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PREPARATION OF NEW IMIDACLOPRID ANALOGUES

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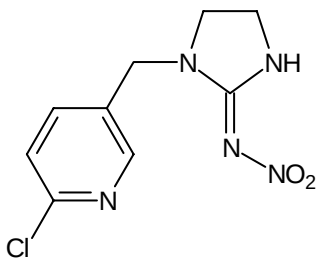
Abstract - A 3-step synthesis of the biologically active metabolites (**2** and **3**) of imidacloprid from aminoacetaldehyde diethyl acetal or ethylenediamine was developed. A series of new imidacloprid analogues were also prepared.

One of the most promising new pest controlling agent is imidacloprid (**1**).[1-5] It shows promise not only as highly active compound against homopteran pests but also for controlling some chewing pests. Furthermore, acting on nicotinic acetylcholine receptor it can be expected to control pests resistant to conventional insecticides.[6-8]

For practical reasons imidacloprid is mainly used in soil application and seed treatment. In both cases two biologically active metabolites (**2** and **3**) were formed and isolated.[9] Compound (**2)** showed sixteen times higher activity than imidacloprid on some aphid pests.[9] The nitroso derivative (**3)** also showed higher aphicidal potency than the parent compound imidacloprid.[9]



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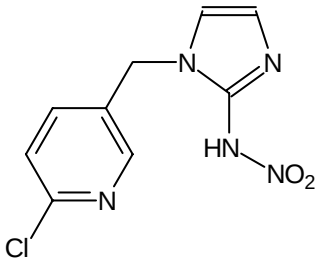

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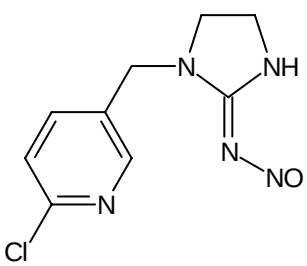
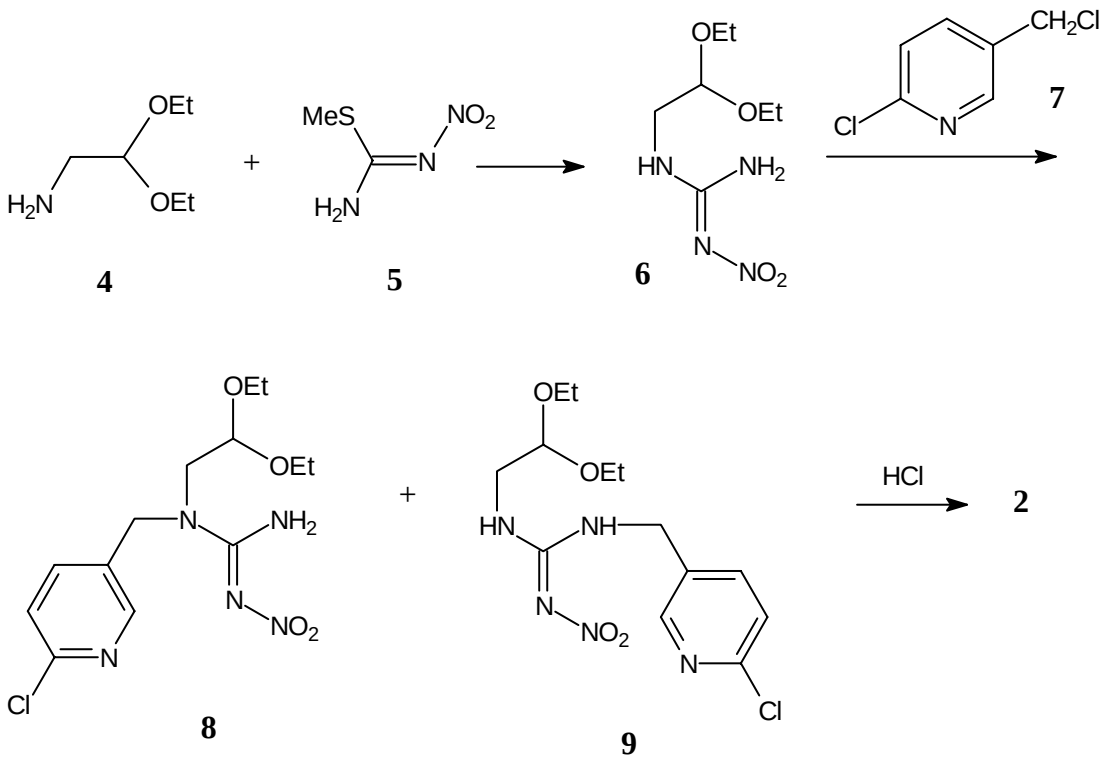


3

Our general interest in the preparation of new potent insecticides prompted us to elaborate efficient synthetic route to biologically active metabolites (**2** and **3**) and to prepare new analogues of imidacloprid.

The synthesis of compound (**2)** was straightforward with *S*-methyl-*N*-nitroisothiourea (**5**)[10] as the starting material (Scheme 1). Thus treatment of isothiourea derivative (**5)** with aminoacetaldehyde diethyl acetal (**4)** in water afforded guanidine derivative (**6)** in 83% yield. Reaction of the latter with 2-chloro-5-chloromethylpyridine (**7**)[11] in the presence of an excess of K_2CO_3 gave a mixture of two isomers which was separated by column chromatography to furnish compounds (**8**) and (**9**) (15 and 41% yields, respectively)[12]. Treatment of either compounds (**8**) or (**9**) with HCl resulted in the formation of the expected product (**2**) (54 and 57% yields, respectively).

