

trated ether solution was red in color. The crude acid weighed 0.3 g. (38% of the theoretical amount).

**Preparation of the Rearranged Hydrocarbon.**—A solution of 0.5 g. of the ethane in 15 cc. of alcohol was heated to boiling in an atmosphere of nitrogen for one hour. Concentration and cooling of the solution yielded 0.25 g. of white crystals melting at 72–76°. When further purified by recrystallization from methyl alcohol this hydrocarbon melted at 82.3–83° (corr.).

*Mol. wt.* (Rast's Method<sup>11</sup>). Subs., 0.0069; camphor, 0.0218;  $\Delta t$ , 19.07° (average calcd. for mean f. p. and mean m. p. for five observations); constant for camphor: 39.7. Calcd. for  $C_{60}H_{78}$ : mol. wt., 678.6. Found: 658.9. *Anal.* Subs., 0.0979:  $CO_2$ , 0.3155;  $H_2O$ , 0.1016. Calcd. for  $C_{60}H_{78}$ : C, 88.41; H, 11.59. Found: C, 87.89; H, 11.61.

### Summary

1. Hexa-(3-ethyl-3-methylpentinyl-1)-ethane has been synthesized.
2. This ethane has been shown to contain a weaker central ethane linkage than hexa-*tert.*-butylethynylethane by comparing their stability toward oxygen, ease of cleavage with alkali metals and tendency toward rearrangement.
3. It is thought that the decrease in stability is due to increasing the molecular weight of the alkyl group.

URBANA, ILLINOIS

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[FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

## COBALT COMPLEXES OF CYSTEINE

BY MAXWELL P. SCHUBERT

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The necessity of a more thorough working out of the chemistry of the heavy metal internal complexes of thiol acids arises out of the great interest shown lately in the catalytic oxidation by iron salts of thiol acids to the corresponding disulfide acids. The beginning of such a purely descriptive chemical study was made with cobalt and thioglycolic acid.<sup>1</sup> The study has now been extended and in this paper will be described the preparation and properties of complexes of cobalt and cysteine.

In the case of cobalt and thioglycolic acid only one type of complex could be found, of which several derivatives were prepared in crystalline form. The complex nucleus in these compounds contains two thioglycolic acid radicals for each cobalt atom and is at an oxidation level corresponding to cobalti bithioglycolate. The situation with cobalt and cysteine was soon found to be more complicated as crystalline complexes were prepared containing cobalt and cysteine in the ratios one to one, one to

<sup>11</sup> Rast, *Ber.*, **55**, 1051, 3727 (1922); Smith and Young, *J. Biol. Chem.*, **75**, 289 (1927).

<sup>1</sup> L. Michaelis and M. Schubert, *THIS JOURNAL*, **52**, 4418 (1930).

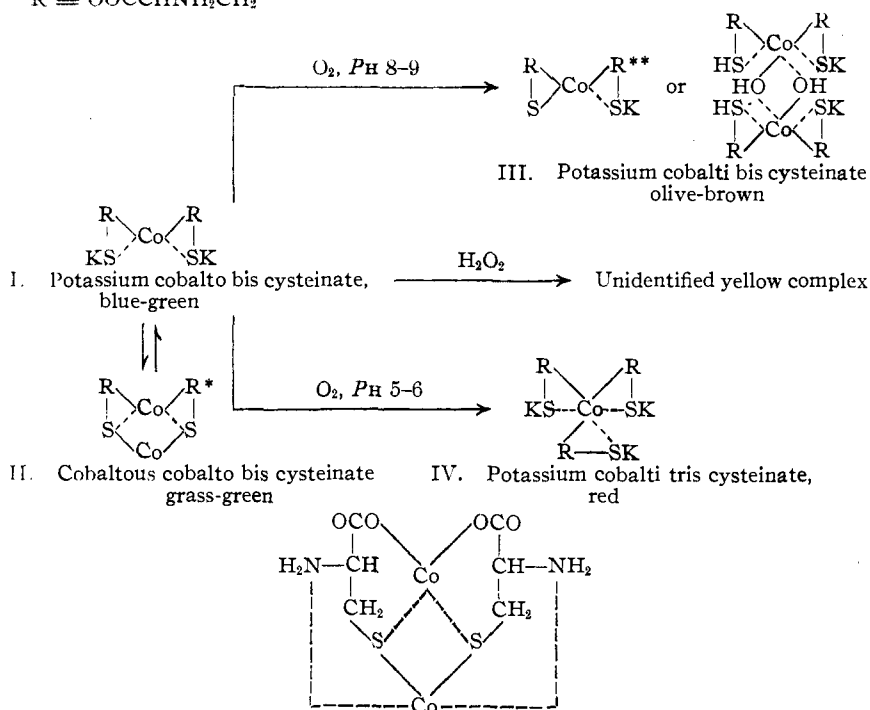
two and one to three. With cobalt and cysteine the study has also been extended to the isolation of complexes in the reduced state by working in the absence of air. In these the cobalt is in the bivalent condition. Finally, one very striking difference between the cysteine complexes and the thioglycolic acid complexes has been partially cleared up. It has been noticed by Michaelis, but not published,<sup>2</sup> that the olive-brown color of the cobalt cysteine complex made in the presence of air could be changed by the addition of hydrogen peroxide to an intense yellow, much more sensitive than the brown for colorimetric work. There is no similar reaction with the cobalt thioglycolic acid complex.

