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ARTICLE

Regiochemistry of nucleophilic substitution of pentachloropyridine with N and O bidentate nucleophiles

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Site reactivity of some enole-imines derived from *N*-aryl formamides with pentachloropyridine under basic conditions in dry CH_3CN was investigated. The aromatic nucleophilic substitution of pentachloropyridine with enole-imines occurs at the 4-position of pyridine ring by both oxygen and nitrogen site of enole-imines. Nucleophilic attack by oxygen of enole-imine gave corresponding oximino compounds as a mixture of *E*- and *Z*-isomers. In contrast nucleophilic attack by nitrogen of enole-imine gave finally unexpected *N*,*N*-di- substituted aryl compounds. The structures of all compounds were confirmed by IR, ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectroscopy as well as elemental analysis and X-ray crystallography.

Introduction

Perhalogenated aromatic and heteroaromatic comounds are important starting materials for synthesis of other heterocycle and macrocycle compounds.[1-3] Great number of review articles and monographs with subject of synthesis and application of pyridines reflects important role of substituted pyridines in organic chemistry, biochemistry, and pharmaceutical chemistry.[4-7] Many researchers concerned on reaction of various N, O, S, C, and P nucleophiles with perhalogenated compounds.[8-12] The nature of nucleophile, reaction condition, solvent, etc. have a basic role in the regiochemistry of reaction. Differentiation reactivity of perfluorinated heteroaromatic compunds into hard and soft nucleophiles was achieved by partial replacement of fluorine by bromine in pentafluoropyridine.[13] In the last few years, we have been pursuing investigations on regiochemistry reaction of different nucleophile with perhalogenated compounds[14]. We showed that 4-substituted tetrafluoropyridine can successfully react with a variety of unequal bidentate nucleophiles. The regioselectivity of nucleophilic substitution in this process was explained by the high nucleophilicity of the secondary or primary amino groups and by the activating influence of pyridine ring nitrogen that significantly activates the *ortho* and *para* sites to itself. In contrast, the major product of the aromatic unequal bidentate nucleophiles such as 2-aminothiophenol, is most likely formed from the initial attack of the S nucleophile and subsequent cycl ization.[14] In another work we showed that pentafluoropyridine successfully reacted with some enolates from oxygen site. The selectivity of nucleophilic substitution in this process is explained based on hard–hard interaction principle.[15]

Aromatic nucleophilic substitution reactions are proceeded *via* the AE-mechanism,[4-6] however, S_{RN1}-,[16-18] EA-[19-21] and S_N(ANRORC)-[22] mechanisms are also observed. Halogen substituents in 2-, 3- and 4- positions of pyridines indicate different reactivity to nucleophiles.[4-6]

Formamide compounds are widely used as intermediates in organic synthesis. *N*-Formyl compounds played a key role in synthesis of important pharmaceutical compounds such as 1,2-dihydroquinolines,[23] cancer chemotherapeutic agents[24] and quinolone antibiotics.[25] Furthermore, they applied as precursor for synthesis of various compounds such as isocyanide,[26] formamidine[27] and amination of azoles.[28] In 1995 Koppang reported disubstitution on hexafluorobenzene with formanilides.[29]

Continuing our research in this area, we would like to report the site selectivity of some N and O bidentate nucleophiles in the reaction with pentachloropyridine.

Results and discussion

Synthesis of precursor formamide compounds

Several papers have been carried out concerning preparation of these important compounds.[30-32] In this paper we established a new method for synthesis of these compounds in a very short reaction time with high yields. Reaction of aromatic amine **1a-l** with formic acid **2** without any solvent in the presence of aminopropyl-silica (APS) **3** as a heterogeneous catalyst using ultrasonic irradiation gave corresponding formamides **4a-l** in 1-5 minutes and 90-95 % isolated yields (table 1). The effect of ultrasound on different reactions has been widely studied during the last two decades[33] and in our earlier studies, we have reported synthesis of some compounds using ultrasonic irradiation.[34,35]

