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1,6-Anhydro-*N*-acetyl-β-*D*-glucosamine in the Oligosaccharide Syntheses: I. Synthesis of 3-Acetate and 3-Benzoate of 1,6-Anhydro-*N*-acetyl-β-*D*-glucosamine via the 4-*O*-Trityl Derivative[1]

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Abstract—3-*O*-Acetyl and 3-*O*-benzoyl derivatives of 1,6-anhydro-*N*-acetyl-β-*D*-glucosamine were synthesized via its selective tritylation followed by the 3-*O*-acylation and removal of the trityl protective group. Tritylium trifluoromethanesulfonate, which can easily be prepared by mixing solutions of triphenylcarbinol and trimethylsilyl trifluoromethanesulfonate in an equimolar ratio, was suggested as a reagent for the effective tritylation of a secondary hydroxyl group.

Key words: carbohydrates, O-tritylation; 1,6-anhydro-N-acetyl-β-D-glucosamine; acylation

Within the context of the studies on the synthesis [1, 2] and application [3] of tumor-associated carbohydrate antigens, we have worked out[3] an approach to the convergent synthesis of three spacered oligosaccharides, fragments of antigens with type 2 chains (H, Le^x, and Le^y), with a common structural moiety, lactosamine Galβ1-4GlcNAc.[4] The choice of the glycosyl acceptor, a glucosamine derivative, for introducing a glycosyl residue into the *O*4-position is the critical point in the synthesis of 4-*O*-glycosyl-substituted derivatives of *N*-acetylglucosamine. This is connected with the reduced nucleophilicity of the C4-hydroxyl group in the glucosamine derivatives, which are in energetically the most favorable $^4C_1$-*D*-conformation [4].

We chose the *N*-acetylglucosamine bicyclic derivative (**I**) with a constrained $_4C^1$-conformation, which is characterized by an increased reactivity of the C4-OH group as compared with that of the C3-OH group [4], as a synthone of the *N*-acetylglucosamine unit. This was used in a number of studies both in an attempt of the selective 4-*O*-glycosylation of 3,4-diol (**I**) [5] and for glycosylation of its 3-*O*-acetyl derivative (**VIII**) [5, 6].[5] 3-Acetate (**VIII**) was found to be an effective acceptor in 4-*O*-glycosyation by the Koenigs–Knorr method [6]. However, the large number of stages in schemes [5–8] of the syntheses of 1,6-AnGlcNAc derivatives and the necessity of opening the anhydro cycle made the authors of [9] abandon the schemes using diol (**I**) and return to more traditional glucosamine derivatives with a $^4C_1$-*D*-conformation.

Earlier, we used diol (**I**) and its derivatives as glycosyl acceptors and intermediates in the syntheses of biologically active oligosaccharides containing an *N*-glucosamine unit [1, 2]. The return to diol (**I**) was caused by a report on its two-stage synthesis from GlcNAc [10] and also by a simple synthesis of 4-trityl ether (**II**) from (**I**) developed by us and the preparation, on the basis of (**II**), of 3-*O*-protected derivatives of 1,6-AnGlcNAc with a free hydroxyl group at C4.

The well-known method for the tritylation of a secondary hydroxyl group in monosaccharides developed by Kochetkov *et al.* includes the treatment of the hydroxyl-containing compound with an excess of $TrClO_4$ in the presence of bases [11–13] in CH_2Cl_2. This method has been employed for the synthesis of various derivatives with secondary trityloxy groups, which were then used as glycosyl acceptors in the oligosaccharide syntheses by the method of tritylcyanoalkylidene condensation [14], when the trityl-substituted hydroxyl group directly participated in the glycoside bond formation. However, the laborious

[1] This paper is dedicated to the 70th birthday of Prof. A.Ya. Khorlin.

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[3] See also the subsequent communications of this series.

[4] Abbreviations: 1,6-AnGlcNAc, 1,6-anhydro-*N*-acetyl-β-*D*-glucosamine; CC, column chromatography; TMS-OTf, trimethylsilyl trifluoromethanesulfonate; TrCl, trityl chloride; $TrClO_4$, tritylium perchlorate; TrOH, triphenylcarbinol; TrOTf, tritylium trifluoromethanesulfonate.

[5] For glycosylation of the glucose analogue of 3-acetate (**VIII**), see [7].

