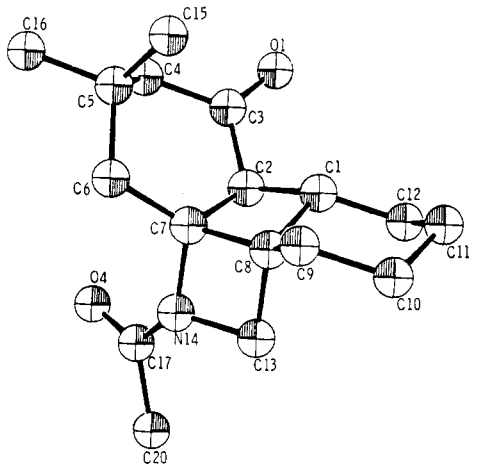

Figure 2. A perspective drawing of one of the independent molecules of **20** generated from the final X-ray coordinates.

multisolution tangent formula approach and refined by using full-matrix least squares. Anisotropic temperature parameters were used for the non-hydrogen atoms, while fixed isotropic parameters were used for the hydrogens. The function minimized was $\sum\omega(|F_o| - |F_c|)^2$ with $\omega = 1/(\sigma F_o)^2$ to give an unweighted residual of 0.053. Tables I–III in the supplementary material contain the final fractional coordinates, temperature parameters, bond distances, and bond angles. There are no abnormally close intermolecular contacts. Figure 1 is a computer-generated drawing of **18** showing the relative configuration.

20: Crystals of **20** formed from ether with symmetry $P2_1/c$ and cell parameters of a = 16.837 (4) Å, b = 15.316 (2) Å, c = 12.557 (3) Å, and β = 100.98 (2)° for Z = 8. An automatic four-circle diffractometer equipped with Cu radiation was used to measure 4486 unique reflections with $2\theta \leq 114°$. Of these 3029 were observed ($I \geq 3\sigma I$) and corrected for Lorentz and polarization effects. A multisolution tangent formula approach to phase solution gave an initial model which was refined with least squares calculations and Fourier difference analysis. The function $\sum\omega(|F_o| - |F_c|)^2$ with $\omega = 1/(F_o)^2$ was minimized to give an unweighted residual of 0.064. Tables IV–VI in the supplementary material contain the final fractional coordinates, temperature parameters, bond distances, and bond angles, while Figure 2 is a drawing of one of the independent molecules of **20**.

The two independent molecules of **20** are related to each other by an approximate translation of one-half the unit cell along X. However, the conformations of the cyclohexanone rings of the two molecules differ. Both rings have half-chair conformations, but in one (shown in Figure 2) C-15 is axial, while in the other C-15′ is equatorial. Both molecules have chair conformations for the cyclohexane ring.

Acknowledgment is made to the Research Corporation (Schering-Plough Corporation Grant) and to the Bryn Mawr College Faculty Research Fund for the support of this research at Bryn Mawr. The acquisition at Bryn Mawr of the preparative liquid chromatograph was made possible by a grant from the National Science Foundation, of a GC/MS system by grants from the Camille and Henry Dreyfus Foundation and the PQ Corporation, and of the 270-MHz NMR spectrometer by grants from the W. M. Keck Foundation and Merck & Co., Inc. We are grateful for the many analytical services provided by Merck Sharp & Dohme Research Laboratories, West Point, PA.

Supplementary Material Available: Tables I–VI containing the final fractional coordinates, temperature parameters, bond distances, and bond angles for **18** and **20** (12 pages). Ordering information is given on any current masthead page.

Spiro and Bicyclic Nucleosides. Preparation of New Structural Types from Ribose Adducts of Diaminomaleonitrile

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The use of ribose adducts of diaminomaleonitrile (DAMN) as starting materials for the synthesis of three new nucleoside structural types is described. Oxidation of ribopyranosyl- and ribofuranosyldiaminomaleonitrile adducts (**3** and **10**, respectively) with DDQ in acetonitrile yields the iminolactones **4** and **11**, respectively, while use of DDQ in methanol yields the spiro derivatives **9** and **12**. Treatment of **4** with *t*-BuOCl and **11** with NBS results in the formation of 2,3-dicyano-5,6,7-triacetoxy-5,6,7,8-tetrahydroimidazo[2,1-*b*][1,3]oxazepine (**16**) and 2,3-dicyano-5,6-bis(benzoyloxy)-7-[(benzoyloxy)methyl]-5*H*-imidazo[2,1-*b*][1,3]oxazine (**15**), respectively. The acyclic DAMN adduct **18** also undergoes cyclization to imidazole **19** on treatment with NBS or *t*-BuOCl. The tosylate of **19** cyclizes to the pyrrolo[1,2-*a*]imidazoles **25** and **27** on heating in toluene. Compound **25** was converted to the aminoimidazolecarboxamide **31** by methanolysis to the monoimidate **29**; Hofmann rearrangement of **29** to the amino nitrile **30**; hydrolysis of **30** to **31**.

Diaminomaleonitrile (DAMN) has proven to be a versatile starting material in both the areas of organic synthesis and prebiotic synthesis.[1,2] In previous studies we reported that DAMN adducts of sugars are useful precursors for the synthesis of both C- and N-nucleosides.[3-5] The facile preparation of spiro and bicyclo nucleosides from ribose adducts of DAMN is reported herein. A preliminary report of some of our findings has appeared.[6]

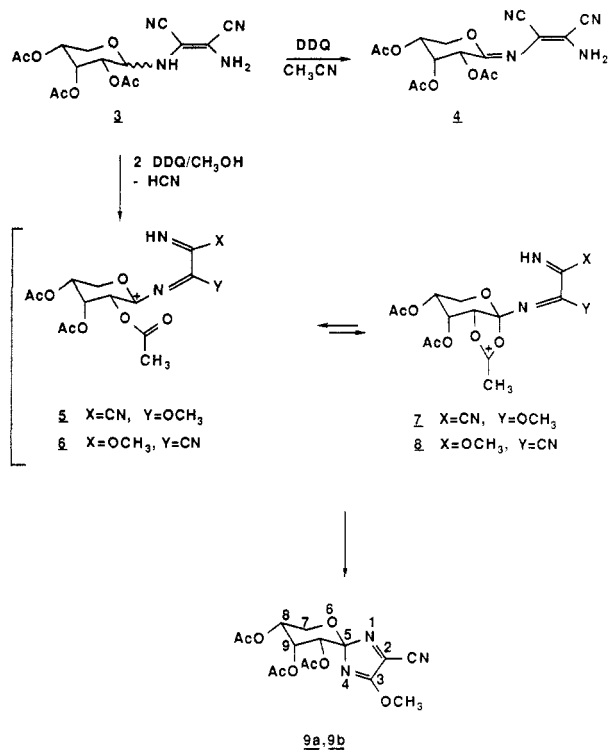
Results and Discussion

The oxidation of ribopyranosyldiaminomaleonitrile (**1**) with 1 equiv of 2,3-dichloro-5,6-dicyanobenzoquinone

