Scalable synthesis of 2,2'-anhydro-arabinofuranosyl imidazoles

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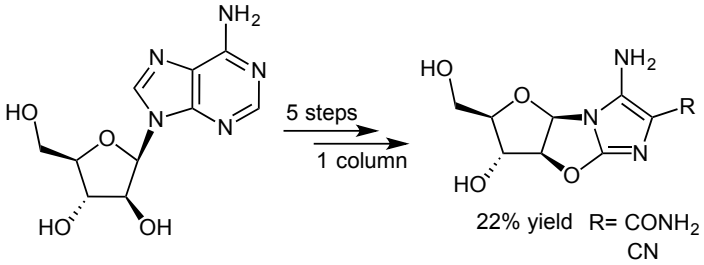

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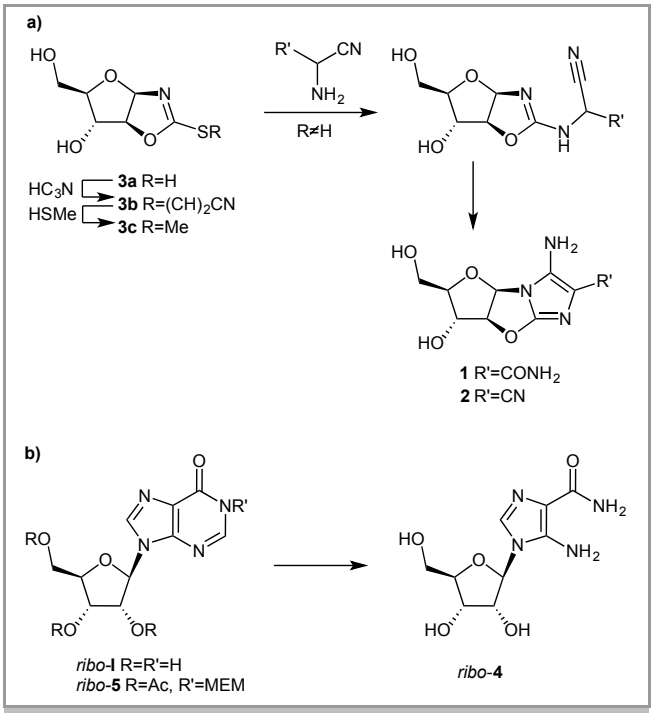
Abstract: We report the efficient and highly scalable synthesis of 2,2'-anhydro-5-amino-1-β-arabinofuranosylimidazole-4-carboxamide (**1**) and 2,2'-anhydro-5-amino-1-β-arabinofuranosylimidazole-4-carbonitrile (**2**) from commercial *arabino*-adenosine (*ara*-**A**). Imidazole **1** is synthesized in only 5 steps with a single chromatographic purification. Additionally, we report a high yielding, three-step conversion of imidazole **1** to imidazole **2**. Imidazoles **1** and **2** are proposed key intermediates of the divergent prebiotic synthesis of ribonucleotides and this facile synthesis is anticipated to be instrumental in continued investigation of the origins of nucleotides.

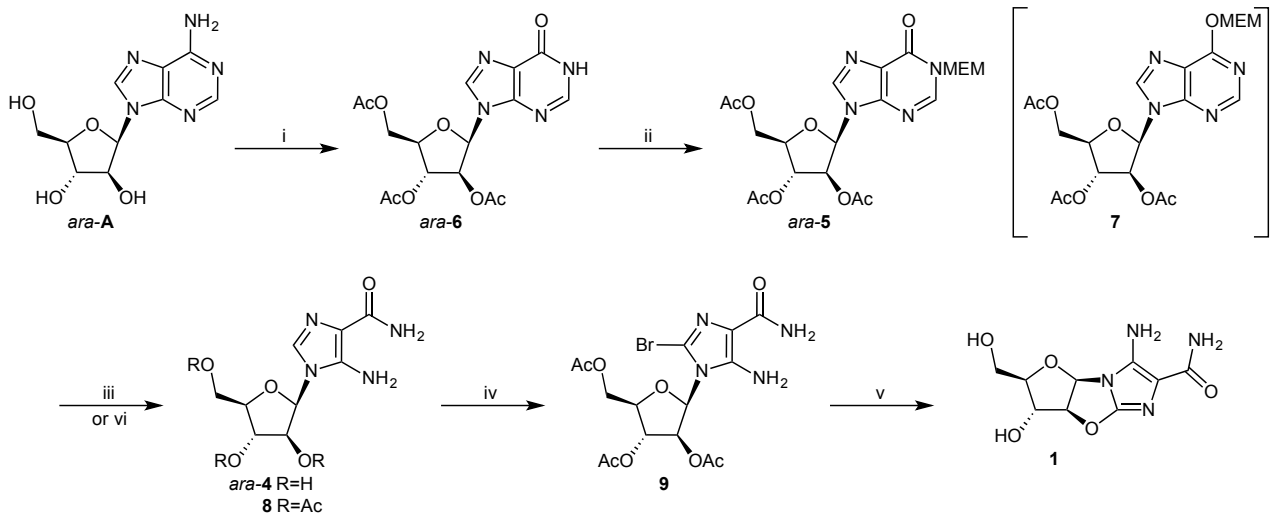
Key words AICAR, nucleosides, arabinosides, purines, prebiotic

