A novel anthranilic acid based multi-component strategy for expeditious synthesis of 4(3*H*)-quinazolinone *N*-nucleosides

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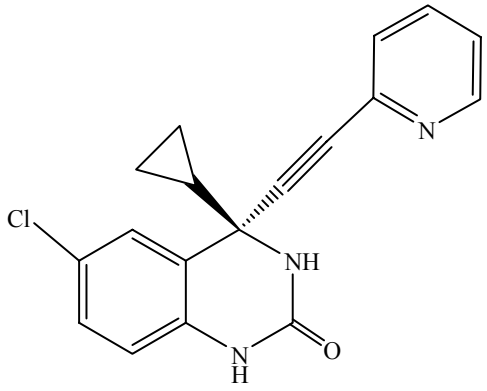
Abstract

A one-pot montmorillonite K-10 clay-supported, three-component reaction of an substituted / unsubstituted anthranilic acid, ribosylamine and a substituted / unsubstituted benzoic acid expeditiously and rapidly yields a 2-aryl-3-(*β*-D-ribofuranosyl)-3H-quinazolin-4-one as a novel *N*-nucleoside in excellent yield using microwave irradiation under solvent-free conditions.

Keywords: Mineral supported, microwaves, solvent-free, quinazolinone *N*-nucleosides, anthranilic acid

Introduction

The development of resistance to inhibition by antiviral agents presently in clinical use has created the need for a new class of inhibitors and this has led to the investigation of quinazolinones.[1-2] Recently quinazolinones have gained recognition as they exhibit anti-HIV activity. 6-Chloro-(4*S*)-cyclopropyl-3,4-dihydro-4(2-pyridyl)ethynylquinazolin-2(1*H*)-one **1**, a novel structural class of non-nucleoside inhibitors of HIV-1 reverse transcriptase (RT), displays synergistic inhibition of RT activity with AZT triphosphate.[3] The fight against HIV, by developing more efficacious drugs has been the prime driving force for the development of a green protocol for the synthesis of 4-(3*H*)-quinazolinone *N*-nucleosides.



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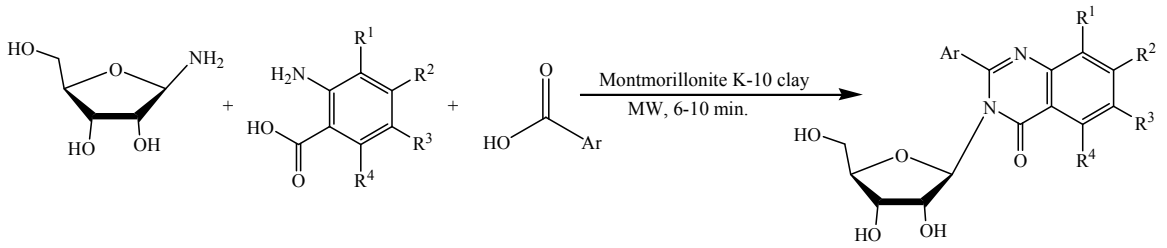
Notably, most available drugs approved by the FDA to treat AIDS patients include protease inhibitors and nucleoside analogues. However, no attempt has been made so far to synthesize nucleoside analogues incorporating a 4(3*H*)-quinazolinone unit as a nucleobase although they appear to be attractive scaffolds for exploiting chemical diversity and generating a drug-like library to screen for lead candidates.

With increasing global environmental concerns, the application of eco-friendly reagents, solid-state procedures, solvent-free reactions, microwave (MW) irradiation techniques[4] and recyclable, less expensive mineral supports for organic transformations has increased dramatically in recent years since the use of expensive and hazardous organic solvents and reagents can be significantly reduced. One-pot multicomponent reactions (MCRS) have gained significant importance in drug discovery processes.[5-11] The application of MW irradiation in conjunction with the use of mineral-supported reagents under solvent-free conditions in a one-pot reaction provides chemical processes with special attributes such as enhanced reaction rates, higher yields of pure products, better selectivity, improved ease of manipulation, rapid optimization of reactions in parallel and several eco-friendly advantages in the context of green chemistry.[12-15] The objective of the present work is to enhance drug-discovery in the form of the development of a general green synthesis of 2-substituted-4(3*H*)-quinazolinone *N*-nucleosides, a novel potent HIV-1 reverse transcriptase inhibitor scaffold from readily available materials.