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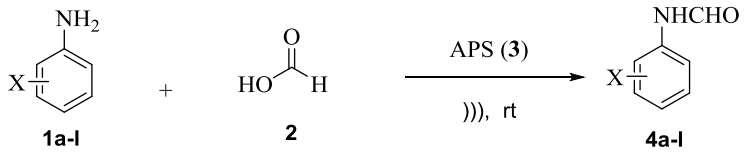
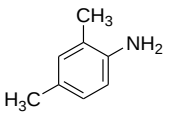
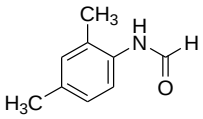
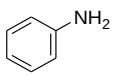
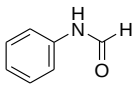
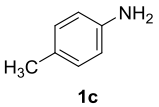
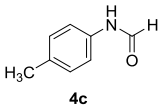
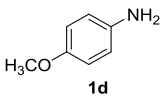
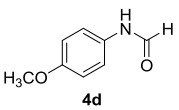
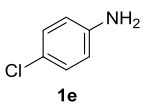
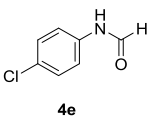
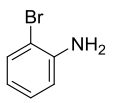
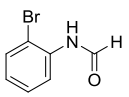
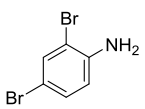
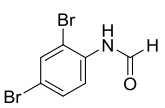
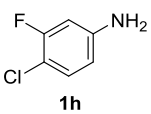
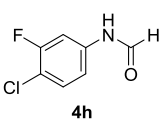
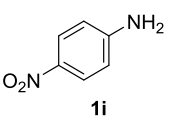
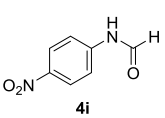
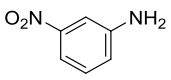
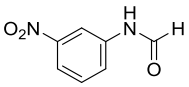
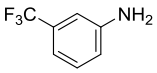
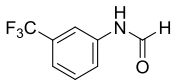
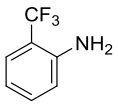
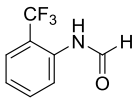
Table 1: Synthesis of aromatic formamides



Entry	Amine	Formamide	Yield(%)	Time (Min)
1	 1a	 4a	93	1
2	 1b	 4b	90	3
3	 1c	 4c	93	1
4	 1d	 4d	95	1
5	 1e	 4e	94	4
6	 1f	 4f	90	3
7	 1g	 4g	92	4
6\8	 1h	 4h	90	4
9	 1i	 4i	90	5

10	 1j	 4j	90	5
11	 1k	 4k	90	5
12	 1l	 4l	90	5

All formamide compounds were identified by comparison of their physical and spectral data with those of authentic samples.[30-32]

The procedure employs a polymeric catalyst and provides a simple and effective procedure for the preparation of *N*-formylamins from good to excellent yields with high purity. This procedure is characterized by heterogeneous and mild reaction conditions, non-toxic content and an easy reaction work-up, making it ideal for both laboratory and large-scale preparations. This method also offers advantages such as the clean persistence of reactions at room temperature without using any solvent, utilizing very low amounts of catalyst, generally completing after 1-5 min, and giving the products with excellent yields. Despite the relative simplicity of this reaction, the attempted acetylation of amine with acetic acid in acetonitrile failed. Similarly, formylation of phenols with formic acid in acetonitrile failed.

Reaction of formamid with pentachloropyridine

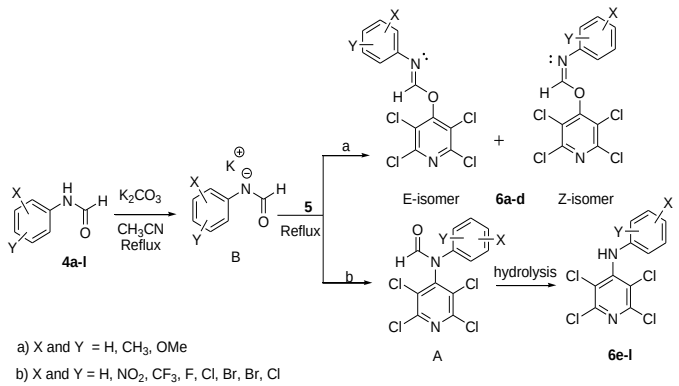
Anions derived from formamides have two nucleophilic sites (O and N) and it is interesting to know which site is attacked in substitution reaction. The reaction conditions were optimized using reaction of pentachloropyridine **5** and *N*-(4-chlorophenyl)formamide **4e** as an example. We investigated the effect of solvent and temperature on the reaction. At room temperature, the reaction gave moderate yield in acetonitrile whereas the yields were low or trace in other solvent. Acetonitrile likewise gave excellent yield at reflux condition (Table 2). the final product was the same in all solvent and temperature. Annelation processes involving reactions between pentachloropyridine **5** and *N*-(2,4-dimethylphenyl)formamide **4a** were studied initially because of the relatively high nucleophilicity of such amine species (Scheme 1, path a). Pentachloropyridine **5** and *N*-(2,4-dimethylphenyl)formamide **4a**, in the presence of potassium carbonate and in dry acetonitrile, gave the desired 2,3,5,6-tetrachloropyridin-4-yl (E and Z)-N-(2,4-dimethylphenyl)formimidate **6a** (Table 3, entry 1) after recrystallization of the crude product eluted by ethanol. ^{1}H NMR analysis of the products showed the presence of **6a** as the major products and as a mixture of E- and Z-isomers. This observation indicated that bidentate nucleophile derived from *N*-(2,4-dimethylphenyl)formamide **4a** reacted with pentachloropyridine from oxygen site. The electron donating effect of methyl group enhanced negative charge density on oxygen by resonance, therefore making it more nucleophile than nitrogen. ^{1}H NMR spectrum of compound **6a** showed one singlet peak at δ = 8.59 ppm and one singlet peak at δ = 8.44 ppm for alkene hydrogens (H_d, $H_{d'}$) of E- and Z-isomers (Scheme 2). It also indicated two singlet peaks in δ = 7.21 and 7.14 ppm for H_a and $H_{a'}$, two doublet peaks in δ = 7.02 and 6.95 ppm for H_b and $H_{b'}$ and two doublet peaks in δ = 6.90 and 6.75 ppm for H_c and $H_{c'}$. Chemical shifts of four methyl groups were located in 2.35, 2.27, 2.26 and 2.20 ppm.

