# A General Synthesis of 4-Substituted 1-(β-D-Ribofuranosyl)imidazo-[4,5-*c*]pyridines †

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The trimethylsilyl derivative (I) of 4,6-dichloroimidazo[4,5-*c*]pyridine was condensed with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide (II) to afford, after removal of protecting groups, the isomeric 1- and 3-(β-D-ribofuranosyl) derivatives [(V) and (VI)]. The reaction of the nucleoside (V) with a variety of nucleophiles afforded various 4-substituted 6-chloro-derivatives. Removal of the 6-chloro-group by catalytic hydrogenation provided a general synthesis of 4-substituted 1-(β-D-ribofuranosyl)imidazo[4,5-*c*]pyridines, including the 4-amino-compound (3-deaza-adenosine).

THE function of the various nitrogen atoms of purine nucleosides in biological systems has been the subject of considerable comment and speculation. It has been postulated that N-3 of the terminal adenylic acid unit in tRNA is essential in the process of protein biosynthesis.[1] Also, N-1 and/or N-3 of the adenine unit have been postulated as binding sites for nicotinamide adenine dinucleotide in various enzymic reactions.[2] The majority of purine and purine-type ribosides exist in the *anti*-conformation, although there have been several reports of these nucleosides existing in the *syn*-conformation in the solid state. In this respect, 3-deazapurine nucleosides are of interest since N-3 of purine nucleosides is thought to be involved in stabilizing the *syn*-conformation by intramolecular hydrogen bonding [O(5′)–H · · · N(3)].[3] Several 3-deazapurine nucleosides have been synthesized previously, but only in low yields, which has precluded adequate chemotherapeutic and biochemical investigations. We report here a route to 6-substituted 3-deazapurine ribosides in sufficient quantities for these purposes.

The principal disadvantage of previous syntheses was the low susceptibility to nucleophilic displacement of the chloro-substituent in 6-chloro-3-deazapurine riboside [4-6] in comparison with 6-chloropurine riboside, a result of

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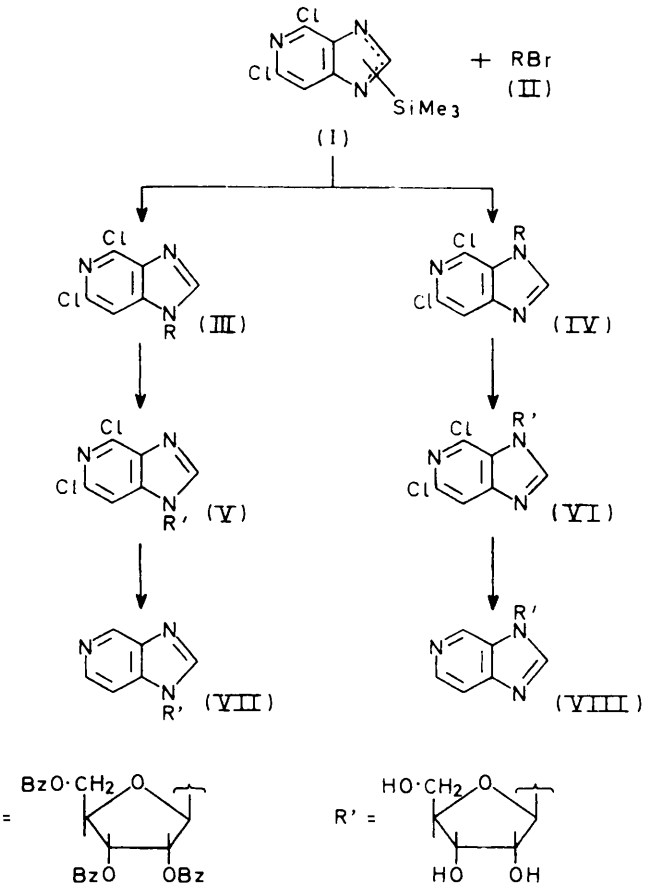
the higher electron density at C-6 in the former nucleoside. This prompted us to attempt the synthesis of a nucleoside carrying a replaceable electron-withdrawing group at C-4, which would decrease the electron density at C-6. We therefore chose 4,6-dichloro-1-(β-D-ribofuranosyl)-imidazo[4,5-*c*]pyridine as our starting material for the synthesis of 4-substituted 1-(β-D-ribofuranosyl)imidazo-[4,5-*c*]pyridines (*i.e.* 6-substituted 3-deazapurine ribosides).