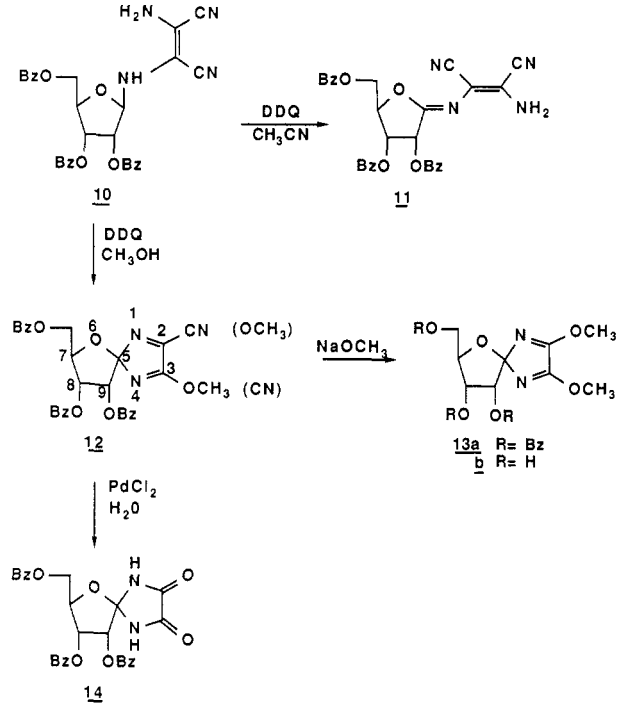
(1) Fukunaga, T.; Begland, R. W. *J. Org. Chem.* **1984**, *49*, 813–821, and previous papers in this series.
(2) Ferris, J. P.; Hagan, W. A., Jr. *Tetrahedron* **1984**, *40*, 1093–1120.
(3) Ferris, J. P.; Huang, H. C. *J. Chem. Soc., Chem. Commun.* **1978**, *1094*–1096.
(4) Ferris, J. P.; Badesha, S. S.; Ren, W. Y.; Huang, H. C.; Sorcek, R. J. *J. Chem. Soc., Chem. Commun.* **1981**, 110–112.
(5) Ferris, J. P.; Devadas, B.; Huang, H. C.; Ren, W. Y. *J. Org. Chem.* **1985**, *50*, 747–754.
(6) Ferris, J. P.; Devadas, B. *Tetrahedron Lett.* **1986**, *27*, 323–326.

0022-3263/87/1952-2355$01.50/0

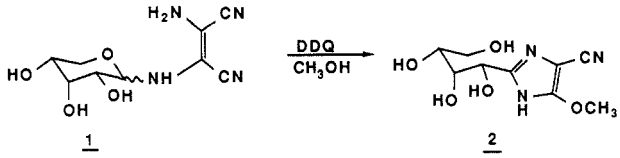
Scheme I



Scheme II



(DDQ) in CH_3OH to 4-cyano-5-methoxy-2-(D-*ribo*-tetrahydroxybutyl)imidazole (**2**) is a key step in the synthesis



of C-nucleoside analogues of bredinin.[4,7] Oxidation of the corresponding triacetyl derivative (**3**) (Scheme I) with DDQ in CH_3CN proceeds by a different pathway to yield the iminolactone ribopyranose **4**. The corresponding iminolactone **11** (Scheme II) was obtained by oxidation of the (tribenzoylribofuranosyl)diaminomaleonitrile adduct **10**. Compounds **4** and **11** exhibited UV maxima at 324 nm, identical with that observed for **18**,[5] and no signal was detected in the ^1H NMR spectrum for a proton at the 1′-position. A 1:1 mixture of isomeric forms of **4** was detected by TLC analysis and multiple acetyl methyl signals in the ^1H NMR spectrum. The exact nature of this isomerism was not determined although syn and anti isomers about the iminolactone nitrogen appear to be likely.

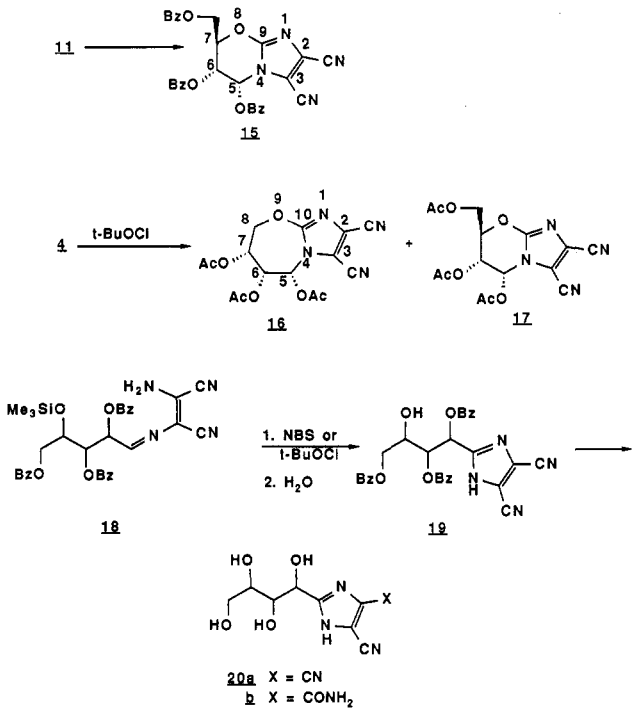
The oxidative cyclization of the Schiff base adducts of DAMN with aldehydes to imidazoles[8] and of alkoxyimino derivatives of DAMN to 2-alkoxyimidazoles[9] prompted investigation of the further oxidation of **4** and **11** by DDQ, but no reaction was observed. The successful oxidative cyclization of **1** in CH_3OH[4] prompted investigation of the oxidation of **3** with 2 equiv of DDQ in CH_3OH. The regioisomers **9a** and **9b** of the spironucleoside 2-cyano-3-methoxy-8,9,10-triacetoxy-1,4-diaza-6-oxaspiro[4.5]deca-1,3-diene were identified by UV absorption at 200 nm characteristic of the isoimidazole ring system[10] and NMR signals near δ 4.0 for the methoxyl groups. The absence of a nitrile stretching band in the isolated mixture of regioisomers of **9** is consistent with the report that 4,5-dicyanoisoimidazoles has weak nitrile absorption in the IR.[10] A 4:1 ratio of the regioisomers of **9** was obtained as determined from the ratio of the methoxyl peaks in the ^1H NMR spectrum.

The corresponding spironucleoside 2(3)-cyano-3(2)-methoxy-8,9-bis(benzoyloxy)-7-[(benzoyloxy)methyl]-1,4-diaza-6-oxaspiro[4.4]nona-1,3-diene (**12**) was obtained by the oxidation of ribofuranosyldiaminomaleonitrile **10** with 2 equiv of DDQ in CH_3OH. Here it was possible to isolate one regioisomer of **12** but the formation of a second regioisomer was suggested by the presence of two methoxyl peaks in the ^1H NMR spectrum of the material in the filtrate. It was not possible to unambiguously assign the location of the methoxyl and cyano groups in **12**. The nitrile group in **12** was displaced with 1 equiv of $NaOCH_3$ in CH_3OH to give the dimethoxy derivative **13a**, a reaction consistent with the presence of an isoimidazole substituted in the 4- or 5-position with a cyano group.[10] A second equivalent of $NaOCH_3$ catalyzed the methanolysis of the three benzoyl groups to yield the deblocked spironucleoside **13b**. The dioxo derivative **14** resulted in the attempted conversion of the nitrile group in **12** to the amide with $PdCl_2/H_2O$.[11] If coordination of Pd^{2+} with the cyano group did take place, it directed the attack of water to the isoimidazole ring and not the nitrile group. The displacement of the methoxyl group by water must proceed by an addition–elimination pathway on the isoimidazole ring system.

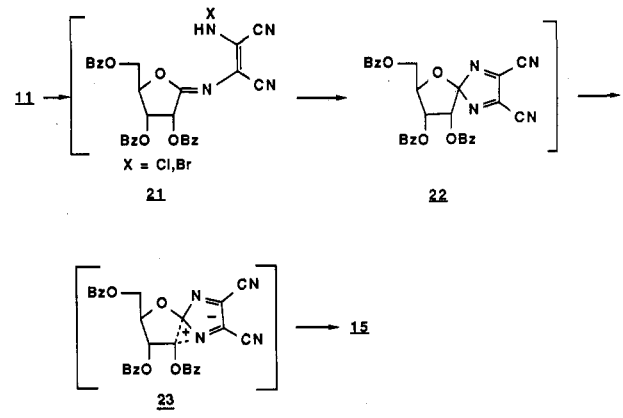
The success of the DDQ/CH_3OH oxidation hinges on the generation of a more easily oxidized intermediate as a consequence of the substitution of a cyano for a methoxyl grouping. It is not due to an increase in the oxidation potential of DDQ in going from CH_3CN to methanol because little difference was observed in the one-electron reduction potential of DDQ in CH_3CN vs. 75% ethanol.[12] The first step in the oxidation in hydroxylic or non-

(7) H. C. Huang, Ph.D. Thesis, Rensselaer Polytechnic Institute, 1977.
(8) Begland, R. W.; Hartter, D. R.; Jones, F. N.; Sam, D. J.; Sheppard, W. A.; Webster, O. W.; Weigert, F. J. *J. Org. Chem.* **1974**, *39*, 2341–2350.
(9) Weigert, F. J. U.S. Pat. 3778446, Dec. 11, 1973; *Chem. Abstr.* **1980**, *80*, 59941n.
(10) Begland, R. W.; Hartter, D. R. *J. Org. Chem.* **1972**, *37*, 4136–4145.
(11) Paraskewas, S. *Synthesis* **1974**, 574–575.
(12) Peover, M. E. *J. Chem. Soc.* **1962**, 4540–4549.

