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Synthesis and antiviral activities of N-substituted-2-substituted-benzimidazole derivatives

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Two series of N-substituted-2-substituted benzimidazole derivatives, viz. 1-benzyl-2-substituted benzimidazole **8-14** and 1-(*p*-chlorophenyl)-2-substituted benzimidazole **15-21** have been synthesized and tested for their antiviral activities. These compounds have been screened for *Tobacco mosaic* viruses and *Sunhemp rosette* viruses and show significant activities.

Keywords: Benzimidazole derivatives, antiviral activities, *Tobacco mosaic, Sunhemp rosette*

IPC: **Int.Cl.[7] C 07 D**

Our interest in imidazole and pyrazole condensed heterocyclic/aromatic[1,2] systems is due to their great therapeutic index[3-5]. A series of analogous and derivatives of benzimidazole have been reported to establish the effect of structure on antiviral activity[6-10].

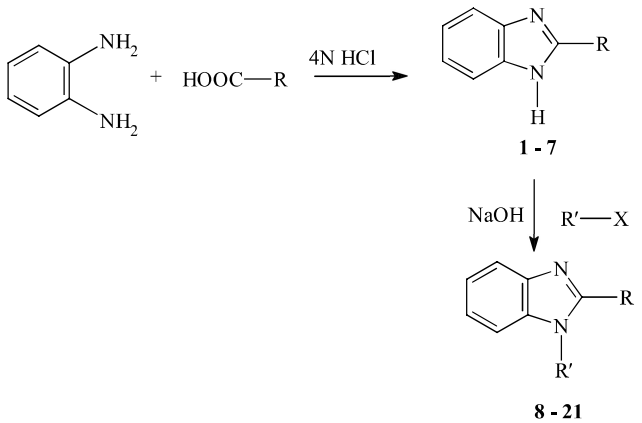
Benzimidazole derivatives have been demonstrated to inhibit Picornaviruses[11], Polioviruses[12], Enteroviruses[13] etc. Broad antiviral applications of benzimidazole derivatives prompted us to synthesize various N-substituted and 2-substituted benzimidazoles and to evaluate their antiviral activities against *Tobacco mosaic* virus and *Sunnhemp rosette* virus. The compounds were synthesized using Phillips condensation, by condensing the *o*-phenylene diamine and carboxylic acid derivatives in 4 *N* HCl, whereas N-substituted derivatives have been synthesized by reaction with alkyl/aryl halide in the presence of base, sodium hydride (**Scheme I**). Two derivatives were synthesized by diazotizing anthranilic acid followed by coupling with β-naphthol (**Scheme II**). This intermediate was then used to synthesize benzimidazole derivatives.

Mass spectral studies of the compounds have been carried out using electron ionization technique and a consistent pattern of mass fragmentation has been observed (**Scheme III**). The general fragmentation pattern of these compounds has started from the substituent at positions 1 and 2. The molecular ion peak has been observed in all the compounds. The base peak in all the spectra has been observed at m/z 118, which is assigned to the unsubstituted benzimidazole nucleus.

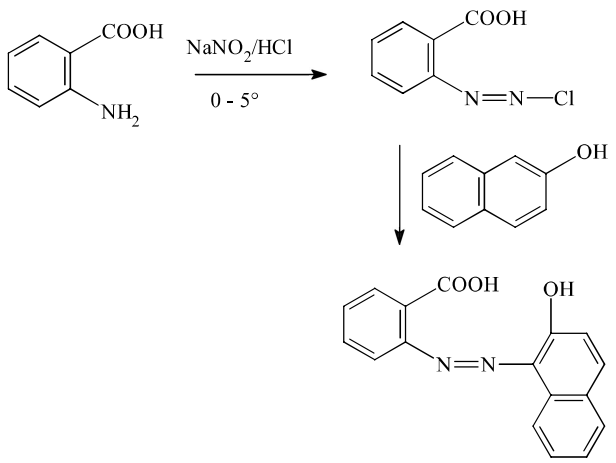
Antiviral activity

Source of inoculum

Cultures of *Tobacco mosaic* virus[14] (TMV, common strain) and *Sunnhemp rosette* virus (SRV) were maintained by regular passage in their systemic hosts *Nicotiana tabacum* L. "NP 31" and *Gotobaria junceal*, respectively.



