Some New Pyrido[2,3-*d*]pyridimines and their Nucleoside of Biological Importance

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Abstract: Chalcones (**I**) reacted with malanonitrile and ammonium acetate yielded 2-amino-3-cyano-4,6-disubstituted pyridines (**II**) in excellent yield. 4-Amino-5,7-disubstituted pyrido [2,3-*d*]pyrimidine-2(1*H*)-thiones (**III**), 4-amino-5,7-disubstituted pyrido[2,3-*d*]pyrimidines (**IV**) and 4-imino-3,5,7-trisubstituted pyrido[2,3-*d*]pyrimidin-2(1*H*)-ones (**V**) have been synthesized by the condensation of compound (**II**) with thiourea, formamide and arylisocyanate respectively. The ribofuranosides *viz.* 4-amino-5,7-disubstituted-1- [2',3',5'-tri-*o*-benzoyl- β , *D*-ribofuranosyl]pyrido[2,3-*d*]pyrimidine-2-(1*H*)-thiones (**VI**) and 4-imino-3,5,7-trisubstituted-1- [2',3',5'-tri-*o*-benzoyl- β , *D*-ribofuranosyl] pyrido [2,3-*d*] pyrimidine-2(1*H*)-one (**VII**) were synthesized by converting compounds **III** and **V** to trimethylsilyl derivative *in situ* by reacting them with hexamethyldisilazane to give corresponding ribofuranosides with β -*D*-ribofuranose-1-acetate-2,3,5-tribenzoate. Compounds **III-V** and their ribofuranosides have been screened for antimicrobial and antifungal evaluations.

Keywords: Chalcones, Nucleosides, Biological activities, Pyrimidine.

Introduction

As a part of large number of therapeutic drugs, the pyrido[2,3-*d*]pyrimidine have been reported in this paper. These derivatives have manifold implications, such as antifungal¹⁻⁴, antibacterial⁵⁻⁹, antiallergic¹⁰ and antiherpes¹¹ *etc.* The ribofuranosides of pyrido[2,3-*d*]pyrimidines have been reported as potential antitumor¹² and anti AIDS agents¹³. The promising multifold exploitations of pyrido[2,3-*d*]pyrimidines and our interest in this area prompted us to synthesize some new pyrido[2,3-*d*]pyrimidines and their ribofuranosides. These derivatives in antibacterial and antifungal studies have shown promising biological activities.

Experimental

Melting points were determined in capillary tubes and are uncorrected. Infrared spectra were recorded on a SHIMADZU F.T.-IR spectrophotometer using in KBr discs and ¹H NMR spectra on JEOL AL-300 NMR spectrophotometer in CdCl₂/DMSO-d₆ using TMS as an internal standard. The purity of the synthesized compounds was checked by TLC using Silica gel G as absorbent and visualization was carried out by UV light or iodine.

Synthesis of 2-amino-3-cyano-4,6-disubstituted pyridine II(a-d)

Chalcone (**I**) (0.05 mole), malononitrile (0.05 mole) and ammonium acetate (0.36 mole) in ethanol (80 mL) were refluxed on a water bath for 15-20 h. After cooling, the contents of the flask were poured into crushed ice with constant stirring to obtain a solid mass, which was washed with water and cold ethanol. The residue was recrystallized from ethanol.

Synthesis of 4-amino-5,7-disubstituted pyrido[2,3-d]pyrimidine-2(1H)-thiones III(a-d)

A mixture of 2-amino-4,6-disubstituted pyridine (**II**) (0.01 mole) and thiourea (0.02 mole) was heated on an oil bath at 120-135 °C for 2 h with constant stirring. The temperature was raised to 180 °C and finally the mixture was heated to 220 °C for 2 h. The residue was washed with water, NaHCO₃ solution and finally with cold ethanol. The crude product was recrystallized from DMF: ethanol (1:2).

4-Amino-5-(4-methylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine-2(1H)-thione (IIIa)

Yield 72%, m. p. = 109°, $\nu_{\max}$ (KBr, cm⁻¹) 3175 (>NH), 3465-3320 (-NH₂), 1225 (>C=S), 1380, 1445, 1490 (>NHCS). δ_{H} (CdCl₃) 6.40-7.41 (9H, m, Ph-H), 3.83 (3H, s, OCH₃), 2.07 (3H, s, -CH₃).

