Oxidative Chlorination of 1,10-Phenanthroline and Its Derivatives by Phosphorus Pentachloride in Phosphoryl Chloride

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Synopsis. Some of aromatic hydrogens of 1,10-phenanthroline and its derivative, 1,10-propano-bridged 1,10-phenanthroline-2,9(1*H*,10*H*)-dione, were oxidatively substituted by chlorine atoms with excess amount of phosphorus pentachloride in phosphoryl chloride to give the polychlorinated products.

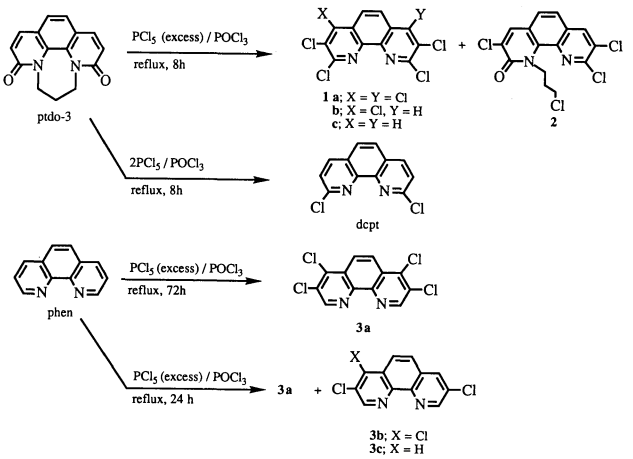
Conversion of 2- and 4-pyridinones to the corresponding chloro-substituted pyridines is known to be an effective method to obtain pyridine derivatives having useful functional groups.[1-3] The familiar reagent is phosphoryl chloride containing phosphorus pentachloride,[1-3] which is added to increase the activity of phosphoryl chloride.[4]

Recently we reported that the method was also useful for chlorination of 1,10-bridged 1,10-phenanthroline-2,9(1*H*,10*H*)-dions to give 2,9-dichloro-1,10-phenanthroline (dcpt).[5] Conversion to dcpt depended on the length of bridged chain, i.e., a propano-bridged derivative (ptdo-3) gave dcpt but an ethano-bridged one (ptdo-2) did not. In the present work, we attempted to control the opening of bridged chains in ptdo-3 and -2 by changing the amount of phosphorus pentachloride. In the presence of *excess* amount of phosphorus pentachloride, oxidative chlorine substitution of some aromatic hydrogens of ptdo-3 occurred, yielding a mixture of polychlorinated derivatives of 1,10-phenanthroline (phen). Such oxidative chlorination also took place in the parent phen, giving the tetrachloro-phen exclusively in almost quantitative yield.

Results and Discussion

Refluxing ptdo-3 in phosphoryl chloride containing two molar amount of phosphorus pentachloride for 8 h gave dcpt in 66% yield (Scheme 1).[5] Chlorination in the absence of phosphorus pentachloride also gave dcpt, in 55% yield. On the other hand, the chlorination product with excess amount of phosphorus pentachloride was quite different. Chlorination of ptdo-3 with ten molar amount of phosphorus pentachloride gave a mixture of polychlorinated phens, 2,3,4,7,8,9-hexachloro-, 2,3,4,8,9-pentachloro-, and 2,3,8,9-tetrachloro-phen (**1a**—**c**, respectively) and a phenanthrolinone, 3,8,9-trichloro-1-(3-chloropropyl)-1,10-phenanthrolin-2(1*H*)-one (**2**) (Scheme 1).

A mixture of **1a**—**c** was obtained as the first fraction of column chromatography. The presence of three components was detected by HPLC analysis. Isolation of **1a**—**c** in preparative amounts by using HPLC were unsuccessful because of low solubilities of these products in methanol. Mass spectrum of the mixture suggested that these were poly (≥4, ≤6) chlorinated phens. Although 2- and 9-chlorines could be introduced in the



Scheme 1.

similar manner to the aforesaid chlorinations, additional chlorines should be introduced by oxidative procedure. ^{1}H NMR spectrum of the mixture (Table 1) was explicable only by considering that the additional chlorines were located 3,8- (**1c**), 3,4,8- (**1b**), and 3,4,7,8- (**1a**) positions.[7] The molar ratios of **1a**:**1b**:**1c** estimated by integral of ^{1}H NMR signals were 1 : 1.1 : 0.4.