Prompted by the above mentioned reports and in pursuing our work on new solvent-free cyclization procedures,[16-20] we devised an original and novel montmorillonite K-10 clay-catalysed MW-activated synthesis of 2-aryl-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-ones **5** from a substituted/ unsubstituted anthranilic acid **3,** ribosylamine **2** and a substituted/ unsubstituted benzoic acid **4** in a one-pot reaction.(Scheme1).



2 **3** **4** **5**

Scheme 1

Compd	Ar	R^1	R^2	R^3	R^4
5a	C_6H_5	H	H	H	H
5b	C_6H_5	OCH_3	H	H	H
5c	C_6H_5	H	Cl	H	H
5d	C_6H_5	H	H	Br	H
5e	C_6H_5	H	H	H	NO_2
5f	4-Cl -C_6H_4	H	H	H	H
5g	4-Cl-C_6H_4	OCH_3	H	H	H
5h	4-Cl-C_6H_4	H	Cl	H	H
5i	4-Cl-C_6H_4	H	H	Br	H
5j	4-Cl-C_6H_4	H	H	H	NO_2

Results and Discussion

The results obtained from the clay-catalysed synthesis of 2-aryl-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-ones **5a-j** under MW irradiation and solvent-free conditions in a one-pot process are summarized in Table 1.

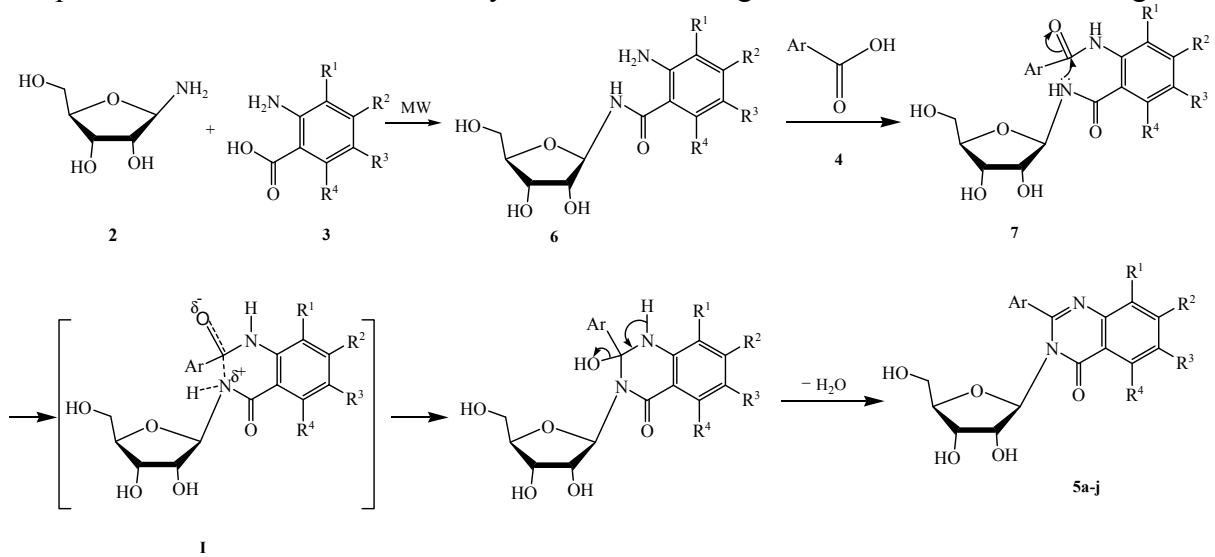
An aromatic acid, anthranilic acid and ribosylamine adsorbed onto K-10 clay were subjected to MW irradiation for the time specified in Table 1, and it was found that the envisaged three-component synthesis (Scheme 1) was successful. Experiments were completed within 6-10 min. as monitored by TLC showing the disappearance of the starting materials.