4-Amino-5-(4-methylphenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine-2(1H)-thione (IIIb)

Yield 69%, m. p. = 120°, $\nu_{\max}$ (KBr, cm⁻¹) 3155 (>NH), 3445-3330 (-NH₂), 1235 (>C=S), 1375, 1455, 1485 (>NHCS). δ_{H} (CdCl₃) 6.85-7.59 (9H, m, Ph-H), 2.09 (3H, s, -CH₃).

4-Amino-5-(4-methylphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine-2(1H)-thione (IIIc)

Yield 80%, m. p. = 125°, $\nu_{\max}$ (KBr, cm⁻¹) 3200 (>NH), 3450-3310 (-NH₂), 1240 (>C=S), 1350, 1430, 1495 (>NHCS). δ_{H} (CdCl₃) 6.89-7.55 (9H, m, Ph-H), 2.06 (3H, s, -CH₃).

4-Amino-5-(2-methylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine-2(1H)-thione (III d)

Yield 85%, m. p. = 145°, $\nu_{\max}$ (KBr, cm⁻¹) 3160 (>NH), 3460-3440 (-NH₂), 1230 (>C=S), 1370, 1410, 1480 (>NHCS). δ_{H} (CdCl₃) 6.75-7.49 (9H, m, Ph-H), 3.87 (3H, s, -OCH₃).

Synthesis of 4-amino-5,7-disubstituted pyrido[2,3-d]pyrimidine IV(a-d)

Compound **II** (0.01 mole) and formamide (0.04 mole) were refluxed on an oil bath for 14 hours. After cooling the reaction mixture was poured in to the crushed ice, solid product obtained, was washed with water, dried and recrystallized with ethanol.

4-Amino-5-(4-methylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine (IVa)

Yield 68%, m. p. = 185°, $\nu_{\max}$ (KBr, cm⁻¹) 3445-3220 (-NH₂), δ_{H} (CdCl₃) 6.70-8.20 (9H, m, Ph-H), 3.75 (3H, s, -OCH₃), 2.07 (3H, s, -CH₃).

4-Amino-5-(4-methylphenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine(IVb)

Yield 71%, m. p. = 172°, $\nu_{\max}$ (KBr, cm⁻¹) 3450-3200 (-NH₂), δ_{H} (CdCl₃) 6.70-8.20 (9H, m, Ph-H), 2.05 (3H, s, -CH₃).

*4-Amino-5-(4-methylphenyl)-7-(4-bromophenyl) pyrido[2,3-*d*]pyrimidine (IVc)*

Yield 65%, m. p. = 112°, $\nu_{\max}$ (KBr, cm^{-1}) 3445-3190 ($-\text{NH}_2$), δ_{H} (CdCl_3) 6.54-8.22 (9H, m, Ph-H), 2.08 (3H, s, $-\text{CH}_3$).

*4-Amino-5-(2-chlorophenyl)-7-(4-methoxyphenyl) pyrido[2,3-*d*]pyrimidine (IVd)*

Yield 67%, m. p. = 215°, $\nu_{\max}$ (KBr, cm^{-1}) 3440-3200 ($-\text{NH}_2$), δ_{H} (CdCl_3) 6.60-8.21 (9H, m, Ph-H), 3.89 (3H, s, $-\text{OCH}_3$).

*Synthesis of 4-imino-3,5,7-trisubstituted pyrido[2,3-*d*] pyrimidin-2(1H)-ones V(a-d)*

A mixture of compound **II** (0.01 mole), appropriate arylisocyanate (0.01mole), dioxane (15 mL) and pyridine (2 mL) was heated, reflux at 150 °C for 20-22 hours. The reaction mixture after cooling dropped in to crushed ice with constant stirring to obtained the yellow solid mass which filtered, washed with water and recrystallized from DMF: ethanol (1:2)

*4-Imino-3-(3-chlorophenyl)-5-(4-methylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-*d*] pyrimidin-2(1H)-one (Va)*

Yield 75%, m. p. = 135°, $\nu_{\max}$ (KBr, cm^{-1}) 3340 ($>\text{NH}$), 3156 ($>\text{C}=\text{NH}$), 1660 ($>\text{C}=\text{O}$), δ_{H} (CdCl_3) 7.05-7.65 (13H, m, Ph-H), 8.30(1H, s, $>\text{NH}$), 8.40 (1H, s, $>\text{C}=\text{NH}$), 3.82 (3H, s, $-\text{OCH}_3$), 2.59 (3H, s, $-\text{CH}_3$).

