

The Walden Inversion in the Reactions of Cobalt Complexes*

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The Walden Inversion in the reactions of cobalt complexes has been known for thirty years, so you may wonder why I have chosen to talk on this subject today. There are two reasons for my choice. First, as developments in our knowledge of optical inversions in reactions of cobalt complexes took place, some interpretations were made which we know now were not correct. I wish to clarify the misunderstandings which have thus arisen. Secondly, we have done some new work on the optical inversion, and have new insights into it. These may be of interest to you.

Paul Walden [1] discovered in 1895 that if *dextro*-ethyl chlorosuccinate were treated with potassium hydroxide, *levo*-ethyl malate resulted, but if silver oxide were used in place of potassium hydroxide, the resultant malate ester was *dextro*. In addition, he showed that the conversion of ethyl malate to ethyl chlorosuccinate also might involve an inversion, depending on whether the chlorinating agent used was phosphorus pentachloride or thionyl chloride. These discoveries were of tremendous importance, because they focussed the attention of chemists upon the importance of reaction mechanisms. Organic chemists made detailed studies of the Walden Inversion, and some thirty different theories were advanced to account for this remarkable phenomenon. Some of these were based on the geometry of the tetrahedron; others, on rate of reaction versus rate of rearrangement; still others, on a possible directive influence of the central carbon atom. In a famous paper [2], published in 1911, Alfred Werner advanced a theory of the Walden Inversion, based upon his investigations of substitution reactions of cobalt complexes in which he observed rearrangement of the *trans* configuration to the *cis*, and vice versa. This theory was based upon the assumption that the metal atom at the center of the complex exerted a directive influence upon incoming groups. In this paper, Werner did not mention the possibility of optical inversion in metal complexes. It was only in that year, that he and his student, V. L. King [3], had resolved the first metal complex and it may well be that Werner's famous paper, to which I have referred, had already been written when the first resolution was effected.

About thirty years ago, convincing evidence was brought forward to show that the Walden Inversion in the reactions of carbon compounds takes place

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by a "back side" attack on the carbon tetrahedron. For example, in the conversion of chlorosuccinate to malate, the hydroxide ion of the attacking molecule approaches the face of the tetrahedron which is opposite the chlorine, and attaches itself to the carbon atom in some fashion. The chlorine then splits off and the three other groups which are attached to the carbon flip over (like an umbrella turning wrong side out) to give an inverted configuration. It is now believed that this is a general mechanism for substitution reactions in carbon compounds. If the overall reaction takes place in an odd number of steps, the product has the inverted configuration; if it takes place in an even number of steps, the product has the same configuration as the starting material.

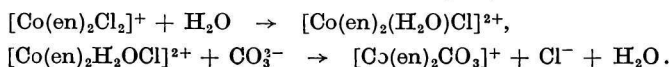
When we first began our search for reactions which might involve optical inversions in metal complexes, we were under the naive impression that substitution reactions in cobalt complexes would be quite comparable to those in organic compounds. This has turned out to be quite erroneous. The geometry of the octahedron is, of course, quite different from that of the tetrahedron, and the bond by which chlorine is attached to cobalt is quite different from that by which chlorine is attached to carbon. The reactions are alike in that each leads to a product of opposite configuration to that of the original material, but beyond this, there is little similarity. Some question has been raised, as a matter of fact, as to whether the inversion reactions shown by octahedral metal complexes should be referred to as Walden Inversions.

The first experiments which we did in our search for optical inversions in the reactions of octahedral complexes were carried out by Robert W. Auten, who was then an undergraduate student at the University. Neither he nor I had ever worked in the field of coordination compounds and neither of us had ever resolved a racemic compound. Our choice of a reaction to study was therefore a somewhat blind one and, as it turned out, an extremely fortuitous one. Werner had reported the preparation and resolution of *cis*-dichloro-bis-ethylenediamine cobalt(III) chloride [4] and had observed that when the *levo* form* of this substance was allowed to react with potassium carbonate in water solution, the *dextro*-carbonato-bis-ethylenediamine cobalt(III) ion was obtained [5]. The preparation and resolution of the starting material looked simple, and the resultant carbonato complex was reported to be stable toward racemization, so this is the system that we chose for study. The resolution of the dichloro complex caused unexpected difficulties. Werner's directions called for the addition of eleven grams of ammonium bromo- α -camphor- π -

* In more recent times, it has become possible to determine absolute configurations. This has introduced some changes in nomenclature, and the isomer of $[\text{Co}(\text{en})_2\text{Cl}_2]^+$ which Werner called *l* is now called *D*.

