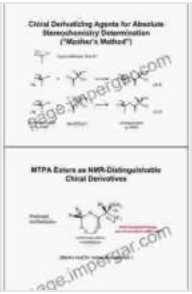
The Assignment of Absolute Configuration by NMR Using Chiral Derivatizing

In the intricate world of organic chemistry, determining the absolute configuration of chiral molecules is paramount to understanding their structure, reactivity, and biological function. Nuclear magnetic resonance (NMR) spectroscopy, a powerful analytical tool, plays a crucial role in this endeavor. By employing chiral derivatizing agents, chemists can harness the power of NMR to unveil the absolute configuration of chiral compounds.

This comprehensive guide delves into the principles and applications of NMR using chiral derivatizing agents. We will explore the theoretical foundations, practical considerations, and real-world examples to empower chemists with the knowledge and skills to confidently assign absolute configuration. Whether you are a seasoned researcher or a budding organic chemist, this definitive resource will illuminate the intricacies of this essential technique.



The Assignment of the Absolute Configuration by NMR Using Chiral Derivatizing Agents: A Practical Guide

by R. Richterich

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Theoretical Foundations: NMR and Chiral Derivatizing

NMR spectroscopy relies on the magnetic properties of atomic nuclei to provide detailed information about the structure and dynamics of molecules. When placed in a magnetic field, certain nuclei, such as ^{1}H and ^{13}C, align with or against the field, resulting in different resonance frequencies. These frequencies correspond to the chemical environment of each nucleus, enabling the identification and characterization of different atoms and groups within a molecule.

Chiral molecules, which lack mirror symmetry, exist as two distinct enantiomers that are non-superimposable mirror images of each other. The absolute configuration of a chiral molecule refers to the spatial arrangement of its atoms or groups around the chiral center. Assigning the absolute configuration is crucial for understanding the molecule's properties and interactions.

Chiral derivatizing agents are molecules that contain a chiral center and can form diastereomeric derivatives with chiral analytes. By derivatizing the analyte with a chiral derivatizing agent, the two enantiomers of the analyte will react to form two distinct diastereomers. These diastereomers have different chemical environments, resulting in distinct NMR signals that can be used to assign the absolute configuration of the analyte.

Practical Considerations: Choosing the Right Chiral Derivatizing Agent

The choice of chiral derivatizing agent is critical for successful NMR analysis. Several factors need to be considered, including:

- **Reactivity:** The derivatizing agent should react efficiently with the analyte under mild conditions.
- **Selectivity:** The derivatizing agent should selectively derivatize the desired functional group(s) without interfering with other parts of the molecule.
- **Stability:** The derivatized product should be stable under the conditions of the NMR experiment.
- **NMR properties:** The derivatizing agent should introduce unique NMR signals that can be easily distinguished from the signals of the analyte.

Commonly used chiral derivatizing agents include:

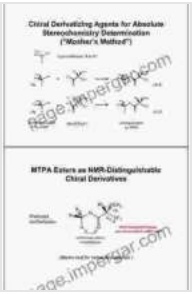
- Mosher's acid and ester
- MTPA (α-methoxy-α-trifluoromethylphenylacetic acid)
- Evans' auxiliary
- CBS (Corey-Bakshi-Shibata) reagent
- BINAP (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl)

Real-World Applications: Case Studies and Examples

The power of NMR using chiral derivatizing agents has been demonstrated in various fields of chemistry, including natural product isolation, pharmaceutical development, and stereoselective synthesis. Here are a few notable examples:

1. **Natural product isolation:** In the isolation of the natural product taxol, NMR analysis using chiral derivatizing agents played a crucial role in determining the absolute configuration of several chiral centers within the molecule.
2. **Pharmaceutical development:** In the development of the HIV protease inhibitor saquinavir, NMR using chiral derivatizing agents was used to assign the absolute configuration of the chiral intermediates, ensuring the synthesis of the correct enantiomer with the desired biological activity.
3. **Stereoselective synthesis:** In the stereoselective synthesis of chiral compounds, NMR using chiral derivatizing agents can be used to monitor the progress of the reaction and determine the enantiomeric purity of the product.

The assignment of absolute configuration by NMR using chiral derivatizing agents is a powerful technique that has revolutionized the field of organic chemistry. By harnessing the principles of NMR spectroscopy and the versatility of chiral derivatizing agents, chemists can confidently determine the spatial arrangement of atoms and groups in chiral molecules. This knowledge is essential for understanding molecular structure, reactivity, and biological function. Whether you are a seasoned researcher or a budding organic chemist, this comprehensive guide provides the foundation and practical insights to master this essential technique.



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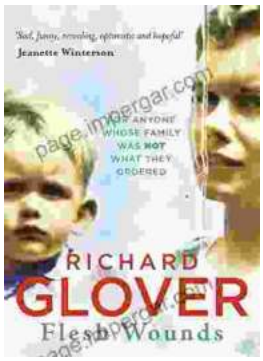

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