

Christopher J. Chandler, Leslie W. Deady and James A. Reiss

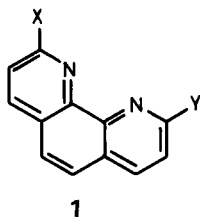
Organic Chemistry Department, La Trobe University, Bundoora, Vic. 3083, Australia

Received October 22, 1980

A series of symmetrically disubstituted compounds, with substituents linked to the ring through a carbon atom, has been prepared from 2,9-dimethyl-1,10-phenanthroline. Nmr data are also reported.

J. Heterocyclic Chem., **18**, 599 (1981).

In this paper we report on the synthesis of symmetrical 2,9-disubstituted-1,10-phenanthrolines (**1**, X = Y), where the substituents are linked to the ring by a carbon atom. Such compounds are potentially interesting as chelating agents and as starting materials for the synthesis of macrocyclic systems.



2 X = Y = CH ₃	7 X = Y = CHNOH
3 X = Y = CHO	8 X = Y = CH ₂ NH ₂
4 X = Y = CO ₂ H	9 X = Y = CH ₂ OH
5 X = Y = CN	10 X = Y = CH ₂ Br
6 X = Y = CO ₂ CH ₃	11 X = Y = CBr ₃
	12 X = Y = CCl ₃

While the analogous monosubstituted compounds (**1**, Y = H) are well known, comparatively little work has been reported on the symmetrically disubstituted compounds. The dialdehyde **3** has been prepared by selenium dioxide oxidation of **2** (no details given), and used in macrocycle formation (**1**), though an earlier report on this oxidation gave an unsymmetrical compound (**1**, X = CHO, Y = CO₂H) as the product (**2**). Preparation of **3**, the diacid **4**, and dinitrile **5** are reported in a Russian journal of limited availability (**3**). In this paper we report details of the preparation of a number of derivatives of interest.

The commercially available **2** was the starting point of the synthetic scheme. This was oxidised with selenium dioxide to **3**. Further oxidation with nitric acid gave **4** which was converted to the ester **6** with methanol and hydrogen chloride. The dialdehyde is a useful intermediate. It was also converted to the oxime **7**, which could then be dehydrated with acetic anhydride to give the nitrile **5**, or hydrogenated over palladium/charcoal to give the aminomethyl derivative **8**. The dialdehyde was also reduced with sodium borohydride to the hydroxy-

methyl compound **9**, from which the bromomethyl derivative **10** was readily prepared. As prepared, **3** and **7** were not analytically pure but the subsequent derivatives gave satisfactory analyses.

Bromination of the dimethyl compound was carried out under a variety of conditions in an attempt to directly prepare **10**, but without success. Under most conditions a mixture of products was formed. Reaction with two moles of bromine in carbon tetrachloride gave a compound assigned as the hydrobromide perbromide of **2**; elemental analysis indicated the presence of three bromine atoms and the nmr spectrum showed that no hydrogens had been replaced.

Replacement of all the methyl hydrogens to give the bis-tribromomethyl compound **11** was readily achieved by reaction with bromine in acetic acid. Hydrolysis with aqueous sulphuric acid had previously been used (**4**) to convert the monotribromomethyl compound to the corresponding acid (**1** X = CO₂H, Y = H) but these conditions did not affect the bis tribromomethyl compound, possibly for solubility reasons. Conversion of **11** to **4** was achieved, however, with hot 80% nitric acid.

Attempts to prepare a bischloromethyl compound by reacting **2** with a controlled amount of *N*-chlorosuccinimide were also unsuccessful. An excess of this reagent gave the bis(trichloromethyl) compound **12** in good yield.

Identification of the reaction products was made on the basis of analysis (a number of the compounds were obtained as hydrates) and spectral data. These symmetrically substituted compounds have simple proton resonance spectra for the aromatic protons, consisting of an AB pattern of H-3,4(7,8), and a singlet for H-5(6). These data are given in Table 1.

