The Ultraviolet Spectra of the Chloropyridines and Chlorinated Pyridines Possessing a Sulfur (-SR), Nitrogen (-NR₂), or Oxygen (-OR) Substituent in Either the 2 or 4-Position: A Convenient Method for Distinguishing such Positional Isomers

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The ultraviolet spectra for a series of 15 chlorinated pyridines which contain a sulfur, nitrogen or an oxygen substituent at either the 2 or 4-position have been examined. A correlation has been established between the position (2 vs 4) of the S, N, or O substituent on the chlorinated pyridines and their ultraviolet spectra. It was found that the chlorinated pyridines with S, N, or O substitution at the 2-position gave ultraviolet spectra whose longest wavelength absorption maxima were enhanced (moved to a greater wavelength and an increased extinction coefficient) when compared to the spectra of the 4-substituted isomers. The difference is great enough so that an easy identification of positional isomers can be made with a relatively high degree of confidence even when only one positional isomer is available. The ultraviolet spectra of all the chlorinated pyridines has been recorded, and it was observed that the number of chlorine atoms, and not their position, was the more significant factor in determining the overall character of the spectra.

During the course of our investigations with chlorinated pyridines, it became necessary to distinguish between isomeric pyridines with the general formula I and II.

X = -SR, -NR₂, -OR
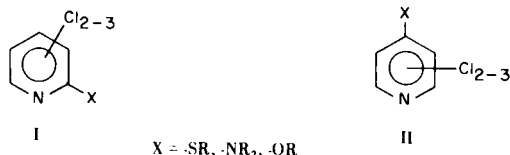
Ultraviolet spectroscopy appeared to have the potential for distinguishing such isomers in addition to being a rapid and convenient analytical tool. Concurrent with this need was a desire to understand the changes in the ultraviolet spectra observed when just chlorine atoms were systematically added to the pyridine ring.

Thus, we wanted to establish a structure-ultraviolet spectra correlation for pyridines I and II, and record the ultraviolet spectra of all the chlorinated pyridines. This paper describes such a correlation as well as the ultraviolet spectra of all the chlorinated pyridines.

Similar ultraviolet data has been reported for non- or mono-chlorinated pyridines containing a -SR, -NR₂ or -OR substituent (2-7). However, the spectra are so different from the polychlorinated analogs that structure identification by spectral comparison was hopeless (compare data in Tables I and II). Likewise, addition of only chlorine atoms

to the pyridine moiety produced spectral changes which appeared to preclude explanation by examining the spectra of only the mono-chlorinated pyridines.

Results

The ultraviolet spectra of the chlorinated pyridines I and II (methanol solution) were characterized by certain general features. Three absorption maxima were usually observed (see Table I); they were labeled Band I (< 230 nm), Band II (230-270 nm), and Band III, (> 270 nm) respectively. The intensity of these bands usually decreased in the order: Band I > Band II > Band III. The data recorded for Band I is open to question, as it was recorded near the lower limit of the instruments sensitivity and the solvent cut-off point.

The most striking relationship between the absorption maxima (methanol solution) for 2 and 4-substituted chloro-pyridines (I and II) was the distance (in nm) between the two longest wavelength absorptions (which were usually Band III and Band II; see Table I). Generally, the distance between these bands for the 2-substituted chloropyridines (I) was twice as large as for the 4-substituted derivatives (II). It is this relationship that is most diagnostic for distinguishing the position (2 or 4) of a chlorinated pyridine possessing a sulfur (-SR), nitrogen (-NR₂) or oxygen (-OR) substituent.

TABLE I (a)