As part of our ongoing investigation of the chemical origins of ribonucleotides,[1] we recently presented a prebiotically plausible divergent synthesis of pyrimidine and 8-oxo-purine ribonucleotides.[1e] Imidazoles **1** and **2** (Scheme 1a) are key intermediates, providing the essential element of regiocontrol required to realise stepwise purine synthesis on an oxazoline scaffold. Oxazolidinone thiones **3b** and **3c**,[1e,2] are both activated towards nucleophilic attack and treatment of either with HCN oligomers gave aminooxazolines that readily cyclized to give imidazoles **1** and **2**.[1e] In the case of **1** (R'=$CONH_2$) a 59% yield was achieved over 3 steps (cyanovinylation, substitution and cyclisation), and remarkably **1** was observed to crystallise directly from the crude reaction mixture. Given the close structural relationship between 8-oxo-purines and canonical purines, the (prebiotically plausible) generational relationship between 8-oxo-purine and pyrimidine ribonucleotides,[1e] and the wide ranging and long standing clinical utility of non-canonical nucleosides,[3] further study of conformationally constrained imidazoles **1** and **2** is warranted. Accordingly, here we report a stereodefined, scalable synthetic route to access **1** and **2** from commercial *arabino*-adenosine (*ara*-**A**).

At first inspection imidazole **1** displays a great deal of similarity to known therapeutic and biosynthetic intermediate AICAR (*ribo*-**4**) (Scheme 1b). The *ribo*-stereochemistry of *ribo*-**4** prohibits a direct 2,2'-annulation to yield **1**, however, the C2'-epimer, AICA arabinoside (*ara*-**4**; Scheme 2) is ideally orientated to allow a facile oxidative ring closing. Specifically, we predicted that activation of the 2 position of *ara*-**4**, for example by bromination, followed by deprotonation of the 2'-hydroxyl would yield imidazole **1**.



Scheme 1 a) Prebiotic synthesis of purine precursor imidazoles **1** and **2**.[1e] b) Kohyama *et al.* synthesis of AICAR (*ribo*-**4**) from inosine (*ribo*-**I**) by hydrolysis of 2',3',5'-*O*-triacetyl *N*1-methoxyethoxymethyl *ribo*-**5**.[7]



Conditions: i) $NaNO_2$, $AcOH_{(aq)}$, RT, 36 h then Ac_2O, Py, RT, 18 h, 74% ii) MEM-Cl, $^iPr_2EtNH_2$, DCM, 0 °C - RT, 18 h, 94% *ara*-**5** iii) NH_3/MeOH, RT, 30 min then 0.2M $NaOH_{(aq)}$, 100 °C, 1 h, then Ac_2O, Py, 0 °C, 1 h, 69% **8** iv) *N*-bromoacetamide, THF, RT, 10 min, 83% v) MeONa/MeOH, reflux, 5 h, 54% vi) NH_3/MeOH, RT, 30 min then 0.2M $NaOH_{(aq)}$, 100 °C, 1 h, 63% *ara*-**4**.

Scheme 2 Synthesis of imidazole **1** by hydrolysis of *N*1-MEM substituted hypoxanthine *ara*-**5**.

