Applications of Chirality in Inorganic Nanomolecules

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Abstract: The term chiral describes two structures, such as molecules and nanoparticles, which are non-superimposable mirror images with sole symmetry operation *E*: 360-degree rotation about an axis. Chiral molecules are optically active enantiomers, meaning they rotate plane polarized light, and may be analyzed with circular dichroism (CD) instrumentation. Diastereomers include achiral compounds which differ in bond arrangement and do not superimpose on the mirror image, although may possess an internal line or plane of symmetry in addition to *E*. This review covers the introduction to inorganic chiral nanostructures, which are valuable in pharmacokinetics and chemical analysis methods. Chemical applications also include separation for enantiomeric selectivity, catalysis based on surface ligand characterization, and sensing chiral molecules from altered single-walled carbon nanotubes (*R*- or *L*-SWNTs).

Introduction

This review focuses on the chirality of individual inorganic nanoparticles as well as chiral nanoparticle assemblies of differing geometries and covers various nanomaterials in a comprehensive analysis. The types of chirality are defined with modeled examples, from chiral inorganic cores to achiral cores with chiral patterns of molecules on the stabilizer shell. The current and proposed applications are also explored, which include descriptions of chiral catalysis and biosensing. Chiral molecules may be classified as inorganic or organic, where chiral inorganic nanomolecules may consist of metals and have the potential for utilization in semiconductors, among other applications, and range in sizing from nanostructures to crystal structures. The synthesis of organic chiral nanoparticles, however, generally involves nucleation where the molecules coat the nanoparticle surface (Vekilov, 2010).

Chiral molecules are classified as non-superimposable, where two molecules side by side may be symmetrical across a central plane, but when superimposed, are not identical (*Figure 1*). In addition, chiral molecules do not have an operation of symmetry besides *E*: 360-degree rotation about a line axis. Chiral molecules include the classification enantiomers, which are mirror images that are non-superimposable. Diastereomers, in contrast, are non-mirror images which are non-superimposable, and are not chiral because they lack mirror image symmetry (*Figure 2*).

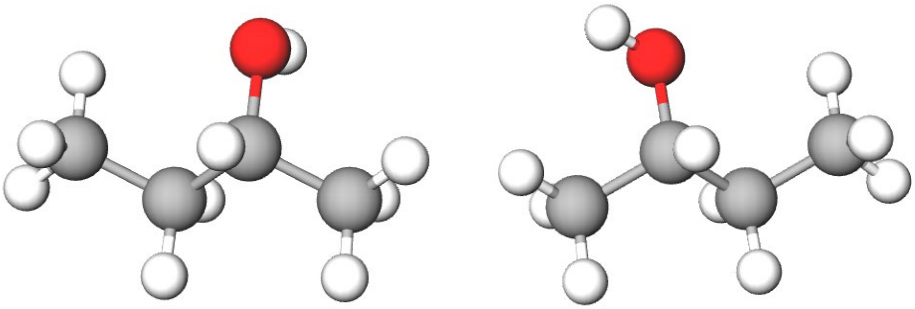

Figure 1: *Butan-2-ol ($CH_3CHOHCH_2CH_3$), commonly known as 2-butanol, is an example of a chiral compound (enantiomer) which exhibits mirror symmetry as (r)-2-butanol (left) and (s)-(+)-2-butanol (right) and is not superimposable; the sole symmetry operation is E (Solomons & Fryhle, 2011).*

