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Fast and efficient microwave synthetic methods for some new 2(1*H*)-pyridone arabinosides

Abstract: Two series of novel 3-cyano-2-(2″,3″,4″-tri-*O*-acetyl-*β*-D-arabinopyranosyloxy)pyridones **5a–h** and **9a,b** were synthesized. Microwave irradiation has been used to obtain these products in high yield under milder conditions by the reaction of 2(1*H*)-pyridone or its salt with an activated arabinose. The silyl method was used to obtain the same nucleosides **5a–h** and **9a,b**. Triethylamine was used to remove the acetyl protecting groups from the sugar moiety and to produce the free nucleosides **6a–h** and **10a,b** in 85–91% yield.

Keywords: microwave; 2-pyridone arabinosides; synthesis.

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Introduction

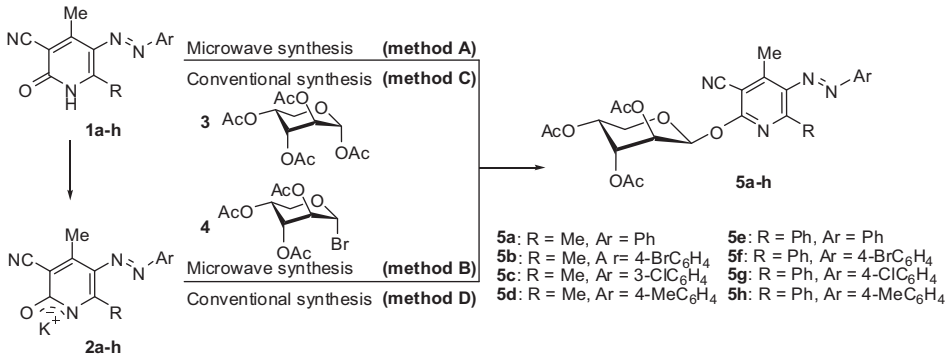
There is great interest in the development of new nucleoside analogs of nucleic acids (Damia and D'Incalci, 2009; De Clercq, 2012; Kale et al., 2012). Some nucleoside analogs have been used in preclinical studies for several therapeutic indications including anticancer activity (Shi and Schinazi, 2001; Kawashima et al., 2011; Chen et al., 2012; Van Poecke et al., 2012).

3-Deazapyrimidine analogs produced significant growth inhibition against L-1210 leukemia cells *in vitro* and have shown antiviral activity against RNA viruses (Abdou and Strekowski, 2000; Shi and Schinazi, 2001; Abdou et al., 2002, 2004; El Sayed et al., 2008). However, the use of some anticancer drugs has led to the development of drug resistance, and some compounds are toxic (Shi and Schinazi, 2001; Reverdito et al., 2012). Consequently, it is essential to discover novel nucleosides as drug candidates that may have low toxicity and more selectivity. Thus, extensive efforts have been conducted on various chemical modifications of nucleoside derivatives through the deletion or change in the nature of the functional groups present on the heterocyclic base or their sugar moieties (Al-Neyadi et al., 2011; Shen et al., 2012; Sun et al., 2012). Varying sugar moieties from D-ribose present in DNA strands to another pentose or hexose have produced modified nucleosides with altered physical and chemical properties. D-Arabinose has been found in the cell wall of mycobacterial species (Briken et al., 2004), and some analogs are the point of attachment of mycolic acids (Brennan and Nikaido, 1995) but a few research groups are interested in using D-arabinose as key starting materials for nucleoside synthesis (Andrzejewska et al., 2002).

Recent reports from our laboratory have described the synthesis of novel pyridine and pyrimidine nucleosides with significant biological and medicinal applications (El-Sayed et al., 2009; Al-Neyadi et al., 2011). D-Arabinose has been the key component for the synthesis of targeted nucleosides. We report here new efficient and convenient ecological methods for the synthesis of a series of novel 2-(*β*-D-arabinopyranosyloxy)pyridine derivatives **5, 6**, **9** and **10**.

Results and discussion

A variety of different modified nucleoside derivatives have been previously synthesized using the classical approaches in solution, which are expensive and time-consuming. In this report we describe new simple, efficient procedures for the synthesis of the target nucleosides **5a–h** and **9a,b**. Four different synthetic strategies to build pyridine nucleosides **5a–h** and **9a,b** were employed, using both new and established methods (Strekowski et al., 2000; El-Sayed et al., 2009) (Schemes 1, 2). Microwave irradiation (methods A and B) was used to obtain the desired products **5a–h, 9a,b** in short time (<10 min) under solvent-free conditions. In method A, silica gel was used as a catalyst to facilitate the reaction between 2(1*H*)-pyridones **1a–h**, **7a–c** and 1,2,3,4-tetra-*O*-acetyl-*α*-D-arabinopyranose (**3**) to produce 3-cyano-2-(2″,3″,4″-tri-*O*-acetyl-*β*-D-arabinopyranosyloxo) pyridines **5a–h** and **9a,b** in 84–91% yields. The same nucleosides **5a–h** and **9a,b** (Schemes 1 and 2) were obtained in high yields under microwave irradiation using the

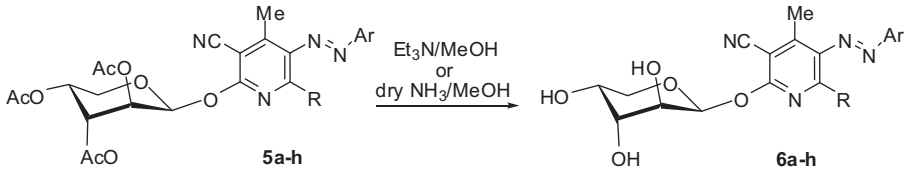


Scheme 1 Synthetic pathways of 2-(tri-*O*-acetyl-*β*-D-arabinopyranosyloxo)pyridines **5a–h**.

