

Alfred Werner's Coordination Chemistry: New Insights from Old Samples**

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Alfred Werner · chirality · cobaltamines · coordination chemistry · spontaneous resolution

Dedicated to Gerhard Ertl on the occasion of his 75th birthday

Alfred Werner (1866–1919) is the undisputed founder of coordination chemistry, but many years passed before his stereochemical insights were accepted. Only after he proved conclusively that metal complexes can be chiral did his model become accepted and earn him the nickname “Inorganic Kekulé” and the Nobel Prize in Chemistry in 1913. But it took more than ten years from the time he predicted chirality in coordination compounds for his group to succeed in separating enantiomers. During the 1980s, reports appeared stating that some of the compounds originally prepared by one of Werner's students, Edith Humphrey, resolve spontaneously into the enantiomers during crystallization. This led to the claim that Werner could have proven his theory much earlier, if he had only tested a single crystal for optical activity. However, our re-examination of the original samples, which are stored in the Werner collection at the University of Zurich, and perusal of the corresponding doctoral theses of Werner's students, reveals new aspects of conglomerate crystallization in the old samples.

A Genius in Stereochemistry

Alfred Werner (Figure 1) was born December 12, 1866 in Mulhouse.^[1] From early on he showed a keen interest in



Figure 1. Alfred Werner in 1913 and the stereochemistry of nitrogen compounds, as introduced by him in his first publication.

chemistry. During his military service he attended lectures at the *Technische Hochschule* in Karlsruhe before he moved to Zürich in 1886 to study at the *Polytechnikum* (now *Eidgenössische Technische Hochschule, ETH*) under the direction of Arthur Hantzsch (1857–1935; Figure 2), Georg Lunge, and William Treadwell. In his doctoral work, supervised by Hantzsch, Werner already showed his strength in stereo-



Figure 2. Alfred Werner and Arthur Hantzsch in 1910.

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chemical imagination. He pointed out that the stereochemistry of nitrogen must be characterized by a tetrahedron and should allow optical isomers (Figure 1), and he challenged Victor Meyer's isomerism model of benzildioximes.^[2] Hantzsch made clear in a final note in the corresponding publication in *Berichte* that Werner was the sole father of this concept.^[3,4] Experimental proof of asymmetric nitrogen was reported ten years later by Pope and Peachey.^[5] After a few months with Berthelot in Paris, Werner returned to Zürich, and in 1892 he submitted his *Habilitation* at the ETH entitled "*Beiträge zur Theorie der Affinität und Valenz*" ("Contributions to the theory of affinity and valence").

Trained as an organic chemist, Werner had not performed a single experiment in the field of coordination chemistry at the time he published his revolutionary paper "*Beitrag zur Konstitution anorganischer Verbindungen*" ("Contribution to the constitution of inorganic compounds").^[6] An unidentified colleague described this work later as "an ingenious impudence".^[7] According to Ernst Berl, Werner's doctoral student and assistant from 1899 to 1910, Werner dreamed about his coordination theory after preparing lectures on inorganic chemistry.^[8] Like Kekulé, Werner had subconsciously worked out the solution to the problem of stereochemistry in metal complexes. He woke up and formulated throughout the night and the next day what would become the foundation of coordination chemistry.^[1]



Karl-Heinz Ernst first trained as a laboratory technician and then studied chemical engineering and chemistry. He obtained his PhD from the Freie Universität Berlin, conducted postdoctoral research at the University of Washington in Seattle, and then joined Empa, the Swiss Federal Laboratories for Materials Science and Technology. In 1995 he founded the Molecular Surface Science Group, specializing in the chirality of two-dimensional molecular crystals, functional surfaces, and single-molecule surface dynamics. He lectures at the ETH Zurich and holds an adjunct faculty position at the University of Zurich.



Heinz Berke received his PhD from the University of Tübingen in 1974. After a postdoctoral stay with Roald Hoffmann at Cornell University in 1977, he finished his *Habilitation* in Konstanz in 1981 and was awarded the Heisenberg Fellowship from the Deutsche Forschungsgemeinschaft and the Dozentenpreis of the Fonds der Chemischen Industrie. After being promoted to professor at the University of Konstanz, he joined the University of Zurich in 1988. His research activities cover various fields of organometallic chemistry, transition-metal hydrides, C–C coupling reactions mediated by transition-metal complexes, and metallacumulenes.