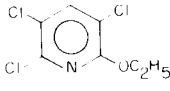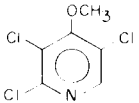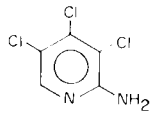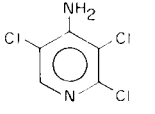Ultraviolet Spectra of 2- and 4- Substituted Polychloropyridines
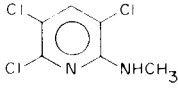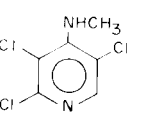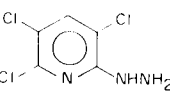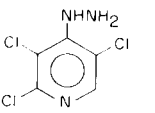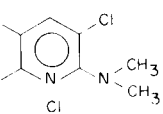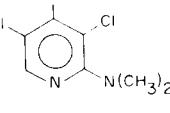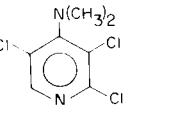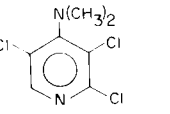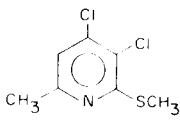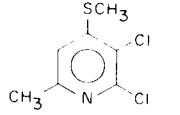
Compound	Band I	Band II	Band III	Solvent (b)
1.	----	234 (9,600)	298 (6,500)	CH_3OH
	----	236 (10,000)	299 (6,600)(c)	hexane
	----	234 (9,500)	298 (6,500)	H^+/CH_3OH
	----	234 (9,800)	298 (6,600)	OH^-/CH_3OH
2.	211 (41,000)	229 (8,500)	276 (2,000) / 283 (1,700)	CH_3OH
	----	228sh (9,200)	277 (1,900) / 285 (1,700)	hexane
	----	229sh (8,300)	275 (1,700) / 282sh (1,500)	H^+/CH_3OH
	----	----	276 (1,900) / 283 (1,800)	OH^-/CH_3OH
3.	215 (20,000)	244 (11,200)	322 (4,800)	CH_3OH
	215 (19,000)	240 (9,200)	313 (4,100)	hexane
	----	243 (6,600)	323 (3,500)	H^+/CH_3OH
	----	243 (7,600)	320 (3,200)	OH^-/CH_3OH
4.	213 (27,000)	248 (18,500)	278sh (1,700)	CH_3OH
	----	234 (10,300)	263sh (1,000)	hexane
	221 (21,000)	----	267 (23,100)	H^+/CH_3OH
	----	248 (18,900)	271sh (2,500)	OH^-/CH_3OH
5.	210 (12,000)	257 (15,300)	329 (6,100)	CH_3OH
	----	254 (13,100)	325 (5,900)	hexane
	----	257 (15,100)	329 (6,000)	H^+/CH_3OH
	----	251 (15,700)	329 (6,000)	OH^-/CH_3OH
6.	224 (23,000)	267 (9,900)	299 (2,300)	CH_3OH
	223 (26,000)	259 (8,600)	288 (1,600) / 298 (1,300)	hexane
	225 (21,000)	267 (9,200)	300sh (2,700)	H^+/CH_3OH
	226sh (24,000)	268 (9,500)	299sh (2,400)	OH^-/CH_3OH
7.	210 (13,000)	256 (12,400)	325 (5,200)	CH_3OH
	----	253 (10,900)	323 (4,800)	hexane
	----	242 (11,600)	306 (5,900)	H^+/CH_3OH
	----	230sh (8,300)	283 (3,700) / 330sh (900)	OH^-/CH_3OH
8.	224 (18,100)	265 (7,900)	295sh (2,600)	CH_3OH
	225 (26,000)	258 (7,800)	290sh (1,200)	hexane
	----	251sh (5,500)	283 (3,100) / 292sh (2,800)	H^+/CH_3OH
	----	----	284 (3,900) / 292 (3,100)	OH^-/CH_3OH
9.	214 (12,000)	270 (13,300)	328 (4,500)	CH_3OH
	211 (14,000)	269 (14,200)	328 (4,800)	hexane
	214 (12,000)	271 (13,400)	327 (4,500)	H^+/CH_3OH
	----	270 (13,200)	327 (4,400)	OH^-/CH_3OH
10.	217 (12,000)	272 (11,000)	322 (3,000)	CH_3OH
	217 (12,500)	270 (10,900)	321 (2,900)	hexane
	218 (14,000)	272 (9,900)	325 (2,600)	H^+/CH_3OH
	211 (51,000)	271 (10,600)	323 (3,000)	OH^-/CH_3OH
11.	225 (11,000)	249 (7,100)	304 (5,500)	CH_3OH
	227 (10,000)	248 (6,700)	293 (4,800)	hexane
	226 (14,000)	250 (9,400)	306 (5,700)	H^+/CH_3OH
	216 (23,000)	250 (8,000)	305 (5,600)	OH^-/CH_3OH

TABLE I (a) (Continued)

Compound	Band I		Band II		Band III		Solvent (b)
12	216	(15,000)	256	(10,700)	302	(5,900)	CH₃OH
	224	(17,000)	265	(12,800)	291sh	(3,000)	CH₃OH
	223	(19,000)	261	(10,500)	281	(2,600)	hexane
13					291	(2,000)	
	224	(18,000)	267	(12,800)	290sh	(3,100)	H⁺/CH₃OH
	212	(61,000)	267	(13,100)	290sh	(3,200)	OH⁻/CH₃OH
	232sh	(18,000)					

(a) Wavelengths are reported in nm and extinction coefficients as molar absorptivities. Spectra were recorded using a Perkin Elmer 202 Visible-ultraviolet spectrometer. (b) Methanolic base was prepared by diluting 1 ml. of 1N sodium hydroxide to 10 ml. with methanol. Methanolic acid was prepared by diluting 1 ml. of 1N sulfuric acid to 10 ml. with methanol. (c) Fine structure present.