Scheme III



Scheme IV



Both NBS and *tert*-butyl hypochlorite effected the efficient conversion of the acyclic ribose derivative **18**[5] to the 2-substituted imidazole **19**. A UV maximum at 260 nm is consistent with the presence of the proposed 2-alkyldicyanoimidazole structure in **19**.[10] The benzoyl groups of **19** were cleaved with $NaOCH_3$ in CH_3OH to give **20a** while treatment of **20a** with aqueous alkali gave the cyano amide **20b**.

A mechanistic pathway for the halogenation–cyclization reaction (Scheme IV) was formulated on the basis of the known chlorination of DISN with Cl_2 or *tert*-butyl hypochlorite.[15,16] The elimination of the halogen[10] from **21** triggers cyclization to the isoimidazole **22**. Isoimidazole **22** undergoes a suprafacial 1,5-shift at room temperature to give **15**, a reaction that proceeds with retention of configuration at C-5. The low temperature (25 °C) at which the isoimidazole intermediate rearranges reflects the stabilization of the positive charge in the dipolar transition state **23** by the ion pair of electrons on the ester oxygen of the 5-benzoyloxy group. In the previous studies without oxygen substituents on the carbon next to the dicyanoisoimidazole ring, temperatures of 80–180 °C were required to effect rearrangement.[10,14] The importance of positive charge stabilization was demonstrated previously by the observation that the rate of isoimidazole rearrangement varied with the 2-substituents in the order $(CH_3)_2CH > CH_3CH_2 > CH_3$.[10] The pronounced charge stabilization by the benzoyloxy substituent in the dipolar transition state **23** is underscored by the observation that the reaction proceeds at 25 °C.

The absence of epimerization at C-5 is consistent with the proposed concerted nature of the rearrangement. The retention of configuration at C-5 is confirmed by $J_{5,6} = 3.8$ Hz for a H–C_5–C_6–H angle of 50° in **15**. In simpler systems it was observed that no *N*-isopropylimidazole was formed in the rearrangement of the 2-propylisoimidazole to the *N*-propylimidazole.[10]

The same mechanistic postulate outlined in Scheme IV accounts for the formation of the acyclic derivative **19** from **18** via a 1,5-shift of a proton in the corresponding isoimidazole intermediate or transition state.

Imidazole **19** proved to be a convenient starting material for the synthesis of pyrrolo[1,2-*a*]imidazole nucleoside derivatives (Scheme V). When **19** is heated with tosyl chloride and Dabco in toluene, two products are obtained (**25** and **27**) that differ in configuration at C-5. The ^1H NMR spectra of **25** and **27** are very similar with the one exception that $J_{5,6}$ in **27** is 1.8 Hz and 7.2 Hz in **25**.

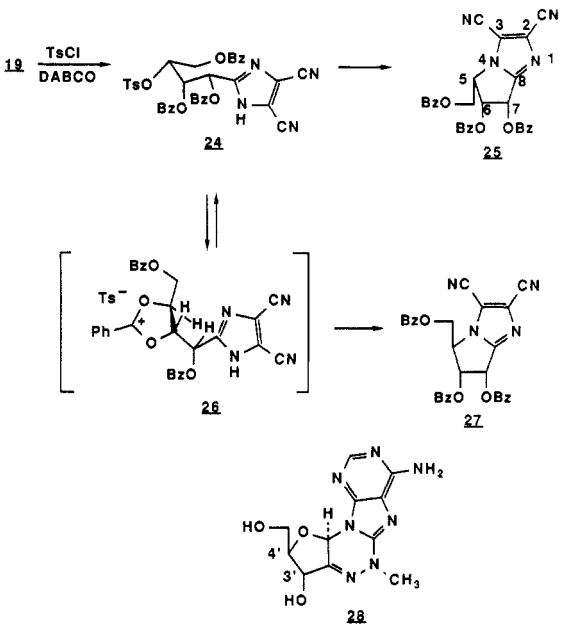
hydroxylic solvents is the abstraction of hydride[13] with the formation of the isomeric aminium cations. Abstraction of a proton from the aminium cations by $DDQH^-$ in weakly nucleophilic solvents yields the iminolactone **4** (Scheme I). Reaction of the aminium cations with methanol, elimination of HCN, and oxidation by a second equivalent of DDQ yields cations **5** and **6**. Cations **5** and **6**, which are stabilized by neighboring group formation of the acetoxonium derivatives **7** and **8**, cyclize to the two regioisomers of **9**.

It was possible to effect the oxidative cyclization of **11** with *N*-bromosuccinimide (NBS) (Scheme III); however, the bicyclic nucleoside, 2,3-dicyano-5,6-bis(benzoyloxy)-7-[(benzoyloxy)methyl]-5*H*-imidazo[2,1-*b*][1,3-oxazine (**15**), formed by the spontaneous rearrangement of the expected spironucleoside **22**, was the reaction product (Scheme IV).[10,14] The structure of **15** was established by a UV maximum at 266 nm, identical with that reported for 2-ethoxy-4,5-dicyanoimidazole.[9] In addition, the NMR signal for H-2′ is shifted from δ 6.37 in **11** to δ 7.4 in **15**, consistent with the migration of C-2′ from carbon to a more electronegative nitrogen atom in **15**.

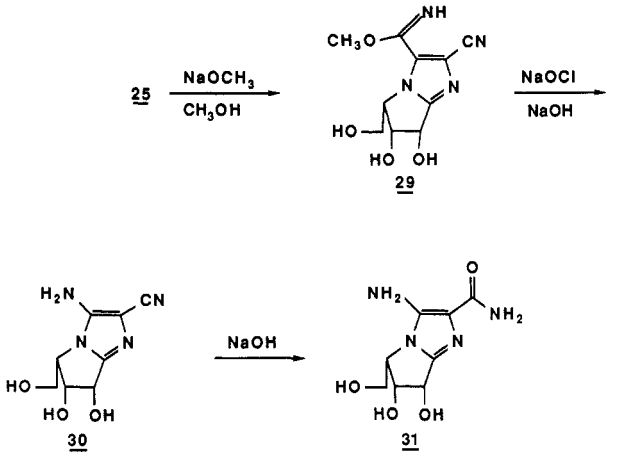
This halogenation–cyclization procedure was also successfully carried out starting with the ribopyranose **4** and the acyclic ribose adduct **18** (Scheme III). Ring expansion of **4** to the seven-membered bicyclic imidazole 2,3-dicyano-5,6,7-triacetoxy-5,6,7,8-tetrahydroimidazo[2,1-*b*][1,3]oxazepine (**16**) proceeded more efficiently with *tert*-butyl hypochlorite than with NBS. Low and variable yields of the isomeric oxazine derivative **17** were also obtained. It is believed that the formation of **17** is due to the presence of a small amount of the corresponding ribofuranosyldiaminomaleonitrile derivative in the starting material. Its presence reflects our inability to crystallize and hence completely separate (triacetylribofuranosyl)-diaminomaleonitrile from the (triacetylribopyranosyl)diaminomaleonitrile.[5]

(13) Walker, D.; Hiebert, J. D. *Chem. Rev.* **1967**, *67*, 153–195.
(14) Replogle, K. S.; Carpenter, B. K. *J. Am. Chem. Soc.* **1984**, *106*, 5751–5753.
(15) Webster, O. W.; Hartter, D. R.; Begland, R. W.; Sheppard, W. A.; Cairncross, A. *J. Org. Chem.* **1972**, *37*, 4133–4136.
(16) Kito, N.; Ohno, A. *J. Org. Chem.* **1974**, *39*, 3373–3375.

