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ORIGINAL PAPER

Synthesis, Characterization and Biological Activity Studies on 6-*p*-Dimethylaminophenyl-5,6-dihydrobenzoimidazo [1,2-*c*]quinazoline: Crystal Structure of the Title Compound and Comparative Study with Related Derivatives

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Abstract Reaction of *o*-aminophenylbenzimidazole with *p*-dimethylaminobenzaldehyde yielded 6-*p*-dimethylaminophenyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline, which was characterized by elemental analysis, IR, UV–Vis, ^{1}H NMR, ^{13}C NMR, mass spectral studies and X-ray crystal structure analysis. Studies on the antimicrobial activity of the compound revealed that it is active against fungus *Yeast* but not *Bacillus subtilis*. The compound crystallized in the space group $P2_1/n$ with the unit cell parameters $a = 10.652(2)$ Å, $b = 11.002(2)$ Å, $c = 15.753(2)$ Å, $\beta = 109.29(2)°$ and the structure was refined to an *R*-factor of 0.0479. The hydropyrimidine ring in the quinazoline moiety is in skew-boat conformation. The dimethylamino group attached to phenyl ring is in conjugation with it. The structure was stabilized by intermolecular C–H–N interactions. A few of the related quinazolines (6-*p*-hydroxyphenyl-5,6-dihydrobenzoimidazo [1,2-*c*]quinazoline; 6-phenyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline; 6-pyridyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline; 6-furyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline) were also examined for their biological activity, in addition to their characterization by IR, UV–Vis, ^{1}H and ^{13}C NMR spectral studies along with structural comparison.

Keywords X-ray crystal structure · NMR · *p*-Dimethylaminobenzaldehyde · *o*-Aminophenylbenzimidazole · Benzoimidazo[1,2-*c*]quinazoline · Biological activity

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Introduction

Quinazolines and their derivatives are of significant focus in the field of medicinal chemistry owing to their broad spectrum of biological properties. They are potent cytotoxic agents [1–4]. Substituted quinazolines exhibit fungicidal, antimicrobial, CNS stimulant, diuretic, anti-inflammatory, anticancer, anti-hypertensive, anti-analgesic, antitumour and anti-HIV properties [5–7]. Some of the derivatives of indole[1,2-*c*]quinazoline show cataleptogenic activity [8]. Imidazole and their derivatives are widely used as ligating groups to transition metal ions [9, 10]. Multidentate N-heterocycles on coordination to metal ions produce organized supramolecules and they appear quite promising for the design of stable light conversion devices [11]. The application of imidazoles in medicinal chemistry [12] and chemistry of natural products/alkaloids [13, 14] are also well known. Heterocycles containing the imidazole moiety are of biological significance and display antibacterial, antifungal activities [15], leukotriene B_4 receptor antagonist properties [16], and potassium channel openers [17]. Benzimidazole and their derivatives as well as their metal complexes exhibit antibacterial, antifungal, veterinary, anthelmintic, insecticidal and virucidal activities [18, 19]. It is likely that the introduction of benzimidazole group into the quinazoline system would appreciably

influence the biological activity of the latter. Benzimidazoquinazolines have been reported to exhibit virucidal properties and antifungal effects against dermatophytes [20]. Benzimidazo[1,2-*c*]quinazolines with 6-alkyl substitution have been evaluated for their bronchodilator activity [21].

Presumably, the biological activity of 6-phenyl-5,6-dihydrobenzimidazo[1,2-*c*]quinazoline is related to its structure and electron donor/acceptor substituents. For instance, the introduction of electron-withdrawing substituents such as Cl, Br, F and NO_2 on the 6-phenyl ring rendered compounds devoid of antifungal activity [22]. On the contrary, an electron donor substituent such as OCH_3 group enhanced the activity of the compound by nearly five times as in *T. mentagrophytes*, *E. floccosum* and *T. rubrum*.

A detailed analysis of the structure of a compound would provide an opportunity to understand the biological function and its implication in the structural ramifications needed for binding to the receptors. In the present study, we have made an attempt to understand the influence of the substituent groups on the conformation of the dihydrobenzoimidazo[1,2-*c*]quinazoline ring system. With this in view, herein we report the synthesis, characterization, crystal structure and biological activity of 6-*p*-dimethylaminophenyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline.