Previous syntheses of *ara*-**4** have either depended on low yielding glycosylations[4] or inefficient C2-hydrolysis of *N*1-oxo derivatives of hypoxanthine arabinosides.[5] In the *ribo*-series however Shaw has shown that *N*1-derivatization of *ribo*-hypoxanthines with benzyl, methoxymethyl, and *p*-toluenesulfonyl allowed facile C2-hydrolysis to give the corresponding aminoimidazole[6], and recently Kohyama *et al.* have shown that *N*1-methoxyethoxymethylated inosine (*ribo*-**5**) is efficiently hydrolysed to *ribo*-**4** (Scheme 1b).[7] Accordingly, we set out develop an improved procedure for synthesis of *ara*-**4**.

Our starting point was commercially available (antiviral drug) 9-β-D-arabinofuranosyl adenine (*ara*-**A**,; Scheme 2). Adenine *ara*-**A** was readily deaminated by treatment with sodium nitrite in aqueous acetic acid to give corresponding hypoxanthine *ara*-**I**, but we found it difficult to reliably isolate pure *ara*-**I**, free from acetate, by crystallization. We were working on 20 g scales and wanted to avoid chromatographic purification methods, and conscious that selective alkylation of *N*1-nitrogen atom precludes the need to protect the 2', 3' and 5' hydroxyl moieties, we chose to acetylate the hydroxyl moieties of *ara*-**I** at this stage to facilitate purification. Treatment of crude *ara*-**I** with acetic anhydride in pyridine smoothly furnished triacetyl hypoxanthine *ara*-**6**, and, gratifyingly, we found that evaporation and trituration with water returned pure *ara*-**6** in 74% yield from *ara*-**A**.

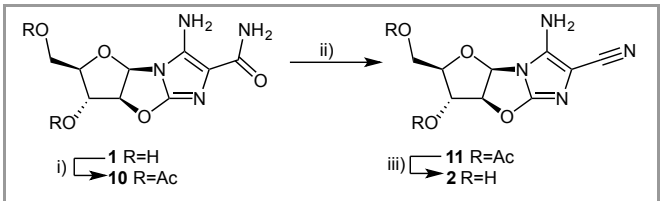
Kohyama *et al.*[7] reported that treatment of 2',3',5'-trisacetoxy inosine (*ribo*-**6**) with 2-methoxyethoxymethyl chloride (MEM-Cl) and $^iPr_2EtNH_2$ in CH_2Cl_2 at 0 °C gave *N*1-MEM *ribo*-**5** derivative in an 86% isolated yield. In our hands, we found that similar treatment of *ara*-**6** gave a 4:1 ratio of MEM derivatised products which we identified as the desired *N*1 substituted *ara*-**5** and *O*6 substituted species **7**, respectively. Whilst chromatographically separable, **7** represented a significant loss of material, so we sought to optimise this alkylation step. An initial solvent screen did not significantly improve the ratio of 4:1, however when the reaction was incubated at room temperature for longer periods we obtained increased yields of product *ara*-**5**. We suspected that *O*6-alkylation was reversible and that our unwanted by-product **7** was converted to the thermodynamically more stable product *ara*-**5**. Remarkably, we found that treatment of *ara*-**6** with excess MEM-Cl (1.5 eq.) at 0 °C followed by incubation at room temperature overnight gave the desired hypoxanthine *ara*-**5** in 94% yield and *ara*-**5** was easily purified by aqueous workup and isocratic elution through a silica plug.

Nucleoside *ara*-**5** was next heated at reflux in aqueous NaOH (0.2M) to bring about simultaneous acetyl deprotection and C2-hydrolysis, however due to poor aqueous solubility of *ara*-**5** the reaction led to a mixture of products. Treatment of *ara*-**5** with saturated methanolic ammonia (30 mins, r.t), however, quantitatively gave the corresponding de-acetylated *N*-MEM hypoxanthine, which was water soluble and smoothly hydrolysed to *ara*-**4** in 63% yield. The product was initially purified by trituration of the crude mixture with hot ethanol followed by chromatography, however we found that direct acetylation of the crude mixture of *ara*-**4** with acetic anhydride in pyridine gave **8** in a 69% yield over 3 steps without requiring chromatography. Importantly it was possible to control acetylation and selectively derivatise the 2', 3' and 5' hydroxyls at 0 °C, however it is of note that a room temperature incubation incurred an additional acetyl at the 5-NH_2. With **8**, the per-*O*-acetylated derivative of our original target *ara*-**4**, in hand we next sought a method of oxidative annulation to install the key 2,2' linkage.