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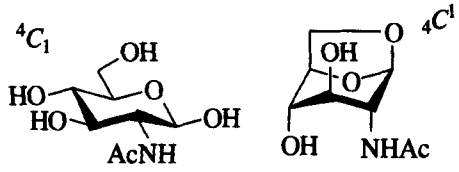
procedure for $TrClO_4$ preparation (a careful treatment of a solution of TrOH in acetic anhydride by 60% perchloric acid and the subsequent washing of the resulting product with a large amount of anhydrous diethyl ether to remove acetic acid and its anhydride) and its explosion hazard, especially when working with large amounts [15], decrease the availability of the resulting trityl ethers.

We suggested a modification that involves the replacement of $TrClO_4$ with TrOTf. The latter is obtained by the addition of a TMS-OTf solution to a TrOH solution in an equimolar ratio and is immediately used in tritylation, performed in the same solvent.[6] This replacement has practically no influence on the effectiveness of tritylation itself but abolishes the disadvantages connected with the preparation and handling of $TrClO_4$.

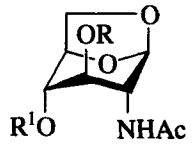
The treatment of diol (**I**) with 3 eq of TrOTf in the presence of 2,4,6-collidine and the subsequent purification by CC resulted in 4-trityl ether (**II**) practically in a quantitative yield. For comparison, we also performed the tritylation with $TrClO_4$ in the presence of collidine. The yield of ether (**II**) after the CC purification was 68%. A preparation of ether (**II**) in 67% yield along with 3-trityl ether (**III**) (8.3%) and a small amount of bistrityl ether (**IV**) by prolonged heating (85–90°C, 62 h) with a TrCl excess in pyridine has been reported [17]. We also isolated bistrityl ether (**IV**) in a low (2–3%) yield from a pooled fraction obtained from several experiments. However, in contrast to the authors of [17], we did not observe the formation of 3-trityl ether (**III**) at the tritylation under our conditions using either $TrClO_4$ or TrOTf. The absence of 3-trityl ether (**III**) in our case may be caused by its easy conversion to the 3,4-bistrityl derivative (**IV**) upon treating with a tritylating agent stronger than TrCl.

Trityl ether (**II**) was then introduced in the benzoylation and acetylation reactions. The benzoylation of 4-trityl ether (**II**) by treating with benzoyl chloride in pyridine diluted with CH_2Cl_2 or benzene gave benzoate (**V**) in a quantitative yield. It should be noted that benzoylation in a mixture of pyridine and CH_2Cl_2 at a large excess of benzoyl chloride (13–14 eq) proceeds at room temperature for 1 h but results in a product requiring the CC purification. The reaction in a mixture of pyridine and benzene with 2.5 eq. of benzoyl chloride proceeds for 16–20 h and practically affords pure derivative (**V**). Detritylation of (**V**) by treating with BF_3Et_2O in the presence of MeOH [18] or by pyridinium perchlorate in a mixture of MeOH and $MeNO_2$ by method [19] results in 3-benzoate (**VI**) with a free hydroxyl group at C4 in 92–95% yield (based on (**II**)).

Sinay *et al.* described one of the shortest possible routes to 3-acetate (**VIII**): this derivative is generated in 2.7% yield as a minor product of the selective acetylation of diol (**I**) with acetic anhydride in pyridine at room temperature. According to these authors, the yield of the major product, 4-acetate (**X**), was 62%. Using acetyl chloride in pyridine diluted with CH_2Cl_2 at cooling allowed us to increase the yield of 3-acetate (**VIII**) up to 16% (the yield of 4-acetate (**X**) was thereby 49%).



(**I**)



(**I**) R = R^1 = H
(**II**) R = H, R^1 = Tr
(**III**) R = Tr, R^1 = H
(**IV**) R = R^1 = Tr
(**V**) R = Bz, R^1 = Tr
(**VI**) R = Bz, R^1 = H
(**VII**) R = Ac, R^1 = Tr
(**VIII**) R = Ac, R^1 = H
(**IX**) R = R^1 = Ac
(**X**) R = H, R^1 = Ac

Taking into account the higher reactivity of the *O*4-axial substituent, we attempted to find a more effective route to 3-acetate (**VIII**) using selective deacetylation of diacetate (**IX**) under conditions of acidic methanolysis [20, 21]. Treating diacetate (**IX**) with hydrogen chloride in a mixture of MeOH and $CHCl_3$ by method [20] gave 3- and 4-acetate (**VIII**) and (**X**) in equal (18%) yields, and the yield of the unreacted diacetate was 60% (at this ratio of the products, diol (**I**) was observed in the reaction mixture).

