

Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for
authors and subscription information:

<http://www.tandfonline.com/loi/gpss20>

SYNTHESIS OF AMIDINE AND BIS AMIDINE PERCURSORS

Nidhi Singhal ^a , Monika Johar ^a , J. W Lown ^b & S. M
Sondhi ^a

^a Department of Chemistry , University of Roorkee
Roorkee , 247 667, U.P., India

^b Department of Chemistry , University of Alberta ,
Edmonton, Alberta, Canada , T6G 2G2

Published online: 04 Oct 2006.

To cite this article: Nidhi Singhal , Monika Johar , J. W Lown & S. M Sondhi (2001)
SYNTHESIS OF AMIDINE AND BIS AMIDINE PERCURSORS, Phosphorus, Sulfur, and Silicon
and the Related Elements, 174:1, 81-92, DOI: [10.1080/10426500108040234](https://doi.org/10.1080/10426500108040234)

To link to this article: <http://dx.doi.org/10.1080/10426500108040234>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

SYNTHESIS OF AMIDINE AND BIS AMIDINE PERCURSORS

NIDHI SINGHAL^a, MONIKA JOHAR^a, J.W LOWN^b and
S.M SONDHI^{a*}

^aDepartment of Chemistry, University of Roorkee Roorkee – 247 667 (U.P.) India
and ^bDepartment of Chemistry, University of Alberta, Edmonton, Alberta, Canada
T6G 2G2

(Received August 17, 1999)

The reactions of substituted *o*-phenylene diamines, *o*-aminophenol, *o*-aminothiophenol, 3,4-diaminopyridine with *p*-cyanobenzaldehyde by refluxing in nitrobenzene gave corresponding benzimidazole, benzoxazole, benzthiazole and imidazopyridine derivatives **Ia**, **b**, **II**, **III**, and **IV**, respectively. Reaction of 4,5-diaminopyrimidine with *p*-cyanobenzaldehyde gave only Schiff's base i.e. **V** or **V'** and not imidazopyrimidine derivative. 2,6-Pyridine dialdehyde on condensation with *p*-aminobenzonitrile gave corresponding dicyano compound **VI**. In an attempt to couple *p*-aminobenzonitrile with 2,6- pyridine dicarboxylic acid using dicyclohexyl carbodiimide or 1,1'-carbonyl diimidazole, only intermediates **VII** & **VIII** were obtained, respectively and no coupled product was formed.

Keywords: Benzimidazole; benzoxazole; benzthiazole; imidazopyridine; Schiff's base; spectral data

INTRODUCTION

Amidines and bis amidines form an important class of compounds exhibiting different types of biological activities, for example distamycin and netropsin are well known antiviral, antitumor agents¹ and DAPI is a well known trypanocidal drug². Famotidine³ is a well known drug used as gastric acid secretion inhibitor. Pentamidine has established activity against the *pneumocystis carinii* pathogen (PCP) which affects a high porportion of AIDS- infected patients^{4,5,6} and is a major cause of mortality in these patients. Pentamidine is one of the two drugs currently used in the clinic,

* Corresponding Author.

has toxic side effects i.e. nephrotoxicity, hepatotoxicity, hypotension and sterile abscesses at injection site⁴. Toxic side effects of pentamidine has prompted a search for related compounds with less toxicity and greater efficacy. With the aim to synthesize different types of amidines and bis amidines and screen then for activity against PCP in future we have synthesized some precursors which we wish to report in this paper.




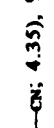



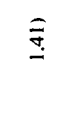

RESULTS AND DISCUSSION

Condensation of 2- cyanopyridine with 1,2- diaminobenzene and 3,4, – diaminopyridine to give corresponding 2- substituted benzimidazole and 2- substituted imidazopyridine respectively have been reported in literature⁷. Reactions of aromatic aldehydes with *o*-aminothiophenol⁸, substituted *o*- phenylenediamines and substituted *o*-aminophenols⁹ have been reported in literature. Reaction of *m*-cyanobenzaldehyde with 4-cyano-*o*-phenylenediamine in boiling glacial acetic acid followed by oxidation with lead tetra acetate to give 5(6) – cyano-2-*m*- cyanophenyl benzimidazole have also been reported in literature¹⁰. We have studied the reactions of *p*-cyanobenzaldehyde with substituted *o*-phenylenediamine, *o*-aminophenol, *o*-aminothiophenol, 3,4 – diaminopyridine and 4, 5 – diaminopyrimidine using nitrobenzene as a solvent and under reflux conditions and the results summarized here.


