# The Total Synthesis of a Glycosidase Inhibitor, Nagstatin#

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A glycosidase inhibitor, nagstatin, has been synthesized from protected L-ribofuranose through the inter- and intramolecular nucleophilic reactions of the imidazole moieties and the regioselective introduction of a carboxymethyl group.

Recently, many kinds of glycosidase inhibitors have become useful as antiobesity drugs, antidiabetes, antifungals, insect antifeedants, and antivirals, including potential therapeutic agents against human immunodeficiency virus (HIV) and tumor metastasis.[1] This extraordinary range of functions results, in part, from the great diversity of carbohydrate structures found in glycoconjugates.[2] Nagstatin (**1**) was discovered in the fermentation broth of *Streptomyces amakusaensis* as a strong and novel inhibitor of *N*-acetyl-$\beta$-D-glucosaminidase ($IC_{50}$ 0.0012 $\mu g\,ml^{-1}$).[3] In several diseases such as diabetes mellitus, leukemia, and cancer, *N*-acetyl-$\beta$-D-glucosaminidase activity in serum has been reported to increase. Therefore, chemical and biochemical studies on nagstatin may lead to understanding the molecular basis of these intractable diseases.[3a] Together with a noteworthy biological activity, nagstatin (**1**) is endowed with a unique structure, distinguished by a fully functionalized 5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine skeleton, which provides a challenging target in organic synthesis (Chart 1).

We have recently communicated the first total syntheses of de-branched nagstatin[4] (**2**) and nagstatin[5] (**1**).

Also, as part of a program to develop glycosidase inhibitors for therapy and to better understand their mode of action, we have already communicated the chemical design and total synthesis of nagstatin analogs (**3**—**9**) possessing different configurations and/or functionalities.[4,6] These syntheses feature a general access to azole-derived nitrogenous carbohydrates by the inter- and intramolecular nucleophilic reactions of the azole moieties. We have also clarified their structure-activity relation.[4—6] Namely, their strong $\beta$-D-glycosidase inhibitory activities indicated that the $\beta$-D-glycosidase recognized especially their C-8a positions as the C-1 position of $\beta$-D-glycopyranosides. Therefore, their substrate-specific activities emphasized that the analogs serve essentially as the antagonists of the corresponding stereochemically oriented $\beta$-D-glycopyranosides.

Independently, carbohydrate-derived heterocycles fused to azole rings have been synthesized, such as the 6-epi-castanospermine analog,[7] the glucosidase I inhibitor,[8] and tetrazole analogs.[9]

Herein, we report full details of the total synthesis of nagstatin (**1**) with reference to the analogs **2**, **3**, and **4** to illustrate a representative example of the useful synthesis of nagstatin related heterocyclic compounds from carbohydrates.

# This paper is dedicated to Prof. Dr. Hans Paulsen in honor of his 75th birthday.

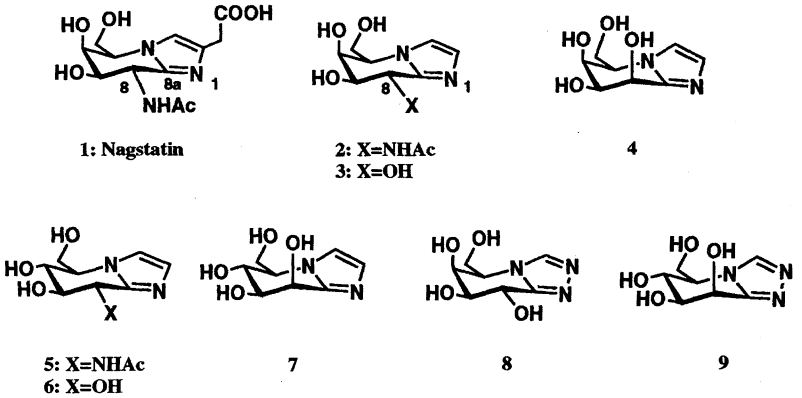



Chart 1.

## Results and Discussion

**Synthesis of De-branched Nagstatin (2).** De-branched nagstatin **2** was effectively synthesized from methyl L-ribofuranoside (Scheme 1).[10] *O*-Benzylation followed by acid hydrolysis gave the protected ribose **10** in 90% overall yield. Reaction of **10** with lithiated *N*-tritylimidazole,[11] which was prepared from *N*-tritylimidazole and *n*-BuLi, gave the L-allose derivative **11**[12] and L-altrose derivative **12**[12] in 47 and 40% yields, respectively. This lack of selectivity was expected from chelation of **10** as shown in Chart 2.[13] The chelation occurred preferentially between the *cis*-oriented oxygen atoms at C-2 and C-3. Therefore, in the nucleophilic reaction, the C-1 hydroxy group was not configurationally biased to give **11** and **12**. However, both imidazoles **11** and **12** were efficiently transformed to useful analogs (**2**—**4**)[6] as well as nagstatin (**1**). The configurations at C-1′ of **11** and **12** were determined by the NMR studies of their corresponding cyclized derivatives **4** and **3** which showed the

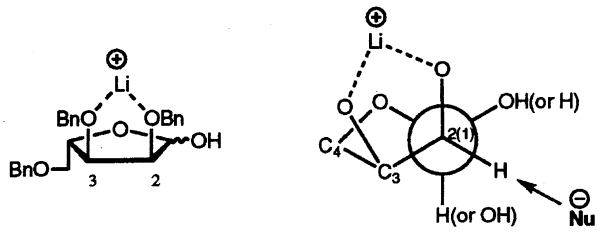
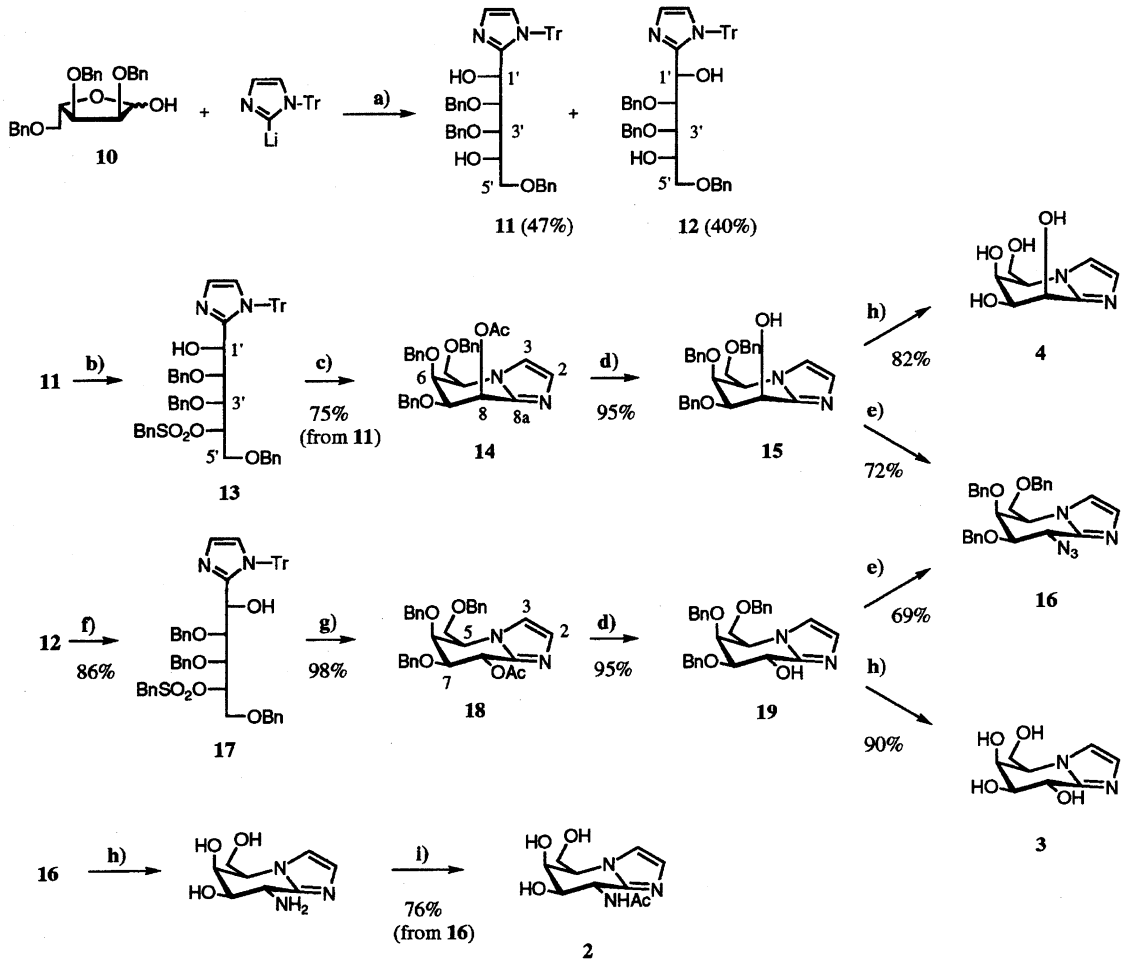


Chart 2.

coupling constants $J_{7,8} = 4$ and 8 Hz, respectively, although the imidazole functionality would enforce a half-chair conformation on the six-membered ring.[8] The imidazoles **11** and **12** were converted into the desired compound **2**, as follows. De-*N*-tritylation and the $S_N2$-type intramolecular cyclization of **11** were performed as a one-pot reaction by treatment with $BnSO_2Cl$ in pyridine to give preferentially the 4′-*O*-sulfonylated **13**, followed by treatment with $Ac_2O$ to yield 75% of the desired acetate **14**, which was de-*O*-acetylated to the D-talose analog **15**.[12] The efficient de-*N*-tritylation



a) THF, -5 °C, 0.5 h; b) $BnSO_2Cl$, pyridine, -15 °C, 1 h; c) $Ac_2O$, 0 → 65 °C, 1.5 h; d) cat. MeONa, MeOH, rt, 1.5 h; e) *n*-$Bu_3P$, $HN_3$ in PhMe, DEAD, THF, rt, 0.5 h; f) $BnSO_2Cl$, pyridine, -10 °C, 1 h; g) $Ac_2O$, pyridine, 65 °C, 1.5 h; h) $H_2$, 10%Pd-C, AcOH, rt, 15 h; i) $Ac_2O$, MeOH, rt, 1 h.

