

1: Hexadehydro Diels-Alder reaction - Wikipedia

Industrial application of the Diels-Alder reaction Di Shen 16/04/ Overview of the use of [4+2] cycloadditions for the manufacture of active pharmaceutical ingredients, agrochemicals, flavors.

This reaction has been successfully utilized in the synthesis of many of the complex organic molecules like Reserpine, Cholesterol, Gibberellic acid, Ambruticins, myrocin C, - colombiasin A, Antibiotic X A etc. Keywords The present review article emphasis on introduction, mechanism, applications and some of Diels Alder Synthesis, the recent advantages of this reaction. A special emphasis has been laid on the application natural products, medicinal of this reaction in the synthesis of natural products and its complete synthesis and also to Chemistry, complete other molecules with known pharmacological actions. Indo American Journal of Pharm Research. Page Vol 3, Issue 4, Sarbjeet Singh Gujral et al. This discovery led both of them the Nobel Prize in Chemistry in the year This Reaction in particular involves a cycloaddition reaction between a conjugated diene and a substituted alkene generally regarded as dienophile to form a substituted cyclohexene system[1][2][3]. Dienophiles Dienophile may be considered to have an electron-withdrawing group conjugated to the alkene part, although it is not a characteristic feature of Diels-Alder dienophiles. There must be some extra conjugation with different groups like phenyl group or chlorine atom is always preferred in order to increase the rate of reaction to many folds. The dienophile should be activated by using different Lewis acids e. Generally either one or both of the reacting species are substituted with different kind of groups which generally does not show any significant effect in the reactivity of the reaction. It has been generalized that all Diels-Alder reactions certain common features: Diels-Alder reaction forms new six-membered rings. The overall reaction is concerted: All bonds break and form in a single step. Diels Alder reaction is highly Diastereoselective. Examples of this distereoselectivity are as follows: Cyclic diene when undergoing Diels Alder reaction gives stereo isomeric products. The endo product is usually favored by kinetic control due to secondary orbital interactions. Niobium pentachloride which also acts a Lewis acid, catalysis the reaction and yields only the endo conformer. Stereo selectivity in DA reactions Diels-Alder reactions generally lead to formation of a array of structural isomers and stereoisomer generally in asymmetrically substituted diene and dienophiles. This can be explained using frontier orbital theory. Generally, the diene molecule contains an electron-releasing group ERG and dienophile contains an electron- withdrawing group EWG. Carbon atom that have the highest coefficients in two frontier orbital begins to for a bond; therefore these carbons will direct the orientation of substituent and thus forms the major product in Diels Alder reaction. Cis principle or Alder-Stein rules According to this rule, the stereochemistry of substituents in the starting material gets preserved in the final product. Application of the Diels -Alder reaction for total synthesis of some of the most complex and diverse organic molecule was first implemented by R. Woodward and his co-workers who at that point of time synthesized some of the complex organic molecules. Some of the applications of Diels alder synthesis in production of some of the pharmacologically important natural compounds are as follows. Reserpine has an antipsychotic effect and is also used as antihypertensive drug which is used widely in Ayurvedic medicine for controlling the high blood pressure and for the treatment of psychotic symptoms. This development of synthesizing such a complex molecule in the lab gave a new direction to the natural product chemistry and also to the vast and successful application to Diels alder reaction. In this synthetic method, a bicyclic molecule serves as the scaffold in the synthetic sequence and use of Diels Alder strategy to form an array of rings and stereocentres which pave the for succeeding stereo controlled expansion to the final target molecule. Structure of Reserpine Page www. In addition to its importance within cells, cholesterol also serves as a precursor for the biosynthesis of steroid hormones, bile acids, and vitamin D. Small quantities are synthesized in other cellular organisms eukaryotes such as plants and fungi. It is almost completely absent among prokaryotes i. This compound can be synthesized using Diels Alder Reaction by the following scheme. Synthesis of Cholesterol Page 3 Gibberellic acid www. It is a plant hormone and is extensively used in plant biotechnology experiments for production of Ex-plants and is generally used in concentrations between 0. The dependence of this hormone was earlier relied on plant sources but now it can be easily prepared using Diels

