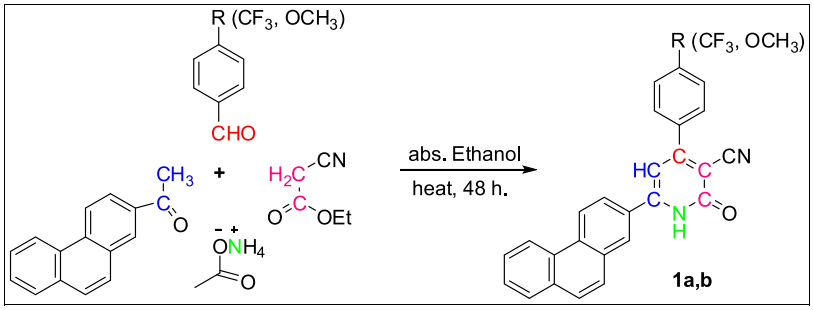
R. A. Haggam,[a]* H. A. El-Sayed,[a] S. A. Said,[a] M. H. M. Ahmed,[b] A. H. Moustafa,[a]* and R. E. Abd-El-Noor[a]

[a]Chemistry Department, Faculty of Science, Zagazig University, Zagazig, Egypt
[b]Chemistry Department, Faculty of Science, Banha University, Banha, Egypt
*E-mail: rhaggan99@hotmail.com; ah_hu_mostafa@yahoo.com

Received November 15, 2015
DOI 10.1002/jhet.2593
Published online 25 January 2016 in Wiley Online Library (wileyonlinelibrary.com).



A series of glycosylation and alkylation reactions of 6-phenanthernyl-2-pyridone derivatives **1a**,**b** containing electron withdrawing and electron donating substituents at 4-position is reported. Regioselective 2-*O*-alkylated/glycosylated products were obtained exclusively, irrespective of the electronic nature of alkylating or the glycosyling agent. Glycosylation of **1a**,**b** with glucosyl/galactosyl and lactosyl bromides afforded **2a**,**b**; **4a**,**b**; and **6a**, respectively. Alkylation of **1a**,**b** with epichlorohydrin, propargyl, allyl bromides, and 3-chloropropanol resulted in compounds **8-10** and **13**, respectively. Deprotection of *O*-glycosylated products under conventional conditions provided the free glycosides **3a**,**b**; **5a**,**b**; **7a**,**12**; and **13**, respectively. The minimal inhibitory concentration for some of the newly synthesized compounds showed high significant activity against Gram (+ve) and Gram (−ve) and antifungal activities. Among the screened compounds, the 4-triflurometyhl phenyl derivatives **2a**, **3a**, **4a**, **8a**, and **11a** exhibited strong antimicrobial activity.

J. Heterocyclic Chem., **54**, 375 (2017).

INTRODUCTION

The 2-pyridones are prominent intermediates in the synthesis of polycyclic compounds of biological significance, as manifested in the antitumor agents, camptothecin [1,2]. They are also structural subunits of naturally occurring products such as the heterocyclic annelated pyridone alkaloid Cerpegin, analgesic, antiulcer, and anti-inflammatory agents [3,4]. Funiculosine (Fig. 1) is another example of biologically active pyridine derivative, which possesses antifungicidal properties [5].

On the other hand, several *O*-glycosyl derivatives of 2-acetamido-2-deoxy-*D*-glucose with hydrophobic aglycons as potential chemotherapeutic agents and *N*-acetyl-*β*-*D*-glucosaminidase and glycosylthioheterocycles have biological inhibitors [6-12], inducers and ligands [13], for affinity chromatography of carbohydrate-process enzymes and proteins. Deprotonation of a 2-pyridone with base provides an ambident anion that can subsequently react on nitrogen or oxygen (Fig. 2). The literature records extensive studies on the influence of base, substituent, electrophile, and solvent on the regioselectivity of *N*-versus *O*-alkylation for the ambident 2-pyridone anion [14-17]. 6-Substituted-2-pyridones are prone to *O*-alkylation, which has been attributed to steric hindrance exerted by the C-6 substitiuent.

As a part of our ongoing program for the synthesis of 2-oxopyridinecarbonitrile derivatives as potential biologically active compounds [18-20], herein, we reported on the glycosylation and alkylation of 2-oxo-4-aryl-6-phenanthrenyl-1,2-dihydropyridine-3-carbonitrile **1a**,**b** derivatives and their evaluation as potential antimicrobial agents.

RESULTS AND DISCUSSION

2-Oxo-4,6-diaryl-1,2-dihydropyridine-3-carbonitrile **1a**, **b** were obtained according to the literature [18] by one-pot multi-component reaction of 3-acetyl phenantherene, ethyl cyanoacetate and aromatic aldehydes in the presence of NH_4OAc/EtOH (Scheme 1). The structure of **1a**,**b** was elucidated by spectral analysis (IR, $^1H/^{13}C$ NMR and elemental analysis). Their IR spectra showed absorption bands at 3440, 3463, 2214, 2220, 1642, and 1687 cm^{-1} corresponding to NH, CN, and C=O groups, respectively. The ^1H NMR exhibited signals at $\delta = 7.13–8.94$, 9.02, 9.06, 9.37, and 9.38 ppm as multiplet, doublet, and singlet,

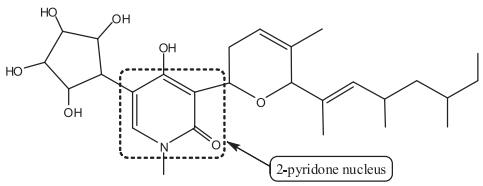


Figure 1. Structure of funiculosine.

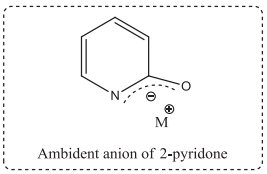


Figure 2. Ambident anion of 2-pyridone.

which are corresponding to aromatic and NH protons, respectively.

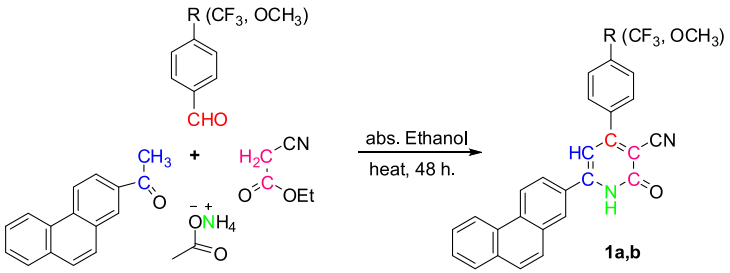
The ambident two sites of 2-pyridones **1a**,**b** are the nitrogen of pyridine and the oxygen atom at position 2. The compounds **1a**,**b** were glycosylated with glucosyl/galactosyl and lactosyl bromides to afford the *O*-glycosides **2a**,**b**; **4a**,**b**; and **6a**, respectively (Scheme 2). The IR spectra showed the absence of the amidic C=O bands, and ^{13}C NMR spectrum of glycoside **2b** showed the anomeric carbon at $\delta = 92.4$ ppm at the low field region. This confirmed the formation of *O*-glycoside not *N*-nucleoside.