The proton decoupled ¹³C nmr spectra of the phenanthrolines were also determined and the data are shown in Table 2. The assignments were made by comparison with those of several dimethylphenanthrolines determined by Marker, Canty and Brownlee (**5**) and are in agreement with those previously published. Also, the proton coupled ¹³C nmr spectra of **2** and **12** showed most of the expected 1-bond and 3-bond couplings. In particular, **2** showed C-4 as a doublet (J_{CH} = 162 Hz) and C-3 as a doublet of

Table 1
¹H Nmr Data for 2,9-Disubstituted-1,10-phenanthrolines

Compound No.	Solvent	Chemical Shift (δ ppm)			
		H-3, 8 (a)	H-4, 7 (a)	H-5, 6 (b)	Other
2	deuteriochloroform	7.45	8.03	7.65	2.9 (CH ₃), 3.0 (H ₂ O)
3	DMSO	8.30	8.75	8.25	10.45 (CHO)
4	DMSO	8.45	8.75	8.20	3.3 (H ₂ O)
5	DMSO	8.45	8.90	8.30	
6	deuteriochloroform	8.33	8.37	7.85	2.7 (H ₂ O), 4.1 (CH ₃)
7	DMSO	8.20	8.55	8.05	8.5 (CH=), 12.0 (OH)
8	deuterium oxide	7.95	8.65	7.98	4.8 (CH ₂)
9	DMSO	7.90	8.50	7.95	4.95 (d, J = 7 Hz, CH ₂), 5.65 (t, OH)
10	deuteriochloroform	7.85	8.25	7.75	4.95 (CH ₂)
11	DMSO	8.55	8.80	8.25	
12	DMSO	8.45	8.85	8.25	

(a) Centre of doublet, J = 9 Hz. (b) Singlet.

Table 2
¹H Decoupled ¹³C Nmr Data for 2,9-Disubstituted-1,10-phenanthrolines

Compound No.	Solvent	Chemical Shift (δ ppm)						Substituent
		C-2	C-10b	C-4	C-4a	C-5	C-3	
2	deuteriochloroform	159.2	145.1	136.2	126.7	125.3	123.4	25.8
2.HBr ₃	DMSO	158.9	141.3	136.5	127.5	126.5	126.4	56.1
3	DMSO	151.9	145.0	137.9	131.0	128.8	119.8	193.3
4	DMSO	148.2	144.6	138.1	130.4	128.3	123.4	166.2
6	deuteriochloroform	148.1	145.5	137.5	130.7	128.3	123.9	165.9 and 53.2
7	DMSO	149.3	144.5	137.3	127.0	128.7	119.6	152.3
8.(HClO ₄) ₂	DMSO	153.5	142.0	138.8	127.0	127.5	122.9	42.9
9	DMSO	162.1	144.2	136.7	127.4	125.8	120.3	64.9
10	deuteriochloroform	157.4	144.6	137.4	128.1	126.6	123.5	34.7
11	DMSO	158.6	141.5	138.7	128.7	127.6	120.1	a
12	DMSO	156.7	142.6	139.4	129.4	128.0	120.0	98.0

(a) Resonance was not observed.

quartets (J_{CH} = 164 and J_{CCCH} = 4 Hz). No 2-bond coupling between either C-3 or C-4 and the corresponding adjacent hydrogen was observed. Similarly, the spectrum of **12** showed C-3 and C-4 as doublets (J_{CH} = 168 and 166 Hz, respectively).

EXPERIMENTAL

Mass spectra were obtained at 75 eV and infrared spectra as potassium bromide discs. Melting points are uncorrected.

1,10-Phenanthroline-2,9-dicarboxaldehyde (**3**).

A mixture of **2** (3 g.) and selenium dioxide (7.5 g.) in dioxan containing 4% water (200 ml.) was heated under reflux for 2 hours and then filtered through celite while hot. The dialdehyde **3**, (2.4 g., 70%) separated from the cold filtrate as yellow crystals, m.p. 231-232° (tetrahydrofuran);

ir: 1720, 1610, 1570, 1360, 1290, 1250, 870, 775 cm⁻¹; ms: m/e (%) 237 (15), 236 (67), 207 (69), 206 (23), 179 (100), 178 (83).

1,10-Phenanthroline-2,9-dicarboxylic acid (**4**).

Compound **3** (0.5 g.) in 80% nitric acid (10 ml.) was heated under reflux for 3 hours. The solution was cooled, poured onto ice, and the precipitated solid was recrystallized from methanol to give the diacid, **4** (as the monohydrate) (0.37 g., 61%), m.p. 238° dec.; ir: 3650-2800, 1725, 1570, 1520, 1460, 880, 775, 730 cm⁻¹; ms: m/e (%) 268 (4), 251 (6), 234 (4), 224 (27), 207 (13), 179 (100), 178 (58).

Anal. Calcd. for C₁₄H₁₀N₂O₅: C, 58.7; H, 3.5; N, 9.8. Found: C, 58.3; H, 3.7; N, 9.65.

The tribromomethyl, **11**, and trichloromethyl, **12**, compounds also gave the diacid when reacted in this manner.