*4-Imino-3-(3-chlorophenyl)-5-(4-methylphenyl)-7-(4-chlorophenyl)pyrido[2,3-*d*] pyrimidin-2(1H)-one (Vb)*

Yield 70%, m. p. = 232°, $\nu_{\max}$ (KBr, cm^{-1}) 3325 ($>\text{NH}$), 3170 ($>\text{C}=\text{NH}$), 1685 ($>\text{C}=\text{O}$), δ_{H} (CdCl_3) 7.02-7.70 (13H, m, Ph-H), 7.92 (1H, s, $>\text{NH}$), 8.44 (1H, s, $>\text{C}=\text{NH}$), 2.53 (3H, s, $-\text{CH}_3$).

*4-Imino-3-(3-chlorophenyl)-5-(4-methylphenyl)-7-(4-bromophenyl)pyrido[2,3-*d*] pyrimidin-2(1H)-one (Vc)*

Yield 78%, m. p.=255°, $\nu_{\max}$ (KBr, cm^{-1}) 3320 ($>\text{NH}$), 3190 ($>\text{C}=\text{NH}$), 1660 ($>\text{C}=\text{O}$), δ_{H} (CdCl_3) 7.12-8.15 (13H, m, Ph-H), 8.09 (1H, s, $>\text{NH}$), 8.39 (1H, s, $>\text{C}=\text{NH}$), 2.59 (3H, s, $-\text{CH}_3$).

*4-Imino-3-(3-chlorophenyl)-5-(2-chlorophenyl)-7-(4-methoxyphenyl)pyrido[2,3-*d*] pyrimidin-2(1H)-one (Vd)*

Yield 81%, m. p. = 175°, $\nu_{\max}$ (KBr, cm^{-1}) 3365 ($>\text{NH}$), 3175 ($>\text{C}=\text{NH}$), 1700 ($>\text{C}=\text{O}$), δ_{H} (CdCl_3) 6.89-7.65 (13H, m, Ph-H), 8.21(1H, s, $>\text{NH}$), 8.47 (1H, s, $>\text{C}=\text{NH}$), 3.82 (3H, s, $-\text{OCH}_3$).

*Synthesis of 4-amino-5,7-disubstituted-1-(2',3',5'-tri-O-benzoyl- β -D-ribofuranosyl) pyrido[2,3-*d*]pyrimidine-2(1H)-thione VI(a-d) and 4-imino-3,5,7-trisubstituted-1-(2',3',5'- tri-O-benzoyl- β -D-ribofuranosyl) pyrido[2,3-*d*]pyrimidin-2(1H)-one VII (a-d)*

Compound **III** / **V** (0.002 mole) in toluene (30 mL) was reacted with hexamethyldisilazane (0.012 mole) in presence of ammonium sulphate. The contents were refluxed for 4 hours. The clear solution when obtained was filtered and the solvent was removed in *vacuo* at 100 °C. The sugar *viz.* β -D-ribofuranose-1-acetate-2,3,5-tribenzoate (0.002 mole) was added to the above pasty mixture and the contents were stirred, at 155-160 °C under. The reaction mixture was stirred for 10 h and during the reaction period *vacuum* was regularly applied for five minutes, at the end of every one-hour. The melt was boiled in methanol for 10 minutes, cooled and filtered. The viscous mass of the ribofuranoside so obtained, was recrystallized from diethyl ether.

4-Amino-5-(4-methylphenyl)-7-(4-methoxyphenyl)-1-(2',3',5'-tri-O-benzoyl- β -D-rebofuranosyl) pyrido[2,3-d]pyrimidine-2-thione (VI a)

Yield 79%, m. p. = 108°, $\nu_{\max}$ (KBr, cm^{-1}) 3430-3320 ($-\text{NH}_2$), 1200 ($>\text{C}=\text{S}$), 1725 ($>\text{C}=\text{O}$), 1075-1025 (C-O-C), δ_{H} (CdCl_3) 7.10-8.04 (24H, m, Ph-H), 3.87 (3H, s, $-\text{OCH}_3$), 2.06 (3H, s, $-\text{CH}_3$).