Coordination Chemistry of the 19th Century

Following isolated studies by Gmelin and others, cobalt complexes gained broader interest after the pioneering work of Genth, Claudet, and Edmond Frémy (1814–1894) published in 1852.^[9] These *flavo*, *croceo*, *luteo*, *purpureo*, *roseo*, *praseo*, and *violeo* compounds had fascinated chemists in the mid-nineteenth century because of their beautiful colors. Werner's revolutionary theory was actually based on experimental data carefully gathered by Sophus Mads Jørgensen (1837–1914), professor of chemistry in Copenhagen. Jørgensen studied intensively the coordination compounds of chromium, cobalt, rhodium, and platinum, and interpreted their structure in the light of the chain theory proposed by the Swedish chemist Christian Wilhelm Blomstrand (1826–1897). Blomstrand had suggested that ammonia molecules could be linked together as $-\text{NH}_3-$ chains, analogous to $-\text{CH}_2-$ chains in hydrocarbons (Figure 3).^[10] This description remained unchallenged until Werner's publication in 1893.^[6]

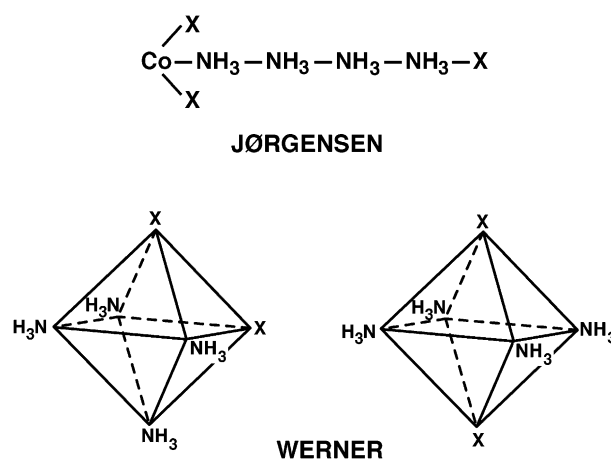


Figure 3. Top: Blomstrand–Jørgensen formula for *praseo* cobalt ammine complexes of the type $[\text{Co}(\text{NH}_3)_4\text{X}_2]^+$ with pentavalent nitrogen atoms. Bottom: Illustration of octahedral *cis* and *trans* isomers of the same complex, $[\text{Co}(\text{NH}_3)_4\text{X}_2]^+$.

Werner rejected the formally pentavalent nitrogen in Blomstrand's chain formulas and abandoned Kekulé's concept of the fixed valency of a chemical element. Instead he introduced the concept of the coordination number as the number of groups around the central metal atom and assumed that ligands could be replaced by other groups. The most frequent coordination numbers were six (octahedral, for example, Co^{III}) and four (square-planar, for example, Pt^{II}). With his remarkable stereochemical perception, he realized immediately that this arrangement must lead to stereoisomers. Like van't Hoff, Werner used the method of isomer counting in order to predict new compounds (Figure 4).^[2] Consequently, he interpreted the *croceo* and *violeo* salts as *cis* and *trans* isomers of an octahedral complex. His new model explained the observation that the neutral $[\text{Co}(\text{NH}_3)_3\text{Cl}_3]$ complex did not form a precipitate upon treatment with silver ions. The Jørgensen–Blomstrand model proposed that chlorine atoms in the chains are weakly bound and can

therefore react with silver ions, while those directly connected to the metal atom cannot. According to this model, however, at least one chlorine atom in $[\text{Co}(\text{NH}_3)_3\text{Cl}_3]$ must be located in

Qui nimium probat, nihil probat^[**]

Although Werner's theory had supporters like Victor Meyer, it was questioned for long time. This may be because Jørgensen, who was very influential and famous at that time, opposed Werner's coordination chemistry.^[15] Henri Moissan actually nominated Jørgensen for the Nobel Prize in 1907, only weeks before his own death.^[16] He wrote to the Nobel committee (in French): "Within this particular area of the chemistry of metal ammonia bases, which connects the inorganic chemistry with the most complicated organic chemistry, Mr. Jørgensen occupies a great position. With a few exceptions, he has coordinated and classified all the series of these compounds with the trivalent metals ... Mr. Jørgensen's work is important and deserves to be bestowed attention." And: "Mr. Werner's investigations and interpretations of this subject have in no way reduced the value of the results achieved by Mr. Jørgensen."^[17]