The *O*-glycoside formation attributed to the steric hindrance of the phenanthrenyl substutuent at 6-position. Although, it was observed that the presence of electronwithdrawing group (CF_3) or electron donating group (OCH_3) at 4-position of phenyl substituent in pyridine ring is not affected on the glycosylation but affected on the chemical and biological activity. The anomeric protons in glcycosides **2a**,**b**; **4a**,**b;** and **6a** appeared in ^{1}H NMR spectra at $\delta = 6.57$–6.84 ppm as doublet with coupling constants $J = 8.0$ or 8.4 Hz, which explains the β-configuration. The deacetylation of *O*-glycosides **2a**,**b**; **4a**,**b**; and **6a** via the procedure described herein [18,20] led to the free glycosides **3a**,**b**; **5a**,**b**; and **7a**, respectively (Scheme 2). The IR spectra of the free *O*-glycosides showed the absence of acetoxy carbonyl groups and presence of bands at 3398–3420 cm^{-1} corresponding to free OH groups. Although, their ^{1}H NMR spectra exhibited absence of acetoxy protons signals and presence of sugar protons at $\delta = 3.42$–4.76 ppm. In addition to, the presence of anomeric protons signals as doublet with high coupling constant indicates the β-configuration with appearance of free OH groups that were exchanged with D_2O (refer to experimental part).

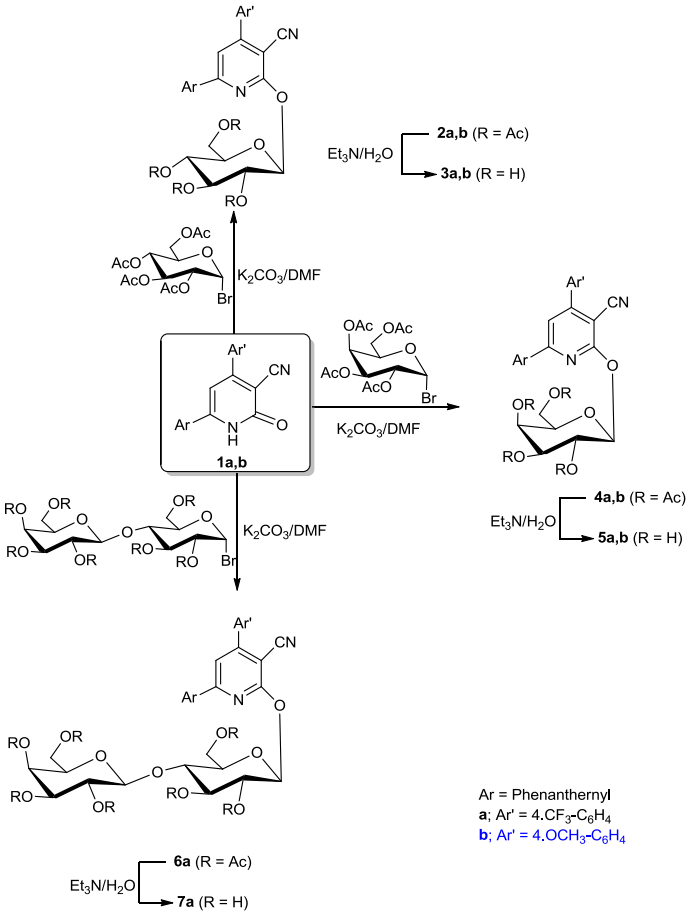
Alkylation of 2-pyridones **1a**,**b** with epichlorohydrin, propargyl/allyl bromides, (2-acetoxyethoxy)methyl bromide [21], 3-chloropropanol and 4-bromobutyl acetate [21] resulted in *O*-alkylated products **8a**,**b**–**10a**,**b** and *O*-acyclic nucleosides **11a**,**b**; **13a**,**b**; and **14a**,**b**, respectively (Scheme 3). The structures of **8a**,**b**–**10a**,**b** and **11a**,**b**–**14a**,**b** were confirmed by their ^{1}H, ^{13}C NMR, IR spectra, and elemental analysis. Spectroscopic data of compounds **8a**,**b**–**10a**,**b** and **11a**,**b**–**14a**,**b** indicate that the alkylation occured at oxygen not nitrogen atom. For instance, in the IR spectra of these products the amidic carbonyl groups (C=O) bands are absent. The ^{1}H NMR spectrum of **8a** showed signals at $\delta = 2.65$–3.06 ppm for (OCH_2) as multiplet, 3.82 ppm proved the (OC*H*) of oxirane ring, and 4.36, 4.93 ppm as doublet of doublet for (OCH*H*) (OC*H*H) characteristic for oxirane ring. While, the ^{1}H NMR spectrum of **9b** revealed the signals at $\delta = 3.64$ ppm for acetylenic (≡C-*H*), 5.35 ppm for (OCH_2). Its ^{13}C NMR spectrum displayed characteristic signals $\delta = 54.7$ ppm for (OCH_2), 77.9, 79.1 ppm for acetylenic carbons (C≡C) and 115.3 ppm (C≡N). Also, ^{1}H NMR spectrum of compound **10b** showed signals at $\delta = 5.20$ ppm [d, 2H, $J = 4.8$ Hz, CH_2(a)], 5.35 ppm [d, 1H, $J = 10.2$ Hz, *H*(d)], 5.54 ppm [d, 1H, $J = 17.4$ Hz, *H*(c)], and 6.25 ppm [m, 1H, *H*(b)]; the high coupling constant indicates that Hc in transconfiguration with Hb. The ^{1}H, ^{13}C NMR and elemental analysis for compounds **8a**, **9a**, and **10a** are in agreement with the proposed structures.

The ^{1}H NMR spectra of the *O*-acyclic nucleosides **11a**,**b** exhibited characteristic signals at $\delta = 1.90$ and 1.91 ppm for the acetoxy methyl groups, in addition to, signals at $\delta = 3.78$, 4.23, and 4.43 and 3.76, 4.33, and 4.48 ppm for CH_2 (c, d, a), respectively. Also, presence of signals for

Scheme 1. One pot synthesis of 2-pyridone 1a,b. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



Scheme 2. Synthetic approaches of nicotnonitrile-2-*O*-glycosides. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



Scheme 3. Alkylation reactions of 2-pyridone 1a,b. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

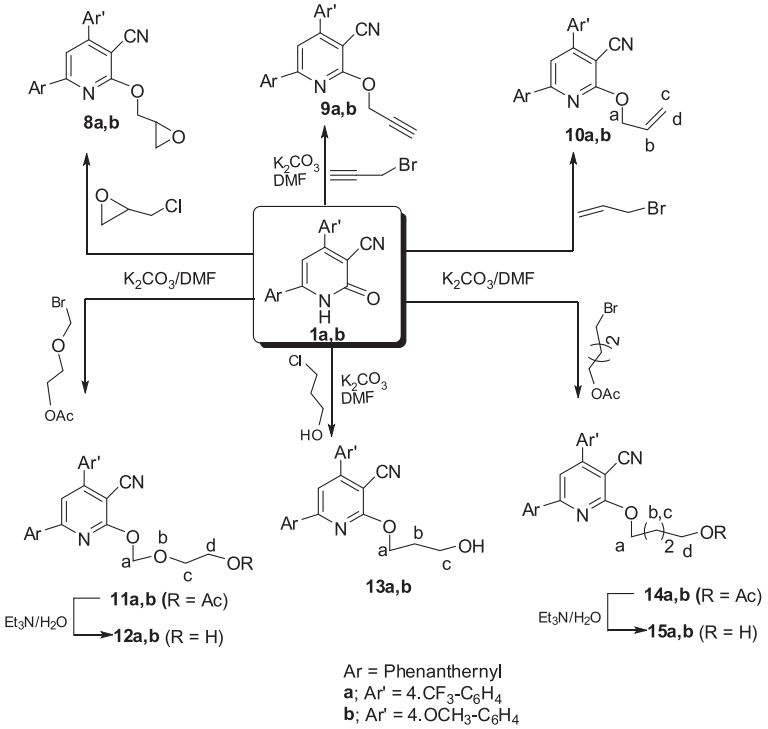


Table 1

The minimal inhibitory concentration (MIC) of **1a**,**b–4a**,**b**; **8a**,**b**; **10a**,**b**; **11a**,**b**; and **14b**

