

NEW DERIVATIVES OF meso-(TETRA-4-PYRIDYL)PORPHINE AND THEIR REACTIONS

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Some reactions of Co-meso(tetra-4-pyridyl)porphine were carried out, and a cyanopyridine complex was isolated. New water-soluble complexes based on Co-meso(tetra-4-N-hydroxyethylpyridyl)porphine were obtained. Aliphatic, aromatic, and heterocyclic amines were examined as ligands.

The effect of the structure and functional substituents of the porphyrine molecule on its biological activity can be examined by studying a large number of different synthetic porphyrines.

The purpose of the present work is to synthesize some cyanamine cobalt complexes of meso(tetra-4-pyridyl)porphine (TPyP), a structural analog of vitamin B₁₂, and to prepare water-soluble analogs of some previously described unsymmetric cobalt complexes [1]. Aliphatic, aromatic, and heterocyclic amines were used as ligands on the central cobalt atom.

The reaction of a chloroform-methanol solution of CoTPyP (2) with 48% hydrobromic acid gave meso-(tetra-4-pyridyl)porphinobromocobalt (III) (3) CoBrTPyP. Treatment of the latter with cyclohexylamine gave the complex 4, also obtained directly from CoTPyP in solution by reaction with cyclohexylamine hydrobromide in cyclohexylamine [1].

Treatment of CoBrTPyP 3 or the complex 4 with excess KCN in methanol gave the complex 5, in which cobalt is present as an anion. By refluxing in glacial acetic acid, followed by chromatography on Al₂O₃ (Brockmann activity grade II), the dicyano complex 5 was converted to the monocyno derivative 6, which with pyridine gave a quantitative yield of the cyanopyridine complex 7.

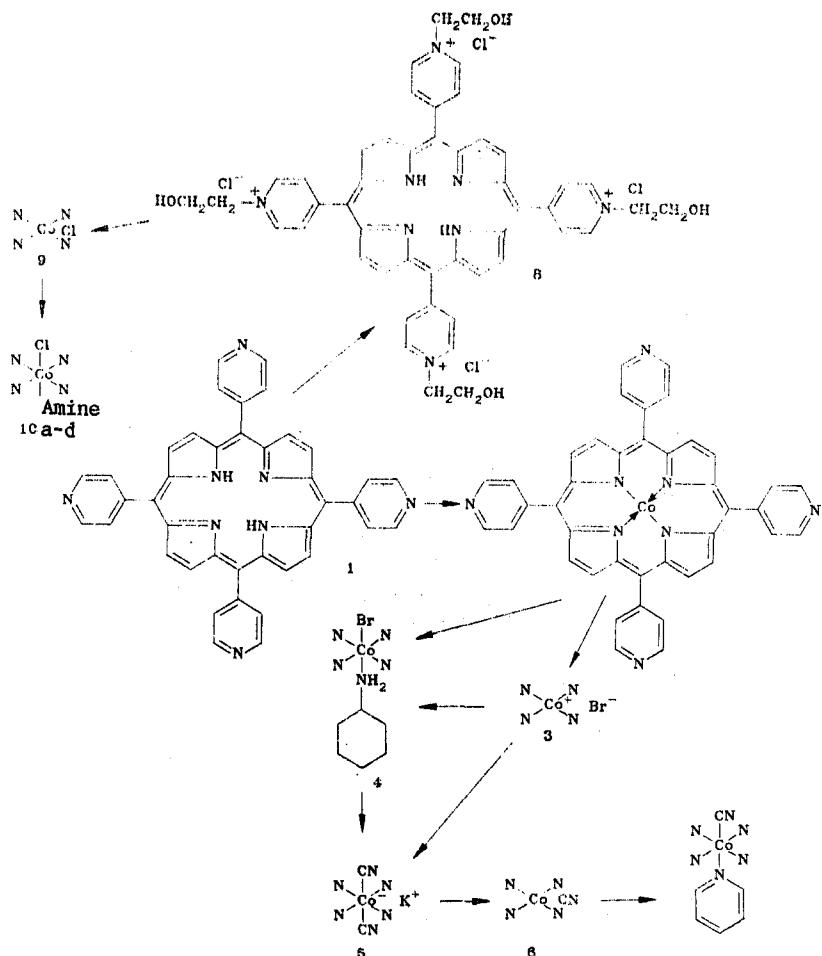
Attempts to synthesize the imidazole and benzimidazole cyano-derivatives of CoTPyP were not successful; in neither case was the complex isolated.

