V. S. Taile, ${ }^{\text {a* }}$ K. M. Hatzade, ${ }^{\text {a,b }}$ P. K. Gaidhane, ${ }^{\text {a }}$ and V. N. Ingle ${ }^{\text {a }}$<br>${ }^{\text {a }}$ Department of Chemistry, Organic Research Laboratory-1, Rashtrasant Tukadoji Maharaj Nagpur<br>University, Nagpur-440 033, India<br>${ }^{\mathrm{b}}$ Department of Chemistry, D. B. Science College, Gondia-441 614, Maharashtra, India<br>*E-mail: vijaytaile@gmail.com<br>Received December 16, 2009<br>DOI 10.1002/jhet. 433<br>Published online 17 June 2010 in Wiley InterScience (www.interscience.wiley.com).




#### Abstract

A series of 2-(4-hydroxyphenyl)-4,5-disubstituted imidazoles (1a-e) prepared from $\alpha$-diketones, ammonium acetate, and $p$-hydroxybenzaldehyde, which were glucosylated by using $\alpha$-acetobromoglucose to form 2-(4-o- $\beta$-D-2,3,4,6-tetra-O-acetyl-glucosidoxyphenyl)-4,5-disubstituted imidazoles (2a-e) which on catalytic deacetylation with $\mathrm{CH}_{3} \mathrm{ONa}$ in methanol afforded the title compound 2-(4-o- $\beta$-d-glucosidox-yphenyl)-4,5-disubstituted imidazoles (3a-e). Compounds were characterized by elemental analysis and by instrumental technique, similarly the title compounds were investigated for antimicrobial and antifungal activity.


J. Heterocyclic Chem., 47, 903 (2010).

## INTRODUCTION

In continuation of our work [1] with imidazole ring which were very important in living systems like vita$\min B_{12}$. Imidazole also forms a part of some important compounds such as purine, adenine, xanthine, guanine, co-enzyme-a. It is also distributed in essential amino acid, e.g., 1-histidine. Imidazoles possess, various biological activities, viz., antibacterial [2,3], antifungal [4], anti-inflammatory [5], antihistaminic [6], and hypertensive [7]. Glucoconjugate and the carbohydrate containing structure [8,9] exhibit a variety of biological and therapeutic properties [10]. As a result, the formation of glucosidic linkage continues to be a dominant theme in carbohydrate chemistry [11,12]. The attached sugar molecules increase water solubility and tissue penetration. In addition to acting as a modifier, carbohydrate can induce biological activity. In view of various biological activities of imidazoles and the importance of glucose moiety in the metabolism, several compounds containing imidazole and glucose moiety have been synthesized. Herein, we reported the synthesis of 2-(4-hydroxyphenyl)-4,5-disubstituted imidazoles and $2-(4-o-\beta-$-d glucosidoxyphenyl)-4, $\quad 5$-disubstituted imidazoles.

## RESULTS AND DISCUSSION

Our general synthetic route starts with the aglycon synthesis $\mathbf{1}$ it was prepared by condensation between $\alpha$ diketones, $p$-hydroxybenzaldehyde, and ammonium acetate in the acetic acid medium [13]. The series of these aglycon prepared by changing substitutions at 4,5 positions (1a-e). The glucosylation is carried out by using modified Koenigs-Knorr method [14] (Scheme 1).

The mechanism of $o$-glucosylation reaction gained immense importance due to its stereo-and regeoselective nature. Glucosylation of 2-(4-hydroxyphenyl)-4,5-disubstituted imidazole with $\alpha$-acetobromoglucose (ACBG) followed by deacetylation leads to the desired $o$-glucoside with distereoselectivity in favors of $\beta$-anomer. o-Glucosylation takes place via $\mathrm{S}_{\mathrm{N}} 1$ and $\mathrm{S}_{\mathrm{N}} 2$ mechanism. In the absence of heavy metal salts or Lewis acid catalyst mostly follows $\mathrm{S}_{\mathrm{N}} 2$ mechanism which mainly leads to $\beta$-anomer as the preferred product. In contrast, the presence of Lewis acid catalyst follows $\mathrm{S}_{\mathrm{N}} 1$ mechanism and is less distereoselective and regioselective.

This leads to the formation of $\alpha$ - and $\beta$-anomers. An ester protecting group on the 2 -hydroxyl group of the donor will lead to the neighboring group participation during $o$-glucosylation reaction and only the 1,2 -transdiaxial glucoside ( $\beta$-anomer) is the preferred product.
Scheme 1




Glucosylation of 2-(4-hydroxyphenyl)-4,5-disubstituted imidazoles with acetobromoglucose (ACBG) followed by deacetylation leads the desired $o$-glucoside FT-IR data of the $o$-glucoside are in agreement with the assigned structure. Anomeric configuration confirmed by ${ }^{1} \mathrm{H}$ NMR since the coupling constant of the compound 8.5 Hz was observed between $\mathrm{H}-1$ and $\mathrm{H}-2$ proton. ${ }^{13} \mathrm{C}$ NMR spectrum, C-1 resonated downfield of the other glucosyl carbon at $\delta 100.26$ consistent with the formation of $o-\beta$ glucosides. $\mathrm{S}_{\mathrm{N}} 2$ mechanism for 1,2-trans glucoside formation 1,2-dioxyacylcarbonium ion (Scheme 2).