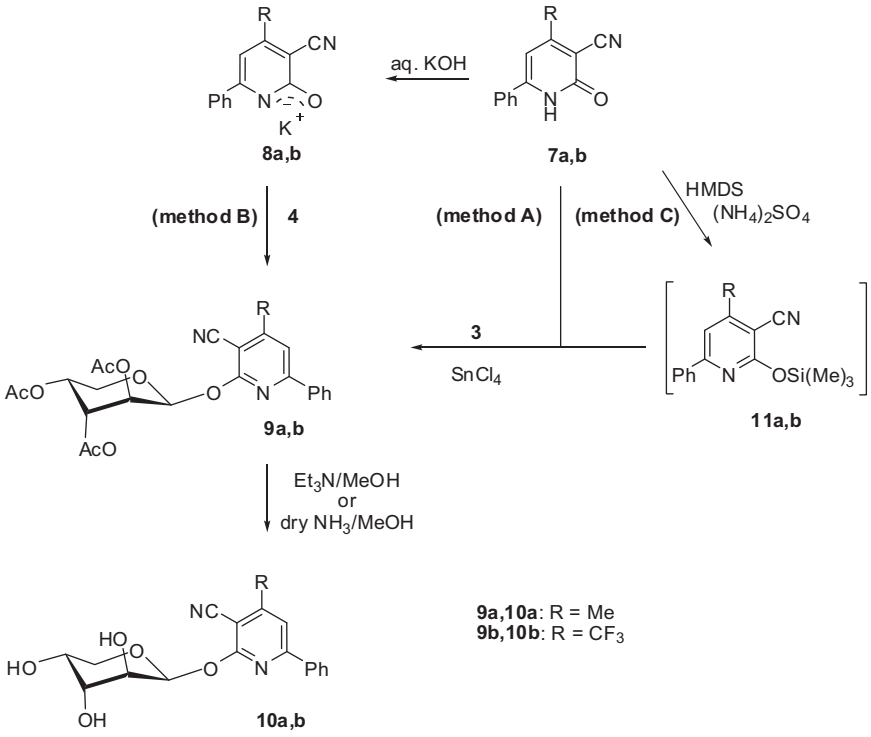
potassium salt of 2(1*H*)-pyridone **2a–h** or **8a,b** and 2,3,5-tri-*O*-acetyl-*α*-D-arabinopyranosyl bromide (**4**) in acetone-DMF (method B). For example, 3-cyano-4-methyl-6-phenyl-5-(4′-chlorophenylazo)-2(1*H*)-pyridone (**1g**) was allowed to react with 2,3,4-tri-*O*-acetyl-*α*-D-arabinopyranosyl bromide (**4**) under microwave irradiation for 2 min to produce 3-cyano-4-methyl-2-(2″,3″,4″-tri-*O*-acetyl-*β*-D-arabinopyranosyloxy)-6-phenyl-5-(4′-chlorophenylazo) pyridine (**5g**) in 88% yield. The same products **5a–h** and **9a,b** can be obtained by using expensive and inconvenient two synthetic methods C and D. In method C, 2(1*H*)-pyridone **1a–h** is allowed to react with hexamethyldisilazane (HMDS) and ammonium sulfate to form a 2-silyloxypyridine intermediate product after 48 h. Then the silyl intermediate is subjected to the reaction *in situ*, under anhydrous conditions, with 1,2,3,4-tetra-*O*-acetyl-*α*-D-arabinopyranose (**3**) in the presence of anhydrous tin(IV)chloride to produce the corresponding product **5a–h**. In method D, 2-pyridone K-salt is a precursor to the same arabinosides **5a–h**. This reaction takes 6 h for completion.

The structures of obtained products **5**, **6, 9** and **10** were established and confirmed on the basis of their elemental analyses and spectral data (MS, IR, 1D and 2D NMR). For example, compound **5g** with a molecular formula $C_{30}H_{27}N_4O_8Cl$ (MS, m/z 606) shows IR absorption at ν 1754 cm^{-1} due to the presence of acetoxy carbonyl groups. The IR spectrum of **5g** does not have a peak that would correspond to the carbonyl carbon at the pyridine C-2, which indicates that the sugar moiety is linked to the pyridine ring through the oxygen atom at C-2 giving *O*-glycoside. The data obtained from ^{1}H NMR spectroscopy support this structure elucidation. Coupling constants were used to establish conformations in solution by the method of averaging of spin-spin coupling (Booth, 1964; Feltkamp and Franklin, 1965; Bozo and Kuszmann, 2000; Andrew and Walter, 2001). The spin-spin coupling $J_{H1'\text{-}H2'}$ < 4 Hz clearly shows that compound **5g** is a *β*-isomer.

The COSY and NOESY spectra were used to assign cross-peak interactions. In compound **5g**, data obtained from NOESY spectrum show that there is no cross-peak interaction between the anomeric proton H-1′ and the *ortho*-aromatic protons at C-2 and C-6, indicating that this compound is an *O*-glycoside. This structural information is supported by analysis of heteronuclear correlation ^{1}H-^{13}C (Ghmbc) chemical shifts. Ghmbc spectral analysis shows that the anomeric proton has cross-peak interactions with C-1′, C-2′ and C-3′ of the sugar moiety, whereas there are no cross-peak interactions between the anomeric proton H-1′ and *ortho*-aromatic carbons at C-2 and C-6. This is further evidence of the formation of *O*-glycoside (Schemes 1–3). Other compounds **5** were analyzed in a similar way.



Scheme 2 Synthesis of 2-(*β*-D-arabinopyranosyloxy)pyridines **6a–h**.



Scheme 3 Synthetic pathways of 2-(*β*-D-arabinopyranosyloxy)pyridines **9a,b** and **10a,b**.

Conclusion

New and efficient methods using microwave irradiation to produce pyridine arabinosides **5a–h** and **9a,b** were described. The solvent-free reaction between 2-pyridones and an acetylated arabinose catalyzed by silica gel produced the targeted products in high yield. The same products **5a–h** and **9a,b** were obtained in high yield under microwave irradiation using an activated sugar in acetone-DMF in the absence of any catalyst. Structures of the obtained products were confirmed using 1D and 2D NMR experiments. ^{1}H ^{1}H NMR and ^{1}H ^{13}C NMR correlations were used to confirm the suggested structures of *O*-nucleoside products **5–10**.

Experimental section

General

Microwave synthesis was conducted using the CEM Microwave system. Melting points were determined on a Gallenkamp apparatus using Pyrex capillaries. Infrared spectra were recorded with a Thermo Nicolet Nexus 470 FT-IR spectrometer using potassium bromide disks. ^{1}H NMR, ^{13}C NMR and 2D NMR spectra were recorded, and the ^{1}H and ^{13}C ^{1}H NMR signals were assigned by means of ^{1}H ^{1}H COSY, NOESY, DEPT, ^{1}H ^{13}C HMQC and ^{1}H ^{13}C HMBC experiments on Varian Gemini spectrometers using Me_4Si as an internal standard. The EI mass spectra were recorded on Shimadzu LCMS-QP 800 LC-MS and AB-4000 Q-trap LC-MS/MS spectrometers. Elemental analysis was obtained from the Central Laboratories Unit (CLU) at United Arab Emirates University. Thin-layer chromatography (TLC) was carried out on precoated Merck silica gel F_{254} plates and UV light was used for visualization. Column chromatography was performed on a Merck silica gel. The reagents were purchased from Aldrich and used without further purification.