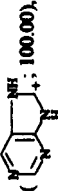

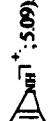
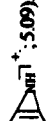


Condensation of 4-chloro –1, 2- phenylene diamine with *p*-cyanobenzaldehyde using nitrobenzene as a solvent and under reflux conditions gave condensed product **Ia** (Scheme -1) The crude product was purified by column chromatography and pure benzimidazole derivative **Ia** was obtained in 25% yield. Spectral data of **Ia** (Table – I) fully support the structure assigned to it. Physical constants and spectral data of **Ia** are reported in Table –I. Similarly reaction of 4, 5 – dimethyl –1, 2, – phenylenediamine with *p*-cyanobenzaldehyde gave compound **Ib** (Scheme – 1). Spectral data of **Ib** is reported in Table – I and is in complete agreement with the structure assigned to **Ib**. Condensation of *o*-aminophenol and *o*-aminothiophenol with *p*-cyanobenzaldehyde gave corresponding benzoxazole (**II**) and benzthiazole (**III**) derivatives in 37 and 19% yields, respectively. Physical constants and spectral data of **II** and **III** are reported in Table – I and is in complete agreement with assigned structures. 3, 4 – Diaminopyridine on condensation with *p*-cyanobenzaldehyde gave compound **IV** which was



purified by crystallization from methanol. ^1H NMR (300 MHz, DMSO- d_6) of **IV** shows signals at δ 5.7 (s, 1H, -NH- exch.), 7.70 (dd, 1H, Ar), 8.05 (d, 2H, Ar), 8.40 (m, 3H, Ar), 9.05 (s, 1H, Ar) HRMS (m/z ; relt. int%) shows M^+ ion peak at m/z 220.07504 (M^+ , 100.00) calcd. for $C_{13}H_8N_4$ 220.07489. Other prominent ion peaks which can arise from the fragmentation of **IV** are reported in Table -I. In case of 4,5- diaminopyrimidine instead of getting bicyclic compound i.e. imidazopyrimidine derivative, only Schiff base i.e. compound having structure **V** or **V'** was obtained in 42 % yield. ^1H NMR (300 MHz; DMSO- d_6) of **V** shows signals at 7.0 (bs, 2H, exch. - NH_2), 7.95 (d, 2H, Ar), 8.1 (s, 1H, - N = CH- C_6H_5), 8.20 (d, 2H, Ar), 8.25 (s, 1H, Ar) and 8.80 (s, 1H, Ar). HRMS (m/z , relt. int. %) of **V** shows M^+ ion peak at 223.08532 (M^+ , 51.48) calcd. for $C_{12}H_9N_5$ 223.08580. Other prominent peaks arising from fragmentation of **V** are mentioned in Table – I. All these cyano compounds i.e. **Ia,b**, **II**, **III** & **IV** are precursors of amidines. 2, 6-Pyridine dicarboxaldehyde and *p*-amino benzonitrile on condensation by refluxing in toluene gave coupled product **VI** in 44% yield. Spectral data of **VI** fully support the structure assigned to it and is reported in Table – I. In an attempt to couple 2,6 – pyridine dicarboxylic acid with *p*-aminobenzonitrile to get the bisnitrile product, pyridine dicarboxylic acid was stirred with 1,3-dicyclohexyl carbodiimide (DCC) and *p*-aminobenzonitrile in DMF at room temperature over night. A white solid product separated out, which was filtered and washed thoroughly with diethyl ether. This product was crystallized from DMF/MeOH to give a white product which was found to be compound **VII** (Scheme – 2). Spectral data of compound **VII** fully support the structure assigned to it and is reported in Table – I. From the formation of **VII** it is clear that *p*-aminobenzonitrile do not react at room temperature with **VII** (which is an intermediate) to give bis-nitrile product. Compound **VII** was stirred with *p*-aminobenzonitrile in DMF at 80°C and work up of the reaction mixture gave unreacted compound **VII** indicating that there was no reaction. Since DCC does not give coupled bis-nitrile so another coupling agent i.e. 1, 1' – carbonyldiimidazole was tried but again an intermediate **VIII** was the only isolable product whose structure was assigned on the basis of IR, ^1H NMR and HRMS. Spectral data of **VIII** is reported in Table –I. After failure of DCC and 1, 1' – carbonyldiimidazole, another coupling agent 1-(3- dimethyl aminopropyl) – 3- ethyl carbodiimide hydrochloride (EDC) was used but in this reaction no identifiable product was obtained.