**The Interrelations among the Cobalt Cysteine Complexes.**—These are most simply brought out in the accompanying diagram. The simplest of the complexes is I. It is formed by mixing deaerated solutions of cysteine, potassium hydroxide and cobalt chloride in an atmosphere of oxygen-free nitrogen. The *PH* of the resulting solution is probably about 11 to 12. If the *PH* be lower, about 7 to 8, a grass-green crop of needles, II, is obtained. II appears to be the cobalt salt of the same complex nucleus that is contained in I. II is quite insoluble in water, but in dilute potassium hydroxide it undergoes decomposition by precipitating half its cobalt as cobaltous hydroxide while the rest goes into solution as an olive-brown complex. This color is due to the oxidation by air of the complex nucleus in I. If II is decomposed by alkali in an oxygen-free environment, the resulting solution has the green color of I.

Oxidation of the reduced green complex can give rise to at least **three** different series of complexes. Oxidation with air gives as the principal product III if the *PH* be in the neighborhood of 8–9, while IV is the main product if the solution is more acid, probably about 5. If the *PH* is too high, over 11, it becomes very difficult to isolate any crystalline products at all. Both III and IV are best isolated as free acids. The free acid of IV is insoluble in water and can be obtained in about 85% yields with only a little cystine as by-product. III, on the other hand, can be obtained at best in yields of only about 60% together with a much larger amount of cystine. This fact is in harmony with the idea that in the process of oxidation of complex I, IV is first formed and then by further oxidation two molecules of IV give III and a molecule of cystine. This idea has already been expressed by Kendall and Holst.<sup>3</sup> On the other hand, it has not been found possible, once III and IV are formed, to convert either into the other; for example, heating III with excess cysteine does not give IV and heating IV with alkali or hydrogen peroxide does not produce III. Certainly under the condition of formation of III or IV, IV cannot be converted to III.

<sup>2</sup> L. Michaelis and S. Yamaguchi, *J. Biol. Chem.*, **83**, 367 (1929).

<sup>3</sup> E. C. Kendall and J. E. Holst, *ibid.*, **91**, 435 (1931).



\* The suggestion that this may be a double internal complex of the following formula will be considered in a later paper.

\*\* As this compound is hydrated, it may be that the normal six coordination places of the trivalent cobalt are completed by the addition of two molecules of water.

Of course the possibility remains that there may be another complex isomeric with IV which acts as the parent substance to III. According to Werner's ideas on the space arrangements of such molecules, IV could exist in two stereoisomeric forms and as a matter of fact the complexes of glycine and alanine<sup>4</sup> with cobalt, which have the same general formula as IV, do exist in two isomeric forms which are supposed to correspond to the possible *cis* and *trans* forms. But, so far, with cysteine, only one form of IV has been found.

In connection with the alanine complexes just mentioned an interesting possibility arises. Alanine coordinates with cobalt through its carboxyl and amino groups. Cysteine has these two groups in the same relative positions and in addition a thiol group. Does cysteine then, coordinate with cobalt through its amino or its thiol group or through both, as well as with its carboxyl group? In other words, does cysteine occupy two or three coordination places on cobalt, and if two, which two of its groups are coordinated?

<sup>4</sup> H. Ley and H. Winkler, *Ber.*, **42**, 3894 (1909); **45**, 372 (1912).