Scheme V



Scheme VI



The structure assignments of the isomeric cyclization products were based on a conformational analysis of **25** and **27** and their respective $J_{5,6}$ values of 7.2 and 1.8 Hz. The E_3 envelope conformation is assigned to **27** where C_6 is above the plane of the pyrroloimidazole ring system,[17] a conformation that relieves the nonbonded repulsions between the 5-(benzoyloxy)methyl and 3-cyano groupings. The H–C_6–C_5–H dihedral angle will be in the 90–120° range in this conformation consistent with the observed $J_{5,6}$ of 1.8 Hz while the H–C_6–C_7–H dihedral angle in the 0–30° range is consistent with $J_{6,7}$ of 6.0 Hz.[18] The ^3E conformation is assigned to **25** because models suggest that the relief of the interaction of the groups in the 3- and 5-positions is more important than the developing interaction between the pseudoaxial 5-(benzoyloxy)methyl and 7-benzoyloxy groups. The dihedral angles between H–C_5–C_6–H and H–C_6–C_7–H will be the same and in the 0–30° range.[19] The observed values of $J_{5,6}$ and $J_{6,7}$ are comparable (7.2 and 6.0 Hz, respectively) and consistent with dihedral angles of this magnitude.[18] The difference in these two coupling constants is probably due to a perturbation of $J_{5,6}$ by the electronegative nitrogen bound to C_5.[18,20]

The 8,2′-cyclonucleoside hydrazone **28**[21] is the closest example of a nucleoside that would be expected to have its sugar ring in an envelope conformation similar to that proposed for **27**. The $J_{3,4}$ value in **28** is reported to be ca. 2 Hz, a value comparable to $J_{5,6}$ of **27**.

The major reaction product **25** is formed by the direct displacement of the tosylate in **19** by the imidazole nitrogen (Scheme V). Compound **27**, with the opposite configuration at C_5, is formed by the initial displacement of the tosylate group by a neighboring benzoate (e.g. **26**) followed by a subsequent displacement of the benzoxonium ion in **26** by the imidazole nitrogen.

The conversion of **25** to the aminoimidazolecarboxamide analogue of 5-amino-1-β-D-ribofuranosylimidazole-4-carboxamide was accomplished by a procedure that was recently devised in this laboratory for another class of nucleosides (Scheme VI).[5] Hydrolysis of **25** with sodium methoxide resulted in the formation of imidate **29**. The structure of **29** was established by its ^1H NMR spectrum, which exhibited two peaks each for both the N–H and OCH_3 groupings as well as other protons in the structure characteristic of hindered rotation of the 3-imidate grouping.[5] The close proximity of the 3-imidate and the 5-hydroxymethyl grouping results in a pronounced downfield shift of the N–H signal in one of the rotomers. This shift is consistent with an imidate conformation where the N–H is on the same side of the ring as the 5-hydroxymethyl group and is H-bonding to it.[22] The selective formation of the 3-imidate may reflect initial attack of the 5-hydroxymethyl on the 3-cyano group to form a cyclic imidate, which is then solvolyzed with methanol to **29**.[5]

The Hofmann reaction of **29** gave the amino nitrile **30**, which was hydrolyzed to the amino amide **31** with sodium hydroxide. The ^1H NMR spectra of **30** and **31** did not exhibit duplicate peaks and were consistent with the assigned structures.

Conclusions

Compounds **9** and **12** represent, to the best of our knowledge, the first reported spironucleoside derivatives. The highly reactive cyanoisoimidazole system present in these structures presents the opportunity for the preparation of a variety of structural types as illustrated by the conversion of **12** to **13** and **14**.

The bicyclic derivatives **15** and **16** also represent an unusual class of nucleoside in which the heterocyclic and sugar rings are fused. The 8,2′-cyclonucleoside hydrazone of adenosine is the only other comparable derivative that has been reported.[21] Ring-fused derivatives are also present in the purine[23] and pyrimidine[24] cyclonucleosides; however, the structural integrity of the ribofuranose ring system is unchanged in these cyclonucleosides. The preparation of **15** and **16** also represents the first successful utilization of cyclic derivatives in this isoimidazole rearrangement. Previous attempts using cyclic ketones as the

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(18) Davies, D. B. In *Progress in Nuclear Magnetic Resonance Spectroscopy*; (Emsley, J. W., Feeney, J., Sutcliffe, L. H., Eds.; Pergamon Press: Oxford, 1978; Vol. 12, Part 3, pp 161–171.
(19) The dihedral angles and the coupling constants are the same for the ^3E and E_3-conformations of **25**.
(20) The same conformational analysis arguments were presented in the preliminary communication but the envelope conformers were designated incorrectly.
(21) Chattopadhyaya, J. B.; Reese, C. B. *J. Chem. Soc., Chem. Commun.* **1978**, 86–87.
(22) James, T. L. *Nuclear Magnetic Resonance in Biochemistry*; Academic Press: New York, 1975; pp 74–75.
(23) Ikehara, M. *Acc. Chem. Res.* **1969**, *2*, 47–53.
(24) Maruyama, S.; Sato, S.; Honjo, M. *Chem. Pharm. Bull. Jpn.* **1982**, *30*, 2688–2697.

starting materials were unsuccessful.[10]

The pyrrolo[1,2-*a*]imidazoles **25** and **27** are a third new class of nucleosides. A nitrogen of the imidazole ring system also serves as the heterocyclic atom of the azaribofuranose in these derivatives. The corresponding purine derivatives will be readily prepared from the functionalized imidazole rings in **30** and **31**.

Compounds **19** and **20** provide convenient starting points for the synthesis of acyclic analogues of substituted imidazole nucleosides which may have useful pharmaceutical activity.[25] For example, the acylic nucleoside of 4-aminoimidazole-5-carboxamide (**20**, X = NH_2) should be the product of the Hofmann reaction of **20b**.

In previous studies we reported the conversion of sugar adducts of DAMN to 5-amino-1-β-D-ribopyranosylimidazole-4-carboxamide[5] and C-nucleoside analogues of bredinin that contain the 5-hydroxyimidazole-4-carboxamide heterocyclic ring system.[4] This previous research coupled with the present report demonstrates that the utility of DAMN as a starting material for the preparation of novel nucleosides is equivalent to its versatility as a starting point for the formation of heterocyclic compounds in reactions that simulate chemical events on the primitive Earth.[2]

Experimental Section[26]

N^3-(2′,3′,4′-Tri-*O*-acetyl-D-ribopyranosylidene)diaminomaleonitrile (4). To a cooled solution of **3** (2 g, 5.5 mmol) in dry acetonitrile (25 mL), at 0–5 °C, was added DDQ (14 g, 6 mmol), and the solution was stirred under nitrogen for 3 h. The reaction mixture was filtered, the filtrate was concentrated, and the residue was triturated with chloroform and filtered to remove 2,3-dichloro-5,6-dicyanohydroquinone ($DDQH_2$). The filtrate was concentrated and chromatographed on 100 g of silica gel using 93:7 $CHCl_3$/acetone as the eluent. Compound **5** (0.9 g, 45%) was isolated as a pale yellow amorphous solid. Crystallization from chloroform/ether/hexane gave **4** as a pale yellow powder: mp 65–70 °C; UV λ_{max} (MeOH) 323 nm (ε 9975), 235 nm (ε 81); IR (Nujol) 3440, 3330, 2240, 2200, 1740, 1670, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2–2.2 (9, CH_3CO), 4.16–4.52 (m, 2, H-5′), 4.7 (br s, 2, NH_2), 5.3 (m, 1, H-4′), 5.6 (2d, 1, H-2′, $J_{2'3'}$ = 3.2 Hz), 5.74 (dd, 1, H-3′, $J_{2'3'}$ = 3.2 Hz, $J_{3'4'}$ = 6 Hz); mass spectrum, *m/e* (relative intensity) 364 (M^+, 56), 304 (M − 60, 66), 244 (41).

