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"SYNTHESIS AND CHARACTERIZATION OF NOVEL SUBSTITUTED BROMOBENZALDEHYDE DERIVATIVES OF 4-AMINOPYRROLO [2, 3-*d*] PYRIMIDINE"

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Abstract:

Substituted bromobenzaldehyde derivatives of 4-aminopyrrolo[2,3-*d*]pyrimidine were reported to act as potent antifungal and antibacterial agents, in this work, a series of novel Substituted bromobenzaldehyde (o-bromobenzaldehyde, m-bromobenzaldehyde, and p-bromobenzaldehyde) derivatives were synthesized. The structures of these compounds were confirmed by elemental analysis, FT(IR), ^{1}H NMR and UV-visible spectral data. All the newly synthesized compounds were evaluated for their in vitro antifungal and antibacterial activities. Most of the screened compounds showed interesting antifungal and antibacterial activities compared with the used reference drugs (fluconazole and streptomycin).

Keywords **—o-Bromobenzaldehydes, 4-aminopyrrolo[2,3-*d*]pyrimidine, m-bromosalicylaldehydes, p-bromobenzaldehyde.**

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I. INTRODUCTION

Pyrimidines and their derivatives have clear scientific importance. Pyrimidines and purines are the most significant naturally occurring heteroaromatic substances. The significance of pyrrolo[2,3-d]pyrimidine derivatives in biology and chemotherapeutics caught the attention of organic chemists. The related fused heterocycles of these molecules are relevant as possible bioactive molecules. They have been found to have biological effects like those of enzyme inhibitors[1], cytotoxic agents[2], antiviral agents[3], anti-inflammatory agents[6], anti-allergenic agents[7], anti-tumor agents[9–12], and antimicrobial and antifungal agents[13]. Research has shown that pyrrolo[2,3-d]pyrimidines, also referred to as 7-deazapurines, have antibacterial, antiviral, anticancer, anti-inflammatory, and antihyperglycemic characteristics. In nucleic acid sequencing, the 7-deazapurine scaffold is used in place of the canonical components of DNA and RNA because its shape is comparable to that of purines.We report the synthesis and antimicrobial activity of a novel series of 4-aminopyrrolo[2,3-d]pyrimidine derivatives of substituted bromobenzaldehydes based on these observations (o-bromobenzaldehyde, m-bromobenzaldehyde, and p-bromobenzaldehyde).

II. EXPERIMENTAL

Unless otherwise specified, all materials were obtained from commercial suppliers and used without purification. On silica gel plates, TLC analysis was performed. None of the melting points have been corrected. FT-IR spectra were collected using KBr pellets on a BRUKER FT-IR spectrophotometer in the 4000-500 cm^{-1} range. At room temperature, UV spectra were recorded on a

JASCO V650 spectrophotometer in methanol solvent. The Brucker ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz in DMSO d_6 with tetramethylsilane as an internal reference. The Microanalytical Centre at Pune University conducted the elemental analyses. All compounds' C, H, and N values were found to be within 0.4% of the theoretical value. Table 1 displays the characteristic data for prepared compounds. The spectral data is shown in Tables 2 through 4.

A. 4-aminopyrrolo[2,3-d]pyrimidine-o-bromobenzaldehyde

A mixture of 4-aminopyrrolo[2,3-d]pyrimidine (0.1 mol) and o-bromobenzaldehyde (0.125 mol) in methanol (45 ml) was refluxed for 2 hours and then allowed to cool to room temperature (r. t.). The precipitate was filtered, washed with methanol, and dried to yield 4-aminopyrrolo[2,3-d]pyrimidine-o-bromobenzaldehyde.

