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From the Selected Works of Otto Vogl

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Chirality and Handedness

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Chirality and Handedness

Otto Vogl and Frank T. Traceski

41,556

A. Prologue

Over six decades I was involved with asymmetry in chemical structures, handedness or chirality.

1.) The **Chiral Carbon Atom**. My first paper in 1948 (in my first year of my thesis) involved the chiral Carbon; the chromatographic separation of epimeric (with hydroxy-groups on 3-position) steric alcohols.

2.) **Molecular Asymmetry**. In 1952 I had to synthesize (with Hilde Mulley) chiral 2,2'-dinitro-6,6'-diphenic acid (by a known procedure) to separate the racemate of a chiral intermediate in our attempted synthesis of the alkaloid cytisine.

3.) First Example of **Macromolecular Asymmetry** (helicity). The anionic polymerization of chloral to polychloral with lithium cholesteroxide as initiator (I did not know anything about what I had done). Three months later Piero Pino gave a talk at the Gordon Conference on Polymers and reported that he had polymerized chiral 3-methylpentene and found the optical rotation was higher than that of the monomer. The optical activity measurements were not well defined.

4.) In 1978, we synthesized by anionic initiators polychloral (PC) with cholesteroxide in film form, and with a **chiral phosphonium salt** (provided by Jan Michalski, Gen Secretary of the Polish Academy and Director of the Academy Institute in Lodz, a student of Lord Todd) also in film form.

5.) At the Gordon Conference on polymers that year I coined the term **Macromolecular Asymmetry**.

6.) With Hatada we used chiral PC for chiral separation (like cellulose acetate) (~1984) of polymer racemates.

7.) With Pino's concurrence we started to develop the technique of measuring **Optical Activity of Solids** in the powder form (~1986). We also measured with the appropriate solid the circular dichroism in one case.

8.) To develop this, we used chiral crystalline **Sodium Chlorate**. The large crystal has the same rotation in all three dimensions. The rotation was also in powder suspension measurements.

9.) At this point we became interested in **Chiral Crystallization** with the focus on **chiral nucleation**. We found, ~ 1988, that crystallization can become isotactic by proper nucleation.

10.) In the next few years with my last two student and post docs, we finished the work as described in **Qin's thesis** and the paper in the Monatshefte.

11.) Back at UMass (with Atkins in Bristol) we calculated the structures of all four polyaldehydes (about 1 1/4 rigid helices).

12.) With ideas from CNRS in Orleans, France the manuscript was expanded, carefully refereed and finally put in publishable form with the proposal that **chirality** was introduced on the **planet Earth** about 3.8 billion years ago by **chiral nucleation**.

Optical Activity: When circular polarized light is passed through an asymmetric substance, a crystal (a solid) or a molecule in solution which has a chiral atom, the plane of the light is shifted; this shift might occur to the left or right. We say the substance is optically active.



Quartz crystals

B. The Chiral Tetrahedral Carbon

If you have followed my writings you will find in one of the commentaries “Degradation, Aging, etc”, I had stated that this subject has followed me all my life. If you have followed my very

first writings and the last part of my communications, you will find that I was equally followed throughout my scientific life, that is, by “handedness” or in more sophisticated way expressed, the chirality.

In my last paper I stated, that we live in a chiral world. I used as an example the hands of my last graduate student at the Polytechnic University in Brooklyn Qin Meifang from Guilin, China as an example.

Over 90 % of the total world population is right handed and 9% left handed. We pointed out that many organs in the body exist in pairs of mirror images. But the central system, the heart and the brain, the reproductive and the digestive systems are solo. Even the stag has a pair of magnificent antlers, one left directional and one right directional.

How did I get so early in life involved in chirality in chemistry? Naturally, it was taught by Professor Spaeth in his Lecture on organic chemistry; optical activity was one of the chapters. But I really got involved, as it so often happened, by accident. As I joined the group of Galinovsky, he gave me as my theme for my thesis the synthesis of pro-vitamin D₂ from Cholesterol. It failed.



The tetrahedral carbon atom.

One day he came and told me that his friend Christiani had succeeded in separating Androstanol from Koprostanol by Tswett type chromatography. They had the 5-hydrogen atom in *cis* or *trans* configuration. Could we not try the same thing for 3 hydroxysteroids, the α form the β form, the *cis* from the *trans*, or better expressed, the **axial** from the **equatorial** form of the steroids with a 3-hydroxy-group attached to the steroid structure. The hydroxyl groups were attached to the tetravalent carbon atom and subject to opposite stereochemistry. I synthesized a number of these pairs of steroids, attempted the separation and it worked after some patient handling of the subject.

