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RESEARCH ARTICLE

SYNTHESIS AND CHARACTERIZATION OF SOME QUINAZOLINE NUCLEOSIDES 6,7-DIMETHOXYQUINAZOLINE-2,4-(1H,3H)-DIONE: MEDICAL SIGNIFICANCE AND FUTURE PROSPECTS

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ABSTRACT

Quinazoline nucleosides are heterocyclic compounds of great importance in medicinal chemistry due to their diverse biological activities, including anticancer, antimicrobial, and anti-inflammatory properties. This article aims to review the methods for the synthesis and characterization of some nucleosides 6,7-Dimethoxyquinazoline-2,4-(*1H,3H*)-Dione, focusing on the reactions between quinazolinones and sugars to produce alpha- and beta-analogues of these nucleosides. This work is expected to contribute to the field of medicinal chemistry and future drug development. The 6,7-Dimethoxy 2,4-(*1H, 3H*)-quinazolinone (2) was reflexed with HMDS from 1day using the Vorbruggen's silylation method. The trimethyl silylquinazolinone (3) was reacted with 1-*O*-acetyl- 2,3,5-tri-*O*-benzoyl-D-ribofuranose (4) afford three protected nucleosides (5,6 and **7**) respectively. Debenzoylation of each of protected nucleosides by sodium metal in dry methanol affore the free nucleosides (8,9 and 10) respectively in good yield . The new synthesized compounds were characterized using the well-known spectroscopic (IR, ^{1}HNMR, ^{13}CNMR and mass spectroscopy).

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INTRODUCTION

Quinazolins and quinazolinones are heterocyclic compounds that have played an important and effective role in the medicinal and pharmacological effect for over two decades (Wolfe *et al*, 1990; Hess *et al*, 1968; Ozaki *et al*, 1985; HISANO *et al*, 1975; ALI, 1988; Lempert-Sréter *et al*, 1983). Quinazolinone compounds have gained importance in medicinal chemistry due to their wide range of pharmacological activities, leading to increased focus on innovative quinazolinone design and synthesis Deharkar *et al*, 2021; Malinowski, 2025). Many 4(3H)-quinazolinones and 2,4-(*1H, 3H*)-quinazolinones exhibit a range of biological activities including antifungal, antibacterial, anticancer, anti-inflammatory, anticonvulsant, immunotropic, anti-HIV, hypolipidemic, antitumor, antiulcer, and analgesic effects (Ghoneim *et al*, 2024; Zayed, 2022; Singh *et al*, 2013; Milićević *et al*, 2020). They also demonstrate potent antimicrobial and cytotoxic activities (Ma & Ns, 1987; Badr *et al*, 1980). Nucleoside derivatives are increasingly important in biological activities, including antiviral effects against hepatitis B virus (HBV) and inhibition of hepatitis C virus (HCV) copying, as well as activity against herpes simplex virus (HSV) and in the treatment of cancer, HIV, and AIDS (Lin & Gao, 1983; Rosendahl *et al*, 1982; Stout & Robins, 1968). The first quinazoline nucleosides were synthesized by Stout and Robins in 1968 (Stout & Robins, 1968). Further synthetic studies in this area were contributed by Dunkel and Pfleiderer in the 1990s (Dunkel & Pfleiderer, 1992). The significance of quinazolinone nucleoside derivatives highlights the importance of continued research and development in this field (ALI, 1988). Several synthetic approaches have been developed for quinazoline nucleosides, including direct glycosylation and multi-component synthetic techniques. (Chien *et al*, 2004; Deharkar *et al*, 2021). The Vorbrüggen silylation method is a widely used technique for the synthesis of nucleosides, playing a significant role in medicinal chemistry due to its efficiency and stereoselectivity (Vorbrüggen *et al*., 1981 Nikolaus *et al*., 2007., Naciuk *et al*., 2023).