TABLE II

Ultraviolet Spectra of 2- and 4-Substituted Pyridines
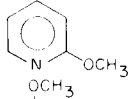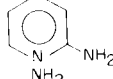Containing Either Zero or One Chlorine Atom
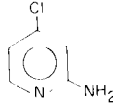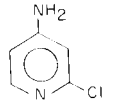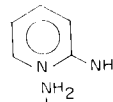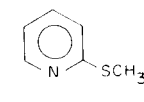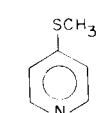
Compound	Band I		Band II		Band III		Solvent	Ref.
	<205	(>5,300)	269	(3,230)	----		pH 1	5
	222	(9,300)	235	(2,000)	----		pH 9	5
	----		229	(9,400)	287	(3,800)	pH 9	4
	241	(14,000)	265	(2,400)	----		pH 12	4
			263	(16,500)	----		pH 1	
	----		234.5	(11,500)	291.5	(3,900)	hexane	1
	----		235	(8,900)	270	(850)	hexane	1
	----		240	(13,000)	303.5	(3,300)	hexane	1
	----		234	(8,700)	272.5	(1.500)	hexane	1
	----		247	(8,700)	292	(4,200)	pH 6	6
	214		263	(12,500)	----		pH 9	4

TABLE III (a)

Ultraviolet Spectra of all the Chloropyridines

| Compound	Band I		Band II		Band III		Solvent (b)
(pyridine)			246sh	(1,800)	----		CH$_3$OH
			251	(2,500)			
			257	(2,700)			
			264	(1,800)			
			251	(1,800)(c)	----		hexane
			254sh	(4,600)	----		H$^+$/CH$_3$OH
			257	(5,000)			
			246sh	(1,800)	----		OH$^-$/CH$_3$OH
			251	(2,400)			
			257	(2,700)			
			263	(1,900)			
(4-chloropyridine)	215	(5,400)	254sh	(1,900)	----		H$^+$/CH$_3$OH
	230sh	(1,900)	259	(2,300)			
			266	(1,600)			
(3-chloropyridine)	213	(5,900)	263sh	(1,300)	274sh	(1,300)	CH$_3$OH
			268	(2,600)			
	213	(8,600)	263	(2,600)	275sh	(2,100)	hexane
			269	(2,800)			
	214sh	(4,500)	----		271	(3,800)	H$^+$/CH$_3$OH
	218	(12,600)	263sh	(2,300)	275sh	(2,000)	OH$^-$/CH$_3$OH
			268	(2,600)			
(2-chloropyridine)	212	(5,000)	260sh	(2,800)	271sh	(2,500)	CH$_3$OH
			264	(3,300)			
	211sh	(5,100)	253sh	(1,600)	271	(2,300)	hexane
			258	(2,300)			
			264	(3,000)			
	213sh	(5,300)	260sh	(2,700)	271sh	(2,400)	H$^+$/CH$_3$OH
			265	(3,300)			
	218	(12,200)	260sh	(2,900)	271sh	(2,500)	OH$^-$/CH$_3$OH
			265	(3,400)			
(3,5-dichloropyridine)	217	(5,600)	----		272sh	(2,300)	CH$_3$OH
					277	(2,700)	
					284sh	(2,200)	
	215	(5,800)	----		272sh	(2,300)	hexane
	218sh	(5,800)			277	(2,800)	
	232sh	(4,200)			285	(2,200)	
	216	(7,000)	----		271sh	(2,300)	H$^+$/CH$_3$OH
					277	(2,700)	
					273sh	(2,400)	
	219	(11,700)	----		271sh	(2,300)	OH$^-$/CH$_3$OH
					278	(2,700)	
					284sh	(2,300)	
(3,4-dichloropyridine)	214sh	(8,300)	261	(1,900)	275	(2,000)	CH$_3$OH
			267	(2,400)			
	214	(7,900)	261sh	(1,600)	275	(1,500)	hexane
	218sh	(6,900)	267	(1,900)			
	223	(4,400)					
	215sh	(7,400)	262sh	(1,700)	275	(1,900)	H$^+$/CH$_3$OH
			267	(2,300)			
	215sh	(7,400)	262sh	(1,800)	275	(1,900)	OH$^-$/CH$_3$OH
			267	(2,300)			
(2,4-dichloropyridine)	212sh	(7,000)	260sh	(1,900)	273	(2,700)	CH$_3$OH
			266	(2,600)			
	213sh	(7,900)	253sh	(1,100)	274	(2,000)	hexane
			265	(2,300)			
	212sh	(6,700)	260sh	(1,700)	273	(2,100)	H$^+$/CH$_3$OH