## BIOLOGICAL ASSAY

Antibacterial activity. The compounds (3a-e) were screened for their antibacterial activities against various pathogenic bacteria Escherichia coli, Klebisilla aerogens, Staphyllococcus aureus, and Bacillus substilis by the cup plate diffusion of $100 \mu \mathrm{~g} / \mathrm{mL}$ by using standard ciprofloxacin and sulphacetamide ( $100 \mu \mathrm{~g} / \mathrm{mL}$ ) for bacteria. The zone of inhibition after 24 h of incubation at $37^{\circ} \mathrm{C}$ was compared with standard drugs (Table 1).

Antifungal activity. The compounds (3a-e) were screened for antifungal activity tasted at $100 \mu \mathrm{~g} / \mathrm{mL}$ concentration in methanol against Aspergillus niger and

Candida albicans by adopting cup plate diffusion method. The zone of inhibition after 7 days at $37^{\circ} \mathrm{C}$ was compared with standard drugs gentamycin and clotrimazole ( $100 \mu \mathrm{~g} / \mathrm{mL}$ ).

## EXPERIMENTAL

The melting points (mp) are taken by using open capillary method and are uncorrected. The FT-IR spectra were recorded on Perkin-Elmer spectrophotometer using KBr disc. The ${ }^{1} \mathrm{H}$ NMR spectra are recorded on Bruker DRX-300 ( 300 MHz FTNMR) instrument using DMSO-d6 as a solvent and TMS as internal standard, and the chemical shift are expressed in $\delta$ ppm values. EI-MS were recorded by direct insertion technique with a Hitachi Perkin Elmer RMU 6D mass Spectrophotometer. Elemental analysis was determined by the FLASH EA 1112 CHN analyzer, Thermo Finigin, Italy.

General procedure for 2-(4-hydroxyphenyl)-4,5-disubstituted imidazoles (1a-e). A mixture of 4-hydroxy benzaldehyde ( 5 mmol ), $\alpha$-diketones ( 5 mmol ), ammonium acetate ( 10 mmol ), and glacial acetic acid ( 50 mL ) was refluxed for 2 h . It was poured on to cold water ( 200 mL ) and neutralized with $\mathrm{NH}_{4} \mathrm{OH}$. The solid obtained was filtered, washed with water, and crystallized from alcohol.

2-(4-Hydroxyphenyl)-4,5-diphenyl imidazole (1a). Yield $1.4 \mathrm{~g}(75 \%), \mathrm{mp} 260^{\circ} \mathrm{C}, R_{f}=0.78$, FT-IR spectrum showed the $3569.4(-\mathrm{OH}$, broad) due to the presence of free phenolic hydroxyl group and $1608\left(\mathrm{C}=\mathrm{N}\right.$, str.), 3165.3-2793.3 $\mathrm{cm}^{-1}$

(aromatic ring, str.), 1235.6 ( $\mathrm{C}-\mathrm{O}$ bend), $3466.6(-\mathrm{NH}) ;{ }^{1} \mathrm{H}$ NMR: $\delta 7.2-7.5(\mathrm{~m}, 14 \mathrm{H}, \mathrm{Ar}-\mathrm{H}), 6.8(\mathrm{~s}, 1 \mathrm{H}, \mathrm{OH}), 7.9(1 \mathrm{H}$, $-\mathrm{NH}, \mathrm{D}_{2} \mathrm{O}$ exchangeable) Anal. Calcd. for $\mathrm{C}_{21} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}$ (312): C, 80.75; H, 5.16; N, 8.97; Found: C, 80.65; H, 5.11; N, 8.85.

2-(4-Hydroxypheny)-5-phenyl imidazole (1b). Yield 54\%; $\mathrm{mp} 175^{\circ} \mathrm{C}$ (ethanol); $R_{f}=0.70$, FT-IR: $3510(-\mathrm{OH}$, broad), $3345.5(-\mathrm{NH}), 1612(\mathrm{C}=\mathrm{N}$, str.), 1218 ( $\mathrm{C}-\mathrm{O}$ bend), 3165.3$2790.3 \mathrm{~cm}^{-1}$ (aromatic ring, str.). ${ }^{1} \mathrm{H}$ NMR: $\delta=6.8(\mathrm{~s}, 1 \mathrm{H}$, $\mathrm{OH}), 10.2\left(1 \mathrm{H},-\mathrm{NH}\right.$, exchangeable with $\left.\mathrm{D}_{2} \mathrm{O}\right), 6.5-7.3(\mathrm{~m}$, 9 H , aromatic). Anal. Calcd. for $\mathrm{C}_{15} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}$ (236): C, 76.25 ; H, 5.12; N, 11.86; Found: C, 76.18; H, 5.20; N, 11.82.