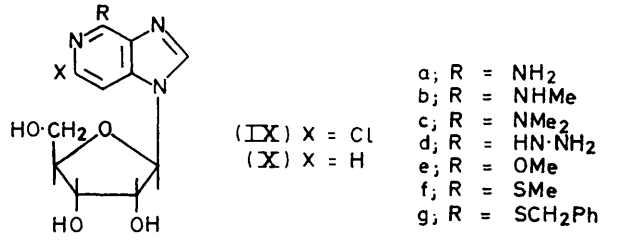
Treatment of 4,6-dichloroimidazo[4,5-*c*]pyridine [7] with *NO*-bistrimethylsilylacetamide in acetonitrile gave a syrup which was assumed to be a monotrimethylsilyl derivative (I). This syrup (I) was condensed with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide (II) [8] in the presence of a catalytic amount of sodium iodide to afford a mixture of protected 1- and 3-ribosides [(III) 49% and (IV) 9%] which was separated by fractional crystallization and column chromatography. The benzoyl groups were removed with methanolic sodium methoxide to give the ribosides (V) (95%) and (VI) (94%). To establish the actual site of glycosidation, compounds (V) and (VI) were dehalogenated by catalytic hydrogenation to afford the imidazo[4,5-*c*]pyridine ribosides (VII) and (VIII), respectively.[9-11]

The anomeric configuration of compounds (VIII) and (IX) has been reported previously as β, but without supporting evidence.[9-11] Since numerous exceptions to the Baker '*trans*' rule are known,[12,13] it was felt that another basis for assigning the anomeric configuration of (V) and (VI) was desirable. The configuration of (V) was established unequivocally as β by its conversion into 3-deaza-adenosine (Xa) as discussed later. In an effort to establish the configuration of (VI) from $^1$H n.m.r. data, the compound was converted into the 2',3'-*O*-isopropylidene derivative, which showed $J_{1',2'}$ 2·3 Hz in deuteriochloroform. However, this value is not sufficiently small to provide unequivocal evidence [14] for the β-configuration. Recently, Imbach and his co-workers [15] have observed that for 2',3'-*O*-isopropylidene ribonucleosides the chemical shift difference (Δδ) between the two isopropylidene methyl signals is greater than 0·18 p.p.m. in the β-series but less than 0·10 in the α-series. For the 2',3'-*O*-isopropylidine derivative of (VI) Δδ is 0·21, which establishes the configuration as β. It follows that the anomeric configuration is also β for (VII) and (VIII).

The reaction of 4,6-dichloro-1-(β-D-ribofuranosyl)-imidazo[4,5-*c*]pyridine (V) with various nucleophiles has afforded the 4-substituted 6-chloro-derivatives (IXa—g). The $^1$H n.m.r. spectrum of each established that only one chloro-substituent had been displaced. Attempts to displace both were unsuccessful as expected, since replacement of one chloro-substituent by an electron-donating group should deactivate the other. The reaction with anhydrous hydrazine gave only (IXd), with no evidence




for the formation of compound (VII).[5] Treatment of the methylthio-derivative (IXf) under the same conditions as employed for the conversion of (V) into (IXa) gave no




reaction, illustrating the greater ease of displacement of the chloro-substituent by nucleophiles.

To establish the site of nucleophilic displacement, the remaining chloro-substituent of (IXa) was removed by

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catalytic hydrogenation to afford 3-deaza-adenosine (Xa) (73%), the properties of which corresponded to those reported.[4,5] Similarly, catalytic hydrogenation of (IXe) gave (Xe). The appearance of an AB coupling pattern in the $^1$H n.m.r. spectra of (Xa) and (Xe) for two of the three aromatic protons confirms the initial site of nucleophilic displacement as C-4.

This method thus represents a new general synthesis of 4-substituted 1-(β-D-ribofuranosyl)imidazo[4,5-*c*]-pyridines in good yield.

These nucleosides have been evaluated as antitumour agents against L-1210 lymphoid leukemia, *in vivo*. Only 6-chloro-4-dimethylamino-1-(β-D-ribofuranosyl)imidazo-[4,5-*c*]pyridine (IXc) showed good antitumour activity.

