisomer was supported undoubtedly by the known configuration of **3**.[7] Concerning the second compound **13** ($R_f \sim 0.2$), the NMR data showed the presence of the piperidinic skeleton and that of two *N*-benzyl groups. Therefore, the formation of the iminosugar proceeded from the nucleophilic attack of two distinct molecules of benzylamine. One of them allowed the expected heterocyclization to form the piperidine; the other one opened the lactone ring, creating a C-3 amide function and liberating a hydroxyl group. The piperidine **13** was identified as its diacetate **14**: both NMR data (^{1}H, ^{13}C and H–C correlation) and elemental analyses corroborated their structures. Attempts to modify yields and/or proportion of these two piperidines by changing the reaction time or the number of equivalents of benzylamine induced no significant modifications of the results described above.



a) 3.0 eq TsCl, $CHCl_3$/pyr: 2/1; b) NH_2Bzl, 120°C, 18h; c) Ac_2O, pyr.

Scheme 3

In summary, we have synthesised new enantiomerically pure polyhydroxylated piperidines by two procedures with decent overall yields (19%, 10%, and 24% respectively for compounds **7**, **12** and **13**) from the same starting material. Further developments using similar short reaction sequences and starting from analogue lactones are currently in progress in our laboratory.

The experimental procedures, analytical techniques and instruments employed were as previously described.[4] Compound **3**, its acetonide derivative, and compound **9** were prepared following the described procedures.[4]

(2*R*,4*S*)-3-Deoxy-2-hydroxymethyl-2,2^1-*O*-isopropylidenepentitol (4):

To a solution of 2,2^1-*O*-isopropylidene-α-D-isosaccharino-1,4-lactone[8] (1.5 g, 7.4 mmol) in anhyd MeOH (15 mL) was added $NaBH_4$ (0.56 g, 14.8 mmol) in small portions. When the reaction was over (monitored by TLC, EtOAc), MeOH was evaporated and the mixture was diluted with water. The overall mixture was extracted continuously (48–60 h) with $CHCl_3$, the organic layer dried and concentrated to give the nearly pure protected pentitol **4**; yield: 1.3 g (85%).

(2*S*,4*S*)-1,4,5-Tri-*O*-acetyl-3-deoxy-2-hydroxymethyl-2,2^1-*O*-isopropylidenepentitol (5):

The triol **4** (0.2 g, 1.0 mmol) was dissolved in anhyd pyridine (3 mL). After addition of Ac_2O (0.5 mL, 1.5 equiv per OH) and a catalytic amount of 4-dimethylaminopyridine (DMAP, 0.1 g), the mixture was stirred overnight. Usual workup and purification by chromatography (1:1 EtOAc/cyclohexane) led to pure triacetate **5**; yield: 0.3 g (93%); $[\alpha]_D$ −15.0 ($c = 1$, $CHCl_3$).

$C_{15}H_{24}O_8$	calc.	C 54.21	H 7.28
(332.4)	found	54.05	7.29

^{1}H NMR (400 MHz, C_6D_6): δ, *J* (Hz) = 1.25 and 1.28 (2s, 6H, $2CH_3$), 1.65, 1.70 and 1.72 (3s, 9H, $3COCH_3$), 1.73 (dd, $J_{3,4} = 5.1$, 1H, H-3), 1.84 (dd, $J_{3,3'} = 14.6$, $J_{3',4} = 7.9$, 1H, H-3′), 3.51 (d, $J_{1,1'} = 8.9$, 1H, H-1), 3.77 (d, 1H, H-1′), 3.93 (dd, $J_{5,5'} = 11.9$, $J_{4,5} = 6.0$, 1H, H-5), 4.00 (d, $J_{2^1,2^{1'}} = 11.4$, 1H, H-2^1), 4.20 (d, 1H, H-2$^{1'}$), 4.35 (dd, $J_{4,5'} = 3.4$, 1H, H-5′), 5.40 (m, 1H, H-4).

