Journal of Advances in Science and Technology
Vol. 20, Issue No. 2, September-2023, ISSN 2230-9659

DOI: https://doi.org/10.29070/a5r3af67

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Density functional theory investigation of reaction mechanisms and stereochemical outcomes

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Abstract: Density functional theory (DFT) is an influential computational technique that is common in studying the electronic structure, reaction pathways, and stereochemical products of chemical reactions. The current project concentrates on DFT use in determining reaction pathways, intermediates, transition states, and activation energies in a bid to learn about the kinetics and thermodynamics that control the chemical transformations. It also examines how stereochemistry, i.e. notions of chirality, enantiomers and diastereomers, can exclude or include certain chemical reactions. The paper states the computational protocols, basis sets, exchange-correlation functionals, catalyst modeling's, and stereochemical control processes utilized in the theoretical studies. Moreover, the difficulties in stereo controlled synthesis and the even more general usability of stereochemistry in other areas, in particular, pharmaceuticals, materials science, agrochemicals, and biological systems, are mentioned. All in all, the combination of DFT-based calculation analysis and chemical theory provides a greater insight into molecular reactivity and stereochemical selectivity, which can be used to design a more efficient and selective chemical process.

Keywords: Density Functional Theory, Reaction Mechanisms, Stereochemistry, Computational Chemistry, Catalysis, Chirality

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INTRODUCTION

Density Functional Theory (DFT) has become one of the most popular methods of computational chemistry being used to research the structures of the systems, their properties and reactivity within the framework of modern theoretical chemistry. Based on quantum mechanics, DFT offers a pragmatic approach to computing electronic structure of atoms and molecules through the use of electron density instead of many-electron wave functions. The theoretical basis of DFT was laid down by the original works of Pierre Hohenberg and Walter Kohn whose efforts changed the face of the field of computational chemistry and its ability to accurately and efficiently perform complex chemical calculations. DFT is now widely used to examine reaction mechanisms, molecular stability and other physicochemical properties of chemical systems.

Learning about reaction mechanisms is one of the primaries aims of chemistry since it shows how reactants will be converted into products in a chain of elementary reactions. Experimental methods can usually give useful data on the results of a reaction and these can be missing detailed information on the pathway, intermediates and transition states that occur at a strictly molecular level. DFT and other computational techniques provide a good solution because it allows the researcher to visualize and analyze the whole reaction pathway in a theoretical manner. Through the use of potential energy surfaces, activation energies

and intermediate structures, DFT aids chemists in gaining better understanding of the kinetics and thermodynamics of chemical reactions.

Stereochemistry, the three-dimensional structure of atoms in molecules and its effects on chemical behavior, is another issue of great importance in chemical reactions. The biological activity, physical properties and functionality of chemical compounds can be defined by the stereochemical outcome of a reaction. The occurrence of certain stereoisomers in most organic and pharmaceutical reactions is of utmost importance in the determination of whether a compound will be active or not. DFT results enable scientists to compute and study stereochemical preferences through an analysis of relative stability of various conformations and transition states of the reaction route.

The use of DFT in reaction kinetics and stereochemistry has been found to gain greater significance in several areas such as organic synthesis, catalysis, and drug design. DFT allows finding an energetically preferable pathway of reactions by modeling them in detail on the basis of molecular coordinates, and it can be used to understand why a particular stereochemical product is preferentially obtained. Moreover, computational forecasts can be used to supplement the experimentations with theoretical validation and experimental design. Such synergy between theoretical and experimental studies has enhanced greatly the study of intricate chemical changes.

Thus, the current work is aimed at the exploration of the mechanism of reactions and stereochemical products with the Density Functional Theory. Using a thorough computational study, the study also seeks to determine important intermediates, transition states, and energy barriers of the chosen chemical reactions. The knowledge gained during this investigation will be used in gaining a better comprehension of molecular reactivity and stereochemical control, hence assist in achieving more effective and selective chemical reactions.

