Synthesis of Pyrazole, Pyrazolo[3,4-*d*]pyrimidine, and 1*H*-1,2,4-Triazole arabino-nucleosides from 2,3,5-Tri-*O*-benzyl-D-arabinose Hydrazone [1]

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The α-arabinofuranosyl pyrazole nucleosides **6a-α** and **12a-14a** were obtained regio- and diastereoselectively from 2,3,5-tri-*O*-benzyl-D-arabinose hydrazone **5a** and acetylacetone, ethoxymethylene malonitrile, ethoxymethylene cyanoacetate, and aminomethylene cyanoacetamide in a one pot procedure *via* two ring closures. Compounds **12a** and **13a** were transformed into the unprotected pyrazolo[3,4-*d*]pyrimidine arabinofuranosyl nucleosides **15b** and **16b** (analogues of adenosine and inosine). Similarly from **5a** and ethyloxalate monothioamide the α-arabinofuranosyl nucleoside analogue of virazole **25** was obtained. *N*-Ethoxymethylene derivatives of oxamide **19** and oxalate monoamide **20** led to 5-substituted 1*H*-1,2,4-triazole arabinofuranosyl nucleosides.

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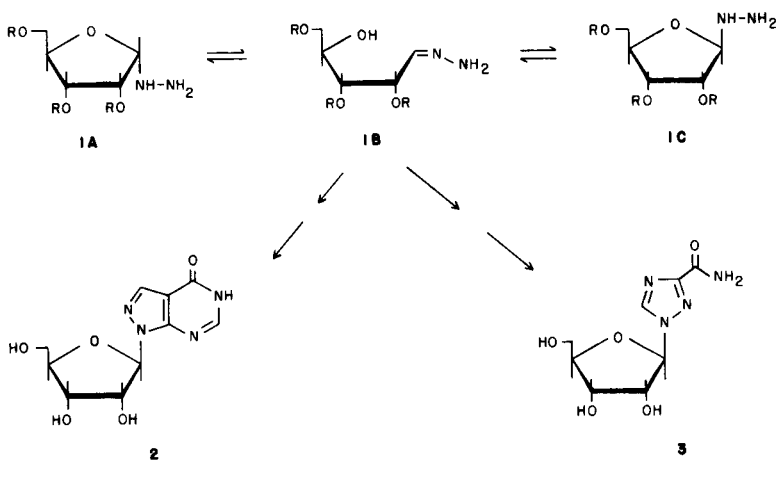
Mixtures of the ribose hydrazones **1A-1C** (scheme 1, $R^1 = R^2 = R^3$ = benzyl; R^1, R^2 = $C(CH_3)_2$, R^3 = H) react with pyrazole and triazole forming compounds regiospecifically and highly diastereoselectively to β-ribofuranosyl pyrazole, pyrazolo[3,4-*d*]pyrimidine, and 1*H*-1,2,4-triazole nucleosides [3-9]. The biologically important allopurinol riboside **2** [3,5] and the antiviral virazole **3** [6,7] were obtained conveniently *via* this route. These investigations were successfully applied to uronic acid derivatives of ribose [8] and to glucose hydrazone [9]. We report here on the extension of this work to D-arabinose.

From earlier investigations it is known, that D-arabinose (**4b**) reacts with hydrazine to yield the corresponding hydrazone **5b** [10], which exists in an equilibrium with the α- and β-hydrazino derivatives (**4bA-C**). However, *O*-protected carbohydrate derivatives have proven to be superior starting materials for nucleoside syntheses [4]. Therefore 2,3,5-tri-*O*-benzyl arabinose **4a** [11] was transformed with anhydrous hydrazine. However, according to the ^{1}H-nmr spectrum the product **5a** obtained in quantitative yield is an inseparable mixture of the hydrazine derivatives **5aA-C**. This mixture, called arabinose hydrazone **5a**, is used for the subsequent reactions.

