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– In this subject, we will discuss Conformations of Cyclohexane: The Chair and the Boat Cyclohexane is more stable than the other cycloalkanes we have discussed, and it has several conformations that are important for us to consider. (1) The most stable conformation of cyclohexane is the chair conformation. (2) There is no angle or torsional strain in the chair form of cyclohexane. – In a chair conformation (Fig.1), all of the carbon–carbon bond angles are 109.5o and are thereby free of angle strain. – The chair conformation is free of torsional strain, as well. – When viewed along any carbon–carbon bond (viewing the structure from an end, Fig.2), the bonds are seen to be perfectly staggered. – Moreover, the hydrogen atoms at opposite corners of the cyclohexane ring are maximally separated. (3) By partial rotations about the carbon–carbon single bonds of the ring, the chair conformation can assume another shape called the boat conformation (Fig.3). (4) The boat conformation has no angle strain, but it does have torsional strain. When a model of the boat conformation is viewed down carbon–carbon bond axes along either side (Fig.4a), the C-H bonds at those carbon atoms are found to be eclipsed, causing torsional strain. Additionally, two of the hydrogen atoms on C1 and C4 are close enough to each other to cause van der Waals repulsion (Fig.4b). This latter effect has been called the “flagpole” interaction of the boat conformation. Torsional strain and flagpole interactions cause the boat conformation to have considerably higher energy than the chair conformation. Although it is more stable, the chair conformation is much more rigid than the boat conformation. The boat conformation is quite flexible. By flexing to a new form—the twist conformation (Fig.5)—the boat conformation can relieve some of its torsional strain and, at the same time, reduce the flagpole interactions. (5) The twist boat conformation of cyclohexane has a lower energy than the pure boat conformation, but is not as stable as the chair conformation. The stability gained by flexing is insufficient, however, to cause the twist conformation to be more stable than the chair conformation. The chair conformation is estimated to be lower in energy than the twist conformation by approximately 23 kJ mol-1. The energy barriers between the chair, boat, and twist conformations of cyclohexane are low enough (Fig.6) to make separation of the conformers impossible at room temperature. At room temperature the thermal energies of the molecules are great enough to cause approximately 1 million interconversions to occur each second. (6) Because of the greater stability of the chair, more than 99% of the molecules are estimated to be in a chair conformation at any given moment. Conformations of Higher Cycloalkanes – Cycloheptane, cyclooctane, cyclononane, and other higher cycloalkanes also exist in nonplanar conformations. – The small instabilities of these higher cycloalkanes appear to be caused primarily by torsional strain and repulsive dispersion forces between hydrogen atoms across rings, called transannular strain. – The nonplanar conformations of these rings, however, are essentially free of angle strain. – X-ray crystallographic studies of cyclodecane reveal that the most stable conformation has carbon–carbon–carbon bond angles of 117o. – This indicates some angle strain. – The wide bond angles apparently allow the molecules to expand and thereby minimize unfavorable repulsions between hydrogen atoms across the ring. – There is very little free space in the center of a cycloalkane unless the ring is quite large. – Calculations indicate that cyclooctadecane, for example, is the smallest ring through which a -CH2CH2CH2– chain can be threaded. – Molecules have been synthesized, however, that have large rings threaded on chains and that have large rings that are interlocked like links in a chain. – These latter molecules are called catenanes. – In 1994 J. F. Stoddart and co-workers, then at the University of Birmingham (England), achieved a remarkable synthesis of a catenane containing a linear array of five interlocked rings. – Because the rings are interlocked in the same way as those of the Olympic symbol, they named the compound Olympiadane. Reference: Organic chemistry / T.W. Graham Solomons, Craig B.Fryhle, Scott A. Snyder, / (eleventh edition) / 2014. InChI=1S/C6H12/c1-2-4-6-5-3-1/h1-6H2InChIKeyInChIKey=XDTMQSROBMDMFD-UHFFFAOYSA-NSMILESC1CCCCC1Canonical SMILESC1CCCCC1Other Names for this SubstanceCyclohexaneBenzene, hexahydro-HexahydrobenzeneHexamethyleneHexanaphthene Organic compound; 6-sided hydrocarbon ring Cyclohexane Cyclohexane 3D structure of a cyclohexane molecule Skeletal formula of cyclohexane in its chair conformation Ball-and-stick model of cyclohexane in its chair conformation Names Preferred IUPAC name Cyclohexane[2] Other names Hexanaphthene (archaic)[1] Identifiers CAS Number 110-82-7 Y 3D model (JSmol) Interactive image Beilstein Reference 1900225 ChEBI CHEBI:29005 Y ChEMBL ChEMBL15980 Y ChemSpider 7787 Y DrugBank DB03561 Y ECHA InfoCard 100.003.461 Gmelin Reference 1662 KEGG C11249 Y PubChem CID 8078 RTECS number GU6300000 UNII 48K5MKG32S Y UN number 1145 CompTox Dashboard (EPA) DTXSID4021923 InChI InChI=1S/C6H12/c1-2-4-6-5-3-1/h1-6H2 YKey: XDTMQSROBMDMFD-UHFFFAOYSA-N YInChI=1/C6H12/c1-2-4-6-5-3-1/h1-6H2Key: XDTMQSROBMDMFD-UHFFFAOYAZ SMILES C1CCCCC1 Properties Chemical formula C_6H_{12} Molar mass 84.162 g·mol−1 Appearance Colourless liquid Odor Sweet, gasoline-like Density 0.7739 g/ml (liquid); 0.996 g/ml (solid) Melting point 6.47 °C (43.65 °F; 279.62 K) Boiling point 80.74 °C (177.33 °F; 353.89 K) Solubility in water Immiscible Solubility Soluble in ether, alcohol, acetone Vapor pressure 78 mmHg (20 °C)[3] Magnetic susceptibility (χ) −68.13·10−6 cm3/mol Refractive index (nD) 1.42662 Viscosity 1.02 cP at 17 °C Hazards GHS labelling: Pictograms Signal word Danger Hazard statements H225, H304, H315, H336 Precautionary statements P210, P233, P240, P241, P242, P243, P261, P264, P271, P273, P280, P301+P310, P302+P352, P303+P361+P353, P304+P340, P312, P321, P331, P332+P313, P362, P370+P378, P391, P403+P233, P403+P235, P405, P501 NFPA 704 (fire diamond) 1 3 0 Flash point −20 °C (−4 °F; 253 K) Autoignitiontemperature 245 °C (473 °F; 518 K) Explosive limits 1.3–8%[3] Lethal dose or concentration (LD, LC): LD50 (median dose) 12705 mg/kg (rat, oral)813 mg/kg (mouse, oral)[4] LCLo (lowest published) 17,142 ppm (mouse, 2 h)26,600 ppm (rabbit, 1 h)[4] NIOSH (US health exposure limits): PEL (Permissible) TWA 300 ppm (1050 mg/m3)[3] REL (Recommended) TWA 300 ppm (1050 mg/m3)[3] IDLH (Immediate danger) 1300 ppm[3] Thermochemistry Std enthalpy offormation (ΔfH298) −156 kJ/mol Std enthalpy ofcombustion (ΔcH298) −3920 kJ/mol Related compounds Related cycloalkanes CyclopentaneCycloheptane Related compounds CyclohexeneBenzene Supplementary data page Cyclohexane (data page) Except where otherwise noted, data are given for materials in their standard state (at 25 °C [77 °F], 100 kPa). Y verify (what is YN ?) Infobox references Chemical compound Cyclohexane is a cycloalkane with the molecular formula C_6H_{12}. Cyclohexane is non-polar. Cyclohexane is a colourless, flammable liquid with a distinctive detergent-like odor, reminiscent of cleaning products (in which it is sometimes used). Cyclohexane is mainly used for the industrial production of adipic acid and caprolactam, which are precursors to nylon.