An amide is a functional group containing a carbonyl group linked to a nitrogen atomor any compound containing the amide functional group. Amides are derived from carboxylic acid and an amine. Amide is also the name for the inorganic anion NH2. It is the conjugate base of ammonia (NH3).An amide is an organic functional group with a carbonyl bonded to a nitrogen or any compound containing this functional group.Examples of amides include nylon, paracetamol, and dimethylformamide.The simplest amides are derivatives of ammonia. In general, amides are very weak bases. Examples of amides include carboxamides, sulfonamides, and phosphoramides. Nylon is a polyamide. Several drugs are amides, including LCD, penicillin, and paracetamol. Amides may be used to form resilient structural materials (e.g., nylon, Kevlar). Dimethylformamide is an important organic solvent. Plants produce amides for a variety of functions. Amides are found in many drugs.March, Jerry (2013). Advanced Organic Chemistry, Reactions, Mechanisms and Structure (7th ed.). Wiley. ISBN 978-0470462591.Monson, Richard (1971). Advanced Organic Synthesis: Methods and Techniques. Academic Press. ISBN 978-0124336803.Montalbetti, Christian A. G. N.; Falque, Virginie (2005). "Amide bond formation and peptide coupling". Tetrahedron. 61 (46): 1082710852. doi:10.1016/j.tet.2005.08.031 By the end of this section, you will be able to:Identify the general structure for an amide.Identify the functional group for an amide.Names amides with common names.Name amides according to the IUPAC system.Compare the boiling points of amides with alcohols of similar molar mass.Compare the solubilities in water of amides of five or fewer carbon atoms with the solubilities of comparable alkanes and alcohols in water.Amides are molecules that contain nitrogen atoms connected to the carbon atom of a carbonyl group. If the two remaining bonds on the nitrogen atom are attached to hydrogen atoms, the compound is a simple amide. If one or both of the two remaining bonds on the atom are attached to alkyl or aryl groups, the compound is a substituted amide (Figure 26.5a.).Figure 26.5a. Amide groups (Credit: Introduction to Chemistry: GOB (V. 1.0).,CC BY-NC-SA 3.0).The carbonyl carbon-to-nitrogen bond is called an amide linkage. This bond is quite stable and is found in the repeating units of protein molecules, where it is called a peptide linkage.Naming AmidesPrimary amides are named by changing the name of the acid by dropping the -oic acid or -ic acid endings and adding -amide.The carbonyl carbon is numbered carbon 1 on its location. It is not necessary to include the location number in the name because it is assumed that the functional group will be on the end of the parent chain.Secondary amides are named by using an upper case N to designate that the alkyl group is on the nitrogen atom. Alkyl groups attached to the nitrogen are named as substituents. The letter N is used to indicate they are attached to the nitrogen.Tertiary amides are named in the same way as secondary amides, but with two NsSimple amides are named as derivatives of carboxylic acids. The ic ending of the common name or the oic ending of the International Union of Pure and Applied Chemistry (IUPAC) name of the carboxylic acid is replaced with the suffix amide (Figure 26.5b.).Figure 26.5b. Comparison of Formic acid and Formamide (Credit: Introduction to Chemistry: GOB (V. 1.0).,CC BY-NC-SA 3.0).Figure 26.5c. Basic structure of an amide showcasing functional groups (credit: General Chemistry 1 & 2 , CC BY 4.0).Amides can be produced when carboxylic acids react with amines or ammonia in a process called amidation. A water molecule is eliminated from the reaction, and the amide is formed from the remaining pieces of the carboxylic acid and the amine (Figure 26.5d.) (note the similarity to formation of an ester from a carboxylic acid and an alcohol discussed in the previous section).Figure 26.5d. Chemical reaction for formation of an amide (credit: General Chemistry 1 & 2 , CC BY 4.0). Give the IUPAC name for the following amides.CH3CH2C=O(NH2)CH3C=O(NH)CH2CH3Solutionpropanamide (proprionamide)N-ethylethanamide (N-ethylacetamide)Write the IUPAC name for each of the following amides.CH3CH2CH2CH2C=O(NH2)CH3CH2CHClCH2C=O(NH2)(credit: 2D structure image of CID 11959 (N-Ethylbenzamide) via PubChem)Check your answers: Name each compound with the common name, the IUPAC name or both.(Credit: Introduction to Chemistry: GOB (V. 1.0).,CC BY-NC-SA 3.0).b.