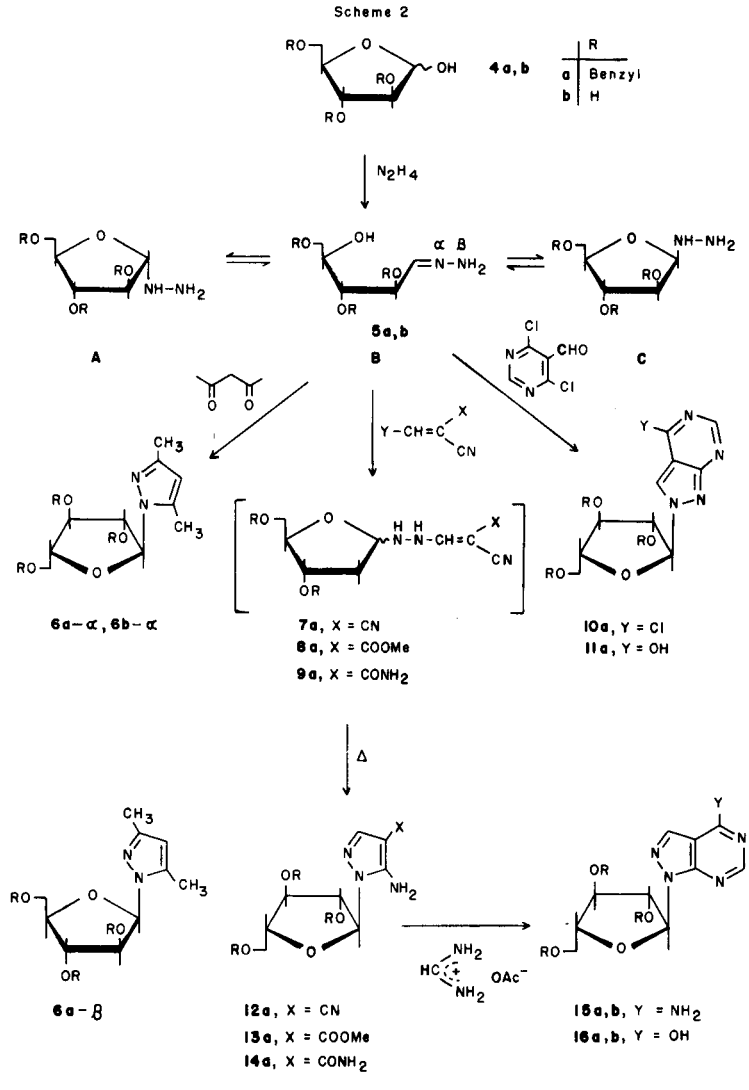
Synthesis of Pyrazole and Pyrazolo[3,4-*d*]pyrimidine Arabinofuranosyl Nucleosides.

Acetylacetone smoothly reacted with **5a** to the α-arabinofuranosyl pyrazole derivative **6a-α**. The ^{1}H-nmr data (H-1′: δ = 5.73, $J_{1',2'}$ 4 Hz) are in agreement with this structural assignment [12]. Further structural proof was obtained by hydrogenolytic deprotonation to **6b-α** and subsequent sodium metaperiodate cleavage of the vicinal diol structure using known procedures [13]. Because the obtained dialdehyde (α^{20}_{578} −20°, c = 2.0, water) was not identical with the cleavage product of the corresponding β-D-ribose derivative [2], the α-connection between pyrazole and arabinose is established. The independent synthesis of the β-anomer **6a-β** (^{1}H-nmr, H-1′: δ = 5.88, $J_{1',2'}$ 5.8 Hz) applying the trichloroacetimidate procedure [14] to 3,5-dimethylpyrazole led to unequivocal structural

Scheme I



Scheme 2



proof, because the anomeric proton of 1′,2′-*cis* nucleosides have been shown to occur at lower field than the corresponding *trans* anomer [15].