	Gram (+ve)		Gram (−ve)	
Comp. no.	*S. aureus* ATCC 6538	*S. epidermidis* ATCC 12228	*P. aeruginosa* ATCC 9027	*E. coli* ATCC 10536
1a	9	13	3	6
1b	7	11	3	6
2a	8	12	3	7
2b	7	11	3	6
3a	8	12	3	6
3b	7	11	3	6
4a	9	14	3	6
4b	7	11	2	6
8a	8	13	2	6
8b	8	12	2	6
10a	8	13	2	6
10b	7	11	3	6
11a	9	15	3	6
11b	7	10	3	6
14b	8	10	3	6
Cefotaxime (5 mg/mL) (control)	10	16	5	10
DMF (control)	—	—	—	—

(MIC), concentration of compound inhibiting the microbial growth (μg/mL).

13a at $\delta = 2.07$, 3.69, 4.67, and 4.77 ppm assigned the CH_2 (b), CH_2(c), (OH, D_2O exchangeable), and OCH_2(a), respectively.

^{1}H NMR spectrum of compound **14b** revealed the signals at $\delta = 1.28$ and 1.85 ppm as multiplet characterized for CH_2(c) and CH_2(b) and triplet at 4.13 and 4.74 ppm for OCH_2(a) and CH_2OCO (d). Deacetylation of **11a**,**b** and **14a**,**b** gave the free acyclic nucleosides **12a**,**b** and **15a**,**b** (Scheme 3). The IR spectra of the deacetylated acyclic nucleosides revealed the absence of the acetoxy carbonyl (C=O) groups and appeared the free hydroxyl groups at 3418, 3448, and 3388 cm^{-1}, respectively. Their ^{1}H NMR spectra showed the absence of the acetoxy methyl groups and appeared the hydroxyl protons, which were exchangeable with D_2O.

ANTIMICROBIAL EVALUATION

The antimicrobial activities of **1a**,**b–4a**,**b**; **8a**,**b**; **10a**,**b**; **11a**,**b**; **and 14b** were assessed against *Staphylococcus aureus* ATCC 6538, *Staphylococcus epidermidis* ATCC 12228 as (Gram +ve), *Escherichia coli* ATCC 10536, *Pseudomonas aeruginosa* ATCC 9027 as (Gram −ve) and fungi namely (*Candida albicans* ATCC 10231 and *Aspergillus niger* ATCC 16404). It is clearly observed that from the obtained data in Table 1, the all tested compounds showed significant antibacterial activity against Gram (+ve) (*S. aureus* and *S. epidermidis*) and significant antibacterial activity against (*E. coli* and *P. aeruginosa*) as Gram (−ve), using the agar well diffusion method [22], compared with Cefotaxime as control. For antifungal

Table 2

The minimal inhibitory concentration (MIC) of **1a**,**b-4a**,**b**; **8a**,**b**; **10a**,**b**; **11a**,**b**; and **14b**

	Fungi	
Comp. No.	*Candida albicans* ATCC 10231	*Aspergillus niger* ATCC 16404
1a	12	11
1b	9	9
2a	8	8
2b	7	7
3a	7	7
3b	8	7
4a	12	11
4b	10	10
8a	12	11
8b	6	6
10a	6	9
10b	12	6
11a	12	11
11b	7	7
14b	9	12
Nystatin (5 mg/mL) (control)	12.5	8.5
DMF (control)	—	—

(MIC), concentration of compound inhibiting the microbial growth (μg/mL).

activity, in Table 2, it was observed that all the tested compounds have a significant antifungal activity against (*A. niger* and *C. albicans*) than the standard drug Nystatin as control.

CONCLUSION

In this article, we studied the minimal inhibitory concentration (MIC) for the most newly synthesized compounds involving variable electron withdrawing and electron donating groups in phenyl groups at 4-position. We found that 2-pyridones containing the electron withdrawing group (CF_3) have the higher chemical reactivity, higher anti-bacterial and anti-fungal activity than that containing the electron donating group (OCH_3). Moreover, the study discovered that the presence of phenanthrenyl group at 6-position preferred the glycosylation and alkylation at *O*- not *N*-products because of the steric hindrance.

EXPERIMENTAL

All melting points are uncorrected and were measured using an Electro thermal IA 9100 apparatus. The IR spectra (KBr discs) were recorded on a Pye Unicam Sp-3-300 or a Shimadzu FTIR 8101 PC infrared spectrophotometer (Cairo University, Cairo, Egypt). The operation frequency was 400 MHz for ^{1}H and 100 MHz for ^{13}C NMR using BRUKER 400 MHz spectrometer at Zagazig University, Nucleic Acid Center Research. The coupling constants (*J*) are given in Hz. The chemical shifts are expressed on the δ (ppm) scale using TMS as the standard reference. Antimicrobial activity was carried at Microbiology Department at Faculty of Pharmacy, Zagazig University. Elemental analyses were determined on a Perkin Elmer 240 (Microanalysis Center, Cairo University, Egypt).

General procedure for synthesis of heterocyclic bases 1a,b. A mixture of 3-acetyl phenantherene (10 mmol), ethyl cyanoacetate (10 mmol), appropriate aldehydes (namely, 4-trifluoromethylbenzaldehyde and 4-methoxybenzaldehyde) (10 mmol) and ammonium acetate (80 mmol) in absolute ehanol (20 mL) was heated under reflux for 48 h; the formed product was filtered off and recrystallized from acetic acid.

General procedure for synthesis of glycosides 2a,b; 4a,b; and 6a. A solution of glucosyl bromide, galactosyl bromide, or lactosyl bromide (10 mmol) in dry DMF (10 mL) was added to a solution of compounds **1a** or **1b** (10 mmol) in dry DMF (15 mL) in the presence of anhydrous K_2CO_3 (11 mmol), the reaction mixture was stirred at room temperature for 24 h and followed by TLC. The solvent was removed under reduced pressure, the residue was washed with distilled water to remove the inorganic residue, and then the formed solid was separated by silica gel chromatography (200–400 mesh) using CH_2Cl_2 as eluent.

General procedure for deacetylation of 2a,b; 4a,b; and 6a. A mixture of synthesized glycoside (10 mmol), triethylamine (1 mL), and few drops of water in methanol (20 mL) was stirred overnight at room temperature, and then the solvent was removed under reduced pressure. The residue was crystallized from methanol.