alder synthesis. Synthesis of Gillerelic Acid Page 4 Ambruticins www. It is known to have a potent antifungal activity and is in the pipeline of becoming as a remedy for certain fungal infections can also be synthesised by Diels alder reaction for its mass production. This drug when tested on various bacterial cultures like Gram-positive bacteria yeasts, fungi etc. This useful compound can also be synthesised using Diels alder reaction. The following total regioselective synthesis of myrocin A was first done by Danishefsky et. Synthesis of Myrocin C 6 - colombiasin A [27] Colombiasin A is a diterpene compound found naturally in gorgonian octacorals [Scientific name: Pseudopterogorgia elisabethae] which was found to have antimicrobial activity against many gram positive as well as gram negative bacteria and also it has found active against Mycobacterium tuberculosis H37Rv. This drug can also be synthetically by using Diels Alder reaction as follows: Synthesis of - colombiasin A Page www. This antibiotic is active against Gram-positive bacteria in various in vitro studies and is also capable of complexing with various divalent as well as monovalent metal cations can now be synthesized using Diels alder reaction with increased percentage yield. Synthesis of Antibiotic X A Page www. It works by interfering and blocking the action potentials in nerves by binding to the voltage-gated, sodium channels in nerve cell membranes and preventing any affected nerve cells from firing by blocking the channels used in the process. Structure of tetrodotoxin Page www. It has been estimated that - Agelastatin A is 1. Structure of Agelastatin A 12 Isochrysohermidin [41] The synthesis of the alkylating subunit of the DNA cross-linking agent, isochrysohermidin, and its subsequent incorporation into conjugates with distamycin A. The DNA binding properties of these agents were compared to that of distamycin A, using a fluorescence intercalator displacement FID assay. Structure of Isochrysohermidin www. It is now possible to synthesize these so called complex alkaloids with Regio-selectivity and confined stereochemistry using Diels Alder synthesis. Structure of norsecurinine 14 Lepicidin A [43] Lepicidin A also known as AA is a tetracyclic macrolide that has been isolated from the culture of soil microbe Saccharopolyspora spinosa. This natural compound has proved to exhibit anti-insecticidal activity particularly against lepidoptera larvae. This compound is effective against a wide variety of bacteria Gram-positive as well as Gram-negative bacteria and also against most anaerobic organisms. The mass production of which is carried out using Diels alder reaction. Colchicum autumnale] and other related species of colchicum. Structure of - Colchicine 16 - -alcolcolchicine [46] It is somewhat structurally related to - Colchicine and is also found in different species of colchicum as a main chemical constituent. It is a well know antimitotic agent that binds to tubulin and inhibits its polymerization and helps in arresting proliferation of tumor cells. This compound can also be synthesized using Diels Alder reaction. Structure of Fostriecin 18 Dolabellatrienone Dolabellatrienone, which have been isolated from a Colombian gorgonian coral of the genus Eunicea can also be synthesized using Diels Alder reaction. Structure of Dolabellatrienone www. It has been proven to have cytotoxic effect against human breast cancer MCF-7 cells. This active anti- carcinogenic compound can also be synthesized by using Diels alder reaction. It has been proven to have antagonizing behavioral effects of nicotine in in- vivo studies. It has been used as an antiresorptive drug for prevention and treatment of osteoporosis in postmenopausal women. Structure of Symbiomine www. Certain natural and synthetic products has been successfully designed using this approach using preferred starting materials. Coniine, Nojirimycin and Phorboxazole are among the most recent examples for such synthesis. Conium maculatum] and the yellow pitcher plant [scientific name: It is lethal to humans and other livestock; an estimate of 0. Structure of Coniine 2 Nojirimycin nojirimycin a group of carbohydrate-like alkaloids or imino sugars found extensively in different species of Streptomyces, but is also found in different plants such as Morus alba and Angylocalyx pynaertii etc in mere quantities. It is a strong inhibitor of enzyme glycosidases and glycosyltransferases. Structure of Nojirimycin Page www. Although the Page method has found many applications in synthesizing many different molecules, there is still much work to do on www. Also there is an urge to focus on the application of the reaction towards the chemistry of natural products so that the natural products which are pharmacologically important and whose occurrence is limited can be synthesized using this reaction Abbreviations used: Synthesis of the hydro aromatic sequence, Ann. Synthesis in the hydroaromatic series, IV. The rearrangement of malein acid anhydride on arylated diene, triene and fulvene, Diels, O. Niobium Pentachloride Activation of Enone Derivatives: Ranganathan Synthesis, Li Name Reactions, 3rd Ed. Journal of the American Chemical Society

