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

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Site reactivity of some enol–imines derived from *N*-aryl formamides with pentachloropyridine under basic conditions in dry CH_3CN was investigated. The aromatic nucleophilic substitution of pentachloropyridine with enol–imines occurs at the 4-position of pyridine ring by both oxygen and nitrogen site of enol–imines. Nucleophilic attack by the oxygen of enol–imine gave corresponding oximino compounds as a mixture of *E*- and *Z*-isomers. In contrast, nucleophilic attack by the nitrogen of enol–imine gave the unexpected *N*,*N*-di-substituted aryl compounds. The structures of all the 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 compounds are important starting materials for the synthesis of other heterocyclic and macrocyclic compounds.[1–3] The great number of review articles and monographs for the synthesis and applications of pyridines, reflects the important role of substituted pyridines in organic chemistry, biochemistry, and pharmaceutical chemistry.[4–7] Many researchers are interested in the reactions of various N, O, S, C, and P nucleophiles with perhalogenated compounds.[8–12] The nature of nucleophile, reaction condition, and solvent have a basic role in the regiochemistry of the reactions. Differentiation reactivity of perfluorinated heteroaromatic compounds into hard and soft nucleophiles was achieved by the partial replacement of fluorine by bromine in pentafluoropyridine.[13] In the last few years, we have been pursuing investigations on the regiochemistry reaction of different nucleophiles with perhalogenated compounds.[14] We have shown 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 cyclization.[14] In another work, we have shown that pentafluoropyridine successfully reacts with some enolates from the oxygen site. The selectivity of nucleophilic substitution in this process was explained on the basis of hard–hard interaction principle.[15]

Aromatic nucleophilic substitution reactions proceed *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 at 2-, 3- and 4-positions of pyridines indicate different reactivities to nucleophiles.[4–6]

Formamide compounds are widely used as intermediates in organic synthesis. *N*-formyl compounds play a key role in the synthesis of important pharmaceutical compounds such as 1,2-dihydroquinolines,[23] cancer chemotherapeutic agents[24] and quinolone antibiotics.[25] Furthermore, they are also applied as precursors for the 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 reported the preparation of these important compounds.[30–32] In this paper, we have established a new method for the synthesis of these compounds in a very short reaction time with high yields. The reaction of the aromatic

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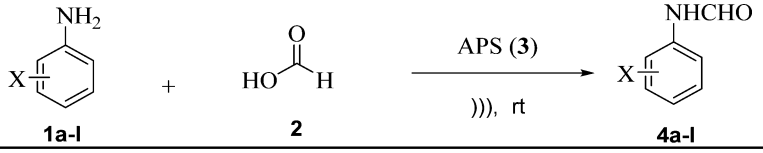
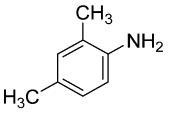
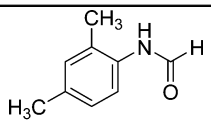
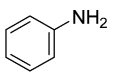
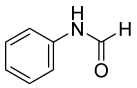
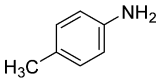
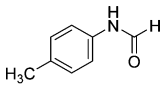
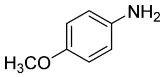
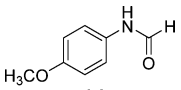
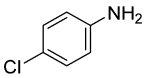
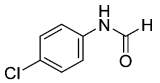
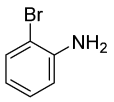
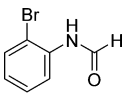
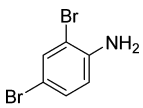
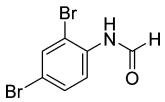
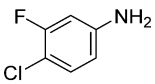
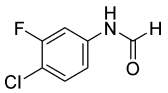
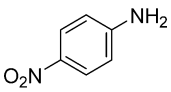
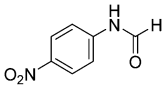
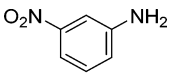
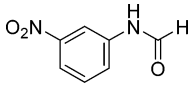
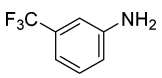
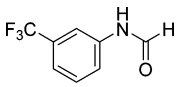
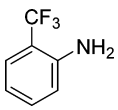
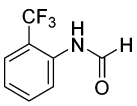
† CCDC 1034368. For crystallographic data in CIF or other electronic format see DOI: 10.1039/c5nj00418g

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	 1h	 4h	90	4
9	 1i	 4i	90	5
10	 1j	 4j	90	5
11	 1k	 4k	90	5
12	 1l	 4l	90	5

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 the corresponding formamides **4a–l** in 1–5 minutes in 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]

All the formamide compounds were identified by the 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*-formylamines with good to excellent yield and 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 the reaction in 1–5 min, and giving the products in excellent yields. Despite the relative simplicity of this reaction, the attempted acetylation of amine with acetic acid in acetonitrile failed. Similarly, the formylation of phenols with formic acid in acetonitrile also failed.