General procedure for synthesis of compounds 8a,b–11a,b; 13a,b; and 14a,b. A mixture of pyridin-2(1*H*)-one **1a**,**b** (0.01 mol) and potassium carbonate (0.01 mol) was stirred in dry DMF (15 mL) for 1 h; then the alkylating agents, namely [epichlorohydrin, propargyl/allyl bromides, (2-acetoxyethoxy)methyl bromide, 3-chloropropanol and 4-bromobutyl acetate] (0.01 mol) was added. The reaction mixture was heated under reflux for 12 h, cooled, and poured onto ice water; the precipitate was collected, dry, and crystallized from methanol.

General procedure for deacetylation of compounds 11a,b and 14a,b. A mixture of synthesized compound **11a**,**b** and **14a**,**b** (10 mmol), triethylamine (1 mL), and few drops of water in methanol (20 mL) was stirred overnight at room temperature, and then the solvent was removed under reduced pressure. The residue was crystallized from methanol.

4-[4-(Trifluoromethyl)phenyl]-2-oxo-6-(phenanthren-2-yl)-1,2-dihydropyridine-3-carbonitrile (1a). This compound was obtained as canary yellow powder, Yield 45%; mp 344–346°C; ir (KBr): NH 3440, C≡N 2214, and 1642 C=O amide cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 7.13 (s, 1H, pyridone-5), 7.66–8.94 (m, 12H, Ar-H), 9.02 (d, 1H, J = 10.4 Hz, Ar-H), and 9.37 (s, 1H, NH). ^{13}C nmr (DMSO-d_6): δ 106.5, 116.1 (C ≡ N), 122.1, 122.7, 123.5, 125.3, 125.5, 125.6, 126.1, 127.1, 127.3, 127.8, 128.5, 128.9, 129.2, 129.6, 129.8, 130.1, 130.5, 131.7, 133.1, 140.1, 151.5, 158.3, and 161.8 (Ar-C and C=O); *Anal.* Calcd. for $C_{27}H_{15}F_3N_2O$ (440.4): C, 73.63; H, 3.43; N, 6.36. Found: C, 73.60; H, 3.39; N, 6.40.

4-(4-Methoxyphenyl)-2-oxo-6-(phenanthren-2-yl)-1,2-dihydropyridine-3-carbonitrile (1b). This compound was obtained as yellow powder, Yield 37%; mp 318−320°C; ir (KBr): NH 3463, C≡N 2220 and 1687 C=O amide cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 3.86 (s, 3H, OCH_3), 7.13–8.17 (m, 13H, Ar-H), 9.06 (d, 1H, J = 10.8 Hz, Ar-H), and 9.38 (s, 1H, NH); *Anal.* Calcd. for $C_{27}H_{18}N_2O_2$ (402.4): C, 80.58; H, 4.51; N, 6.96. Found: C, 80.64; H, 4.47; N, 6.93.

2-(2',3',4',6'-Tetra-O-*acetyl-*β-D-glucopyranosyloxy)-4-[4-(trifluoromethyl) phenyl]-6-(phenanthren-2-yl)-3-carbonitrile (2a). This compound was obtained as yellow powder, Yield 54%; mp 148–150°C; ir (KBr): 2225 C≡N and 1753 C=O for 4CH_3CO cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.68, 2.08, 2.09, 2.13 (4 s, 12H, 4CH_3CO), 4.14 (dd, 1H,

$J_{5,6'}$ = 5.81, $J_{6',6''}$ = 11.36 Hz, H-6′), 4.21 (dd, 1H, $J_{5',6''}$ = 6.0, $J_{6',6''}$ = 11.36 Hz, H-6″), 4.64 (m, 1H, H-5′), 5.12 (t, 1H, J = 9.6 Hz, H-4′), 5.30 (dd, 1H, $J_{2',3'}$ = 9.3, $J_{1',2'}$ = 8.4 Hz, H-2′), 5.76 (dd, 1H, $J_{2',3'}$ = 9.3, $J_{3',4'}$ = 9.6 Hz, H-3′), 6.84 (d, 1H, $J_{1',2'}$ = 8.4 Hz, H-1′), and 7.68–9.73 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{41}H_{33}F_3N_2O_{10}$ (770.7): C, 63.89; H, 4.32; N, 3.63. Found: C, 63.94; H, 4.27; N, 3.61.

2-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranosyloxy)-4-(4-methoxyphenyl)-6-(phenanthren-2-yl)-3-carbonitrile (2b). This compound was obtained as yellow powder, Yield 40%; mp 170–172°C; ir (KBr): 2219 C≡N and 1751 C=O for 4CH_3CO cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.75, 2.01, 2.02, 2.07 (4 s, 12H, 4CH_3CO), 3.88 (s, 3H, OCH_3), 4.10 (dd, 1H, $J_{5',6'}$ = 5.90, $J_{6',6''}$ = 10.4 Hz, H-6′), 4.18 (dd, 1H, $J_{5',6''}$ = 6.11, $J_{6',6''}$ = 10.4 Hz, H-6″), 4.61 (m, 1H, H-5′), 5.10 (dd, 1H, $J_{3',4'}$ = 9.2, $J_{4',5'}$ = 10.0 Hz, H-4′), 5.27 (dd, 1H, $J_{1',2'}$ = 8.0, $J_{2',3'}$ = 9.6 Hz, H-2′), 5.74 (dd, 1H, $J_{2',3'}$ = 9.6, $J_{3',4'}$ = 9.2 Hz, H-3′), 6.81 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1′) and 7.18–9.72 (m, 14H, Ar-H); ^{13}C nmr (DMSO-d_6): δ 20.0, 20.2, 20.3, 20.39 (4$\underline{C}H_3CO$), 55.4 ($O\underline{C}H_3$), 61.8 (C-6′), 68.3 (C-4′), 70.26 (C-3′), 71.6 (C-2′), 72 (C-5′), 92.4 (C-1′), 93.7, 114.2 (C≡N), 122.4, 123.3, 125.7, 126.3, 127, 127.2, 127.7, 128.5, 129, 129.1, 129.8, 129.9, 130, 131.8, 132.2, 133.1, 134.3, 137.3, 156.6, 156.8, 160.9, 161.8, 168.8, 169.3, 169.6 and 169.7 (Ar-C and 4C=O); *Anal.* Calcd. for $C_{41}H_{36}N_2O_{11}$ (732.7): C, 67.21; H, 4.95; N, 3.83. Found: C, 67.18; H, 4.99; N, 3.79.

4-(4-(Trifluoromethyl)phenyl)-2-(β-D-glucopyranosyloxy)-6-(phenanthren-2-yl)-3-carbonitrile (3a). This compound was obtained as pale yellow powder, Yield 88%; mp 180–182°C; ir (KBr): 3414 4OH and 2222 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6 /D_2O): δ 3.44–4.76 (m, 6H, H-6′, H-6″, H-5′, H-4′, H-3′ and H-2′), 6.24 (d, 1H, J = 8.0 Hz, H-1′) and 7.70–9.65 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{33}H_{25}F_3N_2O_6$ (602.56): C, 65.78; H, 4.18; N, 4.65. Found: C, 65.84; H, 4.15; N, 4.62.

2-(β-D-Glucopyranosyloxy)-4-(4-methoxyphenyl)-6-(phenanthren-2-yl)-3-carbonirile (3b). This compound was obtained as white powder, Yield 83%; mp 202–204°C; ir (KBr): 3418 (4OH) and 2221 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6 /D_2O): δ 3.58 (s, 3H, OCH_3), 3.68–4.46 (m, 6H, H-6′, H-6″, H-5′, H-4′, H-3′ and H-2′), 6.56 (d, 1H, J = 8.2 Hz, H-1′), and 7.70–9.65 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{33}H_{28}N_2O_7$ (564.85): C, 70.20; H, 5.00; N, 4.69. Found: C, 70.24; H, 5.03; N, 4.65.

