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Chemoselective Multicomponent One-Pot Assembly of Purine Precursors in Water [*Journal of the American Chemical Society* **2010**, *132*, 16677–16688 DOI: 10.1021/ja108197s]. Matthew W. Powner* John D. Sutherland and Jack W. Szostak

In the course of continued studies of the annulation isomers 6-*exo-trig* **28** and 5-*exo-trig* **32**, the crystal structures of both compounds have now been solved (Schemes 6 and 7). These structures establish the correct stereochemistry of these compounds as *ribo* [2′*R*,3′*R*,4′*S*], not *lyxo* [2′*R*,3′*R*,4′*R*] as previously proposed. This corrected assignment explains the puzzling failure to observe the pyranosyl isomer **40**, as the pyranosyl form was only expected to be favored for the sterically crowded *lyxo* [2′*R*,3′*R*,4′*R*] isomer (Scheme 7). However, the corrected stereochemical assignment leads to a new surprise, which is that equal but opposite diastereoselectivity is observed upon the reaction of the 5-aminoimidazole-4-carboxamide (AICA) and 5-aminoimidazole-4-carbonitrile (AICN) glyceraldehyde imines with 2-aminooxazole **5**, resulting in *lyxo* [2′*R*,3′*R*,4′*R*] selectivity (60%) and *ribo* [2′*R*,3′*R*,4′*S*] selectivity (66%), respectively (Scheme 6). This reversal of imine/iminium facial selectivity may result from amide hydrogen bonding, which is possible for the AICA but not the AICN derivatives. We apologize for any confusion the incorrect 4′-stereochemical assignment of **28**/**32** may have caused. Corrected versions of Schemes S1 and CIF files for **28** and **32** are available as Supporting Information.

EQUILIBRATION OF PURIFIED 32

32 (20 mg) was dissolved in D_2O, and over the course of 2 d it was found to equilibrate to a 4:1 mixture of **32**:**28**. The pD of the sample was measured (pD 6.0) and adjusted with DCl (0.01 mM) to pD 2.0, and over 1 d the sample was observed to re-equilibrate to give a mixture of 10:1 **32**:**28**. Further samples of **32** (20 mg) were dissolved in D_2O at pD 1.0, 4.0, 6.0, 7.0, 8.0, 9.0, and 12.0, and were observed to equilibrate to give mixtures of 50:1, 1:4, 1:4, 1.25:1, 1:1, 3:1, and 5:1 **32**/**28**, respectively, after a period of 3 d. The sample at pD 2.0 was observed to give a ratio of 20:1 after 3 d (Scheme 7).

At low pD (pD < 4), protonation may suppress the nucleophilicity and basicity of the imidazole moiety and increase its leaving group potential, thus kinetically prohibiting and thermodynamically destabilizing **28**, resulting in complete furanosyl selectivity. Evidence for this protonation is provided by the substantial downfield shift of **32**H-(C2) at pD < 4, but not of **28**H-(C2). Some compound degradation (likely hydrolysis) is observed at high pD (pD > 9), and significant imidazole deuteration is observed at pD 12.

ASSOCIATED CONTENT

Supporting Information. Corrected Scheme S1; CIF files for **28** and **32**. This material is available free of charge via the Internet at http://pubs.acs.org.

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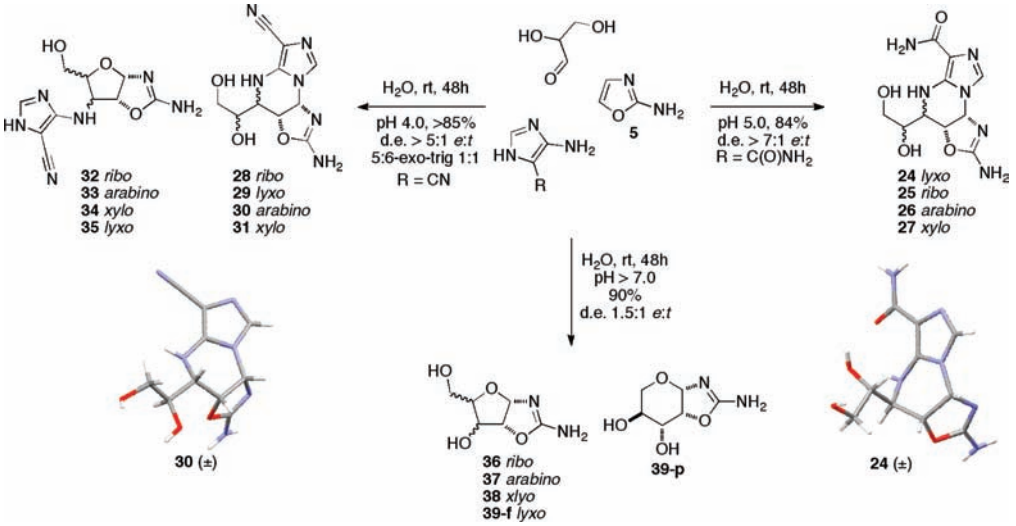
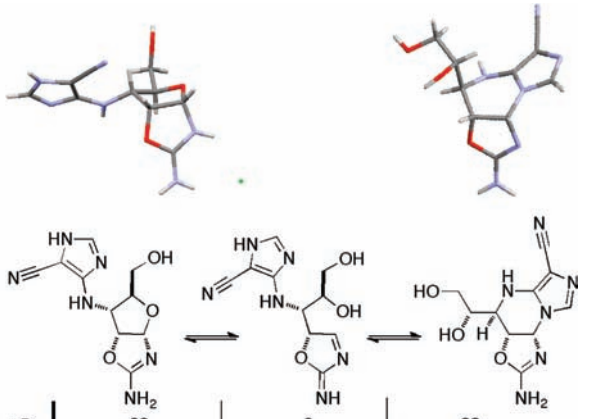
Scheme 6. One-Pot Multicomponent Assembly of *rac*-3′-(Dihydroxyethyl)tetrahydroimidazo-2″-aminooxazolopyrimidines from Glyceraldehyde with Crystal Structures of 24 and 30



Scheme 7. pH-Controlled Isomerization of 32 to 28 in Water after 3 d at Room Temperature[a]



pD	32	9	28
1	>50		1
2	20		1
4	4		1
6	4		1
7	1.25		1
8	1		1
9	3		1
12	5		1

[a] **28** was crystallized at pH 6.5 from phosphate buffer (10 mM), and the hydrochloride salt of **32** was crystallized from water by evaporation at pH 2.0. CIF files for **28** (CCDC 806657) and **32** (CCDC 806658) have been deposited with the Cambridge Structural Database and are available as Supporting Information.

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