According to the scheme proposed by us for obtaining 3-acetate (**VIII**), trityl ether (**II**) purified by CC was acetylated with acetic anhydride in pyridine to give acetate (**VII**) in 85% yield. Its detritylation gave acetate (**VIII**) in 92% yield, which was identical to that described earlier [5, 6].

Thus, both the selective acetylation of diol by the procedure we proposed (although somewhat improved as compared to that reported in [5]) and the selective deacetylation of diacetate are ineffective for the preparation of the target 3-acetate (**VIII**). The selective tritylation of diol (**I**) followed by acylation and detritylation remains the best synthetic route to the target compounds (**VI**) and (**VIII**), having a free hydroxyl group at C4.

Some features of the ^1H NMR spectra of the resulting derivatives of 1,6-AnGlcNAc (**II**)–(**X**) should be mentioned. The introduction of two bulky substituents (Tr and Tr or Bz and Tr) into (**IV**) and (**V**) caused marked changes in the spin-coupling constants $J_{6a,5}$,

[6] The preparation of TrOTf by mixing AgOTf and TrOH solutions is described in [16].

$J_{6b,5}$, and $J_{6b,6a}$ even in such a conformationally rigid structure, whereas these constants were practically invariant in the case of one or two small Ac-substituents or in the case of one bulky (Bz or Tr) substituent in compounds (**II**), (**III**), (**VI**)–(**X**), as well as all other coupling constants in compounds (**II**)–(**X**).

The tritylation method by Kochetkov *et al.* [12–14] was proposed in connection with the synthesis of glycosyl acceptors for the cyanoalkylidene condensation [14]. As a rule, tritylation was thereby the last stage of the glycosyl acceptor synthesis, that is, the single free hydroxyl group was tritylated (for selective tritylation of diols, see, e.g. [22, 23]). Obviously, the simplification of the tritylation procedure we suggested permits this reaction to be used as one of stages for manipulation with protective groups in obtaining intermediates in the oligosaccharide synthesis. The derivatives of 1,6-AnGlcNAc (**VI**) and (**VIII**) obtained in this study as well as 4-trityl ether (**II**) itself were used as glycosyl acceptors (this will be described in the subsequent communications).

EXPERIMENTAL

^{1}H NMR spectra (1D; δ, ppm relative to Me_4Si; *J*, Hz) were registered on WM-500 and WM-250 Bruker instruments in $CDCl_3$. The optical rotation was measured on a Jasco DIP-360 polarimeter at 20°C. CC was performed on Silica gel 60 (Merck). TLC was carried out on precoated Silica gel 60 (Merck, 5553) glass or aluminum plates in (A) 9 : 1 : 1 chloroform–methanol–hexane, (B) 1 : 1 toluene–acetone, (C) 9 : 1 chloroform–hexane, and (D) 1 : 1 ethyl acetate–toluene. The spots were visualized by treating with 7% H_3PO_4 and then heating. The solutions in $CHCl_3$ and benzene were dried by filtration through a cotton layer.

Trimethylsilyl trifluoromethanesulfonate was purchased from Sigma and was also obtained by the method reported for the preparation of bistrimethylsilyl sulfate [24]. Diol (**I**) was synthesized by the method [10]. Tritylium perchlorate was a gift from N.N. Malysheva (Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Moscow). Tritylium trifluoromethanesulfonate was prepared directly before use by the addition of a TMS-OTf solution to a solution of the equimolar amount of TrOH in CH_2Cl_2. Diacetate (**IX**) was obtained by the acetylation of diol (**I**) with acetic anhydride in pyridine; mp 138–139°C (ethyl acetate), $[\alpha]_D^{20}$ –94.7° (*c* 1; $CHCl_3$); lit.: mp 139°C, $[\alpha]_D^{20}$ –97° ($CHCl_3$) [6].