**The Constitution of the Cobalti Bis Cysteinate Complexes.**—Two independent lines of evidence agree with a structure of the complex nucleus III which involves coördination of the carboxyl group and the thiol group leaving the amino group of the cysteine free. The first evidence comes from a comparison of the ultraviolet absorption spectra of solutions of the cysteine complex and of the corresponding thioglycolic acid complex, Fig. 1. Since in the case of thioglycolic acid the coördination must take place through the carboxyl and thiol groups, and since the similarity of absorption spectra probably signifies a similarity of structure, it follows that the cysteine complex probably involves coördination of the carboxyl and thiol groups.

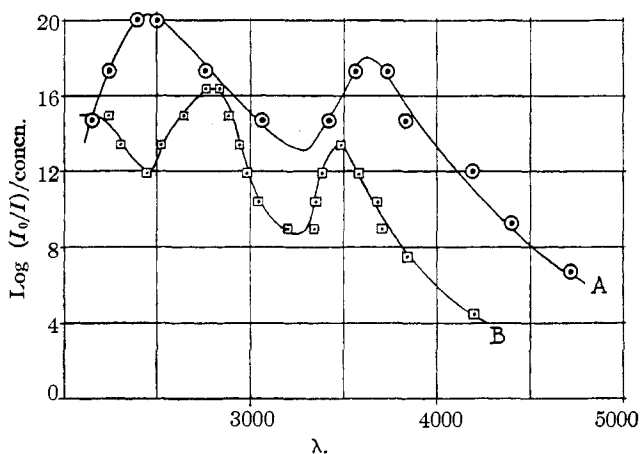


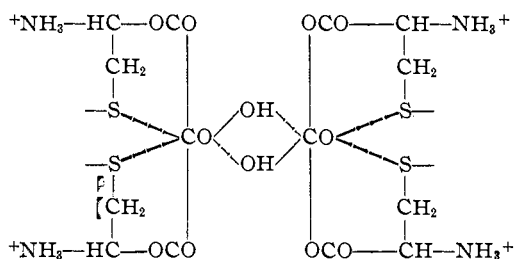
Fig. 1.—A, 0.075 millimolar potassium cobalti bis thioglycolate; B, 0.067 millimolar potassium cobalti bis cysteinate.

Another line of evidence for this comes from a study of the amino group. This method has already been used by Mann<sup>5</sup> in studies on the metal complexes of 1,2,3-triaminopropane to determine how many of these amino groups are coördinated. It is based on the idea that the free electron pair of the nitrogen of an amino group acts as the coördinate link when an amino group coördinates with hydrogen ion or a metal ion. Since there is but one such pair, an amino group cannot coördinate with more than one element at a time. In other words, if the amino group of cysteine is coördinated with the cobalt, it cannot also coördinate with hydrogen ion to form an ammonium salt, a hydrochloride or picrate, for example.

The free acid of III crystallizes in hexagonal plates and complicated patterns of these, and is not very soluble in water but dissolves readily in dilute hydrochloric acid. From concentrated solutions in four to five molar hydrochloric acid a beautifully crystalline crop of olive-brown

<sup>5</sup> G. F. Mann, *J. Chem. Soc.*, 2681 (1926); 890 (1928).

needles can be obtained. These cannot be washed with water as they revert to the hexagonal crystals. If they are dried over sulfuric acid in a vacuum desiccator, great quantities of fumes of hydrochloric acid pour out when the desiccator is opened. Evidently the hydrogen chloride is held only loosely. The same can be said of picric acid. On treatment of an acid solution containing the complex nucleus of III with picric acid, a crop of clean needle-like crystals separates. These can be recrystallized from water saturated with picric acid but not from water alone, as dissociation occurs. The composition of these complexes shows that in the case of hydrochloric acid three-quarters of the total amino groups present form hydrochlorides, while in the case of picric acid half of the amino groups have formed picrates. That these acids do not stick so tightly to the amino group might be due to the stereochemical condition of the complex, to a weakening of the basic character of the amino group due to complex formation or to the fact that the acid character of the SH group is strengthened to such an extent in the complex that it forms a "zwitterion" with the amino group. That the acidity of the thiol group is very much augmented when the complex is formed can also be deduced from the fact that the free acid of III cannot be precipitated by acetic acid but requires hydrochloric acid. If there were internal neutralization, the acid form of III would have the structure



and only the presence of excess of a strong acid would repress the ionization of the thiol group and permit the attachment of an acid at the amino group. At any rate, the fact that picrates and hydrochlorides can be formed at all is sufficient evidence that the amino group cannot be coordinated.