Experimental

Apparatus

The electronic spectra of the *N*-heterocycles (**I**–**V**) were recorded in DMF using Shimadzu UV3101 PC. The IR spectra of the compounds were recorded as Nujol mulls using Shimadzu FTIR 8400S spectrometer. ^{1}H and ^{13}C NMR spectra of the N-heterocycles were recorded on Bruker av 400 MHz instrument using DMSO-d_6 as solvent. The ^{1}H and ^{13}C NMR chemical shifts are reported as δ in parts per million relative to tetramethylsilane as an internal reference and coupling constants (J) are in Hz. The mass spectrum of **I** was recorded on Shimadzu GCMS QP5050.

Synthesis and Spectroscopic Characterization

*6-p-Dimethylaminophenyl-5,6-dihydrobenzoimidazo[1,2-c]quinazoline (**I**)*

o-Aminophenylbenzimidazole was prepared by adopting a literature method [23]. A mixture of *o*-aminophenylbenzimidazole (0.05 mol, 10.45 g) and *p*-dimethylamino benzaldehyde (0.05 mol, 6.66 g) in 200 ml of ethanol was refluxed for 5 h. The resulting solution was evaporated under reduced pressure to a small volume to obtain a yellow compound. It was separated and recrystallized from ethanol to get 6-*p*-dimethylaminophenyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline (**I**) as a cream crystalline solid. Compounds **II** through **V** were prepared as reported earlier [24–27].

Elemental analysis for 6-*p*-dimethylaminophenyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline (**I**) having the molecular formula $C_{22}H_{20}N_4$ requires C 77.63, H 5.92, N 16.45%. Found: C 76.78, H 6.16, N 15.87%. Yield: 60%; mp: 201°C. δ_H (400 MHz, DMSO-d_6) {7.4 (s, NH), 6.86 (s, CH), 7.96 (d, $J = 8.0$, H-7), 7.24 (t, $J = 7.60$, H-8), 6.81 (t, $J = 0.8$, H-9), 6.87 (d, $J = 8.0$, H-10), quinazoline ring protons}, {7.62 (s, H-2′), 7.06 (t, $J = 7.2$, H-3′), 7.02 (t, $J = 7.2$, H-4′), 7.12 (d, $J = 1.2$, H-5′), benzimidazole ring protons}, {7.15 (d, $J = 8.4$, H-2″/6″), 6.63 (d, $J = 8.8$, H-3″/5″), phenyl ring protons}, 2.82 (s, $2CH_3$). δ_C (400 MHz, DMSO-d_6) {147.15 (C-2), 143.61 (C-3), 110.68 (C-4), 68.23 (CH), 127.25 (C-7), 131.39 (C-8), 117.88 (C-9), 114.66 (C-10), quinazoline ring carbons}, {118.47 (C-2′) 121.86 (C-3′), 121.71, (C-4′), 111.88 (C-5′), 132.92 (C-6′), 143.88 (C-7′), benzimidazole ring carbons}, 124.54 (C-1″), 127.07 (C-2″/6″), 111.92 (C-3″/5″), 150.75 (C-4″), phenyl ring carbons}, 40.12 ($2CH_3$).

*6-p-Hydroxyphenyl-5,6-dihydrobenzoimidazo[1,2-c]quinazoline (**II**)*

White solid; Yield: 60%; mp: 295°C. δ_H (400 MHz, DMSO-d_6) 7.46 (s, NH), 6.89 (s, CH), {7.96 (d, $J = 5.6$, H-7), 7.25 (t, $J = 5.60$, H-8), 6.83 (t, $J = 6.0$, H-9), 6.87 (d, $J = 6.8$, H-10), quinazoline ring protons}, {7.64 (d, $J = 6.4$, H-2′), 7.16 (t, $J = 6.4$, H-3′), 7.06 (t, $J = 6.0$, H-4′), 6.96 (d, $J = 6.4$, H-5′), benzimidazole ring protons}, {7.19(d, $J = 6.8$, H-2″/6″), 6.74 (d, $J = 6.8$, H-3″/5″), phenyl ring protons}, 9.65 (s, OH). δ_C (400 MHz, DMSO-d_6) {147.04 (C-2), 143.50 (C-3), 111.70 (C-4), 68.10 (CH), 121.90 (C-7), 131.50 (C-8), 117.90 (C-9), 114.60 (C-10), quinazoline ring carbons}, {118.50 (C-2′) 121.90 (C-3′), 121.70, (C-4′), 110.60(C-5′), 132.80 (C-6′), 143.80 (C-7′), benzimidazole ring carbons}, {130.50 (C-1″), 127.70 (C-2″/6″), 115.30 (C-3″/5″), 158.00 (C-4″), phenyl ring carbons}.