Anal. Calcd for $C_{14}H_{16}N_4O_7$: C, 49.45; H, 4.39. Found: C, 49.59; H, 4.23.

2(3)-Cyano-3(2)-methoxy-8,9,10-triacetoxy-1,4-diaza-6-oxaspiro[4.5]deca-1,3-diene (9). To a solution of **3** (0.9 g, 2 mmol) in CH_3OH (25 mL) cooled in an ice bath was added DDQ (1.2 g, 5.3 mmol), and the mixture was stirred under nitrogen for 2.5 h. The orange solution was concentrated to dryness, the residue was triturated with chloroform, and the $DDQH_2$ was filtered. The filtrate was concentrated to dryness and chromatographed on 50 g of silica gel. Elution with 19:1 $CHCl_3$/acetone gave **9** (0.6 g, 60%), which was purified further by silica gel flash chromatography using 97:3 $CHCl_3$/acetone. Fractions containing **9** were pooled and evaporated to dryness to give 0.3 g as an amorphous solid. Crystallization from chloroform/hexane gave **9** as a yellow powder: mp 110–112 °C; UV λ_{max} (MeOH) 200 nm; IR (Nujol) 1735, 1650, 1595, 1210, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.1, 4.12 (2s, 3, OMe), 4.34 (m, 2, H-7), 4.92, 5.1 (2d, 1, H-10, $J_{9,10}$ = 3.6 Hz), 5.4 (m, 1, H-8), 5.56, 5.64 (2dd, 1, H-9, $J_{8,9}$ = 3.6 Hz); mass spectrum, *m/e* 367 (M^+), 352 (M − OMe), 307 (M − 60).

Anal. Calcd for $C_{15}H_{17}N_3O_8$: C, 49.05; H, 4.63; N, 11.44. Found: C, 49.07; H, 4.87; N, 10.83.

***N*-(2′,3′,5′-Tri-*O*-benzoyl-D-ribofuranosylidene)diaminomaleonitrile (11).** To an ice-cooled solution of *N*-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)diaminomaleonitrile (**10**) (0.16 g, 0.29 mmol) in dry acetonitrile (5 mL) was added DDQ (0.14 g, 0.6 mmol), and the mixture was stirred under N_2 for 2 h. The reaction mixture was concentrated to dryness, triturated with chloroform, and cooled and the $DDQH_2$ was filtered. The filtrate was concentrated to dryness and **11** was isolated by preparative silica gel TLC using 9:1 chloroform/acetone as the eluent. The UV absorbing band was eluted and evaporated to give **11** (80 mg, 50%) as a pale yellow powder. Crystallization from carbon tetrachloride afforded an analytically pure sample: mp 84–85 °C; UV λ_{max} (MeOH) 230 nm (ε 39 940); 324 nm (ε 15 700); IR (Nujol) 3420, 3310, 2220, 2200, 1720, 1600, 1260, 1100, 700 cm^{-1}; NMR ($CDCl_3$) δ 4.72 (dd, 1, H-5′a, $J_{5'a,5'b}$ = 13.2 Hz, $J_{4',5'a}$ = 3.6 Hz), 4.82 (dd, 1, H-5′b, $J_{4',5'b}$ = 3.6 Hz), 4.75 (s, 2, NH_2), 5.25 (m, 1, H-4′), 5.9 (dd, 1, $J_{2',3'}$ = 6 Hz, $J_{3',4'}$ = 1.8 Hz, H-3′), 6.37 (d, 1, H-2′, $J_{2',3'}$ = 6 Hz), 7.3–8.1 (m, 15, Ar).

Anal. Calcd for $C_{30}H_{22}N_4O_7$: C, 65.45; H, 4.00; N, 10.18. Found: C, 65.51; H, 4.26; N, 10.39.

2(3)-Cyano-3(2)-methoxy-7-[(benzoyloxy)methyl]-8,9-bis(benzoyloxy)-1,4-diaza-6-oxaspiro[4.4]nona-1,3-diene (12). To a suspension of *N*-(2′,3′,5′-tri-*O*-benzoyl-β-D-ribofuranosyl)diaminomaleonitrile (**10**) (0.1 g, 0.18 mmol) in dry MeOH (3.5 mL) cooled to 0–5 °C was added DDQ (0.09 g, 0.4 mmol). The mixture was stirred under N_2 for 1 h at 0–5 °C and for 1 h at 25 °C. The mixture was concentrated to dryness, the residue was triturated with acetonitrile, and the $DDQH_2$ was filtered. The filtrate was concentrated to dryness and purified by preparative silica gel TLC using chloroform/acetone (19:1) as the eluent. The major UV absorbing band was eluted, concentrated, and crystallized from ethanol to give **12** (0.05 g, 45%) as a white powder: mp 135–137 °C; UV λ_{max} (MeOH) 229 nm (ε 40 900); IR (Nujol) 1740, 1720, 1655, 1600, 1270, 1100, 700 cm^{-1}; ^1H NMR [$(CD_3)_2SO$] δ 4.0 (s, 3, OCH_3), 4.74 (m, 2, 7-CH_2), 5.18 (m, 1, H-7), 5.92 (d, 1, H-9, $J_{8,9}$ = 6 Hz), 6.04 (dd, 1, H-8, $J_{7,8}$ = 6 Hz), 7.4–8.2 (m, 15, Ar); mass spectrum, *m/e* 553 (M^+), 486.

Anal. Calcd for $C_{30}H_{23}N_3O_8$: C, 65.09; H, 4.16; N, 7.59. Found: C, 64.97; H, 4.31; N, 7.43.

2,3-Dimethoxy-7-[(benzoyloxy)methyl]-8,9-bis(benzoyloxy)-1,4-diaza-6-oxaspiro[4.4]nona-1,3-diene (13a). A solution of **12** (0.55 g, 1 mmol) in dry MeOH (5 mL) was treated with sodium methoxide (50 mg, 0.92 mmol) and stirred under anhydrous conditions for 2 h. The solution was cooled, the precipitate that formed was filtered, and the residue was washed with cold methanol and dried to give 0.23 g of **13a**. An additional 65 mg of **13a** was obtained from the filtrate as a white powder. Crystallization from MeOH gave **13a** as white needles: mp 101 °C; UV λ_{max} (MeOH) 229 nm (ε 40 900); IR (Nujol) 1720, 1650, 1630, 1270, 1100, 700 cm^{-1}; NMR ($CDCl_3$) δ 4.04 (2s, 6, 2 × OCH_3), 4.6–5.0 (m, 2, 7-CH_2), 5.19 (m, 1, H-7), 5.8 (d, H-9, $J_{8,9}$ = 5.4 Hz), 6.16 (dd, 1, H-8, $J_{7,8}$ = 6.6 Hz), 7.4–8.2 (m, 15, Ar); mass spectrum, *m/e* 558 (M^+), 543 (M − CH_3).

Anal. Calcd for $C_{30}H_{26}N_2O_9$: C, 64.51; H, 4.66; N, 5.01. Found: C, 64.53; H, 4.82; N, 4.93.