DFT (DENSITY FUNCTIONAL THEORY)

In applying quantum mechanics to intriguing and difficult chemical issues, density functional theory (DFT) of electronic structure has had an unequalled influence. The number of applications is increasing at a rapid pace, according to recent reviews1 11. Some of the most recent and important studies have focused on topics such as electron transport, solar energy harvesting and conversion, drug design in medicine, understanding and designing catalytic processes in enzymes and zeolites, and many other scientific and technological problems. A key component of DFT's success story is the hunt for the exchange correlation functional, which use the electron density to elucidate the complex many-body processes inside a one-particle framework. Despite density-functional theory's (DFT) widespread use and success, the goal of this study is to shed light on the difficulties that the theory faces both now and in the future. The preciseness of the exchange-correlation functional is crucial for DFT to accurately portray the quantum properties of matter. Whether DFT applications succeed or fail is, in fact, due to the approximate character of the exchange correlation functional.

The inability to have functionals that could provide a good description of both the geometries and dissociation energy of molecules was one of the most fundamental problems in early DFT advances, which targeted the most fundamental problems in chemistry. The determination of chemical reaction kinetics and

the description of van der Waals interactions necessitated the next big problem for DFT: the precise prediction of reaction barrier heights. Much discussion and ongoing research has focused on whether density-functional theory (DFT) can accurately predict the negligible energy differences linked to van der Waals interactions, or whether further corrections or nonlocal functionals of the density are required. Although it is one of the weakest interactions, it is crucial to the correct comprehension of the molecular mechanisms behind several drug-protein and protein-protein interaction advances that are detailed in the literature. Nevertheless, we maintain that DFT, and more especially the exchange correlation functional, faces much more formidable obstacles before it can realize its maximum potential. To assist in the creation of novel functionals, new and more profound theoretical understandings are required. For DFT to progress in the future, they are crucial. In this review, we will attempt to show that one strategy to help this progress is to look more closely at the cases when DFT fails rather badly. One fascinating thing about density-functional theory is that it may reveal the complexities of very small systems, mirroring those of much bigger and more complicated ones. The definition of the word "strong correlation" as used in physics literature is a good illustration of this. In this context, "strong correlation" means that the single-particle model, or even DFT, which relies on a determinant of single-particle Kohn Sham orbitals, is about to collapse. Nevertheless, one must strictly see it as a deconstruction of the presently used density functional approximations. There are substantial additional difficulties for the functional in highly linked systems. We want to show in this study that the behaviour of the energy of a single hydrogen atom may highlight the difficulty of strong correlation for density functionals. With this knowledge, the vast possibilities of DFT may be explored.

CHOICE OF THE COMPUTATIONAL PROTOCOL

Depending on the kind of catalytic system, the accuracy of the DFT findings is highly dependent on the computational process and catalytic model used. This section will compare and contrast homogeneous, heterogeneous, and hybrid catalysts, focusing on the key ways in which their computational techniques and models vary. Additionally, we will quickly go over the key restrictions associated with the DFT approaches that were examined.

- **Basis sets in molecular systems**

In homogeneous systems, the number of atoms is limited and relatively small; but, in heterogeneous catalysts, this number becomes "infinitely" huge. Therefore, using suitable basis sets is one of the key distinctions in managing such diverse systems. A collection of functions used to define the structure of an atom's orbitals is called the basis set for molecular systems. A considerable distance from the nucleus should cause the functions that make up molecular orbitals and complete wave functions—which are produced by taking linear combinations of basic functions and angular functions—to approach zero. Because they are often not demanding and generally accessible in commercial programs like licensed Gaussian and open-source ORCA, Pople basis sets are among the most routinely utilized sets for molecular systems.

- **Effective core potentials**

In contrast to semiempirical approaches, which often employ minimum basis sets for valence electrons and

entirely exclude core electrons, ab initio techniques typically account for all electrons. To account for all heavy atom core electrons and their basis functions, however, requires a lot of computer power. The core area can only be described with sufficient precision by using a large set of Gaussian functions for GTO-based computations, since the electron wave functions in close proximity to the nuclei oscillate at a high rate. It is possible to efficiently substitute potential functions in the Hamiltonian called effective core potentials (ECPs) for core electrons when describing chemical bonding and other physical features, as core electrons are not always crucial. An essential part of accurately describing valence electron characteristics is the inclusion of these words in the description of the electron-electron repulsion of the substituted core orbitals.