4-Amino-5-(4-methylphenyl)-7-(4-chlorophenyl)-1-(2',3',5'-tri-O-benzoyl- β -D-rebofuranosyl) pyrido[2,3-d]pyrimidine-2-thione (VI b)

Yield 71%, m. p. = 85°, $\nu_{\max}$ (KBr, cm^{-1}) 3420-3320 ($-\text{NH}_2$), 1215 ($>\text{C}=\text{S}$), 1730 ($>\text{C}=\text{O}$), 1015-1070 (C-O-C), δ_{H} (CdCl_3) 7.10-8.04 (24H, m, Ph-H), 2.07 (3H, s, $-\text{CH}_3$).

4-Amino-5-(4-methylphenyl)-7-(4-bromophenyl)-1-(2',3',5'-tri-O-benzoyl- β -D-rebofuranosyl) pyrido[2,3-d]pyrimidine-2-thione (VI c)

Yield 67%, m. p. = 76°, $\nu_{\max}$ (KBr, cm^{-1}) 3435-3330 ($-\text{NH}_2$), 1210 ($>\text{C}=\text{S}$), 1710 ($>\text{C}=\text{O}$), 1095-1025 (C-O-C), δ_{H} (CdCl_3) 7.04-8.09 (24H, m, Ph-H) 2.03 (3H, s, $-\text{CH}_3$).

4-Amino-5-(2-chlorophenyl)-7-(4-methoxyphenyl)-1-(2',3',5'-tri-O-benzoyl- β -D-rebofuranosyl) pyrido[2,3-d]pyrimidine-2-thione (VI d)

Yield 82%, m. p. = 125°, $\nu_{\max}$ (KBr, cm^{-1}) 3440-3325 ($-\text{NH}_2$), 1210 ($>\text{C}=\text{S}$), 1710 ($>\text{C}=\text{O}$), 1110-1130 (C-O-C), δ_{H} (CdCl_3) 6.90-8.16 (24H, m, Ph-H), 3.85 (3H, s, $-\text{OCH}_3$).

4-Imino-3-(3-chlorophenyl)-5-(4-methylphenyl)-7-(4-methoxyphenyl)-1-(2',3',5'-tri-O-benzoyl- β -D-rebofuranosyl) pyrido[2,3-d]pyrimidin-2-one (VIIa)

Yield 69%, m. p. = 235°, $\nu_{\max}$ (KBr, cm^{-1}) 1725 ($>\text{C}=\text{O}$), 1130-1070 (C-O-C), δ_{H} (CdCl_3) 6.75-8.19 (28H, m, Ph-H), 8.49 (1H, s, $>\text{C}=\text{NH}$), 3.83 (3H, s, $-\text{OCH}_3$), 2.09 (3H, s, $-\text{CH}_3$).

4-Imino-3-(3-chlorophenyl)-5-(4-methylphenyl)-7-(4-chlorophenyl)-1-(2',3',5'-tri-O-benzoyl- β -D-rebofuranosyl) pyrido[2,3-d]pyrimidin-2-one (VIIb)

Yield 65%, m. p. = 206°, $\nu_{\max}$ (KBr, cm^{-1}) 1750 ($>\text{C}=\text{O}$), 1165-1045 (C-O-C), δ_{H} (CdCl_3) 6.71-8.10 (28H, m, Ph-H), 8.43 (1H, s, $>\text{C}=\text{NH}$), 2.11 (3H, s, $-\text{CH}_3$).

4-Imino-3-(3-chlorophenyl)-5-(4-methylphenyl)-7-(4-bromophenyl)-1-(2',3',5'-tri-O-benzoyl- β -D-rebofuranosyl) pyrido[2,3-d]pyrimidin-2-one (VIIc)

Yield 67%, m. p. = 215°, $\nu_{\max}$ (KBr, cm^{-1}) 1735 ($>\text{C}=\text{O}$), 1100-1025 (C-O-C), δ_{H} (CdCl_3) 6.73-8.12 (28H, m, Ph-H), 8.43 (1H, s, $>\text{C}=\text{NH}$), 2.05 (3H, s, $-\text{CH}_3$).

