Synthesis of 2,9-Dichloro-1,10-phenanthroline from *N,N'*-Annelated Phenanthrolinediones

Masaki YAMADA,* Yoshio NAKAMURA, Shigeyasu KURODA, and Ichiro SHIMAO
Department of Industrial Chemistry, Faculty of Engineering, Toyama University, 3190 Gofuku, Toyama 930
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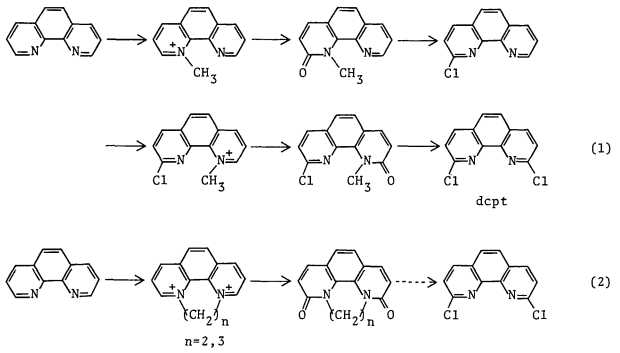
Synopsis. Though the chlorination of an *N,N'*-annelated phenanthrolinedione, 3,6,7,9-tetrahydro-5*H*-[1,4]diazepino-[1,2,3,4-*lmn*][1,10]phenanthroline-3,9-dione, gave 2,9-dichloro-1,10-phenanthroline, another dione, 3,5,6,8-tetrahydropyrazino[1,2,3,4-*lmn*][1,10]phenanthroline-3,8-dione, did not. It demonstrated a simultanous introduction of two chlorine substituents to non-substituted 1,10-phenanthroline via only the former intermediate.

A dichloro derivative of 1,10-phenanthroline (phen), 2,9-dichloro-1,10-phenanthroline (dcpt), is an attractive starting material to construct highly functionalized molecules carrying the phen unit.[1,2] However, using a conventional method dcpt was prepared stepwise by tedious repeating of the chlorination procedure to non-substituted phen (Eq. 1 in Scheme 1).[2,3] *N,N'*-Annelated diones which are prepared by a two-step reaction from non-substituted phen are potential precursors of dcpt. Two chlorine substituents were simultaneously introduced into the diones to give dcpt, as shown in Eq. 2 in Scheme 1.[4]



(1)

(2)

Scheme 1.

In this work concerning the preparation of dcpt, two phenanthrolinediones, 3,5,6,8-tetrahydropyrazino[1,2,3,4-*lmn*][1,10]phenanthroline-3,8-dione (ptdo-2)[4] and 3,6,7,9-tetrahydro-5*H*-[1,4]diazepino[1,2,3,4-*lmn*][1,10]-phenanthroline-3,9-dione (ptdo-3), were subjected to the chlorination procedure. Although dcpt was successfully obtained from propano-bridged dione, ptdo-3, no desired product was prepared from ethano-bridged dione, ptdo-2, under the same conditions. A similar influence of the annelating chain length was observed in analogous diones derived from 2,2'-bipyridine (bpy), 4,6,7,9-tetrahydrodipyrido[1,2-*a*:2,1-*c*]pyrazine-4,9-dione (bpdo-2)[5] and 4,7,8,10-tetrahydrodipyrido-[1,2-*a*:2,1-*c*][1,4]diazepine-4,10-dione (bpdo-3), suggesting the indispensablity of some strain in a ring constructed with an annelating chain in this type of chlorination procedure.

Results and Discussion

Phenanthrolinediones, ptdo-2,[4] ptdo-3, and bipyridinediones, bpdo-2,[5] and bpdo-3 were prepared by the oxidation of the corresponding *N,N'*-annelated bis(quaternary salt)'s[6–8] with potassium hexacyanofer-