TABLE III (Continued)
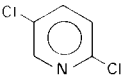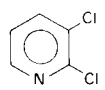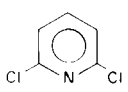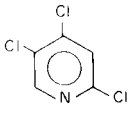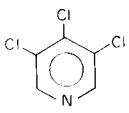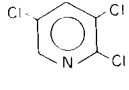
Compound	Band I		Band II		Band III		Solvent
			266	(2,400)			
	217	(14,000)	260sh	(2,400)	273sh	(2,400)	OH⁻/CH₃OH
			266	(2,900)			
	221	(9,200)	----		276	(2,800)	CH₃OH
					282sh	(2,200)	
	222	(11,800)	----		272sh	(2,100)(c)	hexane
					277	(3,600)	
					285	(2,100)	
	221	(9,600)	----		276	(2,700)	H⁺/CH₃OH
					283sh	(2,100)	
	214	(25,500)	----		276	(2,700)	OH⁻/CH₃OH
					283sh	(2,200)	
	218	(6,800)	----		273	(3,500)	CH₃OH
					278sh	(3,000)	
	218	(6,300)	266sh	(2,600)	272	(3,700)	hexane
	222sh	(5,000)	269	(2,800)	281	(3,000)	
	217	(7,300)	----		273	(3,500)	H⁺/CH₃OH
					279sh	(2,900)	
	214	(12,300)	----		273	(3,700)	OH⁻/CH₃OH
					279sh	(2,800)	
	219	(6,000)	----		272	(3,900)	CH₃OH
					278sh	(2,900)	
	218	(7,300)	269	(3,800)	273	(4,400)	hexane
	221sh	(6,700)			280	(3,200)	
	218	(6,000)	----		271	(4,100)	H⁺/CH₃OH
					277	(3,200)	
	218	(9,800)	---		271	(4,200)	OH⁻/CH₃OH
					277sh	(3,300)	
	223	(7,800)	----		277	(2,700)	CH₃OH
					283sh	(2,300)	
	220	(9,100)	----		278	(5,000)	hexane
	227sh	(8,800)			286	(4,300)	
	220	(8,300)	----		277	(2,700)	H⁺/CH₃OH
					284sh	(2,300)	
	213	(28,400)	----		277	(2,500)	OH⁻/CH₃OH
					283sh	(2,200)	
	228	(8,700)	----		283	(4,100)	CH₃OH
					289sh	(3,300)	
	225sh	(9,900)	----		279sh	(4,000)	hexane
	228	(10,100)			283	(4,600)	
					291	(3,500)	
	227	(9,700)	----		282	(4,400)	H⁺/CH₃OH
					289sh	(3,500)	
	215	(25,300)	---		282	(4,200)	OH⁻/CH₃OH
					289sh	(3,400)	
	226	(8,300)	----		283	(3,700)	CH₃OH
					290sh	(3,400)	
	226	(8,600)	----		277sh	(2,800)	hexane
					281sh	(3,500)	
					284	(4,000)	
					293	(3,100)	
	227	(8,900)	----		284	(4,100)	H⁺/CH₃OH
					290sh	(3,500)	
	216	(21,900)	----		284	(4,100)	OH⁻/CH₃OH
					290sh	(3,500)	
	220sh	(6,800)	----		273	(3,600)	CH₃OH
					280sh	(3,100)	

TABLE III (Continued)

