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Reactions of 4-(dimethylamino)pyridinium activated pentachloropyridine with nitrogen nucleophiles and hydride

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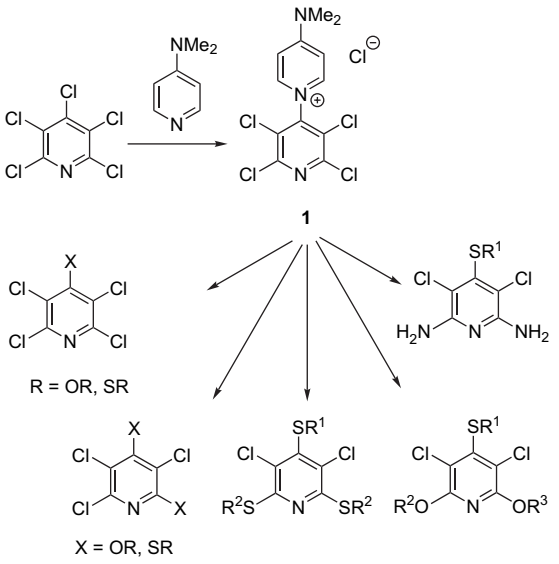
Abstract—Substitution reactions on 2′,3′,5′,6′-tetrachloro-4-dimethylamino-[1,4]bipyridinyl-1-ylium chloride with nitrogen nucleophiles such as *n*-propylamine, isopropylamine, glycine, morpholine, and piperidine were examined. Highly functionalized Cl^2,Cl^3,N^4,Cl^5,Cl^6- and N^2,Cl^3,N^4,Cl^5,Cl^6-substituted pyridines were obtained, in part possessing unsubstituted 4-amino groups due to dealkylation. Detailed NMR studies were performed in order to elucidate the regiochemistry of these dealkylations.

1. Introduction

Substituted pyridines play a crucial role in organic, bioorganic, and pharmaceutical chemistry as well as in material sciences. This is reflected in an impressive number of monographs and review articles dealing with syntheses and properties of functionalized pyridines.[1] Numerous synthetic procedures have been developed during the last decades, among these ring closure reactions from acyclic precursors,[2] Dimroth rearrangements,[3] ring contractions of 1,2-diazocines,[4] multicomponent cascade heterocyclizations,[5] Vilsmeier and the reverse Vilsmeier methods,[6] electrochemical methods,[7] pyrimidine–pyridine ring interconversions,[8] metal-mediated [2+2+2]-cycloadditions,[9] and other metal-organic syntheses.[10] Although nucleophilic substitutions on pentafluoropyridine[11] and approaches from ynamines and ynamides[12] have been studied recently and proved to be promising avenues for the synthesis of highly substituted pyridines, an astonishing large number of simply functionalized pyridines have been unavailable to date. We recently described mono- and oligocationic hetarenium salts with up to ten positive charges within the same molecule,[13] and their broad applicability in heterocyclic synthesis. Thus, 2′,3′,5′,6′-tetrachloro-4-dimethylamino-[1,4]bipyridinyl-1-ylium chloride **1**, readily available in quantitative yields from pentachloropyridine, can be used to prepare Cl^2,Cl^3,O^4,Cl^5,Cl^6- and O^2,Cl^3,O^4,Cl^5,Cl^6-pentasubstituted pyridines[14] as well as their sulfur analogs.[15] Similarly, hitherto unavailable O^2,Cl^3,O^4,Cl^5,O^6-[14] and biologically interesting S^2,Cl^3,S^4,Cl^5,S^6-pentasubstituted pyridines,[15] as well as a broad variety of symmetric and non-symmetric O^2,Cl^3,S^4,Cl^5,O^6-pentasubstituted pyridines are available starting from **1**.[16] The procedure can be extended to the synthesis of first representatives of N^2,Cl^3,S^4,Cl^5,N^6-pentasubstituted pyridines[16] (Scheme 1). The preparation of amino-substituted pyridines, however, remained challenging. 2-Amino-substituted pyridines are available by the Chichibabin reaction,[17] or by nucleophilic substitutions of suitable leaving groups at 2- or 4-position such as halogen atoms.[18] More than one- or twofold substitutions afford vigorous reaction conditions due to the decreased reactivity of chloropyridines substituted with electron-donating groups. Halogen atoms at C-3 are inert toward these substitution reactions[19] unless metal-organic procedures[10] or hetaryne mechanisms are applied.[20] As a consequence, pentasubstituted pyridines with more than one amino-substituent are very rare. According to the



Scheme 1. Synthetic potential of DMAP-activated pentachloropyridine **1**.