Scheme I



Scheme II

Compd	R	R′
1	-CH_2CH_2COOH	H
2	-$C_6H_4OH(o)$	H
3	-CH=CH.C_6H_5	H
4	-$CH_2CH_2CH_2CH_2COOH$	H
5	-CHOH.CHOH.COOH	H
6	-$C_6H_4COOH(o)$	H
7	-C_6H_4N=N-$C_{10}H_6$-OH(2)	H
8	-CH_2CH_2COOH	-$CH_2C_6H_5$
9	-$C_6H_4OH(o)$	-$CH_2C_6H_5$
10	-CH=CH.C_6H_5	-$CH_2C_6H_5$
11	-$CH_2CH_2CH_2CH_2COOH$	-$CH_2C_6H_5$
12	-CHOH.CHOH.COOH	-$CH_2C_6H_5$
13	-$C_6H_4COOH(o)$	-$CH_2C_6H_5$
14	-C_6H_4N=N-$C_{10}H_6$-OH(2)	-$CH_2C_6H_5$
15	-CH_2CH_2COOH	-C_6H_5Cl
16	-$C_6H_4OH(o)$	-C_6H_5Cl
17	-CH=CH.C_6H_5	-C_6H_5Cl
18	-$CH_2CH_2CH_2CH_2COOH$	-C_6H_5Cl
19	-CHOH.CHOH.COOH	-C_6H_5Cl
20	-$C_6H_4COOH(o)$	-C_6H_5Cl
21	-C_6H_4N=N-$C_{10}H_6$-OH(2)	-C_6H_5Cl

Preparation of virus inoculum

Virus inoculum was prepared by grinding 3 to 4 of fresh diseased leaves in a mortax with distilled water (DW, 1 g/mL). The pulp was squeezed through two layers of muslin cloth, and the filtrate was centrifuged and diluted with distilled water to obtain 200-600 lesions on leaves after inoculation with a virus inoculum.

Host Plant

Seeds of N-tabacum 'samsun NN' and *Cyamopsis tetragonoloba* (L) Taub were sown in clay pots. The seedlings were transplanted to 12 cm diameter clay pots filled with compost and transferred to an insect free green house. For experimental work, somsun NN and N Glutinosa L plants were used at the 5 to 6 leaf stage and cyamopsis plants were used at the 4-leaf stage (3 unifoliate leaves and 1 trifoliate leaf). All the experiments were performed with a minimum of three replicates (minimum three plants with three or four leaves) per treatment.

Assay for virus inhibition

Cyamopsis tetragonoloba/SRV and N *Talacum samsun* NN/TMV were the host/virus system employed in the assay for virus infectivity. The two basal leaves of the host plants were treated with buffer extracted and centrifuged sap from *C. aculeatum* leaves or purified protein solution. Post-treatment done 24 hr after the treatment unless otherwise specified. The basal leaves of the control set of plants were treated with distilled water before virus inoculation. Percent inhibition of virus infectively was calculated by the formula:

Percent inhibition = (C - T/C) × 100
C = average number of lesions on control leaves
T = average number of lesions on tested leaves

Minimum time for induction of systemic resistance

The two lower leaves of the test plants, *N. glutinosa* and *Cyomopsis tetragonoloba* were tested with various N-substituted- and 2-substituted-benzimidazoles. After varying treatment intervals, these leaves were removed and the virus SRV was inoculated on the upper untreated leaves 24 hr later. The lesions were counted and percent reduction in number of lesions were calculated using the formula:

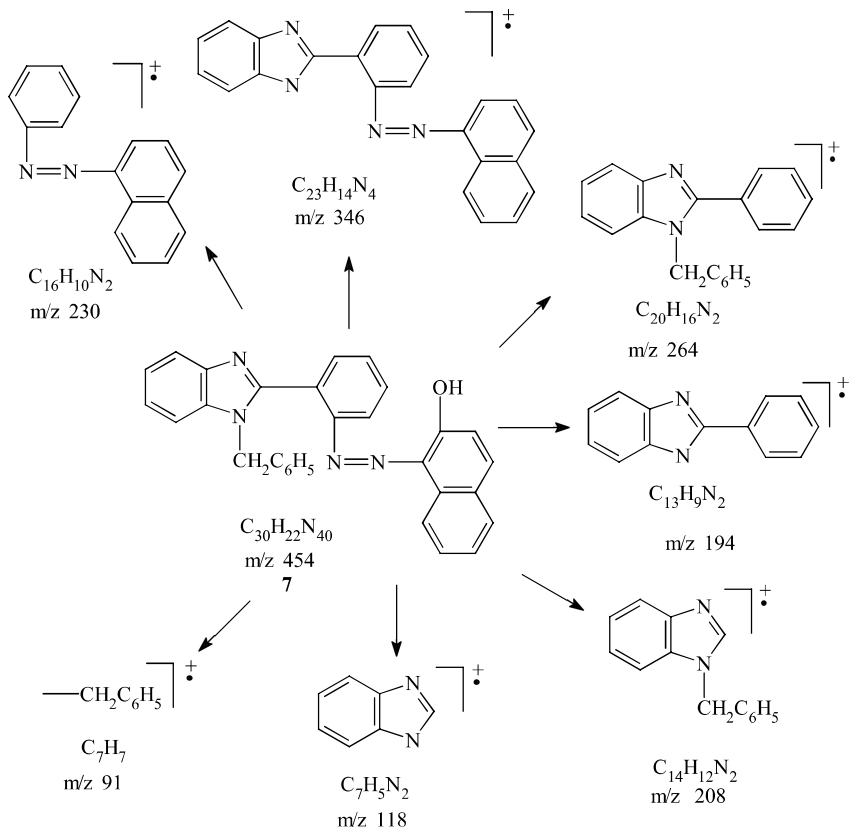
$$\% \text{ inhibition} = \frac{R - L}{L} \times 100$$

Almost all the compounds have shown average % inhibition. Antiviral activities of compounds are summarised in **Table I**

Experimental Section

Melting points were taken in an electrically heated instrument and are uncorrected. Compounds were routinely checked for their purity on silica gel G TLC plates and the spots were visualized by iodine vapours. IR spectra were recorded on a Shimadzu 8201 PC FTIR spectrometer; ^{1}H NMR spectra on a Bruker DRX 300 MHz FT NMR spectrometer using TMS as internal reference (chemical shifts in δ, ppm), and mass spectra on a Jeol SX-102 spectrometer.

Preparation of 2-substituted-benzimidazole 1-7. General procedure. *o*-Phenylenediamine (4 g, 0.04 mole) was condensed with carboxylic acids



Scheme III — Mass spectral fragmentation pattern of 1-benzyl-2-[*o*-phenyl-diazo(β-naphthyl)benzimidazole

Table I – Antiviral activity of 1-benzyl-2-substituted-benzimidazoles and 1-(*p*-chlorobenzyl)-2-substituted-benzimidazoles

Sl. No.	Average number of lesions		% inhibition	
Control	Site leaf	Remote leaf	Site leaf	Remote leaf
	133	130		
1	124	90	12.5	32.3
2	158	85	-17.5	34.6
3	124	88	15.6	28.6
4	119	99	10.9	23.4
5	125	92	20.4	38.1
6	111	98	36.3	15.6
7	120	110	17.9	25.0
8	85	89	36.5	31.9
9	86	90	32.9	23.6
10	125	119	6.7	8.4
11	112	102	24.6	16.3
12	130	127	2.9	2.3
13	100	94	10.5	9.5
14	110	98	17.9	25.0

(0.03 mole) in 50 mL 4 *N*. HCl. The reaction mixture was stirred for about 4 hr with magnetic stirrer at 80°C. The compounds were precipitated by adding concentrated ammonia solution, filtered through suction and washed with cold water. Compounds were recrystallized from water and ethanol.