Similarly, reaction of phenylformamides **4b-d** with pentachloropyridine **5** gives **6b-d** respectively as a mixture of E- and Z-isomers. With this encouraging result in hands, we performed the reaction of formamides containing electron withdrawing group generated by corresponding aromatic amine with pentachloropyridine. Pentachloropyridine **5** and N-(3-nitrophenyl)formamide **4j**, in the presence of potassium carbonate and in dry acetonitrile, gave the desired 2,3,5,6-tetrachloro-*N*-(3-nitrophenyl)pyridin-4-amine **6j** (Table 3) in good yield after recrystallization of the crude product eluted by ethanol. ^{1}H NMR of this compound was quite different from co-

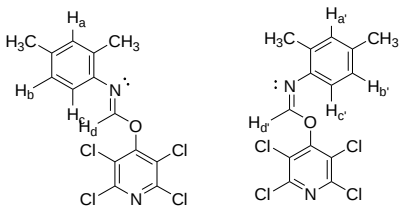
Table 2: Effect of solvent and temperature on the reaction of pentachloropyridine and *N*-(4-chlorophenyl)formamide[a]

Entry	Solvent	Temperature (^{o}C)	Time (h)	Yield (%)
1	THF	r.t.	12	Trace
2	THF	70	15	41
3	Acetone	r.t.	12	30
4	Acetone	60	13	55
5	CH_2Cl_2	r.t.	12	N.R
6	CH_2Cl_2	43	12	N.R
7	CH_3CN	r.t.	10	50
8	CH_3CN	86	12	90
9	$CHCl_3$	r.t.	12	N.R
10	$CHCl_3$	66	12	N.R
11	EtOH	r.t.	12	10
12	EtOH	83	17	30

[a] Reaction conditions: pentachloropyridine (1.0 mmol), Potassium carbonate (1.5 mmol), Solvent (5.0 mL)



Scheme 1: General scheme for reaction of formamide with pentachloropyridine



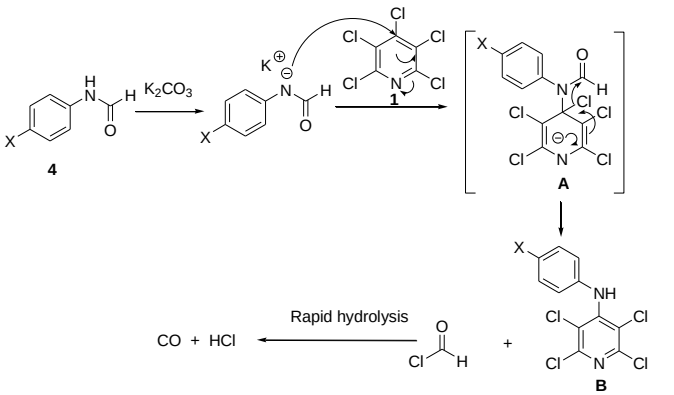
Scheme 2: E and Z isomers of 6a

mpound **6a-6d**. ^{1}H NMR spectrum of compound **6j** showed a broad singlet in 9.4 ppm for NH, two doublets at 7.75 and 7.22 ppm, one triplet in 7.46 ppm and one singlet in 7.71 ppm for aromatic H. There are no signal for aldehyde or alkene hydrogen. The ^{13}C spectrum was at first somewhat puzzling, showing bands for only the ring carbon atoms. The IR spectrum **6j** showed a broad absorption bond at 3335 cm^{-1} for NH stretching. The elemental analysis indicated that the product had the molecular formula $C_{11}H_5Cl_4N_3O_2$. This latter, together with the above data suggested that the compound was 2,3,5,6-tetrachloro-*N*-(4-nitrophenyl)pyridin-4-amine **6j**. The structure was confirmed by X-ray analysis on a single crystal as shown in Fig. 1. A similar reaction occurred with other formamide **4e-l** and **4k, l** to yield the corresponding amines **6e-l** and **4k, l** in moderate to high yields. ^{1}H NMR spectra of compounds **6e-l** showed a singlet in the range of 8.5-10 ppm for NH and some signal in the range of 6.8-8.2 ppm for aromatic hydrogen. In ^{13}C NMR spectra aromatic carbons located in the range 112-153 ppm. In IR spectra, NH stretching bond appeared in the range of 3290-3390 cm^{-1}.