Scheme 1

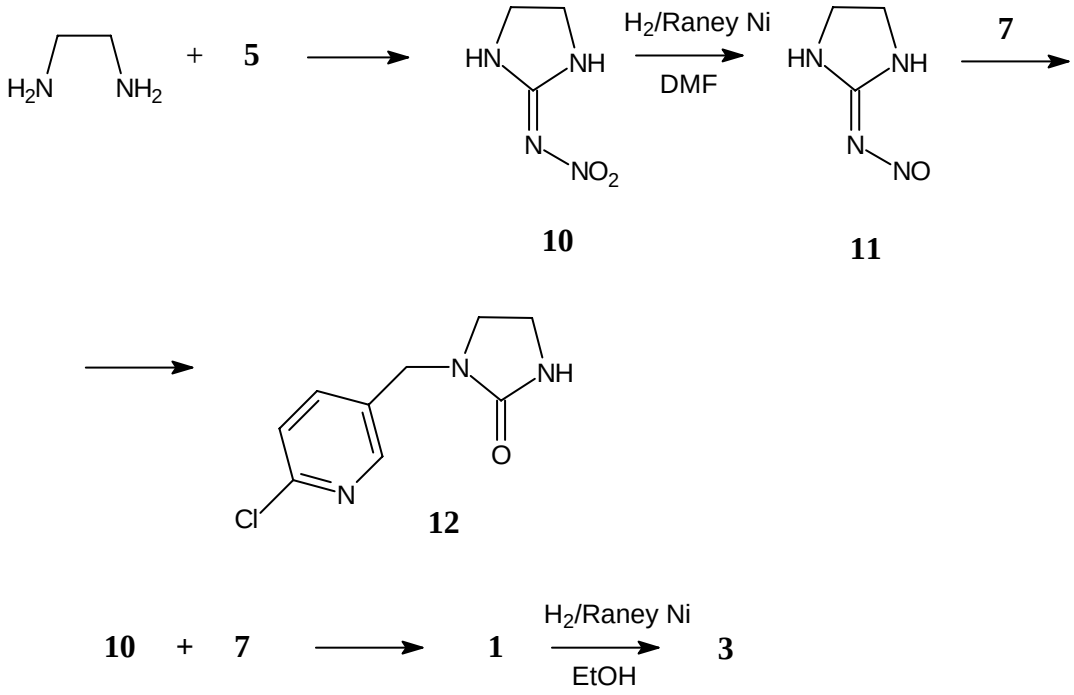


The *N*-nitroso analogue (**3**) of imidacloprid (**1**) was prepared from ethylenediamine (Scheme 2). Treatment of isothiourea derivative (**5**) with ethylenediamine afforded compound (**10**) in 72% yield. Catalytic reduction of **10** in the presence of Raney nickel catalyst afforded the nitroso compound (**11**) in 47% yield. However, the alkylation of compound (**11**) with **7** gave only 2-imidazolidone derivative (**12**). Therefore, we treated the nitro compound (**10**) with **7** to furnish imidacloprid (**1**) and then this was hydrogenated catalytically to give nitroso compound (**3).**

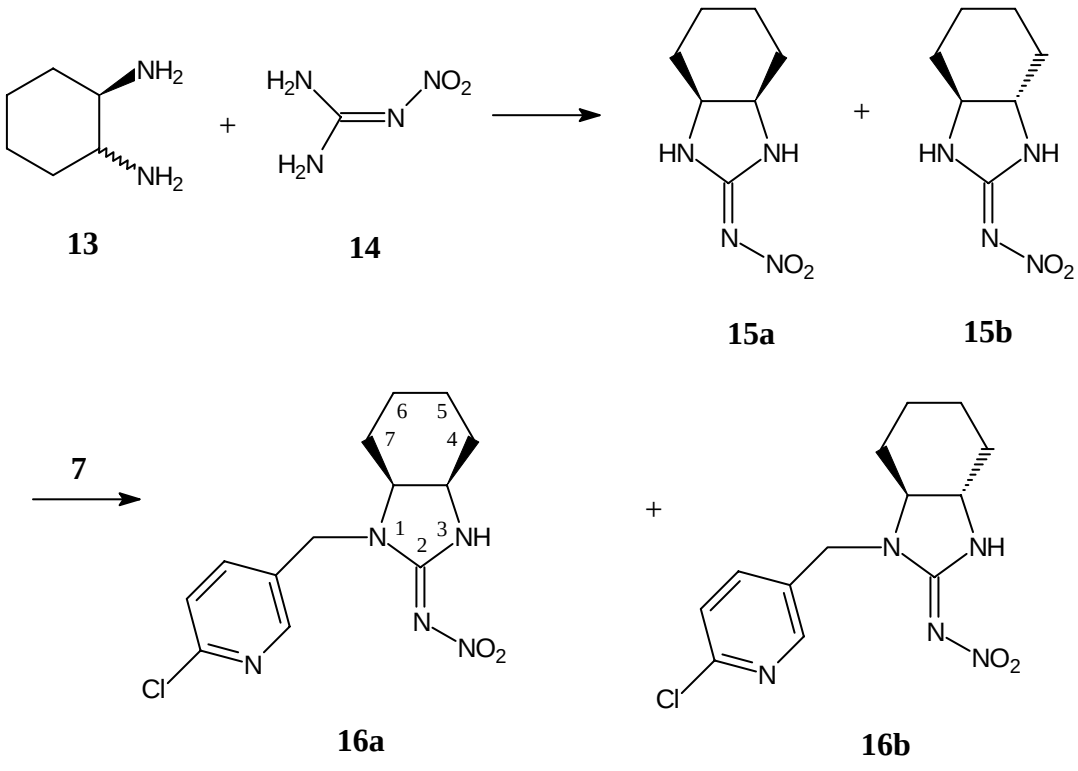
For the preparation of cyclohexano analogue (**16**) of imidacloprid (**1**) 1,2-diaminocyclohexane (a mixture of *cis*- and *trans*-isomers (**13**)) was reacted with nitroguanidine (**14**) to give an unseparable mixture of *cis*-

and *trans*-isomers (**15a,b**). This mixture was then alkylated with compound (**7**) in the presence of K_2CO_3 in boiling acetonitrile. The isomers formed were separated by column chromatography to furnish **16a** and **16b** in 28% yields.[12]

Scheme 2.



Scheme 3.