[5] Cyclohexyl (C_6H_{11}) is the alkyl substituent of cyclohexane and is abbreviated Cy.[6] Cyclohexane is one of components of naphtha, from which it can be extracted by advanced distillation methods. Distillation is usually combined with isomerization of methylcyclopentane, a similar component extracted from naphtha by similar methods. Together, these processes cover only a minority (15-20%) of the modern industrial demand, and are complemented by synthesis.[7] On an industrial scale, cyclohexane is produced by hydrogenation of benzene in the presence of a Raney nickel catalyst.[citation needed] Producers of cyclohexane account for approximately 11.4% of global demand for benzene.[8] The reaction is highly exothermic, with ΔH(500 K) = -216.37 kJ/mol. Dehydrogenation commenced noticeably above 300 °C, reflecting the favorable entropy for dehydrogenation.[9] Unlike benzene, cyclohexane is not found in natural resources such as coal. For this reason, early investigators synthesized their cyclohexane samples.[10] In 1867 Marcellin Berthelot reduced benzene with hydroiodic acid at elevated temperatures.[11][12] In 1870, Adolf von Baeyer repeated the reaction[13] and pronounced the same reaction product "hexahydrobenzene". In 1890 Vladimir Markovnikov believed he was able to distill the same compound from Caucasus petroleum, calling his concoction "hexanaphtene".[citation needed] Surprisingly, their cyclohexanes boiled higher by 10 °C than either hexahydrobenzene or hexanaphthene, but this riddle was solved in 1895 by Markovnikov, N.M. Kishner, and Nikolay Zelinsky when they reassigned "hexahydrobenzene" and "hexanaphtene" as methylcyclopentane, the result of an unexpected rearrangement reaction. In 1894, Baeyer synthesized cyclohexane starting with a ketonic decarboxylation of pimelic acid followed by multiple reductions: In the same year, E. Haworth and W.H. Perkin Jr. (1860–1929) prepared it via a Wurtz reaction of 1,6-dibromohexane. Although rather unreactive, cyclohexane undergoes autoxidation to give a mixture of cyclohexanone and cyclohexanol. The cyclohexanone–cyclohexanol mixture, called "KA oil", is a raw material for adipic acid and caprolactam, precursors to nylon. Several million kilograms of cyclohexanone and cyclohexanol are produced annually.[9] It is used as a solvent in some brands of correction fluid. Cyclohexane is sometimes used as a non-polar organic solvent, although n-hexane is more widely used for this purpose. It is frequently used as a recrystallization solvent, as many organic compounds exhibit good solubility in hot cyclohexane and poor solubility at low temperatures. Cyclohexane is also used for calibration of differential scanning calorimetry (DSC) instruments, because of a convenient crystal-crystal transition at −87.1 °C.[14] Cyclohexane vapour is used in vacuum carburizing furnaces, in heat treating equipment manufacture. Main article: Cyclohexane conformation The 6-vertex edge ring does not conform to the shape of a perfect hexagon. The conformation of a flat 2D planar hexagon has considerable strain because the C-H bonds would be eclipsed. Therefore, to reduce torsional strain, cyclohexane adopts a three-dimensional structure known as the chair conformation, which rapidly interconvert at room temperature via a process known as a chair flip. During the chair flip, there are three other intermediate conformations that are encountered: the half-chair, which is the most unstable conformation, the more stable boat conformation, and the twist-boat, which is more stable than the boat but still much less stable than the chair. The chair and twist-boat are energy minima and are therefore conformers, while the half-chair and the boat are transition states and represent energy maxima. The idea that the chair conformation is the most stable structure for cyclohexane was first proposed as early as 1890 by Hermann Sachse, but only gained widespread acceptance much later. The new conformation puts the carbons at an angle of 109.5°. Half of the hydrogens are in the plane of the ring (equatorial) while the other half are perpendicular to the plane (axial). This conformation allows for the most stable structure of cyclohexane. Another conformation of cyclohexane exists, known as boat conformation, but it interconverts to the slightly more stable chair formation. If cyclohexane is mono-substituted with a large substituent, then the substituent will most likely be found attached in an equatorial position, as this is the slightly more stable conformation. Cyclohexane has the lowest angle and torsional strain of all the cycloalkanes; as a result cyclohexane has been deemed a 0 in total ring strain. Cyclohexane has two crystalline phases. The high-temperature phase I, stable between 186 K and the melting point 280 K, is a plastic crystal, which means the molecules retain some rotational degree of freedom. The low-temperature (below 186 K) phase II is ordered. Two other low-temperature (metastable) phases III and IV have been obtained by application of moderate pressures above 30 MPa, where phase IV appears exclusively in deuterated cyclohexane (application of pressure increases the values of all transition temperatures).[15] Cyclohexane phases[15] No Symmetry Space group a (Å) b (Å) c (Å) Z T (K) P (MPa) I Cubic Fm3m 8.61 4 195 0.1 II Monoclinic C2/c 11.23 6.44 8.20 4 115 0.1 III Orthorhombic Pmnn 6.54 7.95 5.29 2 235 30 IV Monoclinic P12(1)/n1 6.50 7.64 5.51 4 160 37 Here Z is the number structure units per unit cell; the unit cell constants a, b and c were measured at the given temperature T and pressure P. The Flixborough disaster, a major industrial accident caused by an explosion of cyclohexane Hexane Ring flip Cyclohexane (data page) ^ "Hexanaphthene". dictionary.com. Archived from the original on 2018-02-12. ^ "Front Matter". Nomenclature of Organic Chemistry : IUPAC Recommendations and Preferred Names 2013 (Blue Book). Cambridge: The Royal Society of Chemistry. 2014. pp. P001 – P004. doi:10.1039/9781849733069-FP001. ISBN 978-0-85404-182-4. ^ a b c d e NIOSH Pocket Guide to Chemical Hazards. "#0163". National Institute for Occupational Safety and Health (NIOSH). ^ a b "Cyclohexane". Immediately Dangerous to Life or Health Concentrations (IDLH). National Institute for Occupational Safety and Health (NIOSH). ^ Campbell, M. Larry (2011). "Cyclohexane". Ullmann's Encyclopedia of Industrial Chemistry. doi:10.1002/14356007.a08_209.pub2. ISBN 978-3527306732. ^ "Standard Abbreviations and Acronyms" (PDF). The Journal of Organic Chemistry. Archived from the original (PDF) on 1 Aug 2018. ^ Weissermel, Klaus; Arpe, Hans-Jürgen (2008-07-11). Industrial Organic Chemistry. John Wiley & Sons. p. 345. ISBN 978-3-527-61459-2. ^ Ceresana. "Benzene - Study: Market, Analysis, Trends 2021 - Ceresana". www.ceresana.com. Archived from the original on 21 December 2017. Retrieved 4 May 2018. ^ a b Michael Tuttle Musser (2005). "Cyclohexanol and Cyclohexanone". Ullmann's Encyclopedia of Industrial Chemistry. Weinheim: Wiley-VCH. doi:10.1002/14356007.a08_217. ISBN 978-3527306732. ^ Warnhoff, E. W. (1996). "The Curiously Intertwined Histories of Benzene and Cyclohexane". J. Chem. Educ. 73 (6): 494. Bibcode:1996JChEd..73..494W. doi:10.1021/ed073p494. ^ Bertholet (1867). "Nouvelles applications des méthodes de réduction en chimie organique" [New applications of reduction methods in organic chemistry]. Bulletin de la Société Chimique de Paris (in French). series 2 (7): 53–65. ^ Bertholet (1868). "Méthode universelle pour réduire et saturer d'hydrogène les composés