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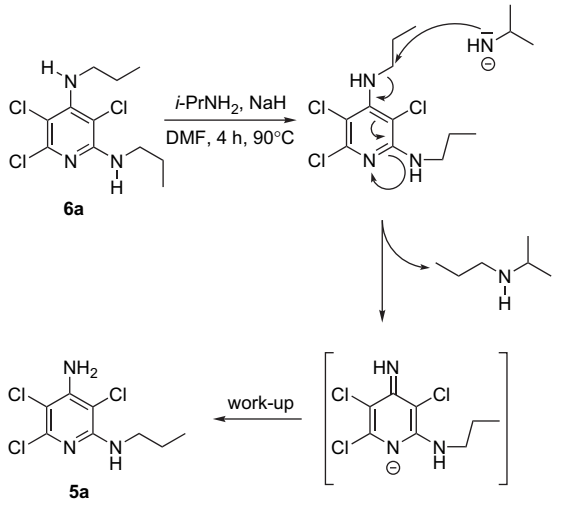
Beilstein cross-fire database, less than 10 representatives of N^2,Cl^3,N^4,Cl^5,Cl^6-pentasubstituted pyridines have been described to date in six publications[21–26] and one patent.[27] We report here our results of studies directed toward the applicability of our synthetic strategy for the preparation of functionalized pyridines starting from hetarenium salts to some nitrogen nucleophiles.

2. Results and discussion

We studied substitution reactions on 2′,3′,5′,6′-tetrachloro-4-dimethylamino-[1,4]bipyridinyl-1-ylium chloride **1** with the nitrogen nucleophiles such as *n*-propylamine, isopropylamine, glycine, morpholine, and piperidine. Nucleophilic substitutions on **1** with *n*-propylamine and isopropylamine were first performed in the presence of sodium hydride as base. Mixtures of substituted pyridines were obtained, which are presented in Table 1, among them new representatives of N^2,Cl^3,N^4,Cl^5,Cl^6-pentasubstituted species.

Surprisingly, *n*-propylamine as nucleophile resulted in the formation of 3,5,6-trichloro-N^2-propyl-pyridine-2,4-diamine **5a** as the main product (Table 1, entry 1), when the reaction was conducted at 50 °C over a period of 4 h. 3,5,6-Trichloro-N^2,N^4-dipropyl-pyridine-2,4-diamine **6a** was isolated in very low yields. The 4-isopropylamino-substituted tetrachloropyridine **4b** was found to be the main product of the reaction of hetarenium salt **1** with isopropylamine under analogous reaction conditions (Table 1, entry 3). 3,5,6-Trichloro-N^2-isopropyl-pyridine-2,4-diamine **5b** was formed in low yields as a by-product. In either case, unmodified starting material was easily separated by filtration over silica gel.