2,9-Bis(carbomethoxy)-1,10-phenanthroline (**6**).

A solution of **4** (0.5 g.) in methanol (100 ml.), was saturated with dry

hydrogen chloride and heated under reflux for 2.5 hours. Dichloromethane (100 ml.) was added to the cooled solution and this was washed with water (2 x 50 ml.), saturated sodium hydrogen carbonate solution (2 x 50 ml.) and brine (2 x 50 ml.). The organic phase was dried and concentrated *in vacuo*. The solid residue was recrystallized from ethanol to give the diester, **6** (as the monohydrate) (0.37 g., 67%) as yellow plates, m.p. 213-214°; ir: 3625-3150, 1730, 1650, 1570, 1455, 1290, 1210, 990, 890, 820, 730 cm⁻¹; ms: m/e (%) 296 (4), 266 (11), 252 (4), 239 (20), 238 (100), 207 (4), 180 (49), 179 (24), 178 (47), 177 (38).

Anal. Calcd. for C₁₆H₁₄N₂O₂: C, 61.1; H, 4.5; N, 8.9. Found: C, 61.0; H, 4.5; N, 9.15.

2,9-Bis(hydroxymethyl)-1,10-phenanthroline (**9**).

A solution of **3** (0.5 g.) and sodium borohydride (0.1 g.) in ethanol (50 ml.) was heated under reflux for 2 hours. The mixture was then concentrated, and the residue recrystallized from water to give the dialcohol, **9** (0.35 g., 68%) as yellow needles, m.p. 197-198° dec.; ir: 3600-3100, 1635, 1605, 1520, 1175, 860 cm⁻¹; ms: m/e (%) 240 (98), 239 (100), 220 (42), 210 (64), 208 (51), 192 (59), 180 (43), 178 (38).

Anal. Calcd. for C₁₄H₁₂N₂O₂: C, 70.0; H, 5.0; N, 11.7. Found: C, 69.7; H, 5.1; N, 11.4.

2,9-Bis(bromomethyl)-1,10-phenanthroline (**10**).

A solution of **9** (0.5 g.) and hydrobromic acid (20 ml., 48%) was heated under reflux for 2 hours and then cooled on ice and treated with solid sodium carbonate until precipitation was complete. Recrystallization from aqueous ethanol gave the bromo compound **10** (0.55 g., 79%) as red plates. Column chromatography on silica gel [dichloromethane/ethyl acetate (5:1)] gave **10** as a pale yellow solid, m.p. 110-111°; ms: m/e (%) 368 (8), 366 (16), 364 (8), 285 (12), 283 (12), 206 (15), 205 (15), 81 (94), 79 (100).

Anal. Calcd. for C₁₄H₁₂Br₂N₂: C, 43.8; H, 3.15; N, 7.3. Found: C, 44.2; H, 3.4; N, 7.4.

1,10-Phenanthroline-2,9-dicarboaldoxime (**7**).

A solution of **3** (0.5 g.), hydroxylamine hydrochloride (1 g.) and pyridine (2 ml.) in ethanol (30 ml.) was heated under reflux for 2 hours. The resulting brown precipitate was recrystallized from ethanol to give the dioxime, **7**, m.p. decomposes slowly above 243°; ir: 3600-2800, 1625, 1515, 1120, 1105, 1005, 1000, 875, 825 cm⁻¹; ms: m/e (%) 266 (17), 265 (40), 248 (10), 223 (55), 204 (38), 179 (100), 178 (75).

1,10-Phenanthroline-2,9-dicarbonitrile (**5**).

A solution of **7** (0.5 g.) in acetic anhydride (10 ml.) was heated under reflux for 2 hours and then cooled on ice. The solid which formed was collected and more was obtained on addition of sodium carbonate to the filtrate. The combined solids were recrystallized from acetone to give the dinitrile **5** (0.35 g., 75%) as a pale yellow powder, m.p. > 350°; ir: 2250, 1615, 1495, 860, 740, 600 cm⁻¹; ms: m/e (%) 231 (22), 230 (100), 204 (47), 203 (20), 178 (29), 177 (18).

Anal. Calcd. for C₁₄H₆N₄: C, 73.0; H, 2.6. Found: C, 72.8; H, 2.8.

2,9-Bis(aminomethyl)-1,10-phenanthroline (**8**).