This method was developed by H. Vorbrüggen and is considered a modification of the silyl-Hilbert-Johnson nucleoside synthesis (Nikolaus *et al*., 2007). The Vorbrüggen silylation method is a technique used for the direct glycosylation of 4-aminoquinazolin-2-one to produce 4-amino-1-(*β*-D-ribofuranosyl) quinazolin-2-one, exclusively yielding the *β*-anomer. (Chien *et al*, 2004). This method involves the ribosylation of 8-trifluoromethyl quinazolin-2,4-(*1H,3H*)-dione through coupling with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-*β*-D-ribofuranose, resulting in a mixture of beta and alpha anomers of benzoylated nucleoside derivatives. (Break, 2021; Break, *et al*, 2013., Mosselhi & Break, 2011). The synthesis of 3'-deoxy-*β*-D-ribofuranosides has been achieved by glycosylation of

trimethylsilylated 2,4-quinazolinediones with an appropriate 3'-deoxyribofuranosyl donor. (Dunkel & Pfleiderer, 1992). This work aims the synthetic route to 6,7-Dimethoxy-2,4-(*1H,3H*)-quinazolinedione (2), prepared initially from 4,5-dimethoxy-2-aminobenzoic acid (1) and potassium cyanate. Compound (2) serves as a precursor for nucleoside derivatives through a subsequent reaction with ribofuranose. The key nucleosidation step involves the Vorbrüggen coupling of the silylated nucleobase with a 1-*O*-acetyl sugar, often catalyzed by a Lewis acid such as trimethylsilyl triflate (TMSOTf).

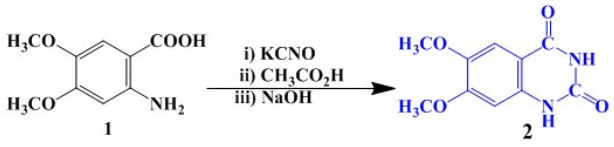
MATERIAL AND METHODS

Purity of the intermediates and final compounds were optimized with thin layer chromatography (TLC) throughout the reaction time. Thin layer chromatography (TLC) was performed on silica gel sheets F1550 LS 254 of Schleicher & Schull and column chromatography on Merck silica gel 60 (particle size 0.063–0.20). The spots were visualized under UV light. All new compound were dried up to a drying over P_2O_5 at a temperature of 70 m and under atmospheric pressure of 200 bar. Melting points were measured on Gallenkamp melting point apparatus (UK) and are uncorrected. IR spectra were recorded for KBr discs on Fourier Transform infrared FTIR and Pie Unicom SP 300 Infrared Spectrophotometers. The ^{1}H and 13C NMR spectra were obtained on a Varian (850 MHz) EM 390 USA instrument. spectrometer (850 MHz). Mass spectra were recorded on a JEOL-JMS-AX500 at King Abdel-Aziz University, Saudi Arabia. Elemental analyses were obtained on an Elementary Vario EL 1150C analyzer. The starting material of 2-amino-4,5-dimethoxy benzoic acid (**1**) was PurchasedPubchem CID: 67865.

GENERAL: All chemicals were supplied in the synthesis of the target compounds by Sigma Aldrich and Merck (Germany). TLC was done using TLC Silica gel 60 F_{254} (sheet 20 cm × 20 cm, aluminum support) and column chromatography on silica gel 60 (particle size 0.063-0.20 mm). Melting points were measured on an electrothermal melting point apparatus and are uncorrected. IR spectra (4000–400 cm^{-1}) were recorded on an FT/IR-4100 Jasco-Japan Fourier transform infrared spectrophotometer. ^{1}H NMR and ^{13}C NMR ($CDCl_3$, CD_3OD and DMSO-d_6) spectra were measured at 850 and 213 MHz on Bruker instruments. Mass spectra were measured on GC MS-QP 2000 EX mass spectrometer at 70 e.V (King Saud University). Elemental analyses were carried out at Characterization Techniques Various advanced analytical methods are employed to confirm the structures and properties of synthesized quinazoline nucleosides (Shaikh & Wagh, 2024).