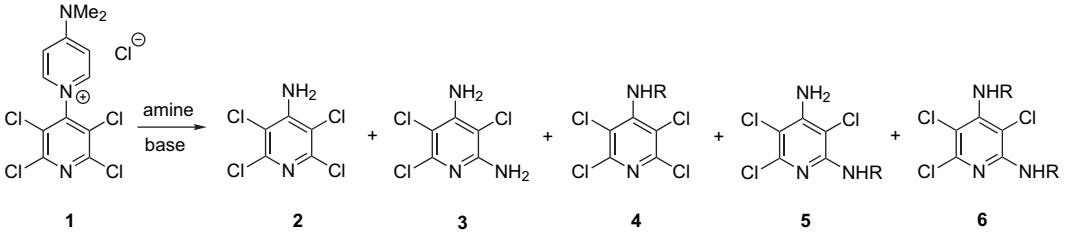
Obviously, the 4-amino groups in **5a** and **5b** were formed from propylamino- and isopropylamino groups, respectively. In a control experiment, the dipropylamino-substituted pyridine **6a** indeed reacted with isopropylamine in the presence of sodium hydride in DMF to give the dealkylated product **5a** (Scheme 2). Several mechanisms can be discussed. The lack of electron-withdrawing groups does not support an $E1_{cb}$-type mechanism and elimination of propene. Nucleophilic attack, however, of propylamide and isopropylamide on the 4-propylamino groups in the initially formed N^2,N^4-dialkyl-pyridine-2,4-diamines **6a** and **6b**, respectively, resulted in the formation of *N*,*N*-dialkylamines and 4-NH_2-substituted pyridines.



Scheme 2. Proposed mechanism for dealkylations.

The regiochemistry of this conversion was unambiguously confirmed by NMR methods. Thus, in the ^1H NMR spectra of **5a**, taken in $CDCl_3$ at rt, two H/D-exchangeable resonance frequencies in a 1:2 ratio are observable at δ=4.82 and 4.95 ppm, which were assigned to the NHR and NH_2

Table 1. Reaction of **1** with amines in the presence of bases



Entry	Amine	Temp/time	Base	Product	R	Yield %
1	*n*-$PrNH_2$	50 °C, 4 h	NaH	**5a**	*n*-Pr	32
				6a	*n*-Pr	5
2			$NaNH_2$	**2**	H	7
				3	H	18
				4a	*n*-Pr	0
				5a	*n*-Pr	40
				6a	*n*-Pr	35
3	*i*-$PrNH_2$	40 °C, 4 h	NaH	**4b**	*i*-Pr	37
				5b	*i*-Pr	5
4			$NaNH_2$	**2**	H	10
				3	H	10
				4b	*i*-Pr	15
				5b	*i*-Pr	30
				6b	*i*-Pr	0

group, respectively. In agreement to the proposed structure, the gs-HMBC (^{1}H–^{13}C) spectrum displays all the expected long range C–H couplings as presented in Figure 1.

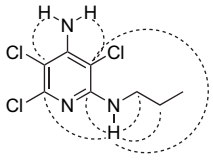


Figure 1. HMBC-detected long range C–H couplings in **5a**.

Among these, the $^{3}J_{CH}$ coupling of the hydrogen atoms of the NH_2 group with C-5 is diagnostically important. However, a 2D INADEQUATE, performed to unambiguously prove the ^{13}C peak assignments, suffered from disadvantageous relaxation times of the aromatic carbon atoms due to the absence of H atoms at the pyridine ring. We solved the problem by considering very large C–C coupling constants within this special pyridine ring (approx. 70 Hz) and by addition of 4% chromium(III) acetylacetonate as a relaxation reagent, and proved the C–C connectivities as shown in Figure 2. Analogous results were obtained with **5b**.

As a result, the ^{13}C NMR peak assignments of the N^2,Cl^3,N^4,Cl^5,Cl^6-substituted pyridines presented in this paper is as shown in Figure 3. A ^{15}N HMBC measurement allowed to assign the resonance frequency δ_N at −310.3 ppm

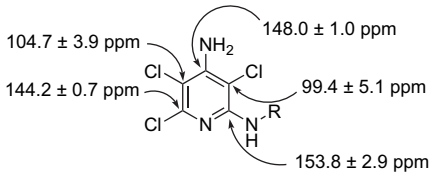


Figure 3. Peak assignments of the ^{13}C NMR resonance frequencies.

to the 4-NH_2-group of **5a**, whereas the signal at −294.5 ppm is caused by the 2-NHR group. The pyridine nitrogen atom could not be detected by ^{15}N NMR spectroscopy.