Spectral analysis of **5a-j** supported the success of the MW-mediated triple one-pot condensation. The ^{1}H NMR spectra of **5 a-j** exhibited aromatic double doublets in the region δ 7.00-8.25 with coupling constants of 8.3 Hz and 2.4 Hz. Multiplets in the region δ 7.29-7.92 for aryl substituents at position-2 were indicative of 4-(3*H*)-quinazolin-4-ones. Multiplets in the region δ 3.66-3.92 due to H-2′, H-3′, H-4′ and H-5′ as well as a doublet at δ 4.64-4.80 with *J*= 4.3 Hz for the anomeric proton as well as a broad singlet at δ 2.00 exchangeable with D_2O due to three–OH groups were indicative of the presence of *β*-D- ribofuranosyl moiety in **5 a-j**. In the ^{13}C NMR spectra, signals in the region δ 122-133 for aromatic carbons, δ 152-153 and δ 164-

168 for C=N, and δ 170-176 for the C=O of the heterocyclic ring as well as signals in the region δ 61.9-84.5 for the sugar carbons supported the formation of **5 a-j**.

For comparison purposes, the temperature was measured by immersing a glass thermometer into the reaction mixture immediately after MW irradiation and was found to be < 95°C. The reactions were also carried out using a thermostated oil-bath at the same temperature (95°C) as for the MW-activated method but for a longer period of time (Table 1) to ascertain whether the MW and montmorillonite combination truly improved the yield or simply increased conversion rates. It was found that with the oil-bath heating method significant lower yields (53-56%) were obtained in comparison to the MW-activated method (Table 1). The MW-activated reactions were cleaner than the corresponding conventional oil-bath reactions. These observations may be rationalized on the basis of the fact that fast, non-contact (super) MW heating of the reaction mixture on a mineral support results in an increase in reaction rate and in an improved yield. Formation of the dipolar activated complex **I** from uncharged adduct (Scheme 2) and greater stabilization of the more polar activated complex by dipole-dipole interaction with electromagnetic field of the microwaves may reduce the activation energy ($\Delta G^{\#}$) resulting in rate enhancement.

In conclusion, we have developed an original mineral-supported facile, inexpensive, high yielding, environmentally benign protocol for the preparation of novel potential anti-HIV reverse transcriptase inhibitors from readily available materials under solvent-free MW irradiation conditions. The amino sugar used in the synthesis was prepared by MW-induced reaction of *β*-D-ribofuranose with $(NH_4)_2CO_3$.[21] The present expeditious and eco-friendly organic transformation has led to synthetically readily manipulable products and may find application in library synthesis of compounds of this structural class. Furthermore this method offers advantages in terms of avoiding protection of sugar functionalities during glycosylation. The present method is an important addition to MW-assisted synthetic methodologies and offers several advantages.



Scheme 2

Experimental Section

General Procedures. Melting points were determined using an open-glass capillary method and are uncorrected. All chemicals used were reagent grade and were used as received without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz on a Bruker AVANCE DPX (400 MHz) FT spectrometer in DMSO-d_6 using TMS an internal reference. Mass spectra were recorded on a JEOL SX-102 (FAB) mass spectrometer at 70 eV. A laboratory Microwave oven (Model BP 310/ 50) operating at 2450 MHz and power output of 600 W was used for all the experiments. Elemental analyses were carried out using a Coleman automatic C, H and N analyzer. The progress of the reaction was monitored by TLC (Merck silica-gel).