2,3-Dimethoxy-7-(hydroxymethyl)-8,9-dihydroxy-1,4-diaza-6-oxaspiro[4.4]nona-1,3-diene (13b). To a suspension of **13a** (0.2 g, 0.36 mmol) in dry MeOH (3 mL) was added sodium methoxide (20 mg, 0.37 mmol), and the mixture was stirred at room temperature under anhydrous conditions. After 2.5 h the reaction mixture was carefully neutralized with Dowex-50W-X8 (H^+), filtered, and concentrated to dryness under reduced pressure. The residue was subjected to preparative silica gel TLC using 89:11 $CHCl_3$/methanol. The UV absorbing band was eluted and evaporated to dryness under reduced pressure to give 50 mg (57%) of **13b** as an amorphous solid. Attempts to crystallize **13b** were unsuccessful: UV λ_{max} (MeOH), end absorption; IR (Nujol) 3500–3100 (br) 1640, 1270, 1050, 970 cm^{-1}; NMR [$(CD_3)_2SO$] δ 3.6 (m, 2, 7-CH_2), 3.9 (br s, 8, 2 × OCH_3, H-9 and H-7), 4.04 (m, 1, H-8), 4.68 (t, 1, 7-CH_2OH), 5.06 (d, 1, 9-OH), 5.44 (br s, 1, 8-OH); mass spectrum, *m/e* 246 (M^+), 231 (M − CH_3). Compound **13b** was extremely hygroscopic so that it was not possible to obtain meaningful combustion analysis.

2,3-Dioxo-7-(hydroxymethyl)-8,9-dihydroxy-1,4-diaza-6-oxaspiro[4.4]nona-1,3-diene (14). To a solution of isoimidazole **12** (55 mg, 0.1 mmol) in dioxane (2 mL) was added $PdCl_2$ (18 mg, 0.1 mmol), and the mixture was heated to reflux under a nitrogen atmosphere for 3 h. Water (0.01 mL) was added and heating was continued for another 6 h and the mixture was left overnight at room temperature. The yellow reaction mixture was filtered and

(25) Dolin, R. *Science (Washington, D.C.)* **1985**, 227, 1296–1303, and references therein.

(26) General experimental procedures are given in ref 5. NMR assignments were made on the basis of proton-decoupling measurements.

the filtrate was concentrated to dryness under vacuum. Purification of the residue by preparative silica gel TLC using 4:1 chloroform/acetone yielded **14** (25 mg, 47%), which was crystallized from ethanol: mp 219–220 °C dec; UV λ_{max} (MeOH) 229 nm (ϵ 49 590); IR (Nujol) 3200–3000 (br), 1770, 1740, 1720, 1600, 1270, 1080, 1070, 720 cm^{-1}; NMR ([$(CD_3)_2SO$] η 4.64 (m, 2, 7-CH_2), 4.8 (m, 1, H-7), 5.74 (d, 1, H-9, $J_{8,9}$ = 5.6 Hz), 5.84 (dd, 1, H-8, $J_{8,9}$ = 5.6 Hz), 7.4–8.1 (m, 15, Ar), 10.73 (br s, 2, 2 × NH).

Anal. Calcd for $C_{28}H_{22}N_2O_9$: C, 63.39; H, 4.15; N, 5.28. Found: C, 63.13; H, 4.23, N, 5.22.

2,3-Dicyano-5,6-bis(benzoyloxy)-7-[(benzoyloxy)methyl]-5*H*-imidazo[2,1-*b*][1,3]oxazine (15). *N*-Bromosuccinimide (0.52 g, 2.9 mmol) was added to an ice cooled solution of **11** (1.45 g, 2.6 mmol) in dry ethyl acetate (50 mL). The mixture was stirred under nitrogen at 0–5 °C for 1 h and at 25 °C for 30 min. The solution was concentrated to dryness and product (**15**) was isolated by silica gel flash chromatography using 19:1 chloroform/acetone as the eluent. Fractions containing **15** were pooled and concentrated to dryness to give 1.0 g of **15** as pale yellow amorphous solid. The product was further purified by crystallization from absolute ethanol to give 0.8 g (55%) of **15**: mp 100–102 °C; UV λ_{max} (MeOH) 230 nm (ϵ 43 840); 266 nm (ϵ 26 030); ^1H NMR ($CDCl_3$) δ 4.7, 4.9 (AB q, 2, 7-CH_2, $J_{a,b}$ = 13.2 Hz, $J_{a,7}$ = 3.6 Hz, $J_{b,7}$ = 2.4 Hz), 5.34 (m, 1, H-7), 6.00 (dd, 1, H-6, $J_{5,6}$ = 3.8 Hz, $J_{6,7}$ = 10.2 Hz), 7.4 (d, 1, H-5, 7.3–8 (m, 15, Ar); ^{13}C NMR 165.02, 163.85, 163.71, 150.69 (C-9), 119.78, 111.92, 107.81, 107.78, 74.19 (C-5), 72.36 (C-6), 62.59 (C-7), 61.26 (7-CH_2); mass spectrum, *m/e* 548 (M^+).

Anal. Calcd for $C_{30}H_{20}N_4O_7$: C, 65.69; H, 3.65; N, 10.22. Found: C, 65.50; H, 3.77; N, 10.03.

2,3-Dicyano-5,6,7-triacetoxy-5,6,7,8-tetrahydroimidazo[2,1-*b*][1,3]oxazepine (16). *tert*-Butyl hypochlorite (0.8 mL, 7 mmol) was added dropwise to a solution of **4** (2 g, 5.0 mmol) in ethyl acetate (50 mL) at 0–5 °C. The solution was stirred under nitrogen for 1.5 h and concentrated to dryness under reduced pressure. The residue was chromatographed on 100 g of silica gel by elution with 9:1 $CHCl_3$/acetone. The fractions collected, which contained a UV absorbing component, were concentrated to give 0.5 g of an amorphous solid, which on crystallization from ethanol gave **17** (40 mg) as needles: mp 175 °C; UV λ_{max} (MeOH) 264 nm; IR (Nujol) 2220, 1765, 1740, 1570, 1210, 1020, 720 cm^{-1}; ^1H NMR δ 2.01, 2.03, 2.16 (3s, 9, 3 × CH_3COO), 4.45 (d, 2, 7-CH_2), $J_{7,7\text{-}CH_2}$ = 3.6 Hz), 5.12 (m, 1, H-7, $J_{6,7}$ = 9 Hz), 5.64 (dd, 1, H-6, $J_{5,6}$ = 3.6 Hz), 6.92 (d, 1, H-5); ^{13}C NMR 170.19, 169.08, 150.67 (C-9), 119.98, 112.32, 108.27, 108.07, 74.86 (C-7), 72.12 (C-5), 62.00 (C-6), 60.93 (C-8); mass spectrum, *m/e* (relative intensity) 362 (M^+, 100), 303 (22), 187 (14).

Anal. Calcd for $C_{15}H_{14}N_4O_7$: C, 49.72; H, 3.86; N, 15.47. Found: C, 49.63; H, 3.89; N, 15.42.

The TLC of the mother liquor from **17** indicated the presence of **16** and **17**, which were separated by preparative silica gel TLC using 88:12 $CHCl_3$/acetone. Crystallization from ethanol gave **16** (0.1 g): mp 147 °C; UV λ_{max} (MeOH) 256 nm (ϵ 9371); IR (Nujol) 2235, 1755, 1730, 1550, 1230, 1060, 980, 810 nm^{-1}; ^1H NMR δ 2.0 (s, 3, CH_3CO), 2.12 (s, 6, CH_3CO), 4.64 (m, 2, H-8, $J_{8a,8b}$ = 13.8 Hz, $J_{8a,7}$ = 3.6 Hz, $J_{8b,7}$ = 1 Hz), 5.56 (m, 1, H-7) 5.64 (dd, 1, H-6, $J_{6,7}$ = 3.0 Hz), 6.8 (d, 1, H-5, $J_{5,6}$ = 1.8 Hz); ^{13}C NMR 170.02, 169.56, 169.48, 154.69 (C-10), 118.61, 112.32, 111.71, 108.34, 76.62 (C-5), 73.24 (C-8), 69.46 (C-7), 68.77 (C-6); mass spectrum, *m/e* (relative intensity) 362 (M^+, 100), 303 (44), 187 (73).

Anal. Calcd for $C_{15}H_{14}N_4O_7$: C, 49.72; H, 3.86; N, 15.47. Found: C, 49.68; H, 3.95; N, 15.43.