Next we used sodium amide as base for the reaction of hetarenium salt **1** with amines. This base gave best results on treatment of **1** with a broad variety of O- and S-nucleophiles.[13–16] In these reactions the amide anion never reacted as nucleophile. Indeed, we found a quantitative conversion of the starting material **1**. Again, the N^2,Cl^3,N^4,Cl^5,Cl^6-substituted pyridine **5a** was isolated as the main product of the reaction with *n*-propylamine at 50 °C (Table 1, entry 2). The diamine **6a** was found in 35% yield. Additional by-products are tetrachloropyridin-4-amine **2** and trichloropyridine-2,4-diamine **3**, isolated in 7% and 18% yield, respectively. The latter mentioned compounds formed also on treatment of pentachloropyridine with ammonia at 170–190 °C, in addition to 2-aminotetrachloropyridine.[21,22] Similar results were obtained starting from isopropylamine (Table 1, entry 4). A mixture of **2**, **3**, **4b**, and **5b** was formed, with **5b** as the

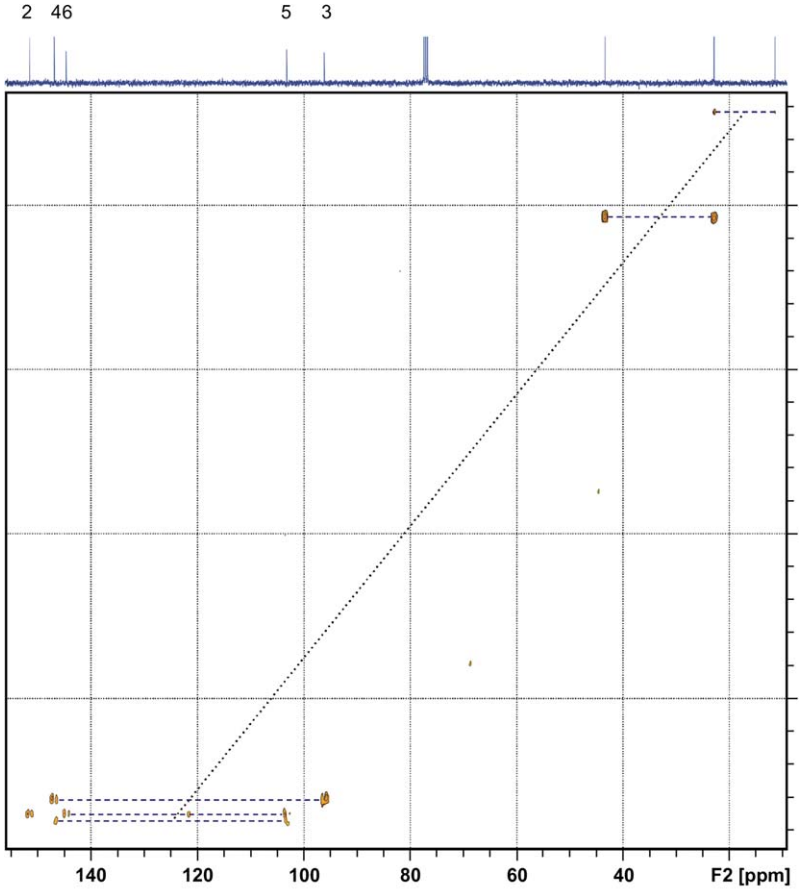
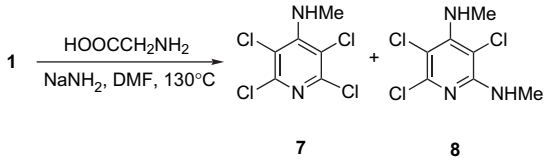


Figure 2. 2D-INADEQUATE of **5a**.

main product. All compounds were easily separated and purified by column chromatography on silica gel.

