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# Synthesis, Glucosylation and Polarographic Studies of Benzofused Pyrimidine Derivatives

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## ABSTRACT

7-Amino-3-methyl-5-(3′-aryl prop-2′-enoyl)-1,2-benzisoxazoles (**2a-j**) were synthesized by the condensation of 5-acetyl-7-amino-3-methyl-1,2-benzisoxazole (**1**) with aldehydes. The reaction of products **2a-j** with urea produced 7-amino-3-methyl-5-(4′-aryl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole derivatives (**3a-j**). Glucosylation of **3a-j** with 2,3,4,6-tetra-*O*-acetyl glucuropyranosyl bromide (TAGBr) and tetrabutylammonium bromide (TBAB) gives corresponding glucosylated 7-amino-(β-D-2,3,4,6-tetra-*O*-acetyl glucopyranosyl)-3-methyl-5-(4′-aryl-2′-pyrimidin-6′-yl)-1,2-benzisoxazoles (**4a-j**). Glucosylated compounds **4a-j** on deacetylation gives target products 7-amino-(β-D-glucopyranosyl)-3-methyl-5-(4′-aryl-2′-pyrimidin-6′-yl)-1,2-benzisoxazoles (**5a-j**). Glucosylation and deacetylation reaction carried out by Knenigs-Knorr reaction. All the synthesized products were characterized by elemental analysis, IR, $^{1}$H NMR, $^{13}$C NMR and mass spectroscopy. The biological and electrochemical activities of all the synthesized compounds were also examined.

## KEYWORDS

Benzisoxazoles, Pyrimidines, Urea, *N*-Glucosides, Electrochemistry.

## INTRODUCTION

Pyrimidine was first prepared by conversion of barbituric acid to 2,4,6-trichloropyrimidine followed by reduction using zinc dust in hot water [1]. The preparation of pyrimidines by barbituric acid from urea and malonic acid in the presence of phosphorus oxychloride [2]. The first synthesized derivative of pyrimidines was reared by condensing ethyl acetoacetate with amidines. Many pyrimidine derivatives have been developed as chemotherapeutics and exhibiting remarkable pharmacological activities [3]. Many heterocyclic compounds occurred in natural products. Hydrolysis of nucleic acid produces several pyrimidines *viz*. uracil, thymine and cytosine. Pyrimidine base shows activities due to presence in uracil, thymine and cytosine, which are essential building blocks in nucleic acid, DNA and RNA. Cytosine is present in both DNA and RNA, while uracil present in RNA and thymine in DNA [4]. Vitamins are essential for life and pyrimidine ring is found in vitamins like riboflavin, thiamine and folic acid [5]. It is also found in many synthetic compounds such as barbiturates and HIV drug, zidovudine and stavudine. Pyrimidine nucleus is present in barbituric acid and its derivatives, veranal and luminal, which are used as hypnotics [6]. 5-Alkylated pyrimidinetrinitrones have been

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reported to show antispasmodic, muscle relaxant and anti-convulsant activity [7]. Natural products like alkaloids also contains pyrimidine ring, these includes xanthine and hypoxanthine which occurs in tea and caffeine, theophylline are also constituents of tea leaves.

The literature indicated that compounds having pyrimidine derivatives possess broad range of biological activities like anticancer, infections of eyes, antiviral, anti-HIV, antibacterial, antimalarial, antihypertensive, antithyroid, H1-antihistamine and as antibiotics [8,9]. Sedative, hypnotics, antihistaminic, anti-inflammatory and antibiotics activities also shown by pyrimidines [10-15]. Phenobarbital is commonly used as anti-convulsant. It also has sedative and hypnotic action. A general anaesthetic barbiturate, methohexital is a short acting and has a rapid onset of action and sodium thiopental is a rapid onset short acting. The majority of anti-HIV agents appears to act as a reverse transcriptase level, most of these inhibitors belong to the class of 2′,3′-dideoxy nucleosides and the compounds of variety of 2′,3′-dideoxy-, 2′,3′-didehydro-, 2′,3′-dideoxy, 3′-azido-, 2′,3′-dideoxy and 3′-fluro-2′,3′-dideoxyribosides of both pyrimidines and purines has been described as potent and selective anti-HIV agents. 3′-Azido-2′,3′-dideoxyrithymidine, the anti-HIV was one of the first nucleosides analogs for clinical use in the treatment of AIDS, lamivudine is used to treat both hepatitis B and AIDS and the antiherpes drug acyclovir are useful carbohydrate based therapeutics [16-18]. 2-Acetamide-5-phenyl-1,3,4-oxadiazoles have antimitotic, analgesic, diuretic, antiemetic, hypnotics, sedative and antidiarrhael properties [19]. In March 2015, NASA Ames scientists reported that for the first time, complex DNA and RNA organic compounds of life, including uracil, cytosine and thymine have been prepared in the laboratory under outer space conditions, using starting chemicals such as pyrimidines, found in meteorites. According to the scientists, pyrimidines, like polycyclic aromatic hydrocarbons (PAHs), the most carbon-rich chemical found in the universe, may have been formed in red giants or in interstellar dust and gas clouds [20-23].

