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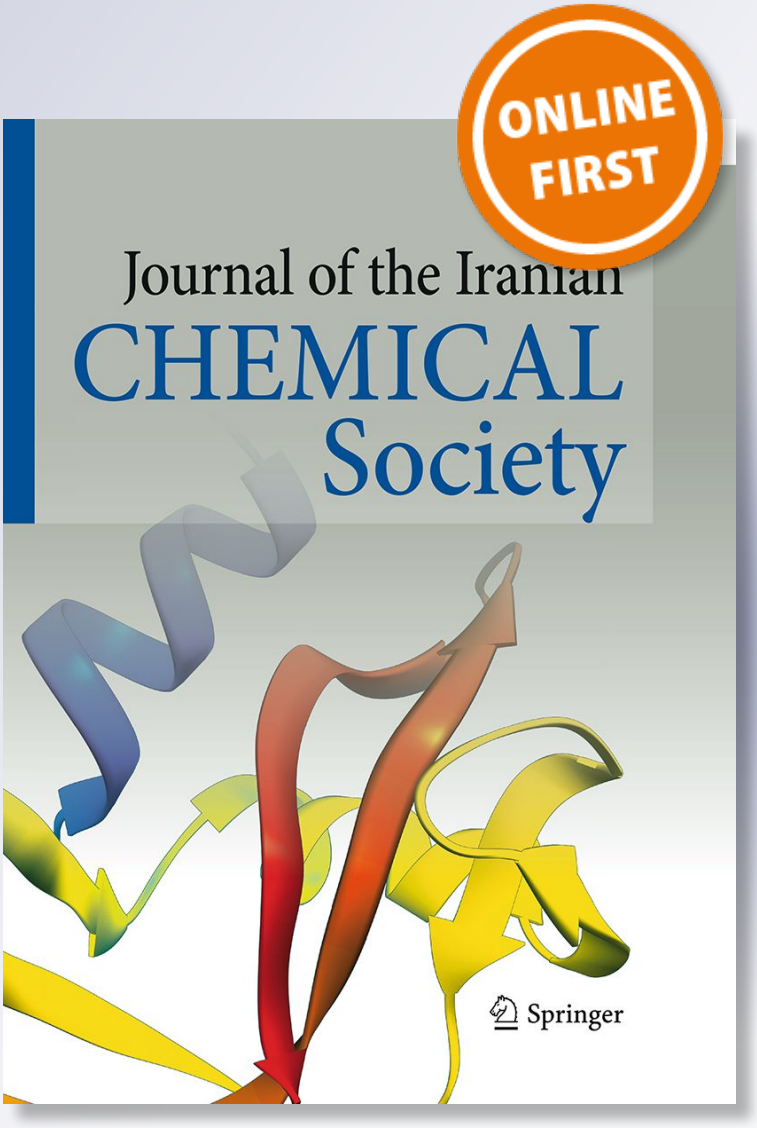

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ORIGINAL PAPER

Microwave in glycosylation reaction: design, and synthesis of highly substituted nicotinonitrile nucleosides

Ahmed H. Moustafa[1] · **Mohammed H. M. Ahmed**[2,3]

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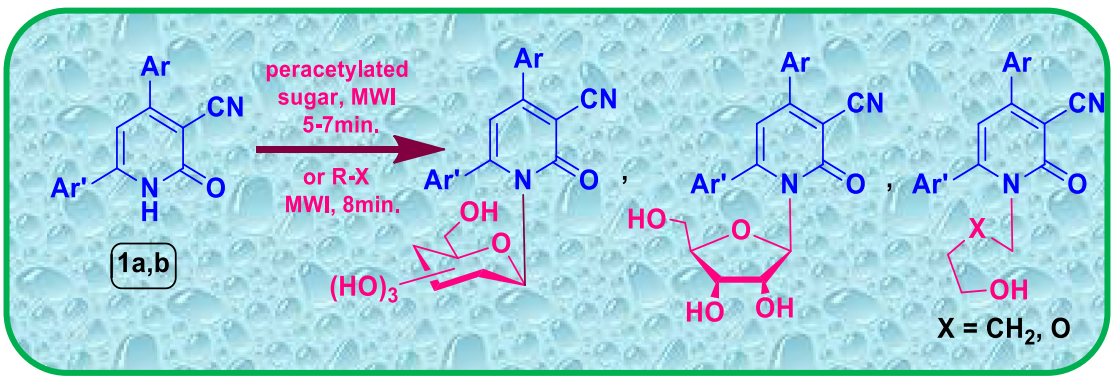
Abstract

An efficient and rapid regiospecific approach for the synthesis of cyclic and acyclic nucleosides of 2-oxonicotinonitriles was performed. Whereas, glycosylation of 2-oxonicotinonitriles **1a, b** with peracetylated sugars (namely, peracetylated glucose, galactose and ribose) under MWI tolerated exclusively the desired *N*-nucleosides **2a, b, 4a, b** and **6a, b** in significant yields (75–86%) and in short reaction time (5–7 min.). The same products were obtained under the conventional conditions, using halo-sugar with low yields in hard conditions. Similarly, the acyclic nucleosides **8a, b** and **9a, b** were obtained under MWI and conventional conditions via reaction of **1a, b** with 4-bromo butyl acetate and 2-acetoxyethoxymethyl bromide. Finally, deprotection of the latter blocked *N*-nucleosides was performed via treatment with aqueous methanolic solution containing a catalytic amount of triethyl amine to give the desired free nucleosides **3a, b, 5a, b, 7a, b, 10a, b** and **11a, b**, respectively. The free nucleosides (**3a, b, 5a, b, 7a, b** and **11a, b**) were evaluated against Gram (+ ve) bacteria, Gram (–ve) bacteria and one pathogenic Fungi namely, *Aspergillus flavus*. Good results were obtained for compounds **7a, b** and **11a, b** compared with the used standard drugs (Cefotaxime and Dermatin).

Graphical abstract



Keywords Microwave · 2-Oxonicotinonitriles · *N*-Glycosylation · Acyclic nucleoside · Antimicrobial activity