Microwave-induced synthesis of 2-aryl-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleosides 5a-j

To a solution of ribosylamine **2** (5.0 mmol), substituted/ unsubstituted anthranilic acid **3** (5.0 mmol) and aromatic acid **4** (5.0 mmol) in DCM (10 mL) was added montmorillonite K-10 clay (0.50 g) with thorough mixing and the solvent then evaporated under reduced pressure. The contents were loaded into a 20 mL vial and subjected to microwave irradiation at 600 W for 2 min. The reaction mixture was then thoroughly mixed outside the microwave for 2 min. and again irradiated for another 2 min. This irradiation-mixing cycle was repeated for the total irradiation time (Table 1). After completion of the reaction as indicated by TLC (Hexane: AcOEt; 8:2, v/v), the product was extracted with DCM (3x50 mL) and the extract was filtered. The filtrate was evaporated under reduced pressure and the final product was recrystallised from ethanol to obtain analytically pure sample of **5a-j**.

Thermal synthesis of 2-aryl-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleosides 5 a-j. Montmorillonite K-10 clay (0.50 g) was added to a solution of ribosylamine **2** (5.0 mmol), substituted/ unsubstituted anthranilic acid **3** (5.0 mmol) and aromatic acid **4** (5.0 mmol) in DCM (50 mL) with constant stirring and the reaction mixture was refluxed on thermostated oil-bath at 95^{o}C for the time specified in Table 1.

Table 1. Mineral supported solvent-free synthesis of 2-aryl-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleosides **5a-j**

Product	Time		Yield (%)		Mp (°C)
	MW (min)	Thermal (h)	MW	Thermal	
5a	7	5	84	55	130-131
5b	8	6	83	53	138-139
5c	6	4	86	56	140-141
5d	7	5	85	55	143-144
5e	6	4	88	55	150-151
5f	6	4	87	54	155-156
5g	10	6	80	50	158-159
5h	8	6	81	52	159-160
5i	8	5	82	53	160-161
5j	6	5	88	55	162-163

After completion of the reaction as indicated by TLC, the reaction mixture was cooled and solvent was evaporated under reduced pressure. The solid product thus obtained was extracted with DCM (3x 50 mL) and filtered. The filtrate was evaporated under reduced pressure and the final product was recrystallised from ethanol to give pure **5a-j**.

2-Phenyl-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleoside (5a). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H, 3′-H, 2 x 5′-H), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.29-7.60 (m, 5H, -C_6H_5), 7.40 (dd, 1H, *J*= 8.3 Hz and 2.4 Hz, 8-H), 7.40-7.50 (dd, 2H, *J* = 8.3 Hz and 2.4 Hz, 6-H, 7-H), 7.90 (dd, 1H, *J* = 8.3 Hz and 2.4 Hz, 5-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 122.1 (8-C), 125.9-132.9 (C_6H_5), 127.0 (4a-C), 127.1 (6-C), 128.6 (5-C), 133.2 (7-C), 152.0 (8a-C), 164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{19}H_{18}N_2O_5$: C, 64.40; H, 5.12; N, 7.91. Found: C, 64.38; H, 5.10; N, 7.88. MS (FAB) *m/z*: 354 (M^+).

2-Phenyl-8-methoxy-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleoside (5b). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H, 3′-H, 2 x 5′-H), 3.73 (s, 3H, -OCH_3), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.29-7.60 (m, 5H, -C_6H_5), 7.30 (dd, 1H, *J*= 8.3 Hz, 6-H), 7.50 (dd, 1H, *J* = 8.3 Hz and 2.4 Hz, 5-H), 8.73 (dd, 1H, *J* = 8.3 Hz and 2.4 Hz, 7-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.3 (OCH_3), 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 118.8 (7-C), 120.9 (5-C), 125.9-132.9 (C_6H_5), 127.1 (6-C), 128.0 (4a-C), 137.6 (8a-C), 155.6 (8-C), 164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{20}H_{20}N_2O_6$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.45; H, 5.22; N, 7.27. MS (FAB) *m/z*: 384 (M^+).