organiques" [Universal method for reducing and saturating organic compounds with hydrogen]. Bulletin de la Société Chimique de Paris (in French). series 2 (9): 8–31. En effet, la benzine, chauffée à 280° pendant 24 heures avec 80 fois son poids d'une solution aqueuse saturée à froid d'acide iodhydrique, se change à peu près entièrement en hydrure d'hexylène, $C_{12}H_{14}$, en fixant 4 fois son volume d'hydrogène: $C_{12}H_6 + 4H_2 = C_{12}H_{14}$ ... Le nouveau carbure formé par la benzine est un corps unique et défini: il bout à 69°, et offre toutes les propriétés et la composition de l'hydrure d'hexylène extrait des pétroles. [In effect, benzene, heated to 280° for 24 hours with 80 times its weight of an aqueous solution of cold saturated hydroiodic acid, is changed almost entirely into hydride of hexylene, $C_{12}H_{14}$, [Note: this formula for hexane (C_6H_{14}) is wrong because chemists at that time used the incorrect atomic mass for carbon.] by fixing [i.e., combining with] 4 times its volume of hydrogen: $C_{12}H_6 + 4H_2 = C_{12}H_{14}$ The new carbon compound formed by benzene is a unique and well-defined substance: it boils at 69° and presents all the properties and the composition of hydride of hexylene extracted from oil.)] ^ Adolf Baeyer (1870). "Ueber die Reduction aromatischer Kohlenwasserstoffe durch Jodphosphonium" [On the reduction of aromatic compound by phosphonium iodide [H_4IP]]. Annalen der Chemie und Pharmacie. 55: 266–281. Bei der Reduction mit Natriumamalgam oder Jodphosphonium addiren sich im höchsten Falle sechs Atome Wasserstoff, und es entstehen Abkömmlinge, die sich von einem Kohlenwasserstoff C_6H_{12} ableiten. Dieser Kohlenwasserstoff ist aller Wahrscheinlichkeit nach ein geschlossener Ring, da seine Derivate, das Hexahydromesitylen und Hexahydromellithsäure, mit Leichtigkeit wieder in Benzolabkömmlinge übergeführt werden können. [During the reduction [of benzene] with sodium amalgam or phosphonium iodide, six atoms of hydrogen are added in the extreme case, and there arise derivatives, which derive from a hydrocarbon C_6H_{12}. This hydrocarbon is in all probability a closed ring, since its derivatives — hexahydromesitylene [1,3,5 - trimethyl cyclohexane] and hexahydromellithic acid [cyclohexane-1,2,3,4,5,6-hexacarboxylic acid] — can be converted with ease again into benzene derivatives.] ^ Price, D. M. (1995). "Temperature Calibration of Differential Scanning Calorimeters". Journal of Thermal Analysis. 45 (6): 1285–1296. doi:10.1007/BF02547423. S2CID 97402835. ^ a b Mayer, J.; Urban, S.; Habrylo, S.; Holderna, K.; Natkaniec, I.; Würflinger, A.; Zajac, W. (1991). "Neutron Scattering Studies of C_6H_{12} and C_6D_{12} Cyclohexane under High Pressure". Physica Status Solidi B. 166 (2): 381. Bibcode:1991PSSBR.166..381M. doi:10.1002/pssb.2221660207. Wikimedia Commons has media related to Cyclohexane. International Chemical Safety Card 0242 National Pollutant Inventory – Cyclohexane fact sheet NIOSH Pocket Guide to Chemical Hazards Cyclohexane@3Dchem Hermann Sachse and the first suggestion of a chair conformation. NLM Hazardous Substances Databank – Cyclohexane Methanol Discovered in Space Calculation of vapor pressure, liquid density, dynamic liquid viscosity, surface tension of cyclohexane Cyclohexane production process flowsheet, benzene hydrogenation technique Retrieved from " Cyclohexan [ACD/IUPAC Name] Cyclohexane [Wiki] [ACD/IUPAC Name] [ACD/Index Name] Cyclohexane [ACD/IUPAC Name] [ACD/Index Name] MFCD00003814 [MDL number] Cyclohexane has a non-polar structure that makes it almost free from ring strain. The most important conformations that it can have included chain conformation and boat conformation. The chair conformation is more stable than the boat conformation. The boat conformation can sometimes be more stable than it is usually, by a slight rotation in the C-C bonds and is called the skew boat conformation. Nevertheless, the chair conformation is the most stable cyclohexane form. A Conformation of cyclohexane can refer to many 3-Dimensional shapes assumed by a cyclohexane molecule without disturbing the integrity of the chemical bonds in it. Table of Contents Conformations of cyclohexane A regular hexagon shape contains internal angles of 120o. However, the carbon-carbon bonds belonging to the cyclohexane ring have a tetrahedral symmetry, with the bond angles corresponding to 109.5o. This is the reason why the cyclohexane ring has a tendency to take up several warped conformations (so that the bond angles are brought closer to the tetrahedral angle (109.5o) and there is reduced overall strain energy). Examples of common conformations of cyclohexane include the boat, the twist-boat, the chair, and the half-chair conformations, which are named based on the shape that the cyclohexane molecule assumes in them. These four cyclohexane conformations have been illustrated below along with some insight into their stability. It can be noted that the cyclohexane molecule has the ability to switch between the conformations listed above and that only the chair and the twist-boat conformations can be isolated into their respective pure forms. Due to hydrogen-hydrogen interactions in these conformations, the bond length and the bond angle vary slightly from their nominal values. The chair conformations of cyclohexane have lower energies than the boat forms. However, the rather unstable boat forms of cyclohexane undergo rapid deformation to give twist-boat forms which are the local minima corresponding to the total energy. The hydrogen atoms belonging to the carbon-hydrogen bonds that are at a perpendicular angle to the mean plane are called axial hydrogens, whereas those belonging to the carbon-hydrogen bonds which are parallel to the mean plane are called equatorial hydrogens. These bonds are also referred to as axial and equatorial bonds respectively. Boat and Chair Forms of Cyclohexane Cyclohexane is the most widely occurring ring in compounds of natural origin. Its prevalence, undoubtedly a consequence of its stability, makes it the most important of the cycloalkanes. The deviation of bond angle in cyclohexane molecules is more than in cyclopentane, it should be more strained and less reactive than cyclopentane. But actually, it is less strained and more stable than cyclopentane. In order to avoid the strain, cyclohexane does not exist as a planar molecule as expected. It exists as a puckered ring which is non-planar and the bond angles are close to tetrahedral bond angles. Two such puckered rings for cyclohexane are called the boat and chair conformations. Stability of conformations of cyclohexane Generally, in the chair-shaped conformation of cyclohexane, there are two carbon-hydrogen bonds of each of the following types: Axial ‘up’ Axial ‘down’ Equatorial ‘up’ Equatorial ‘down’ This geometry of chair cyclohexane conformations is generally preserved when the hydrogen atoms are replaced by halogen atoms such as fluorine, chlorine, bromine, and iodine. The phenomenon wherein the cyclohexane molecule undergoes a conversion from one chair form to a different chair form is called chair flipping (or ring flipping). An illustration detailing chair flipping is provided below. When chair flipping occurs, axial carbon-hydrogen bonds become equatorial and the equatorial carbon-hydrogen bonds become axial. However, they retain the corresponding ‘up’ or ‘down’ positions. It can be noted that at a temperature of 25o Celsius, 99.99% of the molecules belonging to a given cyclohexane solution would correspond