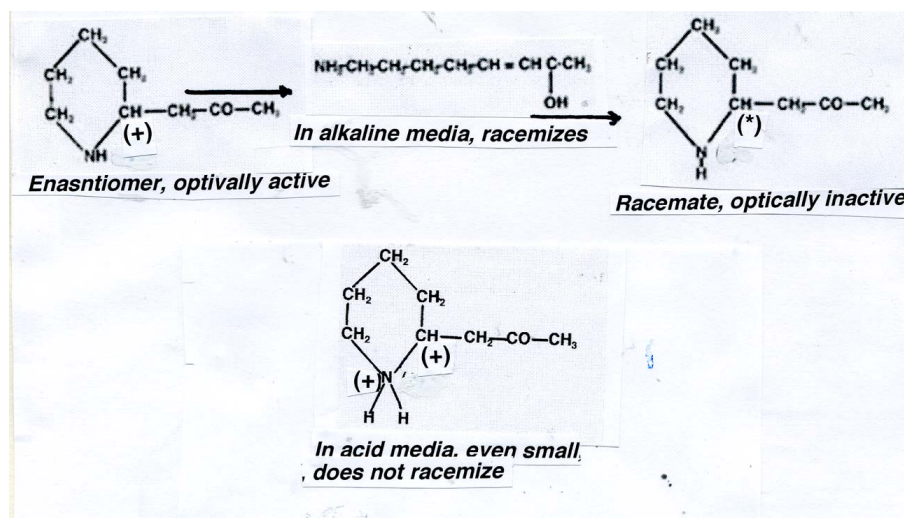
This was only one fundamental contribution to the stereochemistry of the carbon asymmetry.

I later worked on alkaloids, **cytisin** and **isopelletierine**. The cytisin story was trivial. In our attempts to synthesize cytisin, our first attempt was the successful synthesis of tetrahydro-desoxycytisin. This worked and ultimately required the separation of two racemates. But the actual total synthesis failed in the last step.

Incidentally, for one of the separations we used the salt of chiral 2,6,2'6'-dinitrodiphenic acid that Hilde Mulley had prepared in Galinovsky's laboratory as the means of separation. This acquainted me with chirality based on limited (blocked) rotation of the biphenyl basic structure.

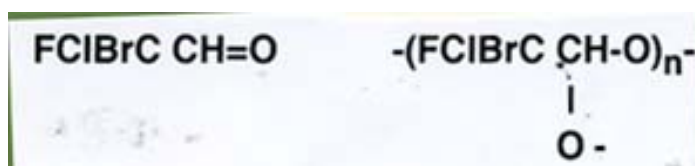
The synthesis of isopelletierin was no problem but the separation of the antipodes and the maintenance of their optical activity was a different story. It required the recognition of the mechanism of the racemization as seen below. The alkaloid must be in acid medium or as a salt. Apparently in the bark of *punicum granatum* the pomegranate tree, the alkaloid is biologically synthesized in the form of a salt with humic acids. And maintained that way.

Under basic conditions, the free base opens up and recycles to the statistically expected racemate.



Isopelletierin

We made an even more important contribution to the stereochemistry of asymmetric Carbon. It started originally with the attempted synthesis of macromolecular asymmetry. – specifically, the synthesis and polymerization of fluorochlorobromoacetaldehyde.



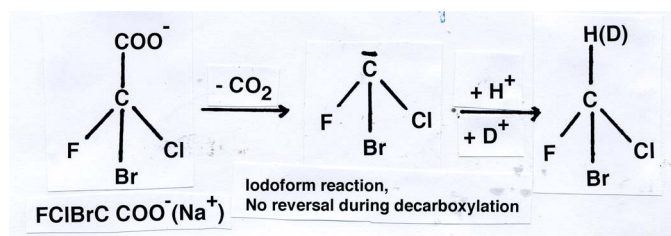
Polymerization of chiral fluochchlorobromoacetaldehyde

Tom Doyle, in my laboratory developed an elegant synthesis of fluorochlorobromoacetic acid and was able to separate the antipodes as strychnine salts. (and synthesized the fluorochlorobromoacetaldehyde by way of the methyl ester of the acid). We had great losses in the recrystallization of the salt and I did not want to have too much strychnine in the laboratory. One day I asked Doyle to see if there was anything in the trap. There was! A colorless liquid with a boiling point about 36°C . What I had forgotten was that during the recrystallization conditions we were subject to the so-called iodoform reaction- the synthesis of pentatomic methanes from halogenated acetic acids.

I realized immediately that we had discovered a gold mine – the possibility of the synthesis of the first and simplest pentatomic molecule with the possibility of synthesizing it in chiral form.

Doyle made more and more of the fluorochlorobromoacetic acid. We were now more careful with the separation and had sufficient quantities and we carried out the iodoform reaction and made chiral fluorochlorobromomethane, and chiral fluorochlorobromodeuteromethane. We did not have the capability or courage to use $^3\text{H}_2\text{O}$ to make the tritiated methane.

These experiments also showed that under the conditions of our iodoform reaction there was no “swinging through” of the fluorochlorobromomethide and the intermediate structure was sterically stable.



Synthesis of fluorochlorobromo(deuterio)methane,

Our paper was sent to JACS and immediately published. I found out that one of the referees, who was knowledgeable on the subject and fair, had worked on the principle of the chiral pentatomic carbon and was happy that we had succeeded.

We were happy with the outcome but it was not all. Five or 10 years later we received a note from a colleague, in Lyon, France. Professor Collet was an expert in structural X-ray measurements. He insinuated that we had inspired him to make the sodium salt of our chiral fluorochlorobromoacetic acid and establish

the absolute configuration of the salt. Together with our earlier results we now had on hand the first pentatomic molecule with its correct absolute configuration.