4-Imino-3-(3-chlorophenyl)-5-(2-chlorophenyl)-7-(4-methoxyphenyl)-1-(2',3',5'-tri-O-benzoyl- β -D-rebofuranosyl) pyrido[2,3-d]pyrimidin-2-one (VIId)

Yield 70%, m. p. = 245°, $\nu_{\max}$ (KBr, cm^{-1}) 1720 ($>\text{C}=\text{O}$), 1140-1065 (C-O-C), δ_{H} (CdCl_3) 6.69-8.04 (28H, m, Ph-H), 8.37 (1H, s, $>\text{C}=\text{NH}$), 3.83 (3H, s, $-\text{OCH}_3$).

Results and Discussion

Chalcone (**I**) were synthesized by refluxing a suitable acetophenone with substituted benzaldehyde in water-ethanol containing sodium hydroxide. These chalcones (**I**), on condensation with malanonitrile in ethanol, in presence of ammonium acetate, gave 2-amino-3-cyano-4,6-disubstituted pyridines (**II**). Compound **II** on treatment with thiourea,

formamide and arylisocyanate afforded compound **III-V** respectively. Compound **III** and **IV** on condensation with hexamethyldisilazane yielded corresponding trimethylsilyl derivatives, which *in situ* when stirred with a sugar *viz.* β -D-ribofuranose-1-acetate-2,3,5-tribenzoate gave ribofuranosides **VI** and **VII**. The proposed structures of the synthesized compounds are well supported by IR and ^1H NMR data and elemental analysis (shown in Table 1).

Table 1. Physical data of compounds **III(a-d)** – **VII(a-d)**

Comp. No.	R ¹	R ²	R ³	Mol. Formula (mol. wt.)	Found % (Calc.)		
					C	H	N
IIIa	4-CH ₃ C ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -		C ₂₁ H ₁₈ N ₄ OS (374)	67.41 (67.38)	4.85 (4.81)	14.95 (14.97)
IIIb	4-CH ₃ C ₆ H ₄ -	4-ClC ₆ H ₄ -		C ₂₀ H ₁₅ N ₄ SCl (378.5)	63.45 (63.41)	3.99 (3.96)	14.93 (14.97)
IIIc	4-CH ₃ C ₆ H ₄ -	4-BrC ₆ H ₄ -		C ₂₀ H ₁₅ N ₄ SBr (423)	56.76 (56.74)	3.56 (3.54)	13.21 (13.24)
IIId	2-ClC ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -		C ₂₀ H ₁₅ N ₄ OSCl (384.5)	62.45 (62.42)	3.92 (3.90)	14.53 (14.56)
IVa	4-CH ₃ C ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -		C ₂₁ H ₁₇ N ₄ O (341)	73.95 (73.90)	5.02 (4.98)	16.39 (16.42)