*6-Phenyl-5,6-dihydrobenzoimidazo[1,2-c]quinazoline (**III**)*

White solid; Yield: 70%; mp: 199°C. δ_H (400 MHz, DMSO-d_6) 7.62 (s, NH), 7.08 (s, CH), {7.95 (d, $J = 6.7$, H-7), 7.27 (m, H-8), 6.82 (t, $J = 7.4$, H-9), 6.86 (d, $J = 8.1$, H-10), quinazoline ring protons}, {7.65 (d, $J = 7.95$, H-2′), 7.25 (m, H-3′), 7.18 (m, H-4′),7.10(d, $J = 7.2$, H-5′), benzimidazole ring protons}, {7.29 (m, H-2″/6″), 7.33 (m, H-3″/5″), 7.15 (m, H-4″), phenyl ring protons}. δ_C (400 MHz, DMSO-d_6) {146.80 (C-2), 143.11 (C-3), 111.80 (C-4), 67.80 (CH), 124.59 (C-7), 131.61

(C-8), 118.13 (C-9), 114.76 (C-10), quinazoline ring carbons}, {118.55 (C-2′) 122.13 (C-3′), 121.98 (C-4′), 110.47 (C-5′), 140.31 (C-6′), 143.80 (C-7′), benzimidazole ring carbons},{132.78 (C-1″), 128.88 (C-2″/4″/6″), 125.94 (C-3″/5″), phenyl ring carbons}.

*6-Pyridyl-5,6-dihydrobenzoimidazo[1,2-c]quinazoline (**IV**)*

White solid; Yield: 60%; mp: 230°C. δ_H (400 MHz, DMSO-d_6) {5.4 (s, NH), 7.72 (s, CH), 7.64 (d, $J = 9.4$, H-7), 7.24 (m, H-8), 7.24 (m, H-9), 7.32 (d, $J = 9.4$, H-10), quinazoline ring protons}, {7.16 (d, $J = 7.02$, H-2′), 7.06 (m, H-3′), 6.80 (m, H-4′), 6.83 (d, $J = 9.4$, H-5′), benzimidazole ring protons}, {7.94 (d, $J = 9.4$, H-3″), 7.74 (m, H-4″), 7.03 (t, $J = 9.4$, H-5″), 8.4(d, $J = 4.7$, H-6″), pyridyl ring protons}. δ_C (400 MHz, DMSO-d_6) {158.40(C-2), 112.10(C-3), 133.00 (C-4), 67.50 (CH), 123.90 (C-7), 122.00 (C-8), 122.20 (C-9), 124.60 (C-10), quinazoline ring carbons}, {110.70 (C-2′) 114.70 (C-3′), 118.10, (C-4′), 118.60 (C-5′), 143.80 (C-6′), 142.90 (C-7′), benzimidazole ring carbons}, {146.9 (C-1″), 137.40 (C-3″), 120.20 (C-4″), 131.50 (C-5″), 149.4 (C-6″), pyridyl ring carbons}.

*6-Furyl-5,6-dihydrobenzoimidazo[1,2-c]quinazoline (**V**)*

Cream solid; Yield: 60%; mp: 211°C. δ_H (400 MHz, DMSO-d_6){7.63 (s, NH), 7.54 (s, CH), 7.94 (d, $J = 6.76$, H-7), 7.29 (t, $J = 8.38$, H-8), 6.87 (t, $J = 7.2$, H-9), 6.94 (d, $J = 8.0$, H-10), quinazoline ring protons}, {7.66 (m, H-2′), 7.24 (m, H-3′), 7.22 (m, H-4′), 7.46 (m, H-5′), benzimidazole ring protons}, {6.34 (H-3″), 6.36 (m, H-4″), 7.46 (m, H-5″), furyl ring protons}. δ_C (400 MHz, DMSO-d_6) {147.18 (C-2), 143.4 (C-3), 112.29 (C-4), 61.83 (CH), 125.14 (C-7), 132.19 (C-8), 118.94 (C-9), 110.62 (C-10), quinazoline ring carbons}, {119.14 (C-2′), 122.93 (C-3′), 122.83 (C-4′), 108.40 (C-5′), 132.9 (C-6′), 143.2 (C-7′), benzimidazole ring carbons},{152.40 (C-2″), 110.80 (C-3″), 110.80 (C-4″), 115.42 (C-5″), furyl ring carbons}.