(credit: credit: 2D structure image of 28774 (N-Methylbutyramide) via PubChem).Check your answers:The reaction between amines and carboxylic acids to form amides is biologically important. It is through this reaction that amino acids (molecules containing both amine and carboxylic acid substituents) link together in a polymer to form proteins. Proteins are large biological molecules made up of long chains of smaller molecules called amino acids. Organisms rely on proteins for a variety of functionsproteins transport molecules across cell membranes, replicate DNA, and catalyze metabolic reactions, to name only a few of their functions. The properties of proteins are functions of the combination of amino acids that compose them and can vary greatly. Interactions between amino acid sequences in the chains of proteins result in the folding of the chain into specific, three-dimensional structures that determine the proteins activity.Enzymes are large biological molecules, mostly composed of proteins, which are responsible for the thousands of metabolic processes that occur in living organisms. Enzymes are highly specific catalysts; they speed up the rates of certain reactions. Enzymes function by lowering the activation energy of the reaction they are catalyzing, which can dramatically increase the rate of the reaction. Most reactions catalyzed by enzymes have rates that are millions of times faster than the non-catalyzed version.For more information on proteins see Chapter 28.3 Amino Acids, Proteins and Enzymes.Acrylamide is found mainly in foods made from plants, that are high in carbohydrates and low in proteins. Examples of such foods include potato products, grain products or coffee. Acrylamide is more likely to build up when foods are cooked for longer periods of time or at higher temperatures. Acrylamide is known to cause cancer in experimental animals and is therefore a possible human carcinogen.Infographic 26.5a. Infographic describing acrylamide and its possible increase in cancer risk. Read more about Chemical Concerns Does Acrylamide in Toast & Roast Potatoes Cause Cancer? by Andy Brunning / Compound Interest, CC BY-NC-ND, or access a text-based summary of infographic 26.5a [New tab].Watch Properties of Amides on YouTube (8 min).Video Source: Professor Dave Explains. (2019, September 19). Properties of Amides.[Video]. YouTube.Figure 26.5e. The molecular structure of urea (credit: Image by NEUROtiker, PDM).Hakarl is a fermented Greenland shark, which is the national dish of Iceland. The process of fermenting the shark is essential as fresh shark meat is poisonous as it contains urea (Figure 26.5e.) and trimethylamine oxide. See the Day 13: Iceland: Hkarl infographic for further information.Physical Properties of AmidesWith the exception of formamide (HCONH2), which is a liquid, all simple amides are solids (Table 26.5a.). The lower members of the series are soluble in water, with borderline solubility occurring in those that have five or six carbon atoms. Like the esters, solutions of amides in water usually are neutralneither acidic nor basic.Table 26.5a.Physical Constants of Some Unsubstituted AmidesCondensed Structural FormulaNameMelting Point (C)Boiling Point (C)Solubility in WaterHCONH2formamide2193solubleCH3CONH2acetamide82222solubleCH3CH2CONH2propionamide81213solubleCH3CH2CH2CONH2butyramide115216solubleC6H5CONH2benzamide132290slightly solubleSource: 15.14: Physical Properties of Amides In Basics of GOB Chemistry (Ball et al.), CC BY-NC-SA 4.0.The amides generally have high boiling points and melting points. These characteristics and their solubility in water result from the polar nature of the amide group and hydrogen bonding (Figure 26.5f.). (Similar hydrogen bonding plays a critical role in determining the structure and properties of proteins, deoxyribonucleic acid [DNA], ribonucleic acid [RNA], and other giant molecules so important to life processes.Figure 26.5f. Hydrogen Bonding in Amides. Amide molecules can engage in hydrogen bonding with water molecules (a). Those amides with a hydrogen atom on the nitrogen atom can also engage in hydrogen bonding (b). Both hydrogen bonding networks extend in all directions. (Credit: Intro Chem: GOB (V. 1.0).,CC BY-NC-SA 3.0, edited by (Ball et al.), CC BY-NC-SA 4.0)Urea (CO(NH2)2) is a diamide containing two amide groups joined by a carbonyl functional group. Urea is the main component of urine consisting of nitrogenous waste products from the metabolic breakdown of proteins. The liver produces enzymes which form urea which is then transported to the kidneys for removal from the body. Urea a colourless, odourless solid which is highly soluble in water and when dissolved in water is neither acidic nor alkaline. Urea is widely used in fertilizers as a nitrogen source and is an important raw material for chemical industry.Figure 26.5g. The molecular structure of urea. (credit: Image by NEUROtiker, PDM).Attribution & ReferencesExcept where otherwise noted, this page is adapted by Caryn Fahey from: References cited in-textNational Center for Biotechnology Information (2024). PubChem Compound Summary for CID 11959, N-Ethylbenzamide. Retrieved February 7, 2024.National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 