Bromination of *ribo*-isomer of **8** has been achieved by treatment with *N*-bromoacetamide in anhydrous THF[8] and pleasingly we found that similar treatment of **8** gave 2-bromo derivative **9** in an 83% yield. Deacetylation of **9** was effected quantitatively by incubation for 30 minutes with saturated methanolic ammonia, but no subsequent cyclisation was observed, even at elevated temperatures (60 °C). However, we found that arabinoside **9** could be directly converted to imidazole **1** by heating at reflux with sodium methoxide in methanol. Furthermore, we found that **1** precipitated directly from the reaction mixture and could be conveniently obtained by filtration in 54% yield from **9** and required no further purification.

With our first target in hand we next sought to dehydrate **1** to access nitrile **2**. Similar amides have previously been dehydrated

with phosphorus oxychloride[4, 9] and p-toluenesulfonyl chloride[10] (TsCl), the latter giving better yields, but due to the incompatibility of these reagents with free hydroxyl groups a protected substrate was required. Treatment of **1** with acetic anhydride in pyridine at 0 °C lead to acetylation of the 3′ and 5′ hydroxyls and the *N*5 nitrogen atom. Cleavage of amides is often difficult and requires extremes of pH or high temperature incubation with methanolic ammonia, which could lead to degradation of the final product. Furthermore, since imidazole **1** is difficult to purify chromatographically, due to its low solubility in organic solvents, the final deprotection step needs to be quantitative with minimal side-products. Recently we have described the use of *N*-acetylimidazole to selectively acetylate hydroxyl groups in the presence of amine functionalities, and this method seemed ideally suited to deliver hydroxyl selective acetylation of **1**.[11]



i) *N*-acetylimidazole, H_2O, RT, 30 min, Quant. ii) TsCl, pyridine, 0 °C, 2 h, 64% iii) NH_3/MeOH, RT, 30 min, 80%

Scheme 3 Synthesis of imidazole **2** by selective *O*-acetylation of imidazole **1** followed by dehydrated and treatment with methanolic ammonia .[1e]

Returning to this strategy,[1e] to avoid *N*5-acetylation, imidazole **1** was suspended in water at pH 8 and treated with *N*-acetylimidazole (6 eq) over 30 minutes. A simple extraction of the mixture with chloroform gave a quantitative yield of analytically pure diacetyl product **10**. This amide was then smoothly dehydrated to nitrile **11** with TsCl in pyridine in 64% isolated yield.[1e] Finally, **11** was deacetylated by a 30 minute incubation with methanolic ammonia and, pleasingly, pure imidazole **2** precipitated directly from the reaction mixture and was isolated in 80% yield.[1e]

In summary, we have successful developed a scalable synthesis of imidazoles **1** and **2**. Our route begins from commercial 9-β-D-arabinofuranosyl adenine (*ara*-**A**) and in 5 steps generates the imidazole **1** in 22% overall yield. The route only requires a single chromatographic purification (of compound **9**); all other intermediates are isolated sufficiently pure for continued synthesis after aqueous workup. Furthermore, we have demonstrated a high yielding, 3-step conversion of amide **1** to nitrile **2** utilizing a selective aqueous acetylation, dehydration and convenient deprotection and isolation protocol.

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Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

NO (this text will be deleted prior to publication)

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2′,3′,5′-Trisacetoxy-9-β-arabinofuranosyl hypoxanthine *ara*-**6**