X-ray Crystallography

Suitable single crystals of **I** for X-ray diffraction study were grown by slow evaporation from concentrated ethanol solution. Measurements were made using graphite monochromated CuKα radiation ($\lambda = 1.54180$ Å) on an Enraf-Nonius CAD-4 diffractometer using ω-2θ scan mode. The crystals of compound **I** belong to the monoclinic space group $P2_1/n$ with unit cell parameters $a = 10.652(2)$ Å, $b = 11.002(2)$ Å, $c = 15.753(2)$ Å, $\beta = 109.00(2)°$. The intensities were corrected for Lorentz, polarization and absorption. The crystal structure was solved by direct methods and refined by full-matrix least squares method using SHELX97 [28]. The non-hydrogen atoms were refined anisotropically and the hydrogen atoms were refined isotropically. The refinement was continued until the maximum shift/e.s.d was zero. Crystal data, intensity collection conditions and refinement parameters are presented in Table 1.

Table 1 Crystal data, intensity collection conditions and refinement parameters for compound **I**

CCDC No.	742983
Empirical formula	$C_{22}H_{20}N_4$
Formula weight	340.42
Temperature (K)	293(2)
Wavelength (Å)	1.54180
Crystal system, space group	Monoclinic, $P2_1/n$
Unit cell dimensions (Å, °)	$a = 10.652(2)$, $b = 11.002(2)$, $c = 15.753(3)$, $\beta = 109.29(2)$
Volume (Å^3)	1742.5(6)
Z, Calculated density (Mg/m^3)	4, 1.298
Absorption coefficient (mm^{-1})	0.616
Absorption correction	Psi-scan [29]
Max. and min. transmission	0.98 and 0.97
Crystal size (mm)	0.13 × 0.11 × 0.10
$F(000)$	720
θ range for data collection (°)	4.42–66.32
Index ranges	$0 \le h \le 12$, $-1 \le k \le 13$, $-18 \le l \le 17$
Reflections collected/unique	3586/3051 [R(int) = 0.0194]
Completeness to	$2\theta = 66.32$, 94.4%
Refinement method	Full-matrix least-squares on F^2
Goodness-of-fit on F^2	1.031
Data/restraints/parameters	3051/0/300
Final R indices ($I > 2\sigma(I)$)	$R1 = 0.0479$, $wR2 = 0.1307$
R indices (all data)	$R1 = 0.0869$, $wR2 = 0.1763$
Largest diff. peak and hole (e Å^{-3})	0.482 and −0.232

Antimicrobial Activity

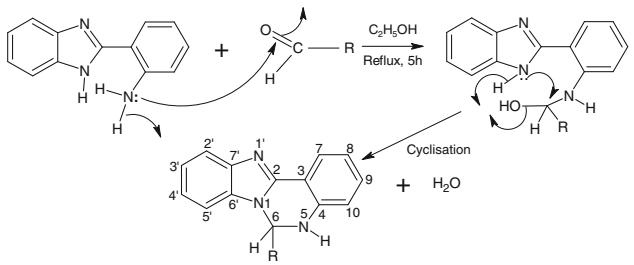
The antimicrobial activity of the N-heterocycles, **I**, **II** and **III** against the bacterial strain *Bacillus subtilis* and the fungus *Yeast* was investigated. The test solutions (50 ppm concentration) were prepared in DMSO for evaluating the biological activity. Cup-plate method was employed and the tests were carried out at room temperature. The experimental plates were incubated for 24 h and the zone of inhibition was measured. The drug action was estimated on the basis of percentage growth inhibition of the cultures.

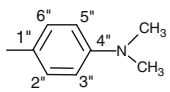
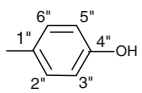
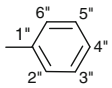
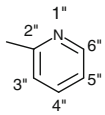
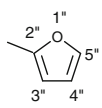
Percentage inhibition was calculated with standard antibiotic *Septran* and standard antifungal agent *Grissoflumin* as reference.

Results and Discussion

o-Aminophenylbenzimidazole reacts with *p*-dimethylamino benzaldehyde in ethanol to produce 6-*p*-dimethylaminophenyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline (**I**). The reaction may occur in two steps, the first one being the nucleophilic attack of amine, *o*-aminophenylbenzimidazole on the aldehyde, *p*-dimethylamino benzaldehyde leading to the formation of carbinolamine by coupling. In the second step, the carbinolamine undergoes cyclisation followed by the loss of a molecule of water to produce the product (**I**) as illustrated in Scheme 1.