Scheme 1.

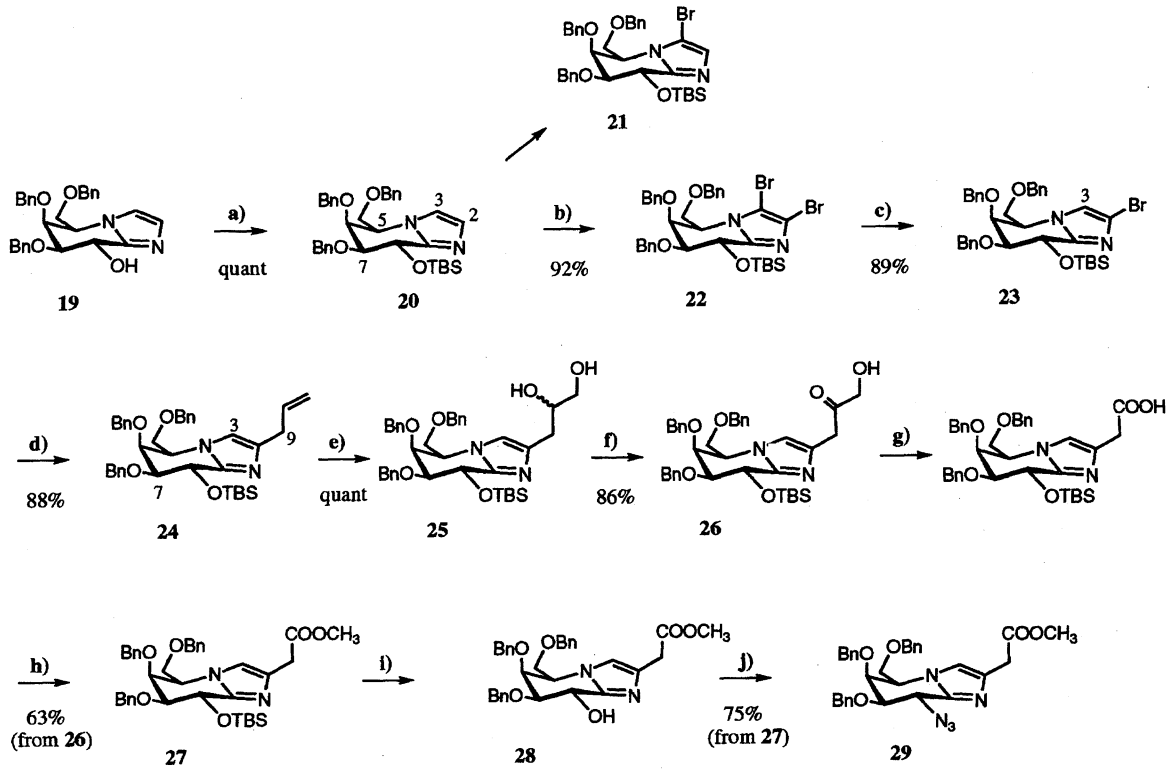
Chart 3.

seemed to be affected by the in situ generated pyridinium acetate to give the cyclic compound **14** and was supported by the stepwise conversion of **17** into **18** as shown later. The substitution of the hydroxy group in **15** under modified Mitsunobu conditions[14] with $HN_3$, *n*-$Bu_3P$, and DEAD (diethyl azodicarboxylate) proceeded with inversion and afforded the azido derivative **16** in 72% yield. The azide was subjected to hydrogenolysis and *N*-acetylation, leading in 76% yield to the *N*-acetyl-D-galactosamine analog **2**,[12] corresponding to de-branched nagstatin.

Alternatively, **16** was prepared from the isomer **12**. *O*-Benzylsulfonylation of **12** gave **17** in 86% yield. This was treated with $Ac_2O$ in pyridine to give the cyclized compound **18** in 98% yield, under concomitant de-*N*-tritylation, as described above. Compound **18** was also obtained by a one pot procedure from **12** as described above. De-*O*-acetylation of **18** to **19** (95%), followed by treatment with $HN_3$ gave the same azide **16** (69%) as described above, with the expected retention of the C-8 configuration. The formal substitution at C-8 is most probably following an elimination/addition mechanism, and the diastereoselectivity is mainly governed by the axial C6–O substituent and N-4 nitrogen atom which are present in the rear site of the C-8. Similar observations have been made in related pyrrole derivatives.[15] In carbohydrate chemistry, the $S_N2$ replacement of equatorial groups at C-2 of glycopyranosides is notoriously difficult because of the combined influence of the ring oxygen, the anomeric substituent, and dipolar effects.[16] In this case, an intermediary carbonium ion would be stabilized by the resonance with the imidazole ring, as shown in Chart 3. This retention was confirmed by the fact that **19** was treated with benzoic acid, *n*-$Bu_3P$, and DEAD to give the corresponding benzoate, which was deacylated to the starting **19**.

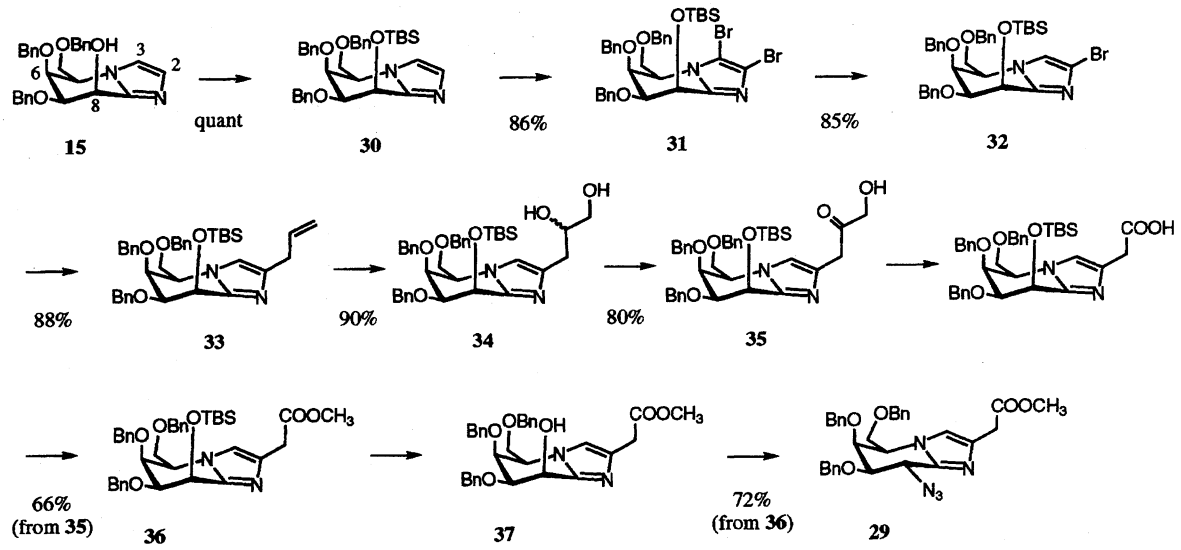
Intermediates **15** and **19** were both hydrogenated to give the nitrogenous D-talose and galactose analogs (**4** and **3**), respectively.

**Total Synthesis of Nagstatin (1).** The results described above suggest that a rational starting point for the synthesis of nagstatin (**1**) would be both isomers **15** and **19** (Schemes 2, 3, and 4). The regioselective introduction of an allyl group at their C-2 positions was investigated under a variety of conditions. According to the general reactivity of imidazoles,[17] the C-2 position of **20** was anticipated to be less reactive than at C-3. Selective bromination of **20**, which was quantitatively prepared by silylation of **19** using TBSOTf and 2,

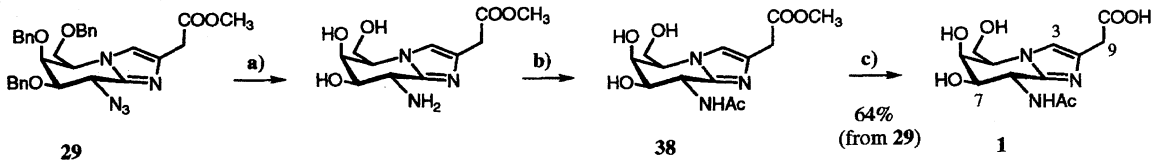


a) TBSOTf, 2,6-lutidine, $CH_2Cl_2$, -10 °C, 0.5 h; b) 2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one, $NaHCO_3$, $CH_2Cl_2$, 20 °C, 2 h; c) *t*-BuLi, THF, $H_2O$, -78 °C, 10 min; d) *n*-BuLi, CuI, THF, allyl bromide, -78 °C, 0.5 h; e) $OsO_4$, NMO, THF-$H_2O$, rt, 4 h; f) $Ag_2CO_3$, PhH, reflux, 12 h; g) $NaIO_4$, MeOH-$H_2O$, rt, 1 h; h) $TMSCHN_2$, THF-MeOH, rt, 10 min; i) TBAF, THF, rt, 1 h; j) *n*-$Bu_3P$, $HN_3$ in PhMe, DEAD, THF, rt, 0.5 h.

Scheme 2.




Scheme 3.




a) $H_2$, 10%Pd-C, AcOH, rt, 15 h; b) $Ac_2O$, MeOH, rt, 1 h; c) NaOH, $H_2O$, 5 °C, 1 h.

Scheme 4.

6-lutidine, gave indeed the undesired C-3 bromo compound **21** (Scheme 2). Consequently, **20** was fully brominated with 2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one to the dibromo compound **22** in 92% yield. Its selective debromination was assayed under several conditions.[18] The best result was obtained by regioselective lithiation with *t*-BuLi followed by quenching with $H_2O$ to give the desired monobromo compound **23** in 89% yield. The structure of **23** was confirmed by the NOE studies of the corresponding allyl derivative **24**, which was obtained in 88% yield from the organocopper derivative of **23** and allyl bromide.[17] Upon irradiating at H-3 ($\delta = 6.85$), NOE enhancements of the $CH_2$-5 ($\delta = 3.76$: 1.7%) and H-5 ($\delta = 4.45$: 3.5%) signals were clearly detected, supporting the substitution at C-2 of **24**.