9-β-Arabinofuranosyl adenine (*ara*-**A**; 23 g, 86 mmol) was suspended in $AcOH_{(aq)}$ (1 L, 2M) and sodium nitrite (29.7 g, 430 mmol) was added. The flask was fitted with a bubbler and the mixture was stirred until evolution of gas ceased (approx. 18 h). Additional sodium nitrite (29.7 g) was added and the solution was stirred for a further 18 h. The mixture was evaporated to dryness and the residue co-evaporated with toluene (4 × 200 mL). The residue was suspended in pyridine (750 mL) and cooled to 0 °C under argon then acetic anhydride (97.5 mL, 1.03 mol) was added in one portion. The mixture was stirred for 1 h at 0 °C and then overnight at room temperature, ethanol (200 mL) was added at 0 °C and the mixture was stirred for 1 h then concentrated to dryness. The residue was co-evaporated with toluene (4 × 200 mL), water (300 mL) was added and the mixture was stirred vigorously for 30 min. The solution was filtered and the filter cake was washed with water (50 mL) and cold ethyl acetate (50 mL) and dried *in vacuuo* to yield hypoxanthine *ara*-**6** as a fine white solid (25.0 g, 63.5 mmol, 74%). Mp. 220-222 °C. IR (Solid, cm^{-1}) 3120 (CH), 3045 (CH), 1738 (OAc), 1691 (HNCO). ^1H NMR (600 MHz, $CDCl_3$) 13.11 (1H, br s, NH), 8.26 (1H, s, H2), 8.06 (1H, s, H8), 6.55 (1H, d, *J* = 4.7 Hz, H1′), 5.52 (1H, dd, *J* = 4.7, 3.1 Hz, H2′), 5.43 (1H, dd, *J* = 4.3, 3.1 Hz, H3′), 4.48 (1H, ABX, *J* = 12.0, 4.3 Hz, H5′), 4.44 (1H, ABX, *J* = 12.0, 6.1 Hz, H5′′), 4.29 (1H, dt, *J* = 6.1, 4.3 Hz, H4′), 2.17 (3H, s, OAc), 2.15 (3H, s, OAc), 1.92 (3H, s, OAc). ^{13}C NMR (151 MHz, $CDCl_3$) 170.7, 169.7, 168.9, 159.1, 148.7, 145.7, 139.3, 124.3, 83.6, 80.2, 75.8, 75.0, 63.0, 20.9, 20.9, 20.4. HRMS (*m/z*) calculated for $C_{16}H_{18}N_4O_8$ $[M+H^+]^+$, 395.1203; found, 395.1203.

2′,3′,5′-Trisacetoxy-β-furanosylarabino-1-(2-methoxyethoxymethyl) hypoxanthine *ara*-**5**

2',3',5'-Trisacetoxy-β-furanosylarabino hypoxanthine (*ara*-**6**; 23 g, 58.4 mmol) was dissolved in dry CH_2Cl_2 (250 mL) and activated 3 Å molecular sieves (5 g) were added. The mixture was cooled to 0 °C and diisopropylethyl amine (20.4 mL, 117 mmol) was added and the mixture was stirred for 1 h. 2-methoxyethoxymethyl chloride (9.9 mL, 87.6 mmol) was added at 0 °C and the mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with water (500 mL) and the pH adjusted to 7 with HCl (1M). The phases were separated, the aqueous phase was extracted with $CHCl_3$ (3 × 250 mL) and the combined organic phases were washed with phosphate buffer (2 × 250 mL, 100mM, pH 7), brine (250 mL) and dried over $MgSO_4$. The solvents were removed under reduced pressure and the resulting residue was eluted through a short silica plug (5cm × 5cm, 5% MeOH/EtOAc) to yield hypoxanthine *ara*-**5** as a colourless oil (26.4 g, 54.7 mmol, 94%). IR (neat, cm^{-1}) 2962 (CH), 1742 (OAc), 1697 (HNCO). ^{1}H NMR (600 MHz, $CDCl_3$) 8.11 (1H, s, H2), 7.89 (1H, s, H8), 6.44 (1H, d, *J* = 4.8 Hz, H1'), 5.52 (1H, AB, *J* = 10.5 Hz, NCH_2O), 5.48 (1H, AB, *J* = 10.5 Hz, NCH_2O), 5.43 (1H, dd, *J* = 4.8, 3.4 Hz, H2'), 5.39 (1H, dd, *J* = 4.3, 3.4 Hz, H3'), 4.40 (1H, ABX, *J* = 12.1, 4.3 Hz, H5'), 4.36 (1H, ABX, *J* = 12.1, 6.2 Hz, H5''), 4.22 (1H, dt, *J* = 6.2, 4.3 Hz, H4'), 3.74 (2H, m, CH_2), 3.46 (2H, m, CH_2), 3.27 (3H, s, OCH_3), 2.10 (3H, s, OAc), 2.06 (3H, s, OAc), 1.84 (3H, s, OAc). ^{13}C NMR (151 MHz, $CDCl_3$) 170.6, 169.7, 168.9, 156.7, 147.9, 147.2, 139.2, 124.0, 83.3, 79.9, 75.7, 75.3, 75.0, 71.6, 69.4, 62.9, 59.1, 20.9, 20.8, 20.4. HRMS (*m/z*) calculated for $C_{20}H_{26}N_4O_{10}$ $[M+H^+]^+$, 483.1727; found, 483.1729.