28774, N-Methylbutyramide. Retrieved February 7, 2024definitionorganic molecule that features a nitrogen atom connected to the carbon atom in a carbonyl groupthe reaction in which an amide group replaces the hydrogen atom on the amino group.Amides represent an essential class of organic compounds characterized by the presence of a carbonyl group (C=O) directly bonded to a nitrogen atom. They are derived from carboxylic acids, whereby the hydroxyl group (OH) is replaced by an amine group (NH2 or NHR, where R represents an alkyl or aryl group). This functional group plays a pivotal role in various biological processes and synthetic applications. Among the diverse range of amides, it is crucial to distinguish between their types based on the nitrogen atom's substitution pattern: Primary Amides: Contain one alkyl or aryl group and are represented by the general formula RCONH2. Secondary Amides: Feature two substituents attached to the nitrogen, expressed as R1CONHR2. Tertiary Amides: Specify three groups bonded to the nitrogen, denoted by R1CONR2R3. Amides exhibit a range of both physical and chemical properties that distinguish them from other functional groups. Their structural integrity arises from hydrogen bonding capabilities, which significantly influence their boiling points and solubility in polar solvents. The ability to form multiple hydrogen bonds allows amides to maintain higher boiling points compared to other carbonyl-containing compounds. "The multifaceted nature of amides not only sustains their significance in organic chemistry but also enhances their relevance in medicinal and industrial applications." The versatility of amides as far as chemical reactivity is concerned cannot be understated. They are commonly involved in various chemical reactions, such as hydrolysis, amidation, and condensation processes. Understanding these reactions and their mechanisms is critical for chemists as it underpins their application in pharmaceutical development and polymer science. In summary, amides stand out as a critical functional group in the realm of organic compounds, bridging many biological and synthetic processes. Their unique characteristics and reactivity make them vital in numerous chemical applications, establishing their importance in both academic research and industry. Definition and General Structure of AmidesAmides are defined as organic compounds that feature the amide functional group, comprising a carbonyl group (C=O) attached to a nitrogen atom (N), forming the general structural formula represented as RCONR'R'', where R, R', and R'' can be hydrogen or hydrocarbon groups. This means that the nitrogen atom can be connected to one or more hydrocarbon chains or other substituents, leading to the classification of amides as primary, secondary, or tertiary. The general structure of amides can be summarized as follows: Primary Amides: RCONH2 - Here, the nitrogen is directly bonded to two hydrogen atoms and one carbon-containing group, exemplifying compounds like acetamide (C2H5NO). Secondary Amides: R1CONHR2 - In this case, the nitrogen is bonded to one hydrogen atom and two carbon groups, as seen in N-methylacetamide (C3H7NO). Tertiary Amides: R1CONR2R3 - These amides have no hydrogen attached to the nitrogen, having three substituents instead, such as N,N-dimethylformamide (C3H7NO). The fundamental property that distinguishes amides from other carbonyl-containing compounds is their ability to engage in hydrogen bonding. This characteristic is due to the electronegative nature of the nitrogen atom, which creates polar interactions with the carbonyl oxygen. Consequently, amides often exhibit distinct physical properties, such as: High boiling points relative to esters and aldehydes of similar molecular weight; Increased solubility in polar solvents, which is crucial for their applications in various chemical processes. "The unique structure and bonding capabilities of amides underscore their roles in both organic chemistry and biochemistry." Overall, the general structure of amides not only defines their chemical identity but also plays a critical role in determining their reactivity and physical characteristics. Understanding this structure is vital for exploring their applications in drug development, polymer synthesis, and biological systems. As we delve deeper into the chemistry of amides, recognizing their diverse forms and inherent properties will be essential for grasping their function and value in scientific endeavors. The nomenclature of amides follows specific rules set forth by the International Union of Pure and Applied Chemistry (IUPAC), which aim to provide a systematic method for naming these compounds. Amides are typically named based on the parent carboxylic acid from which they are derived, replacing the suffix -oic acid with -amide. For example: Acetic Acid