$OsO_4$ Dihydroxylation of **24** afforded the diasteromeric mixture **25** quantitatively, which was oxidized with $Ag_2CO_3$ under modified Fetizon's conditions[19] to give keto alcohol **26** in 86% yield. Periodate oxidation of **26**, followed by esterification, provided the methyl ester **27** in 63% yield.

Direct ozonolysis of **24**, or periodate oxidation of **25** caused concomitant oxidation at C-9.

Conversion of **27** to the azido compound **29** was carried out by de-*O*-silylation to **28**, followed by treatment with $HN_3$ in a similar fashion to that described above. The expected retention of the configuration at the C-8 position was again observed, as described above.

In a similar manner, but with inversion of the configuration (Scheme 3), the isomer **15** possessing an *axial* substituent at C-8 was converted into the azido compound **29** in a ten-step sequence through the allyl derivative **33**, the keto alcohol **35**, and the ester **37**. Thus, inverting azidation of **37** under Mitsunobu conditions[14] using $HN_3$ afforded the azide **29** in 75% yield.

Finally, hydrogenolysis of **29** followed by successive *N*-acetylation to **38** and saponification provided nagstatin (**1**) in 64% overall yield (Scheme 4), which was identical with the natural product in all respects. Namely synthetic nagstatin (**1**) showed the same optical rotation $[\alpha]_D$ +68° ($H_2O$)] and *N*-acetyl-$\beta$-D-glucosaminidase inhibitory activity ($IC_{50}$ 0.0012 $\mu g\,ml^{-1}$)[3,5] as the natural product.

Now, the total synthesis of nagstatin was accomplished to confirm the absolute structure **1**.

## Experimental

The melting points were determined on a micro hot-stage Yanaco MP-S3 and were uncorrected. Optical rotations were measured on a JASCO DIP-370 photoelectric polarimeter. IR spectra were recorded on a JASCO FT/IR-5M spectrometer and $^1H$ NMR spectra on either a JEOL EX270 or a GSX400 spectrometer in $CDCl_3$ using TMS as an internal standard, unless otherwise noted. Mass

spectra were recorded on a JEOL JMS-DX302 mass spectrometer. Silica-gel TLC and column chromatography were performed on a Merck TLC 60F-254 and Fuji-Davison BW-820MH, respectively. In general, the organic solvents were purified and dried by appropriate procedures, and evaporation and concentration were carried out under reduced pressure below 30 °C, unless otherwise noted.

**(5*R*,6*S*,7*S*,8*S*)-8-Acetylamino-5,6,7,8-tetrahydro-6,7-dihydroxy-5-hydroxymethylimidazo[1,2-*a*]pyridine-2-acetic Acid (1: Nagstatin).** To a stirred solution of **38** (0.005 g, 0.016 mmol) in water (0.1 ml) was added 0.1 M NaOH (0.52 ml, 0.052 mmol, M = mol dm$^{-3}$) at 5 °C. After 1 h, the reaction mixture was acidified at 0 °C with 0.1 M HCl to pH 2 and evaporated to a residue, which was subjected to Sephadex LH-20 (7×85 mm) column chromatography developed with 80% aqueous MeOH to afford **1** (0.0045 g, 84%) as a colorless powder: Mp ca. 160 °C (decomp); $R_f$ = 0.29—0.35 (*n*-BuOH–AcOH–$H_2O$ = 2 : 1 : 1); $[\alpha]_D$ +68° (*c* 0.45, $H_2O$); $^1$H NMR (270 MHz, $D_2O$) $\delta$ = 2.14 (3H, s, Ac), 3.82 (2H, br s, H-9), 4.18 (2H, m, H-11), 4.33 (1H, dd, *J* = 10, 2 Hz, H-7), 4.52 (1H, m, H-5), 4.55 (1H, dd, *J* = 2, 2 Hz, H-6), 5.20 (1H, d, *J* = 10 Hz, H-8), and 7.63 (1H, s, H-3); HR-MS (FAB$^+$) Found: *m/z* 300.2914. Calcd for $C_{12}H_{18}N_3O_6$: M, 300.2907. These physicochemical properties were identical with those of the authentic sample of the natural product.

The natural product **1**, which was kindly provided by Dr. T. Aoyagi,[3] was purified by column chromatography on Sephadex LH-20 with 80% aqueous MeOH to give the authentic sample.

**(5*R*,6*S*,7*S*,8*S*)-8-Acetylamino-5,6,7,8-tetrahydro-6,7-dihydroxy-5-hydroxymethylimidazo[1,2-*a*]pyridine (2).** A solution of **16** (0.171 g, 0.345 mmol) in AcOH (4 ml) was hydrogenated in the presence of 10% Pd/C (0.22 g) under an atmosphere of hydrogen (4×10$^5$ Pa) for 15 h at room temperature. The reaction mixture was filtered off and washed with MeOH. The filtrates and washings were combined and evaporated to a residue (0.0328 g). To a solution of the residue in MeOH (0.8 ml) was added acetic anhydride (0.4 ml) at room temperature. After 1 h, the reaction mixture was evaporated and chromatographed on silica gel (4 g) with 1 : 1 $CHCl_3$–MeOH to afford **2** (0.0668 g, 76%) as colorless crystals: Mp 210—212 °C; $R_f$ = 0.32—0.40 ($CHCl_3$–MeOH = 1 : 1); $[\alpha]_D$ +110° (*c* 1.3, $H_2O$); $^1$H NMR (270 MHz, $CD_3OD$) $\delta$ = 2.07 (3H, s, Ac), 4.10 (2H, d, *J* = 6 Hz, H-9), 4.15 (1H, dd, *J* = 9, 2 Hz, H-7), 4.34 (1H, m, H-5), 4.37 (1H, dd, *J* = 2, 2 Hz, H-6), 5.08 (1H, d, *J* = 9 Hz, H-8), 7.39 (1H, d, *J* = 2 Hz, H-2), and 7.78 (1H, d, *J* = 2 Hz, H-3); IR (KBr) 3384, 1639, 1557, 1487, 1442, 1374, 1115, and 1057 cm$^{-1}$; MS (FAB$^+$) *m/z* 242 (M+1); HR-MS (FAB$^+$) Found: *m/z* 242.2547. Calcd for $C_{10}H_{16}N_3O_4$: M, 242.2541.

**(5*R*,6*S*,7*S*,8*S*)-5,6,7,8-Tetrahydro-6,7,8-trihydroxy-5-hydroxymethyl-imidazo[1,2-*a*]pyridine (3).** A solution of **19** (0.119 g, 0.254 mmol) in AcOH (5 ml) was hydrogenated in the presence of 10% Pd/C (0.15 g) under an atmosphere of hydrogen (4×10$^5$ Pa) for 15 h at room temperature. The reaction mixture was filtered off and washed with MeOH. The filtrates and washings were combined and evaporated to a residue. This was dissolved in MeOH and passed through a column of ion exchange resin IRA400 (OH type) with MeOH. The eluents were evaporated to a residue, which was chromatographed on silica gel (6 g) with 1 : 1 $CHCl_3$–MeOH to afford **3** (0.048 g, 90%) as crystals: Mp 79—80 °C; $R_f$ = 0.15—0.25 ($CHCl_3$–MeOH = 1 : 1); $[\alpha]_D$ +30° (*c* 1.6, MeOH); $^1$H NMR (270 MHz, $CD_3OD$) $\delta$ = 3.87 (1H, dd, *J* = 8, 2 Hz, H-7), 4.03 (2H, d, *J* = 5 Hz, H-9), 4.23 (1H, dt, *J* = 5, 4 Hz, H-5), 4.38 (1H, dd, *J* = 4, 2 Hz, H-6), 4.76 (1H, d, *J* = 8 Hz, H-8), 7.05 (1H, d, *J* = 1 Hz, H-2), and 7.36 (1H, d, *J* = 1 Hz, H-3); IR (KBr) 3333, 1638, 1489, 1450, 1360, 1305, 1264, 1144, 1113, 1086, 1065, 1051, 750, and 686 cm$^{-1}$; MS (FAB$^+$) *m/z* 201 (M+1); HR-MS (FAB$^+$) Found: *m/z* 201.2022. Calcd for $C_8H_{13}O_4N_2$: M, 201.2017.

**(5*R*,6*S*,7*S*,8*R*)-5,6,7,8-Tetrahydro-6,7,8-trihydroxy-5-hydroxymethyl-imidazo[1,2-*a*]pyridine (4).** A solution of **15** (0.164 g, 0.349 mmol) was hydrogenated by the same manner, as described above for the preparation of **3**, to afford **4** (0.057 g, 82%) as crystals: Mp 80—81 °C; $R_f$ = 0.15—0.25 ($CHCl_3$–MeOH = 1 : 1); $[\alpha]_D$ +26° (*c* 1.8, MeOH); $^1$H NMR (270 MHz, $CD_3OD$) $\delta$ = 4.04 (1H, dd, *J* = 4, 2 Hz, H-7), 4.07 (1H, dd, *J* = 12, 6 Hz, H-9), 4.09 (1H, dd, *J* = 12, 4 Hz, H-9), 4.21 (1H, ddd, *J* = 6, 4, 4 Hz, H-5), 4.34 (1H, dd, *J* = 4, 2 Hz, H-6), 4.82 (1H, d, *J* = 4 Hz, H-8), 7.12 (1H, d, *J* = 1.5 Hz, H-2), and 7.43 (1H, d, *J* = 1.5 Hz, H-3); IR (KBr) 3383, 2926, 1641, 1486, 1444, 1266, 1100, 1075, 1048, and 768 cm$^{-1}$; MS (FAB$^+$) *m/z* 201 (M+1); HR-MS (FAB$^+$) Found: *m/z* 201.2020. Calcd for $C_8H_{13}O_4N_2$: M, 201.2017.