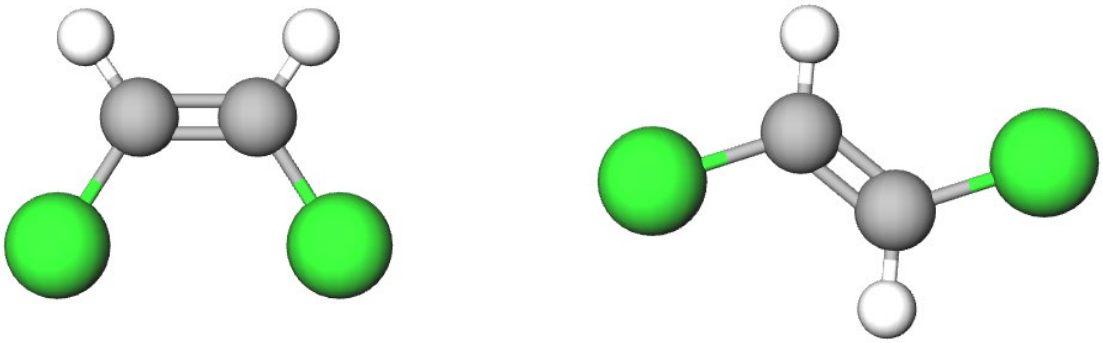

Figure 2: *Cis-1,2-Dichloroethene ($C_2H_2Cl_2$) (left) and Trans-1,2-Dichloroethene ($C_2H_2Cl_2$) (right) are diastereomers due to no mirror image symmetry and differing spatial arrangement (Solomons & Fryhle, 2011).*

Background

For nanoparticles to be chiral, there must be a homochiral biomolecule such as an amino acid or lipid to act as a surface ligand (Ma, Xu, de Moura, Wu, Kuang, Xu & Kotov, 2017). The chiral molecules attach either chemically with bonding, or physically with adsorbing like a film on the ligand. Chiral metal nanoparticles may be made with the aforementioned homochiral biomolecules; however, the difference lies in the chemical reactions which are performed to form the metal (Ma et al., 2017). These may include reduction of salts chemically, electrochemical reduction, thermal or photochemical decomposition of organometallic preceding chemicals, or laser ablation, and according to Ma et al., the most frequently observed method of synthesizing metallic nanoparticles was the chemical reduction method (2017). To improve the yield or better observe the structures, it is recommended to use the "separation techniques [of] chromatography, electrophoresis, and selective precipitation" (Ma et al., 2017).

Nanostructures are measured in nanometers, which should have at least one dimension that is less than 1×10^{-7} m in length, or about the size of a virus particle (CDC, 2022; Pradhan and Chakraverty, 2021). While found in nature, they are also engineered due to a valuable range of applications. These include, but are not limited to: drug delivery, gas storage, optics, cosmetics and electronics (Pradhan and Chakraverty, 2021). The structures vary from planar compounds, to nanotubes such as gallium nitride nanotubes which possess high electrical conductivity potential (Pradhan and Chakraverty, 2021).

To more efficiently examine the behavior and characteristics of chiral inorganic nanostructures, it is recommended to review isomerism. Isomers are two structures with the same chemical formula, which may differ in bond arrangement, spatial arrangement, or symmetry. The structures displayed in Figures 1 and 2 are examples of isomers. The main categories of isomers include configurational and constitutional isomers, both of which contain subcategories as expressed in Figure 3. Configurational isomers include diastereomers and enantiomers which differ in mirror symmetry, and both are non-superimposable. Constitutional isomers consist of coordination, ionization, hydrate and linkage isomers, which differ depending on which ligands are bound to the central ion or atom (Miessler. Fischer & Tarr, 2014).