A solution of **7** (0.5 g.) in ethanol (100 ml.) containing 2% perchloric acid was hydrogenated at atmospheric pressure, over 10% palladium on charcoal. The solution was then heated to boiling, filtered through celite while hot and the filtrate concentrated *in vacuo* until precipitation was complete. The precipitate was recrystallized from ethanol-ether to give the amine **8** as the diperchlorate hemihydrate (0.5 g., 50%), m.p. 283-285° dec.; ir: 3600-2600, 1500, 1150, 1125, 1100, 1050, 875 cm⁻¹.

Thermogravimetric analysis showed a loss of 0.58 moles of water per mole of salt.

Anal. Calcd. for C₁₄H₁₇Cl₂N₄O_{8.5}: C, 37.5; H, 3.8; N, 12.5. Found: C, 37.9; H, 3.8; N, 12.3.

2,9-Dimethyl-1,10-phenanthroline Bromide Perbromide.

A solution of bromine (0.75 g.) in carbon tetrachloride (75 ml.) was added to a stirred solution of **2** (0.5 g.) in carbon tetrachloride. After 4 hours the yellow product was collected and recrystallized from ethanol to give the perbromide (0.8 g., 77%) as yellow needles, m.p. 112-113°; ¹H nmr (DMSO): δ 3.1 (s, 6, CH₃), 6.6-7.3 (s, 1, NH), 8.1 (d, 2, J = 9 Hz, H-3,8), 8.25 (s, 2, H-5,6) 8.9 (d, 2, H-4,7); ms: m/e (%) 209 (9), 208 (54), 207 (18), 162 (152), 160 (100), 158 (57), 81 (18), 79 (18).

Anal. Calcd. for C₁₄H₁₃N₂Br₃: C, 37.45; H, 2.9; Br, 53.4. Found: C, 37.3; H, 2.9; Br, 52.9.

2,9-Bis(tribromomethyl)-1,10-phenanthroline (**11**).

To a stirred solution of **2** (1 g.) and anhydrous sodium acetate (4.4 g.) in acetic acid (150 ml.) at 70°, was added bromine (4.4 g.) in acetic acid (20 ml.) over 0.5 hour. The reaction mixture was kept at 70° for a further 2 hours and then cooled. Water was added and the resultant solid was recrystallized from methanol to give the bromo compound **11**, (2.6 g., 76%) as a yellow solid, m.p. 196-197°; ir: 1550, 1350, 1300, 1060, 990, 880 cm⁻¹; ms: M⁺ peaks about 682 and a complex isotopic pattern in accord with sequential loss of bromines.

Anal. Calcd. for C₁₄H₆Br₆N₂: C, 24.7; H, 0.9; N, 4.1. Found: C, 24.65; H, 0.9; N, 4.2.

2,9-Bis(trichloromethyl)-1,10-phenanthroline (**12**).

A solution of **2** (1.25 g.) and *N*-chlorosuccinimide (1.9 g.) in dry carbon tetrachloride (100 ml.) was stirred and heated under reflux for 15 hours while being irradiated with a tungsten lamp (100 w). Additional *N*-chlorosuccinimide (1.9 g.) was then added and the reaction conditions were maintained for a further 2 hours. The mixture was then cooled, extracted with water (2 x 50 ml.), and the organic phase was dried and concentrated. The solid residue was recrystallized from ethanol to give the chloro compound **12** (1.7 g., 70%) as yellow needles, m.p. 212-214°; ir: 1600, 1510, 1375, 1115, 900, 870, 825 770, 730 cm⁻¹; ms: M⁺ peaks about 414 and a complex isotopic pattern in accord with sequential loss of chlorines.

Anal. Calcd. for C₁₄H₆Cl₆N₂: C, 40.5; H, 1.5; N, 6.75. Found: C, 40.3; H, 1.7; N, 6.9.

Acknowledgment.

We are grateful to Monsanto (Australia) Ltd., for the gift of a quantity of 2,9-dimethyl-1,10-phenanthroline.

REFERENCES AND NOTES

- (1) M. M. Bishop, J. Lewis, T. D. O'Donoghue and P. R. Raithby, *Chem. Commun.*, 476 (1978).
- (2) M. Seyhan and W. C. Fernelius, *Chem. Ber.*, **91**, 469 (1958).
- (3) V. M. Dziomko and B. V. Parusnikov, *Metody Poluch. Khim. Reakt. Prep.*, 112, 285, 289 (1974); *Chem. Abstr.* **83**, 178874q, 178875r, 178876s (1975).
- (4) H. A. Goodwin and R. N. Sylva, *Aust. J. Chem.*, **20**, 217 (1967).
- (5) A. Marker, A. J. Canty and R. T. C. Brownlee, *ibid.*, **31**, 1255 (1978).