One further possibility remains. It seemed possible that the amino groups might be coordinated with the cobalt in alkaline solution but that as the solution is made acid there arises a competition of the cobalt and hydrogen ion for the free electron pair of nitrogen which results in sufficiently acid solution in the displacement of the cobalt from coordination with the amino group. As a matter of fact this is what seems to occur in the case of the alanine complexes, which are also more soluble in acid solution, but in this case with increasing acid there is a very marked color

change. For example, on the addition of sufficient hydrochloric acid the violet color of the alanine complex in water changes to a red suggestive of cobalt chloride. On the other hand, the cobalti bis cysteinate complex does not change in color in hydrochloric acid solutions as concentrated as six molar and the ultraviolet absorption spectrum showed no change in two molar hydrochloric acid. The conclusion seems justified that at no  $P_{\text{H}}$  is the amino group coordinated with the cobalt.

**The Constitution of the Cobalti Tris Cysteinate Complex.**—The same problems arise with the complex IV containing three cysteine radicals for each cobalt atom. Since this complex is so insoluble in acids, it has not been possible to study the acid combining capacity of the amino groups; but a comparison of the absorption spectrum with that of the cobalti tris alanine complex shows, in spite of a similarity of composition, a great difference

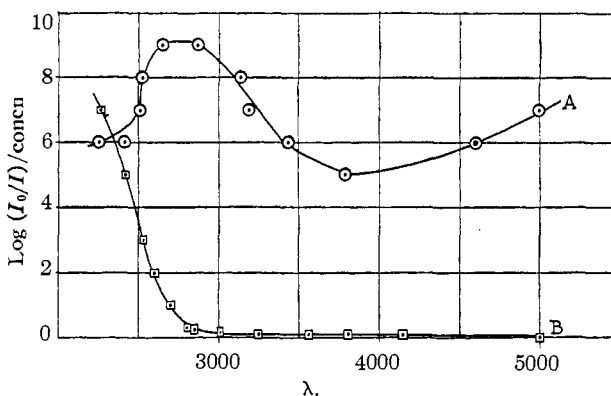


Fig. 2.—A, 0.1 millimolar potassium cobalti tris cysteinate; B, 0.1 millimolar cobalti tris alanine (violet form).

in the spectra (Fig. 2). There is also a difference in the visible part, the alanine complex showing a broad flat band at about 5300 to 5400 Å. and the cysteine complex showing only greatly increasing absorption toward the violet. It seems likely therefore that the cysteine complex involves coordination of three carboxyl and three thiol groups.

Thiohydracrylic acid, which differs from cysteine by the absence of the amino group, also forms cobalt complexes, but as with the other thiol acid complexes there has been considerable difficulty in isolating crystalline chemical individuals, so these complexes have not yet been studied.

**The Reaction of Hydrogen Peroxide with the Cobalti Bis Cysteinate Complex.**—The peroxide reaction first noticed by Michaelis may be carried out as follows. If a dilute solution of a cobaltous salt, about 0.001 molar, is buffered at  $P_{\text{H}}$  7 to 8 with phosphate and excess cysteine is added, an olive-brown color is produced on shaking with air. If now a little dilute hydrogen peroxide solution, about 2%, is added, the color be-

comes an intense yellow. After a few hours this yellow gradually fades. In studying the properties of the complexes isolated, it was soon found that none of the oxidized complexes gives a reaction with hydrogen peroxide but that the blue-green potassium cobalto bis cysteinate does give the same intense yellow color reaction. However, after a solution of the blue-green complex has stood exposed to the air for some hours, it gives only a slight peroxide reaction. This suggested that the olive-brown complex described at the beginning of this paragraph gives the yellow complex with hydrogen peroxide only because the excess cysteine really keeps it partly in the reduced blue-green form and it is this part which gives the reaction. The blue-green color is very much less intense than the brown of the oxidized complex at the same molar concentration and could easily be masked by relatively smaller quantities of the latter.