Table 1. Spectral Properties of Diones

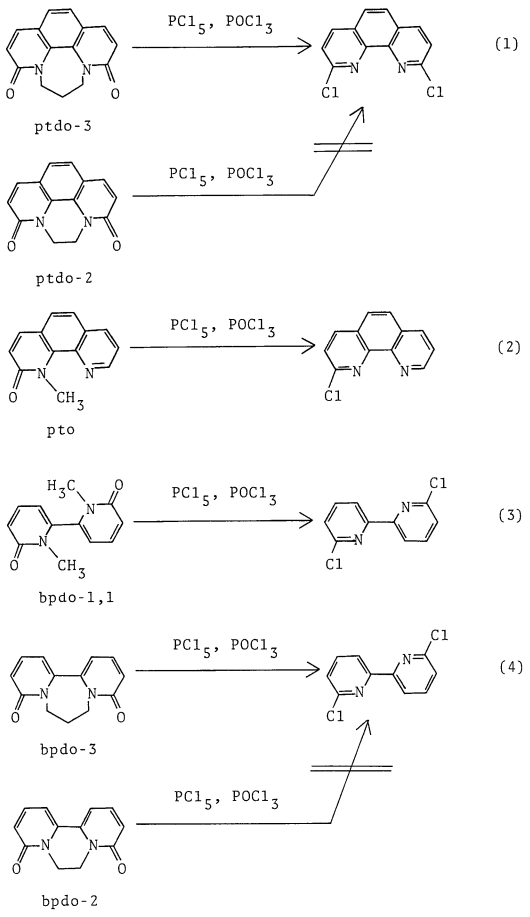
Material	IR/cm^{-1} (KBr)	^{1}H NMR/δ ($CDCl_3$)	λ_{max}/nm (methanol)
ptdo-2	3045w	7.78 (d, J=9.4 Hz, 2H, $H_{1,10}$)	291
	2919w	6.84 (d, J=9.4 Hz, 2H, $H_{2,9}$)	307
	1658vs	7.38 (s, 2H, $H_{11,12}$)	322
	1609s	4.48 (s, 4H, $H_{5,6}$)	337
ptdo-3	3049w	7.72 (d, J=9.5 Hz, 2H, $H_{1,11}$)	290
	2919w	6.79 (d, J=9.5 Hz, 2H, $H_{2,10}$)	312
	1649vs	7.36 (s, 2H, $H_{12,13}$)	327
	1610s	4.32 (t, J=6.5 Hz, 4H, $H_{5,7}$)	342
		2.45 (q,[a] J=6.5 Hz, 2H, H_6)	
bpdo-2	3010w	7.43 (dd, J=9.0 and 7.3 Hz, 2H, $H_{2,11}$)	373
	1645vs	6.69 (dd, J=9.0 and 1.1 Hz, 2H, $H_{3,10}$)	
	1575s	6.72(dd, J=7.3 and 1.1 Hz, 2H, $H_{1,12}$)	
	1531s	4.32 (s, 4H, $H_{6,7}$)	
bpdo-3	3050w	7.38 (dd, J=9.4 and 6.8 Hz, 2H, $H_{2,12}$)	343
	2957w	6.71 (dd, J=9.4 and 1.3 Hz, 2H, $H_{3,11}$)	
	1657s	6.37 (dd, J=6.8 and 1.3 Hz, 2H, $H_{1,13}$)	
	1580s	5.18 (m, 2H, $H_{6,8}$)	
	1540s	3.06 (m, 2H, $H_{6,8}$), 2.22 (m, 2H, H_7)	

a) Quintet.

rate(III) in an aqueous alkaline solution.[2,3,9] The spectral properties of the diones are summarized in Table 1.

A reaction of propano-bridged dione, ptdo-3, with phosphorus pentachloride dissolved in phosphoryl chloride under reflux for 8 h successfully gave dcpt in 66% yield (Eq. 1 in Scheme 2). Although the yield of the intermediate ptdo-3 was lower than that of the corresponding step in a conventional method (Eq. 1 in Scheme 1), this method is attractive because dcpt can be obtained using only three steps from non-substituted phen, without the six tedious steps required in the conventional method.[2,3] A similar treatment of ethano-bridged dione, ptdo-2, on the contrary, gave a tarry intractable mixture as the major product. Furthermore, a noticeable amount (14%) of unchanged ptdo-2 was recovered (see Experimental section).