A rationalization of these observations is shown in Scheme 3. We believe the first step in these reactions is the expected nucleophilic attack by nitrogen of formamide, to give the first formed intermediate **A** which under reaction conditions converted rapidly to main product **B** and formyl chloride. Formyl chloride cannot be isolated, because it decomposes to carbon monoxide (CO) and hydrogen chloride (HCl).

The X-ray structure of 6j

The asymmetric unit of the title compound comprises a molecule of 2,3,5,6-tetrachloro-N-(3-nitrophenyl)pyridin-4-amine **6j** which crystallizes in monoclinic system with spage group *P*2(1)/*n*. The molecular structure of the compound is shown in Fig. 1. The crystal packing of the compound shows weak intermolecular Cl…Cl [Cl(2)…Cl(3)i = 3.4909(11) Å; (i) 1 - x, 1 - y, -z] interactions which are slightly shorter than the sum of the van der Waals radii of Cl atoms [3.50 Å] which is shown in Fig. 2. The crystal packing is further stabilized by the intermolecular π…π interactions in which the centroid to centroid distances are 3.8375(14) and 3.8189(14) Å.



Scheme 3: Proposed explanation for observed B

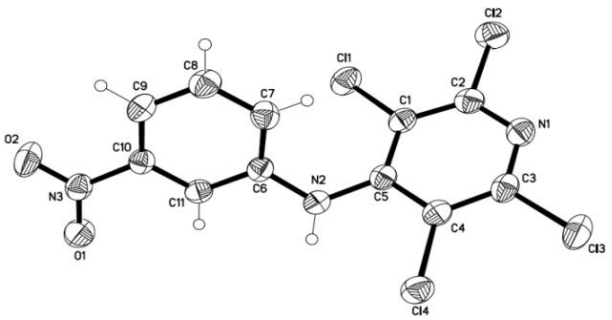


Figure 1: The molecular structure of 6j

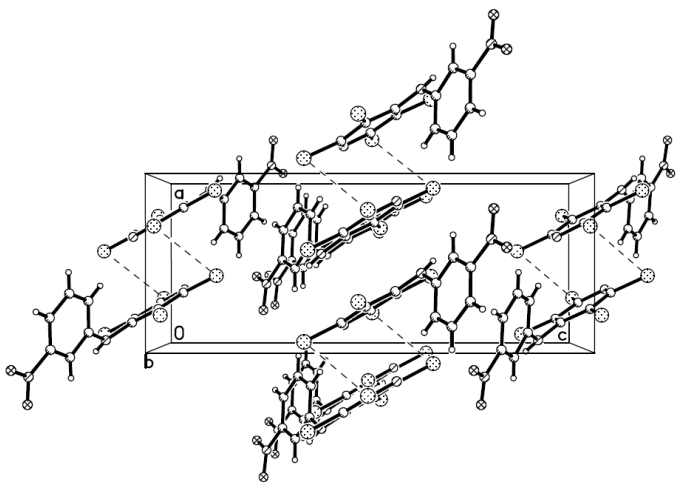
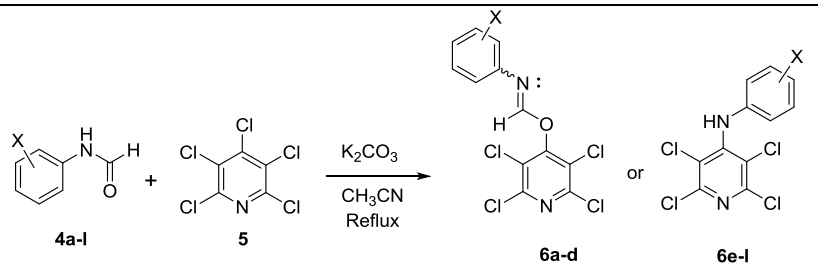
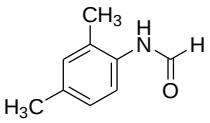
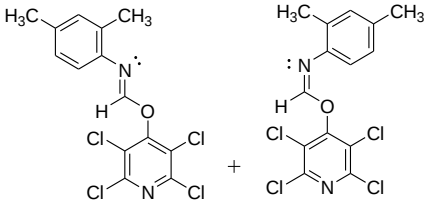
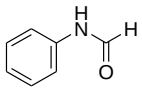
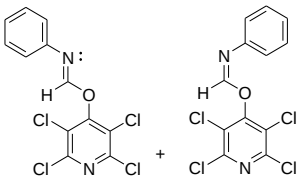
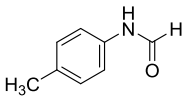
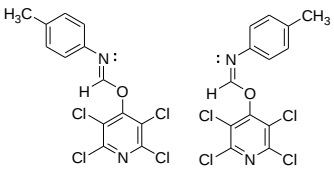
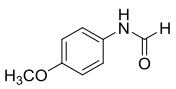
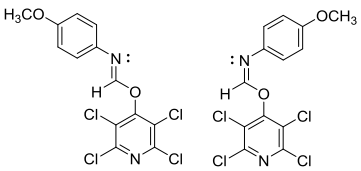
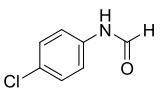
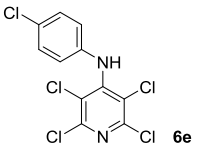
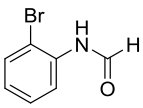
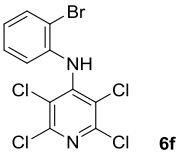
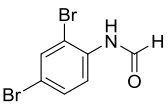
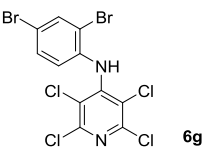