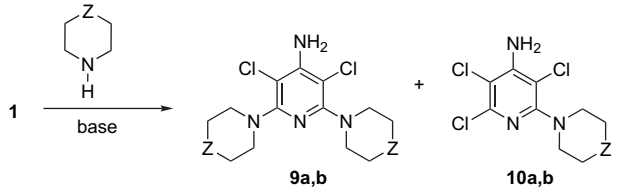
Glycine as nitrogen nucleophile yielded methyl-(2,3,5,6-tetrachloro-pyridin-4-yl)-amine **7**, which is a known compound,[24] and 3,5,6-trichloro-N^2,N^4-dimethyl-pyridine-2,4-diamine **8** in moderate and low yields, respectively (Scheme 3). Obviously, these compounds were formed on decarboxylation of the glycine moieties under the applied reaction conditions. To the best of our knowledge, **8** has never been described before. The pyridylamine **7** was obtained earlier on reaction of pentachloropyridine with methylamine in 1,4-dioxane as a mixture of 2- and 4-isomers after a reaction time of 18 h.[24]



Scheme 3.

Morpholine in the presence of sodium amide converted hetarenium salt **1** into 3,5-dichloro-(2,6-dimorpholin-4-yl)-pyridin-4-ylamine **9a** in 59% yield, which was isolated as a pure compound (Table 2, entry 2). In accordance with the structure, the ^{13}C NMR spectra showed a symmetric molecule. Sodium hydride as the base gives lower yields and considerable amounts of 2,3,5-trichloro-6-morpholin-4-yl-pyridin-4-ylamine **10a** (Table 2, entry 1), the regiochemistry of which was elucidated by HMBC measurements as described above. The morpholine-substituted trichloropyridine with N^2,Cl^3,N^4,Cl^5,Cl^6 substitution pattern is available by substitution of secondary aliphatic amines on (*Z*)-perchloro-1,3-butadiene-1-carbonitrile.[28] Pentachloropyridine reacts with morpholine at the 2-position. Twofold substitution results in the formation of N^2,Cl^3,Cl^4,Cl^5,N^6-morpholino-substituted pyridine. Some earlier published structures had to be revised.[28]

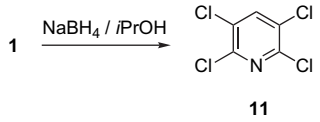
Table 2. Morpholine and piperidine as N-nucleophiles



Entry	Amine	Temp/time	Base	Product	Z	Yield %
1	Morpholine	90 °C, 3 h	NaH	**9a**	O	10
				10a		18
2			$NaNH_2$	**9a**		59
				10a		0
3	Piperidine	100 °C, 3 h	NaH	**9b**	CH_2	54
				10b		18
4			$NaNH_2$	**9b**		37
				10b		25

On reaction of hetarenium salt **1** with piperidine, **9b** and **10b** were obtained under the conditions presented in Table 2 (entries 3 and 4).

2′,3′,5′,6′-Tetrachloro-4-dimethylamino-[1,4]bipyridinyl-1-ylium chloride **1** reacts with sodium borohydride to give 2,3,5,6-tetrachlorpyridine **11** (Scheme 4). Best yields and purities were achieved when 2-propanol was used as solvent. On changing the solvent to ethanol, the yield decreased from 80 to 5% after reaction at rt over a period of 5 h. In DMF, the yield is 46% under analogous reaction conditions. In 2-propanol as solvent, the product was obtained in 95% purity. The 4-(dimethylamino)pyridine could be recovered. The chromatographically separable by-product proved to be 2,3,5-trichloropyridine, as evidenced by GC–MS analysis. Numerous procedures for the preparation of 2,3,5,6-tetrachloropyridine **11** exist, among them the reduction of pentachloropyridine with zinc, ammonium chloride, dimethylphosphonate in water at 89–90 °C,[29] electrochemical methods,[30] the chlorination of 2,3,5-trichloropyridine with hexachloroethane in the presence of *n*-Bu_4NBr in aqueous sodium hydroxide,[31] and some patented procedures.[32]



Scheme 4.

In summary, we supplement our synthetic strategy for the preparation of highly functionalized pyridines from hetarenium salts by results describing scope and limitations of the application of nitrogen nucleophiles.

3. Experimental

3.1. General

The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 and DPX 200 at 400 and 200 MHz, respectively. The chemical shifts are reported in parts per million relative to internal tetramethylsilane (δ=0.00 ppm). FTIR spectra were obtained on a Bruker Vector 22 in the range of 400–4000 cm^{-1} (2.5% pellets in KBr). The GC–MS spectra were recorded on a GC Hewlett–Packard 5980, Series II in combination with a MS Hewlett–Packard 5989 B, and on a Varian GC3900 with SAT2100T mass spectrometer. Melting points are uncorrected.