The reaction of meso-(tetra-4-pyridyl)porphine (TPyP) 1 [3] with excess ethylene chlorohydrin gave the tetrachloride of meso-(tetra-4-N-hydroxyethylpyridyl)porphine (THEtPyP) (8) in quantitative yield. The central cobalt atom was introduced by treating THEtPyP in aqueous medium with a tenfold excess of cobalt chloride followed by concentrated hydrochloric acid; the course of the reaction was monitored spectrophotometrically. The reaction of an aqueous solution of the complex 9 with excess of the corresponding amine yielded the amino derivatives 10a-d.

All the compounds synthesized (8-10) were readily soluble in water at any pH.

In the infrared spectra of compounds 5-7, the cyano group absorbs in the region 2100-2200 cm⁻¹. The two cyano groups of complex 5 give rise to only one absorption band (at 2170 cm⁻¹) indicating that they are equivalent. It can be assumed that both cyano groups are co-ordinated to the cobalt atom and are situated symmetrically relative to the plane of the porphyrine molecule. This structure consists of two normal oscillations: inphase and antiphase. These oscillations include the valency oscillations of the cyano group. Such a structure is unique since only one of the oscillation, i.e. the antiphase oscillation, is IR-active.

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Note. a) n-butylamine, b) cyclohexylamine, c) piperidine, d) pyridine

Infrared spectral data and elemental analysis, show that the conversion of the complex 3 to the complex 5 is accompanied by the dehydrobromination of the peripheral pyridine groups, so that in compound 5 the pyridine groups occur as free bases. Thus, in going from complex 3 to 5 there is a shift of the pyridine ring absorption band from 1640 to 1595 cm^{-1} . Analogous shifts in the absorption for the transition from a pyridine salt to a free base have been reported in the literature [4].

In compound 6, stretching vibrations of the $\text{C}\equiv\text{N}$ group absorb at 2148 cm^{-1} , while the free $\text{C}\equiv\text{N}^-$ ion absorbs at 2080 cm^{-1} . An appreciable change in the frequency indicates that the cyano-group is located in the inner sphere as in the complex 6, where the cyano group is covalently bonded, and not in a structure with separated charges, as was proposed in [5] for etioporphine(cobalt)cyanide.

The infrared spectra of compounds 10a-d contain more absorption bands than that of the complex 9; the frequencies of the additional bands are similar to the vibration frequencies of the coordinated ligands (see Table 1). It should be noted, however, that axial coordination in the test compounds shows up less sharply in the infrared than in previously obtained complexes of CoTPyP with a number of amines [1]. This is to be expected, since the porphyrines which we studied contain hydroxyethyl groups, the vibrations of which partially overlap the region of absorption of the coordinated amines. Thus, some of the bands given in Table 1, appear as shoulders on porphyrin absorption bands, and in several cases bands in the spectrum of the complex are stronger and (or) half as wide as the corresponding bands in complex 9. This is particularly the case for bands due to the stretching vibrations of the $\text{NH}(\text{NH}_2)$ group, which indicate axial coordination. Bands corresponding to these vibrations, are small peaks in the same region as the broad OH stretching absorption band with maximum at 3400 cm^{-1} . However, in all cases these bands are at lower frequencies than in the free amines. This provides evidence for ligand-coordination, since it is known [6] that the coordination of amines is accompanied by a decrease in the frequency of the stretching vibrations of the $\text{N}(\text{NH}_2)$ groups.