We were also working for a short time with **chiral phosphonium salts** in cooperation with the Institute of the Polish Academy of Sciences in Lodz, Poland. First we used some of the chiral phosphonium salts to initiate chloral polymerization. We demonstrated that a chiral counter-ion is sufficient to polymerize chloral to chiral, helical polychloral. When my co-worker Steve Corley, who had done this work in Amherst, spent a semester in Lodz, he worked on some phosphonium salts there.

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F. Galinovsky, O. Vogl and W. Moroz, Synthesis of Tetrahydrodesoxycytisine, *Monatshefte Chem.*, 83, 242 (1952).

F. Galinovsky and O. Vogl, The Alkaloids of Pomegranate Bark, *Monatshefte Chem.*, 83, 1055 (1952).

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Thomas R. Doyle and Otto Vogl, Bromochlorofluoromethane and Deuterobromochlorofluoromethane of High Optical Purity, *J. Am. Chem. Soc.*, 111, 8510 (1989).

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Thomas R. Doyle and Otto Vogl, A Facile Synthesis of Fluorochlorobromoacetic Acid, *Monatshefte Chem.*, 121, 31 (1990).

Thomas R. Doyle and Otto Vogl, Haloaldehyde Polymers 44.Synthesis and Polymerization of Racemic Fluorochlorobromoacetaldehyde, Polymer, 32(15), 2869 (1991).

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Larry Steven Corley, Otto Vogl, Tadeusz Biela, Stanislaw Penczek and Stanislaw Slomkowski, Kinetics of Zwitterion Formation from γ -Propiolactone and Tertiary Phosphines, Makromol. Chem., Rapid Commun. 2, 47 (1981).

Tadeusz Biela, Stanislaw Penczek, Stanislaw Slomkowski and Otto Vogl, Racemic and Optically Active Poly (4-Methyl-2-Oxo-2-Hydro-1,3,2-Dioxaphospholane). Synthesis and Oxidation to the Polyacids, Makromol. Chem., Rapid Commun., 3, 667 (1982).

Gyorgy Deak, Otto Vogl and Leszek B. Kiliman, Poly(10-undecenoic Acid), and some of its Derivatives, J. Macromol. Sci.- Pure and Appl. Chem, A38(3), 221-231 (2001)

Leszek B. Kiliman. Gyorgy Deak and Otto Vogl, Liquid Crystalline Polymers of Polyolefin and Poly (Oxyethylene) Derivatives J. Macromol. Sci.-Pure and Appl. Chem, A38(4), 329-352 (2001)

C. In Preparation to Macromolecular Asymmetry

I had finished my work on the asymmetric carbon in Vienna and had other interests and assignments, until I had joined DuPont. Very soon I was assigned an important project that was expected to fail; the polymerization of higher

aliphatic aldehydes. Indeed, it was scientifically very successful but commercially a failure. It was also for me the beginning of my career in polymer science. Within a year we succeeded (together with my technician Jake Mansure) in the following accomplishments:

- 1.) The polymerization of acetaldehyde (with the recognition [discovery?] of the ceiling temperature of polymerization).
- 2.) Discovery of the polymerization of aldehydes to isotactic polymers.
- 3.) Discovery of "side chain crystallization". This was already the first step toward my interest in crystallization. Up to Butyraldehyde the isotactic polymers have only one crystalline phase, the helical structure of the polyoxymethylene main chain. From the polymers of n-valeraldehyde to n-non(dec)aldehyde. Two melting points are observed, the m.p. of the polymer main chain ($\sim 120^{\circ}\text{C}$) and the "paraffinic" side chain between 40 and 60°C these two phases are reverently immiscible and crystallize independently.
- 3.) Above n-non(aldehyde), only the "paraffinic" m.p. is observed, Apparently, the helical main chain portions do not aggregate any longer.

During this period I also looked (together with Bill Bryant) at the polymerizability of unusual simple monomers and looked at three characteristics: Carbon dioxide, acetone, hexafluoroacetone (which at least copolymerizes). Bryant did some estimates of the ΔG of Polymerization. He found it was near zero or positive, consequently no polymerization. I looked at, first the value of the proton attached to the potentially polymerizable carbonyl group, later (when ^{13}C spectroscopy became available) I looked at the ^{13}C values of the carbonyl carbon of these compounds.

An interesting correlation could be found that coincided with known experience:

- 1.) Formaldehyde and methyl glyoxalate (by ozonization of methyl maleate). They give low molecular weight “oligomers and polymers” in aqueous environment. We looked closer to the polymerization of methyl glyoxalate ?? but could only confirm earlier work on the subject and could never make high molecular weight polymer.
- 2.) Perhaloacetaldehyde polymers. They form hydrates and polymerize. Under the right of the size of the trihalo side groups, they form isotactic polymers, mixture of isotactic and atactic (soluble) polymers or with small side groups, like trifluoroacetaldehyde (fluoral), rubbery atactic polymers like acetaldehyde.
- 3.) They do not form hydrates, and do not polymerize,

With this information in hand I abandoned the polymerization of higher aldehydes and concentrated on the preparation and polymerization of trihalo acetaldehydes, especially the then commercially available trichloroacetaldehyde, chloral.

It turned out that even this project was not without grave hurdles. It took months, even years until we solved it satisfactorily but the project led us into macromolecular asymmetry.

