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Cram felkin-ahn model

Difference between cram's rule and felkin-ahn model. Felkin anh model example. Cram model chemistry. Cram or cramp. Cram model. Felkin-ahn model.

A series of papers published in various journals between 1952 and 2007 discuss the concept of hyperconjugation and its effects on molecular structures. Researchers such as D.J. Cram, M. Cherest, and N.T. Anh contributed to this body of work, exploring the interactions between molecules and their influence on chemical reactions. Studies by R.W. Taft, U. Edlund, and A.S. Cieplak investigated the relationship between molecular structure and reactivity, while others, like G.D. Meakins and F. Rocquet, examined specific aspects of hyperconjugation in different contexts. The papers also report on computational studies using various methods, including the B3LYP/6-31G* level, to predict molecular properties and charges. Researchers such as Y.M. Kobayashi, C. Agami, and G. Mehta used these approaches to investigate hyperconjugation's effects on molecular structure and reactivity. More recent studies by V.K. Yadav, R. Balamurugan, and others have continued to explore the topic of hyperconjugation, with a focus on its implications for chemical reactions and molecular properties. Note that I've removed most of the citations, as they are not necessary for the paraphrased text. If you need them, please let me know! **Asymmetric Induction: A Key Element in Asymmetric Synthesis** In chemistry, asymmetric induction refers to the preferential formation of one enantiomer (a mirror image) over another in a chemical reaction. This phenomenon occurs when a chiral feature present in the substrate, reagent, catalyst, or environment influences the reaction outcome. **The Concept of Asymmetric Induction** Asymmetric induction was first introduced by Hermann Emil Fischer based on his work on carbohydrates. It involves the use of a chiral center to direct the formation of one enantiomer over another. This process is crucial in asymmetric synthesis, where chemists aim to create complex molecules with specific properties. **Types of Asymmetric Induction** There are several types of asymmetric induction, including: 1. **Internal Asymmetric Induction**: A chiral center bound to the reactive site through a covalent bond influences the reaction outcome. 2. **Relayed Asymmetric Induction**: Chiral information is introduced in a separate step and removed again in a separate chemical reaction using chiral auxiliaries. 3. **External Asymmetric Induction**: Chiral information is introduced in the transition state through a catalyst or chiral ligand. **Models of Asymmetric Induction** Several models have been proposed to describe chiral induction at carbonyl carbons during nucleophilic additions. These models, developed by Cram, Cornforth, Felkin, and others, are based on steric and electronic considerations. **The Cram's Rule** Cram's rule states that in certain reactions, the formation of one enantiomer over another is influenced by a chiral center present in the substrate. This rule provides a framework for understanding asymmetric induction and has been widely used in organic synthesis. Overall, asymmetric induction plays a vital role in asymmetric synthesis, allowing chemists to create complex molecules with specific properties. The formation of diastereomers in organic reactions can be influenced by the approach of the entering group to the asymmetric center. The rule states that when the rotational conformation of the C-C bond is such that the double bond is flanked by the two least bulky groups, this will induce the formation of an asymmetric center adjacent to it based on steric hindrance. Two reactions were performed to test this rule. In the first reaction, 2-phenylpropionaldehyde was reacted with a Grignard reagent to form 1,2-diphenyl-1-propanol, resulting in a mixture of diastereomers predominantly the threo isomer. This preference can be explained by the rule, as the active nucleophile attacks the carbonyl group from the least hindered side. The second reaction involved the organic reduction of 1,2-diphenyl-1-propanone with lithium aluminium hydride, resulting in a mixture of diastereomers predominantly the erythro isomer. The Felkin model predicts this stereochemistry, which states that nucleophilic addition reactions to carbonyl groups involve a specific transition state configuration. The Felkin rules also explain how steric interactions influence the formation of diastereomers. The rules state that torsional strain in the transition state represents a substantial fraction of the strain between fully formed bonds, and that attack of the nucleophile occurs according to a specific Dunitz angle. Additionally, polar or electronic effects can stabilize a transition state with maximum separation between the nucleophile and an electron-withdrawing group. The Felkin-Anh model builds upon the Felkin model by addressing its weaknesses and incorporating suggestions from Nguyễn Trọng Anh and Odile Eisenstein. The first weakness addressed was Felkin's assumption of a strong polar effect in nucleophilic addition transition states, leading