The chlorination of *N,N'*-annelated diones might proceed through the same mechanism as in the well-known chlorination reaction of a monoone of phen, 1-methyl-2-hydro-1,10-phenanthroline-2-one (pto, Eq. 2 in Scheme 2),[2,3] and a non-bridged dione of bpy, 1,1'-dimethyl-6,6'-dihydro-2,2'-bipyridine-6,6'-dione (bpdo-1,1, Eq. 3 in Scheme 2).[9] However, the rings constructed with an annelating chain must be open in the present case. A comparison of the two cases, ptdo-2 and ptdo-3, suggests that a strain in the ring was necessary to produce dichloro derivatives, i.e., more strained dihydrodiazepine rings in ptdo-3[10] were opened and finally gave dichloro derivatives, while the complex reaction proceeded in ptdo-2 carring less strained dihydropyrazine rings without ring-opening.



Scheme 2.

This hypothesis was supported by an investigation of analogous bpy derivatives. Though propano-bridged dione derived from bpy, bpdo-3, gave 6,6'-dichloro-2,2'-bipyridine (dcbp) in 11% yield after the reaction of bpdo-3 with phosphorus pentachloride dessolved in phosphoryl chloride under reflux for 20 h, ethano-bridged dione, bpdo-2, gave only a tarry intractable mixture (Eq. 4 in Scheme 2). In addition, the yield of dcbp from bpdo-3 (11%) was much lower than that of dcpt from ptdo-3 (66%). The lower yield of dcbp was rationalized by considering that the strain in the dihydrodiazepine ring in bpdo-3 was released by twisting two pyridone rings around each other.[6,10,11] A twisted conformation of bpdo-3 was confirmed by a largely blue-shifted absorption band, compared with that of bpdo-2, and a magnetic non-equivalence of two of the methylene protons at the 6- or 8-positions indicated by ^{1}H NMR (Table 1).[6,11] The rigid, planar structure of the phenanthrolinedione moiety in ptdo-3 was supported by a small difference in the electronic spectra between that of ptdo-2 and ptdo-3. An ^{1}H NMR measurement of ptdo-3 showed that two of the methylene protons at the 5- or 7-positions were magnetically equivalent, which suggested that the conformation could not be fixed in *twisted stable form* at room temperature.[7,8]

A well-known chlorination procedure of pto and bpdo-1,1 might also be assisted by some strains existing in the starting pyridones. A repulsion between the methyl group and the lone pair of 10-nitrogen seems to be exist in pto, and two pyridone rings in bpdo-1,1 (λ_{max} in electronic spectra; 316 nm in methanol) seem to twist around each other by a larger angle than that in bpdo-3 (Table 1).

In conclusion, a simultanous dichlorination of 2- and 9-positions of phen was successfully achieved in shorter steps by using ptdo-3 as the phenanthroline-dione intermediate. The reaction depends upon the length of the chain and a certain strain in the rings constructed with the annelating chain was indispensable to open the ring forming dichloro-derivatives.

Experimental

Spectral Measurements. IR spectra were recorded on a JASCO IR-810 Spectrophotometer. ^{1}H NMR spectra were measured with a JEOL JNM-FX90Q Spectrometer at room temperature. Electronic spectra was recorded on a Shimadzu UV-265FS Spectrophotometer at 20 °C.

Bis(quanternary salt)'s. 5,6-Dihydropyrazino[1,2,3,4-*lmn*]-[1,10]phenanthroline-4,7-diium dibromide (phenq-2·Br_2),[7] 6,7-dihydropyrido[1,2-*a*:2,1-*c*]pyrazine-5,8-diium dibromide (bpyq-2·Br_2),[6] and 6*H*-7,8-dihydrodipyrido[1,2-*a*:2,1-*c*][1,4]-diazepine-5,9-diium dibromide (bpyq-3·Br_2),[6] were obtained according to a method described in the literature. The synthesis of 6,7-dihydro-5*H*-[1,4]diazepino[1,2,3,4-*lmn*][1,10]-phenanthroline-4,8-diium dibromide (phenq-3·Br_2)[8] was modified as follows: 5 g of 1,10-phenanthroline monohydrate and 25 g of 1,3-dibromopropane dissolved in 30 cm^3 of

Table 2. Modification for Preparation of Diones[a)]

Material	Reaction temperature	Extraction		Column eluent[b)]	Yield
	°C	System	Solvent		%
ptdo-2	40 (3 h)	Solid-liquid	Chloroform	Chloroform	17
ptdo-3	<5	Solid-liquid	Chloroform	20:1 (v/v)-dichloromethane–methanol	30
bpdo-2	Room temperature	Solid-liquid	Hot benzene	—	8.9
bpdo-3	<5	Liquid-liquid	Dichloromethane	Dichloromethane	37

a) General procedure: see text, b) Stationary phase: Merck Kieselgel 60.

nitrobenzene was stirred at 120 °C for 3 h. A yellow precipitate was collected by filtration and washed with benzene. Recrystallization from 5:1 (v/v) ethanol–water gave 8.1 g (84%) of phenq-3·Br_2 as yellow needles.