^{13}C NMR (100 MHz, C_6D_6): δ = 20.29 and 20.34 [$C(CH_3)_2$], 26.78 and 26.90 ($COCH_3$), 37.19 (C-3), 65.61 (C-1 and C-5), 68.71 (C-4), 72.05 (C-2^1), 80.07 (C-2), 110.21 (CMe_2), 169.64, 169.74 and 169.96 (C=O).

(2*S*,4*S*)-3-Deoxy-2-hydroxymethyl-2,2^1-*O*-isopropylidene-1,5-di-*O*-(*p*-toluenesulfonyl)pentitol (6):

To a solution of triol **4** (0.5 g, 2.4 mmol) in a mixture of anhyd $CHCl_3$/pyridine (2:1, 7 mL) at 0°C, was added TsCl (1.1 g, 5.76 mmol). After stirring overnight, the mixture was poured onto ice and neutralized with Na_2CO_3, extracted with CH_2Cl_2, dried and concentrated. The crude product was purified by chromatography (1:2:1 EtOAc/cyclohexane/CH_2Cl_2) to give **6**. The compound is not stable and should be used within a day after its preparation; yield: 0.9 g (69%); $[\alpha]_D$ + 1.5 ($c = 1$, $CHCl_3$).

^{1}H NMR (400 MHz, C_6D_6): δ, *J* (Hz) = 1.11 and 1.16 (2s, 6H, $2CH_3$), 1.47 (m, 2H, H-3, H-3′), 1.85 (s, 6H, 2 ArCH_3), 2.35 (s, 1H, OH-4), 3.47 (d, $J_{1,1'} = 9.5$, 1H, H-1), 3.71 (dd, $J_{5,5'} = 10.2$, $J_{4,5} = 6.4$, 1H, H-5), 3.75 (d, 1H, H-5′), 3.75 (d, 1H, H-1′), 3.82 (m, 1H, H-4), 4.00 (d, $J_{2^1,2^{1'}} = 9.9$, 1H, H-2^1), 4.09 (d, 1H, H-2$^{1'}$), 6.76 (m, 4H, Ar), 7.76 (m, 4H, Ar).

^{13}C NMR (100 MHz, C_6D_6): δ = 21.83 [$C(CH_3)_2$], 27.14 and 27.68 (ArCH_3), 38.28 (C-3), 66.75 (C-4), 71.72, 72.01 and 74.51 (C-1, C-2^1 and C-5), 81.16 (C-2), 110.87 (CMe_2), 128.93, 130.65 and 145.38 (Ar).

(3*R*,5*S*)-3,5-Dihydroxy-3-hydroxymethyl-3,3^1-*O*-isopropylidene-*N*-benzylpiperidine (7) and (2*S*,4*R*)-2-Benzylaminomethyl-4-hydroxymethyl-4-hydroxy-4,4^1-*O*-isopropylidenetetrahydrofuran (8):

A solution of ditosylate **6** (1.4 g, 2.7 mmol) in benzylamine (3.5 mL) was heated at 120°C for 48 h. After cooling, the mixture was partitioned between brine (20 mL) and CH_2Cl_2 (80 mL). Evaporation of the solvent and chromatography (EtOAc) afforded two compounds: **7** (R_f 0.6) as a white solid and the unstable **8** ($R_f \sim 0.4$).

7; yield: 0.4 g (53%); mp 48–50°C; $[\alpha]_D$ + 3.5 (c = 1, $CHCl_3$).

$C_{16}H_{23}NO_3$	calc.	C 69.29	H 8.36
(277.4)	found	69.38	8.17

^{1}H NMR (400 MHz, $CDCl_3$): δ, J (Hz) = 1.32 and 1.40 (2 s, 6H, $2CH_3$), 1.75 (dd, $J_{4,4'}$ = 12.8, $J_{4,5}$ = 2.7, 1H, H-4), 1.83 (dd, $J_{4',5}$ = ~ 6.0, 1H, H-4'), 2.21 (d, J = 10.4, 1H, H-2 or NCH_2), 2.46 (d, J = 9.8, 1H, H-2 or NCH_2), 2.55 (d, 2H, H-2' and NCH_2), 3.10 (s, 1H, OH-5), 3.50 (d, $J_{6,6'}$ = 13.5, 1H, H-6), 3.69 (d, 1H, H-3^1), 3.70 (d, 1H, H-6'), 3.80 (m, 1H, H-5), 3.82 (d, $J_{3^1,3^{1'}}$ = 8.6, 1H, H-3$^{1'}$), 7.20–7.35 (m, 5H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.78 and 27.44 [$C(CH_3)_2$], 44.63 (C-4), 59.65, 60.91 and 62.24 (C-2, NCH_2 and C-6), 66.28 (C-5), 72.96 (C-3^1), 79.34 (C-3), 109.75 (CMe_2), 127.19, 128.27, 128.96 and 137.82 (Ar).