D. L. Funck and O. Vogl, Thermally Stabilized Polyaldehyde Elastomers, U.S. Patent 3,001,966 (1961); C.A. 56, 1307 i (1962)

O. Vogl, Crystalline Aldehyde Polymers, Belgian Patent 580,553 (1959); Australian Patent 239,337 (1959).

O. Vogl, Crystalline Polyaldehydes with Acetal Structure, British Patent 870,775 (1961); C.A. 55, 2657 a (1961), French Patent 1,235,730 (1960), Canadian Patent 628,573 (1961)

O. Vogl, Linear Crystallized Aldehyde Polymers, German Patent 1,144,821 (1963), C.A. 59, P 1782 g (1963).

O. Vogl, Polymerization of Higher Aldehydes, III. Elastomeric Polyacetaldehyde, J. Polym. Sci., A, 2, 4591 (1964).

O. Vogl, Crystalline Aldehyde Polymers, Belgian Patent 580,553(1959)

O. Vogl, Stabilized Crystalline Polyaldehydes Having 2-10 Carbon Atoms, U.S. Patent 3,184,433 (1965)

O. Vogl, Polymerization of Higher Aldehydes. I. The Polymerization of Aldehydes, J. Polym. Sci., 46, 261 (1960).

O. Vogl, Polymerization of Higher Aldehydes. IV. Crystalline Isotactic Polyaldehydes: Anionic and Cationic Polymerization, J. Polym. Sci., A, 2, 4607 (1964).

J.S. Wood, I. Negulescu and O. Vogl, Higher Aliphatic Polyaldehydes. III. Crystal Structure, Crystallinity and Melting Transitions of Isotactic Poly(n-Heptaldehyde), J. Macromol. Sci (Chem.), A11(1), 171 (1971)

Asymmetry in molecules or chemical structures cannot only be caused by asymmetric molecules but also by rigid structures. In the chemical composition I mentioned earlier the hindered rotation of the phenyl rings in 2,2',6,6'-dinitrodiphenyl and which we used for the separation of enantiomers of alkaloids.

When I was a graduate student I had to purify a steroid, which melted between 146 and 148°C. Any further recrystallization did not work and Prof. Galinovsky, my mentor scolded me severely. Today we know the compound had liquid crystalline behavior as do a number of steroids. Later in my career with L. Kiliman we prepared and studied polymers with long flexible side chains that had liquid crystalline groups attached on their ends.

D. Macromolecular Asymmetry

The year 1963 was an important year for the evolution of what later became known as macromolecular asymmetry. I had been working for nearly two years on the polymerization of chloral. Several groups had done it before also. They were relatively unsuccessful. As the initiator was injected in the chloral solution, chloral polymerized and immediately the insoluble polychloral precipitated in bizarre forms and shapes, indicating the shape of the flow of the initiator solution. The entire chloral solution was never initiated but the polymerization occurred only on the surface and within the initiator solution. Every mixing technique more or less failed. And I was frustrated, because I felt that my selected assignment was at the end. On April 12 at 9:00 a.m. I was to present my research to the executive committee of CRD and to Ted Cairns, the General Director. I was sure I had to report my total failure. The same morning, when I woke up in desperation at 3:30 a.m. I had my last idea. Why not inject the initiator solution to that solution of chloral and let it cool off and see the first clear polychloral was produced? By now it was 6:00 a.m. and I had to prepare the experiment to repeat it in front of the executive committee, three hours later without an error or accident. I repeated my simple experiment and it worked every time. What I did not know I had discovered the initiation of a polymerization above the ceiling temperature and it produced a completely insoluble but homogeneous polymer.

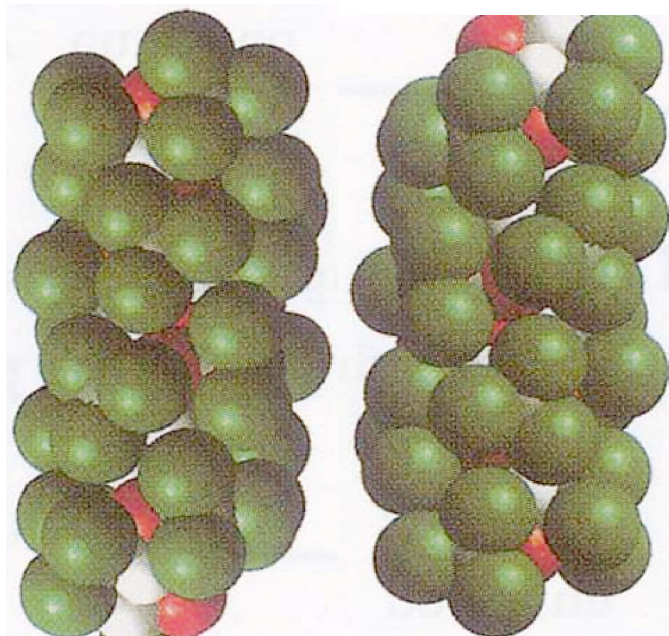
The polymerization worked in front of the committee, the continuation was approved and it almost became a commercial product. The next example was the initiation of chloral with lithium chloresteroxide (from butyl lithium and cholesterol). It worked even better. I will not go into the efforts to stabilize the polymer, but we had made polychloral with cholesteroxide as an optically active polymer. It took us almost 20 years to actually prove this fact.