Compound **1**: Yield 4.6 g (61%), m.p. 256°C; ^{1}H NMR (CD_3OD): δ 7.2 (m, 4H, ArH), 3.4 (t, 2H, H-2′), 3.2 (s, 1H, NH), 2.9 (t, 2H, H-1′); MS: m/z 190 (M^+), 146 ($C_9H_{10}N_2$), 119 ($C_4H_{11}N_2O_2$), 77 (C_6H_5), 74 ($C_3H_{10}N_2$), 55 (C_3H_5N). Anal. Calcd for $C_{10}H_{10}N_2O_2$ C, 63.16; H, 5.26; N, 14.73. Found: C, 62.76; H, 5.32; N, 15.42%.

Compound **2**: Yield 5.7 g (68%), m.p. 145°C; ^{1}H NMR (CD_3OD): δ 7.9 (m, 8H, ArH), 4.8 (s, 1H, OH), 3.2 (s, 1H, NH); MS: m/z 210 (M^+), 194 ($C_{13}H_{10}N_2$), 122 ($C_7H_{10}N_2$), 103 (C_7H_5N), 77 (C_6H_5). Anal. Calcd for $C_{13}H_{10}N_2O$: C, 74.28; H, 4.75; N, 13.33. Found: C, 73.19; H, 5.31; N, 13.76%.

Compound **3**: Yield 6.5 g (74%), m.p. 120°C; ^{1}H NMR (CD_3OD): δ 7.7 (m, 5H, ArH), 7.2 (m, 4H, ArH), 3.9 (d, 1H, H-2′), 3.4 (s, 1H, NH), 3.1 (d, 1H, H-1′); MS: m/z 220 (M^+), 148 ($C_9H_{12}N_2$), 129

(C_9H_7N), 104 (C_8H_8), 93 (C_6H_4N), 77 (C_6H_5). Anal. Calcd for $C_{15}H_{12}N_2$: C, 81.81; H, 5.45; N, 12.72. Found: C, 80.93; H, 6.12; N, 12.93%.

Compound **4**: Yield 6.9 g (79%), m.p. 155°C; ^{1}H NMR (CD_3OD): δ 7.2 (m, 4H, ArH), 3.3 (s, 1H, NH), 2.8 (t, 2H, H-4′), 2.4 (m, 4H, H-2′, H-3′), 2.1 (t, 2H, H-1′); MS: m/z 218 (M^+), 174 ($C_{11}H_{14}N_2$), 146 ($C_6H_{14}N_2O_2$), 102 ($C_5H_{14}N_2$), 93 (C_6H_7N), 83 (C_5H_9N), 77 (C_6H_5), 56 (C_4H_8). Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.05; H, 6.42; N, 12.84. Found: C, 65.87; H, 7.15; N, 12.14%.

Compound **5**: Yield 7.5 g (85%), m.p. 270°C; ^{1}H NMR (CD_3OD): δ 7.3 (m, 4H, ArH), 4.4 (s, 2H, OH), 3.9 (d, 1H, H-2′), 3.4 (d, 1H, H-1′), 3.2 (s, 1H, NH); MS: m/z 222 (M^+), 178 ($C_9H_{10}N_2O_2$), 150 ($C_4H_{10}N_2O_4$), 148 ($C_8H_8N_2O$), 131 ($C_4H_5NO_4$), 106 ($C_3H_6O_4$), 93 (C_6H_7N), 77 (C_6H_5). Anal. Calcd for $C_{10}H_{10}N_2O_4$: C, 54.05; H, 4.50; N, 12.61. Found: C, 54.97; H, 5.01; N, 12.07%.