## EXPERIMENTAL

M.p.s were determined with a Thomas–Hoover capillary apparatus. $^1$H N.m.r. spectra were obtained with Varian A56/60 and XL-100 spectrometers (solutions in [$^2H_6$]dimethyl sulphoxide or [$^2$H]chloroform with sodium 2,2-dimethyl-2-silapentane-5-sulphonate or tetramethylsilane, respectively, as internal standard). U.v. spectra were recorded on a Beckman DK-2 spectrophotometer and optical rotations were obtained with a Perkin-Elmer model 141 automatic digital readout polarimeter. Evaporations were performed under reduced pressure at 40° with a rotary evaporator unless otherwise stated. T.l.c. was run on glass plates coated (0·25 mm) with SilicAR 7GF (Mallinckrodt). Column chromatography was performed on either silica gel (J. T. Baker) or SilicAR CC7 (Mallinckrodt). The 20% palladium–charcoal was purchased from Matthey Bishop, Inc. Elemental analyses were performed by Heterocyclic Chemical Corp., Harrisonville, Missouri, and M-H-W Laboratories, Garden City, Michigan.

4,6-*Dichloro*-1- *and* 3-(2,3,5-*tri*-O-*benzoyl*-β-D-*ribofuranosyl*)*imidazo*[4,5-c]*pyridine* [(III)] *and* (IV)].—*NO*-Bistrimethylsilylacetamide (12 ml) was added to a suspension of 4,6-dichloroimidazo[4,5-*c*]pyridine [7] (5·1 g, 32·2 mmol) in acetonitrile (35 ml) and the solution was stirred at 40° for 1·5 h. The solvent and the excess of silylating agent were removed under reduced pressure leaving a syrup which solidified on cooling. A solution of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide [8] [from 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (15·2 g, 30·0 mmol)] in toluene (20 ml) was added to the silylated product followed by a catalytic amount (50 mg) of sodium iodide. The solvent was removed by vacuum distillation (oil-bath at 50°) and the resulting syrup was stirred under vacuum at 85° for 45 min, then allowed to cool to room temperature. The dark amber glass was dissolved in chloroform (400 ml) and a little starting material was filtered off. The filtrate was washed with saturated aqueous sodium hydrogen carbonate solution (3 × 50 ml) and water (3 × 50 ml), dried ($Na_2SO_4$), and concentrated *in vacuo* to a syrup (25·5 g), which was dissolved in ethyl acetate. The solution was allowed to evaporate at room temperature to furnish a cream coloured solid (8·1 g), which was recrystallized twice from methanol to give white crystals (6·5 g) of (III).

The combined filtrates were concentrated to afford a syrup (15 g) which was dissolved in the minimum amount of benzene and applied to a silica gel column (J. T. Baker; 4·5 × 45 cm) packed in benzene. The column was washed with benzene (2 l) and eluted with benzene–ethyl acetate (9 : 1 v/v), which resolved the isomeric nucleosides, as determined by t.l.c. of individual fractions.

The 3-*riboside* (IV), eluted first, was isolated as an amber syrup. Crystallization from methanol gave white crystals (1·7 g, 9%), m.p. 144—146°; $\lambda_{max.}$ (pH 1) 301sh (ε 17,700), 287 (19,600), and 248 nm (35,000), $\lambda_{max.}$ (MeOH) 283 nm (ε 6000), $\lambda_{max.}$ (pH 11) 301sh (14,500) and 286 nm (16,700); δ ($CDCl_3$) 6·12 (1H, d, $J_{1',2'}$ 2·5 Hz, H-1′) (Found: C, 60·8; H, 3·7; N, 6·85. $C_{32}H_{23}Cl_2N_3O_7$ requires C, 60·75; H, 3·65; N, 6·65%). The 1-*riboside* (III) was obtained as a pale amber syrup. Crystallization from methanol gave white needles (2·8 g) (total yield 9·3 g, 49%), m.p. 145—146°; $\lambda_{max.}$ (pH 1) 274 nm (ε 12,300), $\lambda_{max.}$ (MeOH) 274 nm (9800), $\lambda_{max.}$ (pH 11) 275 nm (15,900); δ ($CDCl_3$) 6·32 (1H, d, $J_{1',2'}$ 4·5 Hz, H-1) (Found: C, 60·9; H, 3·75; N, 6·45%).