2',3',5'-Trisacetoxy-β-furanosylarabino-5-aminoimidazole-4-carboxamide **8**

2',3',5'-Trisacetoxy-β-furanosylarabino-1-(2-methoxyethoxymethyl) hypoxanthine (*ara*-**5**; 24.5 g, 50.8 mmol) was dissolved in MeOH/NH_3 (sat., 300 mL) and stirred for 30 min at room temperature. The solvent was removed under reduced pressure and the resulting residue was dissolved in $NaOH_{(aq)}$ (0.2M, 600 mL) and heated at reflux for 1 h. The solution was neutralised with Dowex 50W×8 (proton form), filtered, flash frozen with liquid nitrogen and lyophilised. The residue was dissolved in pyridine (300 mL), cooled to 0 °C and acetic anhydride (130 mL) was added in one portion. The mixture was stirred at 0 °C for 1 h, quenched with EtOH (200 mL) and the solvents were removed under reduced pressure. The residue was partitioned between H_2O (500 mL) and $CHCl_3$ (250 mL) and the aqueous phase adjusted to pH 7 with sat. $HNaCO_{3(aq)}$. The aqueous phase was further extracted with $CHCl_3$ (4 × 250 mL) and the combined organic phases were washed with brine (250 mL), dried over $MgSO_4$ and the solvents were removed under reduced pressure to yield crude **8** as a pale yellow foam which was sufficiently pure for continued synthesis (13.5 g, 35.2 mmol, 69%). Analytical material can be obtained by silica column chromatography (EtOAc/MeOH, 0% - 5%). Mp. 72-74 °C. IR (Solid, cm^{-1}) 3326 (NH), 3173 (CH), 1742 (OAc), 1643 (HNCO). ^{1}H NMR (600 MHz, $CDCl_3$) 7.16 (1H, s, H8), 6.66 (1H, br s, NH), 5.99 (1H, d, *J* = 5.3 Hz, H1'), 5.70 (1H, br s, NH), 5.47 (1H, dd, *J* = 5.3, 4.0 Hz, H2'), 5.37 (2H, br s, NH_2), 5.39 (1H, dd, *J* = 5.6, 4.0 Hz, H3'), 4.41 (1H, ABX, *J* = 12.3, 4.7 Hz, H5'), 4.37 (1H, ABX, *J* = 12.3, 3.5 Hz, H5'), 4.17 (1H, ddd, *J* = 5.6, 4.7, 3.5 Hz, H4'), 2.13 (6H, s, 2 × OAc), 1.94 (3H, s, OAc). ^{13}C NMR (151 MHz, $CDCl_3$) 170.5, 169.8, 169.6, 167.1, 143.1, 129.1, 113.6, 84.1, 70.1, 75.6, 74.9, 62.2, 20.8, 20.8, 20.3. HRMS (*m/z*) calculated for $C_{15}H_{20}N_4O_8$ $[M+H^+]^+$, 385.1359; found, 385.1361.

2',3',5'-Trisacetoxy-β-furanosylarabino-2-bromo-5-aminoimidazole-4-carboxamide **9**

2',3',5'-Trisacetoxy-β-furanosylarabino-5-aminoimidazole-4-carboxamide (**8**; 3.5 g, 9.11 mmol) was dissolved in dry THF (200 mL) and N-bromoacetamide (1.32 g, 9.57 mmol) was added in a single portion. The mixture was stirred for 10 min at room temperature and then quenched by addition of sat. sodium $bisulfite_{(aq)}$ (100 mL). The mixture was stirred for 15 min then sodium chloride was added until the mixture was fully saturated. The organic phase was separated, washed with brine (100 mL), dried ($MgSO_4$) and concentrated to dryness. The residue was purified by silica column chromatography, eluting with EtOAc/MeOH (1% - 4%) to give 2-bromo-5-aminoimidazole **9** as a white foam (3.52 g, 7.60 mmol, 83%). Mp. 123-126 °C. IR (Solid, cm^{-1}) 3467 (NH), 3341 (NH), 1740 (OAc), 1646 (H_2NCO). ^{1}H NMR (600 MHz, MeOD) 6.25 (1H, d, *J* = 4.9 Hz, H1'), 5.53 (1H, d, *J* = 4.9, 2.8 Hz, H2'), 5.35 (1H, dd, *J* = 5.8, 2.8 Hz, H3'), 4.59 (1H, ABX, *J* = 12.4, 4.2 Hz, H5'), 4.40 (1H, ABX, *J* = 12.4, 2.8 Hz, H5'), 4.27 (1H, ddd, *J* = 5.8, 4.2, 2.8 Hz, H4'), 2.13 (3H, s, OAc), 2.13 (3H, s, OAc), 1.92 (3H, s, OAc). ^{13}C NMR (151 MHz, MeOD) 172.1, 171.6, 170.4, 168.3, 147.8, 113.8, 111.9, 88.6, 80.4, 77.4, 76.9, 63.2, 20.7, 20.6, 20.1. HRMS (*m/z*) calculated for $C_{15}H_{20}N_4O_8Br$ $[M+H^+]^+$, 463.0464; found, 463.0465.

