

methylene triplet (3.77 ppm), while the lower-field one (4.05 ppm) remained unchanged. Finally, decoupling studies showed that the protons in the two methylene groups indeed coupled with each other.

Synthesis of ethyl 4-imidazolidone- Δ 2 α -acetate. 2. Ten g (0.097 mol) of glycine ethyl ester was slowly (ca. 20 min) added to 15.0 g (0.095 mol) of cold (0°C) carbethoxyacetimidic ethyl ester⁴ in a 100 ml argon-flushed, three-necked, round-bottomed flask, equipped with a gas-inlet tube, a dropping funnel and a drying tube (magnesium sulfate). When the addition was complete, the gas stream was interrupted, the flask stoppered and kept at room temperature in the dark. After 24 h a brown, crystalline solid had precipitated. It was separated by filtration and triturated thoroughly, first with methylene chloride and then with diethyl ether. The brown solid was dried, then recrystallized four times from ethanol. Yield: 3.9 g (24 %) of brownish, flaky crystals. Sublimation of this material (140°C/1 torr) gave white crystals, which turned pink after a short exposure to air and/or light. Freshly sublimed samples were used for all measurements. M.p. 177–180°C, IR (KBr): 3380 (NH), 3300–3100 (NH), 1730 (ring C=O), 1695 (ester C=O), and 1595 cm⁻¹ (C=C), UV (ethanol): λ_{\max} at 278 (ϵ =30 000) and 213 nm (ϵ =11 900), NMR (dimethyl sulfoxide- d_6): triplet (J =7 Hz) at 1.17 (3H, CH₃), singlet at 3.94 (2H, SCH₂), quartet (J =7 Hz) at 4.00 (2H, OCH₂), singlet at 4.19 (1H, =CH), broad peak at 7.80 (1H, NH), and a broad peak at 10.90 ppm (1H, NH). (Found: C 49.03; H 5.81; N 16.12. Calc. for C₈H₁₀N₂O₃: C 49.41; H 5.92; N 16.46). MS: M⁺=170.

1. Taylor, P. J. *Spectrochim. Acta* **A 26** (1970) 153.
2. Ceder, O., Stenhede, U., Dahlquist, K.-I., Waisvisz, J. M. and van der Hoeven, M. G. *Acta Chem. Scand.* **27** (1973) 1914.
3. Ceder, O. and Stenhede, U. *Acta Chem. Scand.* **27** (1973) 1923.
4. Lehr, H., Karlan, S. and Goldberg, M. W. *J. Am. Chem. Soc.* **75** (1953) 3640.
5. Jacquier, R., Lacombe, J.-M. and Maury, G. *Bull. Soc. Chim. France* **1971** 1040.
6. Rondeau, R. E. and Sievers, R. E. *J. Am. Chem. Soc.* **93** (1971) 1522.
7. Demarco, P. V., Elzey, T. K., Lewis, R. B. and Wenkert, E. *J. Am. Chem. Soc.* **92** (1970) 5734.
8. Wing, R. M., Early, T. A. and Uebel, J. J. *Tetrahedron Letters* **1972** 4153.

Received March 17, 1973.

Acta Chem. Scand. **27** (1973) No. 6

A New Method for the Preparation of Dianionobis(diamine)cobalt(III) Complexes. Preparation of Carbonatobis(trimethylenediamine)cobalt(III) Salts

JOHAN SPRINGBORG^a and
CLAUS ERIK SCHÄFFER^b

^aDepartment of General and Inorganic Chemistry, Royal Veterinary and Agricultural University, Thorvaldsensvej 40, 2, opg. 4, DK-1871 Copenhagen V, Denmark and
^bChemistry Department I (Inorganic Chemistry), University of Copenhagen, H. C. Ørsted Institute, Universitetsparken 5, DK-2100 Copenhagen Ø, Denmark

Various methods for the preparation of bis(diamine)cobalt(III) complexes are known. In the following, a new method of preparation for this type of complexes is given. We illustrate the method by giving the preparations of the chloride and nitrate salts of the carbonatobis(trimethylenediamine)cobalt(III) ion.