Synthesis of 6,7-Dimethoxy quinazoline-2,4-(1H,3H)-dione (2): A suspension of 2-amino-4,5-dimethoxybenzoic acid (1) (5.00 g, 0.0254 mol) in 200 mL of distilled water containing 2.0 mL of glacial acetic acid was prepared in a three-necked flask. The mixture was cooled in an ice bath (0–5 °C) and stirred vigorously. A solution of potassium cyanate (KCNO) (2.55 g, 0.0314 mol) dissolved in 10 mL of distilled water was added dropwise to the stirred suspension over a period of 1 hour. The reaction mixture was then treated with sodium hydroxide (NaOH) (34.25 g) added gradually to maintain the internal temperature at approximately 40 °C.

The resulting mixture was allowed to cool to room temperature and then stored in a refrigerator for 24 hours to ensure complete precipitation. The crude solid was collected by filtration. The collected solid was dissolved in 70 mL of hot water. The solution was acidified by the dropwise addition of an aqueous solution of sulfuric acid (H_2SO_4) (1:1 v/v) until a precipitate formed. The precipitate was collected by filtration, washed several times with distilled water, and then recrystallized from glacial acetic acid to afford the target compound as a white powder. The final product was dried over phosphorus pentoxide (P_2O_5) at 70 °C under reduced pressure (200 mbar). White powder; 83.42% Yield M.P.: 346 ºC; IR u (cm^{-1}): 3340 (NH str), 1715 (C=O str); ^{1}H NMR (DMSO-D6) d (ppm): 11.12 (s, 1H, NH-1); 10.94 (s, 1H, NH-3); 7.25 (s, 1H, H-5); 6.67 (s, 1H, H-8); 3.82(s, 3H, **6**-OCH_3), 3.78 (s, 3H, **7**-OCH_3). ^{13}C NMR d (ppm): 162.97 C4, 155.43 C-2, 150.95 C-7, 145.56 C-6, 137.08 C-8a, 107.66 C-5 106.72C-4a, 98.29 C-8, 56.35 OCH_3, 56.24 OCH_3. Anal. Calcd. for $C_{10}H_{10}N_2O_4$: C, 54.55; H, 3.64; N, 12.73:Found: C, 54.38; H, 3.65; N, 12.76: ESI-MS (m/z): 222.10 (100) (M^+). chromatography thin layer TLC [1,1-Chloromethane Cl_2CH_2: Methanol CH_3OH by (9: 1)].



Scheme (1):Synthesis of 6,7-dimethoxyquinazolin-2,4-dione

The ribosylation of synthesis of 1-(2,3,5-trihydroxy-ribofuranose)-6,7-dimethoxy quinazoline-2,4- dionederivatives

GENERAL PROCEDURE

The mixture of 4 g (0.018 mol) of 6,7-dimethoxy quniazoline-2,4-dione **2** and 40 ml of HMDS and a few crystals of ammonium sulfate, was refluxed for 4 hours in an oil bath at a temperature of 150 °C until the substance dissolved completely. HMDS excess was evaporated and dried under anhydrous condition to form silylated derivative **3**, which that directly was dissolved in 40 ml dry 1,2-dichloroethane and added of the protected sugar of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-*β*-D- ribofuranose **4** (9.5 g, 0.0189 mol), and 18 ml of a mixture (50 ml trimethylsilyltrifluoromethyl sulphonates $Me_3SiOSO_2CF_3$ triflate + 200 ml of dry 1,2-dichloroethane). The mixture was stirred for 24 hours at room temperature. The mixture of reaction had been washed with a saturated solution of aqueous sodium bicarbonate (100 ml), water (3 × 20 ml) and dried over anhydrous sodium sulfate. The completion of the reaction was confirmed by thin-layer chromatography (TLC) using a solvent system of 1,2-dichloroethane and acetone (9:1, v/v). The chromatogram displayed three distinct spots, indicating the presence of a mixture containing three components. This mixture was subsequently subjected to silica gel column chromatography with the same eluent system (1,2-dichloroethane:acetone, 9:1, v/v), affording three separate fractions. Each fraction was further purified by preparative TLC on a 20 × 20 cm silica gel plate using a solvent ratio of 1,2-dichloroethane:acetone (9.5:0.5, v/v). The purified products were recrystallized from an ethanol–water mixture (8:2, v/v) and subsequently dried over phosphorus pentoxide (P_2O_5) under reduced pressure see (Scheme 2).