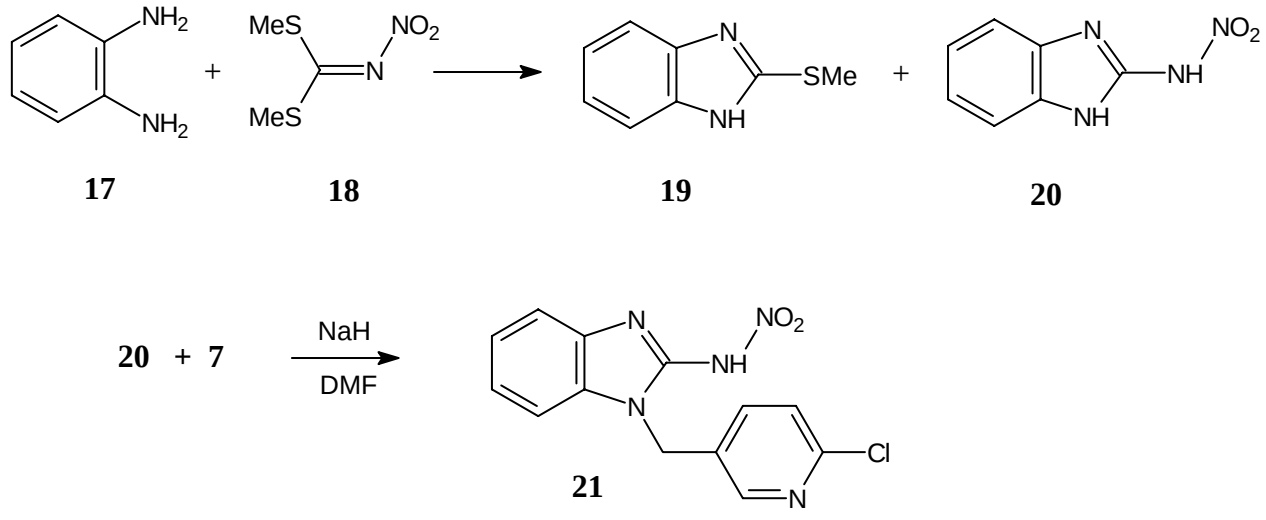
The structural assignment of compounds (**16a**) and (**16b**) was made mainly on the bases of their NMR spectra. For instance, in the *trans*-isomer (**16b**) the axial hydrogen in position 3a is rather close to the methylene group on nitrogen at position 1 generating a strong Van der Waals interaction. Therefore, in the ^{13}C NMR spectrum of **16b** the carbons at positions 3a and 7a resonate at higher field (δ 61.84 and 64.13) than those in the corresponding *cis*-isomer (**16a**; δ 69.45 and 69.70).

The attempted cyclization reaction between 1,2-phenylenediamine (Scheme 4, **17**) and nitroguanidine (**14**) failed. Likewise, the reaction between **17** and **5** also gave negative result. The inefficiency of these reactions was probably due to the lack of reactivity of the relatively weak nucleophile amino groups of **17**.

To overcome this problem we tested a more reactive reagent for the synthesis. The reaction between **17** and dimethyl *N*-nitrodithiocarbamate (**18**)[15] gave the expected product (**20**) in 67% yield, besides some methyl sulfide derivative (**19**).

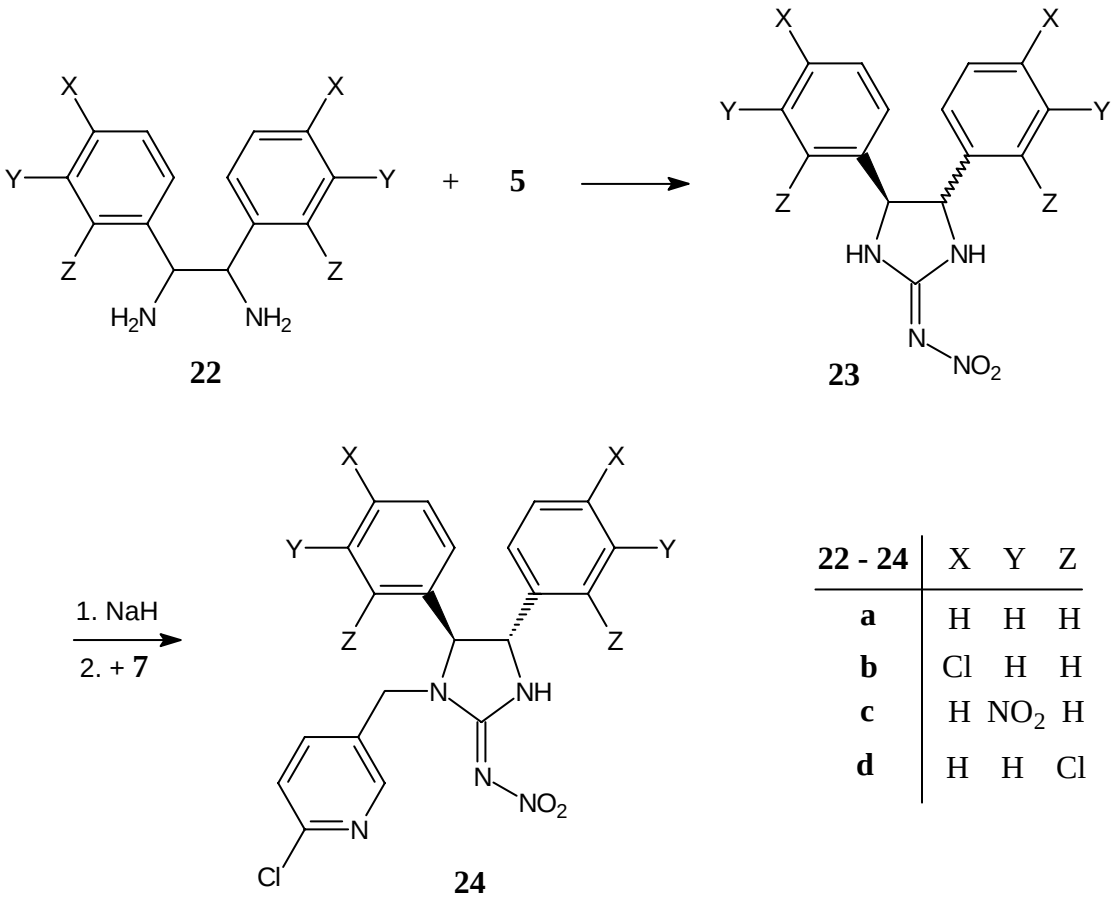
Compound (**20**) was then treated successively with NaH and **7** to furnish the benzimidazole analogue of imidacloprid (**21**).[12]

Scheme 4.



For the preparation of 4,5-diphenylimidacloprid derivatives (Scheme 5, **24**) we used 1,2-diphenylethane derivatives (**22**; a mixture of *meso* and *racemic* stereoisomers).[18] Reaction of **22** with compound (**5**) afforded an unseparable mixture of *cis*- and *trans*-isomers of **23**. This mixture was successively treated with compound (**7**) in the presence of K_2CO_3 to yield a mixture of **24** and its *cis*-isomer[12], from which the *trans*-isomer (**24**) was separated by chromatography.

Scheme 5



22 - 24	X	Y	Z
a	H	H	H
b	Cl	H	H
c	H	NO_2	H
d	H	H	Cl

Comparing the reactivity of the above utilized carbonic acid derivetives (**5**, **14** and **18**) towards amines we generally observed that the reaction rate for nitroguanidine (**14**) was slower as compared with that of compounds (**5**) and (**18**) (Table 1). For the latter two the yields are good or appreciable but slightly lower for compound (**5**) than for compound (**18**). Furthermore, compound (**5**) did not react with aromatic amine (**17**), probably due to the reduced nucleophilicity of its amino groups.