2-(2',3',4',6'-Tetra-O-*acetyl*-β-D-galactopyranosyloxy-4-(4-(trifluoromethyl) phenyl)-6-(phenanthren-2-yl)-3-carbonitrile (4a). This compound was obtained as yellow powder, Yield 58%; mp 174–176°C; ir (KBr): 2220 C≡N and 1752 C=O for 4CH_3CO cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.99, 2.00, 2.02, and 2.03 (4 s, 12H, 4CH_3CO), 4.03 (dd, 1H, $J_{5',6'}$ = 6.12, $J_{6',6''}$ = 11.56 Hz, H-6′), 4.15 (dd, 1H, $J_{5',6''}$ = 6.29, $J_{6',6''}$ = 11.56 Hz, H-6″), 4.68 (m, 1H, H-5′), 5.37 (t, 1H, $J_{3',2'}$ = 10.50, $J_{3',4'}$ = 2.84 Hz, H-3′), 5.43 (t, 1H, $J_{2',1'}$ = 8.40, $J_{2',3'}$ = 10.50 Hz, H-2′), 5.52 (t, 1H, $J_{4',3'}$ = 2.84, $J_{4',5'}$ = 3.30 Hz, H-4′), 6.57 (d, 1H, $J_{1',2'}$ = 8.40 Hz,H-1′), 6.87 (s, 1H, pyridone-H-5), and 7.70–9.65 (m, 13H, Ar-H); *Anal.* Calcd. for $C_{41}H_{33}F_3N_2O_{10}$ (770.7): C, 63.89; H, 4.32; N, 3.63. Found: C, 63.94; H, 4.28; N, 3.67.

2-(2',3',4',6'-Tetra-O-acetyl-β-D-galactopyranosyloxy)-4-(4-methoxyphenyl)-6-(phenanthren-2-yl)-3-carbonitrile (4b). This compound was obtained as yellow powder, Yield 45%; mp 192–194°C; ir (KBr): 2222 C≡N and 1750 C=O for 4CH_3CO cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.99, 2.01, 2.02, 2.20 (4 s, 12H, 4CH_3CO), 3.88 (s, 3H, OCH_3), 4.03 (dd, 1H, $J_{5',6'}$ = 5.26, $J_{6',6''}$ = 11.28 Hz, H-6′), 4.10 (dd, 1H, $J_{5',6''}$ = 6.28, $J_{6',6''}$ = 11.28 Hz, H-6″), 4.18 (m, 1H, H-5′), 5.11 (t,1H, $J_{2',3'}$ = 9.50, $J_{3',4'}$ = 2.0 Hz, H-3′), 5.43 (t, 1H, $J_{1',2'}$ = 8.4, $J_{2',3'}$ = 9.51 Hz, H-2′), 5.45 (t, 1H, $J_{3',4'}$ = 2.0, $J_{4',5'}$ = 2.38 Hz, H-4′), 6.72 (d, 1H, $J_{1',2'}$ = 8.4 Hz, H-1′) and 7.19–9.77 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{41}H_{36}N_2O_{11}$ (732.7): C, 67.21; H, 4.95; N, 3.83. Found: C, 67.17; H, 4.99; N, 3.80.

4-(4-(Trifluoromethyl)phenyl)-2-(β-D-galactopyranosyloxy)-6-(phenanthren-2-yl)-3-carbonitrile (5a). This compound was obtained as yellow crystal, Yield 86%. mp 215–217°C. ir (KBr): 3420 4OH and 2222 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6/D_2O): δ 3.49 (m, 3H, H-3′, H-6′ and H-6″), 3.76 (m, 3H, H-2′, H-4′ and H-5′), 6.38 (d, 1H, $J_{1',2'}$ = 8.22 Hz, H-1′), and 7.16–9.66 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{33}H_{25}F_3N_2O_6$ (602.56): C, 65.78; H, 4.18; N, 4.65. Found: C, 65.72; H, 4.15; N, 4.69.

2-(β-D-Galactopyranosyloxy)-4-(4-methoxyphenyl)-6-(phenanthren-2-yl)-3-carbonitrile (5b). This compound was obtained as white powder, Yield 82%; mp 230–232°C; ir (KBr): 3398 4OH and 2219 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6/D_2O): δ 3.42 (m, 3H, H-3′, H-6′, H-6″), 3.87 (m, 3H, H-2′, H-4′, H-5′), 3.89 (s, 3H, OCH_3), 6.18 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1′), and 7.18–9.75 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{33}H_{28}N_2O_7$ (564.85): C, 70.20; H, 5.00; N, 4.69. Found: C, 70.25; H, 5.03; N, 4.65.

2-(2',3',4',6'-Tetra-O-acetyl-β-D-galactopyranosyl-(1 → 4)-(2',3',6'-tri-O-acetyl-β-D-glucopyranosyloxy)-4-(4-(trifluoromethyl)phenyl)-6-(phenanthren-2-yl)-3-carbonitrile (6a). This compound was obtained as canary yellow powder, Yield 66%; mp 146–148°C; ir (KBr): 2225 C≡N and 1753 C=O for 7CH_3CO cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.66, 2.01, 2.03, 2.07, 2.1, 2.15, 2.21, (7 s, 21H, 7CH_3CO), 4.01–4.07 (m, 3H, H-2′b, H-6′a, H-6′b), 5.10 (dd, 1H, $J_{5'a,6''a}$ = 6.12, $J_{6'a,6''a}$ = 11.80 Hz, H-6″a), 5.26 (m, 1H, H-5′b), 5.28 (m, 2H, H-5′a, H-6″b), 5.35 (d, 1H, $J_{1'b,2'b}$ = 7.85 Hz, H-1′b), 5.38 (m, 1H, H-4′b), 5.50 (m, 1H, H-2′a), 5.58 (dd, 1H, $J_{3'a,4'a}$ = 9.1, $J_{4'a,5'a}$ = 9.93 Hz, H-4′a), 5.61 (m, 1H, H-3′b), 5.75 (m, 1H, H-3′a), 6.75 (d, 1H, $J_{1'a,2'a}$ = 8.4 Hz, H-1′a), and 6.84–9.73 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{53}H_{49}F_3N_2O_{18}$ (1058.95): C, 60.11; H, 4.66; N, 2.65. Found: C, 60.06; H, 4.62; N, 2.70.

4-(4-(Trifluoromethyl)phenyl)-2-(β-D-Galactopyranosyl-(1 → 4x)-(β-D-glucopyran-osyloxy)-6-(phenanthren-2-yl)-3-carbonitrile (7a). This compound was obtained as yellow powder, Yield 86%; mp 240–242°C; ir (KBr): 3420 7 OH and 2220 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 3.04–3.52 (4 m, 12H, H-2'b , H-3'b, H-4'b, H-5'b, H-6'b, H-6"b, H-2'a , H-3'a, H-4'a, H-5'a, H-6'a, H-6"a), 4.19 (d, 1H, OH-4'b), 4.31 (d, 1H, OH-6′b), 4.63 (d, 1H, J = 4.28 Hz, OH-3′b), 4.89 (d, 1H, OH-2′b), 4.99 (d, 1H, OH-6′a), 5.21 (d, 1H, OH-3′a), 5.73 (d, 1H, OH-2′a), 5.82 (d, 1H, $J_{1'b,2'b}$ = 7.65 Hz, H-1′b), 6.10 (d, 1H, $J_{1'a,2'a}$ = 8.84 Hz, H-1′a), and 6.77–9.93 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{39}H_{35}F_3N_2O_{11}$ (764.7): C, 61.26; H, 4.61; N, 3.66. Found: C, 61.23; H, 4.58; N, 3.62.