- **Basis sets in periodic systems**

Investigations of crystalline materials are well-suited to methods based on plane-wave basis sets. Since the energy gap between different levels disappears for infinite systems, the molecular orbitals combine into bands. Then, a complex function in three dimensions may be expressed as an expansion of the orbitals of the electrons in a band along a series of plane waves (PW).

- **Pseudopotentials**

The explicit inclusion of core electrons in PW-based computations is somewhat costly, similar to the situation in molecular systems where a large number of atomic localized functions is required to include all core electrons for heavy atoms. A high number of quickly oscillating functions, i.e. a PW basis with extremely large Ecut, is required to describe the core area properly, as previously stated, since the electron wave functions are in a state of fast oscillation close to the nucleus. To lessen the computing burden, the nuclear charge is smeared and the core electrons are modelled using pseudopotentials (PPs). The minimal energy cutoff that might be used in the calculations is included in each pseudopotential, which is usually defined by a "core radius," , which can be affected by the angular momentum of the valence orbitals. An appropriate analytical function, usually a polynomial or spherical Bessel function, describes the potential for distances less than . The pseudo-wave function and its first and second derivatives must coincide with the reference wave function at . Hence, "hard" pseudopotentials (those with tiny) are computationally more demanding because they need more PW basis functions and higher cutoff energies to describe the area beyond . Conversely, "soft" PPs have fewer PW basis functions, lower cutoff energies, and bigger . A big may drastically reduce the quality of the computed results, even if soft PPs are less computationally intensive.

- **Functionals**

The nature of the exchange-correlation functional is a key differentiator between DFT computations using spatially confined functions and periodic wave functions. The primary drawback of density-functional theory (DFT) approaches used in computational chemistry, which rely on re-introducing orbitals, is the increased complexity from three to three-and-a-half N variables, the return of the electron correlation term, and the resulting inaccurate portrayal of the kinetic energy. Separating this item into an accurately calculable portion and a minor correction term allowed Kohn and Shan to partly solve the kinetic-energy

issue, as shown above. Similar to the Hartree-Fock (HF) formalism, the former is computed with the premise of non-interacting electrons and is the primary factor in the overall kinetic energy. An exchange-correlation term, which incorporates both the interacting electrostatic term and the residual kinetic energy contribution from the interacting electrons, is absorbed.

- **Self-interaction error**

An inherent problem with density-functional theory (DFT) is the so-called self-interacting electron (SIE), which arises from the overall electron density's contribution to an unphysical repulsive contact between an electron and itself. Since the contributions to the energy from exchange precisely balance out the false self-interaction energy, this mistake does not exist in the HF technique. With knowledge of the precise Kohn-Sham functional, the same result would be achieved via density-functional theory (DFT). The incomplete cancellation of the self-interaction energy is present in every approximation DFT functional since that is not the case. The self-interaction mistake is particularly noticeable in transition metal oxides, for instance. Modelling these materials using density-functional theory (DFT) utilizing LDA and GGA approximations fails to adequately account for exchange and correlation effects, producing unreliable results. Although SIC and GW approximations (GWA) provide a more accurate depiction of metal oxide surfaces, both approaches are computationally intensive and hence unsuitable for the massive systems needed for surface and cluster simulations. As previously stated, range-separated functionals and hybrid exchange functionals both partly correct the SIE by include a proportion of the precise exchange energy in the E_{XC} term.