Compound **6**: Yield 7.5 g (79%), m.p. 190°C; ^{1}H NMR (CD_3OD): δ 7.8 (m, 5H, ArH), 7.3 (m, 4H, ArH), 3.1 (s, 1H, NH); MS: m/z 238 (M^+), 194 ($C_{13}H_{10}N_2$), 122 ($C_7H_{10}N_2$), 103 (C_7H_5N), 93 (C_6H_7N), 77 (C_6H_5). Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.59; H, 4.20; N, 11.79. Found: C, 71.14; H, 5.42; N, 12.07%.

Compound **7**: Yield 9.8 g (67%), m.p. 210°C; ^{1}H NMR (CD_3OD): δ 5.4 (1H, s), δ 3.9 (1H, s), 7.9-9.1 (14H, m); MS: m/z 364 (M^+), 194 ($C_{13}H_{10}N_2$), 144 ($C_{10}H_8O$), 128 ($C_{10}H_8$), 122 ($C_7H_{10}N_2$), 103 (C_7H_5N), 93 (C_6H_7N), 77 (C_6H_5). Anal. Calcd for $C_{23}H_{16}N_4O$: C, 75.82; H, 4.39; N, 15.38. Found: C, 75.14; H, 3.99; N, 15.87%.

Preparation of 1-benzyl 2-substituted-benzimidazoles 8-14. General procedure. 2-Substituted-benzimidazoles **1-7** (0.02 mole) were treated with benzyl chloride (2.5 g, 0.02 mole) in the presence of a little quantity of sodium hydride (2 g) in THF. The reaction mixture was stirred for 8-12 hr at 40°C. Excess solvent was removed by distillation and crude product was washed with water, extracted with ethyl acetate and finally recrystallized from water and ethanol.

Compound **8**: Yield 4.16 g (79%), m.p. 102°C; IR (KBr): 3540 (O-H stretching), 1722 (C=O stretching), 1214 cm^{-1} (C-N stretching); ^{1}H NMR ($CDCl_3$): δ 7.4 (m, 9H, ArH), 2.6 (t, 2H, 2″-CH_2), 2.1 (t, 2H, 1″-CH_2), 2.4 (s, 1H, 1′-CH_2); MS: m/z 280 (M^+), 236 ($C_{16}H_{16}N_2$), 208 ($C_{14}H_{12}N_2$), 143 ($C_9H_8N_2$), 140 ($C_6H_8N_2O_2$), 118 ($C_7H_6N_2$), 91 (C_7H_7), 72 ($C_3H_8N_2$), 58 (C_3H_8N). Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 77.27; H, 6.06; N, 10.60. Found: C, 76.03; H, 6.12; N 10.52%.

Compound **9**: Yield 4.10 g (68%), m.p. 238°C; IR (KBr): 3540 (OH stretching), 1216 cm^{-1} (C-N stretching); ^{1}H NMR ($CDCl_3$): δ 8.2 (m, 4H, ArH), 7.7 (m, 5H, ArH), 7.3 (m, 4H, ArH), 4.3 (s, 1H, OH), 2.5 (s, 2H, 1′-CH_2); MS: m/z 300 (M^+), 284 ($C_{20}H_{16}N_2$), 234 ($C_{16}H_{14}N_2$), 208 ($C_{14}H_{12}N_2$), 194 ($C_{13}H_{10}N_2$), 144 ($C_9H_8N_2$), 118 ($C_7H_6N_2$), 103 (C_7H_5N), 91 (C_7H_7). Anal. Calcd for $C_{20}H_{16}N_2O$: C, 80.0; H, 5.33; N, 9.33. Found: C, 80.33; H, 6.12; N 9.14%.