Like Kolbe and his harsh criticism on van't Hoff's theory of the tetrahedral carbon atom,^[2,18] Jørgensen was reluctant to engage in any speculations. He pointed out that compounds predicted by Werner's theory had not been observed, and therefore did not exist. Jørgensen criticized not only Werner's method, but he also claimed that Werner had deliberately misrepresented experimental data. He even accused Werner of unethical behavior by arriving at his results "surreptitiously".^{[**][19]} Fritz Reitzenstein, a chemist from Würzburg, who wrote his *Habilitation* on this controversy, discussed in great detail the work of the two antagonists, responses of numerous chemists concerning the matter, and shortcomings of both theories. His final conclusion was slightly in favor of Werner's theory and he rejected Jørgensen's polemic that "Werner's theory has been received in many quarters with much applause—although hardly from those who have dealt in detail with the metal-ammonia salts."^{[***][20]} In his last comment on Werner's theory, however, Jørgensen's denied that such statements had had any offensive intention.^[21] Jørgensen probably never accepted Werner's model,^[16] although Kauffman claimed that this was the case when Werner reported the synthesis of the previously unknown *cis*- $[\text{Co}(\text{NH}_3)_4\text{Cl}_2]\text{Cl}$ in 1907, a compound predicted by his theory.^[15] Werner's success, however, was yet not sufficient to impress the Nobel Prize committee in Stockholm. In the following years Werner received 19 nominations for the prize, the first together with Jørgensen and others in 1907.^[16] Only after his group proved the chirality of certain coordination compounds did his theory finally become accepted, and Werner was awarded the Nobel Prize in 1913.

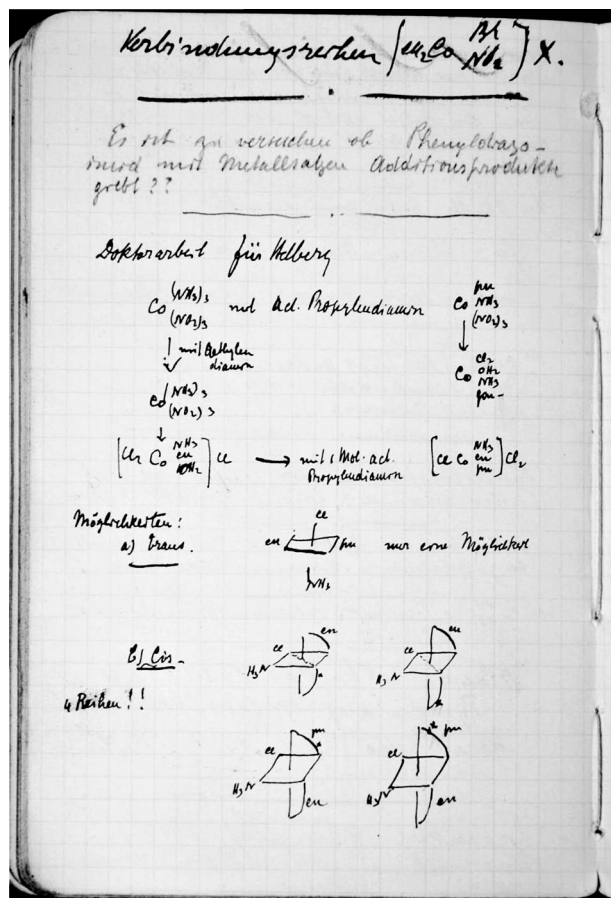


Figure 4. Page from Werner's notebook with the concept for the synthesis of propylene diamine cobalt salts to be pursued by his doctoral student Nathan Helberg, and the prediction of the number of isomers to be expected. (Photographed with permission from the archives of the University of Zurich, Zentralbibliothek Zürich, Werner Nachlass, Signatur 1.2–1.6.)

the chain and precipitation of AgCl was expected to take place. Yet it was not observed. Together with Arturo Miolati,^[11] Werner also presented quite early compelling evidence for his model by electrical conductivity measurements.^[12]

By 1910 Werner had basically deduced the complete chemistry of polynuclear cobalt(III) amines complexes with bridging groups such as NH_2 , OH , SO_4 , NO_2 , and O_2 , and containing up to four cobalt centers, and had predicted accurately their structures.^[13] In 1905 the first edition of his book "Neuere Anschauungen auf dem Gebiete der Anorganischen Chemie" appeared, which guided generations of chemists since then.^[14]

[*] "One who proves too much, proves nothing." Jørgensen on Werner in Ref. [19], p. 323.