CHOICE AND VALIDATION OF THE CATALYST MODEL

One of the key distinctions between heterogeneous and homogeneous catalysts is their size, as previously stated. While the latter has an "infinitely" high number of atoms, the former has a limited and comparatively small number. In theory, the actual structure of a homogeneous catalyst is easy to predict because of its small size. Complexes of transition metals and other homogeneous catalysts often include large organic substituents, which significantly raises the computational cost. These substituents may not always be involved in the catalytic process; in other instances, their only purpose is to stabilize the catalyst's structure. To save computing time and resources without compromising the quality of the findings, it is usual practice to substitute these larger groups with smaller ones in such instances. In one of our publications, for example, the b-diketiminato ligand of Mg and Ca complexes was simplified by substituting H atoms for the two i-Pr substituents of the N-aryl groups. This allowed for an effective dehydrogenation of dimethylamine-borane (DMAB).158 Similarly, the possible chemical pathways of dehydrogenation/dehydrocoupling of amine-boranes have been investigated using a simplified model of the $[Rh(Ph_2P(CH_2)_2\text{-}PPh_2)(C_6H_5F)]^+$ complex, where the methyl groups of the phosphine ligands have been substituted for the phenyl rings.

Modelling heterogeneous catalysts reduces the unlimited number of atoms involved, as indicated before. Periodic boundary condition (PBC) computations and the cluster approach (CA) are the two most used methods. Below, we will provide a quick description of the pros and downsides of each strategy.

With the PBC method, we can study extended surfaces and accurately characterize their structural features as well as those of molecular adsorbates. In addition, by doing PBC calculations at the semilocal

theoretical level, one may get very precise solid-state parameters such bulk moduli, cohesive energies, work functions, elastic and phonon characteristics, surface energies, and equilibrium lattice constants. Having said that, the electronic band gaps are erroneously described since these functionals do not adequately depict the exchange and correlation effects. Using more accurate exchange-correlation functionals in PBC computations is computationally costly, hence the DFT+U technique is the best solution. The spurious interactions between charges in distinct periodic pictures might influence the physical picture, making PBC computations involving charged systems challenging.

It is computationally harder to investigate complicated response processes with several stationary points compared to CA. However, a more precise description of the electrical characteristics may be obtained by using hybrid functionals with reduced computing cost, which is made possible by the CA. The ability to introduce or remove a charge carrier in CAs without causing them to interact with other charge carriers, as a result of PBC, makes them a better choice for investigating charged systems. All the stationary points, including the more complicated transition stages, may be intercepted at much reduced computational cost due to the decreased size of CA. Several of our earlier investigations on catalytic processes made use of cluster models. Choosing a cluster model isn't a walk in the park; picking the right cluster size and methods to saturate the periphery atoms need careful consideration. Clusters are capable of undergoing significant deformations relative to their initial structures, and the presence of dangling bonds at the termination may alter the surface's electronic structure by introducing spurious states, which in turn affects its chemical reactivity. In such cases, one alternative is to embed the cluster in a bigger structure and treat it using inexpensive empirical molecular mechanics methods; another is to use an electrostatic embedding network of polarizable Coulomb point charges, which is similar to a solid's long-range ionic network.

THE ROLE OF STEREOCHEMISTRY IN ORGANIC SYNTHESIS

Stereoselective synthesis, one of the cornerstones of organic synthesis, considers the impact of atomic orientation on chemical reactions inside a product. The potential and variety of products that may be formed from a chemical change are both dictated by the three-dimensional arrangement of atoms. To optimize synthetic pathways leading to complex compounds, whether they be medicines, natural goods, or anything else on the market, stereochemistry is essential. To find stereochemistry in organic synthesis, one needs a systematic approach that combines many goals, challenges, and opportunities. To do so requires exploring the basic concepts of chirality, developing elaborate strategies for achieving stereo control, and understanding the complexities of stereochemical reactions. As the essay progresses, it becomes evident that stereochemistry always throws new chances and difficulties to scientists, necessitating new ways of thinking. We will now go into the much-discussed area of stereochemistry as it pertains to the synthesis of organic compounds.