1,6-Anhydro-2-acetamido-2-deoxy-4-*O*-trityl-β-*D*-glucopyranose (II). A. A solution of TrOTf (1.5 mmol) in CH_2Cl_2 (5 ml) was added dropwise within 5 min to a suspension of anhydride (**I**) [10] (203 mg, 1 mmol) and 2,4,6-collidine (264 μl, 2 mmol) in CH_2Cl_2 (10 ml). The reaction mixture was stirred at room temperature with TLC monitoring (system A, R_f of the starting diol is 0.12, R_f of 4-trityl ether (**II**) is 0.58) for 2 h. Collidine (total 2 mmol) and TrOTf (total 1.5 mmol) were added several times to the reaction mixture till the starting diol disappeared. The reaction was quenched with 300 μl of pyridine and 500 μl of MeOH, diluted with $CHCl_3$, and washed with water. The organic layer was washed with 1 N HCl, water, saturated $NaHCO_3$, and water and dried by filtration through a cotton layer. The filtrate was evaporated, and the residue was purified by CC. Noncarbohydrate trityl-containing impurities were separated by elution with mixture C, and then elution was performed with 0⟶5% MeOH gradient in mixture C to give 480 mg (the stoichiometric yield is 446 mg; the product contained a less polar trityl-positive impurity) of 4-trityl ether (**II**) as white foam, R_f 0.42 (system B) (R_f values of the starting diol (**I**) and of bistrityl ether (**IV**) are 0.05 and 0.78, respectively). Analytical sample of (**II**): $[\alpha]_D^{20}$ –32.2° (*c* 1; $CHCl_3$), lit.: $[\alpha]_D^{21}$ –33.4° ($CHCl_3$) [17]. ^{1}H NMR: 2.198 (3 H, s, Ac), 3.080 (1 H, dd (br. s), $J_{3,4} \leq 1$, H3), 3.538 (1 H, dd, $J_{6b,6a}$ 7.5, $J_{6b,5}$ 5.6, H6b), 3.705 (1 H, dd (br. s), $J_{4,5} \leq 1$, H4), 3.910 (1 H, ddd (d), $J_{5,6a} \leq 1$, H5), 3.973 (1H, ddd (d), J_{NH} 10, $J_{2,1} \leq 1$, H2), 4.350 (1 H, dd, H6a), 5.40 (1 H, d (br. s), H1), 6.350 (1 H, d, NHAc), and 7.28–7.55 (15 H, m, Ar).

B. 2,4,6-Collidine (680 μl, 5.1 mmol) and $TrClO_4$ (1.371 mg, 4.0 mmol) were added in portions within 2 h at room temperature to a suspension of diol (**I**) (500 mg, 2.46 mmol) in CH_2Cl_2 (20 ml). The reaction mixture was treated and the product was purified by CC as described in procedure A to give 740 mg (68%) of trityl ether (**II**) identical to that described above.

1,6-Anhydro-2-acetamido-2-deoxy-3,4-di-*O*-trityl-β-*D*-glucopyranose (IV). The repeated CC of the combined CC fractions from several experiments containing the trityl-positive product (yellow staining at spraying with diluted H_3PO_4, R_f 0.88 (system A) and 0.78 (system B)) resulted in bistrityl ether (**IV**), colorless prisms after recrystallization from ethyl acetate, mp 238–240°C, $[\alpha]_D^{20}$ –61° (*c* 1; $CHCl_3$). ^{1}H NMR: 1.950 (3 H, s, Ac), 3.540 (1 H, ddd (d), $J_{5,6b} \approx 5.8$, $J_{5,6a} \leq 1$, $J_{5,4} \leq 1$, H5), 3.570 (1 H, dd, $J_{6b,6a} \approx 5.8$, H6b), 3.893 (1 H, dd (br. s), $J_{4,3} \leq 1$, H4), 4.185 (1 H, dd (br. s), $J_{3,2} \leq 1$, H3), 4.355 (1 H, ddd (d), $J_{2,NH}$ 10, $J_{2,1} \leq 1$, H2), 4.480 (1 H, dd (d), H6a), 5.708 (1 H, d (br, s), H1), 6.912 (1H, d, NHAc), and 7.20–7.70 (30 H, m, Ar).