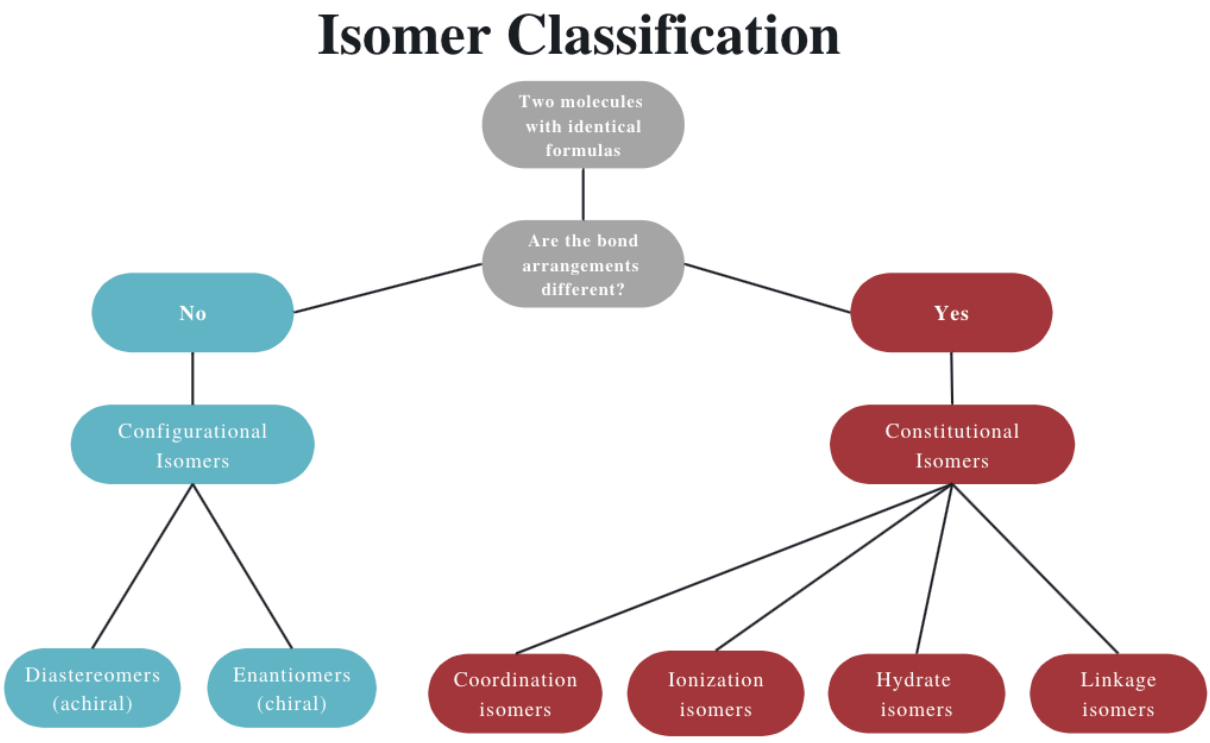

Figure 3: *Guide to classifying configurational and constitutional isomers. (Data from Miessler et al., 2014).*

Experimental Instrumentation

The instrumentation discussed by Ma et al. for investigation of chiral nanomolecules includes

Circular Dichroism (CD), Transmission Electron Microscope (TEM), Scanning Electron Microscope (SEM), Ultraviolet-visible spectroscopy (UV-Vis), and centrifuge. The CD utilization is for optical activity and UV-Vis for fluorescence analysis, as well as surface analysis in the case of SEM. SEM is valuable in measuring the surface of nanostructures as small as 50nm (Swapp, 2017). Modeling software in addition to computational analysis was also utilized. The CD is able to provide data about asymmetric structures such as chiral molecules, which do not possess an internal plane of symmetry.

Additionally, for separation of enantiomers, there are chiral HPLC columns available for utilization in research and commercial fields. This application may aid in entire separation of a racemic mixture, which is a solution composed of 1:1 enantiomers (Blackmond, 2019). A specific chiral HPLC column from Agilent may be utilized for separation and analysis of polar amines and additional separation applications for use in pharmaceutical research (2022) (Ali et al., 2022).

Results and Discussion

The optical activity of nanoparticles is discussed and displayed in various CD spectra in the review by Ma et al. (2017). The optical activity is where the plane of vibration is shifted after a plane polarized light is passed through an optically active liquid, and as compared to nonpolarized light, plane polarized light has an electric field that is only oscillating in one direction (Nafie, 2011). It was observed that chiral molecules result in optically active molecules (Nafie, 2011). This is due to their asymmetry and by utilizing vibrational infrared (IR) with CD, the absorption of the molecules may be analyzed (Andrews and Tretton, 2020). The geometry and arrangement of chiral molecules may be investigated with the use of CD in the infrared region due to the vibration of the structure (Nafie, 2011).