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Schneider, Justus Liebigs Ann. Rolland, Justus Liebigs Ann. Schulze, Justus Liebigs Ann. Journal of the history of the neurosciences 12 2: Kierstead, Tetrahedron , 21 ; b R. For other total syntheses of reserpine using Diels-Alder reactions, see a P. Hanukoglu I Dec J Steroid Biochem Mol Biol 43 8: Olson RE February Retrieved 26 Oct

2: Imine Diels-Alder reaction - Organic Reactions Wiki

The Diels-Alder reaction is an organic chemical reaction (specifically, a [4+2] cycloaddition) between a conjugated diene and a substituted alkene, commonly termed the dienophile, to form a substituted cyclohexene derivative.

Reaction Mechanism[edit] Depending on the substrate chosen, the HDDA reaction can be initiated thermally or by the addition of a suitable catalyst, often a transition metal. The simplest model of an HDDA reaction is the cycloaddition of butadiyne and acetylene to form ortho-benzyne o-benzyne, shown below. The o-benzyne intermediate can be visualized in the two resonance chemistry forms illustrated above. Thermodynamics and Kinetics[edit] The HDDA reaction is often thermodynamically favorable exothermic, but can have a significant kinetic barrier to reaction high activation energy. These two pathways can differ in activation energy depending on substrate and reaction system. Computational studies have suggested that while both pathways are comparable in activation energy for unactivated unsubstituted diynophiles, the stepwise pathway has a lower activation energy barrier, and so is the dominant pathway, for activated diynophiles. As described by Hoye and coworkers, the HDDA reaction can be viewed conceptually as a member of a series of pericyclic reactions with increasing unsaturation by incremental removal of hydrogen pairs. Formally, the hexadehydro Diels-Alder reaction describes only the formation of the benzyne, but this species is an unstable intermediate that reacts readily with a variety of trapping partners, including reaction solvents. Thus, in practice the HDDA reaction describes a two-step cascade reaction of benzyne formation and trapping to yield the final product. The formation of a benzyne intermediate was determined by trapping studies, using benzene or anthracene to trap the benzyne as a Diels-Alder adduct. Since, the HDDA reaction has been an area of renewed interest and has attracted further study by a number of research groups. HDDA reaction of triynes or tetraynes forms benzyne without the direct formation of by-products. In comparison, the formation of benzyne through removal of ortho-substituents on arenes results in stoichiometric amounts of byproducts from those substituents. For example, formation of benzyne from 1 mole of 2-trimethylsilylphenyl trifluoromethanesulfonate triflate produces 1 mole of trimethylsilyl fluoride and 1 mole of triflate ion. Byproducts can compete with other reagents for benzyne trapping, cause side-reactions, and may require additional purification. Additionally, the HDDA reaction can be useful for substrates with sensitive functionality that might not be tolerated by other benzyne formation conditions e. The thermally-initiated HDDA reaction has been shown to tolerate esters, ketones, protected amides, ethers, protected amines, aryl halides, alkyl halides, alkenes, and cyclopropanes. Atom Economy â€” All of the atoms in the HDDA substrate remain in the product after the reaction and atoms of the trapping reagent are incorporated into the product. Reduced Waste â€” Formation of the benzyne species produces no stoichiometric byproducts. Products are often formed in high yield with few side-products. Catalysis â€” HDDA reaction occurs thermally or with a sub-stoichiometric amount of catalyst. Intramolecular Trapping[edit] The HDDA reaction can be used to synthesize multi-cyclic ring systems from linear precursors containing the diyne, diynophile, and the trapping group. For example, Hoye and co-workers were able to synthesize fused, tricyclic ring systems from linear triyne precursors in one step and high yields via a thermally-initiated, intramolecular HDDA reaction. In this case, the pendant silyl ether provided the trapping group, through a retro-Brook rearrangement. Intermolecular Trapping[edit] HDDA-generated benzyne species can also be trapped intermolecularly by a variety of trapping reagents. Careful choice of trapping reagent can add further functionality, including aryl halides, aryl heteroatoms phenols and aniline derivatives, and multiple ring systems. The benzyne serves as the enophile, while the ene can be an alkene Alder ene or an aromatic ring aromatic ene. Lee and co-workers have shown an HDDA-Alder ene cascade reaction that can produce a variety of products, including medium-sized fused rings, spirocycles, and allenes. This desaturates the donor alkane, forming an alkene, and traps the benzyne to a dihydrobenzenoid product. Isotopic labelling and computational studies suggest that the double hydrogen transfer mechanism occurs by a concerted pathway and that the rate of reaction is highly dependent on the conformation of the alkane donor. Lee and co-workers observed that transition metal catalysts induced an HDDA reaction of tetraynes that was intramolecularly