Compound	Band I	Band II	Band III	Solvent
(chlorinated pyridine structure)	217sh (7,700)	267sh (2,600)	273 (3,700) 278 (3,200) 281 (3,200)	hexane
	217 (8,100)	----	273 (4,000) 280sh (3,500)	H⁺/CH₃OH
	215 (23,200)	----	272 (2,600) 279sh (3,200)	OH⁻/CH₃OH
(chlorinated pyridine structure)	222sh (6,600)	----	274 (2,800) 281sh (2,600)	CH₃OH
	219sh (6,900)	267sh (1,900)	274 (2,700) 282 (2,500)	hexane
	222sh (6,900)	265 (2,000)	273 (3,000) 280sh (2,600)	H⁺/CH₃OH
	215 (27,500)	266sh (2,000)	274 (2,800) 281sh (2,600)	OH⁻/CH₃OH
(chlorinated pyridine structure)	227 (9,400) 228 (10,600)	---- ----	282 (4,400) 278sh (4,400) 283 (5,000) 286sh (5,100) 291 (3,500)	CH₃OH hexane
	227 (9,400)	---	281 (4,400)	H⁺/CH₃OH
	215 (23,000)	----	283 (4,400)	OH⁻/CH₃OH
(chlorinated pyridine structure)	228sh (7,200)	----	284 (2,700) 292 (2,700)	CH₃OH
	228sh (9,600)	----	283 (2,800) 292 (2,700)	hexane
	228sh (6,900)	----	284 (2,600) 291 (2,600)	H⁺/CH₃OH
	230sh (8,200)	----	276sh (1,200) 283 (2,200) 293sh (2,300)	OH⁻/CH₃OH
(chlorinated pyridine structure)	213 (10,900) 231sh (7,300) 208 (26,500) 232 (8,100)	---- ----	282 (3,800) 288sh (3,500) 282 (3,900) 289sh (3,600)	CH₃OH hexane
	213 (11,700) 231sh (7,600)	---	282 (3,900) 288sh (3,800)	H⁺/CH₃OH
	216 (24,400) 235sh (7,500)	----	271sh (1,500) 280 (2,000) 289sh (1,700)	OH⁻/CH₃OH
(chlorinated pyridine structure)	---- ----	232 (10,000) 233 (9,900)	290 (5,300) 273sh (1,600) 278sh (2,500) 283sh (3,500) 287 (4,500) 292 (5,300) 296 (4,800) 302 (3,900)	CH₃OH hexane
	----	232 (9,800)	291 (5,200)	H⁺/CH₃OH
	----	232 (9,500)	296 (6,500)	OH⁻/CH₃OH
(chlorinated pyridine structure)	220 (11,800)	240sh (5,900)	291 (4,000) 299 (4,000)	CH₃OH
	214 (28,900)	241sh (5,900)	291 (3,800) 298 (3,800)	hexane
	220 (11,900)	239sh (6,500)	291 (4,000) 297 (4,000)	H⁺/CH₃OH
	219 (22,700)	283sh (7,800)	289 (3,300)	OH⁻/CH₃OH

TABLE III (Continued)

(a) Wavelengths are reported in nm and extinction coefficients as molar absorptivities. Spectra were recorded using a Perkin Elmer 202 Visible-Ultraviolet Spectrometer. The physical constants of the compounds were in agreement with those in the literature (8). (b) Methanolic base was prepared by diluting 1.0 ml. of 1 N sodium hydroxide to 10.0 ml. with methanol. Methanolic acid was prepared by diluting 1 ml. of 1 N sulfuric acid to 10.0 ml. with methanol. (c) Fine structure present.

Since the emphasis of this article is the utility of the ultraviolet spectra as a method for distinguishing positional isomers on the chlorinated pyridines I and II, only a few salient comments concerning their structures will be made. It is known that nucleophilic, aromatic displacement of a chloride on 2,3,5,6-tetrachloropyridine gives products arising only from displacement of the 2-chlorine atom. These products were taken as models for the 2-substituted isomers isolated from nucleophilic, aromatic-displacement reactions on 2,3,4,5-tetrachloropyridine where two isomeric products may be expected (eg. 3 and 4). The validity of this model was shown by the very similar spectra of compounds 9 and 10 where this series (9,10, and 11) were all prepared by unambiguous routes.

Turning attention to the ultraviolet spectra of the chlorinated pyridines, several general features were apparent (Table III). The total number of chlorine atoms have a more pronounced effect on the ultraviolet maxima for the longest wavelength absorption than does the position of the chlorine atoms on the ring. The longest wavelength absorption maxima appeared to increase (bathochromic shift of 7-8 nm) for each additional chlorine atom added to the ring. However, 3,5-dichloro substitution was an exception, and it appeared to cause an additional bathochromic shift of the long wavelength absorption. This shift was found to be 6-11 nm above the normal increment expected for addition of a single chlorine atom on the pyridine ring. Compare, for example, 2,4- and 2,6-dichloropyridine with 3,5-dichloropyridine. Also compare 2,4,6-trichloropyridine with 3,4,5-trichloropyridine.