The traditional method of preparation of the carbonatobis(trimethylenediamine)cobalt(III) ion is based upon the action of carbonate on an aqueous solution of *trans*-dichlorobis(trimethylenediamine)cobalt(III) chloride, possibly combined with removal of chloride by treatment with silver carbonate.^{1,2} *trans*-Dichlorobis(trimethylenediamine)cobalt(III) chloride is obtained by air-oxidation of an ethanolic solution of trimethylenediamine (tn) with an excess of anhydrous cobalt(II) chloride in a yield of 43 %.³

The following new method of preparation of carbonatobis(trimethylenediamine)cobalt(III) chloride utilizes hydrated cobalt(II) chloride directly as the starting material and provides a high yield (67 %) of an almost pure sample. An aqueous solution of cobalt(II) chloride (1 mol) is made to react with the carbamate of trimethylenediamine (2 mol) to give a green, not further identified cobalt(II) solution. This cobalt(II) solution is oxidized with hydrogen peroxide. The resulting mixture of bis(trimethylenediamine)cobalt(III) species is by addition of lithium hydroxide combined with a stream of carbon dioxide converted to the red carbonato complex.

The use of the carbamate of the amine is essential. A single experiment utilizing the free amine was carried out. Besides a large amount of a water-soluble red by-product, which was not identified, only a yield of 25 % impure carbonate complex was obtained.

The nitrate salt is prepared analogously to the chloride (yield 72 %). The perchlorate salt is obtained in high yield (88 %) from the chloride.

These carbonate salts are all excellent starting materials for the preparation of other dianionobis(trimethylenediamine)cobalt(III) compounds; e.g. treatment of the chloride salt with concentrated hydrochloric acid yields *trans*-dichlorobis(trimethylenediamine)cobalt(III) chloride almost quantitatively.

With ethylenediamine the above method has been used with success resulting in new preparations of carbonate- and other dianionobis(ethylenediamine)cobalt(III) salts in high yields.⁴

This new method is probably also useful for preparations of dianionobis(diamine)cobalt(III) complexes with other aliphatic diamines. A single experiment in which trimethylenediamine was replaced by propylenediamine showed that also carbonatobis(propylenediamine)cobalt(III) salts may be obtained in high yields by this method.

Experimental. Materials. Trimethylenediamine with the description *purissimum* was purchased from Fluka. All other chemicals were of reagent grade and were used without further purification.

Spectra. Absorption spectra in the 300–650 nm region, recorded using a Cary Model 14 spectrophotometer, were used as a check of purity and as characterization of the compounds. Data for maxima and minima have been given below as (ϵ, λ) the absorbancy ϵ in liter/mol cm and the wavelength λ in nm.

Preparations. 1. Carbonatobis(trimethylenediamine)cobalt(III) chloride. $[\text{Cotn}_2\text{CO}_3]\text{Cl}\cdot\text{H}_2\text{O}$. A mixture of trimethylenediamine (55.0 ml, 0.656 mol) and water (400 ml) was cooled in ice, and a stream of carbon dioxide was bubbled through the solution for 2–3 h. The stream of carbon dioxide was maintained during the entire preparation. A solution of cobalt(II) chloride 6-hydrate (78.0 g, 0.328 mol) in water (80 ml) at room temperature was then added to the solution with stirring. The addition of the cobalt(II) salt caused a violent evolution of carbon dioxide gas, and the solution became green and gel-like. With

continued cooling and manual stirring, hydrogen peroxide (80 ml, 30 %) was then added dropwise during 15 min. During the addition the temperature increased to about 25° and the reaction mixture became a green homogeneous solution.