## EXPERIMENTAL

Melting points were determined on a melting point apparatus in open capillaries. FT-IR spectra were recorded on Bruker infrared spectrometer, $^{1}$H NMR, $^{13}$C NMR spectra on Bruker Avance II 400 NMR spectrometer and FAB-MS spectra were recorded. Elemental analyses were determined using Perkin-Elmer C, H, N analyzer and Polarogram were recorded on Elico CL-362 polarograph. Purity of compounds was checked on silica gel plates using UV chamber for visualization.

**Synthesis of 5-acetyl-7-amino-3-methyl-1,2-benziso-xazole (1):** It has been synthesized as per literature method [24]. (Yield 12.3 g, 64.73%), m.p.: 136 °C.

**7-Amino-3-methyl-5-(3′-phenyl prop-2′-enoyl)-1,2-benz-isoxazole (2a):** Condensation of 5-acetyl-7-amino-3-methyl-1,2-benzisoxazole (1.90 g, 0.01 M) with benzaldehyde (1.0 mL, 0.01 M) in ethyl alcohol (25 mL) using a few drops of piperidine for 40 min. The reaction mixture was cooled to 0 ºC, yellow solid compound formed was washed with water. Yield 2.10 g, 75.50 %, m.p.: 92 °C and its alcoholic solution turned red with alkali and decolourized with bromine water and it gave dark red colour with conc. $H_2SO_4$. In the same way, 7-amino-3-methyl-5-(3′-aryl prop-2′-enoyl)-1,2-benzisoxazoles (**2b-j**) were synthesized.

**7-Amino-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole (3a):** A mixture of 7-amino-3-methyl-5-(3′-phenyl prop-2′-enoyl)-1,2-benzisoxazole (2.78 g, 0.01 M), urea (0.5 g), ethyl alcohol (15 mL) and KOH (0.4 g) was refluxed on water bath for 4 h. It was cooled and acidified with glacial acetic acid (1.5 mL) and poured on ice-cold water (50 mL), dried and crystallized with aqueous alcohol. Yield 63%, m.p.: 165 ºC. Following the above procedure, other 7-amino-3-methyl-5-(4′-aryl-2′-pyrimidin-6′-yl)-1,2-benzisoxazoles **(3b-j)** were also synthesized. The characterization data of these compounds are summarized in Table-1.

**7-Amino-(β-D-glucopyranosyl)-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole (5a):** To a solution of 7-amino-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole (2.90 g, 0.01 M) and 2,3,4,6-tetra-*O*-acetyl glucuropyranosyl bromide (3.0 g, 0.01 M) in dichloromethane (4 mL) was added tetrabutylammonium bromide (0.32 g) with stirring at 5 ºC. The organic layer was separated, washed with water, 5% aqueous $NaHCO_3$, again with water and dried. The tetraacetyl derivative was deacetylated with 5% sodium methoxide solution. To a solution of 7-amino-(β-D-2,3,4,6-tetra-*O*-acetyl glucopyranosyl)-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole in absolute methanol (25 mL) was added (1.5 mL) of 5% of sodium methoxide solution and kept at room temperature for 45 min. The reaction mixture was neutralized with ion exchange resin (Amberlite IR 120, $H^+$, cation exchanger), filter and dried. A semi-solid mass obtained was crystallized from ethanol as brown syrupy compound was obtained [24-30].

In the same way, other *N*-glucosides 7-amino-(β-D-glucopyranosyl)-3-methyl-5-(4′-aryl-2′-pyrimidin-6′-yl)-1,2-benzisoxazoles **(5b-j)** were synthesized. The characterization data of these compounds are summarized in Table-1.