4,6-*Dichloro*-1-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]*pyridine* (V).—The protected 1-riboside (III) (6·1 g, 9·07 mmol) was dissolved in absolute methanol (100 ml) and sodium methoxide was added to adjust the pH to 10. The solution was heated at reflux for 30 min, cooled to room temperature, and neutralized with Amberlite IRC-50 resin ($H^+$; pre-washed with methanol). The resin was filtered off and the filtrate evaporated to a syrup, which solidified after several co-evaporations with benzene. The solid was triturated with benzene (100 ml) and filtered off. Recrystallization from water furnished the *riboside* (V) (3·0 g, 95%), m.p. 202—203°, $\lambda_{max.}$ (pH 1) 275 (ε 8100) and 258 nm (8900), $\lambda_{max.}$ (MeOH) 275 (7000) and 259 nm (8000), $\lambda_{max.}$ (pH 11) 275 (7100) and 258 nm (8000); δ [$(CD_3)_2SO$] 6·00 (1H, d, $J_{1',2'}$ 5·5 Hz, H-1′) [Found: C, 40·4; H, 3·45; N, 12·55. $C_{11}H_{11}Cl_2N_3O_4,0{\cdot}5H_2O$ (verified by n.m.r.) requires C, 40·1; H, 3·35; N, 12·75%].

4,6-*Dichloro*-3-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]*pyridine* (VI).—The protected 3-riboside (IV) (3·5 g, 5·5 mmol) was treated similarly to furnish the *riboside* (VI) (1·7 g, 94%), m.p. 196—198°; $\lambda_{max.}$ (pH 1) 286 (ε 6600) and 238 nm (6400), $\lambda_{max.}$ (MeOH) 289 (ε 6500) and 239 nm (5400), $\lambda_{max.}$ (pH 11) 289 (6700) and 240 nm (5000); δ [$(CD_3)_2SO$] 6·44 (1H, d. $J_{1',2'}$ 4·0 Hz, H-1′) (Found: C, 41·3; H, 3·5; N, 13·0%).

4,6-*Dichloro*-3-(2,3-O-*isopropylidene*-β-D-*ribofuranosyl*)-*imidazo*[4,5-c]*pyridine*.—To a suspension of the riboside (VI) (480 mg, 1·5 mmol) in acetone (30 ml) and 2,2-dimethoxypropane (5·0 ml) was added a 0·01% solution of sulphuric acid in acetone (40 ml). After stirring at room temperature for 4 h, saturated aqueous sodium hydrogen carbonate (10 ml) was added. The mixture was evaporated and the residue extracted with chloroform (60 ml). The extract was concentrated and applied to a silica gel column (SilicAR CC7; 1 × 25 cm; dry-packed) and eluted with chloroform–methanol (14·5 : 1, v/v). The product fractions afforded a syrup which crystallized from carbon tetrachloride to give the *acetonide* (350 mg, 65%), m.p. 144—146°; $\lambda_{max.}$ (pH 1) 286 nm (ε 6500), $\lambda_{max.}$ (MeOH) 288 (6300) and 239 nm (5950), $\lambda_{max.}$ (pH 11) 288 (6850) and 239 nm (7050); δ [$(CD_3)_2SO$] 1·42 and 1·63 (each 3H, s, $CMe_2$), 6·73 (1H, d, $J_{1',2'}$ 2·3 Hz, H-1′), 7·97 (1H, s, H-7), and 9·06 (1H, s, H-2) (Found: C, 46·6; H, 4·2; N, 12·0. $C_{14}H_{15}Cl_2N_3O_4$ requires C, 46·65; H, 4·15; N, 11·65%).

1-(β-D-*Ribofuranosyl*)*imidazo*[4,5-c]*pyridine* (VII).—Compound (V) (150 mg, 0·47 mmol) in water (50 ml) was hydrogenated over 10% palladium–carbon (100 mg) at 40 lb $in^{-2}$ for 20 h. The white solid resulting from work up was recrystallized from methanol to afford the nucleoside (VII), m.p. 204—205° (lit.,[11] 198—199°); $\lambda_{max.}$ (pH 1) 263 (ε 4300) and 257 nm (4100), $\lambda_{max.}$ (MeOH) 268sh (3400), 261sh (4500), and 249 nm (5600), $\lambda_{max.}$ (pH 11) 267sh (4000), 260sh

(4900), and 243 nm (7000) [lit.,[11] $\lambda_{max.}$ (pH 1·72) 263—264 (4700) and 257—258 nm (4100), $\lambda_{max.}$ (pH 12·35) 268sh (2800), 259sh (4100), and 248 nm (4700)]; $[\alpha]_D^{26}$ −33·4° (*c* 0·5 in $H_2O$) {lit.,[11] $[\alpha]_D^{21}$ −36·0° (*c* 1·0 in $H_2O$)}.