2-(4-Hydroxyphenyl)-imidazole (1c). Yield 72\%; mp $190^{\circ} \mathrm{C}$ (ethanol); $R_{f}=0.68$, FT-IR: 3585 ( -OH , broad), $3358.0(-\mathrm{NH}), 1618$ ( $\mathrm{C}=\mathrm{N}$, str.), 1220 ( $\mathrm{C}-\mathrm{O}$ bend), 3105.5$2788.0 \mathrm{~cm}^{-1}$ (aromatic ring, str.). ${ }^{1} \mathrm{H}$ NMR: $\delta=5.6(\mathrm{~s}, 1 \mathrm{H}$,
$\mathrm{OH})$, $9.5\left(1 \mathrm{H},-\mathrm{NH}\right.$, exchangeable with $\left.\mathrm{D}_{2} \mathrm{O}\right), 6.2-7.4(\mathrm{~m}$, 4 H , aromatic). Anal. Calcd. for $\mathrm{C}_{9} \mathrm{H}_{8} \mathrm{~N}_{2} \mathrm{O}$ (160): C, 67.49; H, 5.03; N, 17.49; Found: C, 67.56; H, 5.10; N, 17.45.

2-(4-Hydroxyphenyl)-4,5-dimethyl imidazole (1d). Yield $62 \%$; $\mathrm{mp} 135^{\circ} \mathrm{C}$ (ethanol); $R_{f}=0.54$, FT-IR: 3424 ( -OH , broad), $3269.0(-\mathrm{NH}), 1614$ ( $\mathrm{C}=\mathrm{N}$, str.), 1224 ( $\mathrm{C}-\mathrm{O}$ bend), 3015.52712. $\mathrm{cm}^{-1}$ (aromatic ring, str.). ${ }^{1} \mathrm{H}$ NMR: $\delta=5.5$ ( $\mathrm{s}, 1 \mathrm{H}$, $\mathrm{OH})$, $9.4\left(1 \mathrm{H},-\mathrm{NH}\right.$, exchangeable with $\left.\mathrm{D}_{2} \mathrm{O}\right), 6.2-7.8(\mathrm{~m}$, 4 H , aromatic). Anal. Calcd. for $\mathrm{C}_{11} \mathrm{H}_{12} \mathrm{~N}_{2} \mathrm{O}$ (188): C, 70.19 ; H, 6.43; N, 14.88; Found: C, 70.25 ; H, 6.40; N, 14.90 .

2-(4-Hydroxyphenyl)-4,5-bis-(4-chlorophenyl)-imidazole (1e). Yield $60 \% ; \mathrm{mp} 245^{\circ} \mathrm{C}$ (ethanol); $R_{f}=0.73$, FT-IR: 3520 ( -OH , broad), $3370.0(-\mathrm{NH}), 1624(\mathrm{C}=\mathrm{N}$, str.), $1222(\mathrm{C}-\mathrm{O}$ bend), $3085-2712 \mathrm{~cm}^{-1}$ (aromatic ring, str.). ${ }^{1} \mathrm{H}$ NMR $\delta=5.8$ $(\mathrm{s}, 1 \mathrm{H}, \mathrm{OH}), 8.5\left(1 \mathrm{H},-\mathrm{NH}\right.$, exchangeable with $\left.\mathrm{D}_{2} \mathrm{O}\right), 6.1-7.5$

Table 1
Antimicrobial activity 4,5-diaryl-2-(4-o- $\beta$-d-glucosidoxyphenyl) imidazoles (3a-e).


[^0](m, 12 H , aromatic). Anal. Calcd. for $\mathrm{C}_{21} \mathrm{H}_{14} \mathrm{Cl}_{2} \mathrm{~N}_{2} \mathrm{O}$ (380): C, 66.16; H, 3.70; N, 7.35; Found: C, 66.32; H, 3.76; N, 7.32.