to a chair-type conformation. The boat conformation of cyclohexane is not a very stable form due to the torsional strain applied to the cyclohexane molecule. The stability of this form is further affected by steric interactions between the hydrogen atoms. Owing to these factors, these conformations are generally converted into twist-boat forms which have a lower torsional strain and steric strain in them. These twist-boat conformations of cyclohexane are much more stable than their boat-shaped counterparts. This conformation has a concentration of less than 1% in a solution of cyclohexane at 25o. In order to increase the concentration of this conformation, the cyclohexane solution must be heated to 1073K and then cooled to 40K. Recommended Videos Cyclohexane conformation free of angle strain: chair conformation is achiral because it has a centre of symmetry because boat conformation is achiral because it has a plane of symmetry. Twist boat conformation is chiral, since there is no element of symmetry. The chair form shown to the right is the most stable conformation of cyclohexane. The C-C-C bonds are very similar to 109.5o, so they are almost free from angle pressure. It is also a completely staggered conformation and is, therefore, free of torsional stress. Boat conformation is the least stable, with the highest strength, has steric hindrance on carbon 1 and carbon 4 between the two equatorial hydrogens, and has torsional stress, as each bond almost fully ellipses other bonds in the Newman projection. Optical activity is the ability of a substance to rotate the plane polarised light. Chirality is the necessary condition for optical activity. Diastereomers lack mirror symmetry and are optically active. Since axial bonds are parallel to each other, substituents larger than hydrogen typically suffer from greater steric crowding when axial rather than equatorial driven. Replaced cyclohexanes would therefore preferentially follow conformations in which the larger substituents assume an equatorial orientation. Home / Cyclohexane Chair Conformation Stability: Which One Is Lower Energy? By James Ashenhurst Last updated: November 21st, 2024 | Finding The Most Stable Conformation Of A Cyclohexane Chair You’re given a structure with two or more substituents on a cyclohexane ring, and you’re asked to draw the most stable conformation. How do you do that? That’s what this post is about. Table of Contents 1. A-Values Are A Useful Measure Of Bulkiness In the last post, we introduced A values and said they were a useful tool for determining which groups are “bulkiest” on a cyclohexane ring. (See post: Ranking the Bulkiness Of Substituents On Cyclohexane Rings With A-Values) The greater the A-value (bulk), the more favoured the equatorial conformer will be (versus axial). We saw that hydroxyl groups (OH) have a relatively low A-value (0.87), methyl groups are higher (1.70) and the t-butyl group is one of the highest of all (>4.5) . We also saw that by knowing the A value (which is essentially the energy difference in kcal/mol) we could figure out the % of axial and equatorial conformers in solution using the formula $\Delta G = -RT \ln K$ In this post we’re going to extend this concept and see what happens when we have MORE than one group on a cyclohexane ring. 2. A-Values Are Additive The nice thing about A values is that they are additive. We can make the (safe) assumption that groups on adjacent carbons don’t bump into one another [Note 1] so figuring out the torsional strain of a cyclohexane chair is simply a matter of adding up the A values of the axial groups in any chair conformation. We can apply this to cyclohexanes with two, three, or even more substituents. Here are some examples: 3. Example: Determining The Most Stable Conformation Of cis- And trans– 1,2-Dimethylcyclohexane That’s nice, you might say, but when might we ever want to do that? The key example is when we are examining two chair conformers of the same molecule. A-values are essential in helping us figure out which one is most stable. Here’s an example of the type of question we might be asked: draw the two chair conformations of cis-1,2-dimethylcyclohexane and trans-1,2-dimethylcyclohexane, and determine which is most stable. Here, I’ve started by drawing the conformer of trans-1,2-dimethylcyclohexane where both CH_3 groups are axial (remember – it’s trans because one group is up and one group is down). The two axial methyl groups give a total of 3.4 kcal/mol of torsional strain. A chair flip converts all axial groups to equatorial and vice versa (but all “up” groups remain “up” and all “down” groups remain “down”!) giving us a conformer where both methyl groups are now equatorial (and therefore do not contribute any strain). Therefore the di-equatorial conformer is favoured by 3.4 kcal/mol. [If we wanted to, we could also figure out the equilibrium constant here: K is about 340, giving a ratio 99.6: 1 in favour of the di-equatorial conformer.] In the case of cis-1,2-dimethylcyclohexane, I’ve started by drawing an axial CH_3 at C-1 and an equatorial CH_3 at C-2 (note that my designation of C-1 and C-2 is completely arbitrary). This has a strain energy of 1.70 kcal/mol due to the single axial CH_3. When we do the chair flip, we convert all axial groups to equatorial and all equatorial to axial, giving us…. a new chair which still has one methyl group equatorial and one axial! The same energy, in other words (1.70 kcal/mol). [The equilibrium constant here is 1, giving a 50:50 ratio] 4. To Determine Chair Conformation Stability, Add Up The A-Values For Each Axial Substituent. The Lower The Number The More Stable It Is Now that we’ve drawn all four possibilities, we can rank them in order of stability if we want, and then determine that for the two isomers of 1,2-dimethylcyclohexane, the di-equatorial conformer of trans-1,2-dimethylcyclohexane is the most stable. 5. Summary: Chair Conformation Stability In the next post we’re going to talk about fused cyclohexane rings, and ask how we can apply what we’ve already learned to understand more about the stability of the conformers of these molecules. Notes Note 1. One key exception to the “A values are additive” assumption is 1,2-di-t-butyl cyclohexane, in which the trans form is actually less stable than the cis despite the fact that both groups are equatorial in the trans. That’s because the two t-butyl groups are held together so closely in space that there is significant “1,2” strain (Van der Waals strain). [Note: it turns out in the trans isomer, the diaxial conformation is favored by 6.2 kcal/mol ! see the References section.] Another exception is the amino alcohol below. What force might be responsible for the fact that the axial conformer is favoured in equilibrium conditions? Quiz Yourself! Click to Flip Click to Flip Click to Flip (Advanced) References and Further Reading This is a topic commonly taught to undergraduates in Organic Chemistry. A-values are empirically derived and denote the thermodynamic preference for a substituent to be in the axial or equatorial position in cyclohexane. A-values can be added, and the total energy thus derived gives the difference in free energy between the all-axial and all-equatorial conformations. Neighboring Carbon and Hydrogen. XIX. t-Butylcyclohexyl Derivatives. Quantitative Conformational Analysis S. Winstein and N. J. Holness Journal of the American Chemical Society 1955, 77 (21), 5562-5578 DOI: 10.1021/ja01626a037 An early paper on the determination of A-values (see Table XII) through kinetic (solvolytic) measurements, which is what Prof. Winstein was well known for. The introduction features a nice summary of how A-values are determined, and later on, Prof. Winstein states “The energy quantity by which a t-butyl group favors the equatorial position is sufficiently large to guarantee conformational homogeneity to most 4-t-butylcyclohexyl derivatives”, in agreement with what is commonly taught in organic chemistry classes today. Conformational analysis. 