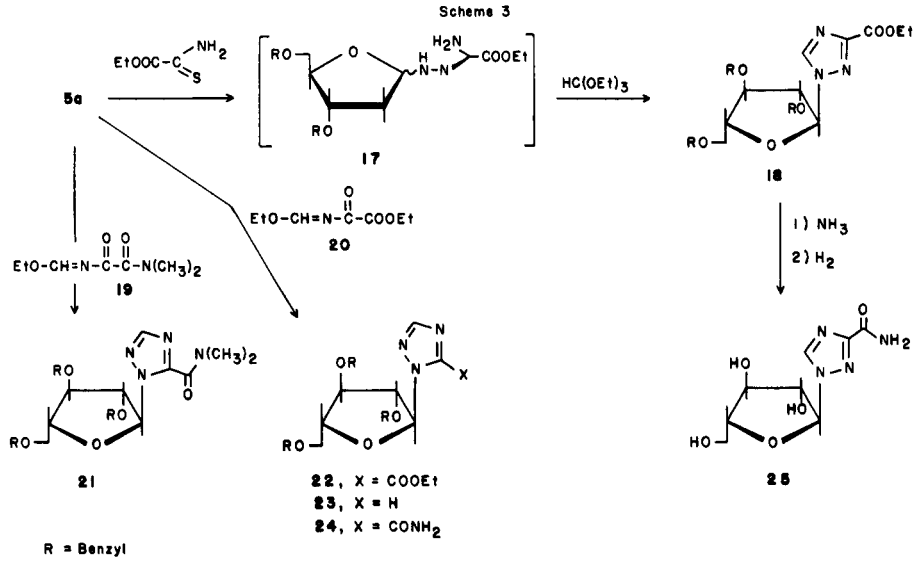
Regioselective reactions with the unsymmetrical β-dicarbonyl derivatives ethoxymethylene malonitrile, ethoxymethylene methyl cyanoacetate, and aminomethylene cyanoacetamide proved possible, because the methylene group, being the more reactive electrophilic centre [16], reacted preferentially with Nβ. This selectivity is presumably due to preferred reaction of **5a** *via* the hydrazone **B** [3,5,6,8,9].

Reaction of **5a** with ethoxymethylene malonitrile led to an intermediate hydrazine derivative **7a**, which was immediately cyclized to the α-arabinofuranosyl pyrazole derivative **12a**. By analogous reactions of **5a** with ethoxymethylene methyl cyanoacetate and aminomethylene cyanoacetamide the pyrazole ester and amide derivatives **13a** and **14a** were obtained *via* the intermediates **8a** and **9a**, which were not isolated. Compounds **12a** and **13a** were transformed into the corresponding pyrazolo[3,4-*d*]pyrimidine derivatives **15a** and **16a** by treatment with excess formamidine acetate. Hydrogenolytic debenzylation led to the analogue of adenosine **15b** and to the allopurinol derivative **16b**. However, reaction of **5a** with 4,6-dichloro-5-formylpyrimidine [17] did not yield the N-1-connected allopurinol derivative **16a**. *N*β-Attack occurred at C-4 of the pyrimidine moiety, which led to the N-2 α-arabinofuranosyl allopurinol derivative **11a** *via* the chloro derivative **10a** as an intermediate.

The structures of these compounds are assigned on the basis of ^{1}H-nmr (H-1′, $J_{1',2'}$) and partly by comparison with published uv data [18].

Synthesis of 1*H*-1,2,4-Triazole Arabino Nucleosides.

A very convenient synthesis of virazole (**3**) was accomplished with ethyl oxalate thioamide as the triazole for-



ming compound [6]. An analogous synthesis of the α-arabinofuranosyl derivative **18** was carried out with **5a** as starting material. The hydrazino derivative **17** obtained as intermediate was not isolated. The structure of **18** was proven by transformation with ammonia and hydrogenolytic deprotection to the known α-arabinofuranosyl derivative of virazole **25** [12].

A convenient synthesis of 5-substituted 1*H*-1,2,4-triazole nucleosides was developed with *N*-alkoxymethylene oxalic acid amide derivatives as triazole forming compounds [6,8,9]. Thus the *N*-ethoxymethylene oxamide derivative **19** reacted with **5a** to the triazole-5-carboxamide **21** in a one pot process. Similarly the *N*-ethoxymethylene oxalate monoamide **20** [6] and **5a** led to the arabinofuranosyl triazole-5-carboxylate **22**. In this reaction the unsubstituted 1*H*-1,2,4-triazole compound **23** was obtained as byproduct. The formation of this byproduct is not unexpected because it is known, that 1*H*-1,2,4-triazole-5-carboxylates are much more rapidly dealkoxycarbonylated than the corresponding 1*H*-1,2,4-triazole-3-carboxylates [6,19]. Compound **22** was transformed into the amide **24**. The ^{1}H-nmr data (δ of H-1', $J_{1',2'}$) are in agreement with the structural assignments.