Based on this research we coined the expression “Macromolecular Asymmetry” in 1979. This is not quite correct. I prepared my talk at a famous Gordon Conference on Polymers and used the term “Molecular Asymmetry” for optical activity based on helicity. My friend Francesco Ciardelli stood up and said generously, “I am sure you meant Macromolecular Asymmetry” not Molecular Asymmetry. This is how macromolecular asymmetry was born in public.

I said 1963 was an important year. On a totally different subject, at the Gordon Conference, Piero Pino was one of the main speakers and he reported a peculiar phenomenon. Having been the lieutenant of Natta in Milan, when Polypropylene was discovered, he was now an independent professor in Pisa, Italy. He thought it would be interesting to study optically active olefins and chose 3-methylpentene as the monomer. It polymerized readily. He found in solution that the optical activity of the polymer was higher as what was expected from the optical activity contributed from the monomers optical activity contribution. They also carried out some measurements in the solid state and found that the optical activity was higher. In the discussion it was concluded that part of the increased contribution of the optical activity might be from partial helical structures that had been encouraged by the chiral monomer units. Twenty five years later in cooperation with Pino and our own much refined techniques of measuring optical activity we re-measured Pino’s sample and indeed it was correct. The contribution of the 3/1 helix of the polyethylene backbone chain (as in PP) seems to contribute 150 degrees for the overall optical activity.

As a matter of fact, we later measured on helical oligomers of chloral the fundamental contribution of the helical backbone chain and concluded it is 400 degrees for polychloral.

Polychloral polymerized with achiral initiators gives completely isotactic polymers. They are 50% left-handed and 50% right-handed and, consequently optically inactive.



Left and right-handed polychloral

O. Vogl, Process for Polymerizing Chloral, U.S. Patent 3,454,527 (1969).

O. Vogl, Chloral-Isocyanate Copolymers and Their Preparation, French Patent 1,528,327 (1968); British Patent 1,151,002 (1969), Canadian Patent 820,418 (1969), Italian Patent 804,395 (1968).

O. Vogl, Chloral-Ketene Copolymers and Their Preparation, French Patent 1,567,895 (1968), British Patent 1,151,003 (1969), Canadian Patent 817,486 (1969), Italian Patent 823,406 (1968).

Talk at the Gordon Conference on Polymers in New London, NH (1979)

We have studied the polymerization behavior of other perhaloacetaldehydes. We found the aldehydes with two fluorine substituents still give soluble, presumably

atactic fraction of the polymers, but larger-sized substituents give only insoluble presumably isotactic polymers.

Polychloral is insoluble in any solvent. In order to measure the optical rotation of chiral polychloral it had to be done on films, actually on stacks of films.

{Polychloral can be made in the form of very thin individual films (as described d. These films were taken out, rinsed with acetone and soaked with diphenyl ether. Diphenyl ether has the same optical behavior as polychloral and eliminates small amounts of birefringence. Then three or four films are placed on top of each other while each film is rotated by 90-120 degrees. The film stacks are now pressed together and from the "stacks" small discs are cut with a cork borer and the stack measured. This technique eliminates any birefringence and gave measurements of +/- 3 % accuracy. Since the film stack is normally relatively large, several samples are taken from the stack and measured. Measurements change with the type of initiator but values as high as 4,000 degrees have been observed. We ascribe this to the fact that the measurements were made perpendicular to the "polymerization direction."

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L. S. Corley, P. Kubisa, B. Yamada and O. Vogl, Effects of Side Group Bulk in Trihaloacetaldehyde Polymers, Polymer Preprints, ACS Division of Polymer Chemistry, 21(1), 205 (1980).

O. Vogl, G.D. Jaycox and J. Zhang, Helical Polymers: Optical Activity Based on Macromolecular Asymmetry, Abstracts, Australian Polymer Symposium, 16, PL 1 (1987)

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L. S. Corley and O. Vogl, Haloaldehyde Polymers. XXI. Optically

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J. Zhang, G.D. Jaycox and O. Vogl, Optical Activity Based on Macromolecular Asymmetry. Initiation of Polymerization, Polymer Preprints, ACS Division of Polymer Chemistry, 26(1), 156 (1985)

E. Tacticity Development in Chloral Polymerization

We have carefully investigated with Hatada in Japan the oligomerization and polymerization of chloral with lithium tert-butoxide. Lithium tert-butoxide exists in several forms. Part of it can be sublimed and is soluble up to one molar solutions in methylcyclohexane. It has a tetrahedral structure, and can be purified by sublimation. When added to chloral (above the ceiling temperature) it degenerates into monomeric species and initiates on chloral molecule. This addition product is the actual initiator.

NMR studies showed that the tetramer of chloral is still flexible, but higher oligomers are still soluble but almost 100% isotactic (helical conformation). Ultimately, the polymer, polychloral is isotactic with 50:50 left and right-handed helices.

Jingyun Zhang, Gary D. Jaycox and Otto Vogl, Polymerization of Chloral with Chiral Anionic Initiators. Stereochemistry of Initiation, Polymer J., 19(5), 603 (1987).