32. Conformational energies of methyl sulfide, methyl sulfoxide, and methyl sulfone groups Ernest L. Eliel and Duraisamy Kandasamy The Journal of Organic Chemistry 1976, 41 (24), 3899-3904 DOI: 1021/jo00886a026 This paper uses the additivity of A-values to determine the A-values of -SCH3, -SOCH3, and -SO2CH3 (Table IV). The gauche interaction in trans-1,2-dimethylcyclohexane Muthiah Manoharan and Ernest L. Eliel Tetrahedron Lett. 1983, 24 (5), 453-456 DOI: 10.1016/S0040-4039(00)81435-5 Although this is generally not covered in introductory organic chemistry, one complication with employing A-values is that groups are on adjacent carbons (as in 1,2-dimethylcyclohexane) can undergo steric repulsion through so-called “gauche interactions”. In this paper, the gauche interaction in trans-1,2-dimethylcyclohexane is calculated to be 0.74 kcal/mol. Conformational analysis. LVII. The calculation of the conformational structures of hydrocarbons by the Westheimer-Hendrickson-Wiberg method Norman L. Allinger, Mary Ann Miller, Frederic A. Van Catledge, and Jerry A. Hirsch Journal of the American Chemical Society 1967, 89 (17), 4345-4357 DOI: 1021/ja00993a017 Tables V-VII in this paper contain conformation energies of disubstituted cyclohexanes, which can be derived from adding the respective A-values. Conformational Studies. VII.1 p-Menthane-2,5-diols and the Relative “Size” of the Isopropyl Group Robert D. Stolow Journal of the American Chemical Society 1964, 86 (11), 2170-2173 DOI: 1021/ja01065a013 1,2-disubstituted cyclohexanes do not add neatly due to repulsive interactions from the groups being so close to each other. Steric Interactions in Organic Chemistry: Spatial Requirements of Substituents Hans Förster, Prof. Dr. Fritz Vögtle Angew. Chem. Int. Ed. 1977, 16 (7), 429-441 DOI: 10.1002/anie.197704291 Conformational analysis. LXXVIII. The conformation of phenylcyclohexane, and related molecules L. Allinger and M. T. Tribble Tet. Lett. 1971, 12 (35), 3259-3262 DOI: 10.1016/S0040-4039(01)97150-3 Oddly enough, in certain phenylcyclohexanes, the phenyl group prefers to be axial, and this paper investigates that using computational methods. Janus face all-cis 1,2,4,5-tetrakis(trifluoromethyl)- and all-cis 1,2,3,4,5,6-hexakis(trifluoromethyl)- cyclohexanes David O’Hagan, Cihang Yu, Agnes Kütt, Gerd-Volker Röschenthaler, Tomas Lebl, David B. Cordes, Alexandra M. Z. Slawin, Michael Bűhl Angew Chem. Int. Ed. 2020, Accepted Article DOI: 10.1002/anie.202008662 This recently published paper is on the synthesis of 1,2,3,4,5,6-hexakis(trifluoromethyl)-cyclohexane. Computational analysis shows that it has a barrier to interconversion of approx. 27.1 kcal/mol. Conformational Study of cis-1,4-Di-tert-butylcyclohexane by Dynamic NMR Spectroscopy and Computational Methods. Gurvinder Gill, Diwakar M. Pawar, and Eric A. Noe J. Org. Chem. 2005, 70, 10726-10731 DOI: 10.1021/jo051654z Although mainly a study of 1,4-Di-t-butylcyclohexane, this paper also presents calculations for comparing the energies of diaxial and diequatorial trans-1,2-Di-t-butylcyclohexane, and finds that the diaxial conformer is more stable than the diequatorial conformer by about 6.2 kcal/mol! Interestingly the twist-boat conformer of this molecule is only slightly lower in energy (0.5 kcal/mol). Structures of cyclohexane A cyclohexane molecule in chair conformation. Hydrogen atoms in axial positions are shown in red, while those in equatorial positions are in blue. Cyclohexane conformations are any of several three-dimensional shapes adopted by cyclohexane. Because many compounds feature structurally similar six-membered rings, the structure and dynamics of cyclohexane are important prototypes of a wide range of compounds.[1][2] The internal angles of a regular, flat hexagon are 120°, while the preferred angle between successive bonds in a carbon chain is about 109.5°, the tetrahedral angle (the arc cosine of −1/3). Therefore, the cyclohexane ring tends to assume non-planar (warped) conformations, which have all angles closer to 109.5° and therefore a lower strain energy than the flat hexagonal shape. Consider the carbon atoms numbered from 1 to 6 around the ring. If we hold carbon atoms 1, 2, and 3 stationary, with the correct bond lengths and the tetrahedral angle between the two bonds, and then continue by adding carbon atoms 4, 5, and 6 with the correct bond length and the tetrahedral angle, we can vary the three dihedral angles for the sequences (2,3,4), (3,4,5), and (4,5,6). The next bond, from atom 6, is also oriented by a dihedral angle, so we have four degrees of freedom. But that last bond has to end at the position of atom 1, which imposes three conditions in three-dimensional space. If the bond angle in the chain (6,1,2) should also be the tetrahedral angle then we have four conditions. In principle this means that there are no degrees of freedom of conformation, assuming all the bond lengths are equal and all the angles between bonds are equal. It turns out that, with atoms 1, 2, and 3 fixed, there are two solutions called chair, depending on whether the dihedral angle for (1,2,3,4) is positive or negative, and these two solutions are the same under a rotation. But there is also a continuum of solutions, a topological circle where angle strain is zero, including the twist boat and the boat conformations. All the conformations on this continuum have a twofold axis of symmetry running through the ring, whereas the chair conformations do not (they have D3d symmetry, with a threefold axis running through the ring). It is because of the symmetry of the conformations on this continuum that it is possible to satisfy all four constraints with a range of dihedral angles at (1,2,3,4). On this continuum the energy varies because of Pitzer strain related to the dihedral angles. The twist-boat has a lower energy than the boat. In order to go from the chair conformation to a twist-boat conformation or the other chair conformation, bond angles have to be changed, leading to a high-energy half-chair conformation. So the relative energies are: chair < twist-boat < boat < half-chair with chair being the most stable and half-chair the least. All relative conformational energies are shown below.[3][4] At room temperature the molecule can easily move among these conformations, but only chair and twist-boat can be isolated in pure form, because the others are not at local energy minima. The boat and twist-boat conformations, as said, lie along a continuum of zero angle strain. If there are substituents that allow the different carbon atoms to be distinguished, then this continuum is like a circle with six boat conformations and six twist-boat conformations between them, three "right-handed" and three "left-handed". (Which should be called right-handed is unimportant.) But if the carbon atoms are indistinguishable, as in cyclohexane itself, then moving along the continuum takes the molecule from the boat form to a "right-handed" twist-boat, and then back to the same boat form (with a permutation of the carbon atoms), then to a "left-handed" twist-boat, and then back again to the achiral boat. The passage from boat → right-twist-boat → boat → left-twist-boat → boat constitutes a full pseudorotation. Another way to compare the stability within two molecules of cyclohexane in the same conformation is to evaluate the number of coplanar carbons in each molecule.