General procedure for 2-(4-o- $\beta$-d-2,3,4,6-tetra-o-acetyl-glucosidoxyphenyl)-4,5-disubstituted imidazoles (2a-e). A solution of 3 g potassium salt of 4,5-disubstituted-2-(4-hydrox-yphenyl)-imidazole in 10 mL of $5 \%$ methanolic KOH was added drop wise to a solution of 5 g of a acetobromoglucose in 20 mL of dry acetone. The resulting mixture was stirred at $0^{\circ} \mathrm{C}$ for 2 h . The reaction was allowed to proceed for an additional 24 h and the solvent remove under reduced pressure. The reaction was monitored by TLC, A brown syrupy mass of 4,5-disubstituted-2-(4-o- $\beta$-d-2,3,4,6-tetra-o-acetyl glucosidoxyphenyl)imidazoles were obtained.
2-(4-o- $\beta$-d-2,3,4,6-Tetra-o-acetyl glucosidoxyphenyl)-4,5-diphenyl imidazole (2a). Yield $3.57 \mathrm{~g}(65 \%) . R_{f}=0.28$. The compound was found to be optically active and the specific rotation $[\alpha]_{\mathrm{D}}{ }^{30}$ in DMSO was found to be -8.12 . FT-IR spectrum of the compound showed following characteristic bands at $v_{\max } 3424(-\mathrm{NH}), 1607(\mathrm{C}=\mathrm{N})$, and $1074(\mathrm{C}-\mathrm{O}) \mathrm{cm}^{-1}$. The characteristic band due to phenolic hydroxyl group (3300-3500 $\mathrm{cm}^{-1}$ ) was absent and the band due to $\mathrm{C}-\mathrm{O}-\mathrm{C}$ which appear at $1231 \mathrm{~cm}^{-1}$ confirms the formation of $o$-glucoside. ${ }^{1} \mathrm{H}$ NMR: 2.02 , 1.95,1.97, $2.01(\mathrm{~s}, 3 \mathrm{H})\left(\mathrm{COCH}_{3}\right), 4.8(\mathrm{~d}, 1 \mathrm{H}$, anomeric proton), 6.4-7.1 (m, 14H, Ar-H), 10.5 (s, 1H, -NH ). Anal. Calcd. for $\mathrm{C}_{35} \mathrm{H}_{34} \mathrm{~N}_{2} \mathrm{O}_{10}$ (642): C, $65.41 ; \mathrm{H}, 5.33$; N, 4.36; Found: C, 65.35 ; H, 5.30; N, 4.38.

2-(4-o- $\beta$-d-2,3,4,6-Tetra-o-acetyl glucosidoxyphenyl)-5-phenyl imidazole (2b). Yield $72 \% ;[\alpha]_{\mathrm{D}}{ }^{30}=-12.56$ (c, 0.1 , DMSO); brown syrup; $R_{f}=0.12$; FT-IR: $3420(-\mathrm{NH}), 2855$ (glucosidic CH), $2420(\mathrm{Ar}-\mathrm{CH}), 1610(\mathrm{C}=\mathrm{N}), 1089(\mathrm{C}-\mathrm{O})$, and $1225 \mathrm{~cm}^{-1}(\mathrm{C}-\mathrm{O}-\mathrm{C}) .{ }^{1} \mathrm{H}$ NMR: 2.02, 1.94, 1.97, 2.01 (s, $3 \mathrm{H})\left(\mathrm{COCH}_{3}\right), 5.1(\mathrm{~d}, 1 \mathrm{H}$, anomeric proton), $6.2-7.0(\mathrm{~m}, 9 \mathrm{H}$, $\mathrm{Ar}-\mathrm{H}), 9.6(\mathrm{~s}, 1 \mathrm{H},-\mathrm{NH})$. Anal. Calcd. for $\mathrm{C}_{29} \mathrm{H}_{30} \mathrm{~N}_{2} \mathrm{O}_{10}$ (566): C, 61.48; H, 5.34; N, 4.94; Found: C, 61.42; H, 5.30; N, 4.93.

2-(4-o- $\beta$-d-2,3,4,6-Tetra-o-acetyl glucosidoxyphenyl) imidazole (2c). Yield $82 \% ;[\alpha]_{\mathrm{D}}{ }^{30}=-2.24$ (c, 0.1, DMSO); brown syrup; $R_{f}=0.22$; FT-IR: $3428(-\mathrm{NH})$, 2828 (glucosidic CH), $2610(\mathrm{Ar}-\mathrm{CH}), 1618(\mathrm{C}=\mathrm{N}), 1085(\mathrm{C}-\mathrm{O})$, and $1210 \mathrm{~cm}^{-1}$ $(\mathrm{C}-\mathrm{O}-\mathrm{C}) .{ }^{1} \mathrm{H}$ NMR: $2.02,1.90,1.96,2.01(\mathrm{~s}, 3 \mathrm{H})\left(\mathrm{COCH}_{3}\right)$, $5.4(\mathrm{~d}, 1 \mathrm{H}$, anomeric proton), $6.0-7.3(\mathrm{~m}, 4 \mathrm{H}, \mathrm{Ar}-\mathrm{H}), 9.8(\mathrm{~s}$, $1 \mathrm{H},-\mathrm{NH})$. Anal. Calcd. for $\mathrm{C}_{23} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{10}$ (490): C, 56.32 ; H , 5.34; N, 5.71; Found: C, 56.38; H, 5.32; N, 5.76.