We go into several subtopics along the way, and each one expands upon a different aspect of the stereochemical trip. Researchers in the field of stereochemistry study the relative merits of asymmetric catalysis and stereo divergent synthesis in order to master the art of stereochemical threading. Creating complex natural product mimics and/or chiral pharmaceuticals isn't without its share of typical challenges, one of which is attaining high degrees of stereochemical selectivity. We also go over some of the practical uses of stereochemistry in areas like material chemistry and medicine. Our objective is to clarify the

function of stereochemistry in light of the potential developments in organic synthesis down the road. Through analyzing the strategies, acknowledging the challenges, and reviewing their applications, our aim is to deepen our understanding of stereochemical processes and open up new avenues for study and development. Following this road will help us understand the three-dimensional interactions between molecules, which will lead to novel approaches to organic chemical production.

Principles of stereochemistry

- **Chirality:**

In stereochemistry, chirality is a fundamental concept. When we talk about optical isomers that can't match or align, we're referring to the chirality idea, which describes how the left and right hands are incompatible. Chiral molecules are also known as optical isomers or "handedness." The presence of chiral centres determines whether a substance is chiralic or not. The significance of stereochemistry cannot be overstated in several emerging domains, including as the biological, medical, and physical sciences.

- **Enantiomers:**

Molecular pairs that are mirror images of one another but cannot superpose are called optical isomers. Because of their optical differences while sharing all other physical properties (such as a melting point, boiling point, solubility, etc.), these two compounds are called optical isomers. Both beams of light will be plane-polarized, but one will go left and the other right. The two enantiomers mirror one another due to their oppositely orientated chiral centres. Stereoisomers known as enantiomers are identical in structure and function but have the opposite side of the molecule. So, although their chemical characteristics are comparable, their reactions to chiral surroundings, such chiral receptors or enzymes, may be different, which might have biological implications. The concept of enantioselectivity is fundamental to the drug development process.

- **Diastereomers:**

Both stereoisomers and diastereomers exist, although diastereomers do not have anti-enantiomer bonds. Diastereomers and enantiomers may have quite different physical properties. Two or more asymmetric centres, along with spatial arrangement change at some centres but none at all, characterize a compound as a diastereomer. The chemical properties and biological effects of diastereomers might vary. When two compounds have the same molecular formula and atomic connectivity but differ in a critical way, this is called stereoisomerism. Enantiomers, diastereomers, and conformers are the subcategories of stereoisomers. At normal temperature, conformers usually interconvert rather fast; they are different spatial geometries of the same molecule that originate from rotation around single bonds.

- **Stereochemical Nomenclature:**

The spatial interactions of atoms in chiral compounds have been modelled in a number of ways by academics. By configuring the chiral centres and arranging the substituent priorities according to atomic number, the R/S system (Cahn-Ingold-Prelog priority rules) is the most prevalent system. An interesting naming technique that uses the orientation of glyceraldehyde to find the location of the chiral centres inside

the molecule is the D/L system.

- **Techniques for Stereochemical Analysis:**

Different methods are used in experiments to find out the stereochemistry of the molecules being studied. The X-ray crystallography, optical rotation, enantioselective chromatography, and nuclear magnetic resonance spectroscopy (including rotating frame Overhauser effect spectroscopy and nuclear spectroscopy) are all examples of such techniques. To create stereoisomers selectively, understand the mechanics of chemical reactions, and predict the properties and actions of target molecules, stereochemistry is necessary. Materials science, asymmetric synthesis, and drug design are just a few of the many fields that rely on it as a basis for their work.

STEREOCHEMICAL CONTROL METHODS

Synthesis stereo control refers to intentionally altering the reaction stereochemistry to produce highly selective stereoisomers. When it comes to synthesizing drugs, crop protection agents, and materials with targeted physical and chemical characteristics, stereochemical control is crucial. For various types of synthesis, several stereochemical control approaches are available.

- **Asymmetric Synthesis:**

Asymmetric synthesis seeks to produce chiral compounds from achiral or prochiral precursors in a manner that provides one enantiomer or a predetermined ratio of the necessary isomers. Typically, chiral reagents, chiral auxiliary products, or chiral catalysts are used in this approach to incorporate chirality into the process. Many asymmetric synthesis methods are in use, including asymmetric hydrogenation, asymmetric aldol processes, and asymmetric epoxidation.