[4] Coplanar carbons are carbons that are all on the same plane. Increasing the number of coplanar carbons increases the number of eclipsing substituents trying to form a 120°, which is unattainable due to the overlapping hydrogens.[5] This overlap increases the overall torsional strain and decreases the stability of the conformation. Cyclohexane diminishes the torsional strain from eclipsing substituents through adopting a conformation with fewer coplanar carbons.[6] For example, if a half-chair conformation contains four coplanar carbons and another half-chair conformation contains five coplanar carbons, the conformation with four coplanar carbons will be more stable.[4] The different conformations are called "conformers", a blend of the words "conformation" and "isomer". The chair conformation is the most stable conformer. At 298 K (25 °C), 99.99% of all molecules in a cyclohexane solution adopt this conformation. The C–C ring of the chair conformation has the same shape as the 6-membered rings in the diamond cubic lattice.[7]:16 This can be modeled as follows. Consider a carbon atom to be a point with four half-bonds sticking out towards the vertices of a tetrahedron. Place it on a flat surface with one half-bond pointing straight up. Looking from directly above, the other three half-bonds will appear to point outwards towards the vertices of an equilateral triangle, so the bonds will appear to have an angle of 120° between them. Arrange six such atoms above the surface so that these 120° angles form a regular hexagon. Reflecting three of the atoms to be below the surface yields the desired geometry. All carbon centers are equivalent. They alternate between two parallel planes, one containing C1, C3 and C5, and the other containing C2, C4, and C6. The chair conformation is left unchanged after a rotation of 120° about the symmetry axis perpendicular to these planes, as well as after a rotation of 60° followed by a reflection in the midpoint plane, resulting in a symmetry group of D3d. While all C–C bonds are tilted relative to the plane, diametrically opposite bonds (such as C1–C2 and C4–C5) are parallel to each other. Six of the twelve C–H bonds are axial, pointing upwards or downwards almost parallel to the symmetry axis. The other six C–H bonds are equatorial, oriented radially outwards with an upwards or downwards tilt. Each carbon center has one axial C–H bond (pointed alternately upwards or downwards) and one equatorial C–H bond (tilted alternately downwards or upwards), enabling each X–C–C–Y unit to adopt a staggered conformation with minimal torsional strain. In this model, the dihedral angles for series of four carbon atoms going around the ring alternate between exactly +60° (gauche+) and −60° (gauche−).[7]:10 The chair conformation cannot be deformed without changing bond angles or lengths. It can be represented as two linked chains, C1–C2–C3–C4 and C1–C6–C5–C4, each mirroring the other, with opposite dihedral angles. The C1–C4 distance depends on the absolute value of this dihedral angle, so in a rigid model, changing one angle requires changing the other angle. If both dihedral angles change while remaining opposites of each other, it is not possible to maintain the correct C–C–C bond angles at C1 and C4. The chair geometry is often preserved when the hydrogen atoms are replaced by halogens or other simple groups. However, when these hydrogens are substituted for a larger group, additional strain may occur due to diaxial interactions between pairs of substituents occupying the same-orientation axial position, which are typically repulsive due to steric crowding.[8] The boat conformations have higher energy than the chair conformations. The interaction between the two flagpole hydrogens, in particular, generates steric strain. Torsional strain also exists between the C2–C3 and C5–C6 bonds (carbon number 1 is one of the two on a mirror plane), which are eclipsed — that is, these two bonds are parallel one to the other across a mirror plane. Because of this strain, the boat configuration is unstable (i.e. is not a local energy minimum). The molecular symmetry is C2v. The boat conformations spontaneously distorts to twist-boat conformations. Here the symmetry is D2, a purely rotational point group with three twofold axes. This conformation can be derived from the boat conformation by applying a slight twist to the molecule so as to remove eclipsing of two pairs of methylene groups. The twist-boat conformation is chiral, existing in right-handed and left-handed versions. The concentration of the twist-boat conformation at room temperature is less than 0.1%, but at 1,073 K (800 °C) it can reach 30%. Rapid cooling of a sample of cyclohexane from 1,073 K (800 °C) to 40 K (−233 °C) will freeze in a large concentration of twist-boat conformation, which will then slowly convert to the chair conformation upon heating.[9] Main article: Ring flip Cyclohexane chair flip (ring inversion) reaction via boat conformation 4. Structures of the significant conformations are shown: chair 1, half-chair 2, twist-boat 3 and boat 4. When ring flip happens completely from chair to chair, hydrogens that were previously axial (blue H in upper-left structure) turn equatorial and equatorial ones (red H in upper-left structure) turn axial.[3] It is not necessary to go through the boat form. The interconversion of chair conformers is called ring flipping or chair-flipping. Carbon–hydrogen bonds that are axial in one configuration become equatorial in the other, and vice versa. At room temperature the two chair conformations rapidly equilibrate. The proton NMR spectrum of cyclohexane is a singlet at room temperature, with no separation into separate signals for axial and equatorial hydrogens. In one chair form, the dihedral angle of the chain of carbon atoms (1,2,3,4) is positive whereas that of the chain (1,6,5,4) is negative, but in the other chair form, the situation is the opposite. So both these chains have to undergo a reversal of dihedral angle. When one of these two four-atom chains flattens to a dihedral angle of zero, we have the half-chair conformation, at a maximum energy along the conversion path. When the dihedral angle of this chain then becomes equal (in sign as well as magnitude) to that of the other four-atom chain, the molecule has reached the continuum of conformations, including the twist boat and the boat, where the bond angles and lengths can all be at their normal values and the energy is therefore relatively low. After that, the other four-carbon chain has to switch the sign of its dihedral angle in order to attain the target chair form, so again the molecule has to pass through the half-chair as the dihedral angle of this chain goes through zero. Switching the signs of the two chains sequentially in this way minimizes the maximum energy state along the way (at the half-chair state) — having the dihedral angles of both four-atom chains switch sign simultaneously would mean going through a conformation of even higher energy due to angle strain at carbons 1 and 4. The detailed mechanism of the chair-to-chair interconversion has been the subject of much study and debate.