2-Phenyl-7-chloro-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleoside (5c). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H,

3′-H, 2 x 5′-H), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.29-7.60 (m, 5H, -C_6H_5), 7.40 (d, 1H, *J*= 2.4 Hz, 8-H), 7.40-7.50 (dd, 1H, *J* = 8.3 Hz and 2.4 Hz, 6-H), 7.90 (d, 1H, *J* = 8.3 Hz, 5-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 122.5 (8-C), 125.1 (4a-C), 125.9-132.9 (C_6H_5), 127.1 (6-C), 130.0 (5-C), 138.5 (7-C), 153.4 (8a-C) ,164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{19}H_{17}ClN_2O_5$: C, 58.69; H, 4.41; N, 7.21. Found: C, 58.66; H, 4.20; N, 7.20. MS (FAB) *m/z*: 388 (M^+).

2-Phenyl-6-bromo-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleoside (5d). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H, 3′-H, 2 x 5′-H), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.29-7.60 (m, 5H, -C_6H_5), 7.30 (d, 1H, *J*= 8.3 Hz, 8-H), 7.70 (dd, 1H, *J* = 8.3 Hz and 2.4 Hz, 7-H), 8.10 (d, 1H, *J* = 2.4 Hz, 5-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 121.7 (6-C), 124.3 (8-C), 125.9-132.9 (C_6H_5), 129.2 (4a-C), 131.9 (5-C), 136.5 (7-C), 151.0 (8a-C), 164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{19}H_{17}BrN_2O_5$: C, 52.67; H, 3.95; N, 6.47. Found: C, 52.65; H, 3.93; N, 6.45. MS (FAB) *m/z*: 432 (M^+).

2-Phenyl-5-nitro-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleoside (5e). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H, 3′-H, 2 x 5′-H), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.29-7.60 (m, 5H, -C_6H_5), 7.80 (dd, 1H, *J*= 8.3 Hz and 2.4 Hz, 8-H), 7.90 (dd, 1H, *J* = 8.3 Hz 7-H), 8.40 (dd, 1H, 8.3 Hz and 2.4 Hz, 6-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 122.1 (4a-C), 122.2 (6-C), 125.9-132.9 (C_6H_5), 128.2 (8-C), 131.9 (5-C), 134.1 (7-C), 152.9 (8a-C), 164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{19}H_{17}N_3O_7$: C, 57.14; H, 4.29; N, 10.52. Found: C, 57.12; H, 4.25; N, 10.50. MS (FAB) *m/z*: 399 (M^+).

2-(*p*-Chlorophenyl)-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleoside (5f). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H, 3′-H, 2 x 5′-H), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.30-7.56 (d, 4H, -C_6H_4), 7.40 (dd, 1H, *J*= 8.3 Hz and 2.4 Hz, 8-H), 7.40-7.50 (dd, 2H, *J* = 8.3 Hz and 2.4 Hz, 6-H, 7-H), 7.90 (dd, 1H, *J* = 8.3 Hz and 2.4 Hz, 5-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 122.1 (8-C), 127.3-135.2 (C_6H_4), 127.0 (4a-C), 127.1 (6-C), 128.6 (5-C), 133.2 (7-C), 152.0 (8a-C) ,164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{19}H_{17}ClN_2O_5$: C, 58.69; H, 4.41; N, 7.21. Found: C, 58.65; H, 4.40; N, 7.20. MS (FAB) *m/z*: 388 (M^+).