- **Chiral Pool Synthesis:**

When chiral precursors like amino acids or carbs are present in nature, the chiral pool synthesis method may be used. These chiral compounds, which are derived from natural sources and retain their enantiomeric purity, are used as building blocks in the synthesis of more complicated molecules. Because it makes use of chiral starting materials to provide improved stereo control and reduce synthesis complexity, chiral pool synthesis is useful in the production of medicines and natural products.

- **Chiral Catalyst:**

Chemicals that possess both catalytic and chirality characteristics are known as chiral catalysts. These chemicals facilitate the formation of the target stereoisomers and, more specifically, quicken the reaction rate. Asymmetric synthesis enzymes, organocatalysts, and transition metal complexes are all instances of chiral catalysts. The excellent stereoselectivity of catalyst-controlled reactions makes them popular in both academic and industrial settings.

- **Chiral Auxiliaries:**

A chiral auxiliary is a short-lived chiral reagent that is connected to a substrate in order to alter the stereochemistry of the process. These auxiliaries may be easily connected to or withdrawn from the

substrate after the reaction has started. Bone Supplements: The chiral auxiliaries mechanism relies on the ability to synthesize the required stereoisomer by precisely positioning the reagents on the substrate. Some examples of chiral auxiliaries are chiral sulfoxides, chiral amino acids, and chiral hydroxyl amine derivatives.

- **Stereoselective Reactions:**

Stereoselective reactions are those that preferentially involve one or more stereoisomers rather than others. These reactions, which manipulate electronic effects, steric fluctuations, or angle constraints, define the stereochemistry of the final product. In the synthesis of several medications and complex natural products, stereoselective methods are very useful due to the fact that the stereochemistry of the molecules greatly influences their biological characteristics.

- **Dynamic Kinetic Resolution (DKR):**

This is the procedure for preparing a racemic mixture of chiral compounds for a stereo controlled reaction. One enantiomer reacts and produces a product in a racemic mixture when a chiral catalyst or enzyme is present; the other enantiomer remains unchanged in DKR. To get high yields of the desired stereoisomer, it is necessary to eliminate the generated enantiomer, which will shift the reaction equilibrium in favour of the selected option.

- **Computational Methods:**

Computer chemistry has greatly aided stereochemical control by supplying energy profiles, transition states, and mechanical characteristics of stereoselective processes. Molecular modelling and density-functional theory (DFT) are two of the computational tools used to develop novel chiral metallic catalysts, predict the stereochemical selectivity of reactions, and find the best reaction conditions for managing the stereochemistry of processes.

TROUBLES IN STEREOCONTROLLED HYBRIDATION/SYNTHESIS

The issue of stereo controlled synthesis, which seeks to create specified stereoisomers during chemical processes, is immense, despite the fact that organic chemistry has made tremendous progress. The intricacy of chemical processes, the necessity for great selectivity, and the structural features of molecules all contribute to this. If we want to build multifunctional molecules with the exact stereochemistry that is required, we must first understand them.

- **Substrate Complexity:**

The stereochemical results of a reaction are known to be determined by the properties of the substrate molecule. As a result, the presence of more chiral centres, functional groups, and stereocenters raises the probability of competing processes and side reactions. Problems with enantio-, diastereo-, and regioselectivity are inevitable with complex substrates and can only be addressed by creating new synthetic techniques and optimizing the reaction parameters.

- **Stereo induction Efficiency:**

Particularly in reactions involving complex structures or several stereocenters, achieving a sufficient degree of stereo induction to cause the desired stereoisomer to develop preferentially may be challenging. Other general factors may also reduce the efficacy of stereo induction in chiral auxiliaries, reagents, or catalysts. A few examples of these include electrical effects, steric hindrance, and solvent polarity effects. Making the right stereo inducing materials and tweaking the reaction conditions are crucial for fixing this problem.