Table 1. Reaction of carbonic acid derivatives with amines

Amines	Product	**14**	**5**	**18**
Ethylenediamine	**10** (%)	57	65	61
13	**15a** + **15b** (%)	62	84	90
22a	**23a** (%)	No reaction	61	88
22b	**23b** (%)	No reaction	74	99
17	**20** (%)	No reaction	No reaction	67

All reaction were carried out in water at 60 °C for 1 h with ratio of amine/carbonic acid derivative 1.2:1

In summary, we have synthesized a series of new imidacloprid analogues and elaborated new method for the preparation of its biologically active metabolites.

EXPERIMENTAL

Reagents were obtained from commercial suppliers and were used without further purification. All reactions were conducted under an atmosphere of dry N_2 or Ar. Melting points were determined on a Büchi apparatus and are uncorrected. IR spectra were obtained with a Spectromom 2000 spectrophotometer. ^{1}H and ^{13}C NMR spectra measurements were carried out using a Bruker DRX-500 spectrometer (500 MHz; internal standard: TMS). MS spectra were obtained on a KRATOS MS25 RFA spectrometer. Merck precoated silica gel 60 F_{254} plates were used for thin-layer chromatography and Kieselgel^{R}60 for column chromatography. All solvents were dried by means of standard methods.

***N*-(2,2-Diethoxyethyl)-*N′*-nitroguanidine** (**6**).

To a stirred suspension of *S*-methylisothionitrourea[10] (**5**; 1.0 g, 7.4 mmol) in water (5 mL) was added 2,2-diethoxyethylamine (**4**; 1.0 g, 7.4 mmol) and the resulting mixture was stirred at rt for 1.5 h. The precipitated product was filtered and dried in vacuum desiccator to afford **6** (1.35 g, 83%), mp 110^{o}C (water). ^{1}H NMR ($CDCl_3$): δ = 1.20 (6H, t, *J*=8 Hz, 2 CH_3), 3.20-4.00 (6H, m, 2 OCH_2 and N-CH_2), 4.55 (1H, t, *J*=5.3 Hz, CH), 7.85 (2H, br s, NH_2), 9.0 (1H, br s, NH).

***N*-(6-Chloropyridin-3-ylmethyl)-*N*-(2,2-diethoxyethyl)-*N′*-nitroguanidine** (**8**) and ***N*-(6-chloropyridin-3-ylmethyl)-*N′*-(2,2,-diethoxyethyl)-*N″*-nitroguanidine** (**9**)

To a stirred solution of **6** (1.0 g, 4.54 mmol) in acetonitrile (40 mL) was added K_2CO_3 (2.2 g, 16 mmol) and 2-chloro-5-chloromethylpyiridine[11] (**7**: 0.72 g, 4.44 mmol), and the resulting mixture was refluxed for 19 h. The mixture was cooled to rt, filtered, the solvent was evaporated *in vacuo*, and then the residue was chromatographed with EtOAc/hexane 4:1 to yield 0.24 g (15%) of **8** and 0.66 g (41%) of **9**.

Compound (8): oil. TLC (EtOAc-hexane 4:1) R_f = 0.49. ^{1}H NMR ($CDCl_3$): δ = 1.25 (6H, m, 2CH_3) 3.37 (2H, d, *J*=4.2 Hz, CH_2), 3.56 (2H, m, OCH_2) 3.77 (2H, m, OCH_2), 4.56 (1H, m, CH), 4.74 (2H, s, N-CH_2), 7.33 (1H, d, *J*=8.2 Hz, C(5')H), 7.78 (1H, dd, *J*=8.2 and 2.0 Hz, C(4')H), 8.14 (2H, br s, NH_2), 8.28 (1H, d, *J*=2.0 Hz, C(2')H). Anal. Calcd for $C_{13}H_{20}N_5O_4Cl$: C, 45.16, H, 5.83, N, 20.25, Cl, 10.25.. Found: C, 45.25, H, 5.89, N, 20.15, Cl, 10.11.

Compound (9): oil. TLC (EtOAc-hexane 4:1) Rf= 0.38. ^{1}H NMR ($CDCl_3$): δ 1.22 (6H, m, 2CH_3), 3.43 (2H, m, CH_2), 3.54 (2H, m, OCH_2), 3.72 (2H, m, OCH_2), 4.50 (2H, d, *J*=5.6 Hz, N-CH_2), 4.53 (1H, m,

CH), 6.78 (1H, br s, NH), 7.32 (1H, d, *J*=8.2 Hz, C(5')H), 7.72 (1H, dd, J=8.2 and 2.2 Hz, C(4')H), 8.33 (1H, d, J=2.2 Hz, C(2')H), 9.53 (1H, br s, NH). Anal. Calcd for $C_{13}H_{20}N_5O_4Cl$: C, 45.16, H, 5.83, N, 20.25, Cl, 10.25. Found: C, 45.21, H, 5.86, N, 20.18, Cl, 10.15.

1-(6-Chloropyridin-3-ylmethyl)-*N*-nitro-1*H*-imidazol-2-ylamine (**2**).

a) A solution of **8**+**9** (2.0 g, 5.79 mmol) in concentrated HCl (20 mL) was stirred at rt for 3 days. The precipitate was collected by filtration, washed with water and dried in vacuum desiccator to yield **2** (0.75 g, 51%).

b) Following the above procedure, using compounds (**8**) or (**9**), with reaction time 2 days, we isolated compound (**2**) in 54 and 57% yields (respectively). mp 190-192^{o}C (decomp); TLC (CH_2Cl_2/MeOH 9:1): R_f = 0.5. IR (KBr): 3340 (NH), 1580, 1536 (NO_2), 1410, 1310 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 5.13 (2H, s, CH_2), 7.01 (1H, s, C(5)H), 7.36 (1H, s, C(4)H), 7.53 (1H, d, *J*=8.3 Hz, C(5')H), 7.77 (1H, dd, *J*=8.3 and 2.2 Hz, C(4')H), 8.40 (1H, d, J=2 Hz, C(2')H), 12.78 (1H, br s, NH). ^{13}C NMR (DMSO-d_6): δ = 45.26 (CH_2), 114.00 (C-4), 117.07 (C-5), 124.60 (C-5'), 131.49 (C-3'), 139.48 (C-4'), 145.87 (C-2'), 149.52 (C-6'), 150.04 (C-2). MS: *m*/*z* = 254 (M^++H, 25), 208 (100). Anal. Calcd for $C_9H_8N_5O_2Cl$: C, 42.62, H, 3.18, N, 27.61, Cl, 13.98. Found: C, 42.45, H, 3.10, N, 27.71, Cl, 14.12.