EXPERIMENTAL

The solvents were purified by conventional methods. Melting points were carried out in a metal block and are uncorrected. The ^{1}H-nmr spectra were taken with a Varian EM 360, Bruker CP 80 Cw. Chemical shifts are reported in parts per million (δ) with TMS as internal reference. Column chromatography was accomplished on silica gel 60 (Fa. Macherey and Nagel, Size 0.05-0.2 mm) and thin layer chromatography (tlc) using silica gel, 0.25 mm layer with a fluorescence indicator (Fa. Macherey and Nagel, "Polygram" SIL G UV_{254}), 4 × 8 cm; eluents are described under each experiment.

2,3,5-Tri-*O*-benzyl-D-arabinose Hydrazone (**5a**).

A solution of 2,3,5-tri-*O*-benzyl-D-arabinose (**4a**, 5.0 g, 11.9 mmoles) (ref [11], see below) was added to a solution of anhydrous hydrazine (3.8 g, 119 mmoles) in 10 ml dry methanol at 0°. The cooling bath was taken off after 10 minutes and the reaction mixture was stirred at room temperature for 6 hours. The solvent and excess hydrazine were evaporated at low pressure finally at 10^{-2} torr. The slightly yellow oil was almost analytically pure, yield 5.0 g (98%).

Methyl 2,3,5-Tri-*O*-benzyl-α-D-arabinofuranoside.

This compound required for the synthesis of **4a** was obtained by the following procedure: Methyl α-D-arabinofuranoside (64 g, 0.4 mmole) (ref [11]) in 800 ml of anhydrous THF was heated to reflux with 400 ml of benzyl chloride and sodium hydride (96 g, 4 mmoles). After 10 hours the reaction mixture was centrifuged, the solid material was washed with anhydrous benzene, the liquid phases were combined, and benzene, THF and excess benzyl chloride were distilled off under vacuum finally at 10^{-2} torr. The slightly yellow oil (15 g, 89%) was pure enough for further reactions.

3,5-Dimethyl-1-(2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl)pyrazole (**6a**-α).

Acetylacetone (1.19 g, 11.9 mmoles) in 10 ml of anhydrous ethanol was added to a solution of **5a** (5.1 g, 11.9 mmoles) in 10 ml of anhydrous ethanol at room temperature. The solution became turbid and warm and clarified afterwards. The solvent was evaporated after 2 hours. The yellow oil was purified by column chromatography (silica gel, benzene:acetone = 95:5), yield 3.8 g (64%); tlc (silica gel, benzene:acetone = 95:5), R_F 0.4; ^{1}H-nmr (deuteriochloroform): δ 5.85 (s, 1H, H-4), 5.73 (d, 1H, H-1', $J_{1',2'}$ 4 Hz), 3.65 (mc, 2H, 2H-5'), 2.26, 2.18 (2s, 6H, $2CH_3$).

Anal. Calcd. for $C_{31}H_{34}N_2O_4$ (498.6): C, 74.67; H, 6.87; N, 5.62. Found: C, 74.73; H, 6.78; N, 5.66.

1-(α-D-Arabinofuranosyl)-3,5-dimethylpyrazole (**6b**-α).

One g of Pd-black was hydrogenated in 25 ml of anhydrous methanol. After 2 hours **6a** (3 g, 6.0 mmoles) and 0.8 ml of concentrated hydrochloric acid in 25 ml of anhydrous methanol were added. The mixture was further hydrogenated. After 20 hours, when the hydrogen uptake had ceased, the catalyst was filtered off, the solution was neutralized with ion exchange resin (Amberlite IRA-402, OH^--form) and the resin washed with methanol. The solvent was evaporated and in this way, a colourless syrup was obtained, which slowly crystallized to colourless needles, yield 1.35 g (99%); tlc (silica gel acetone): R_F 0.50; ^{1}H-nmr (methanol-d_4): δ 5.90 (s, 1H, H-4), 5.72 (d, 1H, H-1', $J_{1',2'}$ 3.5 Hz), 3.70 (mc, 2H, 2H-5'), 2.30, 2.16 (2s, 6H, $2CH_3$).

Anal. Calcd. for $C_{10}H_{16}N_2O_4$ (228.2): C, 52.62; H, 7.07; N, 12.27. Found: C, 52.32; H, 6.99; N, 12.10.