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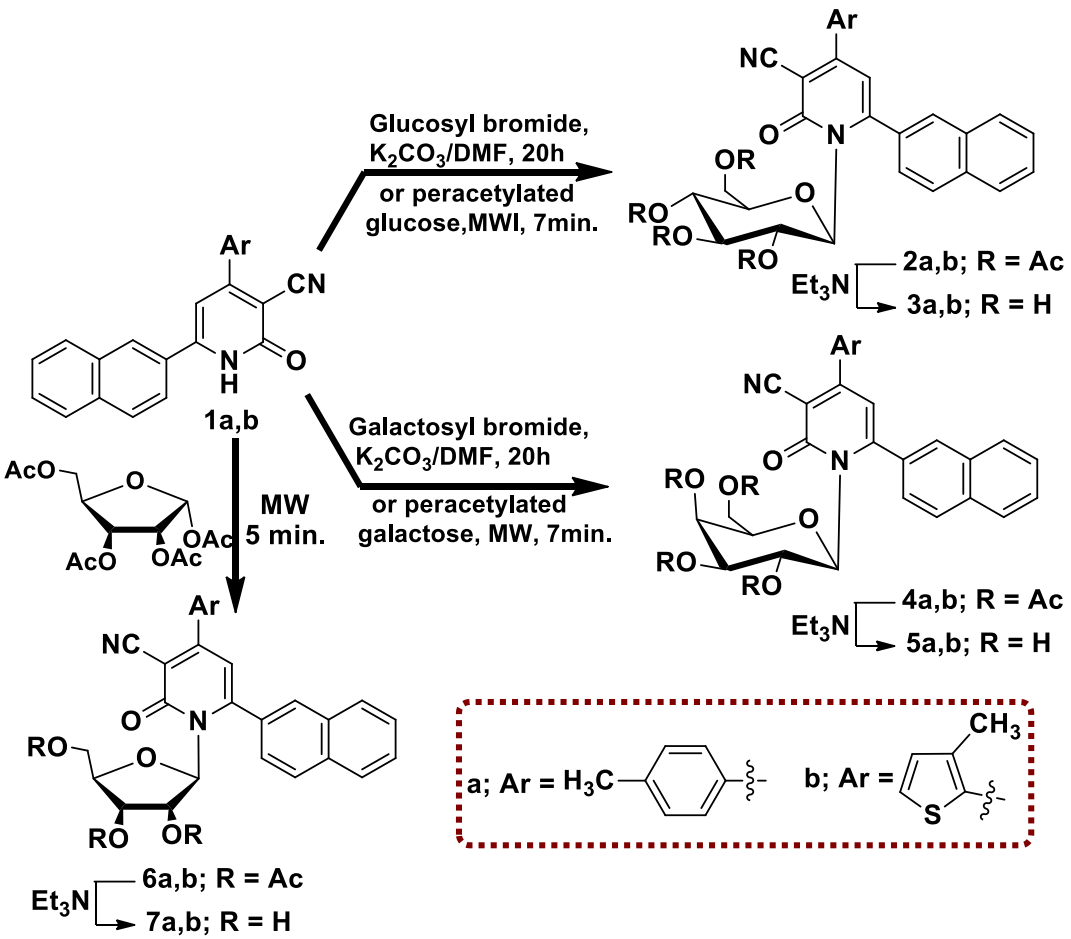
Introduction

2-Oxonicotinonitriles (2-ONN) and derived compounds are one of the most important heterocyclic systems found in several synthetic and naturally occurring applicable compounds, as they have a significant biological activity such as anticancer [1], anticoagulant [2], antimicrobial [3], anti-inflammatory [4], antioxidant [5] anticonvulsant [6], and antifungal activities [7]. Moreover, some glycosides linked 2-ONN have been investigated as potent anti-inflammatory [8], antitumor [9], antimicrobial [10–12], anti-avian influenza virus (H5N1) [13], antimetabolite agents [14] and antiviral [15]. The conventional reported methods for the synthesis of nucleosides are time-consuming, low yields, need extra purification of the products and involve the use of highly poisonous solvent [16, 17]. Microwave irradiation is a one of the green methods with additional advantage to improve the reaction rate, reaction yield and decrease the reaction by-products, in addition to, it gives high yields and more pure products [18]. Our recent papers directed to apply one of the green techniques such as solvent free conditions [19] and MWI [9, 20] in synthesis of biologically important heterocyclic systems. Continuing of these efforts, we repot here a facile, rapid and an efficient method for selectivity synthesis of some 2-ONN nucleoside candidates.

Results and discussion

In this study, the starting nucleobases **1a, b** were synthesized as reported method [9] via one pot condensation of 2-acetylnaphthalene, aromatic aldehyde (namely, tolualdehyde and 3-methylthiophene-2-carboxaldehyde), ethyl cyanoacetate and ammonium acetate. Scheme 1 describes two different methodologies for the synthesis of the target cyclic nucleosides **2a, b, 4a, b** and **6a, b**. The first involves conversion of nucleobases **1a, b** to potassium salt via its reaction with pot. carbonate followed by reaction with glycosyl or/ galactosyl bromide, then stirring at room temperature for long time (20 h) to give **2a, b** and **4a, b** in moderate yield (44–62%,



Scheme 1 MW-assisted glycosylation reaction of 2-ONN 1a, b

Table 1 Comparative data of conventional and MW methods for the synthesis of nucleosides **2–9**

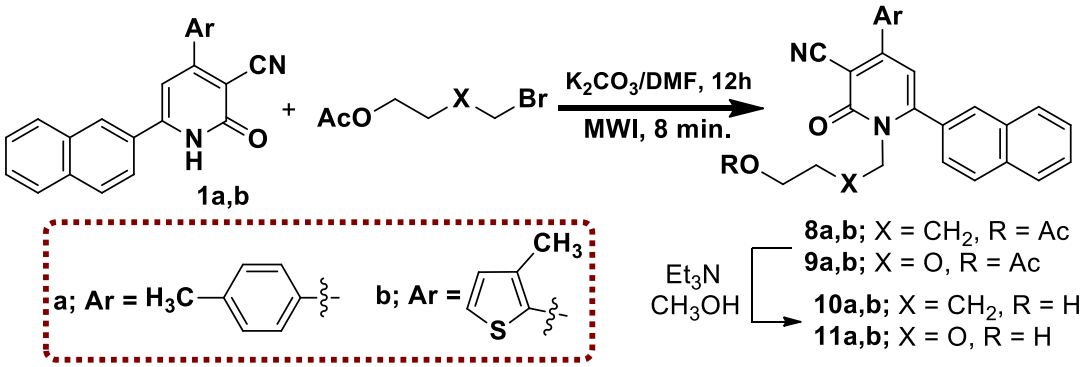
Entry	Compound no.	Conventional method (time, h)	Yield (%)	MW method (time, min)	Yield (%)
1	**2a**	20[a]	62	7	86
2	**2b**	20[a]	44	7	80
3	**4a**	20[a]	51	7	79
4	**4b**	20[a]	62	7	84
5	**6a**	–	–	5	78
6	**6b**	–	–	5	75
7	**8a**	16[b]	35	8	75
8	**8b**	16[b]	42	8	77
9	**9a**	14[b]	32	8	70
10	**9b**	14[b]	44	8	80

[a]Room temperature

[b]Refluxing temperature

Table 1). In the second one, MW was used to simplify the *N*-glycosylation reaction in shorter time and in good yield. Thus, the reaction of 2-ONN **1a, b** with peracetylated sugar (namely, peracetylated glucose / galactose or / ribose) was irradiated with microwave (Discover™ by CEM, 2450 MHz, 300 W, 150 °C) for 5 or 7 min. to give the corresponding 2-ONN nucleosides **2a, b, 4a, b** and **6a, b** in acceptable yields (75–86%, Table 1). The structure of the synthesized nucleosides was agreed with their spectral and microanalysis data. Thus, the presence of the stretching bands of lactam carbonyl (–N–C=O) at frequency 1640–1656 cm^{-1} in the IR data of nucleosides **2a, b** and **4a, b** give a clear evidence for the regiospecific glycosylation on nitrogen atom forming *N*-glycoside as a single isomer. While, the *β*-conformation of the resultant nucleosides **2a, b** and **4a, b** was determined from ^{1}H NMR analysis, which illustrate the diaxial orientation of H-1′ and H-2′ with large coupling constant ($^3J_{1',2'}$ = 8.20–9.20 Hz), in addition to, the presence of four singlets of acetoxy protons at high field (in between *δ* 1.88–2.06 ppm). In the same manner, IR, ^{1}H NMR and ^{13}C NMR spectra confirmed that nucleosides **6a, b** were obtained in *β*-*N*-glycoside configuration as a single isomer.