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trapped by a pendant, sp^3 C-H bond. Deuterium labelling experiments suggest that the sp^3 C-H bond breaking and sp^2 C-H bond forming reactions occur in a concerted fashion. Fluorination[edit] The silver-catalyzed HDDA reaction has also been used to synthesize organofluorine compounds by use of a fluorine -containing counterion.

3: Ch Diels-Alder reaction

The Diels-Alder reaction is one of the most popular transformations for organic chemists to generate molecular complexity efficiently. Surprisingly, little is known about its industrial application for the synthesis of pharmacologically active ingredients, agrochemicals, and flavors and fragrances.

These reactions involve the lowest unoccupied molecular orbital LUMO of the imine, meaning that imines substituted with electron-withdrawing groups on nitrogen are the most reactive. The reaction may be thermal or acid catalyzed. The lowest-energy transition state for the concerted process places the imine lone pair or coordinated Lewis acid in an exo position. Thus, E imines, in which the lone pair and larger imine carbon substituent are cis, tend to give exo products. Thus, the regiochemistry of cycloaddition can be predicted by considering the electron-withdrawing or -donating nature of substituents on the diene. The carbon bearing the largest coefficient in the HOMO of the diene forms a bond to the imine carbon. Use of amino-acid-based chiral auxiliaries, for instance, leads to good diastereoselectivities in reactions of cyclopentadiene, but not in reactions of acyclic dienes. The exo isomer usually predominates particularly when cyclic dienes are used, although selectivities vary. Cycloadditions of these intermediates with dienes give single constitutional isomers, but proceed with moderate stereoselectivity. Regio- and stereoselectivity are unusually high in reactions of this class of dienes. Partial reduction of pyridinium salts has been used, although regioselectivity issues arise when substituted pyridiniums are used. Reactions may be thermal or involve the use of a Lewis acid. For the former, refluxing benzene is common, although reaction temperatures depend on the reactivity of substrates. Boron trifluoride etherate and zinc chloride are commonly used Lewis acids. Simple alkyl or aryl amines are often generated in situ by combining an amine hydrochloride with an aldehyde. Example Procedure [17] 16 To an ice-cooled solution of butyl p-tolylsulfonylimino acetate When the exothermic reaction began to subside, the reaction mixture was kept at room temperature for 12 hours and was then concentrated in vacuo. The residue, which solidified upon standing, was crystallized from Et₂O-hexane 1: Tetrahedron, 54, Tetrahedron, 30,

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The Diels-Alder reaction that involves a nitrogen atom in the diene or dienophile is termed the aza-Diels-Alder reaction. As well as the powerful all-carbon Diels-Alder reaction, the aza-Diels-Alder reaction has also played an important role in the total synthesis of natural products. Herein.