Discussion

One interpretation of the data would require that the delocalization of electron(s) from the unshared pair of electrons on substituent X (for structure types I and II) in the electronically excited state is responsible for differences observed in the ultraviolet spectra of I and II. Thus, resonance forms III and IV would be considered as important contributors to their respective excited states.
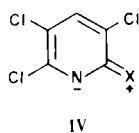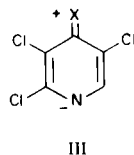

Qualitatively, resonance form IV would be expected to be more favored energetically than resonance form III. The

separation of charges is not as great in IV as in III and resonance form III is cross-conjugated whereas IV is not.

One result of a decreased electronic energy for IV relative to III would be an enhanced absorption at the longer wave-lengths in the ultraviolet spectrum of IV.

The effect of solvents on the ultraviolet spectra suggested a difference in the mode of electronic excitation for the chloropyridines and the chloropyridines containing an oxygen, nitrogen, or sulfur substituent. In direct contrast to the blue-shift noted when changing solvents (hexane to methanol) for oxygen, nitrogen, or sulfur-substituted chloropyridines, essentially no solvent shift was noted for Bands II and III in the simple chloropyridine series. In the former case, chlorine atoms could be viewed as inductively stabilizing a negative charge. In the latter case, the chlorine atoms could be viewed as contributing their non-bonded electrons directly to the π-system. This difference in the effects of chlorine atoms on the electronic excitation can be visualized with resonance pictures for p-chloroaniline and chlorobenzene.
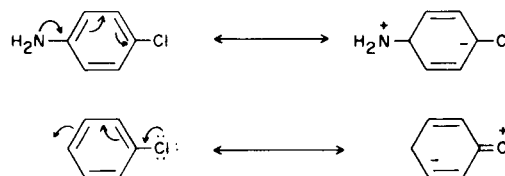
Due to solvation (hydrogen-bonding by methanol) of oxygen, nitrogen, or sulfur substituents and the near absence of solvation of chlorine atoms, the observed solvent effects are as predicted. This assumes the two modes of electronic excitation are weighted as suggested.

EXPERIMENTAL

Melting points were taken using a Thomas-Hoover capillary melting point apparatus and are uncorrected.

2-Ethoxy-3,5,6-Trichloropyridine (1).

Sodium 3,5,6-trichloro-2-pyridinate (1650 g.), sodium carbonate (39.8 g.), dimethylformamide (6 l.) were charged into a flask and heated to 48°. Ethyl iodide (1404 g.) was added with stirring over a period of 90 minutes while maintaining the temperature between 48-60°. The temperature was maintained for an additional 3½ hours at 55-58°. The reaction mixture was poured into ice-water (8 l.) after standing overnight at room temperature. This was extracted with dichloromethane (4 l.) and the dichloromethane layer was separated, washed twice with water, and concentrated under a reduced pressure. The residue was diluted with hexane (2 l.) and the insoluble material was collected by filtration and

discarded. The filtrate was concentrated under a reduced pressure and recrystallized from methanol. Several crops of crystals were obtained which are combined and recrystallized again from methanol to yield a fluffy, white solid (370 g.), m.p. 39.5-40°.

Anal. Calcd. for $C_7H_6Cl_3NO$: C, 37.12; H, 2.67; N, 6.18. Found: C, 37.2; H, 2.8; N, 6.2.·

4-Methoxy-2,3,5-trichloropyridine (2).

2,3,4,5-Tetrachloropyridine (217 g.), and methanol (2 l.) were charged into a 3 l. round bottom flask. This was cooled in an ice bath. Potassium hydroxide (66 g.) dissolved in methanol (250 ml.) was added over a period of 1½ hours, and the reaction mixture was allowed to stir an additional hour at ice bath temperature and then at room temperature for 2 hours. Finally, it was heated under reflux for one hour. The reaction mixture was allowed to stand overnight at room temperature and the potassium chloride was removed by filtration. The filtrate was concentrated under a reduced pressure and the residue recrystallized from methanol to yield a white solid (143 g., 67%); m.p. 62-63.5°.

Anal. Calcd. for $C_6H_4Cl_3NO$: C, 33.91; H, 1.90; N, 6.59. Found: C, 33.9; H, 2.1; N, 6.4.

2-Amino-3,4,5-Trichloropyridine (3).

6-Aminotrichloropicolinic acid (418 g.) was decarboxylated by heating in dimethylformamide (500 ml.) for 2 hours at 130°. Activated charcoal was added to the hot solution and then recovered by filtration. The filtrate was poured into ice-water and a solid was collected by filtration. It was recrystallized from methanol. Only one crop was saved to yield 210 g. of tan needles, m.p. 159-161°.