Synthesis of *1-(2`,3`,5`-tri*-O-*benzoyl*-β-*D-ribofuranosyl)-6,7-dimethoxy quniazoline-2,4-(3H)-dione (5):* White powder; (56%) Yield 0.82 g, (Etanol and H_2O) M.P.: 99-100 ºC. IR (KBr) ν (cm^{-1}) 3310 (NH str), 1710 (C=O str); ^{1}H NMR ($CDCl_3$δ) (ppm): 9.56 (s, 1H, NH-3); 8.08-7.32 (m, 15H, H o,m,p of Bz group's) ; 7.60 (s, 1H, H-5); 6.26 (d, 1H, H-8); 1.25 (s, 1H) H-lactame); 6.78 (d, 1H, J = 6 Hz, $H_{1'}$); 6.3 (d, 1H, $H_{2'}$); 4.85 (dd, 1H, $H_{3'}$); 4.82 (m, 1H, $H_{4'}$); 4.72 (m, 1H, $H_{5'}$); 3.95(s, 3H, 6-OCH_3); 3.94 (s, 3H, 7-OCH_3). ^{13}C NMR (DMSO-D6) δ (ppm): 166.30, 16514, 165.28, 160.52 C-4, 155.38 C-2, 150.02 C-7, 146.29 C-6, 134.55 C-8a, (133.64, 133.42, 133.26) C para, (129.90, 129.74,) C ortho, (129.9, 129.74, 128.81, 128. 5, 128.28, 128.16) C meta ,109 C-5, 108 C-8, 97.28 $C_{1'}$, 79.25 $C_{2'}$, 74.34 $C_{3'}$, 71.18 $C_{4'}$,64.22 $C_{5'}$, 56.48 OCH_3, 56.32 OCH_3. Anal. Calcd. for $C_{36}H_{30}N_2O_{11}$: C, 54.55; H, 3.64; N, 12.73: Found: C, 54.38; H, 3.65; N, 12.76: ESI-MS (m/z): 544.35 (0.79) (M^+ - OBz). Mr. 666.63.

Synthesis of **1-(2`,3`,5`-tri-*O*-benzoyl-*α*-D-ribofuranosyl)-6,7-dimethoxy quniazoline-2,4- (*3H*)-dione (6):** White powder; (32%)Yield 0.75 g, M.P.: 112-116 ºC. IR (KBr) υ (cm^{-1}): 3320 (NH str), 1710 (C=O str). ^{1}H NMR ($CDCl_3$) δ (ppm): 9.35 (s, 1H, NH-3); 8.64 (s, 1H, H-5); 7.45 (s, 1H, H-8); 8.07-7.30(m, 15H, H *o,m,p* of Bz); s,(1.24 2H, H-lactame); 6.79 (d, 1H, *J* = 8.8 Hz, H1');

6.29 (dd, 1H, *J* = 6.6, 2.2 Hz, H2'); 6.19(dd, 1H, *J* = 8.06, 3.60 Hz, H3'); 4.75-4.36 (m, 1H, H4'); 5.45-5.38 (m, 1H, H5'); 3.92 (s, 1H, OCH_3); 3.86 (s, 1H, 7-OCH_3). ^{13}C NMR ($CDCl_3$) δ (ppm): 166.42, 165.64, 165.28, 161.67 C-4, 155.36 C-2, 149.75 C-7, 146.30 C-6, 129.86 C-8a, 129.81 Cp, 128.61 Co, 128.49 Cm, 128.43 C-4a, 108.90 C-5, 108.82 C-8, 97.72 C1', 90.72 C2', 79.37 C3', 71.38 C4', 64.01 C5', 56.58 OCH3, 56.44 OCH3. Anal. Calcd. for $C_{36}H_{30}N_2O_{11}$: C, 54.55; H, 3.64; N, 12.73: Found: C, 54.38; H, 3.65; N, 12.76: ESI-MS (m/z): 222.10(100). Mr. 666.63.