[**] "... a pure subreption": "... so kommt er zu diesem, allen chemischen Begriffen widerstrebendem Resultate durch eine bloße Subreption."

[***] "... weil WERNER'S Theorie von mehreren Seiten mit großem Beifall empfangen worden ist—allerdings kaum von derjenigen Seite, welche sich eingehender mit den Metallammonialsalzen beschäftigt hat—..." Ref. [19], p. 317.

Well, Does It Rotate Yet?

Werner realized early on that certain isomers are like mirror images of each other and that the proof of chirality of such compounds would confirm his model. In a publication with his student Vilmos in 1899 he discussed the chiral cobalt oxalate $[\text{Co}(\text{en})_2\text{C}_2\text{O}_4]\text{X}$ (**1**; en = ethylenediamine).^[22] He stated: “The resulting model allows two configurations that behave like nonsuperimposable image and mirror image.”^[*] He also made clear that this optical isomerism is different from that of organic compounds, since there is no asymmetric carbon atom involved. In addition, he proposed an optically active spiro compound (Figure 5) as an example from the

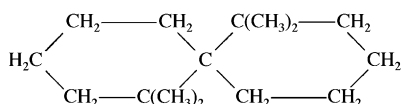


Figure 5. The chiral *spiro*-pentadecane without asymmetric carbon atoms as proposed by Werner.

organic realm. Overlooking van't Hoff's “second case of optical activity” of cumulated dienes,^[2,18] most of the chemists at that time believed that the presence of an asymmetric carbon atom was a necessary condition for optical activity.^[23] Perkin, Pope, and Wallach finally delivered the proof of optical activity in chiral compounds devoid of an asymmetric carbon atom ten years after Werner's proposal.^[24]

Over a period of ten years several people in Werner's laboratory tried unsuccessfully to prove the existence of optically active metal complexes. It is still unclear why it took so long before the American Victor L. King (Figures 6 and 7) succeeded with the resolution of $[\text{Co}(\text{en})_2\text{NH}_3\text{Cl}]\text{Cl}_2$ using *d*-bromocamphorsulfonate.^[25] This method had been established by Pope and Kipping already in 1893.^[26] King recalled in 1942: “After having made these 2000 separate fractional crystallizations which proved that the opposite ends of the system were precisely alike and that we had to do something more drastic, I proposed increasing the dissimilarity of the diastomers by using brom camphor sulfonic acid as a salt-forming constituent having extremely high optical activity. When this was tried, the isomers in the form of these salts literally fell apart. Prior to this, almost everyone in academic circles, knowing the reputation of the problem, used to greet me on the street in Zurich with the inquiry, ‘Well, does it rotate yet?’.”^[27]

After this success, Werner's group managed the separation of more than forty chiral complex compounds, including the carbon-free tetranuclear hexol complex (Figure 8),^[28] which had actually been first synthesized by Jørgensen. They also used separated the enantiomers of 2,3-dimethylsuccinic

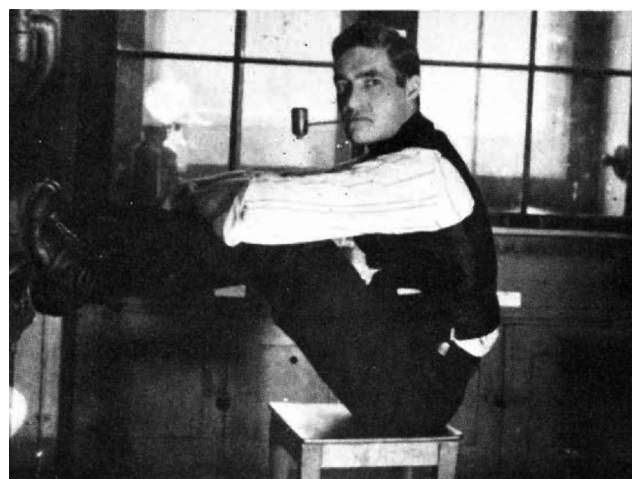


Figure 6. Victor King in Zürich around 1911.