To complete the reaction the mixture was heated to 80–85°, and kept at that temperature for half an hour. During this time the colour changed from green to redviolet. The solution was cooled in ice to approximately 25°. At that temperature, finely powdered lithium hydroxide monohydrate (13.76 g, 0.328 mol) was added with thorough stirring and a vigorous stream of carbon dioxide. The solution became red. The cooling was continued for 3 h, when the stream of carbon dioxide was stopped and the solution left overnight at 0–5°. The filtered solution was then evaporated in a rotating vacuum evaporator at approximately 70° to a volume of 160 to 170 ml. It was found to be important to evaporate to this volume. Evaporation to a volume much larger than 170 ml decreased the yield substantially, and evaporation to a volume less than approximately 150 ml gave an oily product. This super saturated solution was then transferred (while hot) to a preheated beaker and heated to the boiling point with thorough stirring for a few minutes. This caused precipitation of red crystals of carbonatobis(trimethylenediamine)cobalt(III) chloride. The mixture was then cooled in ice for 2 h. The precipitate was filtered, washed with 96 % ethanol (three 100 ml portions) and allowed to dry in air. This yielded 70 g (67 %). This product was not pure, but still suitable for further synthetic work. The pure product was obtained by reprecipitation from water. The crude product (10 g) was dissolved in water (30 ml) at room temperature and filtered. A mixture of acetone (60 ml) and methanol (20 ml) was then added to the stirred solution within a period of 10 min., and red crystals of the chloride salt precipitated. The content of methanol was found to be essential in order to avoid the formation of an oil. The mixture was allowed to stand for another 10 min at room temperature, and was then filtered and washed with 96 % ethanol (three 5 ml portions). Drying in air yielded 7.6 g (76 %). (Found: Co 18.48; C 26.16; N 17.48; H 6.90; Cl 10.99. Calc. for $[\text{Cotn}_2\text{CO}_3]\text{Cl}\cdot\text{H}_2\text{O}$: Co 18.38; C 26.21; N 17.47; H 6.92; Cl 11.06). $(\epsilon, \lambda)_{\text{max}}$: (108.7, 520); (126.7, 360). $(\epsilon, \lambda)_{\text{min}}$: (12.1, 430); (51.2, 327). Medium: water. Literature:² $(\epsilon, \lambda)_{\text{max}}$: (108.5, 520); (127.7, 360).

2. *Carbonatobis(trimethylenediamine)cobalt(III) nitrate*, $[\text{Cotn}_2\text{CO}_3]\text{NO}_3$. Carbonatobis(trimethylenediamine)cobalt(III) nitrate was

prepared analogously to the chloride salt. With the quantities given in preparation No. 1, the cobalt(II) chloride solution was replaced by a solution of cobalt(II) nitrate 6-hydrate (95.5 g, 0.328 mol) in water (80 ml), and the procedure given in preparation No. 1 was followed exactly. The nitrate salt was isolated analogously by evaporation to a volume of 160 to 170 ml. The crude product was washed with 70 % v/v ethanol (three 80 ml portions) and allowed to dry in air. The yield was 82 g of red crystals of the nitrate salt (72 %). This product was not pure. The pure salt was obtained by reprecipitation from water. The crude product (20 g) was dissolved in water (40 ml) at 100° and filtered. Then 96 % ethanol (120 ml) was added quickly to the stirred solution (while hot), and the mixture was cooled for 2 h in ice. The precipitate was filtered and washed with 70 % v/v ethanol (two 20 ml portions). Drying in air yielded 16 g (80 %). (Found: Co 17.11; C 24.25; N 20.45; H 6.43. Calc. for $[\text{Cotn}_2\text{CO}_3]\text{NO}_3$: Co 16.98; C 24.21; N 20.18; H 6.39). $(\epsilon, \lambda)_{\text{max}}$: (107.5, 520); (124.9, 360); $(\epsilon, \lambda)_{\text{min}}$: (11.4, 430); (50.2, 327). Medium: water.