***Synthesis of* 1,3-*Bis*-(2`,3`,5`-tri-*O*-benzoyl-*β*-D-ribofuran-osyl)-6,7-dimethoxy quniazoline-2,4,dione (7):** White powder ; (12%)Yield 0.50 g, M.P.: 100-101 °C. IR (KBr) υ (cm^{-1}) 1710 (C=O str). ; ^1H NMR (DMSO-D6) δ (ppm): 9.32 (s, 1H, H-8); 8.95 (s, 1H, H-5); 8.08-7.97, 7.86-7.79, 7.50-7.32 (m, 15H,$H_{o,m,p}$ of Bz group's); 6.86 (s, 1H, H-1`); 6.79 (s, 1H, H-1``);6.19 (d, 1H, *J* = 5.88 Hz, H-2`); 6.05 (dd, 1H, *J*= 2.92 Hz, H-2``); 5.90 (t, 1H, *J* = 16 Hz, H-3`); 5.82 (t, 1H, *J* = 13.2 Hz, H-3``);4.76-4.41(m, 1H, H-4`); 3.96-3.90 (m, 1H, H-4``); 5.43-5.41(dd, 1H, *J* = 2.9-2.92 Hz, H-5`), 5.22-5.20 (dd,1H, *J* = 5.88, 2.2 Hz, H-5``); 3.96 (s, 3H, OCH_3); 3.95 (s, 3H, OCH_3). ^{13}C NMR δ (ppm): 162.97 C4, 155.43 C-2, 150.95 C-7, 145.56 C-6, 137.08 C-8a, 107.66 C-5 106.72C-4a, , 98.29 C-8, 56.35 OCH_3, 56.24 OCH_3. Anal. Calcd. for $C_{62}H_{50}N_2O_{18}$: C, 54.55; H, 3.64; N, 12.73: Found: C, 54.38; H, 3.65; N, 12.76

Synthesis of free nucleoside of protected nucleoside (5-7) gave new compounds (8-10)

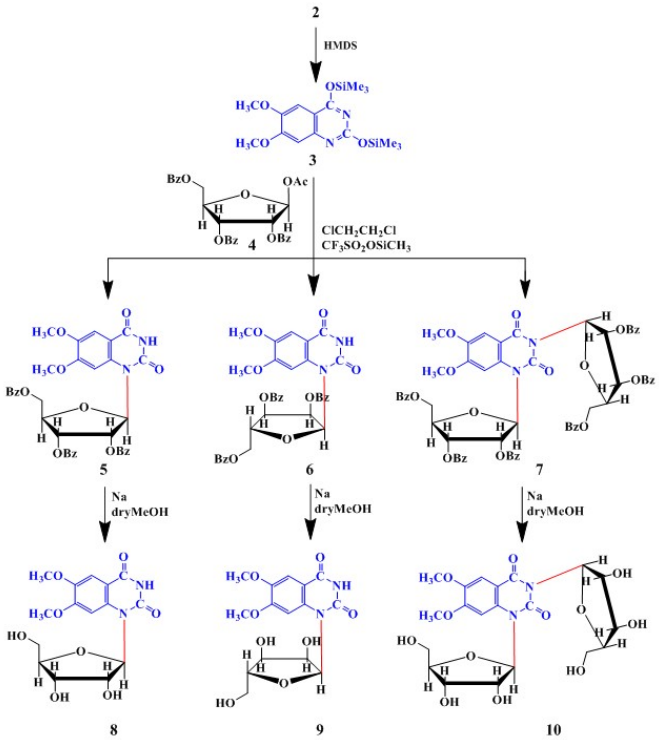
1-(*β*-D-ribofuranosyl)-6,7-dimethoxy quniazoline-2,4-(*3H*)-dione (8) ; 1-(α-D-ribofuranosyl)-6,7- dimethoxy quniazoline-2,4-(*3H*)-dione (9) and **1,3-*Bis*-(*β*-D-ribofuranosyl)-6,7-dimethoxy quniazoline-2,4,dione (10)**