The IR spectrum of *o*-aminophenylbenzimidazole exhibited two bands, one at 3380 cm^{-1} due to υ_{N-H} of benzimidazole group and another split band at 3160 and 3130 cm^{-1} assignable to υ_{N-H} of NH_2 group of phenylene ring. The spectrum of *p*-dimethylamino benzaldehyde displayed a band at 1740 cm^{-1} due to $\upsilon_{C=O}$. The spectrum of **I** did not show any peak around 3380 and 1740 cm^{-1} implying condensation and



Product	R	Name (R)
I		6-p-dimethylaminophenyl
II		6-p-hydroxyphenyl
III		6-phenyl
IV		6-pyridyl
V		6-furyl

Scheme 1 Reaction mechanism of *o*-aminophenylbenzimidazole with substituted benzaldehyde

formation of the quinazoline derivative. However the IR spectrum of **I** showed N–H stretching and in-plane bending vibrations of quinazoline ring at 3182 and 1589 cm^{-1} respectively. The $\upsilon_{C=N}$ coupled with $\upsilon_{C=C}$ of the phenylene rings was observed at 1612 cm^{-1}. The assignments of the other bands along with the spectral data which have not been reported earlier of the related quinazoline derivatives, **II**–**V** are listed in Table 2 [30]. The UV–Vis spectrum of **I** exhibited absorption bands assignable to $\pi \rightarrow \pi*$ transitions and these are listed in Table 3 along with the spectral data of related quinazoline derivatives.

The mass spectrum of **I** showed a parent ion peak at *m/z* 340. The compound undergoes fragmentation and the resultant pattern along with *m/z* values are depicted in Scheme 2.

The ^{1}H NMR spectrum of *o*-aminophenylbenzimidazole exhibited resonance peaks due to NH_2 of the amino group and NH of benzimidazole at 6.97 and 6.75 δ respectively. When this heterocycle was reacted with *p*-dimethylamino benzaldehyde the NH resonance peak was observed at 7.4 δ and the NH_2 resonance disappeared in the spectrum. The aldehydic proton resonance of *p*-dimethylamino benzaldehyde, observed at 9.66 δ, after condensation has undergone upfield shift and it was observed at 6.86 δ. The ^{13}C NMR spectrum of *p*-dimethylamino benzaldehyde exhibited a resonance at 189.72 δ due to aldehydic CH and this has shifted to 68.23 δ in the spectrum of **I** (dihydropyrimidine carbon 6).

The ^{1}H NMR spectrum of **I** exhibited resonances due to NH and CH of dihydropyrimidine ring at 7.40 and 6.86 δ respectively. A peak at 2.58 δ is assigned to CH_3 protons of N–Me_2 moiety. The resonances due to phenyl ring protons 2″, 6″ and 3″, 5″ (Scheme 1) are observed at 7.15 and 6.63 δ as doublets. The protons 2′, 3′, 4′ and 5′ of benzimidazole moiety displayed peaks at 7.62, 7.06, 7.02 and 7.12 δ respectively. The protons 7, 8, 9 and 10 of benzoquinazoline ring displayed peaks at 7.96, 7.24, 6.81 and 6.87 δ respectively.

The ^{13}C NMR spectrum of **I** exhibited methyl carbon resonance at 40.12 δ. The resonances due to quaternary carbons 2, 3, 4, 6′, 7′, 1″ and 4″ are observed at 147.15, 143.61, 110.6, 143.88, 132.92, 124.54 and 150.75 δ respectively. The peaks due to carbons 2′, 3′, 4′ and 5′ of benzimidazole moiety are at 118.47, 121.86, 121.71 and 111.88 δ respectively. The carbons 7, 8, 9 and 10 of benzimidazole ring exhibited the corresponding peaks at 127.25, 131.39, 117.88 and 114.66 δ. The phenyl ring carbons 2″ & 6″ and 3″ & 5″ displayed peaks at 127.07 and 111.92 δ respectively.

The ^{1}H and ^{13}C NMR spectral data of **I** along with those of **II** to **V** are listed under experimental section. Compounds **I**, **II** and **III** possess N–Me_2, OH and H groups in the para position of the phenyl ring. In the dihydropyrimidine ring all the carbon

Table 2 Infrared spectral data (cm^{-1})

I	II	III	IV	V	Assignments
3182	3205	3252	3275	3251	υ_{N-H} of quinazoline ring
1612	1614	1616	1621	1614	$\upsilon_{C=N}$ and $\upsilon_{C=C}$ of benzimidazole and $\upsilon_{C=C}$ of quinazoline.
1589	1587	1582	1595	1585	υ_{N-H} in-plane bending vibration
1527	1531	1528	1538	1529	$\upsilon_{C=C}$ and δ_{CH}
1321	1321	1319	1326	1330	υ_{C-N} and δ_{NH}
1284,	1280,	1296,	1284,	1263,	Benzimidazole ring vibrations
1008,	1007,	1007,	1020,	1007,	
937,	928,	930,	933,	932,	
862	880	891	876	891	
1226	1245	1261	1222	1230	In-plane CH deformation and ring breathing modes
1168	1161	1157	1154	1148	CH out-of-plane deformation of quinazoline ring vibrations
752	748	741	750	748	NH out-of-plane deformation
820	831	829	809	825	CH out-of-plane bending
653	659	674	674	651	Skeletal frequency of quinazoline