TABLE 1. Aminoderivatives of meso-(Tetra-4-N-hydroxyethylpyridyl)porphinochlorocobalt (III) Tetrachloride 10a-d

Compound	Amine	UV spectrum. λ , nm ($\epsilon \cdot 10^{-3}$) [*]	IR spectrum, cm^{-1} †	Found, %			Empirical formula			Calculated, %			Yield, %
				C	H	Cl	C	H	Cl	C	H	Cl	
10a	Butylamine	436 (115), 548 (10.8), 585 sh (4.4)	575 $\text{v}_{\text{C-M-L}}$, 745, 1078 $\text{v}_{\text{C≡N}}$, 1465 $\delta_{\text{(CH}_2, \text{CH}_3)}$, 2968 $\text{v}_{\text{as}}(\text{CH}_3)$, 3200 $\text{v}_{\text{(NH}_2)}$	56.7	4.8	16.0	11.4	$\text{C}_{52}\text{H}_{55}\text{O}_4\text{Cl}_5\text{CoN}_9$	56.4	5.0	16.1	11.4	93
10 b	Cyclohexyl- amine	436 (114), 548 (10.3), 587 sh (3.9)	557 sh $\text{v}_{\text{(M-L)}}$, 705, 898, 1385 $\delta_{\text{(CH}_2)}$, 2868 $\text{v}_{\text{s}}(\text{CH}_2)$, 2945 $\text{v}_{\text{as}}(\text{CH}_2)$, $\text{v}_{\text{s}}(\text{NH}_2)$, 3300 $\text{v}_{\text{as}}(\text{NH}_2)$	57.5	5.2	15.8	11.1	$\text{C}_{54}\text{H}_{57}\text{O}_4\text{Cl}_5\text{CoN}_9$	57.3	5.0	15.7	11.1	91
10c	Piperidine	439 (91.2), 552 (10.4), 591 sh (4.5)	555 $\text{v}_{\text{(M-L)}}$, 1088 $\text{v}_{\text{C≡N}}$, 1385 $\delta_{\text{(CH}_2)}$, 1452 sh $\delta_{\text{(CH}_2)}$, 2750, 2800, 2950 $\text{v}_{\text{as}}(\text{CH}_2)$, 3200 $\text{v}_{\text{(NH)}}$	56.8	4.7	15.8	11.4	$\text{C}_{53}\text{H}_{55}\text{O}_4\text{Cl}_5\text{CoN}_9$	56.9	4.9	15.9	11.3	92
10d	Pyridine	440 (116), 562 (10.1), 601 (4)	696 $\text{v}_{\text{(CH)}}$, 1440, 1598 $\text{v}_{\text{(CC)}}$, $\beta_{\text{(CC)}}$	57.6	4.3	15.9	11.3	$\text{C}_{53}\text{H}_{49}\text{O}_4\text{Cl}_5\text{CoN}_9$	57.2	4.4	16.0	11.3	93

*For complex 9 the corresponding bands were at 435, 546, and 584 nm, and at 412, 530, and 560 nm for Co(II)TPyP.

†Wave numbers for bands not present in the spectrum of complex 9 are given.

For the pyridine ligand, there is no N-H bond and this criterium cannot be used. However, two new bands at 696 and 1598 cm^{-1} in the spectrum can reasonably be attributed to a displacement of the $\nu_{11b}(\text{CH})$, $\nu_{\text{ea}}(\text{CC})$, and $\beta(\text{CCH})$ vibrations on coordination. In free pyridine, these absorptions occur at 702 and 1580 cm^{-1} ; similar displacements have previously been reported for pyridine complexes [4].