The compound **2** revealed three signals of equivalent integral in aliphatic region of ^{1}H NMR spectrum (Table 2) and C=O stretching band at 1642 cm^{-1} in IR spectrum. One of the pyridinone structures should still remained in **2**. Electronic spectrum, which is sensitive to formal π-conjugated systems of phen derivatives,[8] supported the phenanthrolinone structure of **2** (Fig. 1). Spectral pattern of **2** was quite similar to that of another phenanthrolinone 1-methyl-1,10-phenanthrolin-2(1*H*)-one (**8**), while the spectral pattern of a mixture of **1a**—**c** was quite similar to that of dcpt (Fig. 1).[9] The molecular formula shown by mass spectrum and elemental analysis was $C_{15}H_{10}Cl_4N_2O$. Chlorine atom at 9-position of aromatic ring and that in 3-chloropropyl group could be introduced by opening of bridged chain, and two additional chlorines should be done by oxidative chlorination. Additional chlorine atoms were determined to be at 3- and 8-positions by ^{1}H NMR spectroscopy[7] (Table 2).

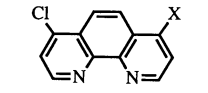
On the other hand, another phenanthrolinedione ptdo-2 gave only a tarry intractable mixture and unreacted ptdo-2 both in the absence of and in the presence of excess amount of phosphorus pentachloride. This result was quite similar to that in the presence of two molar amount of phosphorus pentachloride.[5]

Oxidative chlorination was also observed in the parent phen (Scheme 1). Refluxing phen in phosphoryl

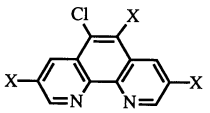
Table 1. ^{1}H NMR Spectra of **1a**—**c**, **3a**—**c**, and Related Chloro-Substituted Phens[a] in $CDCl_3$

Compound	δ (position)				J/Hz (assignment)		Ref. for preparation
1a	—	—	—	8.37s (5, 6)			This work
1b	—	—	—	8.26d (5)	9.2 ($J_{5,6}$)		This work
	—	—	8.33s (7)	7.88d (6)			
1c	—	—	8.33s (4, 7)	7.79s (5, 6)			This work
3a	9.10s (2, 9)	—	—	8.31s (5, 6)			This work
3b	b)	—	—	7.79d (5)	9.2 ($J_{5,6}$) 1.3($J_{2,4}$)		This work
	b)	—	8.27d (7)	8.25d (6)			
3c	b)	—	8.17d (4, 7)	7.71s (5, 6)	2.4 ($J_{2,4}$)		This work
phen	9.14dd (2, 9)	7.57dd (3, 8)	8.18dd (4, 7)	7.72s (5, 6)	8.1 ($J_{3,4}$) 1.8 ($J_{2,4}$)	4.4 ($J_{2,3}$)	Commercial
dcpt	—	7.63d (3, 8)	8.21d (4, 7)	7.81s (5, 6)	8.5 ($J_{3,4}$)		5)
4[a]	9.06d (2, 9)	7.73d (3, 8)	—	8.32s (5, 6)	4.8 ($J_{2,3}$)		
5[a]	9.03d (2)	7.69d (3)	—	8.22d (5)	9.2 ($J_{5,6}$) 4.4 ($J_{2,3}$)	8.1 ($J_{7,8}$) 4.4 ($J_{8,9}$)	
	9.19d[c] (9)	7.64dd (8)	8.25dd (7)	7.91d (6)	1.8 ($J_{7,9}$)		3)
6[a]	9.23dd (2)	7.74dd (3)	8.69dd (4)	—	8.3 ($J_{3,4}$) 4.2 ($J_{2,3}$)	8.1 ($J_{7,8}$) 4.4 ($J_{8,9}$)	Commercial
	9.17dd (9)	7.63dd (8)	8.17dd (7)	7.91s (6)	1.5 ($J_{2,4}$)	1.8 ($J_{7,9}$)	
7[a]	9.08d (2, 9)	—	8.64d (4, 7)	—	2.0 ($J_{2,4}$)		6)[c]

a) **4**: 4,7-dichloro-phen, **5**: 4-chloro-phen, **6**: 5-chloro-phen, and **7**: 3,5,6,8-tetrachlo-phen. b) In the spectrum of a mixture of **3a**—**3c**, the signals of 2- and 9-positions of **3b** and **3c** was observed as an apparent multiplet of δ=9.10—9.02. c) Broad doublet. d) The values are also cited from the reference.



X = Cl; **4**
X= H; **5**



X = H; **6**
X = Cl; **7**

chloride with ten molar amount of phosphorus pentachloride for 24 h gave a mixture of chlorinated products. HPLC analysis indicated that three major components, **3a**—**c**, were produced. Mass and ^{1}H NMR (Table 1)[7] spectra of the mixture were reasonable by considering that these components were 3,4,7,8-tetrachloro- (**3a**), 3,4,8-trichloro- (**3b**), and 3,8-dichloro- (**3c**) phen. Isolation of **3a**—**c** in preparative amounts by using HPLC was also unsuccessful because of low solubilities of these products in methanol. When reaction time was lengthened to 72 h, one of the three components **3a** was obtained exclusively in almost quantitative yield.[10]