- . Jingyun Zhang, Gary D. Jaycox and Otto Vogl, Polymerization of Chloral with Lithium t-Butoxide. Stereochemistry of Initiation and Early Propagation Steps, Polymer, 29(4), 707 (1988).

Otto Vogl, Fu Xi, Frantisek Vass, Koichi Ute, Tohru Nishimura, Koichi Hatada, Direct Formation of the Helical Polymer Conformation in Stereospecific Polymer Synthesis. X-Ray Crystallographic Determination of Linear Chloral Oligomers, Macromolecules, 22, 4658 (1989).

Gary D. Jaycox and Otto Vogl, Haloaldehyde Polymers 41.
Asymmetric Polymerization of Chloral with Chiral Lithium Salts of
Sterols as Initiators, Makromol. Chem., Rapid Comm., 11, 61 (1990)

F. Studies of Chiral Initiation of Chloral Polymerization

With Hatada in Japan and Kratky in Austria, we have studied the stereochemistry of the initiation step of anionic polymerization with chiral alkoxide initiators, with the aim to design the initiating anion in term of structure and bulkiness that is necessary to have.

We investigated also the relative polymerizability of chloral and bromal oligomerization with William Simonsick.

Otto Vogl, L. Steven Corley, William J. Harris, Gary D. Jaycox and J. Zhang, Haloaldehyde Polymers XXVI. Optical Activity Based on Macromolecular Asymmetry, Die Makromolekulare Chemie, Suppl., 13, 1 (1985).

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Meifang Qin, Jan Bartus and Otto Vogl, Stereospecific Polymerization, Chiral Initiation, Chiral Nucleation and Crystallization, Makromol. Chem. Makromol. Symposia, 98, 387 (1995)

Otto Vogl, Chiral Crystallization and the Origin of Chiral Life on Earth
J Polym Sci.: Part A, Polymer Chemistry 49(6) 1299-1308 (2011)

G. The Rigid “Single” Helix

I have used the expression, *Rigid “Single” Helix*, however, that statement is somewhat flawed. The polychloral samples that we had synthesized and called one-handed helixes are aggregates of single helixes. This can be seen in their value of the optical rotation. Optical rotations of carefully prepared films of polychloral show rotations of as many as four thousands of degrees. These high rotations are not based on measurement errors, but represent agglomerates of polymer chains, either oriented by the way they were made, or by arrangement of supermolecular structures, similar to cholesteric structures. The optical rotations of oligomers of chloral in solution level off at about 60 degrees. The inherent rotation of the solid arrangement of polypropylene chains are estimated to be 150 degrees.

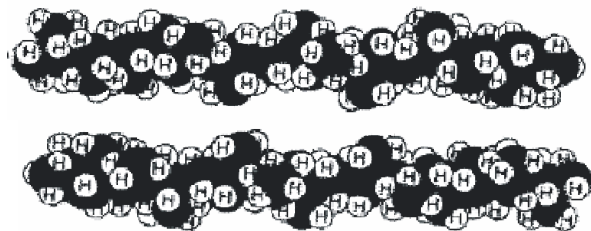
Since the late 1970s, work has also been done on macromolecular asymmetry based on polymers of triarylmethyl methacrylate (Okamoto 1979). These polymers are not crystalline and the solution rotation the same, about 400 degrees.



H. Chirality and Helical Polymers

Polypropylene (PP), discovered in the 1950's and immediately commercialized, is one of the most interesting, best studied and most important polymers in the plastics age. It is a crystalline, isotactic polymer and is melt fabricated. It has the structure of a helical polymer.

PP crystalline as a 3_1 was found to have a helical structure with three monomer units per repeat unit of 0.56 nm and a turn angle of the helix of 120° . PP crystallized from the melt, melts at 165°C . Further investigations showed that PP helices restructure into folded chains with a fold length of about 25 repeat units. PP, like many crystalline helical polymers consists, for statistical reasons of random nucleation, of a 50:50 mixture of left and right-handed helices, like polyoxymethylene, polytetrafluoroethylene and poly(ethylene oxide).



Left and right-handed polypropylene

Isotactic PP, crystallized from the melt, is a semi-crystalline polymer with a crystallinity of about 60% and a melt temperature of about 165°C . It consists of 50% left-handed and 50% right-handed $3/1$ helices. Crystalline PP consists of three phases: the α -phase (monoclinic) with a melt temperature of about 170°C , the β -phase (hexagonal) melting about 155°C , and the triclinic γ -phase for which several melt temperatures between 125°C and 150°C have been reported. The γ -phase crystallizes in the branching points of the spherulitic structure of the α -

phase. The β -phase has to be nucleated and is not found in PP, crystallized from the melt by spontaneous nucleation. The three phases differ from each other by slightly different arrangements of the left- and right-handed helices.

As early as 1996 it was proposed that it should be possible to prepare single handed PP by crystallization with an appropriate chiral nucleation agent (similarly to the strategy to form β -phase of PP by melt). It was even suggested that this might be done by “co-crystallization” with the molten nucleating agent that is able to spontaneously crystallize in chiral form only which then becomes the nucleating agent for the crystallization of PP. PP cannot be formed by oligomerization because PP is too flexible in the non-crystalline form and immediately randomizes its structure in the melt.