General procedure for synthesis of 3-cyano-2-(2″,3″,4″-tri-*O*-acetyl-*β*-D-arabinopyranosyloxy)pyridines **5a–h** and **9a,b**.

Microwave method A A solution of 2(1*H*)-pyridone **1a–h** or **7a,b** (1.0 mmol) and 1,2,3,5-tetra-*O*-acetyl-*α*-D-arabinose (**3**) (0.32 g, 1.0 mmol) in a mixture of dichloromethane/methanol (80:20) was treated with silica gel (200–400 mesh, 1.0 g), and then the solvent was removed by evaporation. The solid residue was transferred into a 10-mL vial and irradiated for 2–3 min using the CEM Microwave system. Purification by flash chromatography (hexanes/EtOAc, 4:1 to 7:3) was used to afford the desired nucleoside products **5a–h** or **9a,b**.

Microwave method B To a solution of 2(1*H*)-pyridone K-salt **2a–h** or **8a,b** (10 mmol) in acetone (5 mL), a solution of 2,3,5-tri-*O*-acetyl-*α*-D-arabinopyranosyl bromide (**4**) (3.79 g, 11 mmol) in acetone (5 mL) was added with stirring at room temperature. The mixture was irradiated for 6–8 min using the CEM Microwave system and then the solvent was removed under reduced pressure. Flash column was used to purify the product using hexanes/EtOAc (4:1–7:3) as eluent to afford the desired products **5a–h** or **9a,b**.

Conventional synthesis method C (silyl method) A mixture of 2(1*H*)-Pyridone **1a–h** or **7a,b** (10.0 mmol), anhydrous hexamethyldisilazane (HMDS) (25 mL) and catalytic amount of ammonium sulfate (0.02 g) was stirred and heated under reflux for 48 h. The excess of HMDS was removed under reduced pressure, providing the silylated base as a colorless oil. To a cold solution of the silylated base in dry MeCN (30 mL) a solution of 1,2,3,5-tetra-*O*-acetyl-α-D-arabinopyranose (**3**) (3.49 g, 11.0 mmol) in dry MeCN (10 mL) was added followed by the addition of tin(IV) chloride (1.60 mL, 13.0 mmol). The mixture was stirred at 0°C for 20 min, then at room temperature for an additional 4–8 h until the reaction was completed as determined by TLC analysis, then poured into saturated $NaHCO_3$ solution (50 mL) and extracted with $CHCl_3$ (3 × 50 mL). The extract was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Silica gel chromatography of the residue eluting with gradient MeOH (0–2%) in $CHCl_3$ afforded pure nucleoside **5a–h** or **9a,b**.

Conventional synthesis method D To a solution of 2(1*H*)-pyridone **1a–h** (10.0 mmol) in DMF (10.0 mL) potassium hydride (1.90 g, 4.76 mmol) was added under a nitrogen atmosphere and the suspension was stirred at 60°C for 2 h. 2,3,4-Tri-*O*-acetyl-*α*-D-arabinopyranosyl bromide (**4**) (4.91 g, 14.5 mmol) was added and the mixture was stirred at room temperature for 19–20 h until the reaction was completed as determined by TLC analysis. The solvent was evaporated and the residue was treated with water (30 mL) and extracted with $CHCl_3$ (3 × 30 mL). The extract was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was subjected to silica gel chromatography (50 g) eluting with gradient MeOH (0–2%) in $CHCl_3$ to afford pure product **5a–h**.

3-Cyano-4,6-dimethyl-2-(2″,3″,4″-tri-*O*-acetyl-*β*-D-arabinopyranosyloxy)-5-phenylazopyridine (5a) Method A, reaction time 3 min, yield 85%; method B, reaction time 7 min, yield 81%; method C, reaction time 53 h, yield 49%; method D, reaction time 20 h, yield 58%; mp 124°C; IR ν 2229 (C≡N), 1750 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.05, 2.10 and 2.17 (3s, 9H, 3 CH_3CO), 2.25 (s, 3H,CH_3), 2.61 (s, 3H,CH_3), 3.76, 3.81 (dd, 1H, H-$5_{a''}$, *J* = 3.8 Hz and 8.4 Hz), 4.15, 4.25 (dd, 1H, H-$5_{b''}$, *J* = 3.8 Hz and 8.4 Hz), 5.31–5.32 (m, 3H, H-2″, H-3″ and H-4″), 6.44 (d, 1H, H-1″, *J* = 2.2 Hz), 7.31–7.89 (m, 5H, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 17.8 (CH_3), 20.9, 20.95 and 21.0 (3 CH_3C=O), 23.0 (CH_3), 59.5 (C-5″), 65.3 (C-4″), 67.4 (C-3″), 68.5 (C-2″), 92.3 (C-1″), 96.8 (C-3), 113.6 (C≡N), 122.5–154.7 (Ar-C), 159.4 (C-2), 168.7, 169.3 and 170.1 (3 C=O); EI-MS: m/z 550 ($M+K^+$). Anal. Calcd for $C_{25}H_{26}N_4O_8$: C, 58.82; H, 5.13; N, 10.97. Found: C, 58.54; H, 5.03; N, 11.02.

3-Cyano-4,6-dimethyl-2-(2″,3″,4″-tri-*O*-acetyl-*β*-D-arabinopyranosyloxy)-5-(4′-bromophenylazo)pyridine (5b) Method A, reaction time 3 min, yield 86%; method B, reaction time 7 min, yield 81%; method C, reaction time 53 h, yield 49%; method D, reaction time 19 h, yield 61%; mp 126°C; IR ν 2230 (C≡N), 1750 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.03, 2. 11 and 2.17 (3s, 9H, 3 CH_3CO), 2.54 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 3.68, 3.72 (dd, 1H, H-$5_{a''}$, *J* = 4.8 Hz and 8.4 Hz), 4.10, 4.15 (dd, 1H, H-$5_{b''}$, *J* = 4.8 Hz and 8.4 Hz), 5.23–5.28 (m, 3H, H-2″, H-3″, H-4″); 6.38 (d, 1H, H-1″, *J* = 2.8 Hz), 7.68 (d, 2H, Ar-H, *J* = 8.8 Hz), 7.61 (d, 2H, Ar-H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.8 (CH_3), 20.8, 20.85 and 20.9 (3 CH_3CO), 23.1 (CH_3), 59.5 (C-5″), 65.3 (C-4″), 67.4 (C-3″), 68.6 (C-2″), 92.5 (C-1″), 97.1 (C-3), 113.7 (C≡N), 124.1–155.5 (Ar-C), 160.0 (C-2), 169.1, 170.0 and 170.5 (3 C=O); EI-MS: m/z 589 ($M+H^+$). Anal. Calcd for $C_{25}H_{25}N_4O_8Br$: C, 50.95; H, 4.28; N, 9.51. Found: C, 51.24; H, 4.34; N, 9.66.