**2-[(1*R*,2*R*,3*S*,4*S*)-2,3,5-Tris(benzyloxy)-1,4-dihydroxypent-1-yl]-*N*-triphenylmethylimidazole (11) and 2-[(1*S*,2*R*,3*S*,4*S*)-2,3,5-tris(benzyloxy)-1,4-dihydroxypent-1-yl]-*N*-triphenylmethylimidazole (12).** To a stirred solution of *N*-tritylimidazole (1.98 g, 6.38 mmol) in dry THF (80 ml) was added 1.6 M *n*-BuLi in hexane (4.01 ml, 6.42 mmol) under Ar at −5 °C. After 10 min, a solution of **10** (1.21 g, 2.9 mmol) in dry THF (8 ml) was added at 0 °C and the resulting solution was stirred at 0 °C for 30 min and then warmed to room temperature. To the reaction mixture were added a small piece of Dry Ice and saturated aqueous NaCl (20 ml). The organic layer was evaporated and chromatographed on silica gel (160 g) with 1 : 1 benzene–EtOAc to afford **12** (0.848 g, 40 %), after recrystallization from EtOAc, as colorless crystals. Other eluents containing **11** were combined, evaporated and rechromatographed on silica gel (120 g) with 2 : 1 $CHCl_3$–EtOAc to afford **11** (1.0 g, 47 %) as a colorless foam.

**11:** Mp 62—67 °C; $R_f$ = 0.61—0.7 (benzene–EtOAc = 1 : 1); $[\alpha]_D$ −112° (*c* 1.0, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 1.98 (1H, br d, *J* = 6 Hz, C1′–OH), 3.54 (1H, dd, *J* = 10, 6 Hz, H-5′), 3.59 (1H, dd, *J* = 10, 4 Hz, H-5′), 3.83 (1H, dd, *J* = 8, 2 Hz, H-3′), 3.92 (1H, ddd, *J* = 8, 6, 4 Hz, H-4′), 4.00 (1H, dd, *J* = 8, 2 Hz, H-2′), 4.25 (1H, d, *J* = 11 Hz, $CH_2Ph$), 4.43 (1H, d, *J* = 11 Hz, $CH_2Ph$), 4.45 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.51 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.52 (2H, s, $CH_2Ph$), 4.53 (1H, dd, *J* = 8, 6 Hz, H-1′), 6.83 (1H, d, *J* = 2 Hz, H-4), 7.09 (1H, d, *J* = 2 Hz, H-5), and 7.0—7.4 (30 H, m, Ph); IR (KBr) 3570, 3357, 3059, 3028, 2858, 1493, 1448, 1215, 1089, 1069, 1029, 1000, 906, 746, 699, and 642 cm$^{-1}$; MS (FAB$^+$) *m/z* 731 (M+1); HR-MS (FAB$^+$) Found: *m/z* 731.9116. Calcd for $C_{48}H_{47}N_2O_5$: M, 731.9097.

Found: C, 78.58; H, 6.29; N, 3.70%. Calcd for $C_{48}H_{46}N_2O_5$: C, 78.88; H, 6.34: N, 3.83%.

**12:** Mp 132.5—133.5 °C; $R_f$ = 0.38—0.50 (benzene–EtOAc = 1 : 1); $[\alpha]_D$ −31° (*c* 1.05, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 1.86 (1H, dd, *J* = 8, 2 Hz, H-2′), 3.29 (1H, dd, *J* = 10, 2 Hz, H-5′), 3.39 (1H, dd, *J* = 10, 7 Hz, H-5′), 3.45 (1H, d, *J* = 10 Hz, C1′–OH), 3.50 (1H, dd, *J* = 8, 4 Hz, H-3′), 3.82 (1H, ddd, *J* = 7, 4, 2 Hz, H-4′), 3.87 (1H, d, *J* = 10 Hz, $CH_2Ph$), 4.05 (1H, d, *J* = 10 Hz, $CH_2Ph$), 4.17 (1H, d, *J* = 10 Hz, $CH_2Ph$), 4.37 (1H, d, *J* = 10 Hz, $CH_2Ph$), 4.45 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.50 (1H, dd, *J* = 10, 2 Hz, H-1′), 4.51 (1H, d, *J* = 12 Hz, $CH_2Ph$), 6.9—6.7 (3H, m, Ph, H-4&5), and 7.0—7.4 (29H, m, Ph); IR (KBr) 3386, 1493, 1448, 1102, 1030, 746, and 700 cm$^{-1}$; MS (FAB$^+$) *m/z* 731 (M+1); HR-MS (FAB$^+$) Found: *m/z* 731.9116, Calcd for $C_{48}H_{47}N_2O_5$: M, 731.9097.

Found: C, 79.13; H, 6.46; N, 4.05%. Calcd for $C_{48}H_{46}N_2O_5$: C, 78.88; H, 6.34; N, 3.83%.

**(5*R*,6*S*,7*S*,8*R*)-8-Acetoxy-6,7-bis(benzyloxy)-5-benzyloxymethyl-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine (14).** To a

stirred solution of **11** (0.535 g, 0.733 mmol) in dry pyridine (15 ml) was added $\alpha$-toluenesulfonyl chloride (0.279 g, 1.46 mmol) at −15 °C. After 1 h, acetic anhydride (0.5 ml) was added to the mixture, and the solution was stirred at 0 °C for 1 h, and then at 60 °C for 1.5 h. After addition of EtOH (0.5 ml), the mixture was stirred at room temperature for 10 min and evaporated to a residue, which was dissolved in EtOAc and washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. The organic layer was dried, evaporated, and chromatographed on silica gel (5 g) with 1 : 1 benzene–EtOAc to afford **14** (0.282 g, 75%) as a colorless syrup: $R_f$ = 0.40—0.46 (benzene–EtOAc = 1 : 2); $[\alpha]_D$ −3.0° (*c* 1.05, $CHCl_3$): $^1$H NMR (270 MHz) $\delta$ = 3.93 (1H, dd, *J* = 10, 8 Hz, H-9), 3.97 (1H, dd, *J* = 10, 4Hz, H-9), 4.09 (1H, dd, *J* = 5, 2 Hz, H-7), 4.21 (1H, dd, *J* = 4, 2 Hz, H-6), 4.35 (1H, ddd, *J* = 8, 4, 4 Hz, H-5), 4.65 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.66 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.76 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.80 (1H, d, *J* = 12 Hz, $CH_2Ph$), 6.25 (1H, d, *J* = 5 Hz, H-8), 7.18 (1H, s, H-2), 7.20 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 3369, 3061, 3030, 2918, 2870, 1735, 1494, 1482, 1452, 1364, 1306, 1233, 1136, 1117, 1098, 1073, 1023, 737, and 698 $cm^{-1}$; MS (FAB$^+$) *m/z* 513 (M+1).

**(5*R*,6*S*,7*S*,8*R*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-5,6,7,8-tetrahydro-8-hydroxyimidazo[1,2-*a*]pyridine (15).** To a stirred solution of **14** (0.181 g, 0.353 mmol) in dry MeOH (10 ml) was added a solution of 28% NaOMe in MeOH (0.015 ml, 0.07 mmol) at room temperature. After 1.5 h, the reaction mixture was evaporated and chromatographed on silica gel (10 g) with 2 : 1 $CHCl_3$–acetone to afford **15** (0.158 g, 95 %) as colorless crystals. Recrystallization from hexane–EtOAc gave an analytically pure sample: Mp 77—78 °C; $R_f$=0.25—0.36 ($CHCl_3$–acetone = 2 : 1); $[\alpha]_D$ −7.8° (*c* 1.0, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 3.90 (2H, d, *J* = 6 Hz, H-9), 3.97 (1H, dd, *J* = 4, 2 Hz, H-7), 4.24 (1H, dd, *J* = 5, 2 Hz, H-6), 4.30 (1H, dt, *J* = 6, 5 Hz, H-5), 4.51 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.54 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.67 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.72 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.90 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.92 (1H, d, *J* = 12 Hz, $CH_2Ph$), 5.02 (1H, d, *J* = 4 Hz, H-8), 7.07 (1H, d, *J* = 2 Hz, H-2), 7.11 (1H, d, *J* = 2 Hz, H-3), and 7.2—7.4 (15H, m, Ph); IR (KBr) 3062, 3029, 2880, 2864, 1493, 1452, 1406, 1356, 1334, 1302, 1265, 1208, 1139, 1120, 1077, 1026, 933, 733, and 697 $cm^{-1}$; MS (FAB$^+$) *m/z* 471 (M+1); HR-MS (FAB$^+$) Found: *m/z* 471.5761. Calcd for $C_{29}H_{31}N_2O_4$: M, 471.5749.

Found: C, 73.07; H, 6.52; N, 5.88%. Calcd for $C_{29}H_{30}N_2O_4$: C, 74.02; H, 6.43; N, 5.95%.

**(5*R*,6*S*,7*S*,8*S*)-8-Azido-6,7-bis(benzyloxy)-5-benzyloxymethyl-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine (16). A) From 15:** To a stirred solution of **15** (0.061 g, 0.127 mmol) and tributylphosphine (0.038 ml, 0.152 mmol) in dry THF (6 ml) were added under Ar successively a solution of 4% $HN_3$ in toluene (0.189 ml, 0.153 mmol) and diethyl azodicarboxylate (0.24 ml, 0.152 mmol) at room temperature. After 30 min at room temperature, the reaction mixture was evaporated and chromatographed on silica gel (5 g) with 5 : 1 benzene–EtOAc to afford **16** (0.045 g, 72 %) as a colorless syrup: $R_f$ 0.38—0.50 (benzene–EtOAc = 5 : 1); $[\alpha]_D$ +98° (*c* 1.2, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 3.81 (1H, dd, *J* = 7, 1.5 Hz, H-7), 3.83 (2H, d, *J* = 6 Hz, H-9), 4.24 (1H, dd, *J* = 4, 1.5 Hz, H-6), 4.28 (1H, dt, *J* = 6, 4 Hz, H-5), 4.49 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.52 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.62 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.74 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.77 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.84 (1H, d, *J* = 12 Hz, $CH_2Ph$), 5.00 (1H, d, *J* = 7 Hz, H-8), 7.07 (1H, d, *J* = 1 Hz, H-2), 7.11 (1H, d, *J* = 1 Hz, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 3062, 3030, 2910, 2870, 2105, 1792, 1727, 1495, 1481, 1453, 1359, 1300, 1259, 1209, 1117, 1094, 1026, 738, and 698 $cm^{-1}$; MS (FAB$^+$) *m/z* 496 (M+1).