8; yield: 0.1 g (11%); $[\alpha]_D$ − 2.3 (c = 0.5, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ, J (Hz) = 1.37 and 1.38 (2 s, 6H, $2CH_3$), 1.72 (s, 1H, NH), 1.80 (dd, $J_{3,3'}$ = 13.1, $J_{3,2}$ = 9.1, 1H, H-3), 2.20 (dd, $J_{3',2}$ = 6.4, 1H, H-3'), 2.65 (dd, $J_{2^1,2^{1'}}$ = 12.3, $J_{2^1,2}$ = 6.8, 1H, H-2^1), 2.80 (dd, $J_{2,2^{1'}}$ = 3.6, 1H, H-2$^{1'}$), 3.74 (d, $J_{5,5'}$ = 9.4, 1H, H-5), 3.80 (d, J = 13.3, 1H, NCH_2), 3.84 (d, 1H, NCH_2), 3.86 (d, 1H, H-5'), 3.91 (d, $J_{4^1,4^{1'}}$ = 8.7, 1H, H-4^1), 3.99 (d, 1H, H-4$^{1'}$), 4.25 (m, 1H, H-2), 7.20–7.35 (m, 5H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.27 and 26.96 [$C(CH_3)_2$], 40.41 (C-3), 52.90 and 53.96 (NCH_2 and C-2^1), 72.51 (C-4^1), 76.87 (C-5), 78.33 (C-2), 87.15 (C-4), 109.74 (CMe_2), 126.99, 128.14, 128.44 and 140.31 (Ar).

(2*S*,4*R*)-2,4-Dihydroxymethyl-4-hydroxy-2^1-*O*-*tert*-butyldiphenylsilyl-4,4^1-*O*-isopropylidenetetrahydrofuran (10):

To a solution of **9** (0.5 g, 1.1 mmol) in anhyd pyridine (3 mL) cooled in an ice bath, was added TsCl (0.7 g, 3.63 mmol). After stirring overnight until the disappearance of the starting material, the solution was heated at 85 – 90°C and stirred for 24 h. The reaction was quenched by addition of water (5 mL) and extracted with CH_2Cl_2, the organic layer dried, evaporated and the residue chromatographed (1:9 EtOAc/cyclohexane) to afford pure **10**; yield: 0.25 g (52%); mp 73–75°C; $[\alpha]_D$ + 4.3 (c = 1, $CHCl_3$).

$C_{25}H_{34}O_4Si$	calc.	C 70.38	H 8.03
(426.6)	found	70.63	8.10

^{1}H NMR (400 MHz, $CDCl_3$): δ, J (Hz) = 1.08 (s, 9H, t-C_4H_9), 1.40 and 1.41 (2 s, 6H, $2CH_3$), 1.99 (dd, $J_{3,3'}$ = 13.2, $J_{3,2}$ = 8.5, 1H, H-3), 2.20 (dd, $J_{3',2}$ = 6.9, 1H, H-3'), 3.68 (dd, $J_{2^1,2^{1'}}$ = 10.9, $J_{2^1,2}$ = 4.2, 1H, H-2^1), 3.74 (dd, $J_{2,2^{1'}}$ = 4.1, 1H, H-2$^{1'}$), 3.80 (d, $J_{5,5'}$ = 9.2, 1H, H-5), 3.87 (d, 1H, H-5'), 3.93 (d, $J_{4^1,4^{1'}}$ = 8.5, 1H, H-4^1), 4.00 (d, 1H, H-4$^{1'}$), 4.25 (m, 1H, H-2), 7.30–7.75 (m, 10H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.32 (CMe_3), 26.35, 26.63, 26.69 and 26.98 (CMe_2 and CMe_3), 38.53 (C-3), 65.76 (C-2^1), 72.00 (C-4^1), 76.89 (C-5), 79.17 (C-2), 87.24 (C-4), 109.77 (CMe_2), 127.76, 129.69, 133.43, 133.47, 134.88, 135.67 and 135.70 (Ar).