ABSTRACT The furan heterocycle is a dienic reagent particularly suitable for the Diels-Alder reaction and maleimides represent a typical family of complementary reagents because of their strong dienophilic character. This paper reviews critically the studies devoted to the exploitation of the Diels Alder reaction between those moieties to synthesise macromolecular materials possessing different structures and properties. The most relevant approaches in this field are i polycondensation reactions calling upon A-A and B-B monomers and ii reversible cross-linking of linear polymers bearing pendant furan or maleimide moieties, based on the temperature sensitivity of the Diels-Alder equilibrium. Diels-Alder reaction, furan polymers, maleimides, polycondensation, reversible cross-linking. Introduction Furan chemistry is a vast domain, but its industrial aspects are essentially based on the exploitation of furfural F and its derivatives, since the former is readily and cheaply prepared from ubiquitous renewable resources in the form of agricultural and forestry by-products[1]. The field of furan polymers, which was thoroughly reviewed in recent years[1,2], represents an area of macromolecular science and technology which stands as a counterpart to petroleum-based materials, because of both the potential availability of the monomer precursors in any country and their renewable character. The furan heterocycle differs substantially in its chemical behaviour, compared with the thiophene and pyrrole homologues, because of its pronounced dienic properties. One of the consequences of this structural feature is that furan and many of its derivatives are ideally suited dienic reagents for the Diels-Alder DA coupling reaction, to the point of being given as typical examples in organic chemistry textbooks, typically with maleic anhydride as the dienophile, viz.: Maleimides are another family of dienophiles, which have been thoroughly studied because of their high reactivity and wide structural variability through the nature of the nitrogen substituents, providing a variety of both monofunctional and polyfunctional derivatives. One of the most relevant aspects of the DA reaction is the high sensitivity to temperature of its equilibrium, which implies that the adducts can be readily reverted to their precursors by heating, a process known as the retro-Diels-Alder RDA reaction. The application of these reactions to macromolecular synthesis has received much attention in the last few decades, but the most fruitful results stem from the more recent investigations. Two distinct approaches dominate this field, namely i the construction of linear or cross-linked polymers through successive DA coupling reactions involving multifunctional complementary monomers, e. In both instances, these polymers can revert to their precursors through the RDA reaction and this feature can be exploited in many applications, like the possibility of recycling or "mending" network-based materials. The purpose of this review is to examine critically the best contributions published recently in these two areas. These polycondensations gave products with molecular weights ranging from 10 to 50 the latter values seem exceedingly high for this type of polymer synthesis, as discussed below, except when the difuran monomer contained silicon atoms linked directly to the C2 positions of the heterocycle. In that case, the DA reaction did not take place because of the electron-withdrawing effect of the Si atoms. The purpose of these studies was to prepare heat-resistant polymers and therefore the authors did not study the RDA behaviour of the polymers, but converted instead the DA adducts along their chains into stable structures by aromatisation, viz.: Multiply substituted furans failed to give high DP because of steric hindrance in the formation of the adducts, whereas unsubstituted difurans linked through both C2 positions gave better results with DPs often higher than A careful study of the polymer structure confirmed that the chain growth had indeed taken place through successive DA couplings, giving a majority of exo structures. A series of papers published in the early nineties[] dealt with systems involving the DA polymerisation between a difuran derivative and a bismaleimide. In more recent years, we carried out a systematic study of the DA polymerisation involving a difuran diacetal F-F and either an aliphatic or an aromatic bismaleimide M-M [9]. The structures of these model adducts were carefully assessed, as were the proportions of exo and endo isomers. With this basic