The frequencies of the porphyrine ring vibrations change little on axial coordination. The strongest bands from the macrocyclic ring are at 800 and 1000 cm^{-1} , and are out-of-plane and in-plane deformation vibrations of the pyrrole CH bonds [7], shifted by 6 cm^{-1} . The greatest shift is observed for the complex with pyridine. Ultraviolet spectral data (see Table 1) also show the greatest bathochromic shift in the spectrum of the complex 10d. Apparently, increased coordination of Co(III) with an aromatic system, which may also involve the dative component of the metal-ligand bond, disturbs the electron system of the macrocyclic ring more strongly, although judging from the small frequency shift, these disturbances are small.

The ultraviolet spectra of the compounds show a small bathochromic shift compared with the complex 9 because of additional coordination. Examples of such bathochromic [8], and also hypsochromic shifts [9] have been reported for absorption bands as a result of axial coordination.

Attempts were made to cleave the axial ligand from the complex at elevated temperatures (70-80°C) and reduced pressure (10⁻⁴ torr). The eliminated ligands were directly precipitated onto a KBr substrate cooled with liquid nitrogen inside a vacuum cryostat, enabling the infrared spectra of the cleaved particles to be taken. In all cases they were found to be starting amines, which, therefore, did not undergo any chemical change during the course of the reaction.

EXPERIMENTAL

Infrared spectra in the range 400-3600 cm^{-1} were taken on a UR-20; samples were prepared as KBr pellets or as suspensions in mineral oil. Ultraviolet spectra over the range 350-800 nm were obtained on a Specord UV-vis using anhydrous chloroform in a 4:1 mixture of chloroform and methanol, or distilled water.

Chromatography was carried out on Al_2O_3 (Brockman activity grade II).

Tetrahydrobromide of meso-(Tetra-4-pyridyl)porphinobromocobalt (III) (3). To 4.25 g (6.28 mmoles) of CoTPyP (2) was added 500 ml of methanol, 500 ml of chloroform, and 12.5 ml of 48% hydrobromic acid. The mixture was vigorously stirred at room temperature for 4 h, evaporated to dryness, and the residue recrystallized from chloroform and ether, and dried for 1 h in a vacuum desiccator at 40°. The violet crystals were carefully washed with dry ether and dried in air to give 6.7 g (99%) of compound 3. Found: C 44.6; H 2.6; Br 37.2; N 10.0%. $\text{C}_{46}\text{H}_{28}\text{Br}_5\text{CoN}_8$. Calculated: C 44.5; H 2.6; Br 37.1; N 10.4%.

Potassium Salt of meso-(Tetra-4-pyridyl)porphinodicyanobromocobalt (III) (5). A. To a solution of 0.3 g (0.36 mmole) of the complex 4 in 300 ml of methanol was added 1.5 g (23 mmoles) of KCN. The reaction mixture was heated at 40°C with periodic stirring for 20 min and then allowed to stand overnight. A further 600 ml of chloroform was added, and after 3 h the mixture was chromatographed on an Al_2O_3 column and evaporated to dryness. Recrystallization from dry ether gave 0.13 g (48%) of 5, R_f 0.12 (Al_2O_3 ; chloroform-methanol, 5:3). Found: C 65.5; H 2.9; N 18.5%. $\text{C}_{42}\text{H}_{24}\text{CoKN}_{10}$. Calculated: C 65.8; H 3.1; N 18.3%.