(2*S*,4*S*)-3-Deoxy-2-hydroxymethyl-2^1,5-di-*O*-*p*-toluenesulfonyl-D-*erythro*-pentono-1,4-lactone (11):

The tosylation of compound **3** (4.5 g, 27.7 mmol) performed as in the preceding procedure, using 3.0 equiv (8.0 g) of TsCl, afforded the ditosylate **11** after purification by chromatography (1:1 EtOAc/cyclohexane); yield: 8.9 g, (68%); mp 103–104°C (lit.[7] mp 110–111°C); $[\alpha]_D$ + 37.1 (lit.[7] $[\alpha]_D$ + 36.0) (c = 1, $CHCl_3$).

$C_{20}H_{22}O_9S_2$	calc.	C 51.06	H 4.71	O 30.60
(470.5)	found	50.77	4.72	30.34

^{1}H NMR (400 MHz, C_6D_6): δ, J (Hz) = 1.55 (dd, $J_{3,3'}$ = 14.1, $J_{3,4}$ = 6.8, 1H, H-3), 1.66 (dd, $J_{3',4}$ = 8.5, 1H, H-3'), 1.83 (s, 6H, 2 Ar*Me*), 2.50 (s, 1H, OH-2), 3.50 (dd, $J_{5,5'}$ = 11.5, $J_{4,5}$ = 5.2, 1H, H-5), 3.72 (dd, $J_{4,5'}$ = 2.9, 1H, H-5'), 3.87 (d, $J_{2^1,2^{1'}}$ = 10.3, 1H, H-2^1), 4.00 (d, 1H, H-2$^{1'}$), 4.03 (m, 1H, H-4), 6.70 (d, J = 8.2, 4H, Ar), 7.70 (d, 4H, Ar).

^{13}C NMR (100 MHz, C_6C_6): δ = 21.12 (Ar*Me*), 33.86 (C-3), 68.77 and 70.31 (C-2^1 and C-5), 74.15 (C-2), 74.43 (C-4), 130.03, 130.07, 144.86 and 145.03 (Ar), 173.17 (C-1).

(1*S*,5*S*)-3-Benzyl-1-hydroxy-7-oxo-6-oxa-3-azabicyclo[3.2.1]octane (12) and (3*S*,5*S*)-3-Benzylamido-3,5-dihydroxy-*N*-benzylpiperidine (13):

Following the same procedure as for **7**, the ditosylate **11** (4.0 g, 8.5 mmol) was heated in the presence of benzylamine. After the same treatment, and purification by chromatography (2:1 EtOAc/cyclohexane) two compounds were obtained respectively **12** (R_f ~ 0.5) and **13** (R_f ~ 0.2).

12; yield: 0.3 g (15%); mp 89–91°C; $[\alpha]_D$ + 8.8 (c = 1, $CHCl_3$).

$C_{13}H_{15}O_3N$	calc.	C 66.94	H 6.48	O 20.58
(233.3)	found	66.30	6.59	19.08

^{1}H NMR (400 MHz, $CDCl_3$): δ, J (Hz) = 1.93 (d, $J_{8,8'}$ = 9.9, 1H, H-8), 2.38 (dd, $J_{8',5}$ = 1.5, 1H, H-8'), 3.92 (d, J = 8.0, 1H, H-2 or NCH_2), 3.96 (d, J = 7.6, 1H, H-2 or NCH_2), 4.03 (d, J = 8.0, 1H, H-2' or NCH_2), 4.24 (d, J = 7.6, 1H, H-2' or NCH_2), 4.48 (dd, br, $J_{4,4'}$ = 14.8, $J_{4,5}$ = 5.8, 1H, H-4), 4.53 (dd, br, $J_{4',5}$ = 6.0, 1H, H-4'), 4.68 (m, 1H, H-5), 7.00 (s, 1H, OH-3), 7.20–7.40 (m, 5H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.60 and 43.25 (C-4 and C-8), 76.21 and 77.00 (NCH_2 and C-2), 78.50 (C-5), 86.50 (C-1), 127.81, 127.97, 128.95 and 137.50 (Ar), 168.00 (C=O).