4,5-Dicyano-2-(D-*ribo*-1′,2′,4′-tri-*O*-benzoyl-3-hydroxybutyl)imidazole (19). Method A. To a solution of **18** (5 g, 8 mmol) in ethyl acetate (125 mL) cooled to 0–5 °C was added *N*-bromosuccinimide (1.6 g, 9 mmol), and the mixture was stirred under nitrogen for 1 h. The reactants were stirred for another 1 h at 25 °C, 25 mL of H_2O was added, and the organic layer was washed with water until the washings were neutral. The organic layer was dried and concentrated to dryness, and the residue was purified by silica gel flash chromatography using 9:1 $CHCl_3$/acetone as the eluant. Fractions containing **19** were combined and evaporated to give an amorphous product (2.66 g, 66%). Crystallization from chloroform/ether/hexane gave **19** as a white powder: mp 92–95 °C; UV λ_{max} (MeOH), 230 nm (ϵ 41 720), 260 nm (ϵ 11 140); IR (Nujol) 3500–3100 (br), 2240, 1720, 1600, 1250, 1100, 710 cm^{-1}; ^1H NMR [$(CD_3)_2SO$] 4.2–4.4 (m, 3, H-3′, H-4′), 5.72 (dd, 1, H-2′, $J_{1',2'}$ = 3.6 Hz, $J_{2',3'}$ = 6.6 Hz), 5.92 (d, 1, 3′-OH, J = 4.8 Hz), 6.44 (d, 1, H-1′), 7.4–8 (m, 15, Ar); mass spectrum (FAB), *m/e* 531 (MH^+), 533 ($MH^+ - H_2O$).

Anal. Calcd for $C_{30}H_{22}N_4O_7 \cdot H_2O$: C, 63.38; H, 4.22; N, 9.85. Found: C, 63.39; H, 4.36; N, 9.89.

Method B. To a solution of **18** (4.6 g, 7.36 mmol) in dry ethyl acetate (75 mL) cooled to 0–5 °C was added *tert*-butyl hypochlorite dropwise (1 mL, 8.85 mmol), and the mixture was stirred under nitrogen for 1.5 h. The reaction mixture was diluted with water (20 mL) and the organic layer was washed with water, dried, and concentrated to dryness. The residue was purified by silica gel column chromatography using 85:15 $CHCl_3/CH_3OH$ as the eluent. The fractions containing **19** were combined and evaporated under reduced pressure to give **19** (2.7 g, 66%) as a pale yellow amorphous material.

4,5-Dicyano-2-(D-*ribo*-1′,2′,3′,4′-tetrahydroxybutyl)imidazole (20a). A solution of **19** (1.3 g, 2.36 mmol) in methanol (11 mL) was cooled to 0–5 °C and a solution of sodium methoxide (from 60 mg of sodium in 5 mL of methanol) was added dropwise. The solution was stirred at 0–5 °C for 30 min and at 25 °C for 2 h. The sodium methoxide was neutralized with Dowex 50W-X8 (H^+) and filtered. The filtrate was concentrated to dryness, triturated with dry ether, and filtered. The brown residue was washed with ether, followed by methylene chloride, and finally crystallized from ethanol to give **20a** (0.35 g, 62.5%) as a crystalline solid: mp 192–193 °C dec; UV λ_{max} (MeOH) 257 nm (ϵ 9279); IR (Nujol) 3500–3100 (br), 2240, 1560, 1520, 1285, 1090, 1020, 880 cm^{-1}; NMR [$(CD_3)_2SO$] δ 3.2–3.8 (m, 8, H-2′, H-3′, H-4′, 2′-OH, 1′-OH, 3′-OH, 4′-OH), 4.92 (d, 1, H-1′, $J_{1',2'}$ = 4 Hz); mass spectrum, *m/e* 238 (M^+), 220 ($M - H_2O$).

Anal. Calcd for $C_9H_{10}N_4O_4$: C, 45.37; H, 4.20; N, 23.53. Found: C, 45.29; H, 4.27; N, 23.43.

4-Cyano-2-(D-*ribo*-1′,2′,3′,4′-tetrahydroxybutyl)imidazole-5-carboxamide (20b). A solution of **20a** (0.4 g, 4.2 mmol) in 4 mL of 1 N NaOH was heated to 55 °C for 4 h under nitrogen. The reaction mixture was cooled, neutralized with 1 N HCl, and freeze-dried. The solid was extracted several times with dry CH_3OH, the extract was concentrated under reduced pressure, and the residue was purified by preparative TLC using EtOAc/MeOH (1:1) as the eluent. The major product (0.2 g, 46%) was crystallized from MeOH to afford an analytical sample of **20b**: mp 206–208 °C dec; UV λ_{max} (MeOH) 254 nm; IR (Nujol) 3480, 3380, 2240, 1660, 1580, 1110, 1060, 1000, 830 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 3.5 (m, 3, H-4′ and H-3′), 3.7 (m, 1, H-2′), 4.38 (t, 1, 4′-OH), 4.63 (br s, 1, 3′-OH), 4.88 (m, 1, 2′-OH, H-1′, $J_{1',2'}$ = 4.2 Hz), 5.92 (br s, 1, 1′-OH), 7.8 (br s, 2, NH_2); mass spectrum, *m/e* 256 (M^+), 238 ($M - H_2O$), 196.

Anal. Calcd for $C_9H_{12}N_4O_5$: C, 42.18; H, 4.68; N, 21.87. Found: C, 41.90; H, 4.78; N, 21.72.

2,3-Dicyano-5-[(benzoyloxy)methyl]-6,7-bis(benzoyloxy)-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]imidazoles 25 and 27. To a solution of **19** (4.4 g, 8 mmol) in 70 mL of dry toluene was added *p*-toluenesulfonyl chloride (3.8 g, 20 mmol) and 1,4-diazabicyclo[2.2.2]octane (1.34 g, 12 mmol), and the mixture was heated to reflux for 10 h under nitrogen. During this period the solution darkened. The TLC (chloroform/methanol, 9:1) of the reaction mixture showed only traces of unreacted starting material. The reaction mixture was filtered and the filtrate was concentrated to dryness under reduced pressure. The dark, gummy product was purified by column chromatography on 200 g of silica gel. Compounds **25** (2 g, 47%) and **27** (1 g, 23.5%) were eluted with chloroform/acetone (49:1) and each was crystallized from ethanol. Compound **25**: mp 82–85 °C; UV λ_{max} (MeOH) 230 nm (ϵ 47 040); IR (Nujol) 2240, 1720, 1595, 1250, 1100, 700 cm^{-1}; NMR ($CDCl_3$) δ 4.8 (dd, 1, 5-CH_{2a}, $J_{A,B}$ = 12 Hz, $J_{A,5}$ = 8.4 Hz), 4.95 (dd, 1, 5-CH_{2b}, $J_{b,5}$ = 4.2 Hz), 5.44 (sextet, 1, H-5, $J_{5,6}$ = 7.2 Hz) 6.36 (dd, 1, H-6, $J_{6,7}$ = 6.0 Hz), 6.7 (d, 1, H-7), 7.3–8.2 (Ar, 15); ^{13}C NMR (Me_2SO-d_6) δ 165.33, 164.14, 164.02, 152.89 (C-8), 112.05, 109.78, 108.46, 108.37, 72.74 (C-6), 65.10 (C-7), 61.72 (5-CH_2), 59.40 (C-5); mass spectrum, *m/e* 532 (M^+), 410.

Anal. Calcd for $C_{30}H_{20}N_4O_6$: C, 67.67; H, 3.76; N, 10.53. Found: C, 67.59; H, 3.93; N, 10.47.