TABLE I Physical constants and spectral data of amidine and bis amidine precursors

Compd	Solvent of cryst./ elution*	yield %	m.p.	IR (KBr) ν cm^{-1}	^1H NMR (DMSO- d_6) δ ; HRMS (m/z, rel. int %)
1	2	3	4	5	
1a	Pet. ether CHCl_3 ; 2:8	25%	232°C	IR 3356 (-NH-), 2352 ($\text{C}\equiv\text{N}$), 1680 ($\text{C}=\text{N}$), 1600 (Ar). ^1H NMR (300 MHz) δ 5.75 (s, 1H; -NH-), 7.30 (dd, 1H; Ar), 7.70 (t, 2H; Ar), 8.05 (d, 2H; Ar), 8.30 (d, 2H; Ar). HRMS Found 255.03811 (M^+ , 33.09) Calcd. for $\text{C}_{14}\text{H}_8\text{N}_3$ 255.03772. Found 253.04072 (M^+ , 100.00) for $\text{C}_{14}\text{H}_8\text{N}_3$ 253.04068. 252.03227 (m/z 253.04072 -H, 5.03), 218.07086 ($+$)  3.57), 128.03775 (NC)  CN^+ ; 1.54), 125.00248 ($\text{C}_6\text{H}_4\text{N}_3^{35}\text{Cl}$, 4.14), 102.03487 ($+$)  CN^+ ; 4.35), 90.03415 ($+$)  NH^+ ; 7.50).	
1b	Pet. ether CHCl_3 ; 2:8	19%	200°C	IR 3413 (NH), 2357 ($\text{C}\equiv\text{N}$), 1615 (Ar). ^1H NMR (300 MHz) δ 2.3 (d, Two singlet look like a doublet, 6H $2\times\text{CH}_3$), 7.3 (s, 1H; Ar), 7.45 (s, 1H; Ar), 8.0 (d, 2H; Ar), 8.30 (d, 2H; Ar), 12.90 (s, 1H; -NH-). HRMS Found 247.11047 (M^+ , 100.00) Calcd. for $\text{C}_{16}\text{H}_{13}\text{N}_3$ 247.11095. 246.10286 (M^+ -H, 38.42); 232.08727 (M^+ - $\dot{\text{C}}\text{H}_3$, 50.25); 129.04498 ($+$)  4.01), 128.03768 (NC)  CN^+ ; 1.78), 119.07175 ($+$)  NH^+ ; 1.41), 118.06539 ($+$)  N^+ ; 7.59), 104.04986 ($+$)  CN^+ ; 5.48).	