Compound **10**: Yield 4.12 g (67%), m.p. 120°C; ^{1}H NMR ($CDCl_3$): δ 8.1 (m, 5H, ArH), 7.5 (m, 5H, ArH), 7.2 (m, 4H, ArH), 4.3 (d, 1H, -CH), 3.9 (d, 1H, -CH), 2.5 (s, 2H, 1′-CH_2); MS: m/z 310 (M^+), 234 ($C_{16}H_{14}N_2$), 220 ($C_{15}H_{12}N_2$), 208 ($C_{14}H_{12}N_2$), 148 ($C_9H_{12}N_2$), 144 ($C_9H_8N_2$), 132 ($C_9H_{10}N$), 118 ($C_7H_6N_2$), 91 (C_7H_7), 77 (C_6H_5). Anal. Calcd for $C_{22}H_{16}N_2$: C, 85.16; H, 5.80; N, 9.03. Found: C, 85.63; H, 5.92; N 9.79%.

Compound **11**: Yield 3.92 g (64%), m.p. 133°C; ^{1}H NMR ($CDCl_3$): δ 7.8 (m, 5H, ArH), 7.3 (m, 4H, ArH), 3.3 (t, 2H, 4″-CH_2), 2.8 (t, 2H, 1″-CH_2), 2.4 (s, 2H, 1′-CH_2), 2.4 (t, 4H, 2″-CH_2, 3″-CH_2); MS: m/z 308 (M^+), 236 ($C_{16}H_{16}N_2$), 208 ($C_{14}H_{12}N_2$), 172 ($C_{11}H_{12}N_2$), 168 ($C_8H_{12}N_2O_2$), 144 ($C_5H_{14}N_2$), 118 ($C_7H_6N_2$), 102 ($C_5H_{14}N_2$), 91 (C_7H_7), 85 ($C_5H_{11}N$), 58 (C_4H_{10}). Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.02; H, 6.49; N, 9.09. Found: C, 74.92; H, 7.15; N, 8.72%.

Compound **12**: Yield 3.96 g (63%), m.p. 180°C; ^{1}H NMR ($CDCl_3$): δ 7.8 (m, 5H, ArH), 7.2 (m, 4H, ArH), 3.5 (d, 1H, 2″-CH), 3.2 (d, 1H, 1″-CH), 2.6 (s, 2H, 1′-CH_2); MS: m/z 312 (M^+), 234 ($C_{16}H_{14}N_2$), 222 ($C_{10}H_{10}N_2O_4$), 208 ($C_{14}H_{12}N_2$), 178 ($C_9H_{10}N_2O_2$), 118 ($C_7H_6N_2$), 91 (C_7H_7). Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.39; H, 5.13; N, 8.97. Found: C, 65.18; H, 6.02; N, 9.33%.

Compound **13**: Yield 5.68 g (87%), m.p. 196°C; ^{1}H NMR ($CDCl_3$): δ 7.8 (m, 5H, ArH), 7.2 (m, 4H, ArH), 3.5 (d, 1H, 2″-CH), 3.2 (d, 1H, 1″-CH), 2.6 (s, 2H, 1′-CH_2); MS: m/z 312 (M^+), 234 ($C_{16}H_{14}N_2$), 222 ($C_{10}H_{10}N_2O_4$), 208 ($C_{14}H_{12}N_2$), 178 ($C_9H_{10}N_2O_2$), 118 ($C_7H_6N_2$), 91 (C_7H_7). Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.39; H, 5.13; N, 8.97. Found: C, 65.18; H, 6.02; N, 9.33%.