Scheme 2 illustrates the regiospecific alkylation of 2-ONN **1a, b** with 4-bromo butyl acetate and 2-acetoxyethoxymethyl bromide in the presence of pot. carbonate using MW and conventional methods forming 2-ONN acyclo nucleosides **8a, b** and **9a, b**. As shown in Table 1, the reaction with the classical method needs long time (14 or 16 h) at refluxing temperature with low yields (32–44%, Table 1). This hard condition was improved using MW method, where, the reaction was finished in 8 min. with significant yields (70–80%, Table 1). The IR data of nucleosides **8a, b** and **9a, b** confirmed the regiospecific alkylation of 2-ONN **1a, b** at nitrogen atom by the appearance of lactam carbonyl (–N–C=O) bands at frequency 1640–1660 cm^{-1}, in addition to the carbonyl ester at frequency 1729–1738 cm^{-1}. The ^{1}H NMR data of nucleosides **8a, b** and **9a, b** illustrate the presence of the glycon moiety at the expected chemical shift. Where, for compound **8a** CH_2 protons of butyl moiety appeared as two multiplets and two triplets at *δ* 1.80, 1.90, 4.12 and 4.55 ppm. In addition to, acetoxy methyl



Scheme 2 MW-assisted synthesis of 2-ONN acyclonucleoside analogues 8–11

protons appeared as singlet at δ 1.99 ppm. The aromatic protons appeared at δ 7.40, 7.06, 7.69, 7.95–8.06, 8.35 and 8.86 ppm as 3 doublets, 2 multiplets and singlets. The ^{1}H NMR spectrum of nucleoside **9b** revealed two singlets and two triplets at δ 2.03, 4.85, 3.35 and 4.50 ppm for acetoxy and glycon moiety protons, the aromatic protons appeared at the expected low field from δ 7.14 to 8.82 ppm as 2 doublets, multiplet and singlet. The ^{13}C NMR was agreed with their structure. The ^{13}C NMR of compound **8a** revealed 6 SP^3 carbons at δ 20.65, 21.01, 24.80, 25.54, 63.48, 66.65 ppm, in addition to, SP and 20 SP^2 carbons at δ 92.01, 113.6, 115.3, 124.2, 126.6, 126.8, 127.4, 127.5, 127.6, 128.3, 128.8, 129.3, 132.7, 132.9, 133.8, 133.9, 139.8, 156.1, 156.9, 163.9 and 170.3 ppm. ^{13}C NMR data of compound **9b** revealed 5 SP^3 carbons at δ 14.81, 20.59, 62.0, 65.15 and 94.3 ppm, in addition to, SP and 20 SP^2-carbons at δ 114.8, 115.4, 124.1, 126.6, 126.9, 127.5, 127.7, 127.8, 128.4, 128.9, 130.5, 130.9, 132.7, 133.5, 133.9, 137.7, 149.8, 156.8, 156.9, 163.5, 170.3 ppm. Finally, the obtained nucleosides **2a, b, 4a, b, 6a, b, 8a, b** and **9a, b** were deacetylated via its treatment with aq. methanol solution containing a catalytic amount of triethyl amine to give the target 2-ONN cyclic and acyclic nucleosides **3a, b, 5a, b, 7a, b, 10a, b** and **11a, b**, respectively in high yields (> 85%). The IR and NMR spectra confirmed the deacetylation reaction. Whereas, the carbonyl ester groups were disappeared in IR spectra, in addition to the appearance of OH groups at frequency 3387–3450 cm^{-1}. Although, the ^{1}H and ^{13}C NMR confirmed the deacetylation reaction by disappearance of acetoxy groups protons and carbons.

Antimicrobial evaluation

Antimicrobial activities of the some synthesized nucleosides were investigated against four pathogenic bacteria (namely, *S. aureus and B. cereus* as Gram (+ve) bacteria and *E. coli and P. aeruginosin* as Gram (−ve) bacteria) and one pathogenic fungi (namely, *Aspergillus flavus*). These activities were screened using well diffusion method and the activity was calculated after 24 h for bacteria and 72 h for Fungi [21]. Table 1 illustrates the obtained results of investigated compounds. Cefotaxime and Dermatin were used as standard drugs for the antibacterial and antifungal activity, respectively. The obtained results were recorded in Table 2, which showed in the inhibition zones. Ten new free nucleosides were tested against the mentioned bacteria and fungi. Four of them (namely, **7a, b** and **11a, b**) showed high activity against the tow type of bacteria compared to the used drug (Cefotaxime) and gave inhibition zones in between 25 and 40 mm. The rest of compounds (namely, **3a, b, 5a, b** and **9a, b**) showed moderate activity against pathogenic bacteria. The observed activity of compounds 7 and **11** may be attributed to the presence of ribose and 2-hydroxyethoxy methyl as glycon moiety containing five-member sugar and acyclic ether, respectively. The antifungal activity was investigated for the same compounds, and showed significant results for compounds **11a, b** (the inhibition zones 23–30 mm), the rest of compounds showed moderate activity compared to Dermatin (Table 2).

Conclusion

In summary, we study the utility of MWI in the synthesis of 2-ONN cyclic and acyclic nucleosides and the obtained results were compared with the classical method. The high yields, short reaction time and pure products were observed with MW method. Ten of the synthesized nucleosides were evaluated against Gram (+ve) bacteria, Gram (−ve) bacteria and one pathogenic fungi namely, *Aspergillus flavus*. and good results were obtained for compounds **7a, b** and **11a, b**.

Table 2 Antimicrobial activity of the synthesized pyridine derivatives, zone of inhibition (mm) calculated using concentration of 100 µg/mL

Compound no.	Gram (+ve) bacteria		Gram (−ve) bacteria		Fungi
	S. aureus	*B. cereus*	*E. coli*	*P. aeruginosa*	*Aspergillus flavus*
3a	22	31	27	30	17
3b	25	28	30	24	12
5a	31	21	34	25	22
5b	30	26	32	16	20
7a	33	25	30	35	25
7b	29	32	32	36	30
9a	33	25	28	32	30
9b	15	12	8	10	25
11a	35	40	33	34	30
11b	34	30	35	36	30
Cefotaxime	31	28	32	34	–
Dermatin	–	–	–	–	31

These advantages encourage us to do further study on such synthetic method and compounds.

Experimental

Melting points were measured using an Electro thermal IA 9100 apparatus with open capillary tube and are uncorrected. Solvents used for extraction and purification were distilled prior to use. Reaction temperatures are reported as bath temperatures. Microwave-assisted reactions were performed using a Discover™ single mode cavity microwave synthesizer (CEM Corp.) producing continuous microwave irradiation at 2450 MHz (300w, 150 °C). The IR spectrum (KBr discs) was recorded on a Pye Unicam Sp^3-300 or a Shimadzu FTIR 8101 PC infrared spectrophotometer. The ^{1}H NMR 400 MHz and ^{13}CNMR 100 MHz spectrum were measured on a JEOL-JNM-LA spectrometer using DMSO as a solvent. All chemical shifts were expressed on the δ (ppm) scale using TMS as an internal standard reference. The coupling constant (*J)* values are given in Hz. Analytical data were obtained from the Microanalytical Center, Cairo University, Cairo, Egypt.

General procedure for preparation of 2-ONN (1a, b)

A mixture of 2-acetylnaphthalene (10 mmol), aromatic aldehydes namely (*p*-tolualdehyde, and 3-methylthiophene-2-carboxaldehyde) (10 mmol), ethyl cyanoacetate (10 mmol), and excess from ammonium acetate (80 mmol), in absolute ethanol (30 mL) was refluxed for 10 h, the reaction mentioned by TLC. The reaction mixture was left behind to cool at room temperature; the formed precipitate was filtered off, washed with ethanol, dried and crystallized from methanol/acetic acid (1:2).