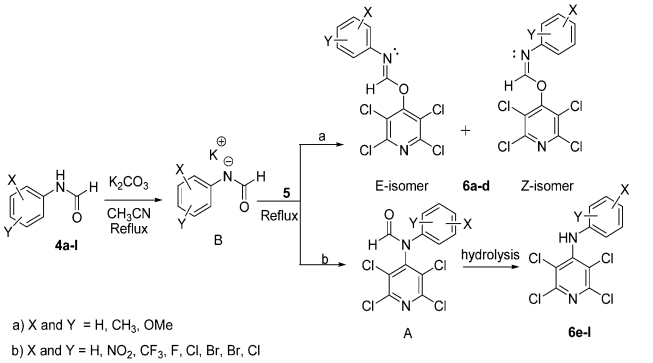
Reaction of formamide with pentachloropyridine

Anions derived from formamides have two nucleophilic sites (O and N) and it is interesting to know which site is attacked in the substitution reaction. The reaction conditions were optimized using the 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 solvents. Similarly, acetonitrile gave excellent yield at reflux condition (Table 2). The final product was the same in all solvents and temperatures. Annelation processes involving reactions between pentachloropyridine **5** and *N*-(2,4-dimethylphenyl)formamide **4a**

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

Entry	Solvent	Temperature (°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).

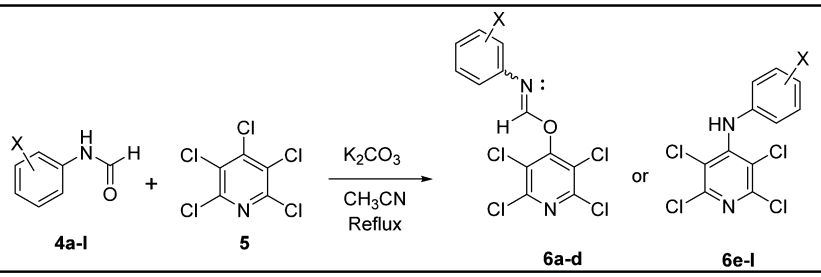


Scheme 1 General scheme for reaction of formamide with pentachloropyridine.

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 product 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 nucleophilic 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 at 2.35, 2.27, 2.26 and 2.20 ppm.

Similarly, the reactions of phenylformamides **4b–d** with pentachloropyridine **5** give **6b–d**, respectively, as mixtures of *E*- and *Z*-isomers. With this encouraging result in hand, 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 compounds **6a–d**. ^{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 at 7.71 ppm for aromatic H. There are no signals for aldehyde or alkene hydrogen. ^{13}C spectrum was at first slightly puzzling, showing bands only for the ring carbon atoms. The IR spectrum **6j** showed a broad absorption band 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, together with the