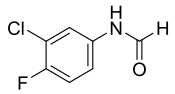
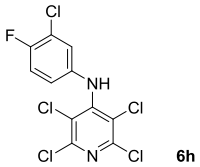
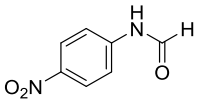
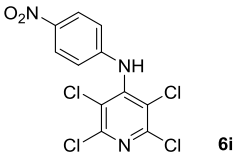
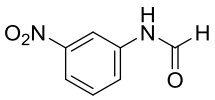
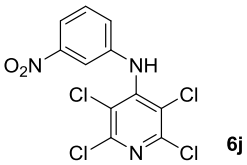
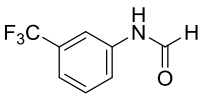
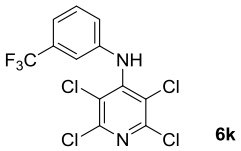
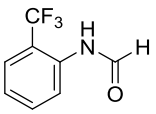
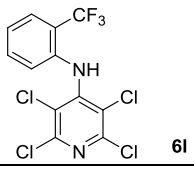
Figure 2: The crystal packing of 6j

Table 3: Reaction of aromatic formamide with pentachloropyridine



4a-l 5 6a-d 6e-l

Entry	Formamide	Product	Yield(%)	M.P(°C)
1	 4a	 6a	31	137-140
2	 4b	 6b	30	169-172
3	 4c	 6c	35	129-132
4	 4d	 6d	53	169-172
5	 4e	 6e	90	150-153
6	 4f	 6f	40	180-183
7	 4g	 6g	75	174-177

8	 4h	 6h	60	135-138
9	 4i	 6i	70	271-274
10	 4j	 6j	65	243-247
11	 4k	 6k	55	141-145
12	 4l	 6l	30	108-111

Conclusion

We demonstrate that pentachloropyridine **5** can successfully react with enole-imines from both oxygen and nitrogen site, depending on X substituent. When X was an electron releasing group, nucleophilic attack was accomplished by oxygen atom and when X was an electron withdrawing group attached to benzene ring, attack to pentachloropyridine was carried out *via* nitrogen site.

Experimental

All solvents and starting materials were obtained commercially (Merck). Solvents were dried using the literature procedures and distilled before use. The ^{1}H NMR spectra were recorded at 500 or 300 MHz. The ^{13}C NMR spectra were recorded at 125 or 75 MHz. The ^{19}F NMR spectra were recorded at 282 MHz. TLC analysis was performed on silica gel TLC plates (Merck).

Preparation of APS

Grafting the silica surface by covalently attaching aminopropyl functional group proceeds via a reaction between silanol groups and aminopropyl triethoxysilane (APTES) in dry toluene.[36,37] Typically, 5 g of silica sample are dispersed in 50 ml dry toluene and stirred for a few minutes at room temperature; then 5 ml of APTES is slowly added to the suspension and refluxed for 10 h. After slow cooling, the resulting solids are filtered, washed with toluene, and dried under reduced pressure for 24 h. The aminopropyl-grafted samples are heated at 120 ˚C for 12 h. The grafted material afterwards is called APS (aminopropyl-silica). Finally, we investigated the formylation of amines with formic acid in the presence of APS as a catalyst.

General procedure for formylation of amines with formic acid

To a mixture of amine (1 mmol) and formic acid (3 mmol), APS (0.005 g) was added. The reaction mixture was irradiated with ultrasound for 1–5 min. The progress of the reaction was monitored by TLC. After completion, the mixture was diluted with water (10 mL) and extracted with dietyl ether (2×10 ml). The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated to afford the pure formamide.