Compound **27**: mp 88–91 °C; UV λ_{max} (MeOH) 230 nm (ϵ 46 941); IR (Nujol) 2240, 1720, 1600, 1250, 1100, 700 cm^{-1}; NMR ($CDCl_3$) δ 4.92 (dd, 1, 5-CH_{2a}, $J_{a,b}$ = 13.2 Hz, $J_{a,5}$ = 3.6 Hz), 5.10

(dd, 1, 5-CH_{2b}, $J_{b,6}$ = 2.4 Hz), 5.14 (br s, 1, H-5), 6.3 (dd, 1, H-6, $J_{6,7}$ = 6.0 Hz, $J_{5,6}$ = 1.8 Hz), 6.5 (d, 1, H-7), 7.3–8.0 (Ar, 15); ^{13}C NMR (Me_2SO-d_6) 165.29; 164.42, 164.16, 153.38 (C-8), 111.97, 109.77, 108.28, 75.41 (C-6), 65.90 (C-7), 62.90 (C-5), 62.58 (5-CH_2) (C-4′); mass spectrum, *m/e* 532 (M^+), 505, 410.

Anal. Calcd for $C_{30}H_{20}N_4O_6$: C, 67.67; H, 3.76; N, 10.53. Found: C, 67.52; H, 3.76; N, 10.44.

Methyl 2-Cyano-5-(hydroxymethyl)-6,7-dihydroxy-5*H*-pyrrolo[1,2-*a*]imidazole-3-carboximidate (29). To a solution of **25** (1 g, 1.8 mmol) in 12 mL of anhydrous MeOH was added NaOH (0.12 g, 2 mmol), and the mixture was stirred at 25 °C for 2 h under nitrogen. The solution was neutralized with Dowex 50 resin (H^+) and filtered, and the filtrate was concentrated under reduced pressure. The gummy residue obtained was triturated with dry ether, filtered, and dried to give 0.47 g of product that was homogenous on TLC ($CHCl_3$/MeOH, 4:1). Crystallization from MeOH gave **29** (0.3 g, 64%) as a white powder: mp 182–85 °C dec; UV λ_{max} 252 nm (ϵ 11 696); IR (Nujol) 3440, 3180, 2230, 1660, 1510, 1140, 770 cm^{-1}; ^1H NMR δ 3.73, 3.77 (2s, 3, OCH_3), 3.6–4.0 (m, 2, 5-CH_2), 4.5–4.84 (m, 3, H-5, H-6, H-7), 5.1–5.6 (m, 2, OH), 5.6–5.9 (2d, 1, OH), 8.8, 9.34 (2s, 1, NH); mass spectrum, *m/e* 252 (M^+).

Anal. Calcd for $C_{10}H_{12}N_4O_4$: C, 47.62; H, 4.76; N, 22.22. Found: C, 47.60; H, 4.85; N, 22.20.

2-Cyano-3-amino-5-(hydroxymethyl)-6,7-dihydroxy-5*H*-pyrrolo[1,2-*a*]imidazole (30). A solution of **29** (0.25 g, 1 mmol) in 2 mL of 5.25% sodium hypochlorite and 1 mL of 1.5 N NaOH was heated to 80 °C for 1 h under nitrogen. The dark brown reaction mixture was cooled and carefully neutralized with 0.5 N HCl. The solution was freeze-dried, and the residue was extracted several times with dry MeOH and filtered. The extract was concentrated, the salt was filtered, and the filtrate was purified by preparative TLC using ethyl acetate/MeOH (3:1). Further purification by crystallization from MeOH furnished **30** as a yellow powder: mp 160 °C dec; UV λ_{max} (H_2O) 249 nm; IR (Nujol) 3460, 3300, 3180, 2220, 1640, 1580, 1140, 1000, 920 cm^{-1}; ^1H NMR δ 3.56 (m, 1, 5-CH_{2a}), 3.74 (m, 1, 5-CH_{2b}), 4.16 (m, 1, H-5), 4.3–4.6 (m, 2, H-7, H-6), 5.36 (d, 1, J = 6 Hz, OH), 5.44 (d, 2, OH), 6.14 (s, 2, NH_2); mass spectrum, *m/e* 210 (M^+), 192 (M – H_2O), 136.

Anal. Calcd for $C_8H_{10}N_4O_3 \cdot 0.3H_2O$: C, 44.57; H, 4.92; N, 25.99. Found: C, 44.82; H, 4.93; N, 25.80.

3-Amino-5-(hydroxymethyl)-6,7-dihydroxy-5*H*-pyrrolo[1,2-*a*]imidazole-2-carboxamide (31). To a suspension of **30** (60 mg, 0.28 mmol) in 0.3 mL of water was added 0.6 mL of 1.5 N NaOH, and the mixture was heated to 100 °C under N_2 for 1 h. The solution was neutralized with 1 N HCl and freeze-dried. The material thus obtained was extracted with dry MeOH and filtered. The filtrate was concentrated and purified twice by preparative TLC using EtOAc/MeOH (7:3). The product was finally purified by crystallization from MeOH/EtOAc to give 30 mg (50%) of **31** is an amorphous solid: UV λ_{max} (H_2O) 271 nm, 240 nm (sh), pH 2, 274 nm, 242 nm; IR (Nujol) 3420, 3300, 1630, 1570, 1510, 1120, 1000 cm^{-1}; ^1H NMR δ 3.56 (m, 1, 5-CH_{2a}, $J_{a,b}$ = 11.25 Hz, $J_{a,5}$ = 6.3 Hz), 3.8 (m, 1, 5-CH_{2b}, $J_{b,5}$ = 2.7 Hz), 4.22 (m, 1, H-5), 4.46 (m, 2, H-7, H-6, $J_{6,7}$ = 5.4 Hz), 5.3 (d, 1, J = 6.3 Hz, OH), 5.5 (m, 1, 2 OH), 5.68 (s, 2, NH_2), 6.6 (br, 2, NH_2); mass spectrum, *m/e* 228 (M^+), 210 (M – H_2O). The picrate salt of **31** was prepared by adding 15 mg of picric acid to a solution of 10 mg of **31** in methanol. Yellow crystals of product were filtered, washed with MeOH, and recrystallized from MeOH; mp 131 °C dec.

Anal. Calcd for $C_{14}H_{15}N_7O_{11} \cdot H_2O$: C, 35.37; H, 3.58; N, 20.63. Found: C, 35.65; H, 3.50; N, 20.62.

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The Synthesis and Configurational Stability of Differentially Protected β-Hydroxy-α-amino Aldehydes

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Syntheses of 1,1-dimethylethyl (*S*)-4-formyl-2,2-dimethyl-3-oxazolidinecarboxylate (**5**) and 1,1-dimethylethyl (4*S-trans*)-4-formyl-2,2,5-trimethyl-3-oxazolidinecarboxylate (**6**) from commercially available serine and threonine derivatives are described. The method involves selective reduction of the corresponding oxazolidine esters **3** and **4** using diisobutylaluminum hydride at low temperature. These differentially protected β-hydroxy-α-amino aldehydes are also shown to be produced in 93–95% enantiomeric excess (via NMR and HPLC analysis of the Mosher ester derivatives **8** and *epi*-**8**)—thus making them useful as chiral, nonracemic synthons for asymmetric synthesis.

Naturally occurring aminoacids constitute an attractive source of chiral, nonracemic starting materials for asymmetric synthesis.[1] This is due in part to the commerical availability of these substances which in many cases includes the unnatural antipode as well. It was in this context that we began to examine the differentially protected β-hydroxy-α-amino aldehydes **5** and **6**, which are derived from L-serine and L-threonine, respectively, as precursors to synthetic amino acids and amino sugars.[2] At the outset of this work, we were aware of three other serine-derived aldehydes analogous to **5** but felt that they would not be suitable for our purposes.[3] This judgement was based on consideration of the following four requirements which we had set: (1) large-scale availability, (2) configurational (and chemical) stability, (3) ability to exert stereocontrol during addition reactions, and (4) ease of subsequent deprotection and manipulation. Herein we describe in detail the synthesis of the oxazolidine aldehydes **5** and **6** as well as an assay of their configurational integrity. Compound **5** has already been shown by us to participate

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