- **Diastereo selectivity:**

It is critical to have diastereoselective transformations that increase the amount of some diastereomers while decreasing the number of others. They found that sometimes it might be difficult to achieve good diastereo selectivity when the energy difference between diastereomeric transition states is not significantly large. Some factors that may affect the level of diastereo selectivity achieved include the solvents utilized, the substrate's flexibility, and the interaction between the catalysts and the substrate. It will need time and effort to improve the response circumstances.

- **Control of Relative and Absolute Stereochemistry:**

The absolute configuration control of starting materials and intermediates is often necessary in the synthesis of natural products, pharmaceuticals, and chiral materials, in addition to the relative and absolute configuration control of the final product. Checking the necessary stereochemical interaction between the target product's stereocenters and determining their relative arrangement is another potentially challenging endeavour. In addition, pinpointing the exact position of the chiral center—the stereochemistry of chiral compounds—remains a challenging endeavour in the realm of chemical research. Additional analytical tools like X-ray crystallography or chiroptical spectroscopy can be needed in some instances.

- **Stereo divergent or Stereo selective Pathway:**

There is a clear distinction between stereoselective synthesis, which mostly produces the target stereoisomer, and stereo divergent synthesis, which depends on producing two or more stereoisomers from a single intermediate. Precise stereo control over the final product at the substrate, reaction design, and mechanistic levels, in addition to meeting the demands for reactivity and selectivity in separate routes, may be rather challenging. Nevertheless, there is always a cost associated with adopting stereoselective and stereo divergent methods: heterogeneity in reaction yield or stereo purity.

- **Scale-up and Producability:**

Many obstacles, including as scalability, reproducibility, and economies of scale, stand in the way of taking stereo controlled synthesis from a benchtop process to an industrial-scale one. Key ideas in the subject include strategies for purification, scalability, and the construction of efficient synthetic methodologies to guarantee the synthesis of greater quantities of molecules that are stereo chemically pure. Another important aspect of industrial stereochemistry is the reduction of stereoisomeric impurities and the maintenance of a product's stereochemical purity during scaling up.

- **Computational Difficulties:**

An accurate representation of the stereochemical outcome may be achieved using computational chemistry,

mechanism, and chiral catalyst/ligand design. Stereo controlled reactions are common, but they need complex quantum mechanical computations that account for solvent effects and molecule dynamics, which adds another computational hurdle to reaction pathway modelling. Coming up with new algorithms for computers and combining theoretical and experimental methods are necessary to overcome these obstacles.

STEREOCHEMISTRY IN DIFFERENT DOMAINS

Stereochemistry is a branch of chemistry that has several generalizable applications. Atomic structure, chemical reactions, and interactions are the main topics covered. The manipulation and harnessing of stereochemical properties allow scientists to produce molecules with specific qualities and uses.

A. Chemistry of Pharmaceuticals

- **Drug Design and Development:**

The pharmacokinetics, safety, and efficacy of drugs are substantially affected by stereochemistry. Enantiomers exhibit distinct pharmacokinetic and pharmacodynamic characteristics upon binding to chiral biosites, such as enzymes, receptors, and transporters. Businesses in the pharmaceutical industry use stereo controlled synthesis to create an enantiomer with enhanced effectiveness, decreased toxicity, and enhanced safety. Amlodipine, a chiral medicine for hypertension, and fluoxetine, a chiral pharmaceutical for depression, are both significantly impacted by stereochemistry throughout their development.

- **Chiral Resolution:**

The enantiomers of chiral medications may be separated from their racemic mixtures using methods such as chromatography, fractional crystallization, and kinetic resolution. When compared to racemic combinations, single enantiomers of many pharmaceutical substances exhibit better pharmacological activity and lower toxicity. Chiral separation techniques used in pharmaceutical chemistry include enzymatic resolution, diastereomeric salt synthesis, and chiral chromatography.