Anal. Calcd. for $C_5H_3Cl_3N_2$: C, 30.42; H, 1.53; N, 14.19. Found: C, 30.5; H, 1.7; N, 14.0.

4-Amino-2,3,5-trichloropyridine (4).

This material was obtained in a manner analogour to the preceding experiment, except 4-aminotrichloropicolinic acid was utilized as the starting material. The product was recrystallized from chloroform-hexane and then from methanol to give light tan crystals, m.p. 152-153°.

Anal. Calcd. for $C_5H_3Cl_3N_2$: C, 30.42; H, 1.53; N, 14.19. Found: C, 30.5; H, 1.6; N, 14.1.

2-Methylamino-3,5,6-trichloropyridine (5).

2,3,5,6-Tetrachloropyridine (100 g.) and aqueous methylamine (100 ml. of 40%) were mixed in a stainless-steel bomb and heated at 150° for 3½ hours. The reaction mixture was mixed with hot methanol (500 ml.), filtered and allowed to stand at room temperature overnight. Crystals were collected by filtration and dried to yield 59 g., m.p. 106-108°.

Anal. Calcd. for $C_6H_5Cl_3N_2$: C, 34.08; H, 2.38; N, 13.25. Found: C, 34.3; H, 2.5; N, 13.0.

4-Methylamino-2,3,5-trichloropyridine (6).

4-Methylsulfonyl-2,3,5-trichloropyridine (10 g.) was dissolved in dimethylformamide (100 ml.) and methylamine (5 ml., 40% aqueous) was added. The reaction mixture was stirred for an hour, poured onto crushed ice and the crystals were collected by filtration. The product was recrystallized from methanol to yield 3.6 g., m.p. 132.5-133.5°.

Anal. Calcd. for $C_6H_5Cl_3N_2$: C, 34.08; H, 2.38; N, 13.25. Found: C, 34.2; H, 2.7; N, 13.3.

3,5,6-Trichloro-2-hydrazinopyridine (7).

One mole (216 g.) of 2,3,5,6-tetrachloropyridine was added to 800 ml. of ethanol in a 2 l. reaction flask equipped with a mechani-

cal stirrer, water-cooled condenser, thermometer and dropping funnel. Two moles of hydrazine hydrate (100 g.) was added and the reaction mixture was heated under reflux for 1.5 hours. After cooling and diluting with water, the solid product was collected by filtration, washed well with water, air dried, and recrystallized from benzene. Yield, 140 g. (66%), m.p. 158.5-161.5°.

Anal. Calcd. for $C_5H_4Cl_3N_3$: C, 28.27; H, 1.90; N, 19.78. Found: C, 28.2; H, 1.6; N, 19.6.

2,3,5-Trichloro-4-hydrazinopyridine (8).

This compound was prepared in a similar manner to 7 and the product recrystallized from methanol. The yield of white solid, m.p. 92.5-95.5° was 51%.

Anal. Calcd. for $C_5H_4Cl_3N_3$: C, 28.27; H, 1.90; N, 19.78. Found: C, 28.1; H, 1.8; N, 19.9.

2-Dimethylamino-3,5,6-trichloropyridine (9).

2,3,5,6-Tetrachloropyridine (217 g.) was dissolved in dimethylformamide and heater under reflux for 26 hours. The black reaction solution was poured onto crushed ice and a solid collected by filtration. The solid was dissolved in hexane and then filtered. The filtrate was cooled in an acetone-dry ice bath to yield a pink solid, 140 g. (62%), m.p. 34-35°.

Anal. Calcd. for $C_7H_7Cl_3N_2$: C, 37.28; H, 3.13; N, 12.42. Found: C, 37.2; H, 3.1; N, 12.2.

2-Dimethylamino-3,4,5-trichloropyridine (10).

This compound was prepared from 2,3,4,5-tetrachloropyridine and dimethyl amine in benzene, using the procedure of Roberts and Suschitzky (9) where 100% of the 2-substituted isomer is obtained by reaction pentachloropyridine and dimethyl amine in benzene. The product, 10, melted at 64-65°.

Anal. Calcd. for $C_7H_7Cl_3N_2$: C, 37.28; H, 3.13; N, 12.42. Found: C, 37.2; H, 3.1; N, 12.2.

4-Dimethylamino-2,3,5-trichloropyridine (11).