GENERAL METHOD: A mixture each one of the protected nucleoside **(5-7)** (0.02mole) and 40 ml dry methanol and 30 mg Natrium, was stirred at room temperature for 24 hours, which was added water and neutralized with few drops of AcOH. Evaporation of the solvent under vacuum gave solid. It was washed three times water. The precipitate was filtered off and was separated using silica gel column chromatography the solvent system: Ethyl acetate: Methanol by (9: 1). It was crystallized from water. Each protected nucleoside (5–7) (0.02 mol) was mixed with 40 mL of anhydrous methanol and 30 mg of sodium, and the mixture was stirred at room temperature for 24 hours. Upon completion of the reaction, water was added, and the solution was neutralized with a few drops of acetic acid. The solvent was evaporated under reduced pressure to afford a solid residue, which was washed three times with water. The resulting precipitate was filtered and purified by silica gel column chromatography using ethyl acetate:methanol (9:1, v/v) as the eluent. The purified compound was recrystallized from water to obtain the final product in pure crystalline form. **The structure and purity of the obtained compound were confirmed by IR, ^1H NMR, and mass spectrometric analyses.**

Synthesis of 1-(+D-ribofuranosyl)-6,7-dimethoxy quniazoline-2,4-(3H)-dione (8): White powder ; (90.94%) Yield 0.34 g (Ethanol), M.P.: 180 °C. IR (KBr) υ (cm^{-1}): 3420 (OH str), 3310 (NH str), 1710 (C=O str); ^1H NMR (DMSO-D6) δ in ppm: 8.90 (s,1H,NH-3); 8.44 (s, 1H, H-8); 7.07 (s, 1H, H-5);1.7 (s, 1H, H-lactame); 6.23 (d, 1H, J = 6.96Hz, $H_{1'}$); 5.67 (q, 1H, $H_{2'}$); 5.43 (q, 1H, $H_{3'}$); 3.34 (m, 1H, $H_{4'}$); 4.70-4.32 (m, 1H, $H_{5'}$); 3.88 (s,3H,OCH_3); 3.82 (s, 3H, OCH_3). ^{13}C NMR δ in ppm: 155 C-4, 149.75 C-2, 136.67 C-5, 133.21 C-7, 129.93, 129.83, 129.74, 128.73, 128.67, 128.60, 128.39 CAromatic 107.86 C-4a, 102.39 C-6, 99.20 C-8, 93.18 $C_{1'}$, 82.25 $C_{2'}$, 75.00 $C_{3'}$, 73.44$C_{4'}$, 64.13$C_{5'}$, 55.21 OCH_3, 56.61 OCH_3. Anal. Calcd. for $C_{15}H_{18}N_2O_8$: C, 54.55; H, 3.64; N, 12.73: Found: C, 54.38; H, 3.65; N, 12.76: ESI-MS (m/z): 354.03 (2.75) (M^+). Mr. 354.31