To test out this idea 0.0002 *M* cobalt chloride solutions in thirtieth molar secondary phosphate were treated with different quantities of cysteine and the peroxide reaction tried before and after bubbling air through these solutions for various lengths of time. In some cases small amounts of iron salts were added to hasten the oxidation of the excess cysteine. It was found that if the molar ratio of cysteine to cobalt were less than four to one, the peroxide reaction was extremely faint. With larger excesses of cysteine, about twelve moles of cysteine per mole of cobalt, the peroxide reaction was quite intense, but after bubbling air through the solutions as described for fifteen hours a greatly diminished but undoubtedly positive reaction was given by the peroxide.

Work along these lines will be continued in this Laboratory, especially with a view to the isolation of the complex formed in the peroxide reaction as well as complexes it has been found possible to form with cystine by choosing the proper conditions. The complexes of cobalto bis cysteinate with carbon monoxide studied indirectly by Cremer<sup>6</sup> are also being taken up.

**Preparation of the Unoxidized Complexes.**—The unoxidized complexes were prepared in crystalline form, filtered, washed and dried in a stream of purified nitrogen using the apparatus sketched in Fig. 3.

Nitrogen freed from oxygen by passage through a tube packed with copper and kept at 450° enters the system through the wide test-tube A at the left. By successively adjusting the various stopcocks, this nitrogen is passed through all parts of the apparatus until air is completely washed out and the solutions deaerated. Test-tube A containing in solution the cysteine hydrochloride is then inverted by twisting in its rubber connections and the solution is pushed over into B by the nitrogen stream. B contains the necessary potassium hydroxide solution. It is then similarly inverted as A and the alkaline cysteine solution is run into the flask C containing the cobalt chloride solution. Here the complex is formed in a reduced state. The flask I contains alcohol or any other precipitating agent which can be forced back into E by blowing into the outlet of I. The whole system A-B-C-D-F within the dotted area is rigidly connected and can be rotated about the axis indicated after freeing the rubber connections with

<sup>6</sup> W. Cremer, *Biochem. Z.*, 206, 228 (1929).

flasks G and J. At D an alundum disk is fused into glass ground into the flask C at E. After turning upside down, the flask F is connected with J and the now upper outlet M of C is connected with G. At the same time the solution in C falls on the alundum disk and filters. If necessary, suction can be applied through K, closing stopcock L. After filtration is complete water in G and alcohol in H can be forced over successively into C by opening the stopcock M now connected to G. The stream of nitrogen is continued, which dries the precipitate on D. When ready the whole part D is taken out and quickly transferred to a desiccator, which is then evacuated. The dried crystalline compounds are stable in air.

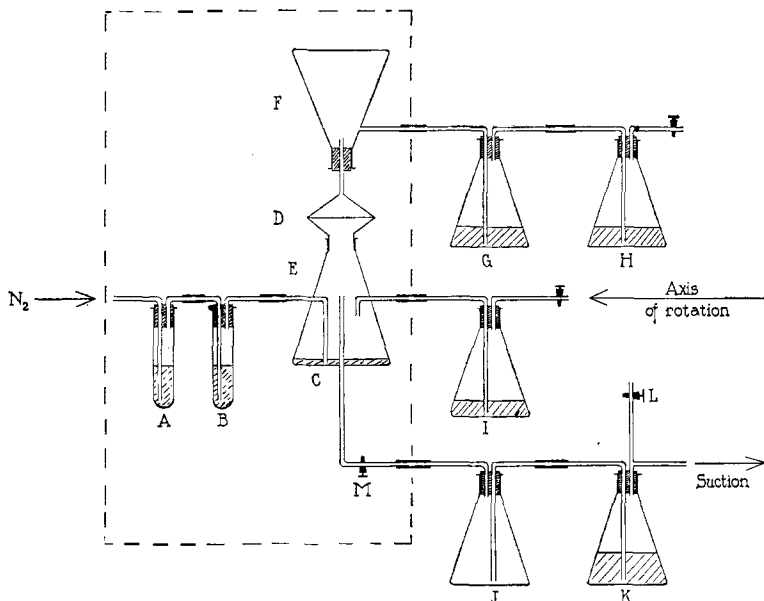


Fig. 3.