3.2. General procedure for the reaction of 2′,3′,5′,6′-tetrachloro-4-dimethylamino-[1,4]bipyridinyl-1-ylium chloride 1 with amines

A suspension of **1** (10 mmol, 3.74 g) in 100 mL of the amine was treated with sodium hydride (50 mmol, 1.25 g) or sodium amide (50 mmol, 1.96 g) and heated at reflux temperature over a period of 5 h. Then, the amine was distilled off in vacuo and the residue was chromatographed (silica gel 60, EtOAc/petroleum ether=1:3).

3.2.1. 2,3,5,6-Tetrachloro-pyridin-4-ylamine (2). Pale yellow solid, mp 210 °C ($C_5H_2Cl_4N_2$ requires C, 25.90; H, 0.87; N, 12.08. Found: C, 25.87; H, 0.86; N, 12.18); δ_H (DMSO-d_6) 7.38 (s, 2H; NH_2); δ_C (DMSO-d_6) 150.8,

144.1, 111.6; ν_{max} (KBr) (cm^{-1}): 3494, 3390, 1583, 1535, 1373, 1250, 1109, 1061, 973; *m*/*z*=233 (MH^+, 100), 195 (M−Cl, 11).

3.2.2. 3,5,6-Trichloro-pyridine-2,4-diylamine (3). Pale yellow solid, mp 168 °C ($C_5H_4Cl_3N_3$ requires C, 28.27; H, 1.90; N, 19.78. Found: C, 29.06; H, 2.11; N, 19.05); δ_H (DMSO-d_6) 6.41 (s, 2H; α-NH_2), 6.31 (s, 2H; γ-NH_2); δ_C (DMSO-d_6) 153.1, 148.7, 143.5, 100.8, 94.3; ν_{max} (KBr) (cm^{-1}) 3453, 3369, 1612, 1573, 1439; *m*/*z*=213 (M, 100), 176 (M−Cl, 28).

3.2.3. Isopropyl-(2,3,5,6-tetrachloro-pyridin-4-yl)-amine (4b). Brownish solid, mp 74 °C ($C_8H_8Cl_4N_2$ requires C, 35.07; H, 2.94; N, 10.22. Found: C, 36.06; H, 2.97; N, 10.23); δ_H ($CDCl_3$) 4.85 (s, 1H; N*H*), 4.61 (h, ^3J=6.4 Hz, 1H; NC*H*), 1.27 (d, ^3J=6.4 Hz, 6H; CH_3); δ_C ($CDCl_3$) 150.0, 146.4, 115.4, 47.2, 24.4; ν_{max} (KBr) (cm^{-1}) 1556, 1539, 1413, 1353, 1259, 1236, 1140, 1021, 912, 708; *m*/*z*=275 (M, 100), 260 (M−CH_3).

3.2.4. 3,5,6-Trichloro-N^2-propyl-pyridine-2,4-diamine (5a). Yellow solid, mp 76 °C ($C_8H_{10}N_3Cl_3$ requires C, 37.75; H, 3.96; N, 16.51. Found: C, 37.56; H, 3.87; N, 16.49); δ_H ($CDCl_3$) 4.85 (br s, 2H; NH_2), 4.78 (br s, 1H; N*H*), 3.38 (dt, ^3J=7.3, 1.5 Hz, 2H; NCH_2), 1.62 (sx, ^3J=7.3 Hz, 2H; CH_2CH$_3$), 0.97 (t, ^3J=7.3 Hz, 3H; CH_3); δ_C ($CDCl_3$) 151.5, 146.9, 144.6, 103.1, 96.1, 43.3, 22.8, 11.4; ν_{max} (KBr) (cm^{-1}) 3511, 3405, 2969, 2929, 2864, 1614, 1583, 1507, 1447, 1298, 1165; *m*/*z*=255 (M, 43); 225 (M−C_3H_7, 100).