Ma et al. extensively covers the four types of chirality, the optical activity of chiral nanostructures, and various nanomaterials with applications, such as ZnO nanobelts for semiconductors (2017). Chirality types two through four as seen in figures 4B-4D are similar in that the inorganic core may be achiral, whereas type one chirality (figure 4A) requires that the inorganic core have a chiral geometry with only a symmetry operation of *E*. Types two through four also consider the surface ligands for classification yet type two requires the surface molecules to have a chiral geometry when bound to the nanoparticle. Type three is also unique in the sense that the surface molecules should be arranged in a chiral pattern, while type four focuses more on the asymmetric high polarization with consideration to the inorganic achiral core. Each of these types have unique applications and characterizations.

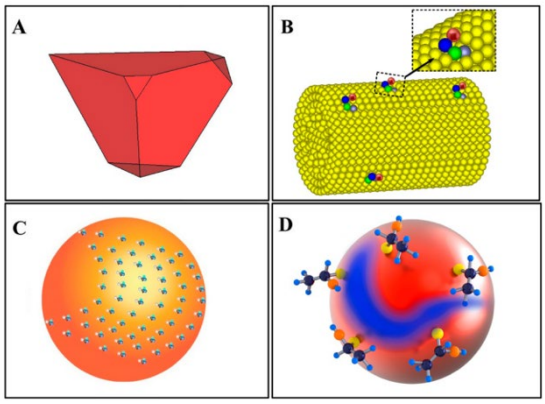

Figure 4: *From the review conducted by Ma et al., the significance of figures 4A-4D are described as followed (2017). (A) Type one chiral non-superimposable geometry based on an inorganic chiral core consisting of a potential inorganic crystal lattice without respect to surface ligands. (B) Type two chirality in which the surface molecules on the nanoparticle have chiral structure, with a potential inorganic achiral core. (C) Type three chirality consists of an achiral core with surface molecules arranged in a chiral pattern in the stabilizer surface ligand shell. (D) Type four chirality with a chiral field effect, consisting of an achiral inorganic core with high asymmetric polarization trends of achiral/chiral, chiral/achiral, and chiral/chiral ligand to adsorption patterns.*

The review by Ma et al. models the bonding and antibonding modes of branched nanorods (top), with sigma at a lower energy and sigma* at a higher energy molecular orbital, as seen in Figure 5 below, which also displays the scanning electron microscope (SEM) images for gold nanoparticles (2017). The SEM images are valuable for evaluating surface structure and texture. Figure 6 from Ma et al. contains the experimental and simulated CD spectra for CdSe and ZnS semiconductor nanorods in L- and D- formation with consideration to natural chiral distortion (2017).

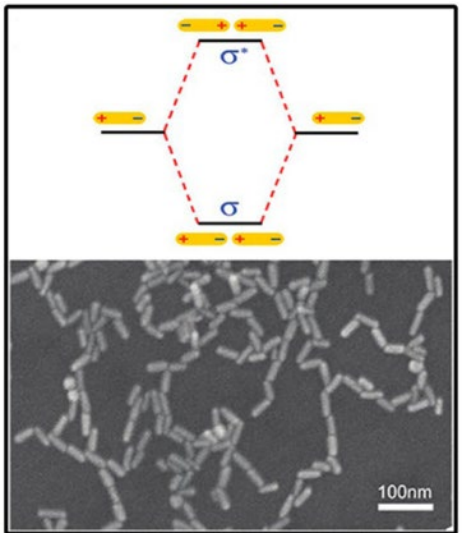

Figure 5: *The branched nanorods of gold (Au) are displayed via SEM, which are approximately 25nm in length each (Ma et al., 2017).*