3-Cyano-4,6-dimethyl-2-(2″,3″,4″-Tri-*O*-acetyl-*β*-D-arabinopyranosyloxy)-5-(4′-chlorophenylazo)pyridine (5c) Method A, reaction time 3 min, yield 89%; method B, reaction time 8 min, yield 80%; method C, reaction time 53 h, yield 49%; method D, reaction time 19 h, yield 66%; mp 118°C; IR ν 2230 (C≡N), 1750 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.03, 2.11 and 2.18 (3s, 9H, 3 CH_3CO), 2.54 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 3.69, 3.72 (dd, 1H, H-$5_{a''}$, *J* = 4.0 Hz and 8.4 Hz), 4.10, 4.15 (dd, 1H, H-$5_{b''}$, *J* = 4.0, Hz and 8.4 Hz), 5.23–5.25 (m, 2H, H-2″ and H-4″), 5.27 (d, 1H, H-3″, *J* = 3.2 Hz), 6.38 (d, 1H, H-1″, *J* = 2.8 Hz), 7.44 (d, 2H, Ar-H, *J* = 4.8 Hz); 7.75 (d, 2H, Ar-H, *J* = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.8 (CH_3), 20.8, 2.86 and 20.9 (3 CH_3CO), 23.1 (CH_3), 59.5 (C-5″), 65.3 (C-4″), 67.4 (C-3″), 68.5 (C-2″), 92.5 (C-1″), 97.1 (C-3), 113.7 (C≡N), 123.9–155.5 (Ar-C), 160.0 (C-2), 169.1, 169.7 and 170.5 (3 C=O); EI-MS: m/z 546 ($M+H^+$). Anal. Calcd for $C_{25}H_{25}N_4O_8Cl$: C, 55.10; H, 4.62; N, 10.28. Found: C, 55.02; H, 4.33; N, 9.98.

3-Cyano-4,6-dimethyl-2-(2″,3″,4″-tri-*O*-acetyl-*β*-D-arabinopyranosyloxy)-5-(4′-methylphenylazo)pyridine (5d) Method A, reaction time 3 min, yield 84%; method B, reaction time 8 min, yield 82%; method C, reaction time 53 h, yield 49%; method D, reaction time 19 h, yield 65%; mp 120°C; IR ν 2227 (C≡N), 1749 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.03, 2.12 and 2.17 (3s, 9H, 3 CH_3CO), 2.39 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 3.70, 3.72 (dd, 1H, H-$5_{a''}$, *J* = 2.4, 8.0 Hz), 4.12, 4.15 (dd, 1H, H-$5_{b''}$, *J* = 2.4, 3.6 Hz), 5.23–5.25 (m, 2H, H-3″ and H-4″), 5.27 (t, 1H, H-2″, *J* = 6.4 Hz), 6.36 (d, 1H, H-1″, *J* = 2.8 Hz), 7.27 (d, 1H, Ar-H, *J* = 8.0 Hz); 7.71 (d, 1H, Ar-H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.5 (CH_3), 20.8, 21.0 and 21.6 (3 CH_3CO), 22.8 (CH_3), 29.7 (CH_3), 59.5 (C-5″), 65.4 (C-4″), 67.4 (C-3″), 68.6 (C-2″), 92.4 (C-1″), 96.8 (C-3), 113.8 (C≡N), 122.5–154.9 (Ar-C), 159.6 (C-2), 169.1, 169.9 and 170.5 (3 C=O); EI-MS: m/z 525 ($M+H^+$). Anal. Calcd for $C_{26}H_{28}N_4O_8$: C, 59.54; H, 5.38; N, 10.68. Found: C, 59.33; H, 5.09; N, 10.53.

3-Cyano-4-methyl-2-(2″,3″,4″-tri-*O*-acetyl-*β*-D-arabinopyranosyloxy)-5-phenylazo-6-phenylpyridine (5e) Method A, reaction time 2 min, yield 90%; method B, reaction time 8 min, yield 85%; method C, reaction time 53 h, yield 49%; method D, reaction time 19 h, yield 63%; mp 162°C; IR ν 2229 (C≡N), 1737 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.11, 2.19 and 2.25 (3s, 9H, 3 CH_3CO), 2.61 (s, 3H, CH_3), 3.76, 3.82 (dd, 1H, H-$5_{a''}$, *J* = 4.2 Hz and 8.4 Hz), 4.16, 4.23 (dd, 1H, H-$5_{b''}$, *J* = 4.2 Hz and 8.4 Hz), 5.34–5.35 (m, 3H, H-2″, H-3″ and H-4″), 6.47 (d, 1H, H-1″, *J* = 2.0 Hz), 7.24–7.75 (m, 10H, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 18.3 (CH_3), 20.9, 21.0 and 21.1 (3 CH_3CO), 59.8 (C-5″), 65.5 (C-4″), 67.6 (C-3″), 68.6 (C-2″), 92.7 (C-1″), 97.9 (C-3), 113.7 (C≡N), 122.7–146.8 (Ar-C), 152.0 (C-2), 168.7, 169.2 and 170.1 (3 C=O); EI-MS: m/z 572 (M). Anal. Calcd for $C_{30}H_{28}N_4O_8$: C, 62.93; H, 4.93; N, 9.79. Found: C, 62.76; H, 4.65; N, 9.83.

3-Cyano-4-methyl-2-(2″,3″,4″-tri-*O*-acetyl-*β*-D-arabinopyranosyloxy)-6-phenyl-5-(4′-bromophenylazo)pyridine (5f) Method A, reaction time 2 min, yield 89%; method B, reaction time 7 min, yield 82%; method C, reaction time 55 h, yield 57%; method D, reaction time 20 h, yield 72%; mp 165°C; IR ν 2229 (C≡N), 1742 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.12, 2.19 and 2.26 (3s, 9H, 3 CH_3CO), 2.63 (s, 3H, CH_3), 3.75, 3.82 (dd, 1H, H-$5_{a''}$, *J* = 4.4, 8.2 Hz), 4.18, 4.27 (dd, 1H, H-$5_{b''}$, *J* = 4.4 Hz and 8.2 Hz), 5.31–5.36 (m, 3H, H-2″, H-3″ and H-4″), 6.50 (d, 1H, H-1″, *J* = 1.6 Hz), 7.26–7.70 (m, 9H, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 18.5 (CH_3), 20.9, 21.0 and 21.1 (3 CH_3CO), 59.7 (C-5″), 65.4 (C-4″), 67.5 (C-3″), 68.5 (C-2″), 92.7 (C-1″), 98.0 (C-3),

113.6 (C≡N), 124.1–154.5 (Ar-C), 159.6 (C-2), 168.7, 169.2 and 170.1 (3 C=O); EI-MS: m/z 649 ($M-H^+$). Anal. Calcd for $C_{30}H_{27}N_4O_8Br$: C, 55.31; H, 4.18; N, 8.60. Found: C, 55.42; H, 3.95; N, 8.44.