3. *Carbonatobis(trimethylenediamine)cobalt(III) perchlorate*, $[\text{Cotn}_2\text{CO}_3]\text{ClO}_4$. Crude carbonatobis(trimethylenediamine)cobalt(III) chloride (20.0 g, 0.062 mol) was dissolved in water (50 ml) at room temperature and the solution was filtered. A saturated solution of sodium perchlorate in water (20 ml) was then added to the stirred solution with cooling in ice. The precipitation of red crystals of the perchlorate salt immediately commenced, and the cooling was continued for half an hour. The precipitate was filtered, washed with ice cold ethanol (50 % v/v, 20 ml) and 96 % ethanol (three 20 ml portions). Drying in air yielded 20.1 g (88 %). (Found: Co 16.06; C 22.74; N 15.46; H 5.52; Cl 9.65. Calc. for $[\text{Cotn}_2\text{CO}_3]\text{ClO}_4$: Co 16.07; C 22.93; N 15.28; H 5.50; Cl 9.67). $(\epsilon, \lambda)_{\text{max}}$: (107.3, 520); (124.7, 360). $(\epsilon, \lambda)_{\text{min}}$: (11.3, 430); (49.2, 327). Medium: water.

1. Werner, A. *Ann.* **386** (1912) 264.
2. Boyle, J. E. and Harris, C. M. *J. Am. Chem. Soc.* **80** (1958) 782.
3. Bailar, J. C. and Work, J. B. *J. Am. Chem. Soc.* **68** (1946) 232.
4. Springborg, J. and Schäffer, C. E. *Inorg. Syn.* **14** (1973) 63.

Received June 22, 1973.

Inhibition of Duodenal Pancreatic Enzymic Activities by Polyphlorethin Phosphate with Special Reference to Phospholipase A₂

B. ARNESJÖ, I. IHSE and I. QVIST

Department of Surgery, University Hospital of Lund, S-221 85 Lund, Sweden

Polyphlorethin phosphate (PPP) is a substance capable of inhibiting the effects of prostaglandins, trombin, and certain enzymes such as alkaline phosphatase and hyaluronidase. Hyaluronidase is completely inhibited in an environment containing 1–2 $\mu\text{g/ml}$ PPP. The molecular weight of PPP is about 15 000 and it is only to a minor extent – if any – split or absorbed from the intestine.^{1,2} It has been shown to be useful in cases with ulcerative colitis.³ This beneficial effect in cases with ulcerative colitis has been ascribed its membrane tightening effect as in this disease the permeability of the colonic mucosa is increased with protein leakage as a consequence. This membrane tightening effect of PPP might be explained by its capability of inhibiting hyaluronidase. Lecithin is another compound that is one of the main components of cell membranes. In the present investigation, therefore, we have found it interesting to study the effect of PPP on the *in vitro* activity of pancreatic enzymes, especially on phospholipase A₂ which in the intestine splits lecithin to lysolecithin the latter of which might be highly toxic to cell membranes in patients with inflammatory intestinal diseases.

Materials and methods. Polyphlorethin phosphate (PPP standard IV batch number Leo 101K) was a gift from AB Leo, Helsingborg, Sweden. It contained 93.5 % PPP. Contaminants were pyridine (2.7 %) sodium chloride (2.4 %), phosphoric acid (0.2 %) and water.

Phospholipase A₂ activity was estimated according to Ihse and Arnesjö,³ lipase according to Erlansson and Borgström,⁴ and trypsin by a modified version of the method of Hummel.⁵ All enzyme assays were run using a pH-stat (Radiometer, Copenhagen) with a TTT2 titrator connected to an ABU11 Burette Unit with a 0.25 ml burette and a thermostatically controlled TTA31 titrator assembly.

Sodium taurodeoxycholate (NaTDC) was synthesized according to Norman⁶ as modified