Diones. All diones, ptdo-2,[4] ptdo-3, bpdo-2,[5] and bpdo-3, were prepared by oxidation of the corresponding *N,N'*-annelated bis(quaternary salt)'s[6–8] with potassium hexacyanoferrate(III) in an aqueous solution. The general procedure was carried out as follows: To an ice-cooled solution of potassium hexacyanoferrate(III) (58.6 g) and sodium hydroxide (26.8 g) in water (100 cm^3) were added in small portions a solution of phenq-3·Br_2 (7.6 g) in water (50 cm^3), whilst maintaining the temperature under 5 °C. The resulting mixture was neutralized by a dropwise addition of concentrated hydrochloric acid with cooling, and then evaporated to dryness. A residual brown solid was extracted with chloroform. The extracted brown solid after removing the chloroform was subjected to column chromatography (Merck Kieselgel 60–20:1(v/v)–dichloromethane–metahnol). Evaporation of eluent and recrystallization from methanol gave 1.5 g (30%) of 3,6,7,9-tetrahydro-5*H*-[1,4]diazepino-[1,2,3,4-*lmn*][1,10]phenanthroline-3,9-dione (ptdo-3) as pale yellow needles. Mp>320 °C. Found: C, 71.41; H, 4.73; N, 10.94%. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10%.

Three other diones (ptdo-2, bpdo-2, and bpdo-3) were prepared by a similar procedure, i.e., a reaction in an aqueous solution, extraction, column chromatography (if necessary), and recrystallization from methanol. Modifications for individual cases are summarized in Table 2. From phenq-2·Br_2 (4.4 g) 0.5 g (17%) of 3,5,6,8-tetrahydropyrazino-[1,2,3,4-*lmn*][1,10]phenanthroline-3,8-dione (ptdo-2) was obtained as yellow needles. Mp 295—297 °C. Found: 70.26; H, 4.24; N, 11.55%. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76%. From bpyq-2·Br_2 (20.0 g) 1.1 g (8.9%) of 4,6,7,9-tetrahydrodipyrido[1,2-*a*:2,1-*c*]pyrazine-4,9-dione (bpdo-2)[5] was obtained as yellowish brown cubes. Mp 313—314 °C (lit,[5] 313—315 °C). From bpyq-3·Br_2 (4.7 g) 1.1 g (37%) of 4,7,8,10-tetrahydrodipyrido-[1,2-*a*:2,1-*c*][1,4]diazapine-4,10-dione (bpdo-3) was obtained as pale yellow needles. Mp>320 °C. Found: C, 68.52; H, 5.39; N, 12.16%. Calcd for $C_{13}H_{12}N_2O_2$:C, 68.41; H, 5.30; N, 12.27%.

Chlorination. Chlorination of ptdo-3: A mixture of ptdo-3 (1.7 g), phosphorus pentachloride (3.0 g), and phosphoryl chloride (20 cm^3) was refluxed for 8 h. After removing the phosphoryl chloride by evaporation, ice water was added: the solution was then basified with aqueous ammonia. A pale-brown precipitate was dried, extracted with hot benzene, and subjected to column chromatography (Merck Kieselgel 60–dichloromethane). Evaporation of the eluent and recrystallization from dichloromethane gave 1.1 g (66%) of dcpt as colorless needles. Mp 249—250 °C (lit,[2] 249—250 °C).

Chlorination of ptdo-2: It was performed similarly, and tarry materials were obtained as precipitates from an aqueous solution basified with aqueous ammonia. The filtrate was evaporated to dryness, and unreacted ptdo-2 was recovered from the residual solid as a chloroform extract.

Chlorination of bpdo-3 and -2: These were performed similarly by refluxing for 20 h. Bpdo-3 (0.8 g) gave 0.09 g (11 %) of dcbp,[9] and bpdo-2 gave only tarry, unidentified black material.

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