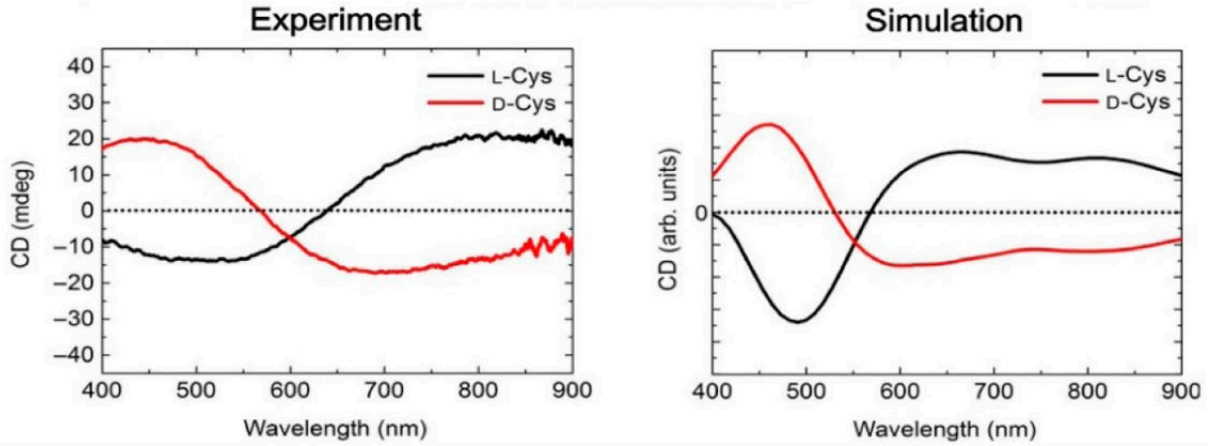

Figure 6: *Displays the CD spectra for the D- and L- Cysteine CdTe nanoparticles (Ma et al., 2017).*

Applications

The study of chiral molecules is valuable in that it connects topics for undergraduates and graduates in the courses of organic chemistry, inorganic chemistry, and instrumental analysis, while providing applications in real-world fields. The purpose of this review is to assist undergraduates and graduates in connecting the topics of chirality, which is typically introduced in organic chemistry courses, and nanostructures, which may be introduced in nanomaterials, inorganic, or instrumentation courses. These applications of chiral nanoparticles include "chiral catalysis, enantiospecific separation, biosensing, chiral memory, and chiroptical devices" (Ma et al., 2017, p. 8079). Chiral catalysis refers to nanoparticles that are utilized for accelerating reactions, where the surface ligands contribute most to the catalytic characteristic. The chiral surface ligands also contribute to the enantioselectivity which is important in pharmacokinetics such as "absorption, distribution, metabolism, and excretion" (Coelho, 2021, p. 2). For example, Iron-Palladium nanoparticles altered with chiral diphosphine ligands [(S)-BINAP] resulted in (S)-binaphthalene with a moderate yield of approximately 50% and enantioselectivity of 48% (Ma et al., 2017). This reaction was tested again without the (S)-BINAP modification, with no enantioselectivity observed (Ma et al., 2017).

In enantiospecific separation, Ma et al. has reported studies on gold and magnetic nanoparticles for efficiency. It was found that chiral gold nanoparticles altered with D- or L-cysteine are able to selectively adsorb one enantiomer from a solution, which leaves the ee remaining in the solution, where ee is the enantiomeric excess (Blackmond, 2019). For this separation, there should be a % major enantiomer – % minor enantiomer to determine the ee, however if the mixture is homochiral or optically pure, there will be 100% ee (Ma et al., 2017). Using a centrifuge is proposed to separate out gold nanoparticles that are modified with L-tyrosine (Ma et al., 2017). When considering magnetic chiral nanoparticles, the results are investigated using chromatography for separation based on the amount of relative solute (Ma et al., 2017). Enantiospecific separation is useful in the medicinal chemistry field for the synthesis of biological medications. Enantiomeric selectivity is the process of synthesizing a specific optically active chiral product, which is a valuable application to achieve desired structures, especially for the medical and electronic fields (Coelho et al., 2021).

In biological systems, there is also crucial chirality in amino acids, DNA, RNA, and polypeptides, the last of which is made up of repeating amino acid units (Blackmond, 2019). While amino acids are naturally left handed (L), the polypeptides they make up, along with DNA and RNA (sugars), are right handed (D) (Blackmond, 2019).

Conclusion

The study of chiral inorganic molecules aids in the bridging of knowledge between organic and inorganic chirality applications in real-world fields, in addition to analysis of nanoparticle behavior. Ma et al. predicts that the investigations on optically active chiral inorganic structures will continue to increase as maximal plane polarization rotation is sought. The applications have high potential and are vast; highlights include altering reactions with chiral catalysis, enantiospecific separation for medicinal chemistry, development of affordable optical instruments, and more efficient drug delivery in pharmacokinetics.