3-Cyano-4-methyl-2-(2″,3″,4″-tri-*O*-acetyl-β-D-arabinopyranosyloxy)-6-phenyl-5-(4′-chlorophenylazo)pyridine (5g) Method A, reaction time 2 min, yield 91%; method B, reaction time 6 min, yield 84%; method C, reaction time 52 h, yield 58%; method D, reaction time 19 h, yield 77%; mp 146°C; IR ν 2228 (C≡N), 1749 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.13, 2.19 and 2.27 (3s, 9H, 3 CH_3CO), 2.64 (s, 3H,CH_3), 3.77, 3.85 (dd, 1H, H-$5_{a″}$, J = 3.0 Hz and 7.8 Hz), 4.20, 4.30 (dd, 1H, H-$5_{b″}$, J = 3.0 Hz and 7.8 Hz), 5.37–5.38 (m, 3H, H-2″, H-3″ and H-4″), 6.52 (d, 1H, H-1″, J =1.6 Hz), 7.28–7.72 (m, 9H, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 18.5 (CH_3), 20.8, 21.0 and 21.1 (3 CH_3CO), 59.7 (C-5″), 65.4 (C-4″), 67.5 (C-3″), 68.5 (C-2″), 92.7 (C-1″), 97.9 (C-3), 113.6 (C≡N), 123.1–154.5 (Ar-C), 159.6 (C-2), 168.7, 169.5 and 170.1 (3 CO); EI-MS: m/z 606 (M). Anal. Calcd for $C_{30}H_{27}N_4O_8Cl$: C, 59.36; H, 4.48; N, 9.23. Found: C, 59.33; H, 4.54; N, 9.12.

3-Cyano-4-methyl-2-(2″,3″,4″-tri-*O*-acetyl-β-D-arabinopyranosyloxy)-6-phenyl-5-(4′-methylphenylazo)pyridine (5h) Method A, reaction time 2 min, yield 88%; method B, reaction time 8 min, yield 80%; method C, reaction time 56 h, yield 51%; method D, reaction time 19 h, yield 69%; mp 137°C; IR ν 2227 (C≡N), 1751 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.11, 2.20 and 2.25 (3s, 9H, 3 CH_3CO), 2.43 (s, 3H, CH_3), 2.60 (s, 3H, CH_3) 3.74, 3.82 (dd, 1H, H-$5_{a″}$, J = 4.2 Hz and 8.2 Hz), 4.20, 4.30 (dd, 1H, H-$5_{b″}$, J = 4.2 Hz and 8.2 Hz), 5.32–5.36 (m, 3H, H-2″, H-3″ and H-4″), 6.48 (d, 1H, H-1″, J = 2.4 Hz), 7.24–7.76 (m, 9H, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 18.2 (CH_3), 20.9, 20.95 and 21.0 (3 CH_3CO), 21.7 (CH_3), 59.8 (C-5″), 65.5 (C-4″), 67.6 (C-3″), 68.5 (C-2″), 92.6 (C-1″), 97.7 (C-3), 113.6 (C≡N), 122.7–153.7 (Ar-C), 159.3 (C-2), 168.7, 169.5 and 170.1 (3 C=O); EI-MS: m/z 585 ($M-H^+$). Anal. Calcd for $C_{31}H_{30}N_4O_8$: C, 63.47; H, 5.15; N, 9.55. Found: C, 63.32; H, 5.07; N, 9.74.

3-Cyano-4-methyl-2-(2″,3″,4″-tri-*O*-acetyl-β-D-arabinopyranosyloxy)-6-phenylpyridine (9a) Method A, reaction time 3 min, yield 88%; method B, reaction time 6 min, yield 85%; method C, reaction time 53 h, yield 58%. mp 137°C; IR ν 2227 (C≡N), 1740 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.10, 2.19 and 2.23 (3s, 9H, 3 CH_3CO), 2.56 (s, 3H, CH_3), 3.76, 3.80 (dd, 1H, H-$5_{a″}$, J = 3.2 Hz and 8.0 Hz), 4.18, 4.23 (dd, 1H, H-$5_{b″}$, J = 3.2 Hz and 8.0 Hz), 5.32–5.34 (m, 3H, H-2″, H-3″ and H-4″), 6.49 (d, 1H, H-1″, J = 1.6 Hz), 7.38 (s, 1H, pyridine H-5), 7.43–7.48 (m, 3H, Ar-H), 7.95–8.00 (m, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.5 (CH_3), 20.75, 20.8 and 20.9 (3 CH_3CO), 59.8 (C-5″), 65.5 (C-4″), 67.6 (C-3″), 68.6 (C-2″), 92.6 (C-1″), 96.0 (C-3), 114.1 (C≡N), 115.9 (C-5), 127.3–136.8 (Ar-C), 155.6 (C-4), 157.8 (C-6), 161.6 (C-2), 169.1, 170.0 and 170.5 (3 CO); EI-MS: m/z 468 (M). Anal. Calcd for $C_{24}H_{24}N_2O_8$: C, 61.53; H, 5.16; N, 5.98. Found: C, 61.49; H, 4.99; N, 5.95.