3,5-Dimethyl-1-(2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl)pyrazole (**6a**-β).

O-(2,3,5-Tri-*O*-benzyl-α-D-arabinofuranosyl)trichloroacetimidate (0.45 g, 0.8 mmole) and 3,5-dimethyl-*N*-trimethylsilylpyrazole (16.8 mg, 0.9 mmole) in 10 ml of dry dichloromethane was treated with 0.5 ml of a 0.4 *M* boron trifluoride etherate solution in dichloromethane at room temperature. After 2 hours the reaction mixture was treated with an equimolar saturated sodium bicarbonate solution. The organic layer was removed, dried over sodium sulfate, the solvent removed, the residue chromatographed on silica gel (toluene:acetone = 95:5), yield 0.28 g (70%) of a viscous oil; tlc (silica gel, toluene:acetone = 95:5), R_F 0.40; ^{1}H-nmr (deuteriochloroform): δ 5.88 (d, 1H, H-1, $J_{1',2'}$ 5.8 Hz), 5.79 (s, 1H, H-4), 2.20, 2.19 (2s, 6H, $2CH_3$).

Anal. Calcd. for $C_{31}H_{34}N_2O_4$ (498.6): C, 74.67; H, 6.87; N, 5.62. Found: C, 74.54; H, 7.07; N, 5.58.

2-(2,3,5-Tri-*O*-benzyl-α-D-arabinofuranosyl)pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (**11a**).

Compound **5a** (2.0 g, 4.6 mmoles) in 20 ml of anhydrous methanol was added to a solution of 4,6-dichloro-5-formylpyrimidine (815 mg, 4.6 mmoles) in 20 ml of anhydrous methanol at −15°. After the addition of 0.5 ml of triethylamine the mixture was stirred at −15° for 1 hour, then at room temperature for 4 hours, and under reflux for 1 hour. The yellow solution, which consisted of the chloro derivative **10a**, was treated with 3.8 ml of sodium hydroxide (10% in water) and 3 ml of hydrogen peroxide (30% in water) at room temperature. The reaction mixture was first cooled with a water bath, then when the exothermic reaction had ceased it was refluxed for 15 minutes. After neutralisation with 3 *N* hydrochloric acid, the mixture was evaporated, extracted with chloroform, the chloroform layer washed with water, dried with sodium sulfate and again evaporated. The residue was chromatographed on silica gel (benzene:acetone = 60:40), yield 1.3 g (53%) of colourless oil; tlc (silica gel, benzene:acetone = 60:40), R_F 0.56; ^{1}H-nmr (deuteriochloroform): δ 11.40 (s, 1H, NH), 8.42 (s, 1H, H-5), 8.18 (s, 1H, H-3), 6.18 (d, 1H, H-1'), 3.72 (mc, 2H, 2H-5'); uv (methanol): λ max 215 nm (log ε = 4.58), 270 nm (log ε = 4.0), 295 nm (log ε = 3.68).

Anal. Calcd. for $C_{31}H_{30}N_4O_5$ (538.6): C, 69.13; H, 5.61. Found: C, 69.16; H, 5.79.

5-Amino-4-cyano-1-(2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl)pyrazole (**12a**).

Compound **5a** (3.0 g, 6.9 moles) in 20 ml of anhydrous methanol was added to a solution of ethoxymethylenemalonitrile (840 mg, 6.9 mmoles) in 20 ml of anhydrous methanol. The mixture was stirred at room temperature for 48 hours. Afterwards the solvent was removed and the residue chromatographed on silica gel (benzene:acetone = 80:20), yield 3.0 g (85%) of colourless oil; tlc (silica gel, benzene:ether = 50:50), R_F 0.55; ^{1}H-nmr (deuteriochloroform): δ 7.45 (5s, 1H, H-3), 5.76 (d, 1H, H-1', $J_{1',2'}$ 3.5 Hz), 3.60 (mc, 2H, 2H-5').

Anal. Calcd. for $C_{30}H_{30}N_4O_4$ (510.6): C, 70.57; H, 5.92; N, 10.97. Found: C, 70.58; H, 5.99; N, 10.73.

Methyl 5-Amino-1-(2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl)pyrazole-4-carboxylate (**13a**).