**B) From 19:** To a stirred solution of **19** (0.120 g, 0.255 mmol) and tributylphosphine (0.078 ml, 0.306 mmol) in dry THF (12 ml) were added under Ar successively a solution of 4 % $HN_3$ in toluene (0.473 ml, 0.506 mmol) and diethyl azodicarboxylate (0.49 ml, 0.306 mmol) at room temperature. After 30 min at room temperature, the reaction mixture was evaporated and chromatographed on silica gel (5 g) with 5 : 1 benzene–EtOAc to afford **16** (0.088 g, 69 %) as a colorless syrup identical with the authentic sample from **15**.

**2-[(1*S*,2*R*,3*S*,4*S*)-2,3,5-Tris(benzyloxy)-4-benzylsulfonyloxy-1-hydroxypent-1-yl]-*N*-triphenylmethylimidazole (17).** To a stirred solution of **12** (1.01 g, 1.39 mmol) in dry pyridine (30 ml) was added benzylsulfonyl chloride (0.397 g, 2.08 mmol) at 0 °C for 1 h. After addition of EtOH, the solution was stirred at room temperature for 10 min, evaporated and chromatographed on silica gel (50 g) with 4 : 1 benzene–EtOAc to afford **17** (1.06 g, 86 %) as a colorless foam: mp = ca. 60°C; $R_f$ = 0.53—0.60 (benzene–EtOAc = 4 : 1); $[\alpha]_D$ −44° (*c* 1.4, $CHCl_3$); $^1$H NMR (400 MHz) $\delta$ = 1.50 (1H, d, *J* = 10 Hz, H-2′), 3.20 (1H, dd, *J* = 12, 2 Hz, H-5′), 3.54 (1H, dd, *J* = 12, 9 Hz, H-5′), 3.73 (1H, dd, *J* = 10, 2 Hz, H-3′), 3.74 (1H, d, *J* = 10 Hz, $CH_2Ph$), 4.03 (1H, d, *J* = 10 Hz, $CH_2Ph$), 4.07 (1H, d, *J* = 10 Hz, $CH_2Ph$), 4.31 (2H, s, $CH_2Ph$), 4.37 (1H, d, *J* = 10 Hz, $CH_2Ph$), 4.42 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.45 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.46 (1H, s, H-1′), 5.08 (1H, ddd, *J* = 9, 2, 2 Hz, H-4′), 6.7—6.8, and 7.0—7.5 (32H, m, Ph, H-4&5); IR (KBr) 3060, 3029, 2922, 2864, 1493, 1449, 1361, 1329, 1218, 1174, 1098, 1030, 1001, 909, 747, and 699 $cm^{-1}$; MS (FAB$^+$) *m/z* 885 (M+1).

**(5*R*,6*S*,7*S*,8*S*)-8-Acetoxy-6,7-bis(benzyloxy)-5-benzyloxymethyl-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine (18).** To a solution of **17** (0.224 g, 0.25 mmol) in pyridine (5 ml) was added acetic anhydride (0.4 ml), and the mixture was warmed at 60 °C for 1.5 h. After addition of EtOH (0.5 ml), the solution was stirred at room temperature for 10 min and evaporated to a residue, which was dissolved in EtOAc and washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. The organic layer was dried, evaporated and chromatographed on silica gel (11 g) with 1 : 1 benzene–EtOAc to afford **18** (0.127 g, 98 %) as a colorless syrup: $R_f$ = 0.53—0.59 (benzene–EtOAc = 1 : 2); $[\alpha]_D$ +75° (*c* 1.4, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 2.06 (3H, s, Ac), 3.81 (1H, dd, *J* = 10, 8 Hz, H-9), 3.98 (1H, dd, *J* = 5, 2 Hz, H-7), 4.00 (1H, dd, *J* = 10, 3 Hz, H-9), 4.21 (1H, dd, *J* = 6, 2 Hz, H-6), 4.45 (1H, ddd, *J* = 8, 6, 3 Hz, H-5), 4.49 (2H, s, $CH_2Ph$), 4.57 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.69 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.70 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.76 (1H, d, *J* = 12 Hz, $CH_2Ph$), 6.22 (1H, d, *J* = 5 Hz, H-8), 7.08 (1H, d, *J* = 1 Hz, H-2), 7.15 (1H, d, *J* = 1 Hz, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 3061, 3030, 2922, 2871, 1744, 1493, 1452, 1367, 1304, 1227, 1093, 1079, 1044, 1026, 967, 740, and 698 $cm^{-1}$; MS (FAB$^+$) *m/z* 513 (M+1).

**(5*R*,6*S*,7*S*,8*S*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-5,6,7,8-tetrahydro-8-hydroxyimidazo[1,2-*a*]pyridine (19).** To a stirred solution of **18** (0.485 g, 0.947 mmol) in dry MeOH (10 ml) was added a solution of 28 % NaOMe in MeOH (0.029 ml, 0.24 mmol) at room temperature. After 1.5 h, the reaction mixture was evaporated and chromatographed on silica gel (50 g) with 2 : 1 $CHCl_3$–acetone to afford **19** (0.427 g, 95 %) as colorless crystals. Recrystallization from hexane–EtOAc gave an analytically pure sample: Mp 112—113 °C; $R_f$ = 0.26—0.35 ($CHCl_3$–acetone = 2 : 1); $[\alpha]_D$ +39° (*c* 1.0, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 3.84 (1H, dd, *J* = 10, 7.5 Hz, H-9), 3.94 (1H, dd, *J* = 10, 3 Hz, H-9), 4.02 (1H, dd, *J* = 5.5, 2 Hz, H-7), 4.35 (1H, dd, *J* = 5, 2 Hz, H-6), 4.39 (1H, ddd, *J* = 7.5, 5, 3 Hz, H-5), 4.49 (2H, s, $Ch_2Ph$), 4.64 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.75 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.82 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.87

(1H, d, $J$ = 12 Hz, $CH_2Ph$), 5.17 (1H, d, $J$ = 5.5 Hz, H-8), 6.98 (1H, d, $J$ = 1.5 Hz, H-2), 7.10 (1H, d, $J$ = 1.5 Hz, H-3), and 7.2—7.6 (15H, m, Ph); IR (KBr) 3104, 2898, 2862, 1495, 1467, 1451, 1366, 1327, 1311, 1289, 1234, 1210, 1180, 1128, 1101, 1052, 1023, 1006, 966, 934, 907, 733, and 694 $cm^{-1}$; MS ($FAB^+$) $m/z$ 471 (M+1); HR-MS ($FAB^+$) Found: $m/z$ 471.5758. Calcd for $C_{29}H_{31}N_2O_4$: M, 471.5749.

Found: C, 73.92; H, 6.59; N, 6.20%. Calcd for $C_{29}H_{30}N_2O_4$: C, 74.02; H, 6.43; N, 5.95%.

**(5*R*,6*S*,7*S*,8*S*)-6,7-Bis(benzyloxy)-5-bezyloxymethyl-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine (20).** To a solution of **19** (0.764 g, 1.63 mmol) and 2,6-lutidine (0.377 ml, 3.26 mmol) in dry $CH_2Cl_2$ (15 ml) was added under $N_2$ at −15 °C *t*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (0.448 ml, 3.26 mmol). After 30 min at the same temperature, saturated aqueous $NaHCO_3$ was added and the mixture was separated. The organic layer was evaporated and chromatographed on silica gel (76 g) with 10 : 1 benzene–EtOAc to afford **20** (0.947 g, 99 %) as a colorless syrup: $R_f$ = 0.48—0.58 (benzene–EtOAc = 5 : 1); $^1H$ NMR (270 MHz) $\delta$ = 0.02 (3H, s, $CH_3$ of TBS), 0.14 (3H, s, $CH_3$ of TBS), 0.82 (9H, s, *t*-Bu of TBS), 3.77 (1H, dd, $J$ = 10, 8 Hz, H-9), 3.88 (1H, dd, $J$ = 4, 2 Hz, H-7), 4.13 (1H, dd, $J$ = 10, 2 Hz, H-9), 4.39 (1H, dd, $J$ = 6, 2 Hz, H-6), 4.4—4.6 (3H, m, $CH_2Ph$ & H-5), 4.62 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.65 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.65 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.68 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.92 (1H, d, $J$ = 4 Hz, H-8), 7.04 (1H, d, $J$ = 1.5 Hz, H-2), 7.14 (1H, d, $J$ = 1.5 Hz, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 2950, 2928, 2855, 1255, 1129, 1092, 1076, 856, 839, 780, 738, and 697 $cm^{-1}$.

**(5*R*, 6*S*, 7*S*, 8*S*)- 6, 7- Bis(benzyloxy)- 5- benzyloxymethyl- 3-bromo-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo-[1,2-*a*]pyridine (21).** To a stirred suspension of **20** (0.175 g, 0.30 mmol) and $NaHCO_3$ (0.05 g, 0.60 mmol) in dry $CH_2Cl_2$ (3.6 ml) was added 2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one (0.12 g, 0.30 mmol) under $N_2$ at 0 °C. After 2 h at 0—5 °C, the reaction mixture was washed with 2 M NaOH (10 ml ×2) and water (5 ml). The organic layer was evaporated and chromatographed on silica gel (18 g) with 10 : 1 hexane–EtOAc to afford **21** (0.149 g, 75 %) as a colorless syrup: $R_f$ = 0.45—0.55 (hexane–EtOAc = 4 : 1); $[\alpha]_D$ +63° (*c* 2.0, $CHCl_3$); $^1H$ NMR (270MHz) $\delta$ = −0.03 (3H, s, $Ch_3$ of TBS), 0.08 (3H, s, $CH_3$ of TBS), 0.77 (9H, s, *t*-Bu of TBS), 3.61 (1H, dd, $J$ = 10.5, 3.5 H, H-9), 3.88 (1H, dd, $J$ = 3.5, 2 Hz, H-7), 4.36 (1H, dd, $J$ = 6, 2 Hz, H-6), 4.43 (1H, dd, $J$ = 10.5, 4 Hz, H-9), 4.52 (2H, m, $CH_2Ph$), 4.63 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.65 (2H, m, $CH_2Ph$), 4.67 (1H, m, H-5), 4.76 (1H, d, $J$ = 3.5 Hz, H-8), 4.80 (1H, d, $J$ = 12.0 Hz, $CH_2Ph$), 7.03 (1H, s, H-2), and 7.2—7.4 (15H, m, Ph); IR (neat) 2950, 2927, 2855, 1455, 1255, 1077, 1027, 851, 839, 780, 737, and 697 $cm^{-1}$; MS ($FAB^+$) $m/z$ 663 and 665 (M+1).