-sulfonate to five grams of the *cis*-dichloro-bis-ethylenediamine cobalt chloride dissolved in 140 ml. of water. He reported that the bromo-camphor- π -sulfonate diastereoisomer precipitated quickly and in good yield. However, when Mr. Auten followed these directions explicitly, no precipitate formed. Two or three repetitions of the experiment did not give any better results. Auten then reasoned that since Americans keep their buildings somewhat warmer than Europeans do, it was possible that Werner had worked at a somewhat lower temperature than he was using. He therefore repeated the experiment, with the solution of the dichloro complex cooled to 16°. This gave results which exactly duplicated Werner's.

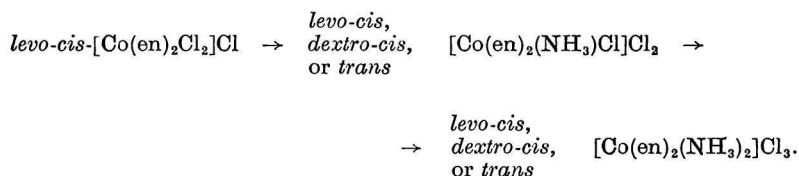
Since Walden had used potassium hydroxide and silver oxide in his famous experiment, we thought it would be logical to study the reaction of silver carbonate with the dichloro-bis-ethylenediamine cobalt(III) ion. Much to our delight, the carbonato complex which was obtained rotated light (at the sodium-*D* line) to the left (that is, *levo* in Werner's notation). We thus had evidence for the first Walden Inversion in the reactions of a cobalt complex [6]. Auten then tried other substituting groups, such as oxalate, but in these other cases he did not find any evidence for optical inversion. Several other students later replaced the coordinated chlorines in the dichloro-bis-ethylenediamine cobalt ion with nitrite, sulfate, and other negative ions, but in no case was there evidence for inversion. We also tried to use other reagents than potassium carbonate and silver carbonate in the carbonate reaction, but those that we tried gave the same result as potassium carbonate [7]. The original observation that potassium carbonate and silver carbonate give different results was confirmed by J. P. Mathieu [8], who also showed, from measurements of circular dichroism, that the carbonato complex which was obtained by the use of potassium carbonate was the non-inverted form. It was later observed in our laboratory, however, that the use of a small amount of silver carbonate gives a product of *dextro* rotation. It was observed also (by J. P. McReynolds [9]) that the reaction between the *levo-cis*-dichloro-bis-ethylenediamine ion and potassium carbonate leads to the *dextro* carbonato complex if relatively small concentrations of potassium carbonate are used, but to the *levo* carbonato complex if a very high concentration of potassium carbonate is used. D. F. Peppard made [10] the significant observation that if dry potassium carbonate is intimately ground in a mortar with *levo-cis*-dichloro-bis-ethylenediamine cobalt(III) ion and water is then added to the mixture, the resultant carbonato compound shows a *levo* rotation. These studies led us to believe that aquation is important in the reaction in which inversion does not take place, and we wrote the following equations:



It was our belief that the reaction which led to an uninverted product resulted from direct substitution. In any event, it was clearly established that the course of the reaction does not depend solely upon the nature of the metallic ion in the reagent.

In a later study, carried out with the help of J. H. Haslam and Eldon M. Jones [11], it was observed that the reaction of dichloro-bis-ethylenediamine cobalt(III) chloride with ammonia gives the *levo* rotatory diammine-bis-ethylenediamine cobalt(III) ion when carried out at dry ice or liquid ammonia temperatures, but a *dextro* rotatory product when carried out at room temperature or at $+80^\circ$. Studies of the optical rotatory dispersion curves indicate that the inversion takes place in the low temperature reaction.

The replacement of the two chloro groups by ammonia molecules is a two-step reaction, and each of the two steps may involve optical inversion or rearrangement in the *cis-trans* sense:



A considerable amount of *trans* diammine is formed at the lower temperatures, as is shown in Table 1 [12].