3-Cyano-6-phenyl-2-(2″,3″,4″-tri-*O*-acetyl-β-D-arabinopyranosyloxy)-4-trifluromethyl pyridine (9b) Method A, reaction time 2 min, yield 92%; method B, reaction time 4 min, yield 89%, method C; reaction time 49 h, yield 45%. mp 112°C; IR ν 2236 (C≡N), 1744 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.02, 2.10 and 2.17 (3s, 9H, 3 CH_3CO), 3.71, 3.75 (dd, 1H, H-$5_{a″}$, J = 3.2 Hz and 8.0 Hz), 4.12, 4.17 (dd, 1H, H-$5_{b″}$, J = 3.2 Hz and 8.0 Hz), 5.24–5.32 (m, 3H, H-2″, H-3″ and H-4″), 6.48 (d, 1H, H-1″, J = 2.8 Hz), 7.43–7.47 (m, 3H, Ar-H), 7.71 (s, 1H, pyridine H-5), 7.91–7.97 (m, 2H, Ar-H); ^{19}F NMR (376 MHz, $CDCl_3$): δ (-63.89) (s, CF_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7, 20.75 and 20.8 (3 CH_3CO), 59.4 (C-5″), 65.1 (C-4″), 67.2 (C-3″), 68.5 (C-2″), 92.4 (C-3), 93.0 (C-1″), 111.0 (C-5), 111.4 (C≡N), 119.8 (CF_3), 127.7–135.6 (Ar-C), 144.5 (C-4), 160.3 (C-6), 162.6 (C-2); 169.1, 170.1 and 170.5 (3 C=O); EI-MS: m/z 545 ($M+Na^+$). Anal. Calcd for $C_{24}H_{21}F_3N_2O_8$: C, 55.18; H, 4.05; N, 5.36. Found: C, 55.24; H, 4.14; N, 5.45.

General procedure for synthesis of 2-(β-D-arabinopyranosyloxy)-3-cyanopyridines 6a–h and 10a,b

Method E Triethylamine (1.0 mL) was added to a solution of protected arabinosides **5a–h** or **10a,b** (1.0 mmol) in MeOH (10 mL with three drops of water). The mixture was stirred overnight at room temperature and then concentrated under reduced pressure. To remove traces of triethylamine, the residue was treated with MeOH and the mixture was concentrated (2×). The resultant solid was purified using silica gel chromatography eluting with chloroform/methanol (9:1). Analytically pure product **6a–h** or **10a,b** was obtained by crystallization from MeOH.

Method F Dry ammonia gas was passed into a solution of protected arabinosides **5a–h** or **9a,b** (0.5 g) in dry methanol (20 mL) at 0°C for 30 min. The mixture was stirred until the reaction was completed as shown by TLC analysis (chloroform/methanol, 9:1) and then concentrated under reduced pressure to afford a solid residue. The obtained solid was purified using silica gel chromatography eluting with chloroform/methanol (9:1) followed by crystallization from MeOH to furnish analytically pure product **6a–h** or **10a,b**.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4,6-dimethyl-5-phenylazopyridine (6a) Method E, yield 88%; method F, yield 80%; mp 156°C; IR ν 3417 (OH), 2233 (C≡N) cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ 2.63 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 3.55–3.89 (m, 5H, H-2″, H-3″, H-4″ and 5″a,b), 4.80–5.39 (3 OH, exchangeable with D_2O), 6.01 (d, J = 6.4 Hz, H-1″), 7.53–7.95 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 17.6 (CH_3), 23.0 (CH_3), 65.6 (C-5″), 66.9 (C-4″), 69.7 (C-3″), 72.1 (C-2″), 95.9 (C-1″), 97.1 (C-3), 113.8 (C≡N), 121.7–154.3 (Ar-C), 160.4 (C-2); EI-MS: m/z 385 ($M+H^+$). Anal. Calcd for $C_{19}H_{20}N_4O_5$: C, 59.37; H, 5.24; N, 14.58. Found: C, 59.26; H, 5.09; N, 14.81.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4,6-dimethyl-5-(4′-bromophenylazo)pyridine (6b) Method E, yield 88%; method F, yield 82%; mp 215°C; IR ν 3405 (OH), 2232 (C≡N) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 2.60 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 3.55–3.83 (m, 2H, H-2″, H-3″, H-4″ and 2H-5″), 4.80–5.37 (3 OH, exchangeable with D_2O), 5.97 (d, H-1″, J = 6.8 Hz), 7.71–7.84 (m, 4H, Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 17.5 (CH_3), 23.0 (CH_3), 65.5 (C-5″), 66.8 (C-4″), 69.6 (C-3″), 72.1 (C-2″), 96.1 (C-1″), 97.2 (C-3), 113.9 (C≡N), 123.7–155.1 (Ar-C), 160.9 (C-2); EI-MS: m/z 462 (M). Anal. Calcd for $C_{19}H_{19}N_4O_5Br$: C, 49.26; H, 4.13; N, 12.09. Found: C, 49.24; H, 4.06; N, 12.33.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4,6-dimethyl-5-(4′-chlorophenylazo)pyridine (6c) Method E, yield 90%; method F, yield 88%; mp 201°C; IR ν 3375 (OH), 2234 (C≡N) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 2.60 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 3.35–3.82 (m, 5H,