Ethoxymethylenemethylcyanoacetate (2.28 g, 14.7 mmoles) in 25 ml of anhydrous methanol was added to a solution of **5a** (6.40 g, 14.7 moles) in 25 ml of anhydrous methanol. The mixture was refluxed for 22 hours, the solvent was evaporated, and the dark yellow oil was chromatographed on silica gel with benzene:methanol = 90:10 and then with carbontetrachloride:methanol = 90:10, yield 7.1 g (89%) of colourless crystals, mp 68° from cyclohexane:*n*-hexane = 2:1; ^{1}H-nmr (deuteriochloroform): δ 7.65 (s, 1H, H-3), 5.80 (d, 1H, H-1', $J_{1',2'}$ 3.4 Hz), 5.06 (dd, 1H, H-2'), 4.13 (dd, 1H, H-3'), 3.78 (s, 3H, OCH_3), 3.60 (mc, 2H, 2H-5').

Anal. Calcd. for $C_{31}H_{33}N_3O_6$ (543.6): C, 68.49; H, 6.12; N, 7.73. Found: C, 68.49; H, 6.25; N, 7.47.

5-Amino-1-(2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl)pyrazole-4-carboxamide (**14a**).

Aminomethylene cyanacetimide (510 mg, 4.6 mmoles) (ref [5]) was added to a solution of **5a** (2.0 g, 4.6 mmoles) in 20 ml of anhydrous ethanol. The mixture was refluxed for 24 hours. The solvent was evaporated and the yellowish residue was chromatographed on silica gel (benzene:acetone = 50:50), yield 0.90 g (73%) of colourless crystals, mp 153° from toluene; tlc (silica gel, benzene:acetone = 50:50), R_F 0.61; ^{1}H-nmr (deuteriochloroform): δ 7.52 (s, 1H, H-3), 5.85 (d, 1H, H-1', $J_{1',2'}$ 3.5 Hz), 3.63 (mc, 2H, 2H-5').

Anal. Calcd. for $C_{30}H_{32}N_4O_5$ (528.6): C, 68.17; H, 6.10; N, 10.60. Found: C, 68.06; H, 6.03; N, 10.86.

4-Amino-1-(2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl)pyrazolo[3,4-*d*]pyrimidine (**15a**).

Compound **12a** (8.5 g, 16.6 mmoles) was heated to 180° under stirring. Formamidinium acetate was added in 200 mg portions every minute until all of **12a** had disappeared. The black reaction mixture was dissolved in benzene, the solution filtered, and the solvent evaporated. The residue was chromatographed on silica gel (chloroform:ethyl acetate = 20:80), yield 7.4 g (83%) of a viscous oil; tlc (silica gel, chloroform:ethyl acetate = 20:80), R_F 0.52; ^{1}H-nmr (deuteriochloroform): δ 8.33 (s, 1H, H-6), 7.82 (s, 1H, H-3), 6.47 (d, 1H, H-1', $J_{1',2'}$ 3.8 Hz), 3.63 (mc, 2H, 2H-5').

Anal. Calcd. for $C_{31}H_{31}N_5O_4$ (537.6): C, 69.25; H, 5.81; N, 13.03. Found: C, 69.43; H, 5.90; N, 13.02.

4-Amino-1-(α-D-arabinofuranosyl)pyrazolo[3,4-*d*]pyrimidine (**15b**).

One g of Pd-black was hydrogenated in 25 ml of methanol for 3 hours. Compound **15a** (2.33 g, 4.06 moles) and 0.5 ml of 9.5 *N* ethanolic hydrogen chloride were added and the mixture again hydrogenated. After 60 hours hydrogen uptake had ceased. The catalyst was filtered off, the solution was neutralized with ion exchange resin (Amberlite IRA 402, OH^--form) and the resin washed with larger quantities of methanol. The solvent was evaporated and the slightly yellow powder recrystallized from methanol, yield 550 mg (51%) of colourless crystals, mp 255°; ^{1}H-nmr (dimethylsulfoxide-d_6): δ 8.32 (s, 2H, H-6 and H-3), 7.80 (s, 2H, NH_2), 6.10 (d, 1H, H-1', $J_{1',2'}$ 4.5 Hz); uv (water): λ max 260 nm.