becomes Acetamide (C2H5NO) Benzoic Acid transforms into Benamide (C7H7NO) When naming amides, the substituents attached to the nitrogen atom are designated using a prefix before the parent name, which provides essential information about the compound's structure. These substituents are indicated by the letters N- followed by the name of the alkyl or aryl group, and they help to distinguish between different isomers. For instance: N-Methylacetamide: This indicates the presence of a methyl group attached to the nitrogen of acetamide. N,N-Dimethylformamide: Here, two methyl groups are attached to the nitrogen of formamide. "The clarity of the nomenclature allows for easy communication and understanding in the field of organic chemistry." In cases where the amide has multiple substituents or branched structures, the rules regarding alphabetical order and numerical designations apply. For example: N-Ethyl-N-propylformamide: This specifies an ethyl group and a propyl group attached to the nitrogen. 3-Methyl-N-ethylcapramide: Here, the numbering indicates that a methyl group is located on the third carbon of the capramide chain. It is important to note that the position of the substituents must be clearly designated. The use of commas to separate numbers and hyphens to divide numbers and letters is standard practice in the naming process. This ensures the names convey the precise structural information needed for understanding the compound. "A well-defined nomenclature system is vital in facilitating efficient collaboration and research within the vast landscape of organic chemistry." The systematic approach to naming amides aids in their identification and differentiation, significantly impacting fields such as pharmaceuticals, where specific amide structures can yield varying biological activities. Researchers must become adept at recognizing and applying these nomenclature rules to foster clarity and avoid miscommunication. As we progress through the exploration of amides, understanding their names will enhance our comprehension of their properties, reactivity, and applications. Types of Amides: Primary, Secondary, and TertiaryAmides can be classified into three main types based on the substitution pattern of the nitrogen atom, which significantly influences their chemical behavior and properties. Understanding these distinctions is crucial for chemists as each type of amide presents unique characteristics and reactivity. Primary Amides: These contain one carbon-containing group attached to the carbonyl carbon and two hydrogen atoms bonded to the nitrogen. Their general formula can be represented as RCONH2. An example is acetamide (C2H5NO), commonly used in various chemical processes. Primary amides exhibit relatively high polarities and can engage in strong hydrogen bonding interactions, which contributes to their higher boiling points compared to other amide types. Secondary Amides: In this class, the nitrogen atom is bonded to one hydrogen atom and two carbon-containing groups, giving them the general formula R1CONHR2. An example of a secondary amide is N-methylacetamide (C3H7NO). Secondary amides typically have reduced reactivity compared to primary amides due to the increased steric hindrance brought about by the additional substituent on the nitrogen. This can affect their formation and reaction pathways, rendering some secondary amides more stable under specific conditions. Tertiary Amides: Tertiary amides have three carbon-containing groups attached to the nitrogen, with no hydrogen atoms bonded to it, represented by the formula R1CONR2R3. A classic example is N,N-dimethylformamide (C3H7NO). Their structure imparts unique properties, making them less polar and often less capable of forming hydrogen bonds compared to primary and secondary amides. Consequently, tertiary amides may exhibit lower boiling points and different solubility characteristics. Each type of amide exhibits unique features that not only determine their reactivity but also their applications in various fields, from pharmaceuticals to polymer chemistry. As chemist Linus Pauling once said, "The key to understanding chemical reactivity lies in the interplay between structure and function." This principle certainly holds true for amides, as their nuanced characteristics directly impact their behavior in synthetic and biological contexts. Furthermore, the classification of amides into primary, secondary, and tertiary types assists researchers in predicting their reactivity and understanding their roles in chemical reactions. For instance, primary amides tend to hydrolyze more readily than secondary and tertiary amides, making them vital in reaction pathways that involve nucleophilic attack, such as in the synthesis of various organic compounds. Recognizing and categorizing amides according to their type is essential for chemists