B. 4-aminopyrrolo[2,3-d]pyrimidine-m-bromobenzaldehyde:

A mixture of 4-aminopyrrolo[2,3-d]pyrimidine (0.1 mol) and m-bromobenzaldehyde (0.11 mol) in methanol (45 ml) was refluxed for 5 hours and then allowed to cool to room temperature (r. t.). The precipitate was filtered, washed with methanol, and dried to yield 4-aminopyrrolo[2,3-d]pyrimidine-m-bromobenzaldehyde.

C. 4-aminopyrrolo[2,3-d]pyrimidine-p-bromobenzaldehyde:

A mixture of 4-aminopyrrolo[2,3-d]pyrimidine (0.1 mol) and p-bromobenzaldehyde (0.15 mol) in methanol (45 ml) was refluxed for 2 hours and then allowed to cool to room temperature (r. t.). The precipitate was filtered, washed with methanol, and dried to yield 4-aminopyrrolo[2,3-d]pyrimidine-p-bromobenzaldehyde.

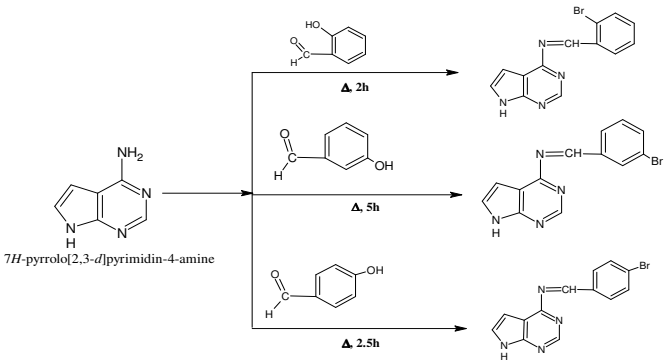

Figure-1: Synthesis of 4-aminopyrrolo[2, 3-d]pyrimidine derivatives of substituted bromobenzaldehydes

III. RESULTS AND DISCUSSION

Under reflux for 2–5 hours, 4-aminopyrrolo[2, 3-d]pyrimidine was reacting with substituted bromobenzaldehydes (o-bromobenzaldehydes, m-bromobenzaldehydes, and p-bromobenzaldehydes). Yields ranging from 76 to 84% were obtained for the target compounds. The physicochemical data of the prepared title compounds are summarised in Table-1. The scheme for the synthesis of 4-aminopyrrolo[2, 3-d]pyrimidine derivatives of substituted bromobenzaldehydes is depicted in Figure 1. 1-(2-bromophenyl)-*N*-(7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl)methanimine (APPoBB), 1-(3-bromophenyl)-*N*-(7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl)methanimine (APPmBB), and 1-(4-bromophenyl)-*N*-(7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl)methanimine (APPpBB). Most organic solvents, but not water, dissolve the prepared compounds. According to the elemental analysis data, all derivatives are expected compositions (**Table-1**). The compounds are coloured powdered solids that are non-hygroscopic. To ensure the purity of the synthesised compounds, TLC was used.

Table-1: Physico-chemical and analytical data of preparedcompounds

Comp	Color	MW	% Yield	MP/DP	Element Content			
					C	H	N	Br
APPoBB	Yellow	314	77.58	206	51.85	3.01	18.60	26.53
APPmBB	Yellow	314	78.39	205	51.85	3.01	18.60	26.53
APPpBB	Yellow	314	79.99	203	51.85	3.01	18.60	26.53