Com. pound	Solvent of cryst. elution*	yield %	m.p.	IR (KBr) ν (cm ⁻¹)	¹ H NMR (DMSO-d ₆) δ ; HRMS (m/z, rel. int. %)
I	2	3	4	5	
II	Pet. ether	37%	182°C	IR 2355 (C≡N), 1455 (Ar). ¹ H NMR (300 MHz) δ 7.50 (m, 2H; Ar), 7.80 (m, 2H; Ar), 8.05 (m, 2H; Ar), 8.35 (m, 2H; Ar). HRMS Found 220.06393 (M ⁺ , 100.00) Calcd. for C ₁₄ H ₈ N ₂ O 220.06366, 219.05552 (M ⁺ -H; 1.35) 128.03735 (NC-CN ⁺ ; 5.47), 102.03445 (+CN; 8.35), 92.02611 (CN ⁺ ; 14.25).	
III	Pet. ether	19%	155°C	IR 2350 (C≡N), 1480 (Ar). ¹ H NMR (300 MHz) δ 7.55 (m, 2H; Ar), 8.0 (m, 2H; Ar), 8.1 (m, 1H; Ar), 8.25 (m, 1H; Ar), 8.30 (m, 2H; Ar). HRMS Found 236.04107 (M ⁺ , 100.00) Calcd. for C ₁₄ H ₈ N ₂ S 236.04082, 235.03249 (M ⁺ -H; 12.72), 210.03423 (M ⁺ -CN; 1.31), 128.03748 (NC-CN ⁺ ; 3.00), 108.00345 (CN ⁺ ; 48.10), 102.03428 (+CN; 3.08).	
IV	MeOH	22%	220(d)	¹ H NMR (300 MHz) δ 5.7 (s, 1H; -NH-, exch), 7.70 (dd, 1H; Ar), 8.05 (d, 2H; Ar), 8.40 (m, 3H; Ar), 9.05 (s, 1H; Ar). HRMS Found 220.07504 (M ⁺ , 100.00) Calcd. for C ₁₃ H ₈ N ₄ 220.07489, 219.06714 (M ⁺ -H; 9.15), 194.07035 (M ⁺ -CN; 1.44), 193.06398 (m/z 194.07035 -H; 2.87), 128.03753 (NC-CN ⁺ ; 1.97), 102.03440 (CN ⁺ ; 6.56), 92.03738 (CN ⁺ ; 5.02), 91.02953 (CN ⁺ ; 1.80).	

Com. pound	Solvent of cryst./ elution*	yield %	m.p.	IR (KBr) ν , cm^{-1}	^1H NMR ($\text{DMSO}-d_6$) δ ; HRMS (m/z , rel. int. \%)
I	2	3	4	5	
V	MeOH	42%	235(d)		IR 3380 (-NH ₂), 2350 (C \equiv N), 1480 (Ar). ^1H NMR (300 MHz) δ 7.0 (bs, 2H; exch.; -NH ₂), 7.95 (d, 2H; Ar), 8.1 (s, 1H; -N=CH-C ₆ H ₄), 8.20 (d, 2H; Ar), 8.25 (s, 1H; Ar), 8.80 (s, 1H; Ar). HRMS Found 223.08532 (M^+ , 51.48) Calcd. for C ₁₂ H ₉ N ₅ 223.08580, 222.07767 (M^+ -H; 42.78), 221.07015 (M^+ - 2H; 28.60), 195.06670 ( , 3.24), -H; 42.78), 221.07015 (M^+ - 2H; 28.60), 195.06670 ( , 100.00), 102.03415 (128.03856 (NC-C \equiv N-  , 4.55), 121.05154 ( , 5.09). (+), 93.03241 ( , 5.09).
VI	MeOH	44%	183°C		IR 2323 (C \equiv N), 1586 (Ar). ^1H NMR (300 MHz): δ 7.50 (m, 4H; Ar), 7.90 (m, 4H; Ar), 8.2 (t, 1H; Ar), 8.3 (d, 2H; Ar), 8.65 (s, 2H; 2x -CH=N-). HRMS Found 335.11691 (M^+ , 100.00) Calcd. for C ₂₁ H ₁₃ N ₅ 335.11710, 334.10912 (M^+ -H, 27.53), 233.08261 (M^+ -C ₆ H ₄ CN, 14.26), 206.07172 ( , 28.18), 129.04514 ( , 20.51), 102.03441 (C ₇ H ₄ N ⁺ ; 60.59).
VII	DMF/MeOH	40%	165°C		IR 3300 (-NH-), 1700 (ester), 1650 (C=N). ^1H NMR (300 MHz) δ 0.8 - 1.9 (m, 40H), 3.2 (m, 2H), 4.10 (m, 2H), 7.55 (d, 2H; Ar), 7.75 (d, 2H; exch. -NH +NH-), 8.0 (m, 1H; Ar). HRMS Found 579.37910 (M^+ , 1.23%) Calcd. for C ₃₃ H ₄₉ N ₅ O ₄ 579.37848, 481.27995 (M^+ - C ₆ H ₁₂ N ₂ ; 1.35%), 356.19631 (M^+ , C ₁₃ H ₂₃ N ₂ O; 2.32) 328.20236 (M^+ - C ₁₄ H ₂₃ N ₂ O ₂ ; 5.29), 98.09716 (C ₆ H ₁₂ N ⁺ ; 100%)