Synthesis of 1-(*α*-D-ribofuranosyl)-6,7-dimethoxy quniazoline-2,4-(3H)-dione (9): White powder; (72.22%) Yield; 0.21 g (Ethanol), M.P.: 223-224 °C. IR (KBr) ν (cm^{-1}): 3450 (OH str), 3320 (NH str), 1715 (C=O str); ^1H NMR (DMSO-D6) δ (ppm): 9.65 (s, 1H, NH-3); (δ7.51 s, 1H, H-8); δ7.12 (s, 1H, H-5); (d,22.6 1H, J = 5.16 Hz, H1'); 4.98 (s, 1H) OH2`, 4.93 (s, 1H, H2'); 4.85 (s, 1H, H3'); 4.62(s, 2H, OH -3`,5`);4.73 (q, 1H, H4'); 4.37 (t, 1H, H5'); 3.96 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3). ^{13}C NMR (DMSO-D6) δ (ppm): 164.46 C4, 150.87 C-2, 141.34 C-8a, 135.62 C-7, 123.01 C- 4a, 115.88 C-6, 114.81 C-8, 94.01 C1', 83.32 C2', 78.65 C3', 72.94 C4', 63.71C5' . Anal. Calcd. For $C_{15}H_{18}N_2O_8$: C, 54.55; H, 3.64; N, 12.73: Found: C, 54.38; H, 3.65; N, 12.76: ESI-MS (m/z): 354.25 (1.04) (M+), 222.10(100) (compound2). Mr. 354.31

Synthesis of 1,3-*Bis*-(*β*-D-ribofuranosyl)-6,7-dimethoxy quniazoline-2,4,dione (10): White powder; (11.38%) Yield 0.10 g (Ethanol); M.P.: 196-200 ° in cmυC. IR (KBr) $^{-1}$3455 (OH str), 1710 (C=O str); ^1H NMR (CD_3OD) δ (ppm): 7.45 (s, 1H, H-8); 7.09 (s, 1H, H-5); 6.56 (d, 1H, J = 3.64 Hz, H-1`); 6.22(d, 1H, J = 5.12 Hz, H-1``); 5.82-5.80 (d, 1H, J = 5.88 Hz, H-2`); 4.73- 4.70 (dd, 1H, J = 5.12, 5.88 Hz, H-2``); 4.41-4.32 (m, 1H, H-3`); 3.91 (d, 1H, J = 5.12 Hz, H-3``); 3.89 (d, 1H, J = 2.92 Hz, H-4`); 3.86(d, 1H, J = 7.36 Hz, H-4``)3.89 (d, 1H, J = 2.92 Hz, H-4`); 3.86(d, 1H, J = 7.36 Hz, H-4``); 3.78 (dd, 1H, J = 3.68, 8.04 Hz, H-5`); 3.72 (dd, 1H, J = 3.68 Hz, H-5``);3.95 (s, 1H, OCH_3); 3.92 (s, 1H, OCH_3). ^{13}C NMR (CD_3OD) δ (ppm): 155.37 C-4, 146.18 C2, 136.99 C-5, 136.40 C-7, 108.55 C-8a 107.86 C-4a, 102.39 C-6, 99.20C-8, 91.00 $C_{1'}$, 89.17 $C_{1''}$,84.21 $C_{2'}$, 83.60 $C_{2''}$, 72.09 $C_{3'}$, 70.45 $C_{3''}$, 70.01 $C_{4'}$, 68.73 $C_{4''}$, 61.68 $C_{5'}$,60.99 $C_{5''}$, 55.19 OCH_3, 55.10 OCH_3. Anal. Calcd. for $C_{20}H_{26}N_2O_{12}$: C, 54.55; H, 3.64; N, 12.73: Found: C, 54.38; H, 3.65; N, 12.76: ESI-MS (m/z): 486.13 (0.20) (M^+). Mr. 486.43.



Scheme (2). Synthesis of 6,7-dimethoxyquinazolin-2,4-dione nucleosides

RESULTS AND DISCUSSION

A suspension of 2-Amino-4,5-dimethoxy benzoic acid was treated solution potassium cyanate KNCO in alkaline medium, the white solid was treated 20% diluted sulfuric acid, gave the base 6,7-dimethoxy quinazolin-2,4-dione 2. which it refluxed with Hexamethyldisilazane (HMDS) was refluxed, then treated with sugar 1-O-Acetyl-2,3,5-tri-O-benzoyl-*β*-ribofuranose 4. TLC were showed be three isomers of protected nucleosides 5. 6 and 7. After separating