[10] The half-chair state (D, in figure below) is the key transition state in the interconversion between the chair and twist-boat conformations. The half-chair has C2 symmetry. The interconversion between the two chair conformations involves the following sequence: chair → half-chair → twist-boat → half-chair′ → chair′. The boat conformation (C, below) is a transition state, allowing the interconversion between two different twist-boat conformations. While the boat conformation is not necessary for interconversion between the two chair conformations of cyclohexane, it is often included in the reaction coordinate diagram used to describe this interconversion because its energy is considerably lower than that of the half-chair, so any molecule with enough energy to go from twist-boat to chair also has enough energy to go from twist-boat to boat. Thus, there are multiple pathways by which a molecule of cyclohexane in the twist-boat conformation can achieve the chair conformation again. Conformations: chair (A), twist-boat (B), boat (C) and half-chair (D). Energies are 43 kJ/mol (10 kcal/mol), 25 kJ/mol (6 kcal/mol) and 21 kJ/mol (5 kcal/mol).[3] The conformer of methylcyclohexane with equatorial methyl is favored by 1.74 kcal/mol (7.3 kJ/mol) relative to the conformer where methyl is axial.In cyclohexane, the two chair conformations have the same energy. The situation becomes more complex with substituted derivatives. A monosubstituted cyclohexane is one in which there is one non-hydrogen substituent in the cyclohexane ring. The most energetically favorable conformation for a monosubstituted cyclohexane is the chair conformation with the non-hydrogen substituent in the equatorial position because it prevents high steric strain from 1,3 diaxial interactions.[11] In methylcyclohexane the two chair conformers are not isoenergetic. The methyl group prefers the equatorial orientation. The preference of a substituent towards the equatorial conformation is measured in terms of its A value, which is the Gibbs free energy difference between the two chair conformations. A positive A value indicates preference towards the equatorial position. The magnitude of the A values ranges from nearly zero for very small substituents such as deuterium, to about 5 kcal/mol (21 kJ/mol) for very bulky substituents such as the tert-butyl group. Thus, the magnitude of the A value will also correspond to the preference for the equatorial position. Though an equatorial substituent has no 1,3 diaxial interaction that causes steric strain, it has a Gauche interaction in which an equatorial substituent repels the electron density from a neighboring equatorial substituent.[11] For 1,2- and 1,4-disubstituted cyclohexanes, a cis configuration leads to one axial and one equatorial group. Such species undergo rapid, degenerate chair flipping. For 1,2- and 1,4-disubstituted cyclohexane, a trans configuration, the diaxial conformation is effectively prevented by its high steric strain. For 1,3-disubstituted cyclohexanes, the cis form is diequatorial and the flipped conformation suffers additional steric interaction between the two axial groups. trans-1,3-Disubstituted cyclohexanes are like cis-1,2- and cis-1,4- and can flip between the two equivalent axial/equatorial forms.[2] Cis-1,4-Di-tert-butylcyclohexane has an axial tert-butyl group in the chair conformation and conversion to the twist-boat conformation places both groups in more favorable equatorial positions. As a result, the twist-boat conformation is more stable by 0.47 kJ/mol (0.11 kcal/mol) at 125 K (−148 °C) as measured by NMR spectroscopy.[10] Also, for a disubstituted cyclohexane, as well as more highly substituted molecules, the aforementioned A values are additive for each substituent. For example, if calculating the A value of a dimethylcyclohexane, any methyl group in the axial position contributes 1.70 kcal/mol- this number is specific to methyl groups and is different for each possible substituent. Therefore, the overall A value for the molecule is 1.70 kcal/mol per methyl group in the axial position.[12] 1,3 Diaxial interactions occur when the non-hydrogen substituent on a cyclohexane occupies the axial position. This axial substituent is in the eclipsed position with the axial substituents on the 3-carbons relative to itself (there will be two such carbons and thus two 1,3 diaxial interactions). This eclipsed position increases the steric strain on the cyclohexane conformation and the confirmation will shift towards a more energetically favorable equilibrium.[13] Gauche interactions occur when a non-hydrogen substituent on a cyclohexane occupies the equatorial position. The equatorial substituent is in a staggered position with the 2-carbons relative to itself (there will be two such carbons and thus two 1,2 gauche interactions). This creates a dihedral angle of ~60°.[14] This staggered position is generally preferred to the eclipsed positioning. Once again, the conformation and position of groups (ie. substituents) larger than a singular hydrogen are critical to the overall stability of the molecule. The larger the group, the less likely to prefer the axial position on its respective carbon. Maintaining said position with a larger size costs more energy from the molecule as a whole because of steric repulsion between the large groups' nonbonded electron pairs and the electrons of the smaller groups (ie. hydrogens). Such steric repulsions are absent for equatorial groups. The cyclohexane model thus assesses steric size of functional groups on the basis of gauche interactions.[15] The gauche interaction will increase in energy as the size of the substituent involved increases. For example, a t-butyl substituent would sustain a higher energy gauche interaction as compared to a methyl group, and therefore, contribute more to the instability of the molecule as a whole. In comparison, a staggered conformation is thus preferred; the larger groups would maintain the equatorial position and lower the energy of the entire molecule. This preference for the equatorial position among bulkier groups lowers the energy barriers between different conformations of the ring. When the molecule is activated, there will be a loss in entropy due to the stability of the larger substituents. Therefore, the preference of the equatorial positions by large molecules (such as a methyl group) inhibits the reactivity of the molecule and thus makes the molecule more stable as a whole.[16] Conformational equilibrium is the tendency to favor the conformation where cyclohexane is the most stable. This equilibrium depends on the interactions between the molecules in the compound and the solvent. Polarity and nonpolarity are the main factors in determining how well a solvent interacts with a compound. Cyclohexane is considered nonpolar, meaning that there is no electronegative difference between its bonds and its overall structure is symmetrical. Due to this, when cyclohexane is immersed in a polar solvent, it will have less solvent distribution, which signifies a poor interaction between the solvent and solute. This produces a limited catalytic effect.[17] Moreover, when cyclohexane comes into contact with a nonpolar solvent, the solvent distribution is much greater, showing a strong interaction between the solvent and solute. This strong interaction yields a heighten catalytic effect. Heterocyclic analogs of cyclohexane are pervasive in sugars, piperidines, dioxanes, etc. They exist generally follow the trends seen for cyclohexane, i.e. the chair conformer being most stable. The axial–equatorial equilibria (A values) are however strongly affected by the replacement of a methylene by O or NH. Illustrative are the conformations of the glucosides.