A. FT(IR) spectra

By comparing the FT(IR) spectra of the synthesised compounds to those of the free 4-aminopyrrolo[2,3-d]pyrimidine, the bonding of the 4-aminopyrrolo[2,3-d]pyrimidine to substituted benzaldehydes was investigated. To investigate the effect of 4-aminopyrrolo[2,3-d]pyrimidine vibration on substituted benzaldehydes, some significant bands were chosen. The absence of stretching vibrations due to the aldehyde (CHO) and amino (NH_2) moiety of amino derivatives confirms the development of the entire set of compounds, with a strong new band forming at region 1659-1674 cm^{-1} corresponding to the azomethine (HC=NN-) group20. A broad aromatic (NH) band in the 3120-3324 cm^{-1} range suggests the presence of the prepared compounds[21-22]. All of the compounds in the 2798-2900 cm^{-1} regions are attributed to (CH) aldehydic bands. Sharp bands at 1583-1588 and 1475-1509 cm^{-1} in the infrared spectra of 2a-c compounds correspond to the >C=C group of an aromatic ring. The 2a-c compounds' FT-IR spectra revealed strong bands in the 1316-1335 cm^{-1}, 722-739 cm^{-1}, and 654-691 cm^{-1} assignable to the aromatic (C–N), di- substituted benzene ring, and monosubstituted benzene ring.

Table-2: FT(IR) spectral data of **2a-c**compounds

Compound	-OH	NH (Aro)	C-H (Aro)	C-H (aldehyde)	>C=C< (aro)	>C=N- (ali)	C-N (aro amine)	Di/tri sub benzene ring	Mono sub benzene ring
APPoBB (2a)	3319	3120	3028	2911	1584/1479	1673	1335	723	691
APPmBB (2b)	3393	3314	3137	2989	1582/1475	1654	1335	723	691
APPpBB (2c)	3381	3187	3098	2796	1588/1480	1655	1316	739	654

B. ^{1}**H NMR spectra**

The broad singlet signals seen at 10.250-10.899 ppm in the ^{1}H NMR spectra of all synthesised compounds are ascribed to the presence of the -NH- moiety in the pyrrolyl ring. All prepared chemicals are classified as belonging to the aldehydic -CH= group by the singlet peak in the range 9.239–9.341 ppm. The 1H NMR spectra of all synthesised derivatives lack the wide singlet signal at 9.84 ppm (2H) that corresponds to the -NH_2 of 4-chloro-7H-pyrrolo[2, 3-d] pyrimidine, demonstrating that Schiff base[23] was successful in replacing the amino group. The ^{1}H NMR bands match those found in published works[23-24].

Table-3: ^{1}H NMR spectral data of **2a-c**compounds

Comp	NH (aro)	CH (aldehydic)	Aromatic Protons
APPoBB (2a)	10.899	9.256	7.436-7.702
APPmBB (2b)	10.815	9.239	7.438-7.702
APPpBB (2c)	10.250	9.341	6.974-8.408

C. UV-Visible spectra

In methanol at ambient temperature, the prepared 2a-c compounds' UV spectra were captured. Table 4 contains the 2a-c substances' UV-vis spectral data. The shift between the benzene rings at 235–275 nm is what is responsible for the 2a–c compounds' aromatic band. The n* transition of the non-bonding electrons present on the nitrogen of the azomethine groups in the 2a-c molecules is what causes the band approach of 315-355 nm.

Table-4: Uv-visible spectral data of **2a-c**compounds

Comp	$\pi \rightarrow \pi^*$	$n \rightarrow \pi^*$
APPoBB (2a)	275	355
APPmBB (2b)	235	315
APPpBB (2c)	269	349

IV. CONCLUSION

New 4-aminopyrrolo[2,3-d]pyrimidine derivatives of 1a-h and 4-aminopyrrolo [2, 3d]pyrimidine derivatives of substituted bromobenzaldehydes have been synthesised in this study (o-bromobenzaldehydes, m-bromobenzaldehydes, and p-bromobenzaldehydes). The analytical data, FT(IR), Uv-vis, NMR spectral studies, and electrochemical data have all verified that the suggested compounds form as they are said to. The produced bezaldehyde-based compounds' 1H/13C NMR, UV-vis, elemental analysis (C, H, N, O), and FT(IR) spectra were documented and studied. The findings suggest a 1:1 ratio of modified bromobenzaldehydes to 4-aminopyrrolo [2,3 d]pyrimidine (o-bromobenzaldehydes, m-bromobenzaldehydes, and p-bromobenzaldehydes).

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