to complete inversion of stereochemistry via SN2 reactions without justification. Anh proposed the antiperiplanar effect as a consequence of asymmetric induction controlled by substituent and orbital effects, where the σ* orbital is aligned parallel to π and π* orbitals, stabilizing the incoming anion. The second weakness in the Felkin Model was its assumption of substituent minimization around the carbonyl R, which cannot be applied to aldehydes. Anh's incorporation of Bürgi-Dunitz angle ideas allowed him to postulate a non-perpendicular attack by the nucleophile on the carbonyl center at an angle of 95° to 105° relative to the oxygen-carbon double bond, favoring approach closer to the smaller substituent and thus solving the problem of predictability for aldehydes. Though the Cram and Felkin-Anh models differ in conformers considered and assumptions, they both attempt to explain the same basic phenomenon: the preferential addition of a nucleophile to the most sterically favored face of a carbonyl moiety. However, many examples exist of reactions displaying stereoselectivity opposite of what is predicted by these models' tenets, leading to products referred to as "anti-Felkin" products. Examples of altered asymmetric induction selectivity include situations where an α-carbon is substituted with a component having Lewis base character (O, N, S, P substituents). In such cases, the introduction of a Lewis acid can result in a bidentate chelation effect that locks the carbonyl and the Lewis base substituent in an eclipsed conformation. The nucleophile then attacks from the side with the smallest free α-carbon substituent. This stereoselective control was recognized early on by Cram, who asserted that his model requires non-chelating conditions. An example of chelation control can be seen in a 1987 paper where methyl titanium chloride forms a Cram-chelate and then dissociates to lead to the anti-Felkin diastereomer. Additionally, a non-chelating electron-withdrawing substituent effect can also result in anti-Felkin selectivity if the α-carbon substituent is sufficiently electron withdrawing. In such cases, the nucleophile will add anti- relative to the electron withdrawing group, even if the substituent is not the smallest. The α-carbon in each of three compounds bonded to it presents distinct explanations for its phenomenon. The Cornforth and original Felkin models proposed a polar effect by placing the EWG substituent and incoming nucleophile anti- to each other, canceling their dipole moments in transition states. A Newman projection illustrates this alignment, regardless of steric bulk between RS and RL. The improved Felkin-Anh model considers molecular orbital interactions for more sophisticated assessment of the polar effect. An illustration of a reaction showcasing anti-Felkin selectivity and its proposed transition structure follows. The stereoelectronic environment at the β-carbon also directs asymmetric induction, with predictive models such as the Cram-chelate model defining its stereoselectivity. Reetz's work extends the Cram-chelate model to predict chelated complexes of β-alkoxy aldehydes and metals. Nucleophiles attack from less sterically hindered sides, leading to anti-adducts in major products. Metal centers must have at least two free coordination sites, with protecting ligands forming bidentate complexes. Recent models include Evans' nonchelate 1,3-induction, where the β-stereocenter is oriented anti- to the incoming nucleophile. The polar X group reduces dipole interactions by being placed anti- to the carbonyl, while Rβ is minimized against the aldehyde group. This results in predicted major products of 1,3-anti-diol. Smaller nucleophiles lead to 1,3 control and determine asymmetry in molecules. Chiral acyclic alkenes also exhibit diastereoselectivity during reactions such as epoxidation and enolate alkylation, where substituents influence the approach of the electrophile from one side of the molecule. The Houk's model predicts that selectivity is stronger for cis than trans double bonds due to steric clash between groups. In contrast, a trans alkene experiences lower selectivity due to less pronounced steric hindrance. The Felkin-Ahn model explains substrate control during nucleophilic addition to chiral aldehydes, considering the molecular framework's influence on stereocentres. Asymmetric induction relies on the molecule's 3D configuration and the interaction between functional groups. This principle guides chemical synthesis by predicting reaction outcomes based on stereochemistry. Computational modelling can provide a more comprehensive approach, while qualitative factors are often used to explain trends in specific synthetic steps. The Felkin-Ahn model describes stereoselectivity in nucleophilic attack at alpha-chiral aldehydes, where the nucleophile approaches the carbonyl group at a specific angle. In contrast, Cram's rule explains selectivity in additions of achiral allylmetals, which are often used to control reactivity at chiral aldehydes. Incorporating organo-aluminum nucleophiles instead of Grignard or organolithium ones can enhance Felkin-Anh selectivity for organometal additions to aldehydes. This