6-(Naphthalen-2-yl)-2-oxo-4-(*p*-tolyl)-1,2-dihydropyridine-3-carbonitrile (1a)

Yellow powder; yield 39%, mp 303–305 °C. IR (KBr): 3455 cm^{-1} (NH), 2219 cm^{-1} (C≡N) and 1682 cm^{-1} (C=O, amide). ^{1}H NMR (DMSO-d_6): $\delta = 2.41$ (s, 3H, $H_{methyl\ ring}$), 6.96 (s, 1H, $H_{2\text{-}ONN}$), 7.39 (d, 2H, $^3J = 7.6$ Hz, H_{aryl}), 7.63 (m, 4H, H_{aryl}), 8.01 (m, 4H, H_{aryl}), 8.55 (s, 1H, H_{aryl}), 12.64 (br, 1H, NH). ^{13}C NMR (DMSO-d_6): $\delta = 20.94$ (C_{methyl}), 97.99, 106.5, 116.6, 124.3, 127.0, 127.6, 127.9, 128.1, 128.2, 128.5, 128.8, 129.3, 132.4, 133.2, 133.8, 140.4, 151.2, 159.6, 162.1 and 172.0, (SP and SP^2-carbons). Anal. Calcd for $C_{23}H_{16}N_2O$ (336.39): C, 82.12; H, 4.79; N, 8.33. Found: C, 82.05; H, 4.82; N, 8.28.

4-(3-Methylthien-2-yl)-6-(naphthalen-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (1b)

Yellow powder; yield 44%; mp 283–285 °C. IR (KBr): 3442 cm^{-1} (NH), 2217 cm^{-1} (C≡N) and 1640 cm^{-1} (C=O, amide). ^{1}H NMR (DMSO-d_6): $\delta = 2.32$ (s, 3H, $H_{methyl\ ring}$), 6.95 (s, 1H, $H_{2\text{-}ONN}$), 7.13 (d, 1H, $^3J = 4.80$ Hz, $H_{thienyl}$), 7.63 (m, 2H, H_{aryl}), 7.79 (d, 1H, $^3J = 4.80$ Hz, $H_{thienyl}$), 8.03 (m, 4H, H_{aryl}), 8.53 (s, 1H, H_{aryl}), 12.92 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): $\delta = 15.20$ (C_{methyl}), 98.5, 107.1, 116.2, 124.2, 127.0, 127.6, 127.9, 128.1, 128.2, 128.5, 128.9, 129.3, 131.0, 131.1, 132.3, 133.8, 138.1, 154.0, 160.2, 169.8 (SP and SP^2- carbons). Anal. Calcd for $C_{21}H_{14}N_2OS$ (342.41): C, 73.66; H, 4.12; N, 8.18. Found: C, 73.59; H, 4.11; N, 8.21.

General method for the synthesis of 2-ONN nucleosides (2a, b, 4a, b, 6a, b, 8a, b and 9a, b)

Conventional method A mixture of 2-ONN **1a** or **/1b** (2 mmol) and anhydrous pot. carbonate (2.1 mmol) was stirred in dry DMF (20 mL) for 1 h., then glycosyl bromide, galactosyl bromide, 4-bromo butyl acetate or/ 2-acetoxyethoxymethyl bromide (2.1 mmol) was added in (10 mL) dry DMF. The reaction mixture was stirred at room temperature for 20 h or refluxed for 14–16 h in case of compounds **8a, b** and **9a, b** (Table 1). The solvent was evaporated under reduced pressure and the residual product was chromatographed on silica gel using methylene chloride / MeOH (99:1) to give the desired product.

MW method A 10 mL process vail was charged with a mixture of **1a** or **/1b** (1 mmol), peracetylated sugar (namely, peracetylated glucose/galactose or/ribose), 4-bromo butyl acetate or/ 2-acetoxyethoxymethyl bromide (1.1 mmol), and dry CH_2Cl_2 (5 mL), then (1.0 g) of silica gel (200–400 mesh) was added (In case of compounds **8a, b** and **9a, b**, pot. carbonate (2.1 mmol) was added). The vail was sealed, placed into the cavity of the irradiated with microwave (Discover™ by CEM, 2450 MHz, 300 W, 150 °C) for 5–8 min (Table 1). The residual product was chromatographed on silica gel using CH_2Cl_2/MeOH (99:1) to give the desired product.

General method for deacetylation reaction

Triethylamine (1 mL) was added to a solution of protected nucleosides (**2a, b, 4a, b, 6a, b, 8a, b** and **9a, b**) (2 mmol) in MeOH (20 mL) and few drops of water. The mixture was stirred at room temperature for overnight, evaporated under reduced pressure. The residue was crystallized from methanol.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyl)-6-(naphthalene-2-yl)-2-oxo-4-(*p*-tolyl)-1,2-dihydropyridine-3-carbonitrile (2a)

Yellow syrup; IR (KBr): 2218 cm^{-1} (C≡N), 1747 cm^{-1} (4C=O, acetoxy) and 1640 cm^{-1} (C=O, amide). ^{1}H NMR (DMSO-d_6): $\delta = 1.94$, 1.95, 1.96 and 2.01 (4 s, 12H, $H_{acetoxy}$), 2.43 (s, 3H, $H_{methyl\ ring}$), 3.98 (d, 1H, $^3J_{6',5'} = 9.20$ Hz, H-6′), 4.10 (d, 1H, $^3J_{6'',5'} = 9.18$ Hz, H-6″), 4.68 (m, 1H, H-5′), 4.84 (t, 1H, $^3J_{3',4'} = 10.01$ Hz, $^3J_{4',5'} = 7.22$ Hz, H-4′), 5.19 (t, 1H, $^3J_{1',2'} = 8.20$ Hz, $^3J_{2',3'} = 9.20$ Hz, H-2′), 5.34 (t, 1H, $^3J_{2',3'} = 9.20$, $^3J_{3',4'} = 10.01$ Hz, H-3′), 6.73 (d, 1H, $^3J_{1',2'} = 8.20$ Hz, H-1′), 7.25 (d, 2H, $^3J = 8.0$ Hz, H_{aryl}), 7.39 (m, 2H, H_{aryl}), 7.65 (d, 2H, $^3J = 8.0$ Hz, H_{aryl}), 7.67–8.06 (m, 3H, $H_{2\text{-}ONN}$ and H_{aryl}), 8.35 (d, 1H, $^3J = 6.8$ Hz, H_{aryl}), 8.45 (s, 1H, H_{aryl}), 8.98 (s, 1H, H_{aryl}). ^{13}C NMR (DMSO-d_6): $\delta = 20.30$, 20.32, 20.41, 20.48 and 20.93 ($5C_{methyl}$), 62.60, 66.22, 68.37, 70.07, 72.35 and 88.93 ($6C_{glucose}$), 93.69, 114.3, 115.4, 124.3, 126.6, 127.5, 128.6, 129.4, 132.6, 132.8, 133.3, 134.0, 139.1, 156.8, 156.9, 161.8, 162.3, 162.9, 169.0, 169.2, 169.5, 169.6, 169.7, 170.0, and 170.1 (SP and SP^2-carbons). Anal. Calcd for $C_{37}H_{34}N_2O_{10}$ (666.22): C, 66.66; H, 5.14; N, 4.20. Found: C, 67.04; H, 5.08; N, 4.23.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyl)-4--(3-methylthien-2-yl)-6-(naphthalene-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (2b)