Table 3 Reaction of aromatic formamide with pentachloropyridine



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

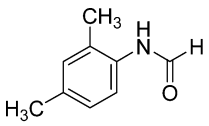
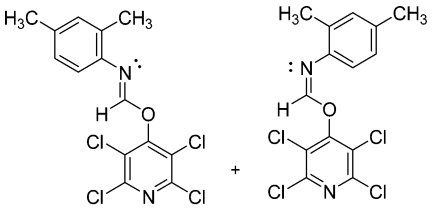
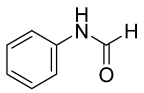
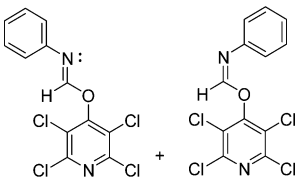
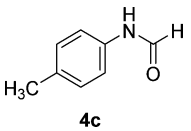
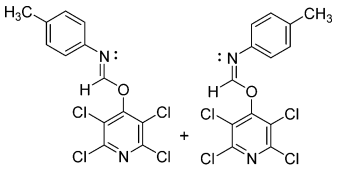
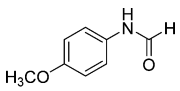
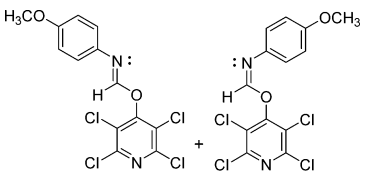
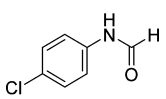
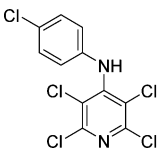
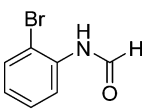
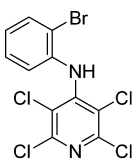
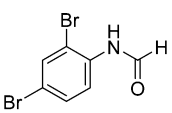
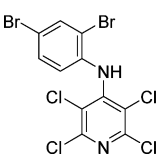
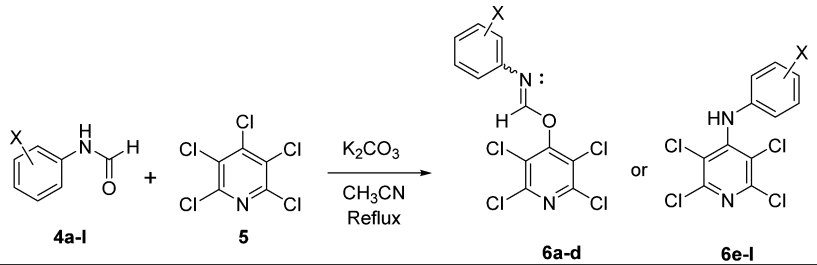
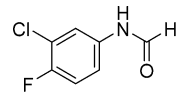
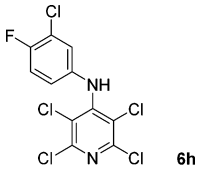
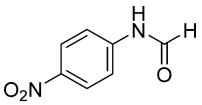
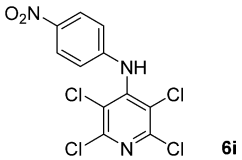
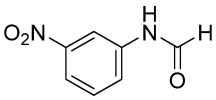
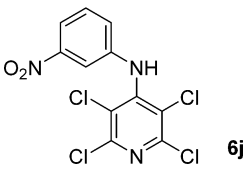
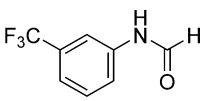
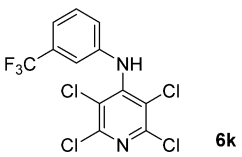
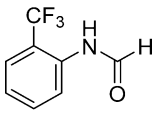
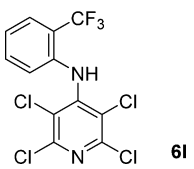
Entry	Formamide	Product	Yield (%)	M.P. (°C)
1	 4a	 6a	31	137–140
2	 4b	 6b	30	169–172
3	 4c	 6c	35	129–132
4	 4d	 6d	53	169–172
5	 4e	 6e	90	150–153
6	 4f	 6f	40	180–183
7	 4g	 6g	75	174–177

Table 3 (*continued*)



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

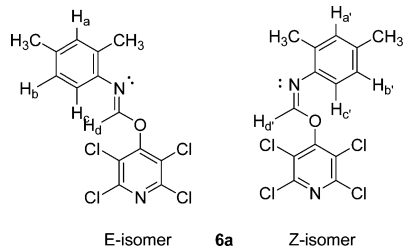
Entry	Formamide	Product	Yield (%)	M.P. (°C)
8	 4h	 6h	60	135–138
9	 4i	 6i	70	271–274
10	 4j	 6j	65	243–247
11	 4k	 6k	55	141–145
12	 4l	 6l	30	108–111

abovementioned NMR 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 were located in the range of 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 the nitrogen of formamide, to give the first formed intermediate **A**, which under reaction conditions converted rapidly to the 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 space 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], as shown in Fig. 2. The crystal packing is further stabilized by the intermolecular π···π



Scheme 2 *E* and *Z* isomers of **6a**.