Imidazolidin-2-ylidenenitroamine (**10**)

To a stirred suspension of **5** (6.0 g, 44 mmol) in water (30 mL) was added ethylenediamine (3 mL, 44 mmol) and the resulting mixture was stirred at 75^{o}C for 1.5 h. After cooling, the precipitate was collected by filtration, washed with water and then dried to afford **10** (4.5 g, 72%), mp 226-228^{o}C (lit.,[20] mp 220-221^{o}C).

Imidazolidin-2-ylidenenitrosoamine (**11**)

Compound (**10**) (5.4 g, 42 mmol) was dissolved in DMF (350 mL) and mixed with Raney nickel catalyst (24 g). The resultant mixture was stirred under H_2 atmosphere until 1.24 equiv. of H_2 (1.22 L) had been absorbed. The catalyst was removed by filtration, the solvent evaporated *in vacuo*, and the residue was purified by column chromatography (CH_2Cl_2-MeOH 5:1) to yield **11** (1.545 g, 33%), and 1.62 g (12.5 mmol) of **10** was recovered, mp 180-182^{o}C (CH_2Cl_2-MeOH 5:1). TLC (CH_2Cl_2-MeOH 5:1): R_f = 0.33. IR (KBr): 3300 (NH), 1620, 1570 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 3.69 (4H, s, 2CH_2), 8.65 (2H, br, 2NH). ^{13}C NMR (DMSO-d_6): δ = 42.17 (C-4 and C-5), 171.50 (C-2). MS: *m*/*z* = 115 (M^++H, 12), 87 (100), 71 (20), 69 (15). Anal. Calcd for $C_3H_6N_4O$: C, 31.58, H, 5.30, N, 49.10. Found: C, 31.65, H, 5.35, N, 49.02.

1-(6-Chloropyridin-3-ylmethyl)imidazolidin-2-one (**12**)

To a suspension of **11** (0.42 g, 3.7 mmol) and K_2CO_3 (1.9 g, 13.7 mmol) in acetonitrile (30 mL) was added compound (**7**) (0.6 g, 3.7 mmol) and the resulting mixture was heated with stirring for 23 h. After cooling, the solid was filtered, washed with acetonitrile and the combined filtrate and washing was evaporated under vacuum. The residue was purified by column chromatography (columm; Al_2O_3, Brockmann II neutral; eluent: CH_2Cl_2-MeOH 5:1, v/v) to give **12** as a white crystal. Yield: 0.12 g (16%), mp 140-142^oC (CH_2Cl_2-MeOH); TLC (Al_2O_3, Brockmann II neutral; CH_2Cl_2-MeOH 14:1): R_f = 0.68. IR (KBr): 3220 (NH), 1690 cm^{-1} (CO). ^1H NMR ($CDCl_3$): 3.32 (2H, t, *J*=6 Hz, CH_2), 3.42 (2H, t, *J*=6 Hz, CH_2), 4.35 (2H, s, CH_2), 5.14 (1H, br s, NH), 7.30 (1H, d, *J*=8.2 Hz, C(5')H), 7.62 (1H, dd, *J*=8.2. and 2.2 Hz, C(4')H), 8.29 (1H, d, *J*=2.2 Hz, C(2')H). ^{13}C NMR ($CDCl_3$): 38.04 (C-4), 44.58 (C-5), 44.64 (CH_2), 124.45 (C-5'), 131.81 (C-3'), 138.82 (C-4'), 149.17 (C-2'), 150.83 (C-6'). MS: *m*/*z* = 211 (M^+, 100), 140 (28), 126 (90), 99 (70).

[1-(6-Chloropyridin-3-ylmethyl)imidazolidin-2-ylidene]nitrosoamine (3)

A mixture of **10** (1.8 g, 14 mmol), compound (**7**) (2.24 g, 14 mmol) and K_2CO_3 (6.80 g, 49 mmol) in acetonitrile (40 mL) was stirred at 70 ºC for 24 h. After cooling, the mixture was filtered, the filtrate was evaporated *in vacuo* and the residue was purified by column chromatography (CH_2Cl_2–MeOH, 5:1) to give imidacloprid (**1**, 1.85 g, 52%). mp 140ºC (EtOH).

Imidacloprid (1.9 g, 7.4 mmol) was dissolved in ethanol (250 mL) and mixed with Raney nickel catalyst (5 g). The resulting mixture was stirred under H_2 atmosphere until 1.05 equiv. of H_2 (193 mL) had been absorbed. The catalyst was removed by filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography (CH_2Cl_2–MeOH, 9:1) to yield **3** (0.65 g, 36%), and 0.6 g (2.4 mmol) of Imidacloprid was recovered, mp 153ºC ($CHCl_3$) (decomp). TLC (CH_2Cl_2–MeOH, 9:1) R_f = 0.25. IR (KBr): 3264 (NH), 1576, 1560, 1424 cm^{-1}. ^1H-NMR (DMSO-d_6): δ = 3.70 (4H, br, $2CH_2$), 4.60 (2H, s, N-CH_2), 7.55 (1H, d, *J*=8 Hz, C(5')H), 7.78 (1H, d, *J*=8 Hz, C(4')H), 8.38 (1H, s, C(2')H), 9.01 (1H, s, NH). ^{13}C-NMR (DMSO-d_6): δ = 40.99 (C-4), 44.09 (C-5), 46.12 (N-CH_2), 124.36 (C-5'), 131.48 (C-3'), 139.44 (C-4'), 149.37 (C-2'), 149.57 (C-6'), 169.58 (C-2). MS: *m/z* = 240 (M^++H, 60), 212 (100), 196 (18), 178 (10). Anal. Calcd for $C_9H_{10}N_5OCl$: C, 45.10, H, 4.21, N, 29.22, Cl, 14.79. Found: C, 45.25, H, 4.40, N, 29.15, Cl, 14.61.