2-(*p*-Chlorophenyl)-8-methoxy-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleoside (5g). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H, 3′-H, 2 x 5′-H), 3.73 (s, 3H, -OCH_3), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.30-7.56 (d, 4H, -C_6H_4), 7.30 (dd, 1H, *J*= 8.3 Hz, 6-H), 7.50 (dd, 1H, *J* = 8.3 Hz and 2.4 Hz, 5-H), 8.73 (dd, 1H, *J* = 8.3 Hz and 2.4 Hz, 7-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 56.3 (OCH_3), 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 118.8 (7-C), 120.9 (5-C), 127.3-135.2 (C_6H_4), 127.1 (6-C), 128.0 (4a-C), 137.6 (8a-C), 155.6 (8-C),164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{20}H_{19}ClN_2O_6$: C, 57.35; H, 4.57; N, 6.69. Found: C, 57.32; H, 4.55; N, 6.66. MS (FAB) *m/z*: 418 (M^+).

2-(*p*-Chlorophenyl)-7-chloro-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleoside (5h). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H, 3′-H, 2 x 5′-H), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.30-7.56 (d, 4H, -C_6H_4), 7.40 (d, 1H, *J*= 2.4 Hz, 8-H), 7.40 (dd,1H, *J* = 8.3 Hz and 2.4 Hz, 6-H), 7.90 (d, 1H, *J* = 8.3 Hz, 5-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 122.5 (8-C), 125.1 (4a-C), 127.3-135.2 (C_6H_4), 127.1 (6-C), 130.0 (5-C), 138.5 (7-C), 153.4 (8a-C), 164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{19}H_{16}Cl_2N_2O_5$: C, 53.92; H, 3.81; N, 6.62. Found: C, 53.90; H, 3.80; N, 6.60. MS (FAB) *m/z*: 422 (M^+).

2-(*p*-Chlorophenyl)-6-bromo-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleoside (5i). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H, 3′-H, 2 x 5′-H), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.30-7.56 (d, 4H, -C_6H_4), 7.30 (d, 1H, *J*= 8.3 Hz, 8-H), 7.70 (dd, 1H, *J* = 8.3 Hz and 2.4 Hz, 7-H), 8.10 (d, 1H, *J* = 2.4 Hz, 5-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 121.7 (6-C), 124.3 (8-C), 127.3-135.2 (C_6H_4), 129.2 (4a-C), 131.9 (5-C), 136.5 (7-C), 151.0 (8a-C), 164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{19}H_{16}BrClN_2O_5$: C, 48.79; H, 3.45; N, 5.99. Found: C, 48.77; H, 3.43; N, 5.97. MS (FAB) *m/z*: 467 (M^+).

2-(*p*-Chlorophenyl)-5-nitro-3-(*β*-D-ribofuranosyl)-3*H*-quinazolin-4-one *N*-nucleosides (5j). ^{1}H NMR (400 MHz, DMSO-d_6), δ 2.00 (brs, 3H, 3 x OH exchangeable with D_2O), 3.65-3.92 (m, 4H, 2′-H, 3′-H, 2 x 5′-H), 3.90-4.00 (m, 1H, 4′-H), 4.64 (d, 1H, *J*= 4.2 Hz, 1′-H), 7.30-7.56 (d, 4H, -C_6H_4), 7.80 (dd, 1H, *J*= 8.3 Hz and 2.4 Hz, 8-H), 7.90 (dd, 1H, *J* = 8.3 Hz, 7-H), 8.40 (dd, 1H, 8.3 Hz and 2.4 Hz, 6-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 61.8 (5′-C), 70.8 (3′-C), 75.7 (2′-C), 76.5 (4′-C), 85.8 (1′-C), 122.1 (4a-C), 122.2 (6-C), 127.3-135.2 (C_6H_4), 128.2 (8-C), 131.9 (5-C), 134.1 (7-C), 152.9 (8a-C), 164.0 (C=N), 170.0 (C=O). Anal. calcd for $C_{19}H_{16}ClN_3O_7$: C, 52.61; H, 3.72; N, 9.69. Found: C, 52.60; H, 3.70; N, 9.68. MS (FAB) *m/z*: 433 (M^+).

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