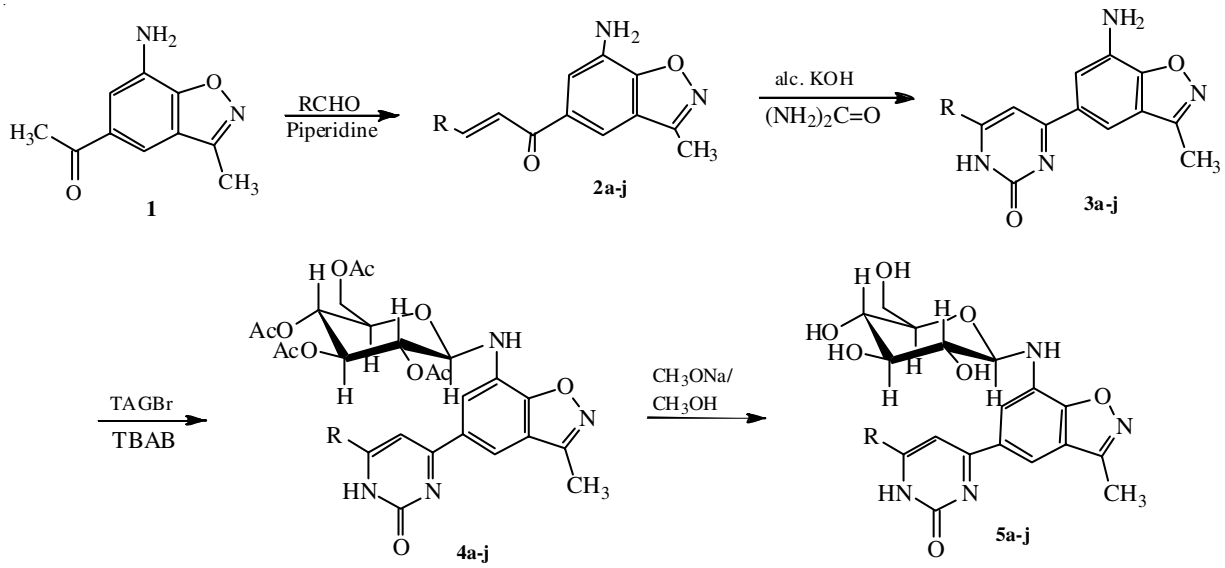
**Polarographic studies:** Polarographic studies of 7-amino-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole and 7-amino-(β-D-glucopyranosyl)-3-methyl-5-((4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole were carried out using Elico CL-362 polarograph based on microprocessor operation. The electrode system consisted of dropping mercury electrode as working electrode, platinum wire as auxiliary electrode and saturated calomel electrode as reference electrode. The supporting electrolyte used was 0.1 M KCl solution. The supporting electrolyte solution was deareated with nitrogen for 15 min and polarograms were recorded in diffusion current (DC) and differential pulse polarography (DPP) modes. To this solution, various concentrations of ethanolic solutions of 7-amino-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole were added and polarograms were recorded for each addition.

## RESULTS AND DISCUSSION

The synthesis of the target compounds **5a-j** is outlined in **Scheme-I**. The characterization of synthesized compounds has been done on the basis of FT-IR, $^{1}$H NMR, $^{13}$C NMR elemental analysis, mass spectroscopy and polarography. The synthesis of 7-amino-3-methyl-5-(3′-aryl prop-2′-enoyl)-1,2-benziso-

TABLE-1
CHARACTERIZATION DATA OF 7-AMINO-3-METHYL-5-(4'-ARYL-2'-PYRIMIDIN-6'-YL)-1,2-BENZISOXAZOLES (**3a-j**) AND 7-AMINO-(β-D-GLUCOPYRANOSYL)-3-METHYL-5-(4'-ARYL-2'-PYRIMIDIN-6'-YL)-1,2-BENZISOXAZOLES (**5a-j**)