information, the actual polymerisation could be carried out in the most adequate conditions and the structure of the ensuing materials assessed. The following mechanism applied to the aromatic bismaleimide: The ^1H NMR spectra of the polymers suggested that chain growth had not been perturbed by detectable side reactions. However, the early precipitation of the polymers from the reaction medium limited their DP to a few tens. A similar study[10] was conducted using much more flexible monomer structures in order to enhance polymer solubility, viz.: Linear polymers from A-B monomers The first attempts to prepare a molecular structure bearing both a furan and a maleimide moiety[12,13] were not corroborated by a convincing structural analysis. It is likely that the conditions used for their synthesis were too severe and the expected products resinified before isolation. We tackled this issue using milder conditions and obtained 2-furfurylmaleimide FM from 2-furfuryl amine and maleic anhydride by the classical two-step synthesis, going through the corresponding Nfurfurylmaleamic acid. FM is a crystalline compound, m. It displayed a high sensitivity to moisture, which induced its ring-opening hydrolysis regenerating the maleamic acid. The soluble fraction, however, gave a ^1H NMR spectrum indicating that regular DA oligomers had indeed been formed according to the following mechanism: The study of A-B monomers is still in progress. Dendrimers and networks The first and hitherto the only application of the DA reaction to prepare thermally responsive dendrons and dendrimers[15] is a very original piece of work based on a furan AB₂ monomer with aromatic ether moieties at C3 and C4 in conjunction with a maleimide bearing a reactive phenolic moiety. The third generation dendrimer MW This nice piece of work constitutes the first example of a thermally labile-reassembling dendrimer exploiting the DA-RDA approach. Different networks, all based on the DA polycondensation between multifunctional furans and maleimides, were prepared and characterised. Scheme 1 shows the synthesis of one such polymer. Cracks were induced in these materials, which were first submitted to a heating treatment to heal them and then slowly cooled to room temperature to reconstitute the heat-opened adducts. Reversible cross-linking reactions An early study dealing with the possibility of synthesizing thermally reversible networks from linear polymers bearing reactive DA functions describes the reaction of difurans with maleimide-substituted polymers[18]. It was however only starting from the nineties that this research topic gained momentum. These results are surprising for two reasons, namely: The same reservations apply to a later study of the same system[21]. Crosslinking readily occurred in solution, but the gels did not revert entirely by the RDA reaction in bulk TGA and the residual proportion of network was the higher, the higher the furan content in the initial copolymer. This problem is associated with the formation of free radicals arising from the methylene group attached to the C2 position in the furfuryl moiety[2] and can be minimised by using an inert atmosphere and adding a radical inhibitor to the substrate. The DA reaction proceeded smoothly in refluxing methylene chloride. The original styrene-furan copolymers were recovered quantitatively after cooling to room temperature, together with the DA adduct of N-phenylmaleimide with 2-methylfuran. The presence of a large excess of 2-methylfuran with respect to the furan moieties appended to the copolymers during the RDA reaction and while cooling the ensuing solution, insured the trapping of all the released maleimide. The same strategy was then applied to the crosslinking and de-cross-linking of the copolymers with MDPBM right-hand side of Scheme 2. The DA reaction produced the expected gelled materials, which were characterised and then submitted to the RDA reaction in the presence of a large excess of 2-methylfuran. The occurrence of de-cross-linking was clearly suggested by the progressive dissolution of the gels and within a few hours all the suspended materials had vanished. The precipitated polymers showed all the structural features of the corresponding initial copolymers, suggesting that the RDA reaction in the presence of the trapping agent had gone to completion. Further studies in this context concerned copolymer with elastomeric properties[10,24,25]. Scheme 3 illustrates this system: The second system was based on the reverse approach, namely the reaction of an elastomeric polydimethylsiloxane PDMS copolymer bearing pendant maleimide moieties with a flexible difuran derivative, as shown in Scheme 4: Two further pieces of evidence were obtained in these studies, concerning the temperature at which the RDA reaction becomes relevant. Figure 1 shows the dynamic mechanical behaviour of one of the cross-linked acrylic copolymers. In both these studies[10,25], the swelling kinetics and equilibria in various media of the networks were investigated in order to determine their cross-link densities and compare them with those obtained from dynamic-mechanical measurements. One of the promising

consequence of these studies is the application of their concepts to the recycling of tyres, an industrial and ecological problem which has found no viable solution to date. The interest of these contributions resides, on the one hand, in a careful study of swelling and mechanical properties of the networks[28] and, on the other hand, in an investigation of the kinetics of both the DA cross-linking[29] and the RDA de-cross-linking processes[27]. Thus, the rate of maleimide consumption was monitored in the case of the DA cross-linking reaction. Conversely, the rate of its regeneration was followed spectroscopically by heating the network in different high-boiling solvents, which induced the progressive RDA de-cross-linking and the consequent solubilisation of the released bismaleimide. *Sci*, 17,

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Diels-Alder Reaction. The [4+2]-cycloaddition of a conjugated diene and a dienophile (an alkene or alkyne), an electrocyclic reaction that involves the 4 π -electrons of the diene and 2 π -electrons of the dienophile.