[2] 1,2,4,5-Tetrathiane ((SCH_2)3) lacks the unfavorable 1,3-diaxial interactions of cyclohexane. Consequently its twist-boat conformation is populated; in the corresponding tetramethyl structure, 3,3,6,6-tetramethyl-1,2,4,5-tetrathiane, the twist-boat conformation dominates. In 1890, Hermann Sachse [de], a 28-year-old assistant in Berlin, published instructions for folding a piece of paper to represent two forms of cyclohexane he called symmetrical and asymmetrical (what we would now call chair and boat). He clearly understood that these forms had two positions for the hydrogen atoms (again, to use modern terminology, axial and equatorial), that two chairs would probably interconvert, and even how certain substituents might favor one of the chair forms (Sachse–Mohr theory [de]). Because he expressed all this in mathematical language, few chemists of the time understood his arguments. He had several attempts at publishing these ideas, but none succeeded in capturing the imagination of chemists. His death in 1893 at the age of 31 meant his ideas sank into obscurity. It was only in 1918 that Ernst Mohr [de], based on the molecular structure of diamond that had recently been solved using the then very new technique of X-ray crystallography,[18][19] was able to successfully argue that Sachse's chair was the pivotal motif.[20][21][22][23][24][25] Derek Barton and Odd Hassel shared the 1969 Nobel Prize in Chemistry for work on the conformations of cyclohexane and various other molecules. Cyclohexane is the most stable of the cycloalkanes, due to the stability of adapting to its chair conformer.[4] This conformer stability allows cyclohexane to be used as a standard in lab analyses. More specifically, cyclohexane is used as a standard for pharmaceutical reference in solvent analysis of pharmaceutical compounds and raw materials. This specific standard signifies that cyclohexane is used in quality analysis of food and beverages, pharmaceutical release testing, and pharmaceutical method development;[26] these various methods test for purity, biosafety, and bioavailability of products.[27] The stability of the chair conformer of cyclohexane gives the cycloalkane a versatile and important application when regarding the safety and properties of pharmaceuticals. ^ Eliel, Ernest Ludwig; Wilen, Samuel H. (2008). Stereochemistry of Organic Compounds. Wiley India. ISBN 978-8126515707. ^ a b c Smith, Michael B.; March, Jerry (2007), Advanced Organic Chemistry: Reactions, Mechanisms, and Structure (6th ed.), New York: Wiley-Interscience, ISBN 978-0-471-72091-1 ^ a b c J, Clayden (2003). Organic chemistry (2nd ed.). Oxford. p. 373. ISBN 9780191666216.{{cite book}}: CS1 maint: location missing publisher (link) ^ a b c d Nelson, Donna J.; Brammer, Christopher N. (2011). 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Java applets of all conformations Archived 2009-09-02 at the Wayback Machine from the University of Nijmegen Retrieved from " Cyclohexane is an alicyclic hydrocarbon comprising a ring of six carbon atoms that plays a crucial role in organic chemistry. Cyclohexanes exhibit great stability due to their ability to adapt to different conformations, minimising strain energy. Understanding the conformation of cyclohexane and its derivatives is essential in chemistry.1.0Understanding the Conformation of CyclohexaneCyclohexanes are non-planar molecules, as a completely planar structure would result in significant angle strain and torsional strain. To bring down these issues, the cyclohexane molecules adopt conformations that reduce the strain energy and increase stability.Chair ConformationBoat ConformationTwist-Boat ConformationHalf-Chair ConformationEach conformation has its own energy profile and stability, which is crucial for understanding the conformation of cyclohexane stability order.2.0Chair Conformation: The Most Stable FormThe most stable conformation of a cyclohexane is the chair conformation. It is named as such because its structure resembles a chair. It eliminates angle strain as the bond angles are close to the tetrahedral 109.5°. It also eliminates torsional strain due to its staggered C-H bonds. In this conformation:Six hydrogen atoms are in axial positions aligned parallel to the ring's imaginary axis.Six hydrogen atoms are in equatorial positions that are aligned roughly in the plane of the ring.The axial and equatorial positions alternate around the ring.Chair Flip: Axial-Equatorial InterconversionThe chair flip is a dynamic process where the molecules rapidly interconvert between two stable chair conformations, switching axial and equatorial substituents. The flipping procedure is crucial to understanding the reactivity of cyclohexane and its derivatives. 3.0Boat and Twist-Boat ConformationsThe cyclohexane boat conformation is less stable than the chair conformation. It is a high-energy structure due to steric strain and eclipsed hydrogen interactions. In this conformation:The molecule resembles a boat with two peaks.Eclipsing interactions cause torsional strain.Flagpole interactions occur due to hydrogen atoms at the bow and stern coming too close together.4.0Twist-Boat ConformationTo relieve strain, the boat conformation distorts to twist-boat conformation, reducing eclipsing interactions and steric hindrance. While it is more stable than the boat form, it is still less stable than the chair conformation. 5.0Half-Chair Conformation: The Transition StateThe half-chair conformation of cyclohexane is a key transitional state during the interconversion between the chair and twist-boat conformations. It represents a high-energy and unstable state where five carbon atoms are coplanar, and one is plucked out of the plane. It is rarely observed in isolated states. 6.0Energy Diagram of Cyclohexane ConformationsTo visualise the stability of different conformations, the conformation of cyclohexane energy diagram is essential. The energy profile follows this order:Chair conformation has the lowest energy. It is also the most stable.Twist-boat conformation has a slightly higher energy than a chair.Boat conformation has an even higher energy due to steric strain.Half-chair conformation has the highest energy, and it is observed in the transition state.7.0Energy Profile DiagramThe conformation of cyclohexane and the energy profile diagram illustrates the energy changes as the molecule undergoes a chair flip:This energy variation explains why cyclohexanes predominantly exist in chair form under normal conditions. 8.0Energy and Stability of Cyclohexane ConformationsRefer to the table below to understand the energy of cyclohexane conformations and the conformation of cyclohexane stability order.9.0Rigid Conformation of Cyclohexane and Its DerivativesCertain cyclohexane derivatives contain bulky substituents that restrict ring flipping, leading to a rigid conformation of cyclohexane. For example:Tert-butylcyclohexane: The bulky tert-butyl group locks the ring in a single chair conformation with the bulky group in the equatorial position.Bicyclo[2]octane and other fused rings: These structures prevent chair flipping due to additional ring strain. The chair conformation is the most stable because it minimizes both steric and torsional strain, while the half-chair has the highest strain due to poor bond angles and steric clashes.