IVb	4-CH ₃ C ₆ H ₄ -	4-ClC ₆ H ₄ -		C ₂₀ H ₁₄ N ₄ Cl (345.5)	69.49 (69.46)	4.09 (4.05)	16.21 (16.23)
IVc	4-CH ₃ C ₆ H ₄ -	4-BrC ₆ H ₄ -		C ₂₀ H ₁₄ N ₄ Br (380)	63.20 (63.16)	3.70 (3.68)	14.70 (14.73)
IVd	2-ClC ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -		C ₂₀ H ₁₄ N ₄ OCl (361.5)	66.42 (66.39)	3.90 (3.87)	15.44 (15.49)
Va	4-CH ₃ C ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -	3-ClC ₆ H ₄	C ₂₇ H ₂₁ N ₄ O ₂ Cl (468.5)	69.19 (69.16)	4.50 (4.48)	11.91 (11.95)
Vb	4-CH ₃ C ₆ H ₄ -	4-ClC ₆ H ₄ -	3-ClC ₆ H ₄	C ₂₆ H ₁₈ N ₄ OC ₂ Cl ₂ (473)	65.99 (65.96)	3.83 (3.80)	11.81 (11.84)
Vc	4-CH ₃ C ₆ H ₄ -	4-BrC ₆ H ₄ -	3-ClC ₆ H ₄	C ₂₆ H ₁₈ N ₄ OCIBr (517.5)	60.31 (60.29)	3.52 (3.48)	10.79 (10.82)
Vd	2-ClC ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -	3-ClC ₆ H ₄	C ₂₆ H ₁₈ N ₄ O ₂ Cl ₂ (489)	63.84 (63.80)	3.70 (3.68)	11.41 (11.45)
VIa	4-CH ₃ C ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -		C ₄₇ H ₃₄ N ₄ O ₈ S (814)	69.32 (69.32)	4.21 (4.18)	6.83 (6.88)
VIb	4-CH ₃ C ₆ H ₄ -	4-ClC ₆ H ₄ -		C ₄₆ H ₃₂ N ₄ O ₇ SCl (819.5)	67.39 (67.37)	3.94 (3.90)	6.81 (6.83)
VIc	4-CH ₃ C ₆ H ₄ -	4-BrC ₆ H ₄ -		C ₄₆ H ₃₂ N ₄ O ₇ SBr (864)	63.92 (63.89)	3.74 (3.70)	6.43 (6.48)
VIId	2-ClC ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -		C ₄₆ H ₃₂ N ₄ O ₈ SCl (835.5)	66.09 (66.07)	3.83 (3.80)	6.68 (6.70)
VIIa	4-CH ₃ C ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -	3-ClC ₆ H ₄	C ₅₃ H ₃₈ N ₄ O ₁₀ Cl (925.5)	68.75 (68.72)	4.14 (4.10)	6.02 (6.05)
VIIb	4-CH ₃ C ₆ H ₄ -	4-ClC ₆ H ₄ -	3-ClC ₆ H ₄	C ₅₂ H ₃₅ N ₄ O ₈ Cl ₂ (914)	68.29 (68.27)	3.83 (3.85)	6.11 (6.13)
VIIc	4-CH ₃ C ₆ H ₄ -	4-BrC ₆ H ₄ -	3-ClC ₆ H ₄	C ₅₂ H ₃₅ N ₄ O ₈ ClBr (958.5)	65.50 (65.10)	3.69 (3.65)	5.81 (5.84)
VIIId	2-ClC ₆ H ₄ -	4-OCH ₃ C ₆ H ₄ -	3-ClC ₆ H ₄	C ₅₂ H ₃₂ N ₄ O ₁₀ Cl ₂ (956)	65.32 (65.27)	3.68 (3.66)	5.83 (5.86)