General procedure for reactions between pentachloropyridine and formamidates

Potassium carbonate (1.5 mmol) was added to a solution of formamide **4** (1 mmol) in dry acetonitrile (5 ml) and the mixture was stirred at room temperature for 30 min. Then pentachloropyridine **5** (1 mmol) was added and the resulting solution was refluxed at 85°C for 12h. The reaction mixture was filtered and the solvent was evaporated. The obtained product was recrystallized from EtOH to give the crude product.

2,3,5,6-tetrachloropyridin-4-yl-N-(2,4-dimethylphenyl)formimidate (6a)

Yield: (31%), white solid, mp 137-140 °C. (Found: C, 46.1; H, 2.7; N, 7.7. $C_{14}H_{10}Cl_4N_2O$ requires: C, 46.2; H, 2.7; N, 7.7%). ^{1}H NMR (500MHz, DMSO-d_6): δ 8.6 (1H, s, alkene-CH), 8.4 (1H, s, alkene-CH), 7.21 (1H, s, Ar-H), 7.14 (1H, s, Ar-H), 7.02 (1H, d, J = 8 Hz, Ar-H), 6.95 (1H, d, J = 9.5 Hz, Ar-H), 6.90 (1H, d, J = 8 Hz, Ar-H), 6.75 (1H, d, J = 8.5 Hz, Ar-H), 2.35 (3H, s, CH_3), 2.27 (3H, s, CH_3), 2.26 (3H, s, CH_3), 2.20 (3H, s, CH_3). ^{13}C NMR (125MHz, DMSO-d_6): δ 148 (Ar-C), 146.2 (Ar-C), 137.1 (Ar-C), 135.7 (Ar-C), 133.2 (Ar-C), 133 (Ar-CH), 132 (Ar-CH), 129.3 (Ar-CH), 129.5 (Ar-CH), 124.9 (Ar-CH), 125.1 (Ar-CH), 22 (CH_3), 21 (CH_3), 19 (CH_3), 18 (CH_3).

2,3,5,6-tetrachloropyridin-4-yl-N-phenylformimidate (6b)

Yield: (30%), white solid, mp 169-172 °C. (Found: C, 42.8; H, 1.7; N, 8.2. $C_{12}H_6Cl_4N_2O$ requires: C, 42.9; H, 1.8; N, 8.3%). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.98 (1H, s, alkene-CH), 8.46 (s, alkene-CH), 7.43-7.29 (5H, m, Ar-H). ^{13}C NMR (75MHz, DMSO-d_6): δ 165 (alkene-CH), 161.4 (alkene-CH), 146.3 (Ar-C), 146 (Ar-C), 137.4 (Ar-C), 137 (Ar-CH), 130.1 (Ar-CH), 129.8 (Ar-CH), 129.1 (Ar-CH), 126.7 (Ar-C), 123.5 (Ar-CH), 121.1 (Ar-CH).

2,3,5,6-tetrachloropyridin-4-yl-N-(4-methylphenyl)formimidate (6c)

Yield: (35%), white solid, mp 129-132 °C. (Found: C, 43.9; H, 2.2; N, 8.0. $C_{13}H_8Cl_4N_2O$ requires: C, 44.1; H, 2.3; N, 8.0%). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.89 (1H, s, alkene-CH), 8.43 (s, alkene-CH), 7.18-7.24 (4H, m, Ar-H), 2.29 (3H, s, CH_3). ^{13}C NMR (75MHz, DMSO-d_6): δ 161.2 (alkene-CH), 146.3 (Ar-C), 146.1 (Ar-C), 136.3 (Ar-CH), 136.1 (Ar-CH), 133.9 (Ar-CH), 130.7 (Ar-CH), 130.2 (Ar-CH), 130.1 (Ar-CH), 129.5 (Ar-CH), 128.9 (Ar-CH), 123.5 (Ar-C), 121.3 (Ar-CH), 121 (Ar-CH), 20.5 (CH_3), 20.4 (CH_3).

2,3,5,6-tetrachloropyridin-4-yl-N-(4-metoxylphenyl)formimidate (6d)

Yield: (53%), white solid, mp 169-172 °C. (Found: C, 42.6; H, 2.1; N, 7.7. $C_{13}H_8Cl_4N_2O_2$ requires: C, 42.7; H, 2.2; N, 7.6%). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.79 (1H, s, alkene-CH), 8.42 (s, alkene-CH), 7.36 (2H, d, J = 5.9 Hz,8.4 Ar-H), 6.92-7 (2H, m, Ar-H), 3.75 (3H, s, CH_3). ^{13}C NMR (75MHz, DMSO-d_6): δ 161.4 (Ar-C), 158.1 (alkene-CH), 157.7 (Ar-C), 147.1 (Ar-C), 146.3 (Ar-C), 130.5 (Ar-CH), 130.2 (Ar-CH), 130 (Ar-CH), 129.1 (Ar-CH), 125.6 (Ar-CH), 123.7 (Ar-CH), 114.9 (Ar-C), 114.2 (Ar-CH), 55.4 (OCH_3).