**Preparation of Potassium Cobalto Bis Cysteinate (I).**—2.4 g. of cysteine hydrochloride dissolved in 10 cc. of water is put in A; 9 cc. of 7.5 *M* potassium hydroxide and 6 cc. of water are put in B; 7.5 cc. of 1 *M* cobalt chloride and 10 cc. of water in C. After deaeration and mixing as described above the flask C is warmed by bringing under it a beaker of hot water (M is closed and disconnected from J). Alcohol is forced over from I, about 60 cc., and the flask system C-D-F gently rocked and cooled. When cool the rigid system is inverted, the product sucked dry and washed with alcohol from G. After drying *in vacuo* over sulfuric acid, almost 2 g. of product is obtained, consisting of short stubby irregular blue-green needles; calculated for  $\text{Co}(\text{OOCCHNH}_2\text{-CH}_2\text{SK})_2 \cdot 2\text{H}_2\text{O}$ , Co, 14.35; N, 6.81; S, 15.57; K, 18.97. Found: Co, 14.60; N, 6.34; S, 15.66; K, 17.85.

**Preparation of Cobaltous Cobalto Bis Cysteinate.**—The grass-green cobalt salt II can be prepared in the same manner as the preceding compound using 14 cc. of the cobalt chloride solution and 6.5 cc. of potash in place of the quantities used there. It crystallizes out spontaneously, as it is quite insoluble. In fact it is so insoluble that it can even be prepared in the presence of air, but its preparation in the absence of air establishes the divalency of the cobalt.



Sixteen cc. of 7.5 *M* potassium hydroxide is poured into a solution of 10 g. of cysteine hydrochloride in 50 cc. of water and this mixture is poured into 60 cc. of 1 *M* cobalt chloride containing 16 cc. of 7.5 *M* potassium hydroxide. The whole is rapidly mixed, covered and set on ice. After half an hour the long, slender, grass-green needles have completely separated and are filtered off, washed with previously boiled water and then with alcohol. After drying in a vacuum over sulfuric acid, 8.2 g. is obtained; calculated for  $\text{Co}(\text{OOCCHNH}_2\text{CH}_2\text{S})_2\text{Co}\cdot 2\text{H}_2\text{O}$ : Co, 30.10; N, 7.14; S, 16.32. Found: Co, 30.18; N, 6.85; S, 17.00.

Another preparation dried for only a few hours *in vacuo* over sulfuric acid gave: calculated for  $\text{Co}(\text{OOCCHNH}_2\text{CH}_2\text{S})_2\text{Co}\cdot 4\text{H}_2\text{O}$ : Co, 27.56; N, 6.54; S, 14.95. Found: Co, 26.96; N, 6.35; S, 15.09.

The percentage of cobalt precipitable by potassium hydroxide in the first preparation is 18.9%. This probably includes some due to decomposition of the complex by the strong alkali.

**Preparation of the Cobalti-tris-cysteinate Complexes.**—The simplest of the oxidized complexes to prepare is the free acid corresponding to IV. Ten cc. of 7.5 *M* potassium hydroxide in 15 cc. of water is added to a solution of 10 g. of cysteine hydrochloride in 40 cc. of water. This mixture is poured into 33 cc. of 1 *M* cobalt chloride containing 9 cc. of 7.5 *M* potassium hydroxide and the mixture quickly stirred and filtered. Air is bubbled through the mixture for an hour. After a day a heavy precipitate has settled out. Under the microscope this appears as opaque masses of platelets somewhat like bunches of grapes. It filters rapidly on a Büchner funnel and is washed with water several times and finally with alcohol. The product is dried by exposure to the air. Yields of about 90% of the theoretical can easily be obtained. It has not yet been found possible to recrystallize this acid. It is extremely insoluble in acids and water but dissolves in alkali giving cherry-red solutions. Calculated for  $\text{Co}(\text{OOCCHNH}_2\text{CH}_2\text{SH})_3\cdot 3\text{H}_2\text{O}$ : Co, 12.46; N, 8.88; S, 20.29. Found: Co, 12.50; N, 8.75; S, 20.06.

Another preparation which after standing for weeks was filtered and first washed with dilute alkali and dilute acid to remove any other complexes, cysteine or cobaltous hydroxide gave the following results: calculated for  $\text{Co}(\text{OOCCHNH}_2\text{CH}_2\text{SH})_3\cdot 4\text{H}_2\text{O}$ : Co, 12.01; N, 8.55; S, 19.55. Found: Co, 12.03; N, 8.36; S, 19.63.