engaged in organic synthesis and medicinal chemistry. Such insights ensure efficient utilization of these compounds and enhance the development of new materials and pharmaceutical agents. Synthesis of Amides: Preparation MethodsSynthesizing amides can be undertaken through several key methods, each tailored to achieve specific outcomes based on the desired properties of the resultant amide. The following are the most prevalent techniques employed in the preparation of amides: Direct Condensation of Carboxylic Acids and Amines: This method involves the reaction of a carboxylic acid with an amine. The reaction is generally straightforward, yielding an amide alongside the elimination of water. The reaction can be represented as follows: RCOOH + R'NH2 RCONHR' + H2O However, this reaction often necessitates heat and potentially a catalyst to drive the equilibrium towards amide formation, especially for less reactive substrates. Acyl Chlorides with Amines: Acyl chlorides react readily with amines to form amides, often under mild conditions. This approach provides a more efficient route than using carboxylic acids due to the greater reactivity of acyl chlorides. The reaction proceeds as follows: RCOCl + R'NH2 RCONHR' + HCl Using Ammonium Salts: Another preparation method is through the reaction of ammonium salts with carbonyl compounds. This process often involves intermediate formation of an imine, followed by reduction to yield the amide. While this route is less common, it can be useful when direct amine substitution is difficult due to steric hindrance. Amidation Reactions: The conversion of carboxylic acids to amides can also be performed through amidation reactions with various reagents like carbodiimides, which activate the carboxylic acid for nucleophilic attack by the amine. This can be represented as: RCOOH + R'NH2 RCONHR' Each of these synthesis methods has distinct advantages and limitations. For instance, while the direct condensation is simple, it might not provide the best yields for sterically hindered amines. Conversely, acyl chlorides, being highly reactive, can lead to side reactions unless properly controlled. As noted by chemist Hermann Emil Fischer, "Chemical synthesis is the language of nature, a dance of atoms and molecules bringing forth the beauty of compounds." Thus, optimal selection of synthesis methods minimizes byproducts and enhances product yields. Overall, understanding the diverse preparation methods for synthesizing amides is crucial for organic chemists, as these methods not only influence the quality of the amide produced but also inform their applications in various fields, including pharmaceuticals, agriculture, and biotechnology. As research continues to evolve, advancements in synthetic methodologies will pave the way for new applications of amides in innovative domains. Reactions of Amides: OverviewThe chemical reactivity of amides encompasses a wide range of reactions that significantly impacts various fields such as organic synthesis, medicinal chemistry, and materials science. Understanding these reactions is fundamental to leveraging the unique properties of amides for specific applications. Below is an overview of key reactions involving amides: Hydrolysis: Amides can undergo hydrolysis, a reaction with water that results in the formation of carboxylic acids and amines. This reaction can be catalyzed by either acids or bases, with the mechanisms varying accordingly. For example: RCONHR' + H2O RCOOH + R'NH2 In acidic conditions, the reaction proceeds through the protonation of the amide nitrogen, enhancing the electrophilicity of the carbonyl carbon, making it more susceptible to nucleophilic attack by water. Amidation Reactions: The process of converting carboxylic acids to amides is pivotal, often involving nucleophilic attack by an amine on the activated carbonyl carbon. As noted earlier, carbodiimides may be utilized to facilitate this reaction, enhancing the yield of amide products. Formation of Imides: Under certain conditions, amides can be transformed into imides through dehydration processes, either by heating or in the presence of dehydrating agents. This transformation is crucial in the synthesis of biologically relevant molecules and polymers. Reductive Amination: In this reaction, amides can serve as substrates for reductive amination, where they are converted to amines by reaction with reducing agents such as lithium aluminum hydride. This reaction underscores the versatility of amides in organic synthesis. Reaction with Acyl Chlorides: Amides react with acyl chlorides to form more complex amide derivatives, illustrating their utility in chemical synthesis. This reaction typically proceeds smoothly in mild conditions, allowing for robust synthetic pathways. "The remarkable versatility of amides allows them to participate in a myriad of chemical