Yellow powder; mp 97–100 °C. IR (KBr): 2218 cm^{-1} (C≡N), 1751 cm^{-1} (C=O, acetoxy) and 1647 cm^{-1} (C=O, amide). ^{1}H NMR (DMSO-d_6): $\delta = 1.88$, 1.94, 1.97 and 2.01 (4 s, 12H, $H_{acetoxy}$), 2.31 (s, 3H, $H_{methyl\ ring}$), 3.95 (dd, 1H, $^2J_{6',6''} = 11.20$, $^3J_{5',6'} = 6.30$ Hz, H, H-6′), 4.07 (dd, 1H, $^2J_{6',6''} = 11.2$, $^3J_{5',6''} = 5.80$ Hz, H, H-6″), 4.64 (m, 1H, H-5′), 4.83 (t,1H, $^3J = 9.6$ Hz, H-4′), 5.18 (t, 1H, $^3J = 9.20$ Hz, H-2′), 5.31 (dd, 1H, $^3J_{2',3'} = 9.2$, $^3J_{3',4'} = 9.60$ Hz, H-3′), 6.80 (d, 1H, $^3J = 9.20$ Hz, H-1′), 7.25–8.96 (m, 10H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$). Anal. Calcd for $C_{35}H_{32}N_2O_{10}S$ (672.70): C, 62.49; H, 4.79; N, 4.16. Found: C; 62.56 H, 4.75; N, 4.11.

1-(β-D-Glucopyranosyl)-6-(naphthalene-2-yl)-2-oxo-4-(*p*-tolyl)-1,2-dihydropyridine-3-carbonitrile (3a)

Brown syrup; yield 95%. IR (KBr): 3395 cm^{-1} (OH), 2224 cm^{-1} (C≡N) and 1641 cm^{-1} (C=O). ^{1}H NMR (DMSO-d_6, D_2O): $\delta = 2.51$ (s, 3H, $H_{methyl\ ring}$), 3.05–3.92 (m, 6H, H-6′, H-6″, H-5′, H-4′, H-3′, H-2′), 6.15 (d, 1H, $^3J = 8.40$ Hz, H-1′), 7.40–8.05 (m, 12H, H_{aryl} and $H_{2\text{-}ONN}$). HRMS (EI): *m/z* [M^+] calcd for $C_{29}H_{26}N_2O_6$: 498.1821; found: 498.1812. Anal. Calcd for $C_{29}H_{26}N_2O_6$ (498.53): C, 69.87; H, 5.26; N, 5.62. Found: C, 69.94; H, 5.23; N, 5.57.

1-(β-D-glucopyranosyl)-4-(3-methylthien-2-yl)-6-(naphthalene-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (3b)

Yellow powder; yield 92%, mp 145–147 °C. IR (KBr): 3425 cm^{-1} (br, 4OH), 2224 cm^{-1} (C≡N) and 1685 cm^{-1} (C=O, amide). ^{1}H NMR (DMSO-d_6): $\delta = 1.32$ (s, 3H, $H_{methyl\ ring}$), 2.84–3.37 (m, 6H, H-6′, H-6″, H-5′, H-4′, H-3′, H-2′), 4.12, 4.41, 4.65, 4.86 (4 m, 4H, 4OH), 6.20 (d, 1H, $^3J = 8.60$ Hz, H-1′), 7.21–8.89 (m, 10H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$). HRMS (EI): *m/z* [M^+] calcd for $C_{27}H_{24}N_2O_6S$: 504.1411; found: 504.1401. Anal. Calcd for $C_{27}H_{42}N_2O_6S$ (504.55): C, 46.27; H, 4.79; N, 5.55. Found: C, 46.35; H, 4.83; N, 5.50.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl)-6-(naphthalene-2-yl)-2-oxo-4-(*p*-tolyl)-1,2-dihydropyridine-3-carbonitrile (4a)

Brown powder; mp 136–138 °C. IR (KBr): 2126 cm^{-1} (C≡N), 1744 cm^{-1} (C=O, acetoxy) and 1656 cm^{-1} (C=O, amide). ^{1}H NMR (DMSO-d_6): $\delta = 1.89$, 1.95, 1.98, 2.06 (4 s, 12H, $H_{acetoxy}$), 2.26 (s, 3H, $H_{methyl\ ring}$), 3.95 (dd, 1H, $^3J_{5',6'} = 5.32$, $^2J_{6',6''} = 11.38$ Hz, H-6′), 4.33 (dd, 1H, $^3J_{5',6''} = 5.80$, $^2J_{6',6''} = 11.38$ Hz, H-6′), 4.74 (m, 1H, H-5′), 4.85 (t, 1H, $^3J_{2',3'} = 9.\ 20$, $^3J_{3',4'} = 2.60$ Hz, H-3′), 5.19 (t, 1H, $^3J_{1',2'} = 8.40$, $^3J_{2',3'} = 9.20$ Hz, H-2′), 5.28 (t, 1H, $^3J_{3',4'} = 2.60$, $^3J_{4',5'} = 2.30$ Hz, H-4′), 6.58 (d, 1H, $^3J_{1',2'} = 8.40$ Hz, H-1′), 7.23–8.91 (m, 12H, H_{aryl}, and $H_{2\text{-}ONN}$). ^{13}C NMR (DMSO-d_6): $\delta = 20.41$, 20.45, 20.59, 20.65 and 34.27 ($5C_{methyl}$), 67.6, 68.2, 69.6, 70.1, 70.5 and 89.4 ($6C_{galactose}$), 96.51, 114.3, 115.8, 124.3, 127.0, 128.1, 128.2, 128.5, 128.7, 128.8, 129.4, 129.5, 130.9, 132.0, 132.4, 133.8, 136.0, 148.3, 154.0, 169.2, 169.8, 170.3, 171.8 and 172.0 (SP and SP^2-carbons). Anal. Calcd for $C_{37}H_{34}N_2O_{10}$ (666.22): C, 66.66; H, 5.14; N, 4.20. Found: C, 66.57; H, 5.17; N, 4.18.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl)-4--(3-methylthien-2-yl)-6-(naphthalene-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (4b)

Yellow powder; m.p 136–138 °C. IR (KBr): 2222 cm^{-1} (C≡N), 1746 cm^{-1} (C=O, acetoxy) and 1642 cm^{-1} (C=O, amide). ^{1}H NMR (DMSO-d_6): $\delta = 1.98$, 1.99, 2.01 and 2.06 (4 s, 12H, $H_{acetoxy}$), 2.31 (s, 3H, $H_{methyl\ ring}$), 3.98 (dd, 1H, $^3J_{5',6'} = 6.13$ Hz, $^2J_{6',6''} = 11.70$ Hz, H-6′), 4.11 (dd, 1H, $^3J_{5',6''} = 6.60$ Hz, $^3J_{6',6''} = 11.70$ Hz, H-6″), 4.58 (m, 1H, H-5′), 5.30 (t, 1H, $^3J_{2',3'} = 10.30$ Hz, $^3J_{3',4'} = 2.84$ Hz, H-3′), 5.34 (t, 1H, $^3J_{1',2'} = 8.40$ Hz, $^3J_{2',3'} = 10.30$ Hz, H-2′), 5.58 (t, 1H, $^3J_{3',4'} = 2.84$ Hz, $^3J_{4',5'} = 3.20$ Hz, H-4′), 6.36 (d, 1H, $^3J_{1',2'} = 8.40$, Hz, H-1′), 7.20–8.85 (m, 10H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$). ^{13}C NMR (DMSO-d_6): $\delta = 20.34$, 20.45, 20.59, 20.64 and 34.26 ($5C_{methyl}$), 69.1, 70.0, 70.1, 70.5, 72.9, 89.4

($6C_{galactose}$), 114.3, 115.6, 124.5, 126.3, 126.8, 127.1, 127.6, 128.0, 128.5, 128.9, 130.6, 131.0, 132.4, 133.9, 135.0, 137.4, 148.8, 152.1, 155.8, 169.2, 170.0, 170.2, 170.4 and 172.0 (SP and SP^2- carbons). Anal. Calcd for $C_{35}H_{32}N_2O_{10}S$ (672.70): C, 62.49; H, 4.79; N, 4.16. Found: C, 62.55; H, 4.83; N, 4.13.