**(5*R*,6*S*,7*S*,8*S*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-2,3-dibromo-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo-[1,2-*a*]pyridine (22).** To a stirred suspension of **20** (1.25 g, 2.14 mmol) and $NaHCO_3$ (0.54 g, 6.24 mmol) in dry $CH_2Cl_2$ (25 ml) was added 2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one (1.93 g, 4.71 mmol) under $N_2$ at 0 °C. After 4 h at 0—10 °C, the reaction mixture was washed with 2 M NaOH (100 ml ×2) and water (50 ml). The organic layer was evaporated and chromatographed on silica gel (120 g) with 15 : 1 hexane–EtOAc to afford **22** (1.46 g, 92 %) as a colorless syrup: $R_f$ = 0.54—0.63 (hexane–EtOAc = 4 : 1); $^1H$ NMR (270 MHz) $\delta$ = 0.00 (3H, s, $CH_3$ of TBS), 0.07 (3H, s, $CH_3$ of TBS), 0.76 (9H, s, *t*-Bu of TBS), 3.60 (1H, dd, $J$ = 10.5, 3.5 Hz, H-9), 3.86 (1H, dd, $J$ = 3.5, 2 Hz, H-7), 4.33 (1H, dd, $J$ = 6, 2 Hz, H-6), 4.40 (1H, dd, $J$ = 10.5, 4 Hz, H-9), 4.50 (2H, m, $CH_2Ph$), 4.5—4.7 (4H, m, $CH_2Ph$ & H-5), 4.74 (1H, d, $J$ = 3.5 Hz, H-8), 4.77 (1H, d, $J$ = 12 Hz, $CH_2Ph$), and 7.2—7.4 (15H, m, Ph).

**(5*R*,6*S*,7*S*,8*S*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-2-bromo- 8- (*t*- butyldimethylsilyloxy)- 5, 6, 7, 8- tetrahydro- imidazo-[1,2-*a*]pyridine (23).** To a stirred solution of **22** (0.178 g, 0.240 mmol) in dry THF (3.6 ml) was added 1.6 M *t*-BuLi in pentane (0.24 ml, 0.384 mmol) under Ar at −78 °C. After 10 min at the same temperature, water (0.013 ml, 1.67 mmol) was added and the mixture was warmed to room temperature. The reaction mixture was concentrated and chromatographed on silica gel (17 g) with 10 : 1 hexane–EtOAc to afford **23** (0.142 g, 89 %) as a colorless syrup: $R_f$ = 0.45—0.51 (hexane–EtOAc = 4 : 1); $[\alpha]_D$ +50° (*c* 1.3, $CHCl_3$); $^1H$ NMR (270 MHz) $\delta$ = 0.03 (3H, s, $CH_3$ of TBS), 0.12 (3H, s, $CH_3$ of TBS), 0.81 (9H, s, *t*-Bu of TBS), 3.75 (1H, dd, $J$ = 10, 8.5 Hz, H-9), 3.85 (1H, dd, $J$ = 4, 2 Hz, H-7), 4.03 (1H, dd, $J$ = 10, 2 Hz, H-9), 4.34 (1H, dd, $J$ = 6, 2 Hz, H-6), 4.43 (1H, ddd, $J$ = 8.5, 6, 2 Hz, H-5), 4.47 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.50 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.59 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.63 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.65 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.84 (1H, d, $J$ = 4 Hz, H-8), 7.09 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); MS ($FAB^+$) $m/z$ 663 and 665 (M+1).

**(5*R*,6*S*,7*S*,8*S*)-2-Allyl-6,7-bis(benzyloxy)-5-benzyloxymethyl-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]-pyridine (24).** To a stirred solution of **23** (0.710 g, 1.07 mmol) in dry THF (15 ml) was added 1.6 M *n*-BuLi in hexane (1.07 ml, 1.71 mmol) under Ar at −78 °C. After 10 min at the same temperature, CuI (0.327 g, 1.71 mmol) was added and the mixture was stirred at −78 °C for 10 min, and then, allyl bromide (0.371 ml, 4.28 mmol) was added. After the reaction mixture was stirred at −78 °C for 15 min and warmed to room temperature, $CH_2Cl_2$ (20 ml) was added. The mixture was washed with saturated aqueous $NH_4Cl$ (20 ml), aqueous $Na_2S$ (10 ml) and water (10 ml), dried, and evaporated. The residue was chromatographed on silica gel (72 g) with 6 : 1 hexane–EtOAc to afford **24** (0.587 g, 88 %) as a colorless syrup: $R_f$ = 0.39—0.46 (hexane–EtOAc = 4 : 1); $[\alpha]_D$ +46° (*c* 1.3, $CHCl_3$); $^1H$ NMR (500 MHz) $\delta$ = 0.00 (3H, s, $CH_3$ of TBS), 0.13 (3H, s, $CH_3$ of TBS), 0.81 (9H, s, *t*-Bu of TBS), 3.34 (2H, m, H-9), 3.76 (1H, dd, $J$ = 10, 8 Hz, H-12), 3.87 (1H, dd, $J$ = 4, 2 Hz, H-7), 4.12 (1H, dd, $J$ = 10, 2 Hz, H-12), 4.38 (1H, dd, $J$ = 6, 2 Hz, H-6), 4.45 (1H, ddd, $J$ = 8, 6, 2 Hz, H-5), 4.49 (2H, m, $CH_2Ph$), 4.62 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.63 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.64 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.68 (1H, d, $J$ = 12 Hz, $CH_2Ph$), 4.92 (1H, d, $J$ = 4 Hz, H-8), 5.05 (1H, m, H-11), 5.13 (1H, m, H-11), 6.01 (1H, dddd, $J$ = 17, 10, 7, 7 Hz, H-10), 6.86 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 2949, 2927, 2856, 1090, 1028, 838, 738, and 697 $cm^{-1}$; HR-MS ($FAB^+$) Found: $m/z$ 625.3434. Calcd for $C_{38}H_{49}N_2O_4Si$: M, 625.3462.

**(5*R*,6*S*,7*S*,8*S*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-8-(*t*-butyldimethylsilyloxy)- 5, 6, 7, 8- tetrahydro- 2- (2, 3- dihydroxypropyl)imidazo[1,2-*a*]pyridine (25).** To a stirred solution of **24** (0.231 g, 0.370 mmol) in THF (4.5 ml) and water (0.45 ml) were added at room temperature aqueous 50 % NMO (*N*-methylmorpholine *N*-oxide monohydrate: 0.182 ml, 0.78 mmol) and aqueous 4 % $OsO_4$ (0.235 ml, 0.037 mmol). After 6 h, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, evaporated and chromatographed on silica gel (10 g) with 1 : 1 benzene–EtOAc to afford **25** (0.237 g, 97 %) as a colorless syrup: $R_f$ = 0.28—0.35 (benzene–EtOAc = 1 : 1); MS ($FAB^+$) $m/z$ 659 (M+1).

**(5*R*,6*S*,7*S*,8*S*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydro-2-(3-hydroxy-2-oxopropyl)imidazo[1,2-*a*]pyridine (26).** A suspension of **25** (0.070 g,

0.106 mmol) and $Ag_2CO_3$ (0.587 g, 2.12 mmol) in benzene (12 ml) was refluxed for 12 h. The reaction mixture was filtered off and washed with benzene. The filtrates and washings were combined, evaporated and chromatographed on silica gel (7 g) with 1 : 1 benzene–EtOAc to afford **26** (0.039 g, 56 %) as a colorless syrup, and recovered **25** (0.025 g, 35 %). The yield of **26** was 86 % on the basis of the consumed **25**.

**26:** $R_f$ = 0.56—0.63 (benzene–EtOAc = 3 : 2); $[\alpha]_D$ +49.6° (*c* 1.9, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 0.06 (3H, s, $CH_3$ of TBS), 0.11 (3H, s, $CH_3$ of TBS), 0.83 (9H, s, *t*-Bu of TBS), 3.69 (1H, d, *J* = 14.5 Hz, H-9), 3.76 (1H, d, *J* = 14.5 Hz, H-9), 3.75 (1H, dd, *J* = 10, 8 Hz, H-12), 3.83 (1H, dd, *J* = 5, 2 Hz, H-7), 4.04 (1H, dd, *J* = 10, 2 Hz, H-12), 4.22 (2H, m, $CH_2Ph$), 4.32 (1H, dd, *J* = 6, 2 Hz, H-6), 4.40 (1H, ddd, *J* = 8, 6, 2 Hz, H-5), 4.49 (2H, m, H-11), 4.60 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.66 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.67 (2H, m, $CH_2Ph$), 4.85 (1H, d, *J* = 5.0 Hz, H-8), 6.98 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 2928, 1717, 1454, 1253, 1077, 1029, 856, 838, 780, 741, and 698 $cm^{-1}$; MS (FAB$^+$) *m/z* 657 (M+1).