H-2″, H-3″, H-4″ and 2 H-5″), 4.80–5.36 (3 OH, exchangeable with D_2O), 5.97 (d, H-1″, J = 6.8 Hz), 7.70 (d, 2H, Ar-H, J = 8.8 Hz), 7.92 (d, 2H, Ar-H, J = 8.8 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 17.5 (CH_3), 22.9 (CH_3), 65.5 (C-5″), 66.8 (C-4″), 69.6 (C-3″), 72.1 (C-2″), 96.1 (C-1″), 97.2 (C-3), 113.8 (C≡N), 124.1–155.1 (Ar-C), 160.9 (C-2); EI-MS: m/z 457 ($M+K^+$). Anal. Calcd for $C_{19}H_{19}N_4O_5Cl$: C, 54.49; H, 4.57; N, 13.38. Found: C, 54.71; H, 4.62; N, 13.19.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4,6-dimethyl-5-(4′-methylphenylazo)pyridine (6d) Method E, yield 89%; method F, yield 85%; mp 210°C; IR ν 3378 (OH), 2233 (C≡N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.47 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 3.61–3.88 (m, 5H, H-2″, H-3″, H-4″ and 2 H-5″), 4.84–5.42 (3 OH, exchangeable with D_2O), 6.01 (d, H-1″, J = 6.8 Hz), 7.49 (d, 2H, Ar-H, J = 8.4 Hz), 7.86 (d, 2H, Ar-H, J = 8.4 Hz); ^{13}C NMR (100 MHz, DMSO-d_6): δ 17.8 (CH_3), 21.5 (CH_3), 23.2 (CH_3), 66.1 (C-5″), 67.4 (C-4″), 70.2 (C-3″), 72.7 (C-2″), 96.5 (C-1″), 97.7 (C-3), 114.5 (C≡N), 122.9–154.9 (Ar-C), 161.1 (C-2); EI-MS: m/z 398 (M). Anal. Calcd for $C_{20}H_{22}N_4O_5$: C, 60.29; H, 5.57; N, 14.06%. Found: C, 60.12; H, 5.76; N, 14.28%.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4-methyl-6-phenyl-5-phenylazopyridine (6e) Method E, yield 91%; method F, yield 84%; mp 134°C; IR ν 3429 (OH), 2230 (C≡N) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 2.55 (s, 3H, CH_3), 3.30–3.93 (m, 5H, H-2″, H-3″, H-4″ and 2H-5″), 4.84 (d, OH, J = 4.4 Hz), 4.94 (d, OH, J = 5.2 Hz), 5.43 (d, OH, J = 5.2 Hz, exchangeable with D_2O), 6.08 (d, H-1″, J = 6.2 Hz), 7.45–7.78 (m, 10H, Ar-H); ^{13}C NMR (50 MHz, DMSO-d_6): δ 17.9 (CH_3), 65.5 (C-5″), 66.8 (C-4″), 69.7 (C-3″), 72.1 (C-2″), 97.0 (C-1″), 97.3 (C-3), 113.8 (C≡N), 122.2–153.2 (Ar-C), 160.3 (C-2). Anal. Calcd for $C_{24}H_{22}N_4O_5$: C, 64.57; H, 4.97; N, 12.55. Found: C, 64.71; H, 4.78; N, 12.39.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4-methyl-6-phenyl-5-(4′-bromophenylazo)pyridine (6f) Method E, yield 89%; method F, yield 82%; mp 140°C; IR ν 3416 (OH), 2232 (C≡N) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 2.54 (s, 3H, CH_3), 3.30–3.87 (m, 5H, H-2″, H-3″, H-4″ and 2H-5″), 4.85 (d, OH, J = 6.2 Hz, exchangeable with D_2O), 4.95 (d, OH, J = 5.6 Hz, exchangeable with D_2O), 5.43 (d, OH, J = 5.2 Hz, exchangeable with D_2O), 6.09 (d, H-1″, J = 6.2 Hz), 7.50–7.87 (m, 9H, Ar-H); ^{13}C NMR (50 MHz, DMSO-d_6): δ 18.1 (CH_3), 65.5 (C-5″), 66.8 (C-4″), 69.7 (C-3″), 72.0 (C-2″), 97.1 (C-1″), 97.4 (C-3), 113.7 (C≡N), 124.1–153.6 (Ar-C), 160.5 (C-2). Anal. Calcd for $C_{24}H_{21}N_4O_5Br$: C, 54.87; H, 4.03; N, 10.66. Found: C, 55.13; H, 4.33; N, 10.80.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4-methyl-6-phenyl-5-(4′-chlorophenylazo)pyridine (6g) Method E, yield 85%; method F, yield 84%; mp 155°C; IR ν 3403 (OH), 2236 (C≡N) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 2.54 (s, 3H, CH_3), 3.32–3.92 (m, 5H, H-2″, H-3″, H-4″ and 2H-5″), 4.84 (d, OH, J = 6.2 Hz, exchangeable with D_2O), 4.94 (d, OH, J = 5.0 Hz, exchangeable with D_2O), 5.43 (d, OH, J = 5.0 Hz, exchangeable with D_2O), 6.08 (d, H-1″, J = 6.4 Hz), 7.48–7.75 (m, 9H, Ar-H); ^{13}C NMR (50 MHz, DMSO-d_6): δ 18.1 (CH_3), 65.5 (C-5″), 66.8 (C-4″), 69.7 (C-3″), 72.1 (C-2″), 97.1 (C-1″), 97.4 (C-3), 113.8 (C≡N), 123.9–153.7 (Ar-C), 160.5 (C-2); EI-MS: m/z 503 ($M+Na^+$). Anal. Calcd for $C_{24}H_{21}N_4O_5Cl$: C, 59.94; H, 4.40; N, 11.65. Found: C, 59.89; H, 4.25; N, 11.52.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4-methyl-6-phenyl-5-(4′-methylphenylazo)pyridine (6h) Method E, yield 88%; method F, yield 81%; mp 131°C; IR ν 3409 (OH), 2231 (C≡N) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 2.38 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 3.36–3.81 (m, 5H, H-2″, H-3″, H-4″ and 2H-5″), 4.79 (d, OH, J = 4.2 Hz, exchangeable with D_2O), 4.89 (d, OH, J = 3.6 Hz, exchangeable with D_2O), 5.37 (d, OH, J = 3.0 Hz, exchangeable with D_2O), 6.02 (d, H-1″, J = 6.2 Hz), 7.33–7.61 (m, 9H, Ar-H); ^{13}C NMR (50 MHz, DMSO-d_6): δ 17.9 (CH_3), 21.2 (CH_3), 65.5 (C-5″), 66.8 (C-4″), 69.7 (C-3″), 72.1 (C-2″), 97.0 (C-1″), 97.3 (C-3), 113.8 (C≡N), 122.3–152.9 (Ar-C), 160.5 (C-2); EI-MS: m/z 561 ($M+H^+$). Anal. Calcd for $C_{25}H_{24}N_4O_5$: C, 65.21; H, 5.25; N, 12.17. Found: C, 65.09; H, 5.35; N, 12.28.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4-methyl-6-phenylpyridine (10a) Method E, yield 88%; method F, yield 80%; mp 151°C; IR ν 3426 (OH), 2222 (C≡N) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 2.50 (s, 3H, CH_3), 3.64–3.88 (m, 5H, H-2″, H-3″, H-4″ and 2H-5″), 4.76–5.35 (3 OH, exchangeable with D_2O), 6.06 (d, H-1″, J = 6.6 Hz), 7.44–7.54 (m, 3H, Ar-H), 7.80 (s, 1H, pyridine H-5), 8.01–8.16 (m, 2H, Ar-H); ^{13}C NMR (50 MHz, DMSO-d_6): δ 20.1 (CH_3), 65.6 (C-5″), 67.0 (C-4″), 69.7 (C-3″), 72.3 (C-2″), 94.8 (C-1″), 96.9 (C-3), 114.2 (C≡N), 115.2 (C-5), 126.9–136.1 (Ar-C), 155.7 (C-4), 156.1 (C-6), 161.8 (C-2); EI-MS: m/z 365 ($M+Na^+$). Anal. Calcd for $C_{18}H_{18}N_2O_5$: C, 63.15; H, 5.30; N, 8.18. Found: C, 63.13; H, 5.34; N, 8.20.