3.2.5. 3,5,6-Trichloro-N^2-isopropyl-pyridine-2,4-diamine (5b). Brownish solid, mp 26 °C ($C_8H_8Cl_3N_3$ requires C, 37.75; H, 3.96; N, 16.51. Found: C, 37.34; H, 3.75; N, 16.26); δ_H ($CDCl_3$) 4.85 (s, 2H; NH_2), 4.60 (s, 1H; N*H*), 4.19 (h, ^3J=6.4 Hz, 1H; NC*H*), 1.22 (d, ^3J=6.4 Hz, 6H; CH_3); δ_C ($CDCl_3$) 150.9, 147.0, 144.7, 103.0, 96.1, 42.9, 23.1, 11.2; ν_{max} (KBr) (cm^{-1}) 3498, 3400, 2972, 1610, 1578, 1504, 1437, 1311, 1182, 1126, 1055; *m*/*z*=254 (M, 100), 238 (M−CH_3).

3.2.6. 3,5,6-Trichloro-N^2,N^4-dipropyl-pyridine-2,4-diamine (6a). Yellow liquid ($C_{11}H_{16}Cl_3N_3$ requires C, 44.54; H, 5.44; N, 14.17. Found: C, 43.67; H, 4.95; N, 14.18); δ_H ($CDCl_3$) 4.86 (s, 1H; N*H*), 4.78 (br s, 1H; N*H*), 3.39 (t, ^3J=7.3 Hz, 2H; NCH_2), 3.36 (t, ^3J=7.3 Hz, 2H; NCH_2), 1.61 (h, ^3J=7.3 Hz, 4H; CH_2), 0.96 (t, ^3J=7.3 Hz, 6H; CH_3); δ_C ($CDCl_3$) 151.5, 146.9, 144.7, 103.2, 96.1, 43.3, 22.9, 11.4; ν_{max} (NaCl) (cm^{-1}) 3398, 2963, 2875, 1582, 1356, 1233, 1070; *m*/*z*=296 (M, 4), 260 (M−Cl, 100), 225 (M−2Cl, 27), 184 (M−2Cl−C_3H_7, 22).

3.2.7. 3,5-Dichloro-(2,6-dimorpholin-4-yl)-pyridin-4-yl-amine (9a). Colorless solid, mp 64 °C ($C_{13}H_{18}Cl_2N_4O_2$ requires C, 46.86; H, 5.44; N, 16.81. Found: C, 46.50; H, 5.70; N, 16.80); δ_H ($CDCl_3$) 4.93 (br s, 2H; NH_2), 3.80–3.85 (m, 8H), 3.26–3.31 (m, 8H); δ_C ($CDCl_3$): 154.3, 148.7, 100.1, 66.9, 49.5; ν_{max} (KBr) (cm^{-1}) 3473, 3321, 2969, 2855, 1621, 1554, 1420, 1392, 1365, 1283, 1257, 1154, 1110, 1067, 1030, 1019, 1007; *m*/*z*=333 (M, 100); 296 (M−Cl, 31).

3.2.8. 3′,5′-Dichloro-3,4,5,6,3″,4″,5″,6″-octahydro-2*H*, 2″*H*-[1,2′,6′,1″]terpyridin-4′-ylamine (9b). Yellow solid, mp 41 °C ($C_{15}H_{22}Cl_2N_4$ requires C, 54.72; H, 6.73; N, 17.02. Found: C, 54.28; H, 7.06; N, 16.81); δ_H ($CDCl_3$) 4.78 (s, 2H; NH_2), 3.10–3.30 (m, 8H; CH_2), 1.50–1.75 (m, 12H; CH_2); δ_C ($CDCl_3$) 155.3, 148.2, 99.7, 50.4, 26.0, 24.7; ν_{max} (KBr) (cm^{-1}): 3480, 3380, 2935, 2918, 2847, 2827, 1611, 1598, 1553, 1541, 1422, 1373, 1283, 1258, 1217, 1117, 1076, 1007, 866; *m*/*z*=330 (MH^+, 100); 294 (M−Cl, 45); 244 (M−$C_5H_{10}N$, 24).