2-(4-o- $\beta$-d-2,3,4,6-Tetra-o-acetyl glucosidoxyphenyl)-4,5-dimethyl imidazole (2d). Yield 78\%; $[\alpha]_{\mathrm{D}}{ }^{30}=-8.16$ (c, 0.1, DMSO); brown syrup; $R_{f}=0.21$; FT-IR (KBr): 3430 $(-\mathrm{NH})$, 2832(glucosidic CH$)$, 2612( $\mathrm{Ar}-\mathrm{CH}$ ), $1625(\mathrm{C}=\mathrm{N})$, $1087(\mathrm{C}-\mathrm{O})$, and $1218 \mathrm{~cm}^{-1}(\mathrm{C}-\mathrm{O}-\mathrm{C}) .{ }^{1} \mathrm{H}$ NMR: 2.00, 1.92, 1.98, $2.01(\mathrm{~s}, 3 \mathrm{H})\left(\mathrm{COCH}_{3}\right), 5.1(\mathrm{~d}, 1 \mathrm{H}$, anomeric proton), 6.2-6.9 (m, 4H, Ar-H), 10.2 (s, 1H, -NH ). Anal. Calcd. for $\mathrm{C}_{25} \mathrm{H}_{30} \mathrm{~N}_{2} \mathrm{O}_{10}$ (518): C, 57.91 ; H, 5.83; N, 5.40; Found: C, 57.95; H, 5.84; N, 5.42.

2-(4-o- $\beta$-d-2,3,4,6-Tetra-o-acetyl glucosidoxyphenyl)- 4,5-bis-(4-chlorophenyl) imidazole (2e). Yield $75 \% ;[\alpha]_{\mathrm{D}}{ }^{30}=$ -4.10 (c, 0.1, DMSO); brown syrup; $R_{f}=0.28 ;$ FT-IR (KBr): 3440 ( -NH ), 2795 (glucosidic CH), 2610 ( $\mathrm{Ar}-\mathrm{CH}$ ), 1620 $(\mathrm{C}=\mathrm{N}), 1090(\mathrm{C}-\mathrm{O})$, and $1215 \mathrm{~cm}^{-1}(\mathrm{C}-\mathrm{O}-\mathrm{C}) .{ }^{1} \mathrm{H}$ NMR: 2.00, 1.94, 1.96, $2.02(\mathrm{~s}, 3 \mathrm{H})\left(\mathrm{COCH}_{3}\right), 5.5(\mathrm{~d}, 1 \mathrm{H}$, anomeric proton), 6.2-6.8 (m, 12H, Ar-H), $11.4(\mathrm{~s}, 1 \mathrm{H},-\mathrm{NH})$. Anal. Calcd. for $\mathrm{C}_{35} \mathrm{H}_{32} \mathrm{Cl}_{2} \mathrm{~N}_{2} \mathrm{O}_{10}$ (710): C, 59.08; H, 4.53; N, 3.94; Found: C, 59.05; H, 4.56; N, 3.96.

General procedure for 2-(4-o- $\beta$-d-glucosidoxyphenyl)-4,5disubstituted imidazoles (3a-e). A solution of 4,5 -disubsti-tuted-2-(4-o- $\beta$-d-2,3,4,6-tetra-o-acetyl glucosidoxyphenyl) imidazole ( 2 g ) in 25 mL of dry methanol was added 1.5 mL of $5 \% \mathrm{CH}_{3} \mathrm{ONa}$ solution .The reaction mixture was kept at room temperature for additional 24 h . It was neutralized with ionexchange resin (Amberlite IR 120, s.d. fine, $\mathrm{H}^{+}$form) filtered and concentrated in vacuum to afford viscous, strongly hygroscopic brown colored syrupy.