2-(β-D-Arabinopyranosyloxy)-3-cyano-4-methyl-6-trifluromethylpyridine (10b) Method E, yield 88%; method F, yield 80%; mp 141°C; IR ν 3409 (OH), 2223 (C≡N) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ 3.54–3.83 (m, 5H, H-2″, H-3″, H-4″ and 2 H-5″), 4.75–5.35 (3 OH, exchangeable with D_2O), 5.96 (d, J = 6.6 Hz, H-1″), 7.50–7.52 (m, 3H, Ar-H), 7.79 (s, 1H, pyridine H-5), 8.11–8.13 (m, 2H, Ar-H); ^{19}F NMR (376 MHz, $CDCl_3$): δ (-61.42) (s, CF_3); EI-MS: m/z 419 ($M+Na^+$). Anal. Calcd for $C_{18}H_{15}F_3N_2O_5$: C, 54.55; H, 3.81; N, 7.07. Found: C, 54.49; H, 3.75; N, 6.98.

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References

Abdou, I. M.; Strekowski, L. A facile synthesis of 6-aryl-5-cyano-1-(β-D-pyranosyl or β-D-furanosyl)-2-thiocytosines. *Tetrahedron* **2000**, *56*, 8613–8636.

Abdou, I. M.; Attia, A. M.; Strekowski, L. Glucopyranosides derived from 6-aryl-5-cyano-2-(methylthio)pyrimidin-4(3*H*)-ones. *Nucleos. Nucleot. Nucl. Acids* **2002**, *21*, 15–21.

Abdou, I. M.; Saleh, A. M.; Zohdi, H. F. Synthesis and antitumor activity of 5-trifluoromethyl-2,4-dihydropyrazol-3-one nucleosides. *Molecules* **2004**, *9*, 109–116.

Al-Neyadi, S.; Hassan, A.; Abdou, I. M. Microwave-assisted synthesis of 2(1*H*)-pyridones and their glucosides as cell proliferation inhibitors. *Nucleos. Nucleot. Nucl. Acids* **2011**, *30*, 120–134.

Andrew, R. V.; Walter, A. S. An examination of the purported reverse anomeric effect beyond acetylated *N*-xylosyl- and *N*-glucosylimidazoles. *J. Org. Chem*. **2001,** *66,* 1097–1102.

Andrzejewska, M.; Kanninski, J.; Kazimierczuk, Z. Microwave induced synthesis of ribonucleosides on solid support. *Nucleos. Nucleot. Nucl. Acids* **2002,** *21*, 73–78.

Booth, H. The average coupling constants of protons on adjacent carbon atoms in mobile cyclohexane systems. *Tetrahedron* **1964**, *20*, 2211–2216.

Bozo, E.; Kuszmann, J. Synthesis of 4-cyanophenyl and 4-nitrophenyl 2-azido-2-deoxy-1,5-dithio-*β*-D-arabino- and -*β*-D-lyxopyranosides possessing antithrombotic activity *Carbohydr. Res*. **2000**, *325*, 143–149.

Brennan, P. J.; Nikaido, H. The envelope of mycobacteria. *Annu. Rev. Biochem*. **1995**, *64*, 29–63.

Briken, V.; Porcelli, S. A.; Besra, G. S.; Kremer, L. Mycobacterial lipoarabinomannan and related lipoglycans: from biogenesis to modulation of the immune response. *Mol. Microbiol*. **2004**, *53*, 391–403.

Chen, L.; Ming, X.; Da Cen, J. Improved and practical synthesis of 2-deoxy-L-ribose by hypophosphite-mediated deoxygenation. *Synth. Commun*. **2012**, *42*, 1–7.

Damia, G.; D'Incalci, M. Contemporary pre-clinical development of anticancer agents – what are the optimal preclinical models? *Eur. J. Cancer* **2009**, *45*, 2768–2781.

De Clercq, E. Ten paths to the discovery of antivirally active nucleoside and nucleotide analogues. *Nucleos. Nucleot. Nucl. Acids* **2012**, *31*, 339–352.

El-Sayed, H. A.; Moustafa, A. H.; Haikal, A. Z.; Abdou, I. M.; El-Ashry, E. S. H. Synthesis and evaluation of antimicrobial activity of some pyrimidine glycosides. *Nucleos. Nucleot. Nucl. Acids* **2008**, *27*, 1061–1071.

El-Sayed, H. A.; Moustafa, A. H.; Haikal, A. Z.; El-Ashry, E. H. Synthesis and antibacterial activity of some glucosyl- and ribosyl-pyridazin-3-ones. *Nucleos. Nucleot. Nucl. Acids* **2009**, *28*, 184–192.

Feltkamp, H.; Franklin, N. C. The conformational free energy (*ΔG*) of the nitro group. *J. Am. Chem. Soc*. **1965**, *87*, 1616–1617.

Kale, R.; Prasad, V.; Kushwaha, D.; Tiwari, K. Facile synthesis of glycosyl tetrazole using benzotriazole methodology. *J. Carbohydr. Chem*. **2012**, *31*, 130–142.

Kawashima, E.; Ohba, Y.; Terui, Y.; Kamaike, K. Synthesis and evaluation of oligonucleotide-conjugated pyrrole polyamide-2′-deoxyguanosine hybrids as novel gene expression control compounds. *Nucleos. Nucleot. Nucl. Acids* **2011**, *30*, 850–872.

Reverdito, M.; Perillo, A.; Salerno, A. Synthesis and synthetic applications of 1-aryl-2-alkyl-4,5-dihydro-1H-imidazoles. *Synth. Commun*. **2012**, *42*, 2083–2097.

Shen, C.; Tseng, C.; Tasi, C.; Shintre, S.; Chen, L.; Sun, C. Traceless polymer-supported divergent synthesis of quinoxalinones by microwave irradiation. *Tetrahedron* **2012**, *68*, 3532–3540.

Shi, J.; Schinazi, R. Asymmetric synthesis of carbocyclic pyrimidine nucleosides via pi-allylpalladium complex. *Nucleos. Nucleot. Nucl. Acids* **2001**, *20*, 1367–1370.

Strekowski, L.; Abdou, I. M.; Attia, M. E.; Patterson, S. The first direct ammonolysis of 2-thiouracil nucleosides to 2-thiocytosine nucleosides. *Tetrahedron Lett*. **2000**, *41*, 4757–4761.

Sun, X.; Zhou, J.; Zhi, J. Efficient one-pot synthesis of tetrahydrobenzo[c]xanthene-1,11-dione derivatives under microwave irradiation. *Synth. Commun*. **2012**, *42*, 1987–1994.

Van Poecke, S.; Sinnaeve, D.; Martins, C.; Balzarini, J.; Calenbergh, S. Synthesis of 5-substitued 2′-deoxyuridine-5′-phosphonate analogues and evaluation of their antiviral activity. *Nucleos. Nucleot. Nucl. Acids* **2012**, *31*, 256–272.