1-(β-D-Galactopyranosyl)-6-(naphthalen-2-yl)-2-oxo-4-(*p*-tolyl)-1,2-dihydropyridine-3-carbonitrile (5a)

Brown powder; yield 92%, mp 142–144 °C. IR (KBr): 3387 cm^{-1} (OH), 2225 cm^{-1} (C≡N) and 1639 cm^{-1} (C=O). ^1H NMR (DMSO-d_6, D_2O): $\delta = 2.50$ (s, 3H, $H_{methyl\ ring}$), 3.06–3.78 (m, 6H, H-6′, H-6″, H-5′, H-4′, H-3′, H-2′), 6.48 (d, 1H, $^3J = 8.20$ Hz, H-1′), 7.60–8.05 (m, 12H, H_{aryl} and $H_{2\text{-}ONN}$).). HRMS (EI): *m*/*z* [M^+] calcd for $C_{29}H_{26}N_2O_6$: 498.1821; found: 498.1811. Anal. Calcd for $C_{29}H_{26}N_2O_6$ (498.53): C, 69.87; H, 5.26; N, 5.62. Found: C, 69.80; H, 5.29; N, 5.66.

1-(β-D-Galactopyranosyl)-4-(3-methylthien-2--yl)-6-(naphthalen-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (5b)

Pale brown powder; yield 93%.; mp 150–152 °C IR (KBr): 3408 cm^{-1} (OH), 2222 cm^{-1} (C≡N) and 1632 cm^{-1} (C=O). ^1H NMR (DMSO-d_6, D_2O): $\delta = 2.51$ (s, 3H, $H_{methyl\ ring}$), 3.04–3.87 (m, 6H, H-6′, H-6″, H-5′, H-4′, H-3′, H-2′), 6.23 (d, 1H, $^3J = 8.40$ Hz, H-1′), 7.39–8.04 (m, 10H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$). HRMS (EI): *m*/*z* [M^+] calcd for $C_{27}H_{24}N_2O_6S$: 504.1410; found: 504.1411. Anal. Calcd for $C_{27}H_{24}N_2O_6S$ (504.55): C, 64.27; H, 4.79; N, 5.62. Found: C, 64.35; H, 4.82; N, 5.57.

1-(2′,3′,5′-Tri-*O*-acetyl-β-D-ribofuranosyl)6-(naphthalene-2-yl)-2-oxo-4-(*p*-tolyl)-1,2-dihydropyridine-3-carbonitrile (6a)

Yellow powder; mp 102–104 °C. IR (KBr): 2215 cm^{-1} (C≡N), 1754 Cm^{-1} (C=O, acetoxy) and 1645 (C=O, amide). ^1H NMR (DMSO-d_6): $\delta = 1.90$, 2.03, 2.08 (3 s, 9H, $H_{acetoxy}$), 2.4 (s, 3H, $H_{methyl\ ring}$), 4.03 (dd, 1H, $^3J_{4',5'} = 4.60$, $^3J_{5',5''} = 12.01$ Hz, H-5′), 4.06 (dd, 1H, $^3J_{4',5''} = 4.20$, $^2J_{5',5''} = 12.01$ Hz, H-5″), 4,07 (m, 1H, H-4′), 4.29 (dd, 1H, $^3J_{2',3'} = 2.40$, $^3J_{3',4'} = 5.60$ Hz, H-3′), 4.71 (dd, 1H, $^3J_{1',2'} = 2.80$, $^3J_{2',3'} = 2.40$ Hz, H-2′), 6.33 (d, 1H, $^3J_{1',2'} = 2.80$ Hz, H-1′), 7.37 (d, 1H, $^3J = 7.60$ Hz, H_{aryl}), 7.62, 8.01 (m, 10H, H_{aryl} and $H_{2\text{-}ONN}$), 8.53 (s, 1H, H_{aryl}). ^{13}C NMR (DMSO-d_6): $\delta = 20.3$, 20.5, 21.1 and 33.8 ($4C_{methyl}$), 70.7, 73.6, 75.6, 79.1, 82.9 ($5C_{ribose}$), 113.0, 116.7, 124.4, 127.1, 127.7, 128.0, 128.2, 128.3, 128.6, 128.9, 129.4, 132.5, 133.3, 133.9, 140.6, 149.2, 151.3, 159.8, 162.3, 169.0, 170.1, 172.2, 178.5 (SP and SP^2-carbons). Anal. Calcd for $C_{34}H_{30}N_2O_8$ (594.61): C, 68.68; H, 5.09; N, 4.71. Found: C, 68.75; H, 5.04; N, 4.67.

1-(2′,3′,5′-Tri-*O*-acetyl-β-D-Ribofuranosyl)-4-(3-methylthien-2-yl)-6-(naphthalene-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (6b)

Yellow powder; mp 165–166 °C. IR (KBr): 2215 cm^{-1} (C≡N), 1732 cm^{-1} (C=O, acetoxy) and 1640 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6): $\delta = 1.90$, 2.03, 2.06 (3 s, 9H, $H_{acetoxy}$), 2.32 (s, 3H, $H_{methyl\ ring}$), 4.03 (dd, 1H, $^3J_{4',5'} = 3.80$, $^3J_{5',5''} = 12.32$ Hz, H-5′), 4.06 (dd, 1H, $^3J_{4',5''} = 3.60$, $^2J_{5',5''} = 12.32$ Hz, H-5″), 4,08 (m, 1H, H-4′), 4.30 (dd, 1H, $^3J_{2',3'} = 2.80$, $^3J_{3',4'} = 6.80$ Hz, H-3′), 4.70 (dd, 1H, $^3J_{1',2'} = 2.40$, $^3J_{2',3'} = 2.80$ Hz, H-2′), 6.33 (d, 1H, $^3J_{1',2'} = 2.40$ Hz, H-1′), 7.11, 8.52 (m, 10H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$). ^{13}C NMR (DMSO-d_6): $\delta = 20.33$, 20.8, 21.0 and 34.5 ($4C_{methyl}$), 71.9, 73.5, 75.5, 79.0, 82.9 ($5C_{ribose}$), 116.3, 124.3, 127.1, 127.6, 128.0, 128.1, 128.2, 128.6, 128.9, 129.4, 131.1, 131.1, 131.2, 132.4, 133.9, 138.2, 142.5, 152.3, 155.3, 168.9, 169.6, 170.0 172.0 (SP and SP^2-carbons). Anal. Calcd for $C_{32}H_{28}N_2O_8S$ (600.64): C, 63.99; H, 4.70; N, 4.66. Found: C, 64.08; H, 4.66; N, 4.69.