B. Materials Science

- **Chiral Materials:**

Stereochemistry is a powerful tool for determining the molecular structure of chiral materials that exhibit desired mechanical, electrical, and optical characteristics. Circular dichroism, optical activity, and selective molecular recognition are chirality-induced features shown by helical-shaped molecular structures, including polymers, liquid crystals, and supramolecular assemblies. Applications for these chiral materials include sensing, photonics, asymmetric catalysis, and drug delivery systems.

- **Stereo controlled Polymerization:**

Stereo controlled polymerization is the subject of research when it comes to the stereochemical characteristics of the resulting polymers. Recent developments in controlled or live polymerization techniques have opened up new possibilities for the synthesis of polymers with inherent properties and functionalities that exhibit stereochemical selectivity. Some examples of these processes are coordination polymerization, ROMP, and ATRP.

C. Pesticides and Agrochemicals

- **Chiral Pesticides:**

For pesticides and agrochemicals to have biological efficacy and environmental sustainability, stereochemistry has to be considered. One enantiomer may be more poisonous or degrade at a slower pace than the other, and it may have different levels of insecticidal, fungicidal, or herbicidal activity. Seed control synthesis allows for the production of environmentally benign, enantiomerically pure pesticides.

- **Chiral Recognition:**

When applied to weeds or pests, chiral herbicides and pesticides are most effective when they bind to specific enzymes or biological receptors. It is known that the stereochemical features of these compounds help to enhance the pesticidal efficiency by targeting the designated targets and minimizing the impact on additional targets. It is already crucial to comprehend the stereochemistry of pesticide-receptor interactions in order to develop more effective and efficient pesticide designs.

D. Scents and Flavors

- **Chiral Aromas:**

The aromas of creams and perfumes, as well as the flavour and aroma of food and drink, are closely related via stereochemistry. Since chiral fragrance molecules include two enantiomers, there is a good chance that their olfactory effects will differ substantially in terms of quality, intensity, and longevity. Stereoselective synthesis is used to generate aroma molecules that are enantiomerically pure, which are utilized in flavour and fragrance applications.

- **Chiral Resolution in Aromas:**

The enantiomers of chiral aromatic compounds are isolated from their racemic mixture by use of chiral separation procedures. We satisfy quality and safety standards for natural food and flavouring ingredients by using enantiomerically pure aroma compounds to develop novel fragrances and flavours, improve the sensory organoleptic qualities of food and drink, and more.

E. Biological Systems

- **Chiral Recognition in Biology:**

Biological processes including signal transmission, enzymes and substrates, and molecular identification rely heavily on stereochemistry. Substances with chirality-induced characteristics include proteins, nucleic acids, and carbohydrates, among many other biological macromolecules. When studying biological processes and developing drugs with specific receptor or enzyme affinities, it is important to consider the stereochemistry of biomolecular interactions.

- **Bioactive Molecules and Chiral Medications:**

Hormones, neurotransmitters, natural substances, and other pharmaceuticals and therapeutics are all

examples of bioactive molecules and chiral medicines. It is common practice to detect stereoisomers by comparing the active, affinity, and metabolic properties of the compounds. Stereochemistry decides the safety and effectiveness of medications and regulates their absorption, transport, metabolism, and elimination from living organisms.

CONCLUSION

In conclusion, the present study highlights the important role of Density Functional Theory (DFT) in understanding reaction mechanisms and predicting stereochemical outcomes in chemical systems. DFT provides a reliable theoretical framework for analyzing reaction pathways, intermediates, transition states, and energy barriers, thereby offering valuable insights into the kinetics and thermodynamics of chemical reactions. The study also emphasizes the significance of stereochemistry, including chirality, enantiomers, and diastereomers, in controlling the selectivity and behavior of organic reactions. By discussing computational protocols, catalyst modeling, and stereochemical control methods, the research demonstrates how computational chemistry can complement experimental approaches to achieve more accurate predictions of chemical reactivity. Furthermore, the wide applications of stereochemistry in areas such as pharmaceuticals, materials science, agrochemicals, and biological systems underline its scientific and industrial importance. Overall, the integration of DFT calculations with stereochemical analysis contributes significantly to the rational design of efficient, selective, and innovative chemical processes.

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