Table 3 Electronic spectral data (cm^{-1})

Ligand	Electronic transitions (cm^{-1})[a]			
I	34317 (14542)	33025 (16200)	27886 (8373)	
II	34352 (11876)	33003 (14590)	27996 (9264)	
III	36390 (6968)	34364 (7042)	33036 (8551)	27996 (5521)
IV	27933 (11342)	33069 (18222)	34388 (18322)	
V	36417 (5379)	34495 (10479)	33091 (9181)	28777 (10267)

[a] ε values in $cm^2\ mol^{-1}$ are given in parentheses

resonances of **I** and **II** have undergone downfield shifts except that of C-4. The electron donating ability of the substituents is in the order N–Me_2 > OH > H and thus the proton and carbon resonances of phenyl ring of **I** and **II** have undergone upfield shifts as compared to those of compound **III**.

X-ray Crystallography of Compound **I**

The X-ray crystallographic study on **I** has shown that the fused benzimidazole ring is roughly planar with a maximum deviation of 0.015(3) Å for atom C9 (Fig. 1). The geometrical parameters of the imidazole ring system are consistent with those reported in the literature [31]. The bond lengths and angles within the central dihydropyrimidine ring are affected by conjugation. The formal single bonds N1–C9 [1.377(3) Å], N1–C2 [1.394(3) Å] and N16–C15 [1.389(3) Å] possess values of a partial double bond (standard: Csp^2–N = 1.39 Å) [32]. The quinazoline ring has deviated from planarity with deviation of 0.272(3) Å at C17 from the least squares plane defined by atoms N1/C9/C10/C15/N16/C17. The imidazole and dihydropyrimidine rings are nearly co-planar as indicated by the dihedral angle of 5.05(2)°. The dihedral angle of 84.85(2)° between the planes of dimethylaminophenyl and the dihydropyrimidine

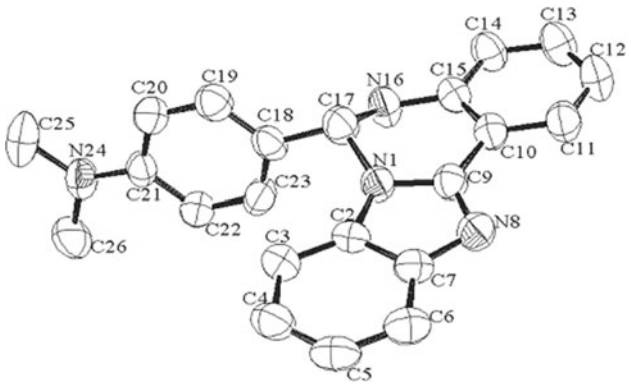
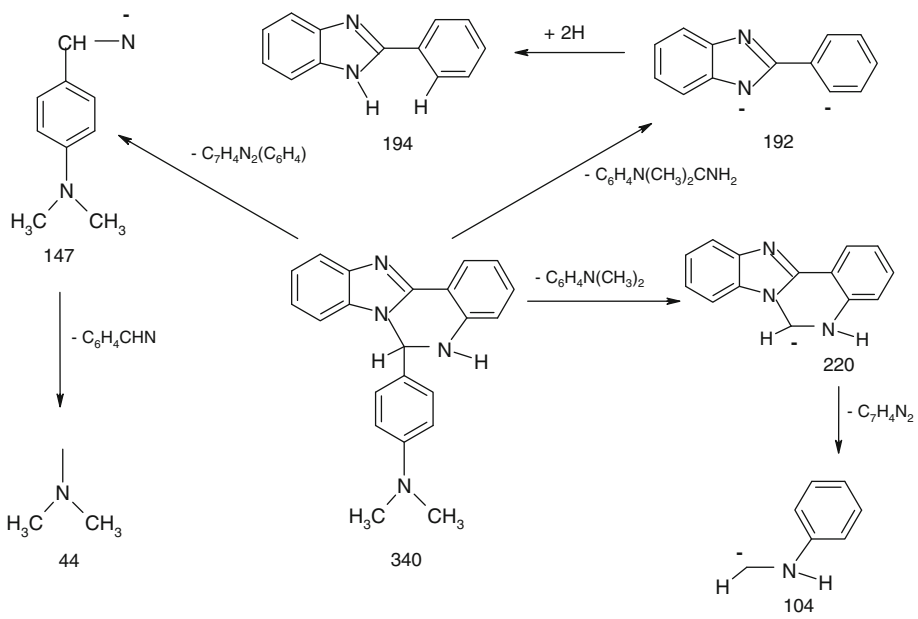