***cis and trans*-(3a,4,5,6,7,7a-Hexahydro-1*H*-benzimidazolidin-2-ylidene)nitroamine** (**15a** and **15b**)

To a solution of KOH (5.0 g, 88 mmol) in water (15 mL) were successively added nitroguanidine (**14**:6.0 g, 58 mmol) and 1,2-diaminocyclohexane hydrochloride (**13**, a mixture of *cis*- and *trans*-isomers: 8.3 g,

44 mmol) and the resultant mixture was stirred at 70°C for 2 h. After cooling, the precipitate was collected by filtration, washed with water and dried to afford **15a,b** (5.0 g, 62%), as a white powder. IR (KBr): 3430, 3200 (NH), 1610 cm^{-1}. ^1H NMR ($CDCl_3$+DMSO-d_6): δ = 1.40 (2H, m, CH_2), 1.52 (2H, m, CH_2), 1.68 (2H, m, CH_2), 1.82 (2H, m, CH_2), 2.18 (0.6H, dm, *J*=10 Hz, CH-*trans*), 3.20 (0.6H, dm, *J*=8 Hz, CH-*trans*), 3.90 (0.8H, s, 2CH-*cis*). ^{13}C NMR ($CDCl_3$+DMSO-d_6): δ = 19.17, 23.2, 26.36, 28.35, 52.88, 61.70, 77.27, 162.83, 164.50. Anal. Calcd for $C_7H_{12}N_4O_2$: C, 45.65, H, 6.57, N, 30.42. Found: C, 45.45, H, 6.49, N, 30.56.

Alternate method for the preparation of compounds **15a** *and* **15b**:

A mixture of *N*-nitrodithiocarbamate[15] (**18**: 3.2 g, 20 mmol) and 1,2-diaminocyclohexane (**13**: 2.73 g, 24 mmol) in water (15 mL) was heated at 60°C for 1 h. After cooling, the precipitate was filtered off, washed with water and dried to afford **15a,b** (3.3 g, 90%).

***cis*- and *trans*-[1-(6-Chloropyridin-3-ylmethyl)-3a,4,5,6,7,7a-hexahydro-1*H*-benzimidazolidin-2-ylidene]nitroamine** (**16a** and **16b**)

A suspension of **15** (3.0 g, 16 mmol), compound (**7**) (2.6 g, 16 mmol) and K_2CO_3 (10.64 g, 76 mmol) in acetonitrile (125 mL) was heated with stirring for 48 h. After cooling, the solid was filtered off, washed with acetonitrile and the combined filtrate and washing was evaporated under vacuum. The residue was purified by column chromatography (column: Al_2O_3, Brockmann II neutral; eluent: hexane-acetone 7:3, v/v) to give pure **16a** (1.4 g, 28%) and **16b** (1.4 g, 28%).

Compound (16a): mp 122-124°C ($CHCl_3$); TLC (hexane-acetone 3:2) R_f = 0.35. ^1H NMR ($CDCl_3$): δ = 1.40 (3H, m, CH_2), 1.59 (1H, m, CH_2), 1.70 (2H, m, CH_2), 1.85 (2H, m, CH_2), 3.58 (1H, m, C(3a)H), 3.95 (1H, m, C(7a)H), 4.21 (1H, d, *J*=15.6 Hz, CH_2-N), 4.86 (1H, d, *J*=15.6 Hz, CH_2-N), 7.34 (1H, d, *J*=8.2 Hz, C(5')H), 7.72 (1H, dd, *J*=8.2 and 2.4 Hz, C(4')H), 8.21 (1H, br s, NH), 8.32 (1H, d, *J*=2.4 Hz, C(2')H). ^{13}C NMR ($CDCl_3$): δ = 24.19, 27.43, 29.24, 31.67, 42.53 (N-*C*H_2), 69.45 (C-3a), 69.70 (C-7a), 124.60 (C-5'), 130.39 (C-3'), 138.97 (C-4'), 149.04 (C-2'), 151.30 (C-6'), 161.56 (C-2). Anal. Calcd for $C_{13}H_{16}N_5O_2Cl$: C, 50.41, H, 5.21, N, 22.61, Cl, 11.45. Found: C, 50.55, H, 5.29, N, 22.51, Cl, 11.31.

Compound (16b): mp 180-182°C ($CHCl_3$); TLC (hexane-acetone 3:2) R_f = 0.37. ^1H NMR ($CDCl_3$): δ = 1.35 (3H, m, CH_2), 1.51 (1H, m, CH_2), 1.89 (2H, m, CH_2), 2.05 (1H, m, CH_2), 2.18 (1H, m, CH_2), 2.91 (1H, m, C(3a)H), 3.29 (1H, m, C(7a)H), 4.48 (1H, d, *J*=15.4 Hz, CH_2-N), 4.58 (1H, d, *J*=15.4 Hz, CH_2-N), 7.32 (1H, d, *J*=8 Hz, C(5')H), 7.74 (1H, d, *J*=8 Hz, C(4')H), 8.30 (1H, s, C(2')H), 8.37 (1H, br s, NH). ^{13}C NMR ($CDCl_3$): δ = 23.67, 23.84, 27.83, 28.81, 43.71 (N-*C*H_2), 61.84 (C-3a), 64.13 (C-7a), 124.65 (C-5'), 130.38 (C-3'), 139.17 (C-4'), 149.17 (C-2'), 151.35 (C-6'), 163.39 (C-2). Anal. Calcd for $C_{13}H_{16}N_5O_2Cl$: C, 50.41, H, 5.21, N, 22.61, Cl, 11.45. Found: C, 50.51, H, 5.31, N, 22.55, Cl, 11.36.

1*H*-Benzimidazol-2-ylnitroamine (**20**) and **2-methylthio-1*H*-benzimidazole** (**19**)

A mixture of *N*-nitrodithiocarbamate[15] (**18**: 3.2 g, 20 mmol) and 1,2-phenylenediamine (**17**: 2.16 g, 20 mmol) in water (15 mL) was heated at 60°C for 1 h. After cooling, the yellow precipitate was filtered off, washed with water.

Compound (20): 2.4 g (67%), as white powder, mp > 230°C (water); TLC (EtOAc): R_f = 0.38. IR (KBr): 3240 (NH), 1620, 1595, 1490, 1390, 1300, 1200 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 7.29 (2H, m, arom. H), 7.46 (2H, m, arom. H), 12.99 (2H, br, 2 NH). ^{13}C NMR (DMSO-d_6): δ = 112.05 (C-4 and C-7), 123.65 (C-5 and C-6), 128.97 (C-3a and C-7a), 151.23 (C-2). MS: *m*/*z* = 178 (M^+, 5), 133 (100), 118 (8), 105 (32). Anal. Calcd for $C_7H_6N_4O_2$: C, 47.19, H, 3.39, N, 31.45. Found: C, 47.25, H, 3.29, N, 31.51.

Compound (19): 0.5 g (15%). mp 202 °C (hexane-EtOAc 2:8). IR (KBr): 3250 (NH), 1620, 1595 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 2.69 (3H, s, S-CH_3), 7.10 (2H, m, arom. H), 7.36 (1H, br, arom. H), 7.49 (1H, br, arom. H), 12.49 (1H, br, NH). ^{13}C NMR (DMSO-d_6): δ = 14.66 (CH_3), 111.06 (C-7), 118.06 (C-4), 121.95 (C-6), 122.27 (C-5), 136.41 (C-7a), 144.59 (C-3a), 152.06 (C-2). MS: *m*/*z* = 164 (M^+, 100), 149 (13), 131 (80), 122 (23), 118 (26), 91 (12).