**Methyl (5*R*,6*S*,7*S*,8*S*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]-pyridine-2-acetate (27).** To a stirred solution of **26** (0.0203 g, 0.031 mmol) in MeOH (2 ml) was added at room temperature a solution of $NaIO_4$ (0.0132 g, 0.0618 mmol) in water (0.22 ml). After 30 min at room temperature, the reaction mixture was concentrated up to 1/10 of the original volume. The concentrates were diluted with water (0.5 ml) and acidified with 1 M HCl to pH 2, and extracted with $CHCl_3$. The extracts were evaporated to a residue. To a stirred solution of the residue in THF–MeOH (10 : 1, 0.4 ml) was added at room temperature 10 % trimethylsilyldiazomethane in hexane (0.112 ml, 0.062 mmol). After 10 min, the reaction mixture was evaporated and chromatographed on silica gel (2 g) with 15 : 1 benzene–EtOAc to afford **27** (0.0128 g, 63 %) as a colorless syrup: $R_f$ = 0.38—0.42 (benzene–EtOAc = 5 : 1); $[\alpha]_D$ +51° (*c* 1.1, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = −0.02 (3H, s, $CH_3$ of TBS), 0.12 (3H, s, $CH_3$ of TBS), 0.80 (9H, s, *t*-Bu of TBS) 3.59 (1H, d, *J* = 16 Hz, H-9), 3.62 (1H, d, *J* = 16 Hz, H-9), 3.68 (3H, s, $OCH_3$), 3.76 (1H, dd, *J* = 10, 8 Hz, H-11), 3.86 (1H, dd, *J* = 4, 2 Hz, H-7), 4.11 (1H, dd, *J* = 10, 2 Hz, H-11), 4.35 (1H, dd, *J* = 6.5, 2 Hz, H-6), 4.45 (1H, ddd, *J* = 8.0, 6.5 2 Hz, H-5), 4.47 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.50 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.60 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.63 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.63 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.66 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.88 (1H, d, *J* = 4 Hz, H-8), 7.05 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph), IR (neat) 2950, 2928, 2855, 1738, 1254, 1094, 838, 738, and 698 $cm^{-1}$; HR-MS (FAB$^+$) Found: *m/z* 657.3387. Calcd for $C_{38}H_{49}N_2O_6Si$: M, 657.3360.

**Methyl (5*R*,6*S*,7*S*,8*S*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-5,6,7,8-tetrahydro-8-hydroxyimidazo[1,2-*a*]pyridine-2-acetate (28).** To a stirred solution of **27** (0.0235 g, 0.036 mmol) in dry THF (0.5 ml) was added 1 M *n*-$Bu_4NF$ in THF (0.040 ml, 0.040 mmol) at room temperature. After 1 h, the reaction mixture was evaporated and chromatographed on silica gel (1 g) with EtOAc to afford **28** (0.0190 g, 97 %) as a colorless syrup: $R_f$ = 0.29—0.35 (EtOAc); $[\alpha]_D$ +18° (*c* 1.4, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$=3.60 (1H, m, H-9), 3.66 (3H, s, $OCH_3$), 3.85 (2H, m, H-11), 3.93 (1H, dd, *J* = 6.5, 1 Hz, H-7), 4.25—4.35 (2H, m, H-5,6), 4.48 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.51 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.65 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.78 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.86 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.90 (1H, d, *J* = 12 Hz, $CH_2Ph$), 5.15 (1H, d, *J* = 6.5 Hz, H-8), 7.03 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 3030, 2917, 2864, 1737, 1355, 1124, 1092, 1050, 1025, 738, and 698 $cm^{-1}$; HR-MS (FAB$^+$) Found: *m/z* 543.2506. Calcd for $C_{32}H_{35}N_2O_6$: M, 543.2495.

**Methyl (5*R*,6*S*,7*S*,8*S*)-8-Azido-6,7-bis(benzyloxy)-5-benzyloxymethyl-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine-2-acetate (29). A) From 28:** To a stirred solution of **21** (0.033 g, 0.061 mmol) and tributylphosphine (0.0233 ml, 0.091 mmol) in dry THF (0.4 ml) were added under Ar successively a solution of 4 % $HN_3$ in toluene (0.150 ml, 0.122 mmol) and diethyl azodicarboxylate (0.144 ml, 0.091 mmol) at room temperature. After 30 min, the reaction mixture was evaporated and chromatographed on silica gel (3 g) with 1 : 2 hexane–ether to afford **29** (0.0266 g, 77 %) as a colorless syrup: $R_f$ = 0.28—0.35 (hexane–ether = 1 : 2); $[\alpha]_D$ +42° (*c* 1.9, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 3.64 (1H, m, H-9), 3.69 (3H, s, $OCH_3$), 3.7—3.9 (3H, m, H-11 & 7), 4.1—4.3 (2H, m, H-5 & H-6), 4.49 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.52 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.61 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.75 (2H, m, $CH_2Ph$), 4.84 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.98 (1H, d, *J* = 7.5 Hz, H-8), 7.06 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 2107, 1737, 1453, 1356, 1260, 1208, 1123, 1092, 1045, 1024, 740, and 698 $cm^{-1}$; HR-MS (FAB$^+$) Found: *m/z* 568.2550. Calcd for $C_{32}H_{34}N_5O_5$: M, 568.2560.

**B) From 37:** To a stirred solution of **37** (0.003 g, 0.061 mmol) and tributylphosphine (0.0233 ml, 0.091 mmol) in dry THF (0.4 ml) were added under Ar successively a solution of 4 % $HN_3$ in toluene (0.150 ml, 0.122 mmol) and diethyl azodicarboxylate (0.144 ml, 0.091 mmol) at room temperature. After 30 min, the reaction mixture was evaporated and chromatographed on silica gel (3 g) with 1 : 2 hexane–ether to afford **29** (0.0259 g, 75%) as a colorless syrup identical with the authentic sample obtained from **28** by the route A.

**(5*R*,6*S*,7*S*,8*R*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine (30).** To a solution of **15** (0.629 g, 1.34 mmol) and 2,6-lutidine (0.232 ml, 2.00 mmol) in dry $CH_2Cl_2$ (12.5 ml) was added *t*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (0.370 ml, 1.61 mmol) under $N_2$ at −15 °C. After 30 min at the same temperature, saturated aqueous $NaHCO_3$ was added and the mixture was separated. The organic layer was evaporated and chromatographed on silica gel (65 g) with 10 : 1 benzene–EtOAc to afford **30** (0.773 g, 99 %) as a colorless syrup: $R_f$ = 0.36—0.48 (benzene–EtOAc = 5 : 1); $^1$H NMR (270 MHz) $\delta$ = 0.25 (3H, s, $CH_3$ of TBS), 0.28 (3H, s, $CH_3$ of TBS), 0.96 (9H, s, *t*-Bu of TBS), 3.89 (1H, dd, *J* = 10.5, 2.5Hz, H-9), 4.0 (2H, m, H-6, H-7), 4.07 (1H, dd, *J* = 10, 8 Hz, H-9), 4.38 (1H, m, H-5), 4.44 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.47 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.65 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.68 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.71 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.89 (1H, d, *J* = 4 Hz, H-8), 4.91 (1H, d, *J* = 12 Hz, $CH_2Ph$), 7.07 (1H, d, *J* = 1.5 Hz, H-2), 7.16 (1H, d, *J* = 1.5 Hz, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 2927, 2854, 1144, 1124, 1097, 837, 736, and 697 $cm^{-1}$.

**(5*R*,6*S*,7*S*,8*R*)-6,7-Dibenzyloxy-5-benzyloxymethyl-2,3-dibromo-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo-[1,2-*a*]pyridine (31).** To a stirred suspension of **30** (1.02 g, 1.75 mmol) and $NaHCO_3$ (0.44 g, 5.23 mmol) in dry $CH_2Cl_2$ (21 ml) was added under $N_2$ 2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one (1.58 g, 3.85 mmol) at 0 °C. After 4 h at 0—10 °C, the reaction mixture was washed with 2 M NaOH (75 ml × 2) and water (40 ml). The organic layer was concentrated and chromatographed on silica gel (95 g) with 15 : 1 hexane–EtOAc to afford **31** (1.12 g, 86 %) as a colorless syrup: $R_f$=0.48—0.55 (hexane–EtOAc=4 : 1), which was used for the next step.

**(5*R*, 6*S*, 7*S*, 8*R*)- 6, 7- Bis(benzyloxy)- 5- benzyloxymethyl- 2-bromo-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo-[1,2-*a*]pyridine (32).** To a stirred solution of **31** (0.461 g, 0.621

mmol) in dry THF (9 ml) was added 1.6 M *t*-BuLi in pentane (0.621 ml, 0.994 mmol) under Ar at −78 °C. After 10 min at the same temperature, water (0.056 ml, 3.10 mmol) was added and the mixture was warmed to room temperature. The reaction mixture was evaporated and chromatographed on silica gel (46 g) with 10 : 1 hexane–EtOAc to afford **32** (0.315 g, 85%) as a colorless syrup: $R_f$ = 0.45—0.48 (hexane–EtOAc = 4 : 1); $[\alpha]_D$ −0.40° (*c* 1.0, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 0.25 (3H, s, $CH_3$ of TBS), 0.29 (3H, s, $CH_3$ of TBS), 0.97 (9H, s, *t*-Bu of TBS), 3.88 (1H, dd, *J* = 10, 8 Hz, H-9), 3.9—4.0 (2H, m, H-6, H-7), 4.03 (1H, dd, *J* = 10, 2 Hz, H-9), 4.32 (1H, m, H-5), 4.44 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.50 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.63 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.66 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.70 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.84 (1H, d, *J* = 4 Hz, H-8), 4.91 (1H, d, *J* = 12 Hz, $CH_2Ph$), 7.12 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 2928, 2855, 1249, 1140, 1097, 838, 736, and 697 $cm^{-1}$; MS ($FAB^+$) *m/z* 663 and 665 (M+11).