3-(β-D-*Ribofuranosyl*)*imidazo*[4,5-c]*pyridine* (VIII).—Compound (VI) (320 mg, 1·0 mmol) in water (100 ml) containing N-sodium hydroxide (2·0 ml) and 10% palladium–carbon (100 mg) was hydrogenated at 40 lb $in^{-2}$ for 1·5 h. The syrupy product was dissolved in ethanol (30 ml) and a little solid was filtered off. Evaporation of the filtrate gave a solid which was recrystallized from methanol to give the nucleoside (VIII) (120 mg, 48%), m.p. 204—207° (lit.,[9] 200—202°; lit.,[10] 195°); $\lambda_{max.}$ (pH 1) 283 (ε 7300) and 252 nm (5100), $\lambda_{max.}$ (MeOH) 275 (6000) and 241 nm (5500), $\lambda_{max.}$ (pH 11) 274 nm (5400) [lit.,[9] $\lambda_{max.}$ (pH 1·3) 283 (7200) and 252 nm (5000), $\lambda_{max.}$ (pH 12·2) 275 (5500) and 242 nm (5600); lit.,[10] $\lambda_{max.}$ (pH 1) 288 (7300) and 252 nm (5400), $\lambda_{max.}$ (pH 7) 270 (4600) and 245 nm (5500)]; $[\alpha]_D^{31}$ −44·7° (*c* 1·0 in $H_2O$) {lit.,[9] $[\alpha]_D^{21}$ −50° (*c* 1·0 in MeOH); lit.,[10] $[\alpha]_D^{21}$ −35·8° (*c* 1·45 in $H_2O$)}.

4-*Amino*-6-*chloro*-1-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]*pyridine* (IXa).—A solution of compound (V) (2·24 g, 7·0 mmol) in liquid ammonia (60 ml) was heated in a steel vessel at 110° for 30 h. The excess of ammonia was removed to afford a tan solid. Recrystallization from water (charcoal) gave the *product* (IXa) (1·95 g, 93%), m.p. 101—103°; $\lambda_{max.}$ (pH 1) 285sh (ε 9200) and 266 nm (11,700), $\lambda_{max.}$ (MeOH) 272 nm (12,500), $\lambda_{max.}$ (pH 11) 270 nm (12,500); δ [$(CD_3)_2SO$] 5·77 (1H, d, $J_{1',2'}$ 5·5 Hz, H-1) and 6·62 (2H, s, 4-$NH_2$) [Found: C, 41·35; H, 5·0; N, 17·3. $C_{11}H_{13}ClN_4O_4$,-1·0$H_2O$ (verified by n.m.r.) requires C, 41·45; H, 4·7; N, 17·6%].

6-*Chloro*-4-*methylamino*-1-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]*pyridine* (IXb).—A solution of compound (V) (800 mg, 2·5 mmol) in methylamine (25 ml) was heated in a steel vessel at 120° for 5 h. The excess of methylamine was evaporated off and the solid was recrystallized from water (charcoal) to give the *product* (IXb) (630 mg, 80%), m.p. 211—212°, $\lambda_{max.}$ (pH 1) 271 nm (ε 15,000), $\lambda_{max.}$ (MeOH) 279 nm (16,400), $\lambda_{max.}$ (pH 11) 278 nm (15,900) δ [$(CD_3)_2SO$] 5·82 (1H, d, $J_{1',2'}$ 5·5 Hz, H-1'), 2·99 (3H, d, Me), 7·20 (1H, s, 4-HN) (Found: C, 46·0; H, 4·9; N, 17·55. $C_{12}H_{15}ClN_4O_4$ requires C, 45·8; H, 4·75; N, 17·75%).

6-*Chloro*-4-*dimethylamino*-1-(β-D-*ribofuranosyl*)*imidazo*-[4,5-c]*pyridine* (IXc).—A solution of compound (V) (40 mg, 2·0 mmol) in dimethylamine (25 ml) was heated in a steel vessel at 115° for 6 h. Evaporation of the excess of dimethylamine gave a solid which was recrystallized from water (charcoal) to give the *product* (IXc) (560 mg, 86%), m.p. 89—94°; $\lambda_{max.}$ (pH 1) 297sh (ε 11,500) and 277 nm (14,400), $\lambda_{max.}$ (MeOH) 286 nm (18,300), $\lambda_{max.}$ (pH 11) 287 nm (ε 17,400); δ [$(CD_3)_2SO$] 5·82 (1H, d, $J_{1',2'}$ 5·5 Hz, H-1') and 3·38 (6H, s, $NMe_2$) [Found: C, 46·4; H, 5·45; N, 16·55. $C_{13}H_{17}ClN_4O_4$,0·5$H_2O$ (verified by n.m.r.) requires C, 46·2; H, 5·05; N, 16·6%].