1,6-Anhydro-2-acetamido-3-*O*-benzoyl-2-deoxy-4-*O*-trityl-β-*D*-glucopyranose (V). A. 4-Trityl derivative (**II**) (280 mg, 0.63 mmol) in a mixture of pyridine (5 ml), CH_2Cl_2 (2 ml), and benzoyl chloride (1 ml, 8.6 mmol) was kept at room temperature for 1 h (R_f of the starting (**II**) is 0.58, R_f of the benzoylation product is 0.83, system A). The mixture was diluted with water

(100 μl), kept for 1 h, and partially evaporated, and the residue was treated with saturated $NaHCO_3$ until CO_2 evolution was over and extracted with $CHCl_3$. The extract was washed three times with saturated $NaHCO_3$, then with water, 1 N HCl, water, $NaHCO_3$, and water; filtered through a cotton layer; and evaporated. The residue was purified by CC in a 0⟶20% gradient of ethyl acetate in toluene to give 309 mg (89%) of benzoate (**V**) as a snow-white foam crystallizing at storage, mp 205–206°C, $[\alpha]_D^{20}$ +32.8° (*c* 1; $CHCl_3$). ^1H NMR: 2.09 (3 H, s, Ac), 3.520 (1 H, ddd (d), $J_{5,6b}$ 6.4, $J_{5,6a} \le 1$, H5), 3.550 (1 H, dd, $J_{6b,6a}$ 6.4, H6), 3.740 (1 H, dd (br. s), $J_{4,5} \le 1$, $J_{4,3} \le 1$, H4), 3.980 (1 H, dd (d), H6a), 4.170 (1 H, ddd (d), $J_{2,NH}$ 9.8, $J_{2,1} \le 1$, H2), 4.880 (1 H, dd (br. s), H3), 5.380 (1 H, d (br. s), H1), 6.440 (1 H, d, NHAc), and 7.25–7.95 (20 H, m, Ar).

B. Chromatographically pure 4-trityl derivative (**II**) (446 mg, 1 mmol) in 2 ml of benzene and 2 ml of pyridine was treated with benzoyl chloride (287 μl, 2.47 mmol) and kept for 16 h at room temperature. The reaction was quenched with 150 μl of water and kept for 1 h, and benzene was evaporated. The residue was poured in water with solid $NaHCO_3$ and triturated. The aqueous layer was decanted, the oily residue was several times treated with saturated $NaHCO_3$ and then with water and dissolved in $CHCl_3$ (20 ml). The solution was washed with 1 N HCl, water, saturated $NaHCO_3$, and water; filtered though a cotton layer; and evaporated. The residue was dried in vacuum to give 540 mg (98%) of chromatographically homogeneous (**V**) as a yellow foam, R_f 0.69 (system B) (R_f of the starting ether is 0.42). The product was detritylated without further purification.

1,6-Anhydro-2-acetamido-3-*O*-benzoyl-2-deoxy-β-*D*-glucopyranose (VI). A. Methanol (0.2 ml) and then a solution of BF_3Et_2O (130 μl) in CH_2Cl_2 (1 ml) were added in 200-μl portions to a solution of the crude benzoate (**V**) (540 mg) obtained in the previous experiment in CH_2Cl_2 (10 ml). The yellow color appearing at the addition of the reagent completely disappeared after shaking. After 20 min, the solution was diluted with $CHCl_3$, washed with saturated $NaHCO_3$ (three times) and water, filtered through a cotton layer, and evaporated to give 560 mg of a crystalline residue; R_f 0.41 (system A) and 0.36 (system D); the starting trityl ether (**V**) had R_f 0.69 in this developing system. The product was treated with ethyl acetate to isolate 215 mg (70%) of crystalline benzoate (**VI**). CC of the residue after mother liquor evaporation gave another 77 mg of (**VI**) (total yield 95% based on (**II**)).