2-(4-o- $\beta$-d-Glucosidoxyphenyl)-4,5-diphenyl imidazole (3a). Yield $65 \% ;[\alpha]_{\mathrm{D}}{ }^{30}=-9.88$ (c, 0.1, DMSO); brown syrup; $R_{f}=0.12$; FT-IR: 3200-3391.7 ( -OH , broad, stretching). 2361.9 (aromatic str.), $1073.7(\mathrm{C}-\mathrm{O}-\mathrm{C}), 1609.9 \mathrm{~cm}^{-1}$ $(\mathrm{C}=\mathrm{N}) .{ }^{1} \mathrm{H}$ NMR: $6.8-7.7 \mathrm{~Hz}(\mathrm{H}, \mathrm{Ar}-\mathrm{H}), 10.5(\mathrm{~s},-\mathrm{NH}), 4.8$ $\left(\mathrm{d}, 1 \mathrm{H}, J_{1,2}=8.5 \mathrm{~Hz}, 1^{\prime} \mathrm{H}\right)$ anomeric proton, $3.9\left(1 \mathrm{H}, 2^{\prime} \mathrm{H}\right)$, $3.4\left(\mathrm{dd}, 1 \mathrm{H}, 3^{\prime} \mathrm{H}\right), 3.7\left(1 \mathrm{H}, 4^{\prime} \mathrm{H}\right), 3.2\left(1 \mathrm{H}, 5^{\prime} \mathrm{H}\right) .{ }^{13} \mathrm{C}$ NMR: $\delta 115-128$ ( $\mathrm{Ar}-\mathrm{C}$ ), sugar moiety: $\delta 100.26$ (s, C-1') anomeric carbon, 81 ( $\mathrm{s}, \mathrm{C}-6^{\prime}$ ), 77 ( $\mathrm{s}, \mathrm{C}-5^{\prime}$ ), 72 ( $\mathrm{s}, \mathrm{C}-4^{\prime}$ ), 70.5 ( $\left.\mathrm{s}, \mathrm{C}-3^{\prime}\right)$, 62 (s, C-2'). EI-MS the molecular ion peak were observed at $474(M+1)(46 \%)$ base peak observed at $312(100 \%), 118$ (10 \%), 77 (08 \%). Anal.Calcd. for $\mathrm{C}_{27} \mathrm{H}_{26} \mathrm{~N}_{2} \mathrm{O}_{6}$ (474): C, 68.34 ; H, 5.52; N, 5.90 ; Found: C, 68.37 ; H, 5.50 ; N, 5.86.

2-(4-o- $\beta$-d-Glucosidoxyphenyl)-5-phenyl imidazole (3b). Yield $58 \% ;[\alpha]_{\mathrm{D}}{ }^{30}=-15.20$ (c, 0.1, DMSO); brown syrup; $R_{f}=0.8$; FT-IR: 3300 ( -OH, broad), $2718.1 \mathrm{~cm}^{-1}$ (aromatic str.), 1079.2 $(\mathrm{C}-\mathrm{O}-\mathrm{C}), 1620.6 \mathrm{~cm}^{-1}(\mathrm{C}=\mathrm{N}) .{ }^{1} \mathrm{H}$ NMR: 6.8-7.8 (m, 9H, $\mathrm{Ar}-\mathrm{H}), 10.4(\mathrm{~s}, 1 \mathrm{H},-\mathrm{NH}), 3.3\left(1 \mathrm{H}, 5^{\prime} \mathrm{H}\right), 3.5\left(1 \mathrm{H}, 4^{\prime} \mathrm{H}\right), 3.4$ $\left(1 \mathrm{H}, 3^{\prime} \mathrm{H}\right), 3.8\left(1 \mathrm{H}, 2^{\prime} \mathrm{H}\right), 5.0\left(\mathrm{dd}, 1 \mathrm{H}, J_{1,2}=8.8 \mathrm{~Hz}, 1^{\prime} \mathrm{H}\right){ }^{13} \mathrm{C}$ NMR: $\delta 115-128(\mathrm{Ar}-\mathrm{C})$, sugar moiety: $\delta 108$ ( $\mathrm{s}, \mathrm{C}-1^{\prime}$ ) anomeric carbon, 80 ( $\mathrm{s}, \mathrm{C}-6^{\prime}$ ), 76 ( $\left.\mathrm{s}, \mathrm{C}-5^{\prime}\right), 71.5$ ( $\mathrm{s}, \mathrm{C}-4^{\prime}$ ), 70.5 ( $\mathrm{s}, \mathrm{C}-3^{\prime}$ ), 60 (s, C-2'). EI-MS: 398 (M) ( $20 \%$ ), 220 ( $58 \%$ ) 116 ( $100 \%$ ) base peak, 105 (10\%), 78(4\%). Anal.Calcd. for $\mathrm{C}_{21} \mathrm{H}_{22} \mathrm{~N}_{2} \mathrm{O}_{6}$ (398): C, 63.31; H, 5.57; N, 7.03; Found: C, 63.34; H, 5.50; N, 7.06.