13; yield: 1.0 g (35%); mp 120–122°C; $[\alpha]_D$ − 25.0 (c = 1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ, J (Hz) = 1.95 (dd, $J_{4,4'}$ = 12.9, $J_{4,5}$ = 9.4, 1H, H-4), 2.03 (dd, br, $J_{4',5}$ = 5.0, 1H, H-4'), 2.18 (m, 1H, NCH_{2a}), 2.55 (d, J = 11.3, 1H, NCH_{2b}), 2.65 (d, 1H, $NCH_{2b'}$), 2.90 (m, 1H, $NCH_{2a'}$), 3.55 (m, 2H, H-2 and H-2'), 3.99 (m, 1H, H-5), 4.38 (dd, $J_{6,6'}$ = 14.6, $J_{5,6}$ = 5.7, 2H, H-6 and OH), 4.45 (dd, $J_{5,6'}$ = 5.9, 1H, H-6'), 5.80 (s, 1H, OH), 7.20–7.35 (m, 10H, Ar), 7.50 (s, 1H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.45 (C-4), 43.22 (C-6), 59.88 and 60.53 (2 NCH_2), 62.09 (C-2), 65.07 (C-5), 73.54 (C-3), 127.54, 127.72, 127.89, 128.51, 128.74, 129.13, 137.15 and 137.94 (Ar), 173.35 (C=O).

(3*S*,5*S*)-3,5-Di-*O*-acetyl-3-benzylamido-3,5-dihydroxy-*N*-benzylpiperidine (14):

The classical acetylation (see, preparation of **5**) of **13** (1.0 g, 2.9 mmol) in the presence of DMAP gave, after column chromatography (1:1 EtOAc/cyclohexane), the diacetate **14**; yield: 0.7 g (55%); mp 117–118°C; $[\alpha]_D$ −4.3 (c = 1, $CHCl_3$).

$C_{24}H_{28}N_2O_5$	calc.	C 67.91	H 6.65	N 6.60
(424.5)	found	67.64	6.72	6.95

^{1}H NMR (400 MHz, $CDCl_3$): δ, J (Hz) = 1.92 (s, 3H, $COCH_3$), 2.00 (dd, $J_{4,4'}$ = ~ 14, $J_{4,5}$ = 5.3, 1H, H-4), 2.09 (s, 3H, $COCH_3$), 2.32 (dd, $J_{4',5}$ = ~ 3.5, 1H, H-4'), 2.46 (d, J = ~ 13, 1H, NCH_{2a}), 2.54 (d, J = ~ 11, 1H, NCH_{2b}), 2.75 (d, 1H, $NCH_{2a'}$), 3.51 (d, $J_{2,2'}$ = 13.0, 1H, H-2), 3.58 (d, 1H, H-2'), 3.66 (d, 1H, $NCH_{2b'}$), 4.27 (dd, $J_{6,6'}$ = 14.8, $J_{5,6}$ = 4.4, 1H, H-6), 4.65 (dd, $J_{5,6'}$ = 6.5, 1H, H-6'), 5.12 (m, 1H, H-5), 7.00–7.40 (m, 10H, Ar), 8.10 (s, 1H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.11 and 21.42 ($COCH_3$), 37.00 (C-4), 43.80 (C-6), 55.64 and 57.05 (NCH_2), 62.31 (C-2), 67.01 (C-5), 78.00 (C-3), 127.50, 127.72, 127.85, 128.56, 128.79, 128.97, 136.19 and 138.06 (Ar), 169.93 and 171.03 (C=O).

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