B. Pyridinium perchlorate [19] (275 mg, 1.53 mmol) was added to a solution of trityl ether (**V**) (280 mg, 0.51 mmol) in a mixture of MeOH (3 ml) and $MeNO_2$ (3 ml), and the resulting mixture was heated for 2 h at 50°C. After the reaction was over (TLC monitoring), the mixture was diluted with $CHCl_3$ (50 ml), washed with saturated $NaHCO_3$ and water, filtered through a cotton layer, and evaporated. The residue was treated with ethyl acetate (10 ml) to isolate 118 mg (75%) of (**VI**). CC of the mother liquor in a 0⟶5% MeOH gradient in $CHCl_3$ resulted in another 31 mg (20%) of (**VI**); mp 187–188°C (ethyl acetate); $[\alpha]_D^{20}$ −46.2° (*c* 1; $CHCl_3$). ^1H NMR: 2.050 (3 H, s, Ac), 3.820 (1 H, dd (br. s), $J_{4,5} \le 1$, $J_{4,3} \le 1$, H4), 3.850 (1 H, dd, $J_{6b,5}$ 5.7, $J_{6b,6a}$ 7.5, H6b), 4.150 (1 H, dd (d), $J_{6a,5} \le 1$, H6a), 4.240 (1 H, ddd (d), $J_{2,NH}$ 9.7, $J_{2,1} \le 1$, $J_{2,3} \le 1$, H2), 4.590 (1 H, ddd (d), H5), 4.950 (1 H, dd (br. s), H3), 5.450 (1 H, d (br. s), H1), 6.510 (1 H, d, NHAc), 7.450 (2 H, t, $J_{m,o}$ 7.4, *m*-H(Ar)), 7.600 (1 H, t, $J_{n,m}$ 7.4, *p*-H(Ar)), and 8.050 (2 H, d, *o*-H(Ar)).

1,6-Anhydro-2-acetamido-3-*O*-acetyl-2-deoxy-4-*O*-trityl-β-*D*-glucopyranose (VII). Acetic anhydride (2.3 ml) was added to a solution of trityl ether (**II**) (1.96 g, 4.4 mmol) in pyridine (7.5 ml); the reaction was kept for 20 h at room temperature and carefully quenched with water (0.5 ml) at cooling with ice. After 40 min, the mixture was diluted with $CHCl_3$ (200 ml); washed with water, saturated $NaHCO_3$, water, 1 N HCl, and water; filtered through a cotton layer; and evaporated. The residue was crystallized from ethyl acetate–ether to give 1.83 g (85%) of acetate (**VII**) as colorless prisms; mp 254–255°C (decomp.); R_f 0.71 (system A) and 0.57 (system B); $[\alpha]_D^{20}$ −5.4° (*c* 1; MeOH). ^1H NMR: 1.850 and 2.15 (2 × 3 H, two s, NAc and OAc), 3.46 (1 H, dd, $J_{6b,6a}$ 7.5, $J_{6b,5}$ 5.8, H6b), 3.80 (1 H, ddd (d), $J_{5,6a} \le 1$, $J_{5,4} \le 1$, H5), 3.87 (1 H, dd (d), H6a), 3.880 (1 H, dd (br. s), $J_{4,3} \le 1$ H4), 4.420 (1 H, ddd (d), $J_{2,NH}$ 9, $J_{1,2} \le 1$, H2), 5.200 (1 H, ddd (br. s), 5.680 (1 H, d (br. s), H1), 7.20–7.70 (15 H, m, Ar), and 8.150 (1 H, d, NHAc).

1,6-Anhydro-2-acetamido-3-*O*-acetyl-2-deoxy-β-*D*-glucopyranose (VIII). Boron trifluoride etherate (0.5 ml) in CH_2Cl_2 (1 ml) was added to a solution of trityl ether (**VII**) (1.83 g, 3.77 mmol) in a mixture of anhydrous $CHCl_3$ (20 ml), MeOH (0.7 ml), and pyridine (3 ml). After the reaction was over (15 min, TLC monitoring), the reaction mixture was diluted with pyridine (10 ml) and evaporated to dryness. The residue was chromatographed in a 0⟶5% MeOH gradient in $CHCl_3$ to isolate 850 mg (92%) of acetate (**VIII**); mp 143–144°C (ethyl acetate); $[\alpha]_D^{20}$ −82° (*c* 1; MeOH) (lit.: mp 143–144°C [5] and 147–148°C [6]; $[\alpha]_D^{20}$ −82° (*c* 1; MeOH) [5], −71° (c 1, $CHCl_3$) [6], and −79.6° (*c* 1, MeOH) [25]); ^1H NMR: 2.032 and 2.113 (2 × 3 H, two s, NAc and OAc), 3.669 (1 H, dd (br. s), $J_{4,5} \le 1$, $J_{4,3} \le 1$, H4), 3.817 (1 H, dd, $J_{6b,6a}$ 7.5, $J_{6b,5}$ 5.5, H6b), 4.050 (1 H, ddd (d), $J_{2,NH}$ 9.3, $J_{2,1} \le 1$, $J_{2,3} \le 1$, H2), 4.070 (1 H, dd (d), $J_{6a,5} \le 1$, H6a), 4.551 (1 H, ddd