| Compd. | R | m.f. | m.w. | m.p. (°C) | Yield (%) | Elemental analysis (%): Calcd. (found) | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N |
| **3a** | $C_6H_5$ | $C_{18}H_{14}N_4O_2$ | 318 | 165 | 54 | 70.33 (70.32) | 4.86 (5.20) | 19.30 (19.32) |
| **3b** | 4-$ClC_6H_4$ | $C_{18}H_{13}ClN_4O_2$ | 352 | 145 | 65 | 62.87 (63.25) | 4.03 (4.32) | 17.25 (18.10) |
| **3c** | 2-$NO_2C_6H_4$ | $C_{18}H_{13}N_5O_4$ | 363 | 126 | 45 | 60.89 (60.25) | 3.91 (4.25) | 20.89 (20.28) |
| **3d** | 4-$NO_2C_6H_4$ | $C_{18}H_{13}N_5O_4$ | 363 | 135 | 52 | 60.89 (61.56) | 3.91 (4.89) | 20.89 (21.20) |
| **3e** | 4-$OHC_6H_4$ | $C_{18}H_{14}N_4O_3$ | 334 | 142 | 67 | 66.66 (65.58) | 4.61 (4.90) | 18.29 (19.52) |
| **3f** | 2-$OHC_6H_4$ | $C_{18}H_{14}N_4O_3$ | 334 | 175 | 70 | 66.66 (67.85) | 4.61 (5.10) | 18.29 (18.10) |
| **3g** | 2-$C_4H_3O$ | $C_{16}H_{12}N_4O_3$ | 308 | 172 | 62 | 64.28 (64.35) | 4.32 (4.58) | 19.99 (19.25) |
| **3h** | 2-$CH_3OC_6H_4$ | $C_{19}H_{16}N_4O_3$ | 348 | 145 | 52 | 67.49 (68.47) | 5.03 (5.65) | 17.49 (18.00) |
| **3i** | 4-$CH_3OC_6H_4$ | $C_{19}H_{16}N_4O_3$ | 348 | 156 | 43 | 67.49 (68.33) | 5.03 (5.46) | 17.49 (18.24) |
| **3j** | 6-$CH_3OC_6H_4$ | $C_{19}H_{16}N_4O_3$ | 348 | 125 | 45 | 67.49 (67.56) | 5.03 (5.22) | 17.49 (18.50) |
| **5a** | $C_6H_5$ | $C_{24}H_{24}N_4O_7$ | 480 | – | – | 61.05 (62.05) | 5.35 (5.24) | 12.38 (11.67) |
| **5b** | 4-$ClC_6H_4$ | $C_{24}H_{23}ClN_4O_7$ | 514 | – | – | 56.74 (57.70) | 4.76 (4.85) | 11.51 (11.98) |
| **5c** | 2-$NO_2C_6H_4$ | $C_{24}H_{23}N_5O_9$ | 525 | – | – | 55.53 (56.32) | 4.66 (4.86) | 14.08 (14.80) |
| **5d** | 4-$NO_2C_6H_4$ | $C_{24}H_{23}N_5O_9$ | 525 | – | – | 55.53 (56.74) | 4.66 (4.56) | 14.08 (13.59) |
| **5e** | 4-$OHC_6H_4$ | $C_{24}H_{24}N_4O_8$ | 496 | – | – | 58.97 (60.20) | 5.16 (5.25) | 11.96 (12.54) |
| **5f** | 2-$OHC_6H_4$ | $C_{24}H_{24}N_4O_8$ | 496 | – | – | 58.97 (58.60) | 5.16 (4.36) | 11.96 (12.36) |
| **5g** | 2-$C_4H_3O$ | $C_{22}H_{22}N_4O_8$ | 470 | – | – | 57.01 (58.25) | 5.01 (5.20) | 12.06 (11.85) |
| **5h** | 2-$CH_3OC_6H_4$ | $C_{25}H_{26}N_4O_8$ | 510 | – | – | 59.74 (61.02) | 5.43 (5.50) | 11.61 (10.98) |
| **5i** | 4-$CH_3OC_6H_4$ | $C_{25}H_{26}N_4O_8$ | 510 | – | – | 59.74 (60.58) | 5.43 (5.72) | 11.61 (11.32) |
| **5j** | 6-$CH_3OC_6H_4$ | $C_{25}H_{26}N_4O_8$ | 510 | – | – | 59.74 (58.96) | 5.43 (5.35) | 11.61 (11.87) |




R: (a) $C_6H_5$; (b) 4-$ClC_6H_4$; (c) 2-$NO_2C_6H_4$; (d) 4-$NO_2C_6H_4$; (e) 4-$OHC_6H_4$; (f) 2-$OHC_6H_4$; (g) 2-$C_4H_3O$; (h) 2-$CH_3OC_6H_4$; (i) 4-$CH_3OC_6H_4$; (j) 6-$CH_3OC_6H_4$