4-(4-(Trifluoromethyl)phenyl)-1-(oxiran-2-ylmethyl)-2-oxo-6-(phenanthren-2-yl)- 1,2-dihydropyridine-3-carbonitrile (8a). This compound was obtained as brown powder, Yield 41%; mp 180–182°C; ir (KBr): 2218 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 2.65–3.06 (m, 2H, OCH_2), 3.82 (m, 1H, OC*H*, oxiran ring), 4.36 (dd, 1H, J = 6.6 Hz, OCH*H*), 4.93 (dd, 1H, J = 2.7, 2.4 Hz, OC*H*H), 7.68 - 8.33 (m, 11H, Ar-H), 8.54 (d, 1H, J = 8.4 Hz, Ar-H), 9.07 (d, 1H, J = 7.8 Hz, Ar-H) and 9.65 (s, 1H, Ar-H); *Anal.* Calcd. for $C_{30}H_{19}F_3N_2O_2$ (496.4): C, 72.58; H, 3.86; N, 5.64. Found: C, 72.55; H, 3.90; N, 5.61.

4-(4-Methoxyphenyl)-1-(oxiran-2-ylmethyl)-2-oxo-6-(phenanthren-2-yl)-1,2-dihydropyridine-3-carbonitrile(8b). This compound was obtained as dark brown powder, Yield 31%; mp 212–214°C; ir (KBr): 2217 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 2.36–2.90 (m, 2H, OCH_2), 3.85 (s, 3H, OCH_3), 3.91 (m, 1H, OC*H*, oxirane ring), 4.41 (dd, 1H, J = 6.8 Hz, OCH*H*), 4.97 (dd, 1H, J = 2.8, 2.89 Hz, OC*H*H), 7.14–8.11 (m, 12H, Ar-H), 9.04 (d, 1H, J = 8.4 Hz, Ar-H) and 9.61 (s, 1H, Ar-H); *Anal.* Calcd. for $C_{30}H_{22}N_2O_3$ (458.5): C, 78.59; H, 4.84; N, 6.11. Found: C, 78.53; H, 4.87; N, 6.08.

4-[4-(Trifluoromethyl)phenyl]-6-(phenanthren-2-yl)-2-(prop-2-yn-1-yloxy) nicotinonitrile (9a). This compound was obtained as yellow powder, Yield 59%; mp 202–204°C; ir (KBr): 2216 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 3.73 (t, 1H, J = 1.8 Hz, ≡C-*H*), 5.38 (d, 2H, J = 1.8 Hz, OCH_2), 7.68-8.33 (m, 11H, Ar-H), 8.54 (d, 1H, J = 8.4 Hz, Ar-H), 9.07 (d, 1H, J = 7.8 Hz, Ar-H) and 9.65 (s, 1H, Ar-H); ^{13}C nmr (DMSO-d_6): δ 55.01 (OCH_2), 78.09, 78.9 (C≡C), 92.5, 114.7, 114.9 (C≡N), 122.4, 122.8, 123.3, 125.4, 125.6, 126.3, 127.1, 127.2, 128.6, 128.8, 129.1, 129.7, 130.02, 130.3, 131.8, 133.1, 132.0, 134.3, 139.8, 155.2, 157.3 and 162.5 (Ar-C); *Anal.* Calcd. for $C_{30}H_{17}F_3N_2O$ (478.4): C, 75.31; H, 3.58; N, 5.85. Found: C, 75.27; H, 3.61; N, 5.82.

4-(4-Methoxyphenyl)-6-(phenanthren-2-yl)-2-(prop-2-yn-1-yloxy)nicotinonitrile (9b). This compound was obtained as yellow powder, Yield 41%; mp 200–202°C; ir (KBr): 2216 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 3.64 (s, 1H, ≡C-*H*), 3.84 (s, 3H, OCH_3), 5.35 (s, 2H, OCH_2), 7.14–8.11 (m, 11H, Ar-H), 8.47 (d, 1H, J = 8.10 Hz, Ar-H), 9.04 (d, 1H, J = 8.4 Hz, Ar-H) and 9.61 (s, 1H, Ar-H); ^{13}C nmr (DMSO-d_6): δ 54.7 (OCH_2), 55.3 (OCH_3), 77.9, 79.1 (C≡C), 91.8, 114.2, 114.5, 115.3 (C≡N), 122.2, 123.3, 125.4, 126.3, 127.1, 127.4, 127.8, 128.3, 128.5, 129, 129.7, 130, 130.1, 130.3, 131.7, 132.9, 134.6, 156.2, 156.7, 160.8 and 162.7 (Ar-C); *Anal.* Calcd. for $C_{30}H_{20}N_2O_2$ (440.4): C, 81.80; H, 4.58; N, 6.36. Found: C, 81.75; H, 4.61; N, 6.31.

2-(Allyloxy)-6-(phenanthren-2-yl)-4-[4-(trifluoromethyl) phenyl]nicotinonitrile (10a). This compound was obtained as yellow powder, Yield 61%; mp 150–152°C; ir (KBr): 2218 cm^{-1} C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 5.24 (d, 2H, J = 4.8 Hz, OCH_2(a)), 5.36 (d, 1H, J = 10.8 Hz, C*H* (d)), 5.56 (d, 1H, J = 17.2 Hz, C*H*(c)), 6.21-6.27(m, 1H, C*H*(b)), 7.69-8.15 (m, 11H, Ar-H), 8.32 (s, 1H, Ar-H), 8.53 (d, 1H, J = 8.4 Hz, Ar-H) and 9.08 (d, 1H, J = 8.0 Hz, Ar-H); ^{13}C nmr (DMSO-d_6): δ 6.75 (OCH_2), 92.4, 114.3, 114.9 (C≡N), 118.04, 122.2, 123.3, 125.3, 125.5, 125.6, 126.2, 127.03, 127.1, 128.4, 128.5, 129.1, 129.2, 129.7, 129.8, 129.9, 131.7, 132.9, 133, 134.5, 139.8, 154.9, 157.4, and 163.3 (Ar-C and CH = CH_2); *Anal.* Calcd. for $C_{30}H_{19}F_3N_2O$ (480.4): C, 74.99; H, 3.99; N, 5.83. Found: C, 74.95; H, 3.97; N, 5.80.

2-(Allyloxy)-4-(4-methoxyphenyl)-6-(phenanthren-2-yl) nicotinonitrile (10b). This compound was obtained as pale yellow powder, Yield 53%; mp 210–212°C; ir (KBr): 2214 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 3.90 (s, 3H, OCH_3), 5.20 (d, 2H, J = 4.8 Hz, CH_2(a)), 5.35 (d, 1H, J = 10.2 Hz, *H*(d)), 5.54 [d, 1H, J = 17.4 Hz, *H*(c)], 6.25 [m, 1H, *H*(b)], 7.16 (d, 1H, J = 8.4 Hz, Ar-H), 7.69–8.17 (m, 10H, Ar-H), 8.49 (d, 1H, J = 8.1 Hz, Ar-H), 9.07 (d, 1H, J = 8.1 Hz, Ar-H) and 9.59 (s, 1H, Ar-H); *Anal.* Calcd. for $C_{30}H_{22}N_2O_2$ (442.5): C, 81.43; H, 5.01; N, 6.33. Found: C, 81.38; H, 5.04; N, 6.37.