Sulfuryl chloride in thionyl chloride is known to be another chlorination reagent for phen.[6] Phosphorus pentachloride in phosphoryl chloride, however, was much more useful reagent because this gave only one product under appropriate conditions, while the product in the use of sulfuryl chloride is a mixture of several derivatives carrying a variety of numbers (4—8) of chlorine substituents.[6]

Experimental

IR spectra were recorded on a JASCO IR-810 Spectrometer. Electronic spectra were taken on a Shimadzu UV-265FS Spectrophotometer at 20°C. ^{1}H NMR spectra were recorded on a JEOL FX-90Q Spectrometer at room temperature. HPLC analyses were performed by Shimadzu LC-8A system at 40°C (column: Shim-pack PREP-ODS(H) Kit; 4.6 mm ϕ ×25 cm L, eluent: methanol).

Materials. 1,10-Phenathroline (phen) monohydrate and 5-chloro-1,10-phenanthroline (**6**) were commercially obtained and used without purification. Preparation of 6,7-dihydro-5*H*-[1,4]diazepino[1,2,3,4-*lmn*][1,10]phenanthroline-3,9-dione (ptdo-3), 5,6-dihydropyrazino[1,2,3,4-*lmn*][1,10]phenanthroline-3,8-dione (ptdo-2), and 2,9-dichloro-1,10-phenanthroline (dcpt) was reported elsewhere.[5] The following compounds were prepared by literature procedure: 4,7-dichloro-1,10-phenanthroline (**4**); mp 254—256°C (lit,[3] 249—250°C), 4-chloro-1,10-phenanthroline (**5**); 163—165°C (lit,[11] 163—165°C), 1-methyl-1,10-phenanthrolin-2(1*H*)-one (**8**); mp 129—130°C (lit,[2] 129—130°C). Other chemicals were also obtained commercially, and some of them were purified by conventional methods prior to use.

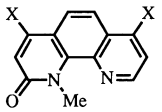
Chlorination in the Presence of Excess Amount of Phosphorus Pentachloride. Chlorination of ptdo-3: A mixture of ptdo-3 (1.24 g, 4.92 mmol), phosphorus pentachloride (10.3 g, 49.2 mmol), and phosphoryl chloride (20 cm^3) was refluxed for 8 h. After evaporating the phosphoryl chloride, ice water was added: The solution was then made basic with aqueous ammonia. Pale brown precipitates were collected by filtration, dried, and subjected to column chromatography (Merck Kieselgel 60, dichloromethane). Removal of solvent of the first fraction gave 0.47 g of a mixture of 2,3,8,9-tetrachloro-1,10-phenanthroline (**1c**), 2,3,4,8,9-pentachloro-1,10-phenanthroline (**1b**), and 2,3,4,7,8,9-hexachloro-1,10-phenanthroline (**1a**), as white needles. MS (EI, 70 eV) *m/z* (rel intensity) 390 (21), 388 (46), 386 (56), 384 (31), 356 (23), 354 (68), 352 (100), 350 (68), 319 (20), 318 (25), 317 (38), 316 (32), 315 (30), and 314 (15). ν_{max} (KBr) 1550m, 1526m, 1448s, 1376s, 1210s, 1160s, 958s, 850s, 724 cm^{-1}. The molar ratios of **1a** : **1b** : **1c** were not changed by repeated recrystallyzation from benzene.

Evaporation of solvent of the second fraction gave 0.85 g

Table 2. ^{1}H NMR Spectra of **2** and Related Phenanthrolinones[a] in $CDCl_3$

Compound	δ (position)				J/Hz (assignment)	Ref. for preparation
2	—	—	8.01s (4)	7.58s 7.59s		This work
	—	—	8.29s (7)	(5, 6)	($J_{1,2}$ and $J_{2,3}$ in 3-chloropropyl group, respectively).	
	5.20t, 3.89t, 2.58q[b] (3-chloropropyl group)					
8	—	6.91d (3)	7.77d (4)	7.55s (5, 6)	9.3 ($J_{3,4}$) 8.2 ($J_{7,8}$) 4.1 ($J_{8,9}$) 1.9 ($J_{7,9}$)	2)
	8.94dd (9)	7.50dd (8)	8.17dd (7)			
	4.49s (methyl group)					
9[a]	—	7.08s (3)	—	8.03d (5)	9.2 ($J_{5,6}$) 4.6 ($J_{8,9}$)	This work
	8.80d (9)	7.62d (8)	—	8.17d (6)		
	4.34s (methyl group)					

a) **9**: 4,7-dichloro-1-methyl-1,10-phenanthrolin-2(1*H*)-one. b) Quintet.