6-*Chloro*-4-*hydrazino*-1-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]*pyridine* (IXd).—A solution of compound (V) (1·44 g, 4·5 mmol) in anhydrous hydrazine (15 ml) was heated at reflux for 1 h. The mixture was evaporated to afford an amber syrup which was co-evaporated with ethanol to give a solid. Recrystallization from ethanol–water (charcoal) gave the *product* (IXd) (1·03 g, 72%), m.p. 126—129°; $\lambda_{max.}$ (pH 1) 316 (ε 6000) and 264 nm (11,500), $\lambda_{max.}$ (MeOH) 280 nm (12,600), $\lambda_{max.}$ (pH 11) 277 nm (9800); δ [$(CD_3)_2SO$] 5·79 (1H, d, $J_{1',2'}$ 5·5 Hz, H-1'), 8·25 (1H, s, *H*N·$NH_2$), and 3·36 (2H, s, HN·N*H*$_2$) [Found: C, 40·6; H, 4·75; N, 21·6. $C_{11}H_{14}ClN_5O_4$,0·5$H_2O$ (verified by n.m.r.) requires C, 40·65; H, 4·6; N, 21·6%].

6-*Chloro*-4-*methoxy*-1-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]-*pyridine* (IXe).—A solution of sodium methoxide (from 50 mg of sodium) in methanol (10 ml) was added to compound (V) (250 mg, 0·75 mmol) and the resulting solution was heated in a steel vessel at 110° for 20 h. The mixture was filtered and the filtrate neutralized with Amberlite IRC-120 resin ($H^+$); the resin was then filtered off. Silica gel (1 g) was added to the filtrate and the methanol was evaporated off. The resulting mixture was placed on a silica gel column (SilicAR CC7; 2·5 × 20 cm; dry-packed) and eluted with chloroform–methanol (13 : 2 v/v) to give the *product* (IXe) (180 mg, 76%). Recrystallization from methanol gave white crystals, m.p. 135—137°; $\lambda_{max.}$ (pH 1) 259 nm (ε 9500), $\lambda_{max.}$ (MeOH) 257 nm (11,600), $\lambda_{max.}$ (pH 11) 256 nm (12,000); δ [$(CD_3)_2SO$] 5·92 (1H, d, $J_{1',2'}$ 5·5 Hz, H-1') and 3·86 (3H, s, OMe) (Found: C, 45·4; H, 4·5; N, 13·0. $C_{12}H_{14}ClN_3O_5$ requires C, 45·65; H, 4·45; N, 13·3%).

6-*Chloro*-4-*methylthio*-1-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]-*pyridine* (IXf).—A solution of compound (V) (1·6 g, 5·0 mmol) in ethanol (175 ml) containing sodium (160 mg) and methanethiol (2·01 ml) was heated at reflux for 16 h, neutralized with Amberlite IRC 120 resin ($H^+$), filtered, and evaporated to a residue which solidified when triturated with chloroform. This crude solid was extracted (Soxhlet) with diethyl ether for 48 h. The extract was evaporated to afford a syrup which solidified when triturated with chloroform (50 ml). Recrystallization from acetone–water gave the *product* (IXf) (1·02 g, 62%), m.p. 153—154°; $\lambda_{max.}$ (pH 1) 298 nm (ε 10,100), $\lambda_{max.}$ (MeOH) 247sh (13,100) and 291 nm (14,100), $\lambda_{max.}$ (pH 11) 295 nm (11,400); δ [$(CD_3)_2SO$] 5·96 (1H, d, $J_{1',2'}$ 5·5 Hz, H-1) and 2·66 (3H, s, SMe) (Found: C, 43·15; H, 4·2; N, 12·35. $C_{12}H_{14}ClN_3O_4S$ requires C, 43·45; H, 4·2; N, 12·65%).