2,3,5,6-tetrachloro-N-(4-chlorophenyl)pyridin-4-amine (6e)

Yield: (90%), white solid, mp 150-153°C. (Found: C, 38.7; H, 1.4; N, 8.1. $C_{11}H_5Cl_5N_2$ requires: C, 38.6; H, 1.5; N, 8.2%). IR (KBr): 3364.1 (NH) cm^{-1}. ^{1}H NMR (300MHz, DMSO-d_6): δ 9.05 (1H, s, NH), 7.29 (2H, d, J = 5.9 Hz, Ar-H), 6.95 (2H, d, J = 5.8 Hz, Ar-H). ^{13}C NMR (75MHz, DMSO-d_6): δ 147.7 (Ar-C), 145.6 (Ar-C), 139.4 (Ar-C), 128.4 (Ar-CH), 126.6 (Ar-C), 121.4 (Ar-CH), 120.8 (Ar-C).

2,3,5,6-tetrachloro-N-(2-bromophenyl)pyridin-4-amine (6f)

Yield: (40%), pale gray solid, mp 180-183°C. (Found: C, 34.2; H, 1.4; N, 7.3. $C_{11}H_5BrCl_4N_2$ requires: C, 34.1; H, 1.3; N, 7.2%). IR (KBr): 3370 (NH) cm^{-1}. ^{1}H NMR (300MHz, DMSO-d_6): δ 8.75 (1H, s, NH), 7.60 (1H, d, J = 7.9 Hz, Ar-H), 7.31 (1H, t, J = 7.6 Hz, Ar-H), 7.18 (1H, d, J = 8 Hz, Ar-H), 7.10 (1H, t, J = 7.3 Hz, Ar-H): ^{13}C NMR (75MHz, DMSO-d_6): δ 148.4 (Ar-C), 145.4 (Ar-C), 139.4 (Ar-C), 132.4 (Ar-CH), 128 (Ar-CH), 126.6 (Ar-CH), 119.2 (Ar-C), 117.5 (Ar-C).

2,3,5,6-tetrachloro-N-(2,4-dibromophenyl)pyridin-4-amine (6g)

Yield: (75%), pale yellow solid, mp 174-177°C (Found: C, 28.3; H, 1.0; N, 6.1. $C_{11}H_4Br_2Cl_5N_2$ requires: C, 28.4; H, 0.9; N, 6.0%). IR (KBr): 3364.1 (NH) cm^{-1}. ^{1}H NMR (300MHz, DMSO-d_6): δ 8.31 (1H, s, NH), 7.73 (1H, d, J = 1.9 Hz, Ar-H), 7.39 (1H, dd, J = 8.5 Hz, J = 2 Hz, Ar-H), 6.93 (1H, d, J = 8.5 Hz, Ar-H). ^{13}C NMR (75MHz, DMSO-d_6): δ 148.7 (Ar-C), 144.9 (Ar-C), 142 (Ar-C), 133.7 (Ar-CH), 130.4 (Ar-CH), 126 (Ar-CH), 118.7 (Ar-C), 117 (Ar-C), 114 (Ar-C).

2,3,5,6-tetrachloro-N-(3-chloro-4-fluorophenyl)pyridin-4-amine (6h)

Yield: (60%), white solid, mp 135-138°C. (Found: C, 36.5; H, 1.2; N, 7.6. $C_{11}H_4Cl_4FN_2$ requires: C, 36.7; H, 1.1; N, 7.8%). IR (KBr): 3384.8 (NH) cm^{-1}. ^{1}H NMR (300MHz, DMSO-d_6): δ 9.07 (1H, s, NH), 7.19 (1H, dd, J = 9 Hz, Ar-H), 7 (1H, dd, J = 2.6 Hz, J = 6.49, Ar-H), 6.81 (1H, m, Ar-H). ^{13}C NMR (75MHz, DMSO-d_6): δ 152.4 (Ar-CF, J = 237.8), 148.2 (Ar-C), 145.2 (Ar-C), 141.2 (Ar-C), 121.3 (Ar-CH), 120.3 (Ar-CH, J = 6.8 Hz), 119 (Ar-C), 118.8 (Ar-CH, J = 18.5 Hz), 116.2 (Ar-C, J = 21.4 Hz). ^{19}F NMR (282 MHz, DMSO-d_6): δ -126.1 (1F).