1-(β-D-Ribofuranosyl)-6-(naphthalen-2-yl)-2-oxo-4-(*p*-tolyl)-1,2-dihydropyridine-3-carbonitrile (7a)

Yellow powder; yield 91%, mp 189–191 °C. IR (KBr): 3421 cm^{-1} (OH), 2215 cm^{-1} (C≡N) and 1635 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6, D_2O): $\delta = 2.45$ (s, 3H, $H_{methyl\ ring}$), 3.38–3.72 (m, 5H, H-5′, H-5″, H-4′, H-3′, H-2′), 6.05 (d, 1H, $^3J = 3.80$ Hz, H-1′), 7.38 (d, 1H, $^3J = 8.0$ Hz, H_{aryl}), 7.61–8.07 (m, 10 H, H_{aryl}), 8.55 (s, 1H, H_{aryl}). HRMS (EI): *m*/*z* [M^+] calcd for $C_{28}H_{24}N_2O_5$: 468.1723; found: 468.1724. Anal. Calcd for $C_{28}H_{24}N_2O_5$ (468.50): C, 71.78; H, 5.16; N, 5.98. Found: C, 71.70; H, 5.12; N, 6.03.

1-(β-D-Ribofuranosyl)-4-(3-methylthien-2-yl)-6-(naphthalen-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (7b)

Yellow powder; yield 90%; mp 182–185 °C IR (KBr): 3417 cm^{-1} (OH), 2214 cm^{-1} (C≡N) and 1639 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6, D_2O): $\delta = 2.29$ (s, 3H, $H_{methyl\ ring}$), 3.20–3.87 (m, 5H, H-5′, H-5″, H-4′, H-3′, H-2′), 6.44 (d, 1H, $^3J = 3.20$ Hz, H-1′), 7.11 (d, 1H, $^3J = 5.0$ Hz, $H_{thienyl}$), 7.60–7.89 (m, 7H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$), 8.02 (d, 1H, $^3J = 8.50$ Hz, H_{aryl}), 8.49 (s, 1H, H_{aryl}). HRMS (EI): *m*/*z* [M^+] calcd for $C_{27}H_{24}N_2O_4S$: 472.1524; found: 472.1523. Anal. Calcd for $C_{26}H_{22}N_2O_5S$ (474.53): C, 65.81; H, 4.67; N, 5.90. Found: C, 65.76; H, 4.71; N, 5.87.

4-(3-Cyano-6-(naphthalen-2-yl)-2-oxo-4-(*p*-tolyl) pyridin-1(2*H*)-yl)butyl acetate (8a)

Pale brown powder, mp 120–122 °C. IR (KBr): 2220 cm^{-1} (C≡N) and 1735 cm^{-1} (C=O, acetoxy), 1640 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6): $\delta = 1.80$ (m, 1H, $CH_{2(c)}$), 1.90 (m, 2H, $CH_{2(b)}$), 1.99 (s, 3H, $H_{acetoxy}$), 2.42 (s, 3H, $H_{methyl\ ring}$), 4.12 (t, 2H, $^3J = 5.40$ Hz, $CH_{2(d)}$), 4.55 (t, 2H, $^3J = 5.60$ Hz, $CH_{2(a)}$), 7.40 (d, 2H, $^3J = 7.60$ Hz, H_{aryl}), 7.06 (m, 2H, H_{aryl}) 7.69 (d, 2H, $^3J = 7.20$ Hz, H_{aryl}), 7.95–8.06 (m, 4H, H_{aryl}), 8.35 (d, 1H, $^3J = 8.40$ Hz, H_{aryl}), 8.86 (s, 1H, H_{aryl}). ^{13}C NMR (DMSO-d_6): $\delta = 20.65$, 21.01, 24.80, 25.54, 63.48, 66.65 (SP^3-carbons), 92.01, 113.6, 115.3, 124.2, 126.6, 126.8, 127.4, 127.5, 127.6, 128.3, 128.8, 129.3, 132.7, 132.9, 133.8, 133.9, 139.8, 156.1, 156.9, 163.9, 170.3 (SP and SP^2-carbons). Anal.Calcd for $C_{28}H_{26}N_2O_3$ (450.33): C, 77.31; H, 5.82; N, 6.22. Found: C, 77.24; H, 5.86; N, 6.17.

4-(3-Cyano-4-(3-methylthiophen-2-yl)-6-(naphthalene-2-yl)-2-oxopyridin-1(2*H*)-yl)butyl acetate (8b)

Pale brown powder; mp 130–132 °C. IR (KBr): 2221 cm^{-1} (C≡N) and 1731 cm^{-1} (C=O, acetoxy), 1646 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6): $\delta = 1.79$ (m, 1H, $CH_{2(c)}$), 1.91 (m, 2H, $CH_{2(b)}$), 1.98 (s, 3H, $H_{acetoxy}$), 2.29 (s, 3H, $H_{methyl\ ring}$), 4.10 (t, 2H, $^3J = 5.36$ Hz, $CH_{2(d)}$), 4.55 (t, 2H, $^3J = 5.74$ Hz, $CH_{2(a)}$), 7.11 (d, 1H, $^3J = 4.88$ Hz, $H_{thienyl}$), 7.60–7.89 (m, 7H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$), 8.01 (d, 1H, $^3J = 8.74$ Hz, H_{aryl}), 8.52 (s, 1H, H_{aryl}). ^{13}C NMR (DMSO-d_6): $\delta = 20.64$, 20.85, 24.85, 25.60, 63.50, 66.61 (SP^3-carbons), 92.01, 114.0, 115.2, 124.5, 126.4, 126.7, 127.4, 127.6, 127.6, 128.0, 128.8, 129.4, 132.8, 132.9, 133.8, 133.9, 138.8, 155.8, 156.8, 165.9, 171.1 (SP and SP^2-carbons). Anal.Calcd for $C_{27}H_{24}N_2O_3S$ (456.56): C, 71.03; H, 5.30; N, 6.14. Found: C, 70.92; H, 5.27; N, 6.19.

2-((3-Cyano-6-(naphthalene-2-yl)-2-oxo-4-(*p*-tolyl) pyridin-1(2*H*)-yl)methoxy)ethyl acetate (9a)

Brown syrup; IR (KBr): 2219 cm^{-1} (C≡N), 1729 cm^{-1} (C=O, acetoxy). 1660 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6): $\delta = 2.03$ (s, 3H, $H_{acetoxy}$), 2.43 (s, 3H, $H_{methyl\ ring}$), 4.50 (t, 2H, $^3J = 4.50$ Hz, $CH_{2(d)}$), 4.87 (t, 2H, 4.50 Hz, $CH_{2(c)}$), 5.26 (s, 2H, $CH_{2(a)}$), 7.41 (d, 2H, $^3J = 8.10$ Hz, H_{aryl}), 7.59 (m, 2H, H_{aryl}), 7.71 (d, 2H, $^3J = 8.10$ Hz, H_{aryl}), 8.04–8.10 (m, 4H, H_{aryl}), 8.39 (d, 1H, $^3J = 7.80$ Hz, H_{aryl}), 8.88 (s, 1H, H_{aryl}). HRMS (EI): *m/z* [M^+] calcd for $C_{28}H_{24}N_2O_4$: 452.1710; found: 452.1711. Anal. Calcd for $C_{28}H_{24}N_2O_4$ (452.17): C, 74.32; H, 5.35; N, 6.19. Found: C, 74.35; H, 5.34; N, 6.18.