Figure 7. Original vials containing the *l,l'* diastereomer of $[\text{Co}(\text{en})_2\text{NH}_3\text{Cl}]$ bromocamphorsulfonate (top) and the *d* enantiomer of $[\text{Co}(\text{en})_2\text{NH}_3\text{Cl}]\text{Br}_2$ (bottom), both prepared by Victor King in Werner's laboratory.

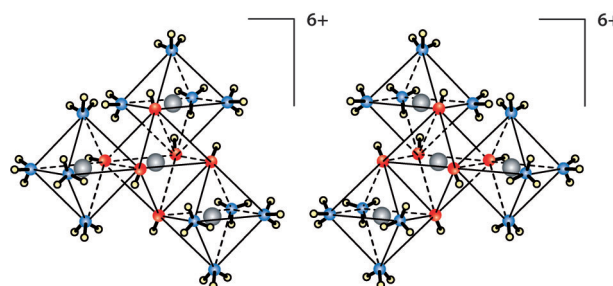


Figure 8. Enantiomeric cations of the carbon-free cobalt complex $[\{(\text{H}_3\text{N})_4\text{Co}(\mu\text{-OH})_2\}_3\text{Co}]^{6+}$; gray Co, yellow H, blue N, red O.

acid using the enantiopure coordination compound $[\text{Co}(\text{en})_3]\text{Br}_3$ as the resolving agent.^[29]

An Overlooked Opportunity

After reports of the spontaneous resolution of salts originally prepared by Werner's students, Bernal and Kauffman made the case, decades later, of the so-called “overlooked opportunity”, stating that Werner and his student Edith Ellen Humphrey (1875–1977) had overlooked the possibility of conglomerate crystallization.^[30] They claimed

[*] “Das unter dieser Voraussetzung sich ergebende Modell ist jedoch, stereochemisch gesprochen, ein asymmetrisches, d. h. es kann in zwei räumlichen Anordnungen, die sich verhalten wie Bild und Spiegelbild und die nicht zur Deckung gebracht werden können, konstruiert werden” (from Ref. [22]).

that by just picking out a single crystal and measuring its optical activity, Werner could have had the necessary proof years earlier and without all the tedious attempts at diastereomeric salt crystallization. This view has been frequently repeated by others.^[31]

Edith Humphrey enrolled at the University of Zurich in the Fall 1898 for her doctoral project.^[32] In the first part of her doctoral thesis (Figure 9),^[33] Humphrey gave a review on how different ligands bind to the central metal atom, while the



Figure 9. Right: The cover page of Humphrey's doctoral thesis entitled: "About the binding site of metals in their compounds and about dinitritodiethyleneaminecobalti salts". Left: The original sample of *cis*-[Co(NO₂)₂(en)₂]Br prepared by Humphrey in 1899 or 1900.

second part described her syntheses of *cis* and *trans* (*flavo* and *croceo*) bis(ethylenediamine)dinitro cobalt salts [Co(NO₂)₂(en)₂]X; X = Cl, Br, I, NO₂, NO₃, 1/2 SO₄, 1/2 [PtCl₆], 1/2 [PtCl₄], [AuCl₄]; Figure 10). Another one of Werner's students, the Austrian Adolph Grün, synthesized at that time compounds of same type, [Co(NO₂)₂(en)₂]X (X = Cl, I, NO₃, 1/2 SO₄).^[34] Interestingly, Werner believed that these complexes were nitrito compounds, in which the oxygen is

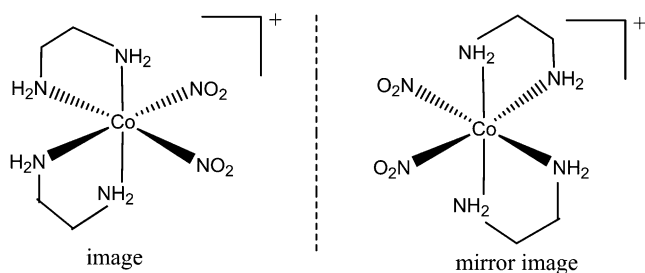


Figure 10. Structure models of the enantiomers of the chiral *flavo*-bis(ethylenediamine)dinitrocobalt cation of **2** and **3**.