2-{[(3-Cyano-6-(phenanthren-2-yl)-4-(4-(trifluoromethyl) phenyl)pyridin-2-yl)oxy]methoxy}ethyl acetate (11a). This compound was obtained as yellow powder, Yield 52%; mp 208–210°C; ir (KBr): 2219 C≡N and 1738 C=O, acetoxy cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.90 (s, 3H, CH_3CO), 3.78 [t, 2H, J = 5.7 Hz, OCH_2 (c)], 4.23 [t, 2H, J = 5.7 Hz, CH_2OCO (d)], 4.43 [s, 2H, OCH_2O (a)], and 7.75–9.78 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{32}H_{23}F_3N_2O_4$ (556.5): C, 69.06; H, 4.17; N, 5.03. Found: C, 69.12; H, 4.21; N, 4.99.

2-{[(3-Cyano-4-(4-methoxyphenyl)-6-(phenanthren-2-yl) pyridin-2-yl)oxy]-methoxy}ethyl acetate (11b). This compound was obtained as yellow powder, Yield 40%; mp 224–226°C; ir (KBr): 2216 C≡N and 1742 C=O, acetoxy cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.91 (s, 3H, CH_3CO), 3.76 [t, 2H, J = 5.7 Hz, OCH_2 (c)], 3.89 (s, 3H, OCH_3), 4.33 [t, 2H, J = 5.7 Hz, CH_2OCO (d)], 4.48 [s, 2H, OCH_2O (a)], and 7.03–9.60 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{32}H_{26}N_2O_5$

(518.5): C, 74.12; H, 5.05; N, 5.40. Found: C, 74.07; H, 5.02; N, 5.43.

4-[4-(Trifluoromethyl)phenyl)-2-[(2-hydroxyethoxy) methoxy]-6-(phenanthren-2-yl)nicotinonitrile (12a). This compound was obtained as yellow powder, Yield 86%; mp mp 228–230°C; ir (KBr): 3418 OH and 2218 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 2.65 (t, 2H, J = 6.3 Hz, CH_2 (c)), 3.31 (t, 1H, OH, D_2O exchangeable), 3.79 [q, 2H, J = 7.2 Hz, CH_2OH (d)], 6.39 [s, 2H, OCH_2O(a)], and 7.23–9.69 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{30}H_{21}F_3N_2O_3$ (514.5): C, 70.12; H, 4.08; N, 5.44. Found: C, 70.06; H, 4.13; N, 5.39.

2-[(2-Hydroxyethoxy)methoxy]-4-(4-methoxyphenyl)-6-(phenanthren-2-yl)nicotinonitrile (12b). This compound was obtained as yellow powder, Yield 82%; mp 250–252°C; ir (KBr): 3448 OH and 2222 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 2.56 [t, 2H, J = 6.3 Hz, CH_2 (c)], 3.45 (t, 1H, OH, D_2O exchangeable), 3.69 (s, 3H, OCH_3), 3.89 [q, 2H, J = 7.2 Hz, CH_2OH (d)], 6.29 [s, 2H, OCH_2O(a)] and 7.38–9.78 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{30}H_{24}N_2O_4$ (476.5): C, 75.61; H, 5.08; N, 5.88. Found: C, 75.66; H, 5.05; N, 5.92.

4-[4-(Trifluoromethyl)phenyl]-2-(3-hydroxypropoxy)-6-(phenanthren-2-yl)nicotinonitrile (13a). This compound was obtained as pale yellow powder; Yield 43%; mp 142–143°C; ir (KBr): 3331 OH and 2217 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 2.07 (m, 2H, CH_2(b)), 3.69 (t, 2H, J = 4.8 Hz, CH_2(c)), 4.67 (t, 1H, J = 5.4 Hz, OH, D_2O exchangeable), 4.77 [t, 2H, J = 4.8 Hz, OCH_2(a)], 7.69 (s, 1H, Ar-H), 7.72-8.31 (m, 8H, Ar-H), 8.54 (s, 1H, Ar-H), 8.57 (s, 1H, Ar-H), 9.09 (s, 1H, Ar-H), 9.12 (s, 1H, Ar-H) and 9.64 (s, 1H, Ar-H); *Anal.* Calcd. for $C_{30}H_{21}F_3N_2O_2$ (498.5): C, 72.28; H, 4.25; N, 5.62. Found: C, 72.21; H, 4.22; N, 5.59.

2-(3-Hydroxypropoxy)-4-(4-methoxyphenyl)-6-(phenanthren-2-yl)nicotinonitrile (13b). This compound was obtained as yellow powder, Yield 33%; mp 134–135°C; ir (KBr): 3410 OH and 2216 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 2.03 [t, 2H, J = 6.4 Hz, CH_2(b)], 3.68 [t, 2H, J = 6.5 Hz, CH_2(c)], 3.88 (s, 3H, OCH_3), 4.73 (t, 1H, J = 5.4 Hz, OH, D_2O exchangeable), 4.76 [t, 2H, J = 6.1 Hz, OCH_2 (a)], 7.17 (s,1H, Ar-H), 7.19–8.17 (m, 10H, Ar-H), 8.51 (d, 1H, J = 8.4 Hz, Ar-H), 9.09 (d, 1H, J = 8 Hz, Ar-H), and 9.62 (s,1H, Ar-H); ^{13}C nmr (DMSO-d_6): δ 31.7 [CH_2(b)], 55.3 (OCH_3), 57.2 [CH_2(c)], 64.4 [OCH_2(a)], 90.3, 91.9, 114.2 (C≡N), 122.1, 123.3, 125.4, 126.3, 127.1, 127.2, 128.1, 128.3, 128.5, 129.1, 130.2, 131.7, 132.8, 134.9, 156.1, 157.1, 160.7, and 164.2 (Ar-C); *Anal.* Calcd. for $C_{30}H_{24}N_2O_3$ (460.5): C, 78.24; H, 5.25; N, 6.08. Found: C, 78.29; H, 5.19; N, 6.12.

4-{[3-Cyano-6-(phenanthren-2-yl)-4-(4-(trifluoromethyl) phenyl)pyridin-2-yl]oxy}butyl acetate (14a). This compound was obtained as pale brown powder, Yield 56%; mp 176–177°C; ir (KBr): 2219 C≡N and 1731 C=O, acetoxy cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.76 [m, 2H, CH_2 (c)], 1.83 [m, 2H, CH_2 (b)] , 1.99 (s, 3H, $C\underline{H}_3CO$), 4.09 [t, 2H, J = 6.0 Hz, OCH_2 (a)], 4.47 (t, 2H, J = 6.3 Hz, CH_2OCO (d)), and 6.85–9.88 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{33}H_{25}F_3N_2O_3$ (554.5): C, 71.47; H, 4.54; N, 5.05. Found: C, 71.41; H, 4.58; N, 5.01.