Infrared studies

The IR spectra of 2-amino-3-cyano-4,6-disubstituted pyrimidines **II** showed-CN and -NH₂ bands of moderate intensity in the region 2280-2180 cm⁻¹ and 3430-3310 cm⁻¹, respectively. Compound **III** showed sharp band due to >C=S and three characteristic bands of medium intensity due to >NHCS moiety in the region 1225-1255 cm⁻¹ and 1350-1520 cm⁻¹, respectively. Compound **III** also showed band due to -NH₂ and >NH groups in the region 3435-3310 cm⁻¹ and 3155-3200 cm⁻¹, respectively. In compound **IV**, -NH₂ band appeared at 3445-3190 cm⁻¹. >C=O band in compound **V** was obtained in the region 1700-1660 cm⁻¹. The new band appeared in compound **VI** and **VII** at 1710-1750 cm⁻¹ due to >C=O group and >NH band disappeared in the IR-spectra of these compounds confirmed the ribosilation at this position. The symmetric and asymmetric stretching vibration due to the C-O-C linkage in compound **VI** and **VII** have appeared in the region 1165-1025 cm⁻¹.

Scheme 1

R¹ = (a) 4-CH₃C₆H₄, (b) 4-CH₃C₆H₄, (c) 4-CH₃C₆H₄, (d) 2-ClC₆H₄

R² = (a) 4-OCH₃C₆H₄, (b) 4-ClC₆H₄, (c) 4-BrC₆H₄, (d) 4-OCH₃C₆H₄

R³ = 3-ClC₆H₄

¹H NMR studies

The ¹H NMR spectra of all the pyrido[2,3-*d*]pyrimidines and their ribofuranosides exhibit a multiplet in the region δ 6.50-8.22 due to aromatic protons. The -NH₂ protons gave a signal, which merged with aromatic protons and has been confirmed by integration of the multiplet. A sharp singlet of -CH₃ protons observed in the range δ 2.25 -2.33 while a singlet due to the -OCH₃ protons in the region δ 3.82-3.86. The >NH proton in compound **III** appeared as a singlet at δ 7.92-8.30. A peak due to >NH was found to be absent in compound **VI** and **VII**, indicating the site of attachment of sugar. Proton at C-1' (in the sugar part) caused a singlet at δ 6.35-6.50, confirming the formation of β -configuration. C-2' and C-3' protons of sugar moiety appeared in the region δ 5.70-5.95 as a multiplet and protons at C-4' and C-5' causing a multiplet in the region δ 4.35-4.87.

Screening for antimicrobial activities

Antimicrobial evaluations of all the synthesized compounds were carried out against *Escherichia coli* (gram negative bacteria), *Staphylococcus aureus* (gram positive bacteria) and fungi *e.g.* *Aspergillus niger*, *Aspergillus flavus*. These compounds were tested at conc. 100 μ g/disc in agar-agar media following the method due to Bauer *et al*¹⁴. These results have been tabulated in the form of inhibition zones (mm) and activity indices (inhibition area of sample/inhibition area of the standard). Streptomycin and Mycostain were taken as the reference compounds in the antibacterial and antifungal activities, respectively. Comparison of activity indices show that the ribofuranosides *i.e.* **VI** and **VII** show better activities than corresponding precursor heterocyclic compounds **III** and **V**. All the compounds were found to be moderately active against various bacteria and fungi but compound **IIIa** was significantly active against gram negative bacteria *Escherichia coli*. The results of antimicrobial evaluations have been presented in Table 2.

Table 2. Antimicrobial activities of compounds **III(a-d)**–**VII(a-d)** zone of growth inhibition (mm)(activity index)

Comp. No.	<i>Escherichia coli</i> (gram –ve)	<i>Staphylococcus aureus</i> (gram +ve)	<i>Aspergillus niger</i>	<i>Aspergillus flavus</i>
IIIb	9.0 (0.74)	8.9 (0.71)	8.8 (0.73)	8.5 (0.70)
IIIc	7.9 (0.65)	7.5 (0.61)	8.9 (0.74)	9.2 (0.77)
IIId	12.1 (0.99)	12.5 (1.02)	7.7 (0.64)	7.5 (0.62)
IVa	9.1 (0.74)	9.7 (0.79)	12.0 (1.00)	11.8 (0.98)
IVb	9.5 (0.78)	8.7 (0.71)	8.6 (0.71)	7.9 (0.65)
IVc	8.0 (0.78)	8.5 (0.70)	9.0 (0.75)	9.2 (0.76)
IVd	11.7 (0.95)	11.9 (0.97)	7.9 (0.65)	7.6 (0.63)
Va	8.9 (0.73)	9.5 (0.78)	11.8 (0.98)	12.2 (1.02)
Vb	9.2 (0.75)	9.9 (0.81)	8.5 (0.70)	8.3 (0.69)
Vc	7.6 (0.62)	8.0 (0.95)	9.6 (0.80)	8.9 (0.74)
Vd	12.3 (1.008)	11.5 (0.94)	7.6 (0.63)	8.3 (0.69)
VIa	10.2 (0.82)	10.0 (0.80)	12.3 (1.03)	12.0 (1.00)
VIb	9.9 (0.80)	9.2 (0.74)	9.0 (0.75)	8.8 (0.73)
VIc	9.3 (0.75)	9.5 (0.77)	10.2 (0.85)	9.8 (0.81)
VIId	12.3 (0.99)	12.1 (0.97)	8.6 (0.72)	8.2 (0.68)
VIIa	10.6 (0.85)	10.9 (0.87)	11.7 (0.97)	11.4 (0.95)
VIIb	9.8 (0.79)	8.8 (0.72)	8.9 (0.74)	9.2 (0.76)
VIIc	10.8 (0.87)	10.5 (0.86)	9.5 (0.79)	8.9 (0.74)
VIIId	9.7 (0.79)	10.1 (0.81)	8.7 (0.72)	9.3 (0.77)

Activity Index: inhibition area of the sample/inhibition area of the standard

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