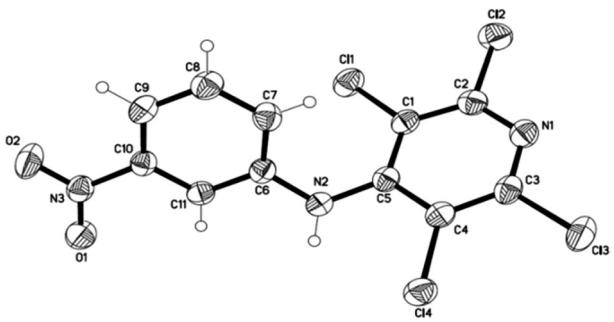
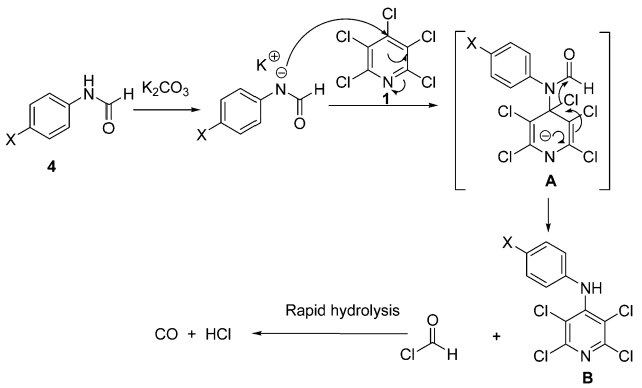


Fig. 1 The molecular structure of **6j**.



Scheme 3 Proposed explanation for observed **B**.

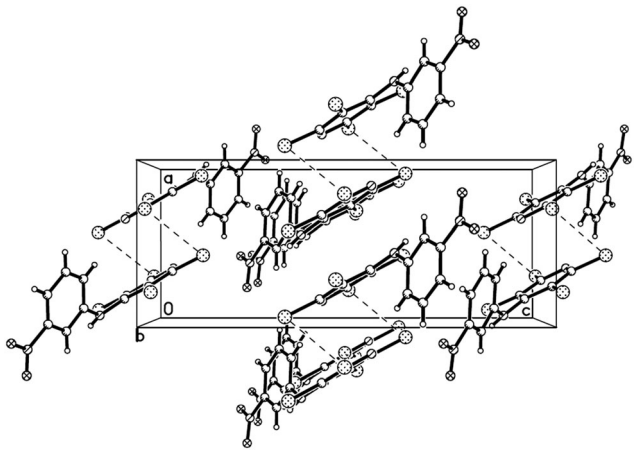


Fig. 2 The crystal packing of **6j**.

interactions in which the centroid to centroid distances are 3.8375(14) and 3.8189(14) Å.

Conclusion

We have demonstrated that pentachloropyridine **5** can successfully react with enol–imines from both oxygen and nitrogen site, depending on the X substituent. When X is an electron-releasing group, nucleophilic attack is accomplished by oxygen atom and when X is an electron-withdrawing group attached to benzene ring, pentachloropyridine is attack to *via* a nitrogen site.

Experimental

All the solvents and starting materials were obtained commercially (Merck). Solvents were dried using the literature recommended procedures and distilled before use. ^{1}H NMR spectra were recorded at 500 or 300 MHz. ^{13}C NMR spectra were recorded at 125 or 75 MHz. ^{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 attached 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 was dispersed in 50 ml dry toluene and stirred for a few minutes at room temperature. Then, 5 ml of APTES was slowly added to the suspension and refluxed for 10 h. After slow cooling, the resulting solids were filtered, washed with toluene, and dried under reduced pressure for 24 h. Aminopropyl-grafted samples were heated at 120 °C for 12 h. The grafted material obtained afterwards was 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 the 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 diethyl ether (2 × 10 ml). The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated to afford 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 12 h. 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 (500 MHz, 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 (125 MHz, 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 (75 MHz, 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 (75 MHz, 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 (75 MHz, 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 (300 MHz, 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 (75 MHz, 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 (300 MHz, 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 (75 MHz, 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 (300 MHz, 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 (75 MHz, 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 (300 MHz, 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 (75 MHz, 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 (300 MHz, 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 (75 MHz, 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 (300 MHz, 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 (75 MHz, 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 (300 MHz, 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 (75 MHz, 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 (300 MHz, 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 (75 MHz, 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 performed 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 U_{iso} (H) = 1.2 U_{eq} (C). The N-bound hydrogen atom was located from the difference Fourier map and constrained to refine with the parent atoms with U_{iso} (H) = 1.2 U_{eq} (N). CCDC 1034368.

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