Compd	yield %	IR (KBr)	¹ H NMR (DMSO- <i>d</i> ₆)
1	3	4	5
VIII	66%	212°C	IR 1700 & 1750 (anhydride), 1680 (COOH), 1620 (C=N). ¹ H NMR (300 MHz) δ 7.10 (d, 2H) 7.85 (s, 1H), 8.1–8.30 (m, 3H). HRMS 150.01915 (M ⁺ -O-C-N  ; 2.60), 122.07308 (M ⁺ -O-C-N  ; 9.62), 105.02149(m/z 150.01915 -COOH: 55.32), 77.02660 (C ₅ H ₃ N; 50.16), 67.02955 (C ₃ H ₃ N ₂ ; 9.90).

EXPERIMENTAL

Melting points were determined on JSGW apparatus and are uncorrected. Only principal sharply defined IR peaks are reported. ^1H NMR spectra were recorded in a ca. 5–15% (w/v) solution in DMSO-d_6 . Line positions are recorded in ppm from the reference. The MS spectrometer peak measurements were made by comparison with perfluorotributylamine using an AEI MS-9 double focusing high resolution mass spectrometer at a resolving power of 15000. TLC was performed on Silica Gel G for TLC (Merck) and spots were visualized by iodine vapour or by irradiation with UV light (254 nm). Column chromatography was performed by using Qualigens Silica Gel for column chromatography (60–120 mesh).

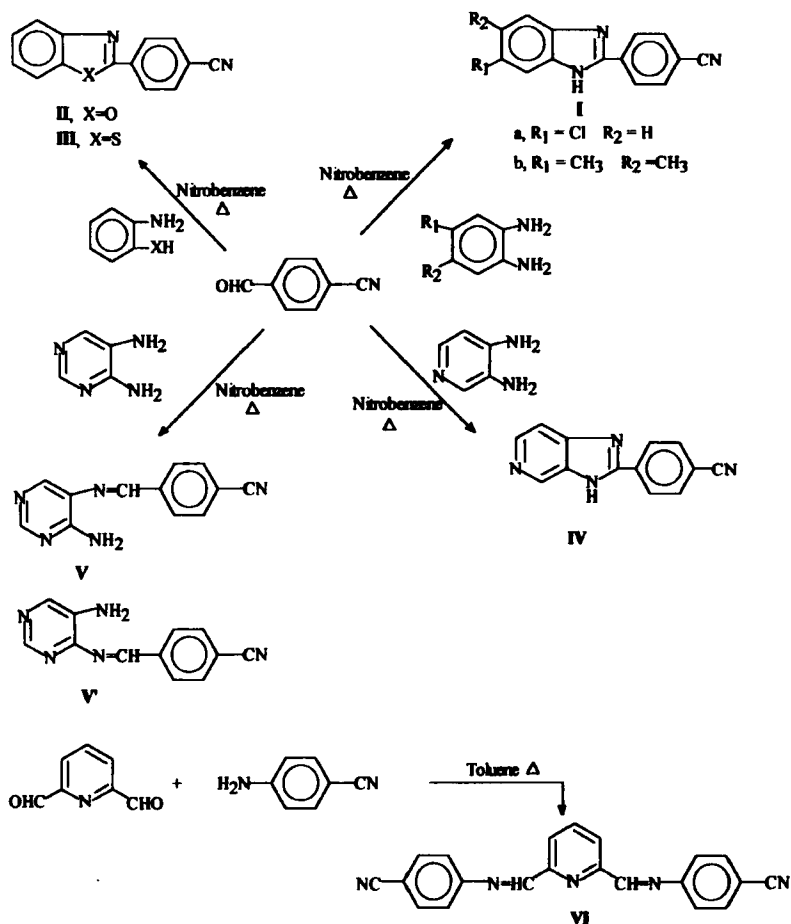
Synthesis of benzimidazole derivative i.e. **Ia,b**

4-Chloro-1,2-phenylenediamine (145mg, 1m mol) and p-cyanobenzaldehyde (130 mg; 1 m mol) were mixed in nitrobenzene (20 ml) and heated at $140^\circ\text{--}150^\circ\text{C}$ for 24 hrs. Nitrobenzene was removed under reduced pressure. To the residue left behind was added pet. ether and the reaction contents were scratched. A crude solid product separated out; it was purified by column chromatography over silica gel. Elution with pet.ether: chloroform (5:5) removed side products and elution with pet.ether:chloroform (2:8) gave the pure compound **Ia**. Yield 70 mg (25%), m.p.. 232°C .