X = H; **8**
X = Cl; **9**

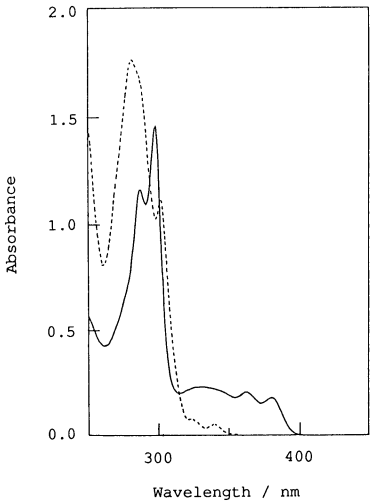


Fig. 1. Electronic spectra of **2** (——, 3.33×10^{-5} mol dm^{-3}) and a mixture of **1a**—**c** (---, 13 mg dm^{-3}) in acetonitrile.

(46%) of 3,8,9-trichloro-1-(3-chloropropyl)-1,10-phenanthrolin-2(1*H*)-one (**2**) as white needles. Mp (benzene) 225—228 °C. MS (EI, 70 eV) *m/z* (rel intensity) 378 (M^{**+}, 20), 376 (M^{*+}, 40), 374 (M^+, 31), 343 (35), 341 (94), and 339 (100). Elemental analysis: Found: C, 47.82; H, 2.78; N, 7.38%. Calcd for $C_{15}H_{10}Cl_4N_2O$: C, 47.91; H, 2.68; N, 7.45%. ν_{max} (KBr) 1642vs, 1616s, 1442s, 1366s, 1172s, 902s, 758s cm^{-1}.

Chlorination of phen: A mixture of phen monohydrate (1.00 g, 5.04 mmol), phosphorus pentachloride (10.5 g, 50.4 mmol), and phosphoryl chloride (15 cm^3) was refluxed for 72 h, and then treated as described above. Removal of solvent after subjection to column chromatography (Merck Kieselgel 60, chloroform) gave 1.51 g (94%) of 3,4,7,8-tetrachloro-1,10-phenanthroline (**3a**) as white needles. Mp (benzene) 291—294 °C. MS (EI, 70 eV) *m/z* (rel intensity) 322 (M^{***+}, 11), 320 (M^{**+}, 48), 318 (M^{*+}, 100), 316 (M^+, 86). Elemental analysis: Found: C, 45.04; H, 1.40; N, 8.52%. Calcd for $C_{12}H_4Cl_4N_2$: C, 45.33; H, 1.27; N, 8.81%. ν_{max} (KBr) 1572m, 1462s, 1406s, 1352s, 1186s, 820s, 720s cm^{-1}.

The reaction for 24 h gave 1.31 g of mixture of **3a**—**3c**. MS (EI, 70 eV) *m/z* (rel intensity) 322 (10), 320 (48), 318 (100), 316 (77), 286 (16), 284 (48), 282 (50), 250 (17), 248 (37).

4,7-Dichloro-1-methyl-1,10-phenanthrolin-2(1*H*)-one (9). This was prepared from **4**[3] by a procedure analogous to that of preparation of **8** from phen.[2] 2.15 g (8.63 mmol) of **4** gave 1.80 g (75%) of **9** as brown plates. Mp (benzene) 209—213 °C. MS (EI, 70 eV) *m/z* (rel intensity) 282 (M^{**+}, 8), 280 (M^{*+}, 40), 278 (M^+, 65), 215 (100). Elemental analysis: Found: C, 55.84; H, 3.01; N, 10.11%. Calcd for $C_{13}H_8Cl_2N_2O$: C, 55.94; H, 2.89; N, 10.04%. ν_{max} (KBr) 1664vs, 1496s, 1458s, 1018s, 878s, 840s cm^{-1}.

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7) A notable deshielding effect due to chloro substituents was recognized by interaction of chlorine groups in 4-, 5-, 6-, and 7-positions with the protons in their *peri*-positions, 5-, 4-, 7-, and 6-positions, respectively (observed in **4**—**7** and **9**, $\Delta\delta$=ca. 0.5). Any other locational relationship between chlorine and hydrogen did not give such large effects ($\Delta\delta<0.2$).

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9) In spite of the presence of three components, the electronic spectrum of a mixture of **1a**—**c** was quite simple (Fig. 1). This is not in conflict with the aforesaid conclusion because effects of chlorine substituents at 4- and 7-positions of phen to λ_{max} values are almost negligible: M. N. Ackermann and L. V. Interrante, *Inorg. Chem.,* **23**, 3904 (1984).

10) This result indicated that chlorination of phen proceeded stepwise. But in the case of ptdo-3, less chlorinated products were not converted to more chlorinated ones even if reaction time was lengthened to 72 h. And chlorinations of 3,4,7,8-positions of dcpt did not take place under similar conditions, indicating dcpt was not intermediate of **1a**—**c**. Different reaction mechanism might be present.

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