4-*Benzylthio*-6-*chloro*-1-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]-*pyridine* (IXg).—Compound (V) (620 mg, 2·0 mmol) was dissolved in ethanol (75 ml) to which sodium (70 mg) was added, followed by toluene-α-thiol (0·35 ml, 3·0 mmol). The mixture was heated at reflux for 6 h, filtered, and evaporated. The syrupy residue was suspended in water (20 ml) and neutralized (N-HCl) to furnish a solid. This was collected, washed with water (2 × 10 ml), and triturated with benzene. Recrystallization from isopropyl alcohol gave the *product* (IXg) (690 mg, 85%), m.p. 100—103°; $\lambda_{max.}$ (pH 1) 300 nm (ε 11,860), $\lambda_{max.}$ (EtOH) 299 (14,600) and 292 nm (14,700), $\lambda_{max.}$ (pH 11) 298 nm (14,300); δ [$(CD_3)_2SO$] 5·96 (1H, d, $J_{1',2'}$ 5·5 Hz, H-1'), 4·60 (2H, s, PhC$H_2$), and 7·38 (5H, m, Ph) [Found: C, 53·25; H, 5·45; N, 9·4. $C_{18}H_{18}ClN_3O_4S$,0·5$CH_3CHOHCH_3$ (verified by n.m.r.) requires C, 53·6; H, 5·05; N, 9·6%].

4-*Amino*-1-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]*pyridine* (3-*Deaza-adenosine*) (Xa).—The 4-amino-6-chloro-derivative (IXa) (450 mg, 1·5 mmol) was dissolved in water (150 ml) to which sodium hydroxide (60 mg, 1·5 mmol) was added, followed by wet 20% palladium–carbon (40 mg; as 90 mg of catalyst containing 54·9% water). This mixture was hydrogenated at 40 lb $in^{-2}$ for 15 h and filtered through Celite which was washed with water (30 ml); the filtrate was then concentrated. The white solid was filtered off, washed with cold water (15 ml), and air-dried to give 3-deaza-adenosine (290 mg, 75%), m.p. 229—231° (lit.,[4,5] 225—226°); $\lambda_{max.}$ (pH 1) 262 nm (ε 11,600), $\lambda_{max.}$ ($H_2O$) 264 nm (11,900), $\lambda_{max.}$ (pH 11) 265 nm (12,000) [lit.,[4,5] $\lambda_{max.}$ (pH 1)

262 nm (10,300), $\lambda_{max.}$ (pH 11) 265 nm (10,800)]; δ [$(CD_2)_2SO$] 5·99 (1H, d, $J_{1',2'}$ 3·0 Hz, H-1'), 8·63 (2H, s, $NH_2$), 7·47 (1H, d, $J_{6,7}$ 3·5 Hz, H-7), 7·83 (1H, d, $J_{6,7}$ 3·5 Hz, H-6), and 8·77 (1H, s, H-2); $[\alpha]_D^{26}$ −44·5° (*c* 1·00 in $H_2O$) {lit.,[4] $[\alpha]_D^{26}$ −48·3° (*c* 1·03 in $H_2O$)}.

4-*Methoxy*-1-(β-D-*ribofuranosyl*)*imidazo*[4,5-c]*pyridine* (Xe).—The 6-chloro-4-methoxy-derivative (IXe) (360 mg, 1·1 mmol) was dissolved in water and N-sodium hydroxide (1·1 ml) was added, followed by 20% palladium–carbon (300 mg; as 660 mg of catalyst containing 54·9% water). This mixture was hydrogenated at 45 lb $in^{-2}$ for 3 h, filtered through Celite, and evaporated to a syrup which crystallized from a small amount of water to give the *product* (Xe) (210 mg, 69%). A sample recrystallized from water had m.p. 101—103°; $\lambda_{max.}$ (pH 1) 261 nm (ε (7600), $\lambda_{max.}$ (MeOH) 251 nm (10,700), $\lambda_{max.}$ (pH 11) 251 nm (10,100); δ [$(CD_3)_2SO$] 3·99 (3H, s, OMe), 5·82 (1H, d, $J_{1',2'}$ 5·5 Hz, H-1'), 7·34 (1H, d, $J_{7,6}$ 5·0 Hz, H-7), 7·75 (1H, d, $J_{6,7}$ 5·0 Hz, H-6), and 8·33 (1H, s, H-2) (Found: C, 51·4; H, 5·55; N, 14·7. $C_{12}H_{15}N_3O_5$ requires C, 51·25; H, 5·35; N, 14·95%).

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