Similarly 4,5-dimethyl-1,2-phenylenediamine was condensed with p-cyanobenzaldehyde to give compound **Ib**. Yield 19%, m.p. 200°C . Spectral data of **Ia** and **Ib** is reported in Table-I.

Synthesis of substituted benzoxazole (**II**) and benzthiazole derivative (**III**)

o-Aminophenol (218mg, 2m mol) and p-cyanobenzaldehyde (260mg; 2m mol) were taken in nitrobenzene (40 ml) and heated at $140^\circ\text{--}150^\circ\text{C}$ for 24 hours. Nitrobenzene was removed under reduced pressure and the residue left behind was diluted with pet.ether and scratched. A crude product separated out; it was filtered and subjected to column chromatography over silica gel. Elution with pet. ether gave compound **II**. Yield 150 mg (37%), m.p. 182°C .



SCHEME 1

Similarly o-aminothiophenol was condensed with p-cyanobenzaldehyde and the crude product was purified by column chromatography over silica gel. Elution with pet. ether gave the final compound **III**. Yield 70 mg (19%), m.p. 155°C. Spectral data of **II** and **III** is reported in Table I.

Synthesis of substituted imidazopyridine derivative IV

3,4-Diaminopyridine (218 mg, 2 m mol) and p-cyanobenzaldehyde (260mg; 2m mol) were mixed in nitrobenzene (50 ml) and heated at

140°-150°C for 24 hrs. and then the volume of the solvent was reduced to 15 ml. The reaction mixture was allowed to cool at room temperature and a solid compound separated out it was filtered, washed with pet. ether and air dried. The crude product was purified by crystallization from methanol to give compound **IV**. Yield 90 mg (23%), m.p. 220°C(d). Spectral data of compound **IV** is reported in Table I.

Condensation of 4,5-diaminopyrimidine with p-cyanobenzaldehyde to give V or V'

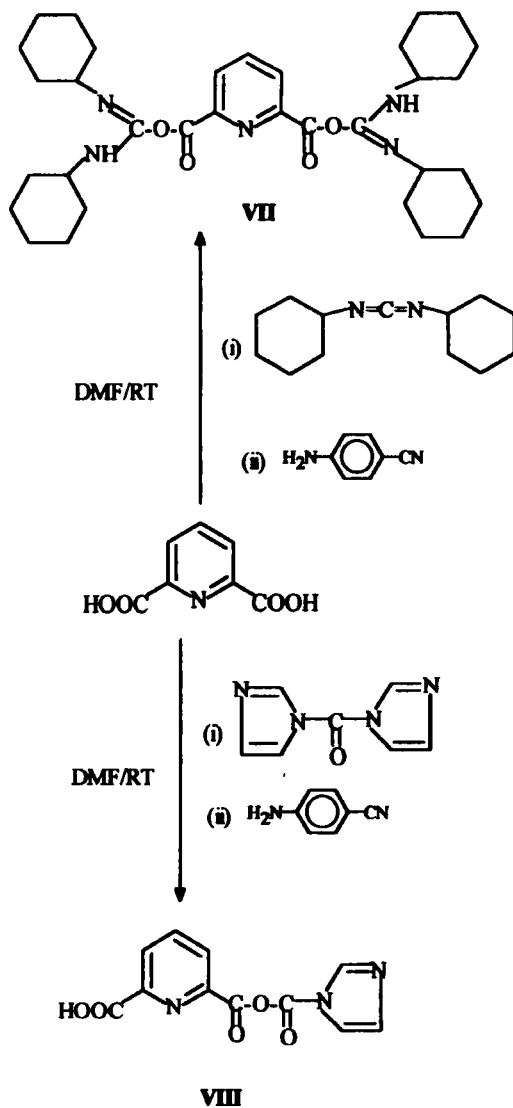
4,5-Diaminopyrimidine (220mg, 2m mol) and p-cyanobenzaldehyde (260 mg, 2 m mol) were mixed in nitrobenzene (50ml) and heated at 140°-150°C for 24 hrs. Nitrobenzene was removed under reduced pressure and to the residue left behind was added pet.ether. A solid product separated out; it was filtered, washed with pet. ether and air dried to give a crude product which was purified by crystallization from methanol to give a Schiff base which may have structure **V** or **V'**. Yield 190 mg (42%), m.p. 235°C. Spectral data of the Schiff base is reported in Table –1.