Table 1

Products formed in the reaction
 $\textit{levo-cis}\text{-}[\text{Co(en)}_2\text{Cl}_2]\text{Cl} \rightarrow [\text{Co(en)}_2(\text{NH}_3)_2]\text{Cl}_3$

Temperature of reaction, 0°	Configuration of product (ratio <i>cis/trans</i>)	$[\alpha]_D$ of <i>cis</i> product
-77	2.5/1	-32°
-33	2.85/1	-22°
+25	3.7/1	+18°
+80	∞	+38°

In the reaction between the dichloro complex and ammonia at 80° , the reaction takes place while the complex is in the solid state. This may account, in part, for the fact that there is no inversion at that temperature and no detectable rearrangement to the *trans* form. That this is not the sole factor

is indicated, however, by the fact that the optical activity of the product obtained from liquid ammonia, as well as the relative amounts of the *cis* and *trans* isomers, varies with the temperature.

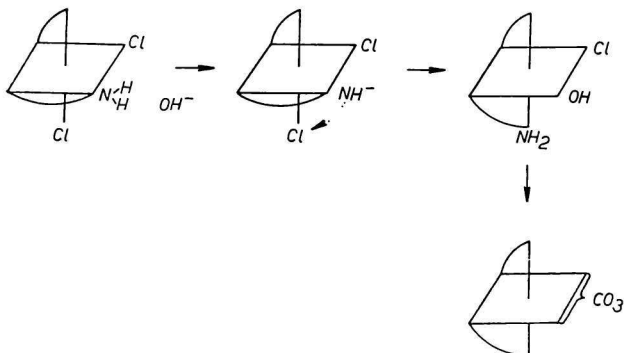
It was our original belief that since each step of the reaction with ammonia involved the replacement of a chloro group by an ammonia molecule, the mechanisms of the two steps would be the same and that the product could not be inverted under any set of experimental conditions. We were therefore somewhat surprised to discover that the diammine can be formed in either the inverted or non-inverted form. It is a little difficult to study the first step, because by the time an appreciable amount of chloro-ammine-diethylenediamine cobalt(III) ion is formed, some of it has reacted further to give the diammine. Earl Greenwood [12] studied the second step of the replacement — that is, the conversion of the chloro-ammine complex to the diammine complex, and found no evidence for optical inversion under any conditions. More recently, Dr. Ronald Archer has made a careful study of the first step of the reaction [13] and has confirmed the fact that the inversion takes place in the replacement of the first chlorine atom. Evidently, the substitution of the first ammonia molecule for a chlorine so alters the nature of the complex that the replacement of the second chlorine follows a different mechanism.

Encouraged by the discovery of an optical inversion in the reaction of ammonia with the dichloro complex, we attempted to replace the chlorine atoms by other neutral molecules, but in no case did we obtain evidence for an inversion. Charles Hance [14] studied the reaction of ammonia with the analogous dichloro-bis-ethylenediamine chromium(III) ion, but found no evidence for optical inversion. This was a great disappointment to us, for we had hoped that we could make a detailed comparison of the cobalt(III) and chromium(III) complexes.

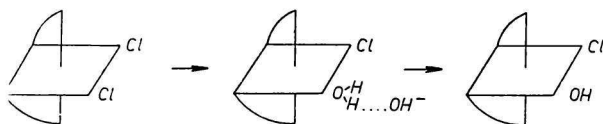
At the outset of our study of the reaction between ammonia and the dichloro-bis-ethylenediamine cobalt(III) ion, we encountered an interesting phenomenon which almost caused us to miss the discovery of the inversion. Throughout our studies, we had made all of our measurements of optical rotation at the sodium-*D* line. When Mr. Haslam prepared the diammine complex from the optically active dichloro compound for the first time, he reported to me that the product was optically inactive; this suggested that the reaction led to complete racemization. This seemed strange, for the reaction conditions were quite mild. I therefore asked him to repeat the experiment. The result was the same. I then suggested that he measure the optical rotation of the product at some other wavelength. When he made the measurements at the mercury-*E* line, he observed that the product had optical activity. The rotatory dispersion curve of the diammine complex, like that of other colored compounds, is quite anomalous, and the same sample shows *dextro* rotation at one wave-

length and *levo* rotation at another. It happens that, with this compound, the dispersion curve crosses the zero line very close to the sodium-*D* line, so the substance is optically active but at that wave length shows zero rotation.