The potassium salt of this complex has been made by dissolving 1 g. of the free acid in 25 cc. of water with 1.5 cc. of 7.5 *M* potassium hydroxide. The solution was evaporated somewhat and methyl alcohol and ethyl alcohol added in about equal parts until about 50 cc. had been added. Long red needle-like crystals separated. Calculated for  $\text{Co}(\text{OOCCHNH}_2\text{CH}_2\text{SK})_3\cdot 2\text{H}_2\text{O}$ : Co, 10.37; N, 7.38; K, 20.57. Found: Co, 10.21; N, 7.47; K, 20.25.

The conditions under which these latter crystals are formed have not been fully worked out and it frequently happens that the product obtained instead of being crystalline is amorphous or liquid. This complex gives extremely insoluble alkaline earth salts which have not been crystallized.

**Preparation of the Cobalti-bis-cysteinate Complexes.**—The free acid corresponding to the oxidized complex III has been prepared, starting with both bivalent and trivalent cobalt. Either procedure gives the same crystalline product in about 50–60% of the theoretical yield. Only the procedure starting with bivalent cobalt need be described. Five grams of cysteine hydrochloride is dissolved in 20 cc. of water and 7.5 cc. of 7.5 *M* potassium hydroxide is added. This solution is poured into 16 cc. of 1 *M* cobalt chloride containing 4.5 cc. of 7.5 *M* potassium hydroxide. The mixture is stirred and filtered into a flask and air is sucked through for about an hour. Then concentrated hydrochloric acid is added drop by drop until the amorphous precipitate first formed redissolves

or crystallization begins. Then 50 cc. of 95% alcohol is added and the whole set on ice. The crystals usually come out in the form of hexagonal plates and complicated patterns of these, but occasionally the crystal shape was altogether different. They are filtered, washed with a little cold water and then with alcohol. The yield after drying by exposure to the air is 3.7 g. The product may be recrystallized by dissolving in potassium hydroxide and reprecipitating with hydrochloric acid and alcohol. The mean of results from several independent preparations follows. Calculated for  $[\text{Co}(\text{OOCCH}_2\text{NH}_2\text{CH}_2\text{SH})_2\text{OH}]_2 \cdot 8\text{H}_2\text{O}$ : Co, 15.20; N, 7.22; S, 16.50. Found: Co, 15.39; N, 7.26; S, 16.99.

The potassium salt of this complex was obtained by following the above procedure through the sucking of air through the mixture for one hour then alcohol is slowly added till precipitation begins. The crystallization of this potassium salt is, like that of the potassium tris-cysteinate complex previously described, subject to undetermined factors which frequently lead to amorphous or liquid precipitates. The latter usually form if the solution is too alkaline. The analysis of a crop of needle-like brown crystals growing in dense sheaves is given. Calculated for  $[\text{Co}(\text{OOCCHNH}_2\text{CH}_2\text{S})_2\text{HK}(\text{OH})_2] \cdot 4\text{H}_2\text{O}$ : Co, 15.10; N, 7.18; S, 16.42; K, 10.01. Found: Co, 15.29; N, 7.49; S, 16.22; K, 9.35.

The corresponding barium salt has also been crystallized by starting with the free acid previously described, dissolving in water with the aid of a little potassium hydroxide and adding barium chloride solution. The crystals are cubical. Calculated for  $[\text{Co}(\text{OOCCHNH}_2\text{CH}_2\text{S})_2\text{H}(\text{OH})_2] \cdot \text{Ba} \cdot 9\text{H}_2\text{O}$ : Ba, 14.75; Co, 12.70; S, 13.78; N, 6.01;  $\text{H}_2\text{O}$ , 19.38. Found: Ba, 14.70; Co, 12.71; S, 14.01; N, 5.73;  $\text{H}_2\text{O}$ , 19.26.

This is the only one of the cysteine complexes in which water could be determined by heating to constant weight at  $110^\circ$ , all the others slowly undergoing decomposition during which nitrogen is lost. Water could not well be determined in a vacuum over sulfuric acid as in most cases even after weeks no definite end-point could be found.