4-((3-Cyano-4-(4-methoxyphenyl)-6-(phenanthren-2-yl) pyridin-2-yl)oxy)butyl acetate (14b). This compound was obtained as brown powder, Yield 45%; mp 186–187°C; ir (KBr): 2216 C≡N and 1736 C=O, acetoxy cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.28 [m, 2H, CH_2 (c)], 1.85 [m, 2H, CH_2 (b)] , 1.97 (s, 3H, $C\underline{H}_3CO$), 3.29 (s, 3H, OCH_3), 4.13 [t, 2H, J = 6.0 Hz, OCH_2 (a)], 4.74 [t, 2H, J = 6.3 Hz, CH_2OCO (d)] and 7.68–9.63 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{33}H_{28}N_2O_4$ (516.5): C, 76.73; H, 5.46; N, 5.42. Found: C, 76.68; H, 5.41; N, 5.46.

4-(4-(Trifluoromethyl)phenyl)-2-(4-hydroxybutoxy)-6-(phenanthren-2-yl) nicotinonitrile (15a). This compound was obtained as pale yellow powder, Yield 86%; mp 196–197°C; ir (KBr): 3448 OH and 2220 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.78 [m, 2H, CH_2 (c)], 1.84 [m, 2H, CH_2 (b)], 3.36 [q, 2H, J = 6.3 Hz, CH_2OH (d)], 4.19 [t, 2H, J = 5.12 Hz, OCH_2 (a)], 4.56 (t, 1H, J = 5.4 Hz, OH, D_2O exchangeable) and 7.45–9.78 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{31}H_{23}F_3N_2O_2$ (512.5): C, 72.65; H, 4.52; N, 5.47. Found: C, 72.60; H, 4.55; N, 5.42.

2-(4-Hydroxybutoxy)-4-(4-methoxyphenyl)-6-(phenanthren-2-yl)nicotinonitrile (15b). This compound was obtained as pale yellow powder, Yield 81%; mp 210–211°C; ir (KBr): 3388 OH and 2218 C≡N cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 1.48 (m, 2H, CH_2 (c)), 1.85 (m, 2H, CH_2 (b)) , 3.69 (s, 3H, OCH_3), 4.13 [t, 2H, J = 6.0 Hz, OCH_2 (a)], 4.36 (t, 1H, J = 5.4 Hz, OH, D_2O exchangeable), 4.74 [t, 2H, J = 6.3 Hz, CH_2OCO (d)] and 7.48–9.73 (m, 14H, Ar-H); *Anal.* Calcd. for $C_{31}H_{26}N_2O_3$ (474.6): C, 78.46; H, 5.52; N, 5.90. Found: C, 78.52; H, 5.56; N, 5.86.

ANTIMICROBIAL EVALUATION

Mueller-Hinton agar plates were surface-inoculated with the tested strains suspensions adjusted to match 0.5 McFarland standards, and the inoculated were spread over the surfaces of plates using sterile cotton swabs. After drying of the plates, cups (10 mm diameter) were punched in the agar. Samples were dissolved in DMF. Different concentrations of each tested compound were calculated (100–500 µg), using the MIC. The (MIC) of each compound was calculated from the authentic concentration. Then 100 µL from each tested sample or the antimicrobial agents (control) were added into the cups. The plates were incubated at 37°C for 24 h for bacteria and at 30°C for 5 days for fungi growth [22]. The antibacterial activity was determined by

measuring the diameter of the zone of inhibition and comparing to the antimicrobial agents (control). The experiment was repeated three times, and the mean inhibition zones were calculated. The plate cultures were incubated, and the development of the inhibition growth zones was observed.

Acknowledgments. We are thankful for Dr. Nader Abo Ttaleb, assistant Lecturer of Microbiology and Immunology, Faculty of Pharmacy, Zagazig University, for performing the biological activities described in this article.

REFERENCES AND NOTES

[1] Comins, D. L.; Nolan, J. M. Org Lett 2001, 3, 4255.

[2] Josein, H.; Ko, S.-B.; Bom, D.; Curran, D. P. Chem Eur J 1998, 4, 67.

[3] Ryu, H. C.; Seo, S.; Lee, J.-Y.; Ha, T.-A.; Lee, S.; Jung, A.; Ann, J.; Kim, S.-E.; Yoon, S.; Hong, M.; Blumberg, P. M.; Frank-Foltyn, R.; Bahrenberg, G.; Schiene, K.; Stockhausen, H.; Christoph, T.; Frormann, S.; Lee, J. Eur J Med Chem 2015, 93, 101.

[4] Lazaar, J.; Hoarau, C.; Mongin, F.; Tre'court, F.; Godard, A.; Que'guiner, G.; Marsais, F. Tetrahedron Lett 2005, 46, 3811.

[5] Buck, J.; Madeley, J. P.; Pattenden, G. J Chem Soc Perkin Trans 1992, 1, 67.

[6] Awad, O. M. E.; Attia, W. E.; El Ashry, E. S. H. Carbohydr Res 2004, 339, 469.

[7] El Ashry, E. S. H.; Rashed, N.; Shobier, A. H. S. Pharmazie 2000, 55, 251.

[8] El Ashry, E. S. H.; Rashed, N.; Shobier, A. H. S. Pharmazie 2000, 55, 331.

[9] El Ashry, E. S. H.; Rashed, N.; Shobier, A. H. S. Pharmazie 2000, 55, 403.

[10] El Ashry, E. S. H.; El Nemr, A. Synthesis of Naturally Occurring Nitrogen Heterocycles from Carbohydrates; Blackwell: Oxford. UK, 2005.

[11] Kuhn, C. S.; Lehmann, J.; Steck, J. Tetrahedron 1990, 46, 3129.

[12] Blane-Muesser, M.; Vigne, L.; Driguez, H.; Lehmann, J.; Steck, J.; Urbhns, K. Carbohydr Res 1992, 224, 59.

[13] El Ashry, E. S. H.; Awad, L. F.; Atta, A. I. Tetrahedron 2006, 62, 2943.

[14] Reddy, A. C. S.; Narsaiah, B.; Venkataratnam, R. V. J Fluorine Chemistry 1996, 78, 21.

[15] Diez-Barra, A. E.; de la Hoz, A. Synth Commun 1994, 24, 1057.

[16] Sato, T.; Yoshimatsu, K.; Otera, A. J Synlett 1995, 845.

[17] Comins, D. L.; Jianhua, G. Tetrahedron Lett 1994, 35, 2819 and references therein.

[18] El-Sayed, H. A.; Moustafa, A. H.; Haikal, A. Z.; Abu-El-Halawa, R.; El Ashry, E. H. Eur J Med Chem 2011, 46, 2948.

[19] Moustafa, A. H.; El-Sayed, H. A.; Haikal, A. Z.; Abd El-Hady, R. A. Nucleosides Nucleotides Nucleic Acids 2013, 32, 1.

[20] Moustafa, A. H.; El-Sayed, H. A.; Haikal, A. Z.; Abu-El-Halawa, R.; El Ashry, E. H. Nucleosides Nucleotides Nucleic Acids 2011, 30, 340.

[21] Lazrek, H. B.; Taourite, M.; Barascut, J. L.; Imbach, J. L. Bull Soc Chem Belg 1996, 105, 391.

[22] Barry, A. L. In Procedures Antibiotics in Laboratory Medicine; Lorin Williams Wilkians Co.: Baltimore, 1980, pp 1–23.