References

Andrews, S. S., & Tretton, J. (2020). Physical principles of circular dichroism. *Journal of Chemical Education*, *97*(12), 4370–4376. https://doi.org/10.1021/acs.jchemed.0c01061

CDC. Masks against COVID-19 - Centers for Disease Control and Prevention. (2022) https://www.cdc.gov/museum/pdf/cdcm-pha-stem-lesson-masks-against-covid-19-data.pdf

Chemistry Department, P. U. Chirality and Optical Activity. (2022). https://chemed.chem.purdue.edu/genchem/topicreview/bp/1organic/chirality.html

Chemistry Department, P. U. Optical Activity. (2020). https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Supplemental_Modules_(Organic_Chemistry)/Chirality/Optical_Activity

Coelho, M. M., Fernandes, C., Remião, F., & Tiritan, M. E. (2021). Enantioselectivity in drug pharmacokinetics and toxicity: Pharmacological relevance and analytical methods. *Molecules*, *26*(11), 3113. https://doi.org/10.3390/molecules26113113

Davis, U. of C. 5.1: Chiral molecules. (2015). https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Map%3A_Organic_Chemistry_(Vollhardt_and_Schore)/05._Stereoisomers/5.1%3A_Chiral_Molecules

Golberg, D., Bando, Y., Huang, Y., Terao, T., Mitome, M., Tang, C., & Zhi, C. (2010). Boron nitride nanotubes and nanosheets. *ACS nano*, *4*(6), 2979–2993. https://doi.org/10.1021/nn1006495

Gunawardena, G. (2022, February 28). *Stereocenter*. Chemistry LibreTexts. Retrieved from https://chem.libretexts.org/Ancillary_Materials/Reference/Organic_Chemistry_Glossary/Stereocenter

Libretexts, T. (2022, April 16). *Circular Dichroism*. Chemistry LibreTexts. Retrieved from https://chem.libretexts.org/Bookshelves/Physical_and_Theoretical_Chemistry_Textbook_Maps/Supplemental_Modules_(Physical_and_Theoretical_Chemistry)/Spectroscopy/Electronic_Spectroscopy/Circular_Dichroism#:~:text=Circular%20Dichroism%2C%20an%20absorption%20spectroscopy,with%20metals%20and%20other%20molecules.

Ma, W.; Xu, L.; de Moura, A.; Wu, X.; Kuang, H.; Xu, C.; Kotov, N. (2017). In *Chemical Reviews*, ACS publications. Chiral Inorganic Nanostructures. https://pubs-acs-org.ezp.twu.edu/doi/pdf/10.1021/acs.chemrev.6b00755

Miessler, G. L.; Fischer, P. J.; Tarr, D. A. (2014). In *Inorganic Chemistry*; Pearson Education, 2014; pp 75–116.

Pradhan, K. K. and Chakraverty, S. (2021) Introduction to nanostructures. In *Nano Scaled Structural Problems: Static and Dynamic Behaviors*, edited by S. Chakraverty, AIP Publishing. https://aip.scitation.org/doi/pdf/10.1063/9780735422865_001

PubChem. (2022). *2-butanol*. National Center for Biotechnology Information. PubChem Compound Database. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/2-Butanol

Pub, C. (2022). *Dichlorofluoromethane*. National Center for Biotechnology Information. PubChem Compound Database. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Dichlorofluoromethane

Swapp, S. (2017). *Scanning Electron Microscopy (SEM)*. Integrating Research and Education. Retrieved from https://serc.carleton.edu/research_education/geochemsheets/techniques/SEM.html

UCLA. Optical Activity, 2022. http://www.chem.ucla.edu/~harding/IGOC/O/optical_activity.html

Vekilov, P. G. Nucleation | crystal growth & design - ACS publications, 2010. https://pubs.acs.org/doi/10.1021/cg1011633 (accessed Nov 6, 2022).