attached to the Co atom.^[33–35] But after his group had synthesized true nitrito compounds,^[36] he referred to Humphrey's and Grün's samples correctly as nitro complexes.^[37] Humphrey focused on the different stability of the *cis* and *trans* isomers for different ligands and counterions, but did not discuss chirality and optical activity. Interestingly, she described the *trans*-to-*cis* conversion as "... an *autoracemizing-like process*" ("... einen 'autoracemisierungsähnlichen' Prozess ..."). This statement indicates that Humphrey was aware of chirality, since this isomerization creates both *cis* enantiomers from the achiral *trans* isomer.

The first report in modern times on conglomerate crystallization of these compounds appeared in 1973.^[38] Based on solubility data for the racemate and the pure enantiomers, spontaneous resolution was concluded to occur for *flavo*-bisethylenediaminedinitrocobalt chloride (**2**) and bromide (**3**). Hence, the measured optical activity of a solution of an individual crystal would have proved Werner's theory indeed much earlier. Bernal later delivered the first X-ray structure analysis of **2** and the enantiopure *cis*-[Co(NO₂)₂(en)₂]I (**4**),^[*] and also determined their absolute configurations using the Bijvoet method.^[39] Structural data from X-ray diffraction for a pure enantiomer of **3** were first reported in 1988.^[40] Compounds **2** and **3** crystallize into the space group *P*₂₁, and Bernal reported on the spontaneous resolution of both of them.^[**]

Werner was certainly aware that conglomerate crystallization and enantiomorphic crystals may occur and that this would provide the way to successful separation.^{[***][22]} In his first paper mentioning the possibility of chiral complexes, he concluded for **1** that their "small crystal size and their unsuitable form" ("in wenig geeigneter Form") make them improper for such analysis,^[22] but he also stated: "... that this type of negative result would be of limited value." And furthermore (loosely translated):^[****] "The importance of the possibility of this type of isomerism led us investigate two series of isomers of the type [Co(NO₂)₂(en)₂]X and two series of isomers of the type [Co(SCN)₂(en)₂]X, whereby new

[*] The crystals obtained from the racemate of **4** were, according to Bernal, "useless for single crystal X-ray diffraction".

[**] Bernal mentioned investigations of **3** several times, but gives insufficient references ("Clearfield Symposium", "Submitted for publication to J. Coord. Chem.", see Ref. [39c]), such that we could not find this original work.

[***] "Es scheint aber doch nicht ausgeschlossen zu sein, daß sich solche Isomere durch Enantiomorphie an ihren Krystallen charakterisieren könnten und dadurch der Weg zur Trennung derselben geboten würde." Cited from Ref. [22]. ("It seems possible that such isomers could be characterized through the enantiomorphism of their crystals which provides the route to their separation.")

[****] "Bei der Wichtigkeit, die der Entscheidung in Bezug auf die Möglichkeit des Auftretens derartiger Isomeren zukommt, sind Versuche in ähnlicher Richtung möglichst variiert worden; so sind z. B. zwei isomere Verbindungsreihen, [Co(NO₂)₂(en)₂]X, und zwei isomere Reihen, [Co(SCN)₂(en)₂]X, genauer untersucht worden, wobei, zwar nicht für die asymmetrische Isomerie, wohl aber in anderer Hinsicht, neue Ergebnisse von weittragender Bedeutung gewonnen worden sind, wie ich in einer demnächst erscheinenden Publikation zeigen werde." Surprisingly, this statement, as well as the previous citation from Ref. [22], has never been mentioned by Kauffman.

important results were obtained, not in terms of asymmetry, but in other respects, that will be reported in a forthcoming publication.”^[22] This statement indicates that Humphrey’s and Grün’s samples were tested, maybe for enantiomorphism only, but with negative results. Hence, it is puzzling that Humphrey and Grün never tested single crystals of their samples for optical activity, a technique established in Werner’s group after Humphrey’s departure,^[*] but available in Zürich at that time.