It was finally concluded that all polymers that are helical should be capable of crystallizing in the single helical form if properly nucleated by chiral initiators.

Otto Vogl and Gary D. Jaycox, Crystalline Helical Polymers, POLIMERI 18(3 & 4), 141-149 (1997),

Zvonimir Janovic, Ante Jukic and Otto Vogl, Spacer groups in macromolecular structures, POLIMERI 31, 1:14-21 (20

I. Crystallization vs Polymerization

Crystallization is in simple terms the reorganization of molecules or ion pairs into an organized well-defined structure in the solid phase. It is the three-dimensional structure of the crystal.

Polymers, on the other hand, are long one-dimensional, macromolecules of cross-linked three dimensional structures whose single units, the monomer units are permanently connected to each other as macromolecules. The linear macromolecules can still be soluble, capable of crystallization and can melt.

Crystals are also macromolecules but regular assemblies of molecules or ion pairs that are not actually connected with each other and exist as three-dimensional macromolecules only in the solid crystalline form.

Let's compare known everyday structures. Sugar is a molecule formed by a combination of glucose and fructose. Let us simplify it and say it is glucose. Glucose can be, has been combined by special enzymes to large macromolecules, cellulose. Because of the similarity to sugar type structures we call the entire family polysaccharides.

One of the fundamental features in crystallization is the beginning of the crystallization – Nucleation. Microscopic particles, they could be even still soluble aggregates of the molecules to be crystallized (it has to be supersaturated) form larger aggregates and, ultimately these nucleation sites become large enough and the crystal begins to grow merrily and the crystals of various sizes start to precipitate.

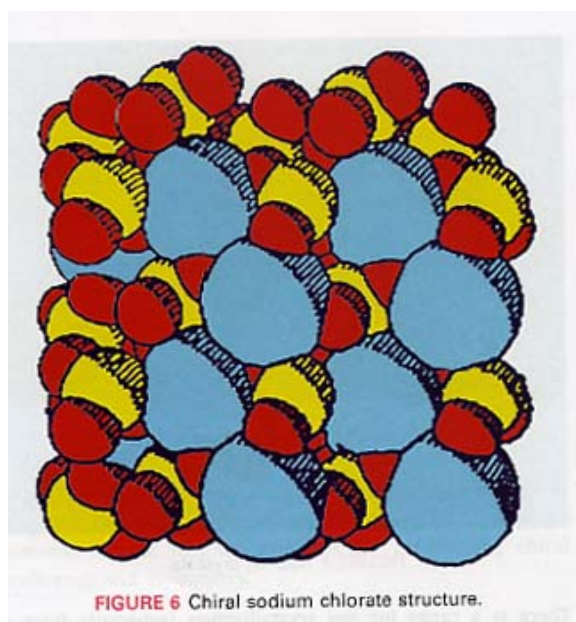
This is not only true for simple molecules but also for macromolecules if they are capable of crystallizing (usually from the melt).

J. Chiral Crystallization

Since 1856, since Hofmann first observed that Sodium chlorate crystallizes in large crystals that are chiral, sodium chlorate crystallization has been studied for centuries off and on without a significant breakthrough. How was it approached? Primarily by studying the crystal growth. When sodium chlorate crystals are allowed to grow, it was traditionally done by allowing the water in a most quiescent situation in a Petri dish, covered with filter paper to avoid the introduction of impurities from the air in the laboratory. What happens is slow but random crystallization, random nucleation to form large crystals, when the optical activity of these large crystals became available, they gave optical rotations near 130 degrees in all three directions. Checking the number of crystals, the size of the crystals, and the weight of the crystals did traditional research. Something did not fit. The number of crystals of one chirality to the other changed from

experiment to experiment. It became clear that the start of the crystal growth, the nucleation was random.

Years went by and we became interested in the subject. We were in part inspired because we needed to develop a technique to measure optical activity in the solid state in powder form. Sodium chlorate was the obvious test case. The other was a lecture by Prof. McBride of Yale, which he gave at the Polytechnic University. It was on a different subject but he had been working on the subject of sodium chlorate crystallization. And had numerous undergraduate students counting the various individual crystals.



Structure of sodium chlorate crystal

How did people know whether the crystals were left or right-handed? Easily done, by measuring large crystals. Some people believed they could differentiate smaller crystals by a difference of the hue of the individual crystals. I never believed that rather questionable technique.

Scientists at AT&T, in about 1978, even determined the crystal structure.