switch has been shown to significantly improve stereoselectivity by Claude Spino and co-workers, specifically when transitioning from vinylgrignard to vinylalane reagents with chiral aldehydes. The outcome of adding achiral allylmetals to aldehydes is determined by the chirality of the α-carbon on the substrate. Cram's rule explains this stereoselectivity through considering a transition state where the oxygen lone pair interacts with the boron center, and the allyl group adds to the carbon end of the carbonyl group. The steric demand in this transition state is minimized by positioning the largest group away from the congested carbonyl group and the allylmetal group approaching past the smallest group on the α-carbon center. For example, (R)-2-methylbutanal reacts with an allylboron reagent to produce two diastereomers, of which the (R, R)-isomer is the major product. Cram's model for this reaction places the carbonyl group trans to the ethyl group and shows the allyl boron approaching past the hydrogen, a small group. This results in nucleophilic addition happening at the face where the hydrogen is located, producing the (R, R)-isomer as the major product. Asymmetric stereoinduction can be achieved by using chiral auxiliaries that may be reversibly attached to the substrate, inducing diastereoselective reactions prior to cleavage. These include Evans' chiral oxazolidinone auxiliaries for asymmetric aldol reactions and pseudoephedrine amides or tert-butanesulfinamide imines. Macrocyclic substrates often exhibit higher levels of stereo induction compared to linear ones due to their more rigid conformations. Early experiments by W. Clark Still and colleagues have shown that medium- and large-ring organic molecules can provide striking levels of stereo induction in reactions such as kinetic enolate alkylation, dimethylcuprate addition, and catalytic hydrogenation, even with a single methyl group biasing the diastereomeric outcome. among others, helped challenge widely-held scientific belief that large rings are too floppy to provide stereochemical control. Several total syntheses have utilized macrocyclic stereocontrol to achieve desired reaction products. In (−)-cladiella-6,11-dien-3-ol synthesis, a strained trisubstituted olefin was dihydroxylated diasetereoselectively with N-methylmorpholine N-oxide and osmium tetroxide, in the presence of an unstrained olefin. Route to (±)-periplanone B involved facial selective epoxidation of enone intermediate using tert-butyl hydroperoxide in the presence of two other alkenes. Sodium borohydride reduction of 10-membered ring enone intermediate proceeded as predicted by molecular modelling calculations accounting for lowest energy macrocycle conformation. Substrate-controlled synthetic schemes have many advantages since they do not require use of complex asymmetric reagents to achieve selective transformations. In organic synthesis, reagent control approach selectively forms one stereoisomer out of many, stereoselectivity determined by structure and chirality of reagent used. When chiral allylmetals are used for nucleophilic addition reaction to achiral aldehydes, chirality of newly generated alcohol carbon is determined by chirality of allymetal reagents. Chirality of allymetals usually comes from asymmetric ligands used. Various chiral ligands have been developed to prepare chiral allylmetals for reaction with aldehydes. H. C. Brown reported first chiral allylboron reagents for asymmetric allylation reactions with aldehydes. TADDOL ligands developed by Dieter Seebach were used to prepare chiral allyltitanium compounds for asymmetric allylation with aldehydes. Jim Leighton developed chiral allysilicon compounds in which release of ring strain facilitated stereoselective allylation reaction, 95% to 98% enantiomeric excess could be achieved for range of achiral aldehydes. The Felkin-Nguyen model, named after its proponents, is a way to describe the stereochemistry of carbonyl addition reactions. The model suggests that the reaction occurs with an asymmetric induction, meaning that one stereoisomer is favored over the other. This concept was first proposed by Nguyen and Eisenstein in 1977, and has since been supported by numerous studies (Bürgi et al., 1973; Anh et al., 1980). The model suggests that the Felkin-Nguyen transition state is more stable than other possible transition states, leading to a preferential formation of one stereoisomer. Several researchers have contributed to our understanding of this phenomenon, including Cram and Elhafez (1952), Reetz et al. (1987), and Evans et al. (1996). These studies have shown that the Felkin-Nguyen model can be applied to a wide range of carbonyl addition reactions. The concept of asymmetric induction has important implications for organic synthesis, as it allows chemists to predict the stereochemistry of products in complex reaction schemes. As a result, the Felkin-Nguyen model has been widely adopted and is now considered a fundamental principle of organic chemistry. Note: I removed most of the references and citations to make the text more concise and focused on the main idea. Let me know if you'd like me to add anything back in!