Thirteen years later, Humphrey and Grün’s salts were prepared again in Werner’s group, this time by Richard Hessen.^[41] Hessen separated the enantiomers of **2** and **3** by the Pope–Kipping method. He then resolved pure enantiomers by seeding racemic solutions with enantiopure crystals, but referred to this as “spontaneous resolution”.^[**] Moreover, he compared the solubility of the racemate and the pure enantiomers. In contrast to the work from 1973,^[38] he found a higher solubility for the pure enantiomers of **3**, but concluded, in agreement with the sixty-years-later work,^[38] a higher solubility for the racemate of **2**. In their doctoral theses Humphrey, Grün, and Hessen all reported that crystals of **2** show a multiple, parallel, striped pattern, penetrating the crystal (“in vertikaler Richtung sehr tief gestreift”; “seitlich vielfach gestreifte”; “parallele Flächenstreifung”). Hessen proposed twinning of *d* and *l* crystals as the reason for this appearance, a scenario that was first shown for another compound by the Zürich-born geochemist Viktor Moritz Goldschmidt, a year after Hessen’s thesis appeared.^[42] Hessen supported his proposal by the observation that solutions of crystals obtained after seeding with pure enantiomers show lower optical activity than solutions of the pure enantiomers themselves. Hessen also reported differences in shapes of the enantiopure and “racemate” crystals of **2** and **3**, but his description of the racemate crystals is in accordance with those given by Humphrey and Grün.

In order to test whether spontaneous resolution had indeed occurred, we re-examined the original samples prepared by Humphrey, Grün, and Hessen by means of X-ray crystallography. For Humphrey’s original *flavo-3* sample (Figure 11), we come to the following conclusion: the larger crystals are racemic and do not show enantiomorphism. So, if Humphrey had tested solutions of large single crystals for optical activity, she would have failed to observe it. According to Humphrey, crystals of **3** also show striped patterns, although less pronounced than in **2**. The larger crystals of **3** (5–10 mm) are prisms and plates possessing mirror symmetry (Figure 11), thus exhibiting no enantiomorphism. However, our inspection also revealed—after tedious examination of the crystals in the vial shown in Figure 9—the existence of a

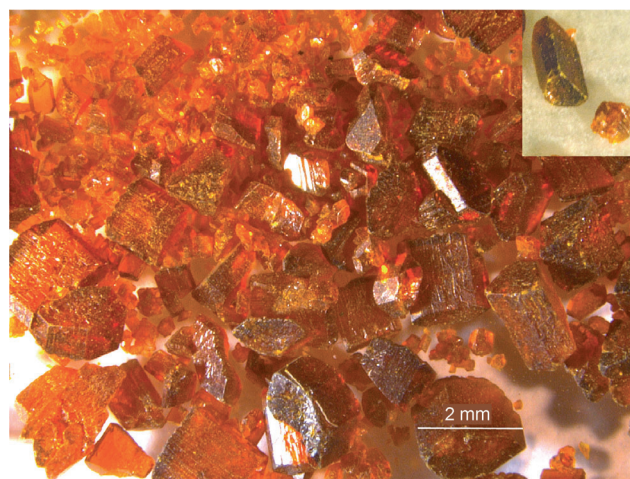


Figure 11. Humphrey’s crystals of **3**. The large crystals (inset) do not show enantiomorphism.

few enantiomorphous crystals (Figure 12). Flack parameter analysis^[44] of the X-ray diffraction pattern showed that only small crystals (< 1 mm) had an enantiomeric excess. This is in line with the circular dichroism (CD) spectrum of a solution prepared from a very small crystal (*M* = 856 µg)^[***] of Humphrey’s original sample,^[31a] which supported the conclusion of conglomerate crystallization of **3**.

While Bernal claimed perfect spontaneous resolution for **2** and **3**, we did not find a single enantiopure crystal in Humphrey’s original sample of **3**. This observation is in agreement with more recent crystallographic analyses.^[45] As concluded already by Hessen, the crystals are probably lamella twins of both enantiomers. We also performed X-ray diffraction measurements of five different crystals of the original racemic sample of **2** prepared by Grün. Like Humphrey’s sample of **3**, the *P*₂₁ space group was confirmed.^[39a] However, Flack parameter analysis of the diffraction pattern showed that one crystal was racemic, two were enantioenriched, and two were enantiopure.