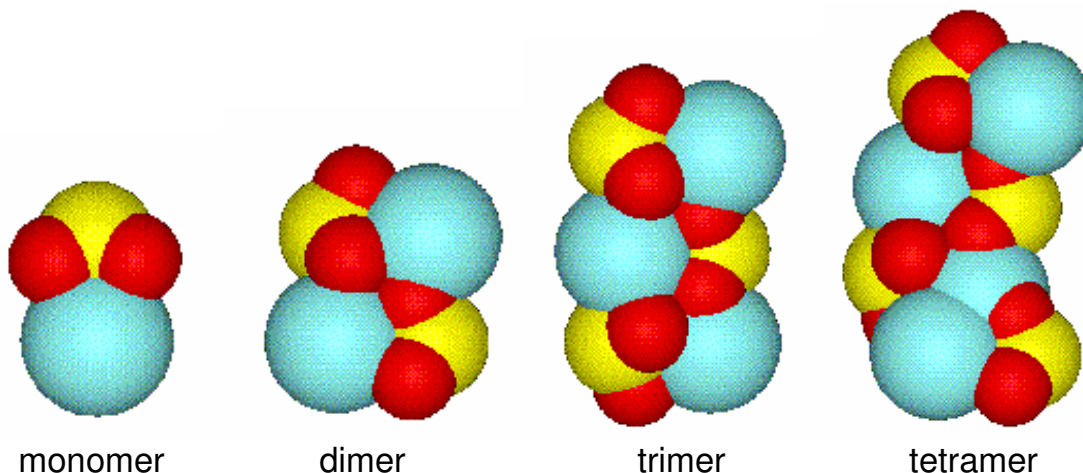
Another interesting question came up. Yes there is chiral crystal, not only sodium chlorate, but also sodium bromate, some sodium iodate and nonionic crystals like benzyl. They were reported to give chiral crystals. We repeated this crystallization and indeed it is true.

The questions came up, why sodium chlorate and not sodium perchlorate. The difference in the size of the positive and negative ions was not the question. It required, as we found also a certain dissymmetry. It was actually chloral and the polymerization, the stereospecific polymerization of chloral that gave us the clue. Indeed the difference of the smaller group vis a vis the larger “asymmetric” guiding group was the answer. The small carbonyl group needed for the polymerization was equivalent to the small sodium ion for crystallization. The larger asymmetric trichloromethyl group on the other hand was or the asymmetric chlorate groups the guidance for the asymmetric crystallization.

Another guidance came from the commercial sample of sodium chlorate. By now in Brooklyn we had mastered the techniques of measuring the optical activity of solids. We measured the optical activity “from the bottle” and it was inactive. So we had run out of our starting material and ordered a new batch of sodium chlorate. Now being more careful, we measured the optical activity of this new bottle right in the beginning as the bottle was opened. The “new” sample had full optical activity of about 128 degrees.

By chance, an article came out in science, in which a non-quiescent crystallization of sodium chlorate was discussed. And a breakup crystal was made responsible for the favored formation of excess in optical activity of the final crystals. Still then, the color scheme (which has never been established on a scientific basis) was used for these measurements and their interpretation.

After we had solved the problem of accurately measuring optical activity of solids in their solid form, as suspensions, the crux of the matter became obvious. For over 100 years scientists in the field had been hunting for an explanation for the erratic behavior, observed when carefully crystallizing sodium chlorate.



1.) Sodium chlorate had a bulky asymmetric anion, as is the bromate in sodium bromate and other salts. Benzil, although building a molecular crystal behaves similarly.

2.) Sodium chlorate crystallization is nucleated by asymmetric nucleating agents.

3.) Rotation seems to break up the INITIAL nucleating agent and overwhelms the nucleation. Still remembering the questionable “color” identification.

Subsequently we found the solution.

Create a slightly supersaturated solution of sodium chlorate, and add at this point shaved pure chiral sodium chlorate crystals. It worked. Sodium chlorate crystals obtained this way were 100% optically pure.

2.) This crystallization has to be done under agitation, in our case by rotation of the nucleated solution. If the nucleation is done above the saturation concentration, the nucleation unit dissolves down to the monomer, which is not chiral, and random crystallization occurs.

3.) We knew that the sodium chlorate crystal, if translated into a single helical structure gave a 2/1 helical structure. Knowing that the chloral polymerization requires 4-6 monomer units to form a $1\frac{1}{2}$ turn of the polymer helix before the structure becomes a completely isotactic stereospecific propagation.

4.) This knowledge gave us confidence that for the chiral crystallization to form isotactic propagation in the crystallization we need a trimer or a tetramer not more for completely stereospecific crystallization. We therefore called it isotactic crystallization. – and ultimately, only isotactic crystals are formed.

5.) One point needs to be made with respect to isotactic nucleation. The chiral structure of sodium chlorate depends on its optical sign directly on the crystal structure. Not on the sign of the optical rotation. For example, (+) chiral sodium chlorate is produced by nucleation of the supersaturated solution with (+) sodium chlorate crystals. And (-) sodium chlorate crystals are formed by nucleating with (-) sodium chlorate nuclei. (+) Sodium chlorate crystals are only formed by nucleation with (-) sodium bromate crystals and (-) sodium chlorate crystals are formed by nucleation with (+) sodium bromate crystal. (+) sodium chlorate crystals have the same fundamental crystal structure as does (-) sodium bromate.

6.) Naturally (+) sodium, bromate crystals are formed by nucleating with (+) sodium bromate and vice versa.

Finally, it should be mentioned that chiral crystallization was carried out by slowly creating supersaturation by decreasing the temperature. We have also demonstrated that this phenomenon could also be achieved by adding water miscible non-solvents, like methanol or acetone, to create the supersaturation. Methanol provides a smoother environment and provides 100% chiral sodium chlorate.

Talk at the Gordon Conference on Polymers in Herkimer, NH (1996)

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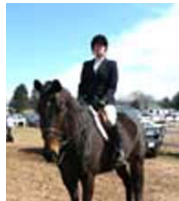
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Cover page: Chiral Crystallization



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