2-((3-Cyano-4-(3-methylthien-2-yl)-6-(naphthalene-2-yl)-2-oxopyridin-1(2*H*)-yl)methoxy) ethyl acetate (9b)

Brown powder, mp 168–170 °C. IR (KBr): 2219 cm^{-1} (C≡N), 1738 cm^{-1} (C=O) and 1656 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6): $\delta = 2.03$ (s, 3H, $H_{acetoxy}$), 2.29 (s, 3H, $H_{methyl\ ring}$), 3.35 (t, 2H, $^3J = 5.20$ Hz, $2H_{(c)}$), 4.50 (t, 2H, $^3J = 5.20$ Hz, $2H_{(d)}$), 4.85 (s, 2H, $2H_{(a)}$), 7.14 (d, 1H, $^3J = 5.20$ Hz, $H_{thienyl}$), 7.58–7.03 (m, 7H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$), 8.30 (d, 1H, $^3J = 8.50$ Hz, H_{aryl}), 8.82 (s, 1H, H_{aryl}). ^{13}C NMR (DMSO-d_6): $\delta = 14.81$, 20.59 ($2C_{methyl}$), 62.0, 65.15, 94.3 ($3C_{methylene}$), 114.8, 115.4, 124.1, 126.6, 126.9, 127.5, 127.7, 127.8, 128.4, 128.9, 130.5, 130.9, 132.7, 133.5, 133.9, 137.7, 149.8, 156.8, 156.9, 163.5, 170.3 (SP and SP^2-carbons). Anal. Calcd for $C_{26}H_{22}N_2O_4S$ (400.45): C, 68.10; H, 4.84; N, 6.11. Found: C, 68.16; H, 4.81; N, 6.15.

1-(4-Hydroxybutyl)-6-(naphthalene-2-yl)-2-oxo-4-(*p*-tolyl)-1,2-dihydropyridine-3-carbonitrile (10a)

Brown powder; yield 98%; mp 150–151 °C. IR (KBr): 3430 cm^{-1} (OH), 2210 cm^{-1} (C≡N) and 1642 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6, D_2O): $\delta = 1.51$ (m, 2H, $CH_{2(b)}$), 1.65 (m, 2H, $CH_{2(c)}$), 2.43 (s, 3H, $H_{methyl\ ring}$), 3.15 (t, 2H, $^3J = 6.01$ Hz, $CH_{2(a)}$), 3.51 (t, 1H, $J = 5.80$ Hz, OH, exchange with D_2O), 4.65 (t, 2H, $^3J = 6.00$ Hz, $CH_{2(d)}$), 7.42 (d, 2H, $^3J = 7.20$ Hz, H_{aryl}), 7.60 (d, 2H, $J = 7.20$ Hz, H_{aryl}), 7.69 (d, 2H, $J = 7.60$ Hz, H_{aryl}), 7.97 (m, 2H, H_{aryl}), 8.06 (d, 2H, $^3J = 8.0$ Hz, H_{aryl}), 8.37 (d, 1H, $^3J = 8.40$ Hz, H_{aryl}), 8.85 (s, 1H, Ar-H). HRMS (EI): *m/z* [M^+] calcd for $C_{27}H_{24}N_2O_2$: 408.1831; Found: 408.1823. Anal. Calcd for $C_{27}H_{24}N_2O_2$ (408.49): C, 79.39; H, 5.92; N, 6.76. Found: C, 79.47; H, 5.89; N, 6.73.

1-(4-Hydroxybutyl)-4-(3-methylthiophen-2-yl)-6-(naphthalene-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (10b)

Brown powder; yield 95%; mp 178–180 °C. IR (KBr): 3435 cm^{-1} (OH), 2218 cm^{-1} (C≡N) and 1644 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6, D_2O): $\delta = 1.51$ (m, 2H, $CH_{2(b)}$), 1.66 (m, 2H, $CH_{2(c)}$), 2.27 (s, 3H, $H_{methyl\ ring}$), 3.16 (t, 2H, $^3J = 5.58$ Hz, $CH_{2(a)}$), 4.60 (t, 2H, $^3J = 6.18$ Hz, $CH_{2(d)}$), 7.13 (d, 1H, $^3J = 4.38$ Hz, $H_{thienyl}$), 7.59–7.89 (m, 7H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$), 8.03 (d, 1H, $J = 8.40$ Hz, H_{aryl}), 8.55 (s, 1H, H_{aryl}). HRMS (EI): *m/z* [M^+] calcd for $C_{25}H_{22}N_2O_2S$: 414.1834; found: 414.1835. Anal. Calcd for $C_{25}H_{22}N_2O_2S$ (414.52): C, 72.44; H, 5.35; N, 6.76. Found: C, 72.52; H, 5.31; N, 6.72.

1-((2-Hydroxyethoxy)methyl)-6-(naphthalene-2-yl)-2-oxo-4-(*p*-tolyl)-1,2-dihydropyridine-3-carbonitrile (11a)

Brown powder; yield 95%; mp 140–142 °C. IR (KBr): 3450 cm^{-1} (br, OH), 2222 cm^{-1} (C≡N) and 1640 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6, D_2O): $\delta = 2.42$ (s, 3H, $H_{methyl\ ring}$), 3.33 (t, 2H, $^3J = 4.56$ Hz, $CH_{2(d)}$), 3.87 (t, 2H, $^3J = 4.56$ Hz, $CH_{2(c)}$), 4.68 (s, 2H, $CH_{2(a)}$), 7.43 (d, 2H, $^3J = 8.10$ Hz, H_{aryl}), 7.60 (m, 2H, H_{aryl}), 7.69 (d, 2H, $^3J = 8.10$ Hz, H_{aryl}), 7.95–8.07 (m, 4H, H_{aryl}), 8.37 (d, 1H, $^3J = 6.80$ Hz, H_{aryl}), 8.86 (s, 1H, H_{aryl}). Anal. Calcd for $C_{26}H_{22}N_2O_3$ (410.46): C, 76.08; H, 5.40; N, 6.82. Found: 76.14; H, 5.37; N, 6.86.

1-((2-Hydroxyethoxy)methyl)-4-(3-methylthiophen-2-yl)-6-(naphthalene-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile (11b)

Brown powder; yield 91%; mp 148–150 °C. IR (KBr): 3404 cm^{-1} (OH), 2221 cm-1 (C≡N) and 1673 cm^{-1} (C=O, amide). ^1H NMR (DMSO-d_6, D_2O): $\delta = 2.29$ (s, 3H, $H_{methyl\ ring}$), 3.80 (t, 2H, $^3J = 6.20$ Hz, $2H_{(d)}$), 4.78 (t, 2H, $^3J = 4.60$ Hz, $CH_{2(c)}$), 4.85 (s, 2H, $CH_{2(a)}$), 7.18 (d, 1H, $^3J = 5.22$ Hz, $H_{thienyl}$), 7.46–7.14 (m, 7H, H_{aryl}, $H_{2\text{-}ONN}$ and $H_{thienyl}$), 8.35 (d, 1H, $^3J = 8.50$ Hz, H_{aryl}), 8.94 (s, 1H, H_{aryl}). HRMS (EI): *m/z* [M^+] calcd for $C_{24}H_{20}N_2O_3S$: 416.1235; found: 416.1233. Anal. Calcd for $C_{24}H_{20}N_2O_3S$ (416.49): C, 69.21; H, 4.84; N, 6.73. Found: C, 69.15; H, 4.81; N, 6.77.

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