The free acid of this series dissolves only slightly in water but readily on addition of hydrochloric acid. From sufficiently strong hydrochloric acid long brown needle-shaped crystals of a hydrochloride deposit and are stable so long as the acid concentration is maintained high enough. Preparations were made as follows. Two grams of the free acid is dissolved in 15 cc. of water with 15 cc. of concentrated hydrochloric acid and 5 to 10 cc. of alcohol is added. The mixture is set on ice for an hour or two, then filtered on a Büchner funnel and sucked as dry as possible. The compound cannot be washed with water or alcohol as it readily loses hydrogen chloride, giving the free acid again. Drying in a vacuum over concentrated sulfuric acid causes dissociation of considerable hydrogen chloride, as is evident on opening the desiccator. Analysis of the compound so dried gave these figures: calculated for  $[\text{Co}(\text{OOCCH}_2\text{NH}_2\text{CH}_2\text{SH})_2\text{OH}]_2 \cdot 3\text{HCl} \cdot \text{H}_2\text{O}$ : Co, 15.54; N, 7.38; Cl, 14.03. Found: Co, 15.71; N, 7.12; Cl, 14.10.

The corresponding picrate was prepared by dissolving 1.7 g. of the free acid in 60 cc. of water with the aid of 10 cc. of concentrated hydrochloric acid and then adding 150 cc. of saturated picric acid. A crystalline precipitate consisting of brown needles and a few square plates settled out. This, like the hydrochloride, could not be washed but was merely sucked as dry as possible. After drying in a vacuum over concentrated sulfuric acid, 3 g. was obtained. The analyses corresponded to  $[\text{Co}(\text{OOCCHNH}_2\text{CH}_2\text{SH})_2] \cdot \text{C}_6\text{H}_2(\text{NO}_2)_3\text{OH} \cdot 9\text{H}_2\text{O}$ . Calculated: Co, 8.56; N, 10.15; S, 9.29. Found: Co, 8.58; N, 11.64; S, 9.64.

The very high nitrogen content is probably due to the fact that the precipitate could not be washed, and retained some of the mother liquors containing excess picric acid.

Oxygen consumption studies on the formation of the oxidized complexes similar to those described in the study of the thioglycolic acid complexes show that one equivalent of oxygen is taken up for each mole of cobalt.

### Summary

A number of cobalt complexes of cysteine in both reduced and oxidized states have been crystallized and their chemical constitutions, properties and interrelationships discussed.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE LABORATORY OF FOODS AND SANITATION, UNIVERSITY OF WISCONSIN]

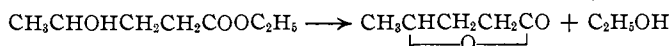
## LEVULINIC ACID. III. THE HYDROGENATION OF CERTAIN OF ITS ALKYL ESTERS IN THE PRESENCE OF PLATINUM CATALYST

BY RALPH W. THOMAS, H. A. SCHUETTE AND MILFORD A. COWLEY

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The discovery<sup>1</sup> that levulinic acid readily may be converted to  $\gamma$ -hydroxy-*n*-valeric acid with hydrogen in the presence of platinum catalyst logically leads to a study of the behavior of its alkyl esters under similar conditions. The resulting compounds of such a reaction, the esters of  $\gamma$ -hydroxy-*n*-valeric acid, have not yet been described. Neugebauer<sup>2</sup> reported the synthesis of the ethyl derivative from the silver salt of the acid and ethyl iodide. On attempting to purify the resulting ester by fractional distillation, he found, however, that it underwent decomposition with the formation of ethanol and *n*-valerolactone, as follows



This observation is of interest in that it suggests that the alkyl esters of  $\gamma$ -hydroxy-*n*-valeric acid show that same instability which is characteristic of the parent acid.

That this instability is not alone a property of the ethyl ester and that the rate of hydrogenation is a function of the size of the alkyl residue and the solvent employed, if any, have been demonstrated in this Laboratory. The presentation of pertinent data is the object of this communication.

**Rate of Hydrogenation.**—Two series of hydrogenations of the methyl, ethyl, *n*- and isopropyl, and *n*- and isobutyl esters<sup>3</sup> of levulinic acid were carried out with portions of the same preparation of catalyst<sup>4</sup> in the usual mechanical shaker operating with hydrogen under a pressure of two to three atmospheres and at a temperature of 22–24°. No solvent was em-

<sup>1</sup> Schuette and Thomas, *THIS JOURNAL*, **52**, 3010 (1930).

<sup>2</sup> Neugebauer, *Ann.*, **227**, 101 (1885).

<sup>3</sup> Schuette and Cowley, *THIS JOURNAL*, **53**, 3485 (1931).

<sup>4</sup> Voorhees and Adams, *ibid.*, **44**, 1397 (1922).