Mechanism[edit] The reaction is an example of a concerted pericyclic reaction. As such, the Diels-Alder reaction is governed by orbital symmetry considerations: Such a scenario is termed an inverse electron demand Diels-Alder reaction. Regardless of which situation pertains, the HOMO and LUMO of the components are in phase and a bonding interaction results as can be seen in the diagram below. Since the reactants are in their ground state, the reaction is initiated thermally and does not require activation by light. Despite the fact that the vast majority of Diels-Alder reactions exhibit stereospecific, syn addition of the two components, a diradical intermediate has been postulated [6] and supported with computational evidence on the grounds that the observed stereospecificity does not rule out a two-step addition involving an intermediate that collapses to product faster than it can rotate to allow for inversion of stereochemistry. There is a notable rate enhancement when certain Diels-Alder reactions are carried out in polar organic solvents such as dimethylformamide and ethylene glycol. Pairing these two coefficients gives the "ortho" product as seen in case 1 in the figure below. A diene substituted at C2 as in case 2 below has the largest HOMO coefficient at C1, giving rise to the "para" product. Similar analyses for the corresponding inverse-demand scenarios gives rise to the analogous products as seen in cases 3 and 4. Examining the canonical mesomeric forms above, it is easy to verify that these results are in accord with expectations based on consideration of electron density and polarization. In general, with respect to the energetically most well-matched HOMO-LUMO pair, maximizing the interaction energy by forming bonds between centers with the largest frontier orbital coefficients allows the prediction of the major regioisomer that will result from a given diene-dienophile combination. The maximization of orbital interaction correctly predicts the product in all cases for which experimental data is available. For instance, in uncommon combinations involving X groups on both diene and dienophile, a 1,3-substitution pattern may be favored, an outcome not accounted for by a simplistic resonance structure argument. E- and Z-dienophiles, for example, give rise to the adducts with corresponding anti- and syn-stereochemistry: For normal demand Diels-Alder scenarios, with electron-withdrawing substituents such as carbonyls attached to the dienophile, the endo transition state is typically preferred, despite often being more sterically congested. This preference is known as the Alder rule. Endo selectivity is typically higher for rigid dienophiles such as maleic anhydride and benzoquinone; for others, such as acrylates and crotonates, selectivity is not very pronounced. Dienes with bulky terminal substituents C1 and C4 decrease the rate of reaction, presumably by impeding the approach of the diene and dienophile; [23] however, bulky substituents at the C2 or C3 position actually increase reaction rate by destabilizing the s-trans conformation and forcing the diene into the reactive s-cis conformation. Anthracene, being less aromatic and therefore more reactive for Diels-Alder syntheses in its central ring can form a 9,10 adduct with maleic anhydride at 80 degrees Celsius and even with acetylene, a weak dienophile, at degrees. The dienophile undergoes Diels-Alder reaction with a diene introducing such a functionality onto the product molecule. A series of reactions then follow to transform the functionality into a desirable group. The end product cannot not be made in a single DA step because equivalent dienophile is either unreactive or inaccessible. This is a "masked functionality" which can be then hydrolyzed to form a ketone. Chlorosulfonyl isocyanate can be utilized as a dienophile to prepare the Vince lactam. The complexed dienophile becomes more electrophilic and more reactive toward the diene, increasing the reaction rate and often improving the regio- and stereoselectivity as well. Lewis acid catalysis also enables Diels-Alder reactions to proceed at low temperatures, i.

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Well-known and extensively studied for many decades, the Diels-Alder reaction remains as one of the most frequently

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employed synthetic methods for the construction of six-membered ring systems) The high regio- and stereoselectivity typically displayed by this pericyclic process and the ease of execution have contributed toward its popularity.

Zoogeography of Caribbean insects Ten lives of the Buddha The Theology of John Wesley National lampoons truly tasteless cartoons British animals extinct within historic times Declarative invitation with supporting warrant (4:15/16) Geometry Grade 5 (Intermediate Geometry) Health seeking behaviour definition Using Illustrator 9 The sum of my parts Do you really need a home computer? Design and Development of Fuzzy-Logic Controllers Little Jack of all trades Target job application usa Simple elements of garden design by children Collecting Fossils Human Factors in Simple and Complex Systems, Second Edition Yours Till The End Of Time The Ideals country treasury The Georges Pompidou Centre Night watch, by T. Heggen. Report of the Boulder Committee of the Royal Society of Edinburgh A survey analysis of dance wellness-related curricula in American higher education When I Think About You, My Friend Glad Rags And All That Jazz Late afternoon woman Allies of the Night (Cirque Du Freak) Parts of a flower worksheet Moral education in a secular society A Short History Of English Law Tall Trees, Tough Men Collins/Janes warships of World War II How to Draw Dinosaurs (Kids Guide to Drawing) Network operating systems George R. Taylor Anthony R. Curtis George R. Taylor Michael Trumbull George R. Taylor Susan Branch Dessert Recipe 2003 Calendar Crime in Victorian Britain Trigger point therapy The Lion King Flute Ncert 10th maths solutions