Condensation of 2,6-pyridinedicarboxaldehyde with p-amino benzonitrile to give VI

2,6-Pyridinedicarboxaldehyde (270 mg, 2 m mol) and p-amino benzonitrile (470 mg; 4 m mol) were mixed in toluene (25ml) and heated under reflux for 14 hrs. The solvent was removed under reduced pressure and the solid residue left behind was purified by crystallization from methanol to give pure compound **VI** Yield, 250 mg (44%), m.p. 183°C. Spectral data of **VI** is summarized in Table I.

Coupling of 2,6-pyridinedicarboxylic acid with p-amino benzonitrile using DCC as a coupling agent to give VII

2,6-Pyridinedicarboxylic acid (330 mg, 2 m mol) and dicyclohexylcarbodiimide (820 mg, 4 m mol) were added to dry DMF (30 ml). To this p-amino benzonitrile (470 mg; 4m mol) was added and the reaction contents were allowed to stirr overnight. During stirring a white compound separated out which was filtered, washed with diethylether and air dried to



SCHEME 2

give compound **VII** which was recrystallized from DMF/MeOH. Yield 450 mg (40%), m.p. 165°C. Spectral data of **VII** is summarized in Table-1.

Coupling of 2,6-pyridinedicarboxylic acid with p-amino benzonitrile using 1,1'-carbonyldiimidazole as a coupling agent to give VIII

2,6-Pyridinedicarboxylic acid (330 mg, 2 m mol) and 1,1'-carbonyldiimidazole (770 mg, 4.4 m mol) were taken in dry DMF (30 ml) and stirred at room temperature for half an hour and then filtered. In the filtrate p-amino benzonitrile (470 mg; 4 m mol) was added and the reaction contents were stirred for overnight. The compound which separated out was filtered and washed with diethyl ether to give a first crop of the product. The filtrate was evaporated to dryness under vacuum and the solid residue left behind was washed with diethyl ether to give a second crop of the product. The total product was purified by crystallization from DMF to give pure compound VIII. Yield 370 mg (66%), m. p. 212°C. Spectral data of VIII is reported in Table –1.

Acknowledgements

We are thankful to the technical staff of chemistry department, University of Roorkee, Roorkee for IR spectra. Financial help from UGC New Delhi (Nidhi Singhal) is gratefully acknowledged.

References

1. S.M. Sondhi, B.S.P Reddy, and J.W. Lown, *Current Medicinal Chemistry*, **4**, 321 (1997).
2. K. Jansen, P. Lincoln, and B. Norden, *Biochemistry*, **32**, 6605 (1993).
3. A.S. Taha, N. Hudson, C.J. Hawkey, A.J. Swannell, P.N. Trye, J. Cottrell, S.G. Mann, T.J. Simon, R.D. Sturrock, and R.I. Russell, *N. Engl. J. Med.*, **334**, 1435 (1996).
4. R.R. Tidwell, S.K. Jones, J.D. Gertaz, K.A. Ohemeng, M. Cory, and J.E. Hall, *J. Med. Chem.*, **33**, 1252 (1990).
5. I.O. Donkor, R.R. Tidwell, and S.K. Jones, *J. Med. Chem.*, **37**, 4554 (1994).
6. J.O. Trent, G.R. Clark, A. Kumar, W.D. Wilson, D.W. Boykin, J.E. Hall, R.R. Tidwell, B.L. Blagburn, and S. Neidle, *J. Med. Chem.*, **39**, 4554 (1996).
7. H.C. Francis, *J. Het. Chem.*, **4**, 157 (1967).
8. T.C. Deligorgiev, *Dyes Pigm.*, **12**, 243 (1990).
9. Y. Bathini, K.E. Rao, R.G. Shea and J.W. Lown, *Chem. Res. Toxicol.*, **3**, 268, (1990).
10. J.D. Bower, F.F. Stephens and D.G. Wibberley, *J. Chem. Soc.*, 3341 (1950).