B. To a solution of 0.3 g (0.28 mmole) of compound 3 in 200 ml of methanol was added 1.5 g (23 mmoles) of KCN. The reaction mixture was heated at 40°C for 0.5 h and 400 ml of chloroform added. After standing overnight, the mixture was chromatographed on an Al_2O_3 column and then evaporated to dryness. The residue was recrystallized from dry ether to give 0.2 g (95%) of the salt, 5, R_f 0.12 (Al_2O_3 ; chloroform-methanol, 5:3). Found: C 65.8; H 3.0; N 18.4%. $\text{C}_{42}\text{H}_{24}\text{CoKN}_{10}$. Calculated: C 65.8; H 3.1; N 18.3%.

meso-(Tetra-4-pyridyl)porphinocyanocobalt (III) (6). A solution of 0.15 g (0.17 mmole) of the complex 5 in 50 ml of glacial acetic acid was refluxed for 0.5 h. When cool, the reaction mixture was passed through an Al_2O_3 column (chloroform-methanol 5:3). After evaporation of the eluate, the residue was recrystallized from dry ether to give 0.1 g (83%) of compound 6, R_f 0.85 (Al_2O_3 ; chloroform-methanol, 5:3). Found: C 70.2; H 3.2; N 17.6%. $\text{C}_{41}\text{H}_{24}\text{CoN}_9$. Calculated: C 70.2; H 3.4; N 18.0%.

meso-(Tetra-4-pyridyl)porphinocyanopyridinocobalt (III) (7). The complex 6 (0.05 g; 0.07 mmole) was dissolved in 20 ml of pyridine by heating at 70°C for 10 min. The solution was

chromatographed on an Al_2O_3 column and eluted with a chloroform-methanol-pyridine (10:1:3) mixture. The eluate was evaporated to dryness and the residue recrystallized from dry ether to give 0.055 g (99%) of the complex 7, R_f 0.75 (Al_2O_3 ; chloroform-methanol, 8:1). Found: C 70.9; H 3.5; N 18.0%. $\text{C}_{46}\text{H}_{29}\text{CoN}_{10}$. Calculated: C 70.8; H 3.7; N 17.9%.

Tetrachloride of meso-(Tetra-4-N-hydroxyethylpyridyl)porphine (8). A mixture of 1 g (16 mmoles) of the TPyP 1 in 100 g (1.24 moles) of ethylenechlorhydrin was refluxed for 2 h (course of the reaction monitored by chromatography). The reaction mixture was evaporated to dryness *in vacuo* and the dry residue recrystallized from ether. The crystalline material was washed with chloroform and recrystallized from a mixture of water and propanol (1:10) to give 1.5 g (99%). Found: C 61.0; H 4.9; Cl 14.7; N 11.9%. $\text{C}_{48}\text{H}_{46}\text{Cl}_4\text{N}_8\text{O}_4$. Calculated: C 61.3; H 4.9; Cl 15.1; N 11.9%.

Tetrachloride of meso(Tetra-4-N-hydroxyethylpyridyl)porphinochlorocobalt (III) (9). To a solution of 8 g (8.5 mmoles) of compound 8 in 500 ml of distilled water was added 8 g (61 mmoles) of CoCl_2 in 10 ml of distilled water. The solution was refluxed for 2 h with simultaneous distillation of water until the volume was reduced to 100 ml (course of reaction was monitored spectrophotometrically). After the addition of 12 ml of concentrated HCl, the reaction mixture was evaporated to dryness *in vacuo*, recrystallized from ether, washed with acetone, and recrystallized from a mixture of water and ethanol (1:10) to give 8.5 g (97%) of the complex 9. Found: C 55.5; H 4.7; Cl 17.4; N 10.8%. $\text{C}_{48}\text{H}_{44}\text{Cl}_5\text{CoN}_8\text{O}_4$. Calculated: C 55.8; H 4.3; Cl 17.2; N 10.8%.

Aminoderivatives of meso-(Tetra-4-N-hydroxyethylpyridyl)porphinochlorocobalt (III) Tetrachloride (10a-d, Table 1). To a solution of 0.1 mmole of compound 9 in 10 ml of distilled water was added 0.4 mmole of the corresponding amine. After 10 minutes the reaction mixture was evaporated to dryness, the dry residue recrystallized from absolute ether and then further recrystallized from a mixture of water and the corresponding amine (1:10). The crystalline material was filtered off and washed with the corresponding amine and absolute ether.

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