**Scheme-I:** Synthesis of 7-amino-(β-D-glucopyranosyl)-3-methyl-5-(4′-aryl-2′-pyrimidin-6′-yl)-1,2-benzisoxazoles

xazoles (**2a-j**) was achieved by reacting with different aldehydes. The reaction of **2a-j** 7-amino-3-methyl-5-(3′-aryl prop-2′-enoyl)-1,2-benzisoxazoles with urea produced 7-amino-3-methyl-5-(4′-aryl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole derivatives (**3a-j**).The IR of compound **3a** showed the characteristic absorption bands at 3243 (-$NH_2$), 3027-2849 (C-H *str.* in benzene), 1640 (amide -NH-C=O, *str*. in pyrimidine), 1605 (C=N arom. *str*.). The $^1$H NMR spectrum displayed signals at δ 12.34 (s, 1H, NH-pyrimidine), δ 8.13-6.91 (7H, Ar-H), δ 5.38 (s, 1H, pyrimidine), δ 4.78 (s, 2H, $NH_2$), δ 2.53 (s, 3H, $CH_3$). The $^{13}$C NMR spectrum of the product displayed signals δ 167.38 (pyrimidine), δ 166.89 (pyrimidine), δ 160.61 (C=O in pyrimidine), δ 159.07 (C-3 in benzisoxazole), δ 151.57 (C-3a in benzisoxazole), δ 141.77 (C-1′ in benzene), δ 129.01 (C-3′ in benzene), δ 128.63 (C-5′ in benzene), δ 130.96 (C-4′ in benzene), δ 136.89 (C-7), δ 128.26 (C-2′ in benzene), δ 127.20 (C-6′ in benzene), δ 126.34 (C-5 in benzisoxazole), δ 121.30 (C-7a in benzisoxazole), δ 116.30 (C-6 in benzisoxazole), δ 115.65 (C-4 in benzisoxazole), δ 114.79 (pyrimidine), δ 19.78 ($CH_3$). The FAB-MS of the product confirmed the molecular formula $C_{18}H_{14}N_4O_2$. It shows molecular ion peak at *m/z* 317.8 $[C_{18}H_{14}N_4O_2]^+$. The base peak appear at *m/z* 172.4 $[C_{10}H_8NO_2]^+$.

Glucosylation of synthesized compounds **3a-j** with TAGBr and tetrabutylammonium bromide gives corresponding glucosylated 7-amino-(β-D-2,3,4,6-tetra-*O*-acetyl glucopyranosyl)-3-methyl-5-(4′-aryl-2′-pyrimidin-6′-yl)-1,2-benzisoxazoles