2-(4-o- $\beta$-d-Glucosidoxyphenyl) imidazole (3c). Yield $60 \%$; $[\alpha]_{\mathrm{D}}{ }^{30}=-5.22$ (c, 0.1, DMSO); brown syrup; $R_{f}=0.15$; FTIR: 3400 ( -OH, broad), 2818.1 (aromatic str.), 1088.2 $(\mathrm{C}-\mathrm{O}-\mathrm{C})$ glucosidic linkage, $1624 \mathrm{~cm}^{-1}(\mathrm{C}=\mathrm{N}) .{ }^{1} \mathrm{H}$ NMR: 6.5-7.9 (m, Ar-H), $11.4(\mathrm{~s}, 1 \mathrm{H},-\mathrm{NH}), 3.2\left(1 \mathrm{H}, 5^{\prime} \mathrm{H}\right), 3.4(1 \mathrm{H}$, $\left.4^{\prime} \mathrm{H}\right), 3.5\left(1 \mathrm{H}, 3^{\prime} \mathrm{H}\right), 3.9\left(1 \mathrm{H}, 2^{\prime} \mathrm{H}\right), 5.5\left(\mathrm{dd}, 1 \mathrm{H}, J_{1,2}=10.2\right.$ $\left.\mathrm{Hz}, 1^{\prime} \mathrm{H}\right)$ anomeric proton. ${ }^{13} \mathrm{C}$ NMR: $\delta 116-130(\mathrm{Ar}-\mathrm{C})$, sugar moiety: $\delta 110$ (s, C-1 ${ }^{\prime}$ ) anomeric carbon, 82 (s, C-6'), 77 (s, C$5^{\prime}$ ), 72.5 (s, C-4'), 71.5 ( $\mathrm{s}, \mathrm{C}-3^{\prime}$ ), 63 (s, C-2'). EI-MS: 322 (M) $(28 \%), 160(100 \%)$ base peak $146(15 \%), 77(4 \%)$ Anal.Calcd. for $\mathrm{C}_{15} \mathrm{H}_{18} \mathrm{~N}_{2} \mathrm{O}_{6}$ (322): C, 55.90 ; H, 5.63 ; $\mathrm{N}, 8.69$; Found: C, 55.88; H, 5.60; N, 8.65.

2-(4-o- $\beta$-d-Glucosidoxyphenyl)-4,5-dimethyl imidazole (3d). Yield 68\%; $[\alpha]_{\mathrm{D}}{ }^{30}=-11.10$ (c, 0.1, DMSO); brown syrup; $R_{f}=0.16$; FT-IR: 3380 ( -OH , broad), 2910 (aromatic str.), $1085.0(\mathrm{C}-\mathrm{O}-\mathrm{C})$ glucosidic linkage, $1630 \mathrm{~cm}^{-1}(\mathrm{C}=\mathrm{N})$.
${ }^{1} \mathrm{H}$ NMR: $6.0-7.4(\mathrm{~m}, \mathrm{Ar}-\mathrm{H}), 10.2(\mathrm{~s}, 1 \mathrm{H},-\mathrm{NH}), 3.0\left(1 \mathrm{H}, 5^{\prime} \mathrm{H}\right)$, $3.2\left(1 \mathrm{H}, 4^{\prime} \mathrm{H}\right), 3.5\left(1 \mathrm{H}, 3^{\prime} \mathrm{H}\right), 3.7\left(1 \mathrm{H}, 2^{\prime} \mathrm{H}\right), 5.6\left(\mathrm{dd}, 1 \mathrm{H}, J_{1,2}=\right.$ $\left.9.8 \mathrm{~Hz}, 1^{\prime} \mathrm{H}\right)$ anomeric proton. ${ }^{13} \mathrm{C}$ NMR: $\delta 120-136(\mathrm{Ar}-\mathrm{C})$, sugar moiety: $\delta 115$ (s, C-1') anomeric carbon, 88 (s, C-6'), 86 (s, C-5'), 76 ( $\mathrm{s}, \mathrm{C}-4^{\prime}$ ), 70. ( $\mathrm{s}, \mathrm{C}-3^{\prime}$ ), 65 ( $\mathrm{s}, \mathrm{C}-2^{\prime}$ ). EI-MS: 350 (M) $(25 \%), 170(100 \%)$ base peak $118(12 \%), 78(8 \%)$. Anal.Calcd. for $\mathrm{C}_{17} \mathrm{H}_{22} \mathrm{~N}_{2} \mathrm{O}_{6}$ (350): C, 58.28; H, 6.33; N, 8.00; Found: C, 58.32; H, 6.36; N, 8.05.