Compound **14**: Yield 7.3 g (80%), m.p. 275°C; ^{1}H NMR ($CDCl_3$): δ 8.1 (m, 8H, ArH), 7.6 (m, 7H, ArH), 7.2 (m, 4H, ArH), 2.4 (s, 2H, 1′-CH_2); MS: m/z

454 (M^+), 346 ($C_{23}H_{14}N_4$), 264 ($C_{20}H_{16}N_2$), 230 ($C_{16}H_{10}N_2$), 208 ($C_{14}H_{12}N_2$), 194 ($C_{13}H_{10}N_2$), 128 ($C_{10}H_8$), 118 ($C_7H_6N_2$), 91 (C_7H_7). Anal. Calcd for $C_{30}H_{22}N_4O$: C, 79.29; H, 4.85; N, 12.33. Found: C, 78.13; H, 5.01; N, 12.33%.

Preparation of 1-(*p*-chlorophenyl)-2-substituted benzimidazoles 15-21. General procedure. A mixture of 2-substituted benzimidazoles **1-7** (0.02 mole) and *p*-dichlorobenzene (2.92 g, 0.02 mole) dissolved in ethanol (20 mL) in the presence of a little quantity of sodium hydride (2 g) and tetrahydrofuran (40 mL) stirred for 10-16 hr at 40°C. The precipitated product was filtered and excess solute was removed by distillation. The crude product was washed with water, extracted with ethyl acetate and finally recrystallized from water and ethanol.

Compound **15**: Yield 4.62 g (77%), m.p. 178°C; ^{1}H NMR ($CDCl_3$): δ 7.8 (m, 4H, ArH), 7.2 (m, 4H, ArH), 2.8 (t, 2H, 2″-CH_2), 2.3 (t, 2H, 1″-CH_2); MS: m/z 300 (M^+), 256 ($C_{15}H_{13}N_2Cl$), 248 ($C_{12}H_9N_2O_2Cl$), 228 ($C_{13}H_9N_2Cl$), 194 ($C_{13}H_{10}N_2$), 146 ($C_9H_{10}N_2$), 118 ($C_7H_6N_2$), 112 (C_6H_5Cl), 77 (C_6H_5), 72 ($C_3H_8N_2$), 57 (C_3H_7N). Anal. Calcd for $C_{16}H_{13}N_2O_2Cl$: C, 64; H, 4.33; N, 9.33. Found: C, 63.87; H, 5.01; N, 10.07%.

Compound **16**: Yield 5.2 g (81%), m.p. 148°C; ^{1}H NMR ($CDCl_3$): δ 8.1 (m, 4H, ArH), 7.7 (m, 5H, ArH), 7.1 (m, 4H, ArH), 4.3 (s, 1H, OH); MS: m/z 320 (M^+), 304 ($C_{19}H_{13}N_2Cl$), 228 ($C_{13}H_9N_2Cl$), 216 ($C_{15}H_8N_2$), 194 ($C_{13}H_{10}N_2$), 144 ($C_{10}H_{10}N_2$), 118 ($C_7H_6N_2$), 112 (C_6H_5Cl), 77 (C_6H_5). Anal. Calcd for $C_{19}H_{13}N_2OCl$: C, 73.54; H, 4.19; N, 9.03. Found: C, 73.87; H, 4.77; N, 9.88%.

Compound **17**: Yield 4.86 g (74%), m.p. 58°C; ^{1}H NMR ($CDCl_3$): δ 7.9 (m, 8H, ArH), 7.1 (m, 5H, ArH), 2.9 (d, 1H, 2″-CH), 2.4 (d, 1H, 1″-CH); MS: m/z 330 (M^+), 254 ($C_{15}H_{11}N_2Cl$), 228 ($C_{13}H_9N_2Cl$), 194 ($C_{13}H_{10}N_2$), 148 ($C_9H_{12}N_2$), 144 ($C_{10}H_{10}N_2$), 131 (C_9H_9N), 118 ($C_7H_6N_2$), 112 (C_6H_5Cl), 104 (C_8H_8), 77 (C_6H_5). Anal. Calcd for $C_{21}H_{15}N_2Cl$: C, 76.36; H, 4.54; N, 8.49. Found: C, 77.03; H, 4.93; N, 8.94%.