[1-(6-Chloropyridin-3-ylmethyl)-1*H*-benzimidazol-2-yl]nitroamine (**21**).

To a stirred solution of **20** (1.3 g, 7 mmol) in dry DMF (30 mL) were successively added NaH (0.4 g (50% purity), 8 mmol) and compound (**7**) (1.18 g, 7 mmol). The resulting mixture was heated at 80°C for 2 h. After cooling, the solvent was evaporated *in vacuo*, the residue was washed with acetone and water. The crude product was dissolved in $CHCl_3$, filtered and the filtrate was evaporated *in vacuo* to afford 0.8 g (36%) of **21**, as light yellow crystals, mp 221 °C ($CHCl_3$) (decomp); TLC (EtOAc): R_f = 0.63. IR (KBr): 3328 (NH), 1560, 1496, 1280, 1136 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 5.41 (2H, s, CH_2), 7.32 (2H, m, arom. H), 7.47 (1H, d, *J*=8.4 Hz, C(5')H), 7.60 (1H, m, arom. H), 7.63 (1H, m, arom. H), 7.79 (1H, dd, *J*=8.4 and 2.5 Hz, C(4')H), 8.50 (1H, d, *J*=2.5 Hz, C(2')H), 13.26 (1H, br, NH). ^{13}C NMR (DMSO-d_6): δ = 42.48 (*C*H_2), 110.44 (C-4), 112.91 (C-7), 123.89 (C-5), 124.01 (C-6), 124.34 (C-5'), 128.83 (C-3'), 129.02 (C-3a), 130.90 (C-7a), 138.98 (C-4'), 149.11 (C-2'), 149.73 (C-6'), 149.92 (C-2). MS: *m*/*z* = 303 (M^+, 5), 258 (62), 132 (100), 126 (62). Anal. Calcd for $C_{13}H_{10}N_5O_2Cl$: C, 51.41, H, 3.32, N, 23.06, Cl, 11.67. Found: C, 51.55, H, 3.39, N, 22.91, Cl, 11.45.

(4,5-Diphenylimidazolidin-2-ylidene)nitroamines (**23**). **General Procedure**

A stirred suspension of appropriate ethylenediamine derivative (15 mmol)[18] and compound (**5**) (3.7 g, 27 mmol) in water (10 mL) was heated at 90-95°C for 2 h. After cooling, the solid was filtered and purified by column chromatography (CH_2Cl_2-MeOH 10:1), as a white powder.

Compound (23a): Yield 61%. TLC (hexane-acetone 6:4) R_f = 0.33. ^{1}H NMR ($CDCl_3$): δ = 5.42 (2H, s, 2CH), 6.90 (4H, m, arom. H), 7.08 (6H, m, arom. H), 8.05 (2H, br, 2NH). ^{13}C NMR ($CDCl_3$): δ = 63.30 (C-4 and C-5), 127.09, 128.2, 128.29, 134.73 (C-1' and C-1''), 163.42 (C-2).

Compound (23b): Yield 74%; TLC (CH_2Cl_2-MeOH 5:1) R_f = 0.68. IR (KBr): 3420 (NH), 1600 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 5.42 (2H, s, 2CH), 6.88 (4H, d, *J*=8 Hz, arom. H), 7.17 (4H, d, *J*=10 Hz, arom. H), 8.24 (2H, br s, 2NH). ^{13}C NMR ($CDCl_3$): δ = 62.62 (C-4 and C-5), 128.40, 128.72, 133.06 (C-1' and C-1''), 134.61 (C-4' and C-4''), 163.27 (C-2).

Compound (23c): Yield 52%; TLC (CH_2Cl_2-MeOH 9:1): R_f = 0.44. IR (KBr): 3400 (NH), 1600, 1520, 1360 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 5.74 (2H, s, 2CH), 7.41 (4H, m, arom. H), 7.83 (2H, s, arom. H), 7.91 (2H, d, *J*=8 Hz, arom. H), 8.33 (2H, br s, 2NH). ^{13}C NMR (DMSO-d_6): δ = 60.99 (C-4 and C-5), 121.92 (C-4' and C-4''), 122.61 (C-2' and C-2''), 129.73 (C-5' and C-5''), 133.83 (C-6' and C-6''), 138.95 (C-1' and C-1''), 147.29 (C-3' and C-3''), 163.25 (C-2).

Compound (23d): Yield 40%; TLC (CH_2Cl_2-acetone 4:1): R_f = 0.71. IR (KBr): 3420 (NH), 1600 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 5.83 (2H, s, 2CH), 7.15 (6H, m, arom. H), 7.21 (2H, m, arom. H), 9.17 (2H, br s, 2NH). ^{13}C NMR ($CDCl_3$): δ = 58.98 (C-4 and C-5), 127.43, 129.80, 130.20, 130.40, 133.38 (C-2' and C-2''), 134.37 (C-1' and C-1''), 163.92 (C-2).

Alternate method for the preparation of compounds **23a** *and* **23b**:

A mixture of *N*-nitrodithiocarbamate[15] (**18**: 1.6 g, 10 mmol) and 1,2-diamino-1,2-diphenylethane (**22a**: 2.5 g, 12 mmol) or 1,2-diamino-1,2-bisz(4-chlorophenyl)ethane (**22b**: 3.35 g, 12 mmol) in water (10 mL) was heated at 60^{o}C for 1 h. After cooling, the precipitate was filtered off, washed with water and dried to afford **23a** (2.5 g, 88%) or **23b** (3.45 g, 99%).

[1-(6-Chloropyridin-3-ylmethyl)-4,5-diphenylimidazolidin-2-ylidene]nitroamines (**24**). **General Procedure**

To a suspension of compound (**23**) (4 mmol) and compound (**7**) (0.65 g, 4 mmol) in acetonitrile (40 mL) was added K_2CO_3 (3.0 g, 20 mmol), and the resulting mixture was heated for 24 h. After cooling, the reaction mixture was filtered, the solid washed with acetonitrile and then the combined filtrate and washing was evaporated *in vacuo*. The residue was purified by column chromatography (CH_2Cl_2-methanol 20:1 as eluent) to yield **24**.