Anal. Calcd. for $C_{10}H_{13}N_5O_4$ (267.2): C, 44.94; H, 4.90; N, 26.21. Found: C, 45.16; H, 4.91; N, 26.37.

1-(2,3,5-Tri-*O*-benzyl-α-D-arabinofuranosyl)pyrazolo[3,4-*d*]pyrimidin-4-one (**16a**).

Compound **13a** (750 mg, 1.38 mmoles) was treated with formamidinium acetate as described for **15a**. The residue was chromatographed on silica gel (benzene:acetone = 60:40), yield 750 mg (95%) of a slightly yellow, viscous oil; tlc (silica gel, benzene:acetone = 60:40), R_F 0.60; ^{1}H-nmr (deuteriochloroform): δ 8.20 (s, 1H, H-6), 7.92 (s, 1H, H-3), 6.38 (s, 1H, H-1', $J_{1',2'}$ 4 Hz), 3.62 (mc, 2H, 2H-5').

Anal. Calcd. for $C_{31}H_{30}N_4O_5$ (538.6): C, 69.13; H, 5.61; N, 10.40. Found: C, 69.18; H 5.55; N, 10.13.

1-(α-D-Arabinofuranosyl)pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-one (**16b**).

Compound **16a** (500 mg, 0.93 mmole) was hydrogenated as described for **15a**, yield 105 mg (42%) of colourless crystals, mp 244° after desiccation over phosphorus pentoxide; ^{1}H-nmr (deuteriumoxide): δ 8.32 (s, 1H, H-6), 8.25 (s, 1H, H-3), 6.10 (d, 1H, H-1', $J_{1',2'}$ 3.5 Hz); uv (methanol): λ max 254 mm.

Anal. Calcd. for $C_{10}H_{12}N_4O_5$ (268.2): C, 44.78; H, 4.51; N, 20.89. Found: C, 44.70; H, 4.54; N, 21.12.

Ethyl 1-(2,3,5-Tri-*O*-benzyl-α-D-arabinofuranosyl)-1*H*-1,2,4-triazole-3-carboxylate (**18**).

Ethyl oxalate monothioamide (0.27 g, 2.0 mmoles (ref [6]) was added to a solution of **5a** (0.87 g, 2.0 mmoles) in 10 ml of anhydrous dichloromethane at room temperature. After 4 hours the solvent was evaporated, the hydrazone **17** formed as an intermediate was treated with 4 ml of triethylorthoformate in 10 ml of toluene at reflux temperature. After 4 hours

the volatile compounds were evaporated and the residue chromatographed on silica gel (acetone:chloroform = 5:95), yield 0.48 g (44%) of colourless oil; tlc (silica gel, chloroform:acetone = 95:5), R_F 0.64; ^{1}H-nmr (deuteriochloroform): δ 8.42 (s, 1H, H-5), 6.13 (d, 1H, H-1', $J_{1',2'}$ 2.0 Hz).

Anal. Calcd. for $C_{31}H_{33}N_3O_6$ (543.6): C, 68.49; H, 6.12; N, 7.73. Found: C, 68.49; H, 6.05; N, 7.53.

N,N-Dimethyl-*N'*-ethoxymethyleneoxamide (**19**).

The synthesis of **19** follows the procedure given for **20** [6]. From *N,N*-Dimethyloxamide (2.33 g, 20.0 mmoles) and diethoxymethyl triethylaminonium tetrafluoroborate (17.40 g, 60.0 mmoles) (ref [20]) in 30 ml of dichloromethane 2.26 g (66%) of **19** was obtained as a colourless oil (bp 85°, 0.006 torr); ^{1}H-nmr (deuteriochloroform): δ 8.35 (s, 1H, H-α), 4.38 (q, 2H, OCH_2), 3.08, 3.00 (2s, 2H, 2N-CH_3), 1.38 (t, 3H, CH_3).

Anal. Calcd. for $C_7H_{12}N_2O_3$ (172.2): C, 48.83; H, 7.03; N, 16.27. Found: C, 48.48; H, 7.38; N, 16.38.

N,N-Dimethyl 1-(2,3,5-Tri-*O*-benzyl-α-D-arabinofuranosyl)-1*H*-1,2,4-triazole-5-carboxamide (**21**).