Compound **18**: Yield 5.32 g (81%), m.p. 240°C; ^{1}H NMR ($CDCl_3$): δ 7.8 (m, 5H, ArH), 7.3 (m, 4H, ArH), 3.2 (t, 2H, 4″-CH_2), 2.7 (t, 2H, 1″-CH_2), 2.2 (m, 4H, 2″-CH_2, 3″-CH_2); MS: m/z 328 (M^+), 284 ($C_{17}H_{17}N_2Cl$), 256 ($C_{15}H_{14}N_2Cl$), 232 ($C_{13}H_{13}N_2Cl$), 228 ($C_{13}H_9N_2Cl$), 194 ($C_{13}H_{10}N_2$), 172 ($C_{11}H_{12}N_2$), 118 ($C_7H_6N_2$), 112 (C_6H_5Cl), 102 ($C_5H_{14}N_2$), 85 ($C_5H_{11}N$), 77 (C_6H_5), 58 (C_4H_{10}). Anal. Calcd for $C_{18}H_{17}N_2O_2Cl$: C, 65.85; H, 5.18; N, 8.53. Found: C, 65.12; H, 5.29; N, 8.87%.

Compound **19**: Yield 4.88 g (73%), m.p. 82°C; ^{1}H NMR ($CDCl_3$): δ 7.8 (m, 4H, ArH), 7.1 (m, 4H, ArH), 4.3 (d, 1H, 2″-CH), 3.7 (d, 1H, 1″-CH); MS: m/z 332 (M^+), 288 ($C_{15}H_{13}N_2O_2Cl$), 254 ($C_{15}H_{11}N_2Cl$), 228 ($C_{13}H_9N_2Cl$), 194 ($C_{13}H_{10}N_2$), 148 ($C_4H_8N_2O_4$), 118 ($C_7H_6N_2$), 112 (C_6H_5Cl), 89 ($C_3H_7NO_2$), 77 (C_6H_5). Anal. Calcd for $C_{16}H_{13}N_2O_4Cl$: C, 57.83; H, 3.91; N, 8.43. Found: C, 57.13; H, 3.12; N, 9.06%.

Compound **20**: Yield 4.48 g (64%), m.p. 316°C; ^{1}H NMR ($CDCl_3$): δ 8.2 (m, 4H, ArH), 7.5 (m, 4H, ArH), 7.1 (m, 4H, ArH); MS: m/z 348 (M^+), 304 ($C_{19}H_{13}N_2Cl$), 270 ($C_{19}H_{14}N_2$), 228 ($C_{13}H_9N_2Cl$), 194 ($C_{13}H_{10}N_2$), 118 ($C_7H_6N_2$), 112 (C_6H_5Cl), 77 (C_6H_5). Anal. Calcd for $C_{20}H_{13}N_2O_2Cl$: C, 68.96; H, 3.73; N, 8.04. Found: C, 69.33; H, 4.08; N, 8.88%.

Compound **21**: Yield 4.74 g (50%), m.p. 318°C; ^{1}H NMR ($CDCl_3$): δ 8.2 (m, 8H, ArH), 7.7 (m, 6H, ArH), 7.1 (m, 4H, ArH), 4.4 (s, 1H, OH); MS: m/z 474 (M^+), 304 ($C_{19}H_{13}N_2Cl$), 270 ($C_{19}H_{14}N_2$), 230 ($C_{16}H_{10}N_2$), 228 ($C_{13}H_9N_2Cl$), 218 ($C_{15}H_{10}N_2$), 194 ($C_{13}H_{10}N_2$), 176 ($C_9H_6N_2Cl$), 128 ($C_{10}H_8$), 118 ($C_7H_6N_2$), 112 (C_6H_5Cl), 77 (C_6H_5). Anal. Calcd for $C_{29}H_{19}N_4OCl$: C, 73.41; H, 4; N, 11.81. Found: C, 73.87; H, 4.32; N, 11.91%.

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