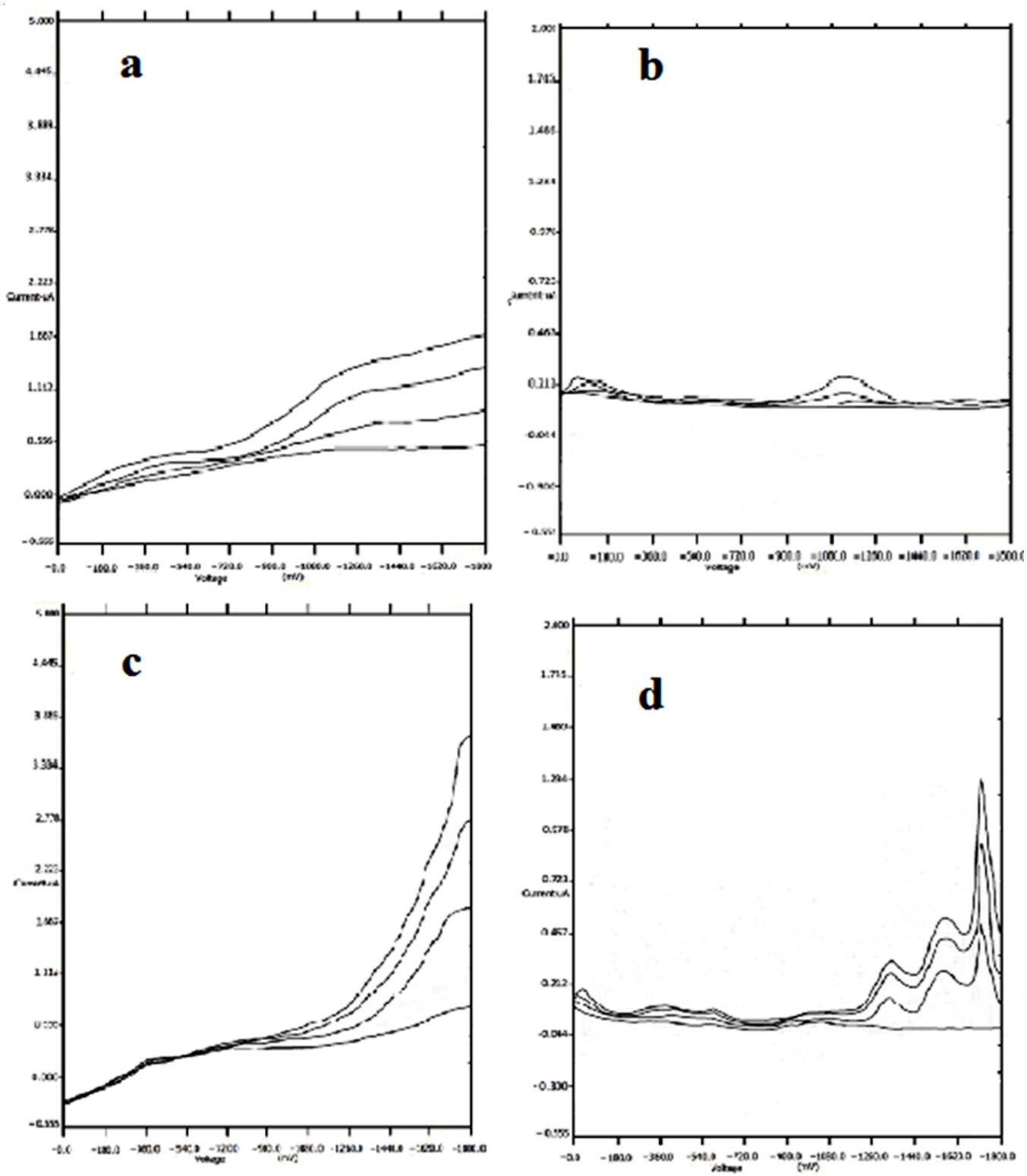



Fig. 1. (a) DC polarograms of 7-amino-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole, (b) DP polarograms of 7-amino-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole, (c) DC polarograms of 7-amino-(β-D-glucopyranosyl)-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole, (d) DP polarograms of 7-amino-(β-D-glucopyranosyl)-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole

(**4a-j**). Glucosylated compounds **4a-j** on deacetylation gives target products 7-amino-(β-D-glucopyranosyl)-3-methyl-5-(4′-aryl-2′-pyrimidin-6′-yl)-1,2-benzisoxazoles (**5a-j**). The IR spectra showed distinct absorption bands, ($\lambda_{max}$, $cm^{-1}$): 3391 (str. OH), 2962-2875 (C-H str. in benzene), 1620 (amide (NH-C=O) stretching vibration in pyrimidine), 1569 (C=N). The $^1$H NMR spectrum displayed signals at $^1$H NMR: δ 12.05 (s, 1H, NH-pyrimidine), δ 8.44-7.73 (m, 7H, Ar-H), δ 4.65 (s, 1H, pyrimidine), δ 4.54-4.47 (m, 1H in glucose), δ 4.20 (s, 1H, NH), δ 3.96-2.70 (6H, glucose), δ 2.56 (s, 3H, $CH_3$). Signals due to hydroxyl protons of the carbohydrate were not observed because of fast exchange of non-hydrogen bonded -OH groups

and the acidic phenolic functions. The $^{13}C$ NMR spectrum displayed signals δ 168.63 (C-6 in pyrimidine), δ 166.85 (C-2 in pyrimidine), δ 157.17 (C-3 in benzisoxazole), δ 155.66 (C in amide –NH-C=O), δ 148.10 (C-3a), δ 142.45 (C-5 in benzisoxazole), δ 138.37 (C-1′ in benzene), δ 135.77 (C-4′ in benzene), δ 132.66 (C-5′ in benzene), δ 132.39 (C-3′ in benzene), δ 129.85 (C-2′ in benzene), δ 129.15 (C-6′ in benzene), δ 128.00 (C-7 in benzisoxazole), δ 122.63 (C-7a in benzisoxazole), δ 116.20 (C-6 in benzisoxazole), δ 112.32 (C-4 in benzisoxazole), δ 103.19 (C-3 in pyrimidine), δ 89.15 (C-1″ in glucose), δ 81.82 (C-5″ in glucose), δ 74.22 (C-3″ in glucose), δ 67.77 (C-4″ in glucose), δ 63.45 (C-2″ in glucose), δ 57.76 (C-6″ in glucose), δ 19.20 ($CH_3$). FAB-MS confirmed the molecular formula $C_{24}H_{24}N_4O_7$. It shows molecular ion peak at *m/z* 481 $[C_{24}H_{24}N_4O_7]^+$. The base peak appear at *m/z* 243 $[C_{12}H_{10}N_4O_2+2H^+]^+$. On the basis of above chemical and spectral evidences, the product (**5a)** was assigned to be 7-amino-(β-D-glucopyranosyl)-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole [24-26,28-30].