N,N-Dimethyl *N'*-ethoxymethyleneoxamide (**19**; 0.86 g, 5.0 mmoles) in 20 ml of anhydrous THF was added to a solution of **5a** (2.17 g, 5.0 mmoles) in 50 ml anhydrous THF at 0°. Compound **19** had disappeared already after 5 minutes. The solvent was evaporated and the residue heated to 120° for 1 hour. The product was chromatographed on silica gel (chloroform:methanol = 96:4), yield 1.32 g (48%) of a colourless oil; tlc (silica gel, chloroform:methanol = 96:4), R_F 0.42; ^{1}H-nmr (deuteriochloroform): δ 8.00 (s, 1H, H-3), 6.60 (d, 1H, H-1', $J_{1',2'}$ 3.2 Hz), 3.06, 3.20 (2s, 6H, $2CH_3$).

Anal. Calcd. for $C_{31}H_{34}N_4O_4$ (542.6): C, 68.62; H, 6.32; N, 10.32. Found: C, 68.86; H, 6.39; N, 10.29.

Ethyl 1-(2,3,5-Tri-*O*-benzyl-α-D-arabinofuranosyl)-1*H*-1,2,4-triazole-5-carboxylate (**22**).

Ethyl *N*-ethoxymethyleneoxalate monoamide (**20**; 0.86 g, 5.0 mmoles) (ref [6]) in 20 ml of anhydrous THF was added to a solution of **5a** (2.17 g, 5.0 mmoles) in 20 ml of anhydrous THF at 0°. After 30 minutes the solvent was evaporated and the residue was heated to 100° for 45 minutes. The product was chromatographed on silica gel (ethyl acetate:petroleum ether (40-60° bp) = 60:40), yield 1.26 g (47%) of a colourless oil; tlc (silica gel, ethyl acetate:petroleum ether = 60:40), R_F 0.62; ^{1}H-nmr (deuteriochloroform): δ 8.08 (s, 1H, H-3), 6.95 (d, 1H, H-1', $J_{1',2'}$ 3.4 Hz), 3.65 (mc, 2H, 2H-5'), 1.43 (t, 2H, CH_3).

Anal. Calcd. for $C_{31}H_{33}N_3O_6$ (543.6): C, 68.49; H, 6.12; N, 7.73. Found: C, 68.68; H, 6.09; N, 7.59.

As a byproduct of this reaction, 220 mg (5%) of **23** was obtained as a colourless oil. The characterization was accomplished by ^{1}H-nmr (deuteriochloroform): δ 8.25 (s, 1H, H-5), 7.95 (s, 1H, H-3), 6.00 (d, 1H, H-1', $J_{1',2'}$ 2 Hz).

Anal. Calcd. for $C_{28}H_{29}N_3O_4$ (471.6): C, 71.32; H, 6.20; N, 8.91. Found: C, 71.46; H, 6.09; N, 8.87.

1-(2,3,5-Tri-*O*-benzyl-α-D-arabinofuranosyl)-1*H*-1,2,4-triazole-5-carboxamide (**24**).

Compound **22** (0.98 g, 1.81 mmoles) was treated with 30 ml of ethanol saturated with ammonia at 0°. After 7 hours at room temperature all **22** had disappeared. The volatile compounds were evaporated, the oily residue crystallized in colourless needles, yield 0.93 g (qu), mp 106-108°; ^{1}H-nmr (deuteriochloroform): δ 8.05 (s, 1H, H-3), 6.48 (d, 1H, H-1', $J_{1',2'}$ 3.5 Hz), 3.70 (mc, 2H, 2H-5').

Anal. Calcd. for $C_{29}H_{39}N_4O_5$ (514.6): C, 67.69; H, 5.88; N, 10.89. Found: C, 67.84; H, 5.96; N, 10.73.

1-(α-D-Arabinofuranosyl)-1*H*-1,2,4-triazole-5-carboxamide (**25**).

Compound **18** (0.54 g, 1.0 mmole) was treated with 20 ml of ethanol saturated with ammonia at 0°. After 6 hours at room temperature all of **18** had disappeared. The volatile compounds were evaporated, the residue was hydrogenated as described for **16b**. The nucleoside **25** obtained crystallized on standing, mp 128-130°, yield 0.19 g (78%). this material was identical with the material obtained according to ref [12] (mixed mp, ^{1}H-nmr).

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