Our analyses of the historic samples of the Werner collection clearly demonstrate that the spontaneous resolution of racemic chiral compounds of **2** and **3**, prepared by Werner’s students Humphrey, Grün, and Hessen, is far more complex than previously claimed in the literature. Not all the crystals show enantiomeric enrichment, and in those that do, the enrichment decreases with increasing crystal size. Nevertheless, it remains a mystery why Werner apparently did not test the crystals for optical activity earlier, although he considered the possibility of spontaneous resolution in one of his previous publications. However, the dubious achievement of an “overlooked opportunity” should go to Adolf Grün rather than Edith Humphrey. At least for salt **2**, his sample contained enantiopure crystals in addition to racemic twinned crystals.

[*] Werner later purchased two polarimeters, Lippich Nos. 7517 and 8142, from Franz Schmidt & Haensch, a company still in business in Berlin today.

[**] George B. Kauffman attributed this work mistakenly to Jakob Bosshart, who simultaneously performed similar work on **2** and oxalo salts.^[43] Werner did not publish with Hessen, so his work is recorded only in his doctoral thesis. For the same reason, Kauffman was not aware of the doctoral work of Grün and of several other of Werner’s students (Werner later published other results together with Grün).

[***] From Ref. [31d]. The original reference [31a] states 856 mg, which would be an enormous crystal, but the given concentration suggests the 1000-fold smaller value.

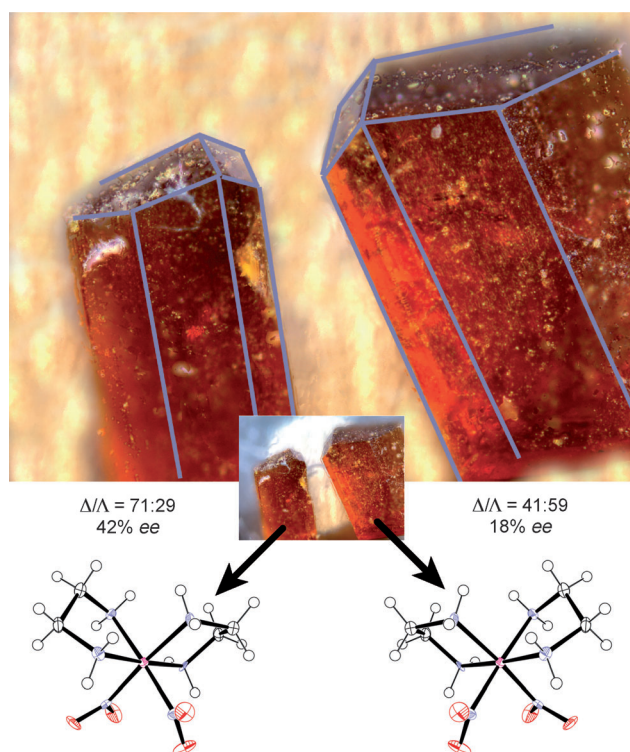


Figure 12. Microscope images of enantiomorphous crystals of **3**. The crystal edges are highlighted with blue lines. The absolute structures were determined by X-ray analysis; large white centers C, small white balls H, pale blue centers N, red centers O. The two opposite-handed crystals have opposite enantiomeric excesses.

On account of the overwhelming success of Werner's coordination theory, his other quite remarkable achievements are often forgotten.^[46] Werner was the first to suggest that the periodic table could have periods of different length and placed two periods with 18 elements after two short periods with eight elements.^[47] He correctly proposed structures for ammonium and oxonium salts, introduced the hydrogen bond in $(\text{HF})_2$, and anticipated our modern acid–base theory long before Brønsted and Lowry.^[46,48] He used early modern techniques like electrical conductivity measurements and polarimetry for molecular structure determination. In this context, his implementation of UV/Vis spectroscopy^[50] and optical rotation dispersion (ORD)^[51] is especially noteworthy. Shortly after receiving the Nobel Prize, Werner became seriously ill and could not work regularly from 1915 on. He retired in 1918 and died in 1919 at the age of 53 after suffering from arteriosclerosis.^[51,52]

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