2,3,5,6-tetrachloro-N-(4-nitrophenyl)pyridin-4-amine (6i)

Yield: (70%), orange solid, mp 271-274°C. (Found: C, 37.5; H, 1.5; N, 11.9. $C_{11}H_5Cl_4N_3O_2$ requires: C, 37.4; H, 1.4; N, 11.9%). IR (KBr): 3290.2 (NH) cm^{-1}. ^{1}H NMR (300MHz, DMSO-d_6): δ 9.79 (1H, s, NH), 8.11 (2H, d, J = 8.6 Hz, Ar-H), 6.97 (2H, d, J = 8.7 Hz, Ar-H). ^{13}C NMR (75MHz, DMSO-d_6): δ 148 (Ar-C), 146.7 (Ar-C), 145.3 (Ar-C), 140.4 (Ar-C), 125.2 (Ar-CH), 125 (Ar-CH), 116 (Ar-C).

2,3,5,6-tetrachloro-N-(3-nitrophenyl)pyridin-4-amine (6j)

Yield: (65%), yellow solid, mp 243-247°C. (Found: C, 37.4; H, 1.5; N, 12.0. $C_{11}H_5Cl_4N_3O_2$ requires: C, 37.4; H, 1.4; N, 11.9%). IR (KBr): 3355.1 (NH) cm^{-1}. ^{1}H NMR (300MHz, DMSO-d_6): δ 9.41 (1H, s, NH), 7.75 (1H, d, J = 6.8 Hz, Ar-H), 7.71 (1H, s, Ar-H), 7.46 (1H, t, J = 7.8 Hz, Ar-H), 7.22 (1H, d, J = 7.2 Hz, Ar-H). ^{13}C NMR (75MHz, DMSO-d_6): δ 148.1 (Ar-C), 147.5 (Ar-C), 145.6 (Ar-C), 143.3 (Ar-C), 129.6 (Ar-CH), 124.9 (Ar-CH), 121.5 (Ar-CH), 115.9 (Ar-C), 112.9 (Ar-CH).

2,3,5,6-tetrachloro-N-(3-(trifluoromethyl)phenyl)pyridin-4-amine (6k)

Yield: (55%), white solid, mp 141-145°C. (Found: C, 38.2; H, 1.4; N, 7.7. $C_{12}H_5Cl_4F_3N_2$ requires: C, 38.3; H, 1.3; N, 7.6%). IR (KBr): 3390.8 (NH) cm^{-1}. ^{1}H NMR (300MHz, DMSO-d_6): δ 9.25 (1H, s, NH), 7.43 (1H, t, J = 7.6 Hz, Ar-H), 7.26 (1H, d, J = 8.1 Hz, Ar-H), 7.25 (1H, s, Ar-H), 7.12 (1H, d, J = 7.5 Hz, Ar-H). ^{13}C NMR (75MHz, DMSO-d_6): δ 147.6 (Ar-C), 145.6 (Ar-C), 142.4 (Ar-C), 130 (Ar-C4), 129.3 (Ar-CH) 124 (CF3), 122.7 (Ar-CH), 121 (Ar-CH), 118.1 (Ar-C), 115.6 (Ar-CH). ^{19}F NMR (282 MHz, DMSO-d_6) δ -61.2 (CF_3).

2,3,5,6-tetrachloro-N-(2-(trifluoromethyl)phenyl)pyridin-4-amine (6l)

Yield: (30%), white solid, mp 108-111°C. IR (KBr): 3388.6 (NH) cm^{-1}. ^{1}H NMR (300MHz, DMSO-d_6): δ 8.37 (1H, s, NH), 7.66 (1H, d, J = 7.7 Hz, Ar-H), 7.52 (1H, t, J = 7.5 Hz, Ar-H), 7.28 (1H, t, J = 7.5 Hz, Ar-H), 7.12 (1H, d, J = 7.9 Hz, Ar-H). ^{13}C NMR (75MHz, DMSO-d_6): δ 148.6 (Ar-C), 145.4 (Ar-C), 145.4 (Ar-C), 132.7 (Ar-CH), 129.1 (Ar-CH), 126.3 (Ar-CH), 125.8 (CF_3), 117.9 (Ar-CH).

X-ray crystallography

Single crystal X-ray data of the compound was collected at 298(2) K on STOE IPDS 2T diffractometer with Mo Kα radiation (λ = 0.71073 Å). The unit Cell parameters refinement, data reduction and correction for Lp and decay were performed using X-AREA[38] software. Absorption corrections were applied using MULABS[39] routine in PLATON.[40] The structures were solved by direct methods and refined by the least squares method on F2 using the SHELXTL program package.[41] All of the calculations were done by PLATON. All non-hydrogen atoms were refined anisotropically. The C-bound hydrogen atoms were positioned geometrically and refined with a riding

model approximation with their parameters constrained to the parent atom with Uiso (H) = 1.2 Ueq (C). The N-bound hydrogen atom was located from the difference Fourier map and constrained to refine with the parent atoms with Uiso (H) = 1.2 Ueq (N). Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1034368 for the compound. Copy of this information may be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html or from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336-033; email: deposit@ccdc.ac.uk).

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