Our inability to find other examples of the Walden Inversion always bothered me, for I was afraid that we had made some mistake. Mathieu's qualitative check on our results in the carbonate reaction gave me some comfort, but did not completely convince me that we really had an optical inversion. Some of my students also questioned whether our results were correct, and I am sure that many other chemists did, also. Among those who expressed his doubts was Professor Frank P. Dwyer, who undertook to test our experiments and conclusions. He made the significant observation that in the two cases in which optical inversions had been observed, the reagents were basic. From this, he theorized that the presence of a base, as well as the presence of silver ion, is necessary, to produce the inversion [15]. He quickly demonstrated that the reaction of nitrite ion with dichloro-cobalt(III) ion in neutral solution gives a dinitro compound of the same configuration as the initial material, even in the presence of silver ion, but in a basic solution, the same reagents give a compound with inverted configuration. Professor Dwyer's untimely death occurred soon after he made this key discovery. Dr. Laurence Boucher and Dr. Eishun Kyuno, working in my laboratory, have extended Professor Dwyer's work and have shown that the presence of silver ion is not necessary, although inversion appears at lower basicities if silver ion is present [16]. Boucher and Kyuno have demonstrated that in aqueous solution, at least, the inversion takes place in the reaction of the dichloro-bis-ethylenediamine cobalt(III) ion with the hydroxide ion. This yields the inverted form (and much of the *trans* form) of chloro-hydroxo-bis-ethylenediamine ion. This ion is not suitable for study because it racemizes very rapidly. Once it has been formed, however, the hydroxo and chloro groups can be replaced by nitro, carbonato, acetylacetonato, or other groups to yield products which are optically stable and which can be isolated in optically active form. The key to the whole inversion reaction is the removal of a proton from the complex. The observations which Dr. Boucher and Dr. Kyuno have made lead us to believe that this proton is lost from one of the coordinated nitrogen atoms. This leaves a negative charge on that nitrogen atom and allows it to move toward an adjacent coordinated chlorine atom. An hydroxide ion from the solution now takes the place which the nitrogen originally occupied, and the chlorine atom is released from the complex. This release is facilitated by the presence of silver ion, but is effected in the absence of silver ion if the concentration of hydroxide ion is sufficiently large. The amine nitrogen eventually combines with a proton from the solvent to become, again, part of an NH_2 group. The course of the reaction is shown by the following diagrams:



If attack by the base is preceded by aquation, the proton will be lost from the aquo ligand rather than from the less acidic amine ligand. This leads to the formation of the non-inverted hydroxo-chloro complex, in accordance with the observations of McReynolds and Peppard.



Depending upon which nitrogen atom is attacked in the reaction of $[\text{Co}(\text{en})_2\text{Cl}_2]\text{Cl}$ with hydroxide ion, the hydroxo-chloro complex can have either the *cis* or *trans* configuration. If these two ligands are replaced by nitro or other unidentate groups, the product can be either *cis* or *trans*. If, however, the replacing group is bidentate (carbonate, oxalate, acetylacetonate, etc.), the product must have a *cis* configuration. Any complex ions which have gone through an intermediate *trans* configuration can, of course, be either *dextro* or *levo*. This accounts for the fact that a rather large amount of racemization takes place. A similar mechanism can be postulated for the reaction between the dichloro complex and ammonia.

If this hypothesis is correct, complexes containing diamines which have no hydrogen atoms attached to the nitrogen atoms should not undergo inversion reactions. To test this point, we have attempted to prepare the *cis*-dichloro-bis(1,10-phenanthroline)-cobalt(III) ion and the *cis*-dichloro-bis-(*N,N,N',N'*-tetramethylethylenediamine)-cobalt(III) ion, which we have hoped to use in studies of the inversion. Unfortunately, we have not been able to obtain either of these ions. In the first case, only the tris-1,10-phenanthroline complex has been obtained and, in the second case, the tertiary nitrogens seem unable to coordinate firmly to the cobalt, and no compound stable enough for study has been isolated. However, we are still hoping to find a diamine or other bidentate group which will serve our purpose. We have

also attempted to prepare the *cis*-dichloro-bis-trimethylenediamine cobalt(III) ion, but have been able to obtain only the *trans* form. We hope ultimately, also, to find inversion reactions in other types of cobalt complexes and in complexes of other metals.

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