2-(4-o- $\beta$-d-Glucosidoxyphenyl)-4,5-bis-(4-chlorophenyl) imidazole (3e). Yield $62 \% ;[\alpha]_{\mathrm{D}}{ }^{30}=-6.80$ (c, 0.1, DMSO); brown syrup; $R_{f}=0.20$; FT-IR: 3420 ( -OH , broad), 3015 (aromatic str.), $1088.0(\mathrm{C}-\mathrm{O}-\mathrm{C})$ glucosidic linkage, $1630 \mathrm{~cm}^{-1}(\mathrm{C}=\mathrm{N})$.
${ }^{1} \mathrm{H}$ NMR: $6.0-7.3(\mathrm{~m}, \mathrm{Ar}-\mathrm{H}), 10.5(\mathrm{~s}, 1 \mathrm{H},-\mathrm{NH}), 3.0\left(1 \mathrm{H}, 5^{\prime} \mathrm{H}\right)$, $3.4\left(1 \mathrm{H}, 4^{\prime} \mathrm{H}\right), 3.5\left(1 \mathrm{H}, 3^{\prime} \mathrm{H}\right), 3.8\left(1 \mathrm{H}, 2^{\prime} \mathrm{H}\right), 5.2\left(\mathrm{dd}, 1 \mathrm{H}, J_{1,2}=\right.$ $\left.9.0 \mathrm{~Hz}, 1^{\prime} \mathrm{H}\right)$ anomeric proton. ${ }^{13} \mathrm{C}$ NMR: $\delta 114-136(\mathrm{Ar}-\mathrm{C})$, sugar moiety: $\delta 103$ ( $\mathrm{s}, \mathrm{C}-1^{\prime}$ ) anomeric carbon, 78 (s, C-6'), 77 (s, C-5'), 75 (s, C-4'), 73 ( $\left.\mathrm{s}, \mathrm{C}-3^{\prime}\right), 67$ ( $\mathrm{s}, \mathrm{C}-2^{\prime}$ ). EI-MS: 542 (M) ( $32 \%$ ), $380(10 \%) 246(100 \%)$ base peak, $163(24 \%), 137(12$ \%), 77 (32 \%). Anal.Calcd. for $\mathrm{C}_{27} \mathrm{H}_{24} \mathrm{Cl}_{2} \mathrm{~N}_{2} \mathrm{O}_{6}$ (542): C, 59.68; H, 4.45; N, 5.16; Found: C, 59.72; H, 4.48; N, 5.15.

Acknowledgments. The authors are thankful to the Director, Sophisticated Analytical Instrument Facility (SAIF) Chandigarh, IIT-Powai, Mumbai, for providing necessary spectral analysis, to the Head Department of Chemistry for providing necessary laboratory facilities, and to the Head Department of Pharmacy for the biological activities.

## REFERENCES AND NOTES

[1] Ingle, V. N.; Hatzade, K. M.; Taile, V. S.; Gaidhane, P. K.; Kharche, S. T. J Carbohydr Chem 2007, 26, 107.
[2] Kondo, H.; Taguchi, M.; Inoue, Y.; Sakamoto, F.; Tssukamoto, G. J Med Chem 1990, 33, 2012.
[3] Dickens, J. P.; Ellames, G. J.; Hare, N. J.; Lawson, K. R.; McKay, W. R.; Mutters, A. P.; Myers, P. L.; Pope, A. M. S.; Upton, R. M. J Med Chem 1991, 34, 2356.
[4] Ogata, M.; Matsumoto, H.; Hamada, Y.; Takehara, M.; Tawara, K. J Med Chem 1983, 26, 768.
[5] Bhatia, M.; Naithani, P. K.; Bhalla, T. N.; Saxena, A. K. J Indian Chem Soc 1992, 60, 594.
[6] Rama Sarma, G. V. S.; Reddy, V. M. Indian J Heterocycl Chem 1993, 3, 111.
[7] Carini, D. J.; Dunica, J. V.; Aldrich, P. E.; Chiu, A. T.; Johnson, A. L.; Pierce, M. E.; Price, W. A.; Santella, J. B., III; Wells, G. J.; Wexler, R. R.; Wong, P. C.; Yoo, S. E.; Pieter, B. M.; Timmermans, W. M. J Med Chem 1991, 34, 2525.
[8] Dwek, R. A. Chem Rev 1996, 96, 683.
[9] Davis, B. G. J Chem Soc Perkin Trans 1 1999, 3215.
[10] McAuliffe, J. C.; Hundsgaul, O. Chem Ind 1997, 170.
[11] Gupta, A.; Sharma, R.; Prakash, L. J Indian Chem Soc 1994, 71, 635.
[12] Huryn, D. M.; Okabe, M. Chem Rev 1992, 92, 1745.
[13] Steck, E. A.; Day, A. R. J Am Chem Soc 1943, 65, 452.
[14] Koenig, W.; Knorr, E. Chem Ber 1901, 34, 957.


[^0]:    ${ }^{\text {a }}$ Average zone of inhibition in mm .
    ${ }^{\mathrm{b}}$ Concentration of test compounds and standard $100 \mu \mathrm{~g} / \mathrm{mL}$. (Activity index) $=$ Inhibition zone of the sample/inhibition zone of the standard.
    ${ }^{\mathrm{c}}$ Activity index against std. 1.
    ${ }^{\text {d }}$ Activity index against std. 2.For antibacterial activity: Std. $1=$ Ciprofloxacin and Std. $2=$ Sulphacetamide, for antifungal activity: Std. $1=$ Gentamycin and Std. $2=$ Clotrimazole.