2,2'-Anhydro-5-aminoimidazole-4-carboxamide-β-furanosylarabinoside **1**

Sodium (75 mg, 3.24 mmol) was dissolved in dry methanol (20 mL) and 2',3',5'-trisacetoxy-β-furanosylarabino-2-bromo-5-aminoimidazole-4-carboxamide (**9**; 1 g, 2.16 mmol) was added. The mixture was heated at reflux for 5 h, cooled to room temperature and NH_4Cl (69 mg, 1.1 mmol) was added. The mixture was allowed to stand at -20 °C for 1 h then filtered to give imidazole **1** as a fine white powder (300 mg, 1.17 mmol, 54%). Mp. 234–238 °C. IR (solid, cm^{-1}) 3493 (NH), 3359 (NH), 3210 (OH), 1638 (H_2NCO), 1581 (C=N), 1533 (C=C). ^{1}H NMR (600 MHz, D_2O) 6.46 (1H, d, *J* = 5.4 Hz, H1'), 5.68 (1H, d, *J* = 5.4 Hz, H2')), 4.60 (1H, br s, H3'), 4.38 (1H, ddd, *J* = 6.8, 4.9, 1.9 Hz, H4'), 3.56 (1H, ABX, *J* = 12.4, 4.9 Hz, H5'), 3.42 (1H, ABX, *J* = 12.4, 6.8 Hz, H5''). ^{13}C NMR (151 MHz, D_2O) 169.1, 152.6, 140.0, 109.9, 97.9, 89.3, 86.5, 75.3, 61.5. HRMS (*m/z*) calculated for $C_9H_{12}N_4O_5$ $[M+H^+]^+$, 257.0880; found, 257.0882. [1e]

3',5'-Bisacetoxy-2,2'-anhydro-5-aminoimidazole-4-carboxamide-β-furanosylarabinoside **10**

2,2'-Anhydro-5-aminoimidazole-4-carboxamide-β-furanosylarabinoside (**1**; 256mg, 1 mmol) was suspended in water (20 mL) at RT, adjusted to pH 8 with 1M $NaOH_{(aq)}$ and *N*-acetylimidazole (220 mg, 2 mmol) was added. The reaction was stirred at RT for 10 min and during this time kept at pH 8 by manual dropwise addition of 1M $NaOH_{(aq)}$. *N*-acetylimidazole (2 × 220 mg) was added and stirred at pH 8. After the third addition of reagent the reaction was stirred for 10 min then the solution was adjusted to pH 5 with 1M $HCl_{(aq)}$. The reaction was extracted with $CHCl_3$ (20 × 20 mL) and the combined extracts were dried ($MgSO_4$) and evaporated to dryness to give 3',5'-bisacetoxy-2,2'-anhydro-5-aminoimidazole-4-carboxamide-β-furanosylarabinoside (**10**) as a pale yellow powder (343mg, 1 mmol, quant.). Mp. 163-166 °C. IR (Solid, cm^{-1}) 3330, 1740, 1649, 1597. ^{1}H NMR (600 MHz, D_2O) 6.52 (1H, d, *J* = 5.7 Hz, H1'), 5.91 (1H, d, *J* = 5.7 Hz, H2'), 5.52 (1H, d, *J* = 1.9 Hz, H3'), 4.75 (1H, dt, *J* = 1.9, 4.1 Hz, H4'), 4.20 (2H, d, *J* = 4.1 Hz, H5'), 2.20 (3H, s, OAc), 1.98 (3H, s, OAc). ^{13}C NMR (151 MHz, D_2O) 174.3, 173.5, 169.0, 152.2, 140.2, 109.7, 96.0, 87.3, 84.7, 78.7, 64.4, 20.8, 20.3. HRMS (*m/z*) calculated for $C_{13}H_{16}N_4O_7$ $[M+H^+]^+$, 341.1092; found, 341.1090.