each isomer alone, were removed from their respective protective groups debenzoylation using the method of Zemplen free nucleosides desired 8, 9 and 10 (scheme 2) (Zemplen, *et al* 1936; Break, 2021; Kamaraj, & Mukhopadhyay, 2023). The ^{1}H NMR spectrum of the base 6,7-dimethoxy quinazolin-2,4-(1H, 3H)-dione 2 11.12δappeared two singlet signals for amide groups proton at (s, 1H, NH-1); 10.94 (s, 1H, NH-3).δ δ 7.25 (s, 1H, H-5); δTwo protons appeared in the aromatic region at 6.67 (s, 1H, H-8), and shows two signals a singlet for methoxy groups protons at δ 3.78 (s, 3H, 7-OCH_3 3.82 (s, 3H, 6-OCHδ) $_3$). The ^{13}C NMR of the compound 2 showed two lines of the two sets of carbonyl amide HN-C=O, C atoms of quinazolinone. The mass spectra of compound 2 shown the molecular ion at M.$^{+}$= 222.10 (100%) with a relative abundance of 100%, which this indicates that quinazolinone moiety is the most stable. The glycoside bond were appeared doublet signals in ^{1}H NMR at δ 6.78 (d, 1H, *J* = 6 Hz, H-1`) and δ 6.23 (d, 1H, *J* = 6.96 hz, H-1`) for Anomeric β (5) and anomeric α (6) respectively. Aromatic region have been appeared to be more complicated in the ^{1}H NMR spectrum of nucleosides protected (5, 6) 8.08-7.32 (m, 1H, Hδat $_{o,m,p}$ of Bz) which that represent benzoyl groups protons due to overlapping benzoyl protons with quinazolinone protons H-5, H-8. Deprotection of the benzoyl group of protected nucleoside (5-7) was used sodium metal in dry methanol at room temperature for 24 h to give the corresponding free nucleoside (8-10). The ^{1}H NMR the benzoyl protons were disappeared in free nucleosides (8-10) and showed the prospective base moiety protons and the sugar moiety protons and hydroxyl groups protons.

The successful glycosylation of a quinazolinone molecule with two sugar molecules was confirmed using nuclear magnetic resonance (NMR) spectroscopy of two compounds**7** and 10. Specifically, the ^{1}H NMR the two proton glycoside bonds gave doublet signals that were assigned at doublet signals at δ6.69 (d, 1H, *J* = 5.1 Hz) H1'' and 5.69–5.63 (d,1H; *J* = 4.25 Hz) H1' for compound **7**, and at 6.56 (d, 1H, *J* = 3.64 Hz,H-1`) and 6.22 (d, 1H, *J* = 5.12 Hz, H-1``) for compound 10, respectively. Also, ten distinct signals appeared in the sugar region of the ^{13}C NMR spectrum, including two glycosidic bonds at 91.00 C1' and 89.17 C1', providing conclusive evidence of the formation of two glycosidic bonds linked to the nitrogen atoms N-1 and N-3 of the quinazolinone ring of isomers of compound 10 91.00 C1`, 89.17δ . C1``. which involves the ribosylation of a quinazolinone compound with a sugar derivative. (Break & Al-harthi, 2018; Break *et al*, 2022).

CONCLUSION

In conclusion, this work a successful of Ribosylation of silated compound (**3**) with 1-*O*-acetyl-2,3,5-tri-*O*β-benzoyl- -D-ribofuranose (**4**) afforded mixture three isomers *β*-anomeric5, *–α*anomeric 6 and 1,3-*bis*-*β*-anomeric of the benzoylated nucleoside derivatives (**5**), (**6**) and (**7**), respectively. Deprotection of the latter by using dry absolute methanol and sodium metal gave new free N- nucleosides **(8), (9)** and **(10)**, respectively, in moderate yields. The successful synthesis of nucleosides were demonstrated using analytical methods such as IR, ^{1}H NMR, & ^{13}C NMR and MASS spectroscopy. We expect the newly synthesized compounds to have a promising future and a significant impact in the medical field.

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