2,3,5-Trichloro-4-methylaminopyridine (6) was methylated according to the procedure of Cook and Wakefield (10) who methylated 4-methylaminotetrachloropyridine. 2,3,5-Trichloro-4-methylaminopyridine (42.3 g.) was dissolved in diethyl ether and cooled to -75°. A 2N solution (100 ml.) of n-butyl lithium was added dropwise over a period of twenty minutes. The reaction was stirred for an additional ½ hour at -75° and then allowed to warm at room temperature for 15 minutes. The temperature was reduced to -75° again and dimethyl sulfate (25 g.) was added during 10 minutes. The temperature was allowed to come to room temperature and then heated under reflux for 45 minutes. The reaction solution was washed with water, dried, and concentrated under a reduced pressure to yield 46.5 g. of residue. This was dissolved in a mixture of benzene-hexane and cooled to yield 2 crops (17.5 g.) of starting material (6). The filtrate was concentrated under a reduced pressure and distilled, b.p. 82° at 0.1 mm Hg to yield 8.65 g. of a light yellow oil identified as the product 11; nmr (deuteriochloroform): 3.0 δ (6H, singlet, $N(CH_3)_2$), 8.1 δ (1H, singlet, pyridyl proton).

Anal. Calcd. for $C_7H_7Cl_3N_2$: C, 37.28; H, 3.13; N, 12.42. Found: C, 37.1; H, 3.0; N, 12.1.

6-Methylthio-4,5-dichloro-2-picoline (12) and 4-Methylthio-5,6-dichloro-2-picoline (13).

A 3-neck 1-liter flask was fitted with a dry-ice condenser, and stirring paddle. The flask was charged with sodium hydride (12.4 g.), tetrahydrofuran (300 ml.), and methylmercaptan. 4,5,6-Trichloro-2-picoline was dissolved in tetrahydrofuran (100 ml.) and

added dropwise over a period of 10 minutes. Dimethylformamide (200 ml.) was added to facilitate the reaction of the methylmercaptan and sodium hydride. The reaction mixture was then warmed to 40° for one hour after which time it was shown by vpc that all the starting material was consumed. The reaction was poured onto ice and a solid was collected by filtration, washed with water and air dried to yield 49.2 g. of a buff-colored solid. This solid was analyzed by vpc (2 ft. SE 30 column, isothermal at 225°) which showed 4 components present: (retention time/relative amount), 1.4 minutes/17, 2.4 minutes/68, 4 minutes/5, 5 minutes/10. The first two components in order of elution were later identified as the monothio ethers, **13** and **12** respectively. The third component (4 minutes) from the vpc chromatogram was unidentified, and the fourth component (5 minutes) was isolated (3 g.) by column chromatography (150 g. silica gel eluted with benzene) and identified as: 4,6-bis(methylthio)-5-chloro-2-picoline; m.p. 96-98°, nmr (DMSO-d₆): 2.38, 2.42, and 2.50 δ (methyl singlets), 6.47 δ (pyridyl proton).

The buff colored solid (49.2 g.) was dissolved in hot cyclohexane (350 ml.) and some insoluble material removed by filtration. The filtrate was allowed to cool slowly to yield gold-colored crystals, 28 g., m.p. 126-128°. This material was shown by elemental analysis and nmr spectrum (deuteriochloroform): 2.49 δ (6H, singlet, -SCH₃, and -CH₃ on pyridine ring) to be the 4-methylthio-5,6-dichloro-2-picoline (**13**), since it is known that the 4-position of a substituted pyridine is more susceptible to nucleophilic attack than the position adjacent to the nuclear nitrogen atom. Thus, the mono-methylthio material in greater amount is the 4-methylthio **13**, and the material in lesser amount is the 6-methylthio compound, **12**. The UV data (see Table I) is also consistent with these structures.

The mother liquors from the isolation of **13** were concentrated under a reduced pressure and a distillation was attempted. The

product crystallized and clogged the distillation apparatus (b.p. about 80° at 0.5 mm Hg). This solid was isolated (2.8 g.) and identified as the 6-methylthio-4,5-dichloro-2-picoline (**12**); m.p. 72-74°, nmr (deuteriochloroform): 2.48 and 2.57 δ methyl singlets and 7.02 δ (pyridyl proton).

Compound 12.

Anal. Calcd. for C₇H₇Cl₂NS: C, 40.40; H, 3.39; N, 6.73. Found: C, 40.7; H, 3.6; N, 6.8.

Compound 13.

Anal. Calcd. for C₇H₇Cl₂NS: C, 40.40; H, 3.39; N, 6.73. Found: C, 40.2; H, 3.5; N, 6.9.

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