**(5*R*,6*S*,7*S*,8*R*)-2-Allyl-6,7-bis(benzyloxy)-5-benzyloxymethyl-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]-pyridine (33).** To a stirred solution of **32** (0.288 g, 0.434 mmol) in dry THF (6 ml) was added 1.6 M *n*-BuLi in hexane (0.434 ml, 0.694 mmol) under Ar at −78 °C. After 5 min at the same temperature, CuI (0.132 g, 0.694 mmol) was added and the mixture was stirred at −78 °C for 10 min, and then, allyl bromide (0.150 ml, 1.74 mmol) was added. After the reaction mixture was stirred at −78 °C for 15 min and warmed to room temperature, $CH_2Cl_2$ (8 ml) was added. The mixture was washed with saturated aqueous $NH_4Cl$ (8 ml), aqueous $Na_2S$ (5 ml) and water (5 ml), dried, and evaporated. The residue was chromatographed on silica gel (30 g) with 6 : 1 hexane–EtOAc to afford **33** (0.238 g, 88 %) as a colorless syrup: $R_f$ = 0.26—0.37 (hexane–EtOAc = 4 : 1); $[\alpha]_D$ −8.0° (*c* 1.1, $CHCl_3$); $^1$H NMR (500 MHz) $\delta$ = 0.25 (3H, s, $CH_3$ of TBS), 0.26 (3H, s, $CH_3$ of TBS), 0.95 (9H, s, *t*-Bu of TBS), 3.32 (2H, m, H-9), 3.89 (1H, dd, *J* = 10, 8 Hz, H-12), 3.9—4.0 (2H, m, H-6, H-7), 4.04 (1H, dd, *J* = 10, 2 Hz, H-12), 4.28 (1H, m, H-5), 4.46 (2H, m, $CH_2Ph$), 4.64 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.68 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.69 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.88 (1H, d, *J* = 4 Hz, H-8), 4.90 (1H, d, *J* = 12 Hz, $CH_2Ph$), 5.03 (1H, dddd, *J* = 10, 2, 1, 1 Hz, H-11), 5.13 (1H, dddd, *J* = 17, 2,2,2 Hz, H-11), 6.03 (1H, dddd, *J* = 17, 10, 7, 7 Hz, H-10), 6.85 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 2927, 2854, 1249, 1139, 1097, 837, 779, 736, and 697 $cm^{-1}$; HR-MS ($FAB^+$) Found: *m/z* 625.3477. Calcd for $C_{38}H_{49}N_2O_4Si$: M, 625.3462.

**(5*R*,6*S*,7*S*,8*R*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydro-2-(2,3-dihydroxypropyl)imidazo[1,2-*a*]pyridine (34).** To a stirred solution of **33** (0.169 g, 0.271 mmol) in THF (3.2 ml) and water (0.32 ml) were added at room temperature aqueous 50% NMO (0.133 ml, 0.569 mmol) and aqueous 4 % $OsO_4$ (0.172 ml, 0.027 mmol). After 6 h, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, evaporated and chromatographed on silica gel (9 g) with 1 : 1 benzene–EtOAc to afford **34** (0.161 g, 90 %) as a colorless syrup: $R_f$ = 0.25—0.32 (benzene–EtOAc = 1 : 1); MS ($FAB^+$) *m/z* 659 (M+1).

**(5*R*,6*S*,7*S*,8*R*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydro-2-(3-hydroxy-2-oxopropyl)imidazo[1,2-*a*]pyridine (35).** A suspension of **34** (0.617 g, 0.937 mmol) and $Ag_2CO_3$ (5.17 g, 18.7 mmol) in benzene (30 ml) was refluxed for 12 h. The reaction mixture was filtered off and washed with benzene. The filtrates and washings were combined, concentrated and chromatographed on silica gel (30 g) with 1 : 1 benzene–EtOAc to afford **35** (0.331 g, 54%) as a colorless syrup, and recovered **34** (0.204 g, 33%). The yield of **35** was 80% on the basis of the consumed **34**.

**29:** $R_f$ = 0.53—0.56 (benzene–EtOAc = 3 : 2); $[\alpha]_D$ +23.6° (*c* 1.5, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 0.20 (3H, s, $CH_3$ of TBS), 0.25 (3H, s, $CH_3$ of TBS), 0.97 (9H, s, *t*-Bu of TBS), 3.65 (1H, d, *J* = 14 Hz, H-9), 3.82 (1H, d, *J* = 14 Hz, H-9), 3.86 (1H, dd, *J* = 10.5, 8 Hz, H-12), 3.94 (1H, dd, *J* = 6, 1.5 Hz, H-6), 4.00 (1H, dd, *J* = 4, 1.5 Hz, H-7), 4.08 (1H, dd, *J* = 10.5, 2 Hz, H-12), 4.23 (2H, m, H-11), 4.36 (1H, m, H-5), 4.43 (1H, d, *J* = 11 Hz, $CH_2Ph$), 4.47 (1H, d, *J* = 11 Hz, $CH_2Ph$), 4.60 (2H, m, $CH_2Ph$), 4.71 (1H, d, *J* = 12.5 Hz, $CH_2Ph$), 4.77 (1H, d, *J* = 4 Hz, H-8), 4.90 (1H, d, *J* = 12.5 Hz, $CH_2Ph$), 6.99 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 2928, 2855, 1716, 1453, 1138, 1095, 1062, 1027, 838, 736, and 698 $cm^{-1}$; MS ($FAB^+$) *m/z* 657 (M+1).

**Methyl (5*R*,6*S*,7*S*,8*R*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-8-(*t*-butyldimethylsilyloxy)-5,6,7,8-tetrahydroimidazo[1,2-*a*]-pyridine-2-acetate (36).** To a stirred solution of **35** (0.124 g, 0.188 mmol) in MeOH (12 ml) was added at room temperature a solution of $NaIO_4$ (0.081 g, 0.376 mmol) in water (1.3 ml). After 30 min, the reaction mixture was concentrated up to 1/10 of the original volume. The concentrate was diluted with water (2 ml) and acidified with 1 M HCl to pH 2, and extracted with $CHCl_3$. The extracts were evaporated to a residue. To a stirred solution of the residue in THF–MeOH (10 : 1, 2.5 ml) was added 10 % trimethylsilyldiazomethane in hexane (0.540 ml, 0.376 mmol) at room temperature. After 10 min, the reaction mixture was evaporated and chromatographed on silica gel (12 g) with 15 : 1 benzene–EtOAc to afford **36** (0.0814 g, 66%) as a colorless syrup: $R_f$ = 0.37—0.40 (benzene–EtOAc = 5 : 1); $[\alpha]_D$ −6.4° (*c* 1.7, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$ = 0.24 (3H, s, $CH_3$ of TBS), 0.25 (3H, s, $CH_3$ of TBS), 0.95 (9H, s, *t*-Bu of TBS), 3.61 (2H, m, H-9), 3.70 (3H, s, $OCH_3$), 3.90 (1H, dd, *J* = 10.5, 8 Hz, H-11), 3.9—4.0 (2H, m, H-6, H-7), 4.05 (1H, dd, *J* = 10.5, 2.0 Hz, H-11), 4.33 (1H, m, H-5), 4.45 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.48 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.63 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.67 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.70 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.86 (1H, d, *J* = 5 Hz, H-8), 4.90 (1H, d, *J* = 12 Hz, $CH_2Ph$), 7.07 (1H, s, H-3), and 7.2—7.4 (15H, m, Ph); IR (neat) 2949, 2926, 2854, 1739, 1250, 1140, 1097, 837, 736, and 697 $cm^{-1}$; MS ($FAB^+$) *m/z* 657 (M+1).

**Methyl (5*R*,6*S*,7*S*,8*R*)-6,7-Bis(benzyloxy)-5-benzyloxymethyl-5,6,7,8-tetrahydro-8-hydroxyimidazo[1,2-*a*]pyridine-2-acetate (37).** To a stirred solution of **36** (0.0414 g, 0.063 mmol) in dry THF (1.0 ml) was added 1 M *n*-$Bu_4NF$ in THF (0.070 ml, 0.070 mmol) at room temperature. After 1 h, the reaction mixture was evaporated and chromatographed on silica gel (2 g) with EtOAc to afford **37** (0.0328 g, 96 %) as a colorless syrup: $R_f$ = 0.53—0.56 (benzene–EtOAc = 3 : 2); $[\alpha]_D$ −9.8° (*c* 1.2, $CHCl_3$); $^1$H NMR (270 MHz) $\delta$=3.61 (1H, d, *J* = 17 Hz, H-9), 3.65 (1H, d, *J* = 17 Hz, H-9), 3.68 (3H, s, $OCH_3$), 3.89 (2H, m, H-11), 3.94 (1H, dd, *J* = 4, 2 Hz, H-7), 4.2—4.3 (2H, m, H-5 & H-6), 4.51 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.54 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.64 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.72 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.88 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.90 (1H, d, *J* = 12 Hz, $CH_2Ph$), 4.98 (1H, d, *J* = 4 Hz, H-8), 7.05 (1H, s, H-3), and 7.2—7.4 (15 H, m, Ph); IR (neat) 1738, 1452, 1155, 1130, 1087, 1025, 736, and 698 $cm^{-1}$; HR-MS ($FAB^+$) Found: *m/z* 543.2504. Calcd for $C_{32}H_{35}N_2O_6$: M, 543.2495.

**Methyl (5*R*,6*S*,7*S*,8*S*)-8-Acetylamino-5,6,7,8-tetrahydro-6,7-dihydroxy-5-hydroxymethylimidazo[1,2,-*a*]pyridine-2-acetate (38).** A solution of **29** (0.024 g, 0.0423 mmol) in AcOH (1 ml) was hydrogenated in the presence of 10% Pd/C (0.03 g) under an atmosphere of hydrogen ($4\times 10^5$ Pa) for 15 h at room temperature.

The reaction mixture was filtered off and washed with MeOH. The filtrates and washings were combined and evaporated to a residue (0.0164 g). To a solution of the residue in MeOH (1.6 ml) was added acetic anhydride (0.8 ml) at room temperature. After 1 h at room temperature, the reaction mixture was evaported and chromatographed on silica gel (3 g) with 2 : 1 $CHCl_3$–MeOH to afford **38** (0.010 g, 76 %) as colorless crystals: Mp 197—199 °C; $R_f$ = 0.28—0.35 ($CHCl_3$–MeOH = 2 : 1); $[\alpha]_D$ +89° (*c* 0.3, $H_2O$); $^1$H NMR (270 MHz, $D_2O$) $\delta$ = 2.10 (3H, s, NAc), 3.66 (2H, m, H-9), 3.72 (3H, s, $OCH_3$), 4.04 (1H, dd, *J* = 11, 6 Hz, H-11), 4.1—4.2 (2H, m, H-11, 7), 4.29 (1H, m, H-5), 4.46 (1H, dd, *J* = 2, 2 Hz, H-6), 5.03 (1H, d, *J* = 9.5 Hz, H-8), and 7.23 (1H, s, H-3); HR-MS (FAB$^+$) Found: *m/z* 314.1339. Calcd for $C_{13}H_{20}N_3O_6$: M, 314.1352.

Found: C, 48.15; H, 6.28; N, 12.91%. Calcd for $C_{13}H_{19}N_3O_6$: C, 49.84; H, 6.11; N, 13.41%.

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