**Polarographic studies:** The DC polarograms have been shown in Fig. 1a while DP polarograms have been shown in Fig. 1b. The diffusion current (DC) polarogram shows a distinct polarographic wave with half wave potential ($E_{1/2}$) -1.170 V which matches with the literature value for heterocyclic ring *i.e.* pyrimidine group. The differential pulse polarogram shows a distinct peak with peak potential -1.150 V.

The supporting electrolyte solution was deareated with nitrogen for 15 min and polarograms were recorded in diffusion current (DC) and differential pulse polarography (DPP) modes. To this solution, various concentrations of ethanolic solutions of 7-amino-(β-D-glucopyranosyl)-3-methyl-5-(4′-phenyl-2′-pyrimidin-6′-yl)-1,2-benzisoxazole were added and polarograms were recorded for each addition. The DC polarograms have been shown in Fig. 1c, while DP polarograms have been shown in Fig. 1d. The DC polarogram shows a distinct polarographic wave with half wave potential ($E_{1/2}$) -1.690 V, which matches with the literature value for sugar group [31,32]. The differential pulse polarogram shows a distinct peak with peak potential -1.770 V.

**Antimicrobial studies:** Compounds **5a-j** were screened for their antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* by disc diffusion method. The standard ciprofloxacin was used for the comparison of results. The screening result showed all compounds shows activity against both bacteria tested at 800 µg/mL concentration. Compounds **5c**, **5g** and **5i** were active whereas remaining compounds showed moderate to less activity against bacteria *E. coli*. Compounds **5f** and **5i** shows moderate to less active and compound **5d** was inactive, whereas the remaining compounds were active against *S. aureus*. Similarly, antifungal screening of compounds **5a-j** were carried out against two fungi *viz.*, *Candida albicans* and *Aspergillus niger* adopting the disc diffusion method. The comparison of results was done by using nystatin as a standard. The compounds **5d**, **5e** and **5g** were less active and remaining compounds were active against *C. albicans* at 800 µg/mL concentration. Compounds **5a**, **5d** and **5i** showed less active whereas remaining compounds showed moderate to active against fungi *A. niger* (Table-2).

TABLE-2
ANTIMICROBIAL ACTIVITIES OF 7-AMINO-(β-D-GLUCOPYRANOSYL)-3-METHYL-5-(4'-ARYL-2'-PYRIMIDIN-6'-YL)-1,2-BENZISOXAZOLES (**5a-j**)

| Compd. | Zone of inhibition (mm) Concentration (µg/mL) | | | |
|---|---|---|---|---|
| | Bacteria | | Fungi | |
| | *E. coli* | *S. aureus* | *C. albicans* | *A. niger* |
| **5a** | 9.2 | 12.2 | 10.1 | 9.3 |
| **5b** | 9.4 | 10.4 | 11.5 | 11.2 |
| **5c** | 13.2 | 10.5 | 11.9 | 10.5 |
| **5d** | 7.3 | 6.3 | 8.4 | 7.2 |
| **5e** | 9.1 | 11.0 | 8.9 | 11.3 |
| **5f** | 8.2 | 9.2 | 10.8 | 11.6 |
| **5g** | 15.6 | 12.3 | 9.2 | 10.3 |
| **5h** | 9.2 | 11.0 | 10.5 | 11.6 |
| **5i** | 10.5 | 9.8 | 10.3 | 9.5 |
| **5j** | 9.6 | 10.2 | 11.1 | 10.6 |
| Std | 33 | 24 | 12.7 | 13.3 |
| | Ciprofloxacin (100 µg/mL) | | Nystatin (100 µg/mL) | |

Zone of inhibition in mm ± 0.3; Blank: 6.3 mm

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