Fig. 1 Single crystal X-ray structure of **I** with thermal ellipsoids at 50% probability

rings indicates that the latter is nearly orthogonal to the former. A study of the torsion angles, asymmetric parameters and least squares plane calculations reveal that the dihydropyrimidine ring is in the skew-boat conformation, which is confirmed by the puckering parameters [33], $Q = 0.402$ Å, $\theta = 60.1°$ and $\phi = 286.99°$. Similar skew boat conformations were reported in 5,6-dihydroimidazo[1,2-*c*]quinazolines [26, 34, 35]. There are several reported structures where the dihydropyrimidine ring existed in half chair/flat boat type conformation [36–43].

Scheme 2 Mass spectral fragmentation of **I**



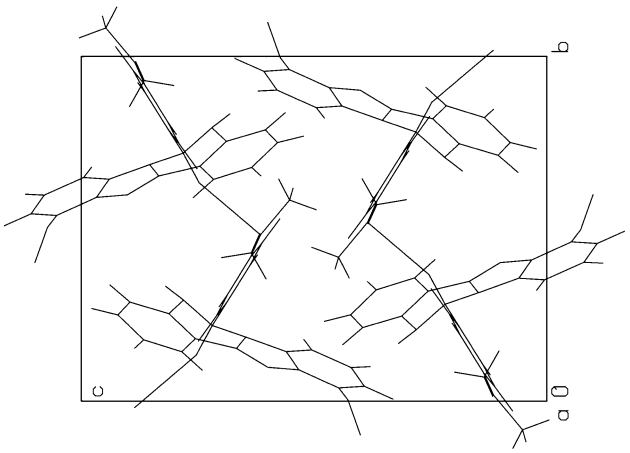


Fig. 2 Packing of molecules down *a*-axis of **I**

Table 4 Comparison of bond lengths (Å) and angles (°) in 6-phenyl groups

Bonds/angle	Compound		
	I	**II**	**III**
C22–C23	1.399(4)	1.386(3)	1.385(2)
C21–C22	1.399(4)	1.386(3)	1.374(3)
C20–C21	1.398(4)	1.386(3)	1.374(3)
C19–C20	1.370(4)	1.374(3)	1.381(3)
C18–C19	1.364(4)	1.390(3)	1.383(2)
C18–C23	1.379(4)	1.382(3)	1.387(2)
C20–C21–C22	116.4(3)	119.0(2)	119.9(2)

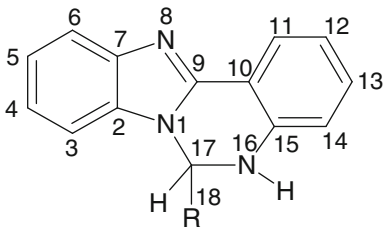


Fig. 3 **I**: R = dimethylaminophenyl; **II**: R = hydroxyphenyl; **III**: R = phenyl

The torsion angles of 63.0(3)° and −55.5(4)° for N16–C17–C18–C23 and N1–C17–C18–C23 respectively determine the inter-ring conformation of the junction between dimethylaminophenyl ring and the dihydrobenzimidazoquinazoline ring. This value being close to 60° indicates that the dimethylaminophenyl ring bisects the plane of the dihydrobenzimidazo quinazoline ring. The molecule possesses a chiral center at C17. The dimethylamino group is essentially planar (sum of the bond angles at N24 is 358°) and nearly coplanar with the adjacent phenyl ring C18/C19/C20/C21/C22/C23 (dihedral angles 170.6(3)° and 11.1(4)°). The atoms N24, C25 and C26 of the dimethylamino group have deviations of 0.051(3) Å, −0.059(3) Å and −0.150(3) Å respectively from the least squares plane of the phenyl ring C18/C19/C20/C21/C22/C23. The planarity of the dimethylamino group may increase the conjugation with the phenyl ring. The dimethylamino group is clearly conjugated with phenyl ring as indicated by the N24–C21 bond length [1.377(4) Å] and the bond angles around N24. The packing of molecules down *a*-axis is shown in Fig. 2. The structure exhibits intermolecular hydrogen bonds of the type C–H–N. The intermolecular hydrogen bonds are between the nitrogen of the imidazole ring of one molecule and the