Compound (24a): Yield 54%, mp 103-104^{o}C (CH_2Cl_2-MeOH). TLC (hexane-acetone 4:1, Al_2O_3): R_f = 0.15. ^{1}H NMR ($CDCl_3$): δ = 3.79 (1H, d, *J*=15.2 Hz, CH_2), 4.89 (1H, d, *J*=9.8 Hz, CH), 5.14 (1H, d, *J*=15.2 Hz, CH_2), 5.35 (1H, d, *J*=9.8 Hz, CH), 6.77 (2H, d, *J*=7.2 Hz, arom. H), 6.89 (2H, d, *J*=6.6 Hz, arom. H), 7.15 (6H, m, arom. H), 7.32 (1H, d, *J*=8.2 Hz, C(5')H), 7.66 (1H, dd, *J*=8.2 and 2.2 Hz, C(4')H),

8.03 (1H, d, *J*=2 Hz, C(2')H), 8.57 (1H, s, NH). ^{13}C NMR ($CDCl_3$): δ = 43.25 (*C*H_2), 62.79 (C-4), 65.30 (C-5), 124.71 (C-5'), 126.89, 128.00, 128.44, 128.61, 128.75, 129.08, 129.51 (arom. C), 131.67 (C-3'), 134.25 (arom.C), 139.64 (C-4'), 149.64 (C-2'), 151.68 (C-6'), 161.79 (C-2). MS: *m*/*z* = 409 (15), 407 (M^+, 45), 363 (16), 361 (48), 256 (22), 229 (38), 180 (48), 126 (100). Anal. Calcd for $C_{21}H_{18}N_5O_2Cl$: C, 61.84, H, 4.45, N, 17.17, Cl, 8.69. Found: C, 61.65, H, 4.29, N, 17.31, Cl, 8.81.

Compound (24b): Yield 68%; mp 205-208^{o}C (hexane-acetone). TLC (hexane-acetone 4:1, Al_2O_3): R_f = 0.12. ^{1}H NMR ($CDCl_3$): δ = 3.81 (1H, d, *J*=15.2 Hz, CH_2), 4.92 (1H, d, *J*=9.7 Hz, CH), 5.22 (1H, d, *J*=15.2 Hz, CH_2), 5.40 (1H, d, *J*=9.7 Hz, CH), 6.81 (2H, d, *J*=8.2 Hz, arom. H), 6.92 (2H, d, *J*=8.3 Hz, arom. H), 7.23 (2H, d, *J*=8.4 Hz, arom. H), 7.26 (2H, d, *J*=8.2 Hz, arom. H), 7.41 (1H, d, *J*=8.2 Hz, C(5')H), 7.72 (1H, dd, *J*=8.2 and 2.2 Hz, C(4')H), 8.11 (1H, d, *J*=2 Hz, C(2')H), 8.63 (1H, s, NH). MS: *m*/*z* = 477 (12), 475 (M^+, 8), 433 (98), 432 (100), 398 (80), 306 (28). Anal. Calcd for $C_{21}H_{16}N_5O_2Cl_3$: C, 52.91, H, 3.38, N, 14.69, Cl, 22.31. Found: C, 53.05, H, 3.49, N, 14.51, Cl, 22.11.

Compound (24c): Yield 32%, mp 244-246^{o}C (hexane-acetone). TLC (hexane-acetone 7:3, Al_2O_3): R_f = 0.28. IR (KBr): 3410 (NH), 1590, 1540, 1480 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 4.08 (1H, d, *J*=16 Hz, CH_2), 4.83 (1H, d, *J*=16 Hz, CH_2), 5.57 (1H, d, *J*=10.3 Hz, CH), 5.79 (1H, d, *J*=10.3 Hz, CH), 7.33 (1H, d, *J*=6.8 Hz, arom. H), 7.37-7.40 (2H, m, arom. H and C(5')H), 7.48 (2H, t, J=8.4 Hz, arom. H), 7.67 (1H, br s, arom. H), 7.76 (1H, dd, *J*=8.2 and 2.2 Hz, C(4')H), 7.86 (1H, s, arom. H), 7.92 (2H, m, arom. H), 8.20 (1H, d, *J*=1.5 Hz, C(2')H), 9.82 (1H, s, NH). ^{13}C NMR (DMSO-d_6): δ = 43.49 (*C*H_2), 61.10 (C-4), 63.38 (C-5), 121.86, 122.40, 123.03 (arom.C), 124.21 (C-5'), 129.49, 129.91 (arom.C), 131.02 (C-3'), 133.78, 136.11, 138.63 (arom. C), 139.70 (C-4'), 147.14, 147.33 (arom. C), 149.50 (C-2'), 149.58 (C-6'), 161.13 (C-2). Anal. Calcd for $C_{21}H_{16}N_7O_6Cl$: C, 50.66, H, 3.24, N, 19.69, Cl, 7.12. Found: C, 50.50, H, 3.19, N, 19.51, Cl, 7.21.

Compound (24d): Yield 55%, mp 232-234^{o}C (CH_2Cl_2-MeOH). TLC (CH_2Cl_2-acetone 9:1): R_f = 0.69. IR (KBr): 3200 (NH), 1560, 1540, 1460 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 3.75 (1H, d, *J*=15 Hz, CH_2), 5.07 (1H, d, *J*=15 Hz, CH_2), 5.66 (1H, d, *J*=9.7 Hz, CH), 5.90 (1H, d, *J*=9.7 Hz, CH), 6.82 (1H, d, *J*=7.4 Hz, arom. H), 7.05 (1H, t, *J*=7.5 Hz, arom. H), 7.16 (4H, m, arom. H), 7.21 (1H, m, arom. H), 7.25 (1H, d, *J*=8 Hz, arom. H), 7.34 (1H, d, *J*=8.2 Hz, C(5')H), 7.65 (1H, dd, *J*=8.2 and 2.2 Hz, C(4')H), 8.12 (1H, d, *J*=2 Hz, C(2')H), 8.54 (1H, s, NH). ^{13}C NMR ($CDCl_3$): δ = 43.70 (*C*H_2), 58.92 (C-4), 60.05 (C-5), 124.87 (C-5'), 126.87, 126.92, 128.33 (arom. C), 129.27 (C-3'), 129.47, 129.51, 129.86, 130.25, 130.32, 130.55, 132.08, 133.82, 135.16 (arom. C), 139.87 (C-4'), 150.18 (C-2'), 151.98 (C-6'), 161.87 (C-2). Anal. Calcd for $C_{21}H_{16}N_5O_2Cl_3$: C, 52.91, H, 3.38, N, 14.69, Cl, 22.31. Found: C, 52.75, H, 3.29, N, 14.71, Cl, 22.41.

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