(d), H5), 4.651 (1 H, ddd (br. s), H3), 5.403 (1 H, d (br. s), H1), and 6.435 (1 H, d, NHAc).

Selective deacetylation of diacetate (IX). A solution of HCl in MeOH (obtained by the addition of 200 μl of acetyl chloride to 2 ml of MeOH) was added at cooling with ice to a solution of diacetate (**IX**) (580 mg, 2.02 mmol) in anhydrous $CHCl_3$ (1 ml) and MeOH (2 ml). The mixture was kept for 3.5 h at 0°C and for 3 h at 5°C. The reaction mixture, containing (TLC, system A) the starting diacetate (**IX**), monoacetates (**X**) and (**VIII**), and traces of diol (**I**) (R_f 0.20), was diluted with pyridine (2 ml) and evaporated. The residue was coevaporated with toluene (4 × 2 ml) and chromatographed in a 0⟶2% MeOH gradient in $CHCl_3$ to isolate in the elution order:

The starting diacetate (**IX**), R_f 0.58, yield 350 mg (60%). ^{1}H NMR: 2.048, 2.137, and 2.200 (3 × 3 H, three s, NAc and 2 × OAc); 3.840 (1 H, dd, $J_{6b,6a}$ 7.5, $J_{6b,5}$ 5.5, H6b); 4.118 (1 H, ddd (d), $J_{2,NH}$ 9, $J_{2,1} \le 1$, $J_{2,3} \le 1$, H2); 4.160 (1 H, dd (d), $J_{6a,5} \le 1$, H6a); 4.610 (1 H, ddd (d), $J_{5,4} \le 1$, H5); 4.680 (1 H, dd (br. s), $J_{3,4} \le 1$, H3); 4.740 (1 H, dd (br. s), H4); 5.384 (1 H, d (br. s), H1), and 5.888 (1 H, d, NHAc).

4-Acetate (**X**), R_f 0.35, yield 90 mg (0.37 mmol, 18.5%); ^{1}H NMR: 2.005 and 2.161 (2 × 3 H, two s, NAc and OAc), 3.684 (1 H, dd (br. s), $J_{3,4} \le 1$, $J_{3,2} \le 1$, H3), 3.812 (1 H, dd, $J_{6b,6a}$ 7.5, $J_{6b,5}$ 5.5, H6b), 4.110 (1 H, ddd (d), $J_{2,NH}$ 9.5, $J_{2,1} \le 1$, H2), 4.342 (1 H, dd (d), $J_{6a,5} \le 1$, H6a), 4.616 (1 H, ddd (d), $J_{5,4} \le 1$, H5), 4.780 (1 H, dd (br. s), H4), 5.430 (1 H, dd (br. s), H1), and 5.934 (1 H, d, NHAc).

3-Acetate (**VIII**), R_f 0.32, yield 90 mg (0.37 mmol, 18.2%), identical to the sample described above.

Selective acetylation of diol (I). Acetyl chloride (95 μl, 1.3 mmol) in CH_2Cl_2 (200 μl) was added at 0°C to a solution of diol (**I**) (203 mg, 1 mmol) in pyridine (1 ml). The resulting mixture was kept for 5 h at room temperature, and a solution of AcCl (200 μl, 2.7 mmol) in CH_2Cl_2 (600 μl) was added in portions at TLC monitoring (system A). Pyridine (200 μl) was then added to the reaction mixture, and the solvents were removed by coevaporation with toluene and heptane. The residue was chromatographed as described above to isolate in the elution order: 80 mg (28%) of diacetate (**IX**), 120 mg (49%) of 4-acetate (**X**), 40 mg (16%) of 3-acetate (**VIII**), and (with 10% MeOH in $CHCl_3$) 16 mg (8%) of the starting diol (**I**).

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