Table 5 Comparison of bond lengths (Å) and angles (°) of dihydropyrimidine ring

Compound	r_{C-NH}	$r_{C-C(R)}$	$r_{C-N(ring)}$	N–C–N	C–NH–C
I	1.446(4)	1.510(4)	1.476(4)	105.2(2)	120.5(2)
II	1.459(3)	1.514(3)	1.459(3)	106.5(2)	122.6(2)
III	1.452(2)	1.521(2)	1.457(2)	106.6(1)	121.4(2)
IV	1.462(5)	1.525(5)	1.456(5)	107.4(3)	123.7(3)
V	1.450(3)	1.490(3)	1.453(3)	107.2(2)	121.0(2)

Table 6 Percentage inhibition shown against Bacillus subtilis and Yeast

Compound	Bacillus subtilis	Yeast
I	Nd[a]	70
II	Nd[a]	70
III	46	40
Standard	76	67

[a] Not detected

hydrogen of phenylene ring of adjacent molecule. The hydrogen bonding parameters are given below.

D–H ···A	Symm	H···A	D···A	D–H···A
C(6)–H(6)··· N(8)	−x, 1 − y, − z	2.6029 Å	3.5977Å	171°

The bond lengths in the 6-phenyl group of **I** have changed compared with other derivatives due to the para substitution of the dimethylamino group (Table 4). While the bond lengths C22–C23, C21–C22 and C20–C21 (Fig. 3) are elongated, the bond lengths C19–C20, C18–C19 and C18–C23 are shortened (Table 4) as compared to para OH substituted phenyl group in 6-*p*-hydroxyphenyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline (**II**) [24] and the non-substituted phenyl group in 6-phenyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline (**III**) [25]. The N1–C17 bond in the dihydropyrimidine ring of compound **I** is lengthened (1.477(4) Å) when compared to the respective bond lengths in **II**: 1.459(3) Å, **III**: 1.457(2) Å, **IV**: 1.453(3) Å [26] and **V**: 1.456(5) Å [27]. The N1–C17–N16 bond angle (105.0(2)°) has decreased as compared to 106.5(2)°, 106.6(1)°, 107.2(2)° and 107.4(3)° respectively in compounds **II**, **III**, **IV** and **V**. The dihedral angle between dimethyl aminophenyl ring and the dihydrobenzoimidazoquinazoline plane in compound **I** is 80.9(2)° whereas the corresponding angle is 86.26(1)° and 87.4(2)° in compounds **IV** and **V** respectively. Bond lengths and bond angles of dihydropyrimidine ring of compounds **I**–**V** are compiled in Table 5.

The antimicrobial activity of **I**, **II** and **III** against the bacterial strain *Bacillus subtilis* and the fungus *Yeast* reveal that **I** and **II** are slightly more toxic as compared to the standard with respect to *Yeast* but showed no toxicity against *Bacillus subtilis* (Table 6). The substituents in *para* positions (dimethyl amino group in **I** and hydroxyl group in **II**) are electron donating and do not show any bacterial growth inhibition. These substituents show appreciable growth inhibition as compared to the standards in the case of the fungus *Yeast*. The substituent in **III** (phenyl) which has hydrogen in the *para* position shows moderate antimicrobial activity for both the microbes as compared to **I** and **II**.

Conclusion

In conclusion, the reaction of *o*-aminophenyl benzimidazole with substituted aldehydes has resulted in the formation of quinazoline derivatives via cyclisation with the elimination of water molecule(s). ^{1}H and ^{13}C NMR spectral data have supported the formation of cyclised products. X-ray crystallographic studies have confirmed the cyclisation and have revealed the influence of the substituent R on the dihydropyrimidine ring with respect to bond lengths and bond angles. The dihydropyrimidine ring is in a skew-boat conformation in **I** and the dimethylamino group is clearly conjugated with the phenyl ring which it is attached to. Antimicrobial activity of **I**, **II** and **III** against the bacterial strain *Bacillus subtilis* and the fungus *Yeast* reveal that **I** and **II** are slightly more toxic as compared to the standard with respect to *Yeast* but showed no toxicity against *Bacillus subtilis*.

Supplementary Material

Crystallographic data for the structural analysis of compound **I** have been deposited with the Cambridge Crystallographic Data Centre (CCDC) as 742983. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, U.K.; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

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