3.2.9. 2,3,5-Trichloro-6-(morpholin-4-yl)-4-amino-pyridine (10a). Colorless solid, mp 144 °C ($C_9H_{10}Cl_3N_3O$ requires C, 38.26; H, 3.57; N, 14.87. Found: C, 38.23; H, 3.12; N, 14.34); δ_H ($CDCl_3$) 5.11 (s, 2H; 10H), 3.77–3.90 (m, 4H; 9H), 3.25–3.40 (m, 4H; 8H); δ_C ($CDCl_3$) 155.6, 148.9, 144.2, 108.2, 104.3, 66.8, 49.5; ν_{max} (KBr) (cm^{-1}): 3445, 3334, 1622, 1559, 1525, 1417, 1367, 1254, 1112; *m*/*z*=283 (M, 100).

3.2.10. 3′,5′,6′-Trichloro-3,4,5,6-tetrahydro-2*H*-[1,2′]bipyridinyl-4′-ylamine (10b). Yellow oil. δ_H ($CDCl_3$) 5.04 (s, 2H; NH_2), 3.13–3.30 (m, 4H; CH_2), 1.50–1.77 (m, 6H; CH_2); δ_C ($CDCl_3$) 156.7, 148.7, 144.0, 107.3, 104.4, 50.4, 25.8, 24.4; *m*/*z*=281 (M, 100), 245 (M−Cl, 25); 86 ($C_5H_{10}N$, 31).

3.3. General procedure for the reaction of 2′,3′,5′,6′-tetrachloro-4-dimethylamino-[1,4]bipyridinyl-1-ylium chloride (1) with glycine

A suspension of pyridinium salt **1** (3.74 g, 10 mmol) in 100 mL of DMF was treated with sodium amide (1.96 g, 50 mmol) and glycine (1.5 g, 20 mmol) and heated for 5 h at 120 °C. After cooling, the reaction mixture was poured in water, and pH was adjusted to 5 with hydrochloric acid. The mixture was then evaporated to dryness, and the residue was chromatographed (silica gel, ethyl acetate/petroleum ether=1:4).

3.3.1. 2,3,5,6-Tetrachloro-4-(*N*-methylamino)-pyridine (7). Oil, δ_H ($CDCl_3$) 4.82 (s, 1H; 5H), 2.91 (s, 3H; 6H); δ_C ($CDCl_3$) 155.0, 148.5, 97.7, 41.5; ν_{max} (KBr) (cm^{-1}): 3498, 3397, 3945, 1601, 1553, 1484, 1396, 1325, 1045, 843, 705; *m*/*z*=247 (MH^+, 100), 214 (M−CH_4N, 75). No satisfactory elemental analysis achieved.

3.3.2. 2,3,5-Trichloro-4,6-di-(*N*-methylamino)-pyridine (8). Colorless solid, 69 °C ($C_7H_8N_3Cl_3$ requires C, 34.96; H, 3.35; N, 17.47. Found: C, 35.22; H, 2.90; N, 17.55); δ_H ($CDCl_3$) 5.07 (br s, 2H; 7H, 9H), 2.94 (s, 6H; 8H, 10H); δ_C ($CDCl_3$) 156.3, 148.8, 143.6, 106.5, 102.4, 41.4 (overlapped); ν_{max} (KBr) (cm^{-1}) 3502, 3402, 1601, 1563, 1525, 1397, 1327, 1043, 938; *m*/*z*=241 (MH^+, 100), 210 (M−CH_4N, 15).

3.3.3. 2,3,5,6-Tetrachloropyridine (11). A suspension of salt **1** (3.74 g, 10 mmol) in 100 mL of anhydrous 2-propanol was treated with sodium borohydride (0.57 g, 15 mmol) at rt and stirred for 6 h. Then, the solution was poured in diluted hydrochloric acid and extracted twice with diethyl ether. The organic layer was separated, evaporated, and chromatographed (silica gel, ethyl acetate/petroleum ether=1/1). All spectroscopic data are in agreement to an authentic sample.

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