reactions, each adding to their significance in organic chemistry." Amides also play crucial roles in biochemical processes, serving as intermediates in the synthesis of amino acids and peptides. Their unique structural characteristics enable preferential interactions with other biomolecules, contributing to their essential functions in biological systems. In conclusion, a deep understanding of the reactions involving amides is vital for chemists striving to exploit their potential in various synthetic and biological pathways. The breadth of reactions, including hydrolysis, amidation, and transformation into other functional groups, illustrates the central role amides occupy in the landscape of organic chemistry, catering to both scientific inquiry and practical applications. Hydrolysis of Amides: Mechanism and ConditionsHydrolysis of amides is a significant reaction in organic chemistry, as it involves the conversion of amides into carboxylic acids and amines. This reaction can occur under various conditionsacidic, basic, or neutraland understanding the underlying mechanisms and factors influencing this process is essential for chemists. The general hydrolysis reaction can be represented as follows: RCONHR' + H2O RCOOH + R'NH2 In acidic conditions, the mechanism begins with the protonation of the nitrogen atom in the amide, which increases the electrophilicity of the carbonyl carbon. This facilitation leads to an enhanced susceptibility to nucleophilic attack by water. The following steps summarize the mechanism: The protonation of the carbonyl oxygen increases the carbon's partial positive charge. Water acts as a nucleophile, attacking the carbonyl carbon to form a tetrahedral intermediate. The intermediate subsequently collapses, regenerating a carbonyl group and releasing the protonated amine. Finally, deprotonation of the protonated amine forms free amine, yielding the final productscarboxylic acid and amine. Conversely, in basic conditions, the mechanism alters slightly. Instead of acidity catalyzing the reaction, the hydroxide ion serves as a nucleophile. The steps involved are: The hydroxide ion performs a nucleophilic attack on the carbonyl carbon. This results in a negatively charged tetrahedral intermediate, which subsequently undergoes proton transfer. Finally, the breakdown of the intermediate leads to the formation of carboxylic acid and amine. The conditions of hydrolysis significantly affect the rates and yields of the reaction. Factors such as: Temperature: Elevated temperatures generally enhance reaction rates. Concentration of Reactants: Higher concentrations of water or the amide increase the likelihood of the reaction occurring. Type of Catalyst: Depending on whether an acidic or basic catalyst is used, the mechanism and efficiency of the hydrolysis can vary. "Hydrolysis of amides underpins essential processes in organic synthesis, showcasing the beautiful complexity of chemical reactivity." Understanding the conditions and mechanisms involved in amide hydrolysis is crucial for numerous applications, including drug design and environmental chemistry. The reactions yield key intermediates valued in the synthesis of various bioactive compounds, such as amino acids and pharmaceuticals. This highlights not only the importance of amides but also the broader implications of their hydrolysis in biochemical pathways and industrial processes. The formation of amides via condensation reactions is a fundamental process in organic chemistry, wherein a carboxylic acid reacts with an amine, resulting in the elimination of a small molecule, typically water. This reaction not only exemplifies the synthesis of amides but also demonstrates an essential principle of organic transformation: the coupling of two functional groups while ejecting a byproduct. The general reaction can be illustrated as follows: RCOOH + R'NH2 RCONHR' + H2O This reaction process typically proceeds under specific conditions that favor amide formation. Factors critical for optimizing yields include: Heat: Applying heat increases the kinetic energy of the molecules involved, thereby driving the reaction towards product formation. Catalysts: The use of acid catalysts can enhance the reaction rate by protonating the carbonyl oxygen, making the carbonyl carbon more electrophilic. Stoichiometry: Maintaining a favorable stoichiometric ratio of reactants ensures that both the carboxylic acid and amine remain in adequate concentrations to promote successful reactions. "Condensation reactions represent the elegance of chemistry, where simple molecules unite to form complex structures and functional capabilities." Amides can also be synthesized through other methods involving condensation reactions, including: Activation of Carboxylic Acids: This process involves converting carboxylic acids into more reactive intermediates such as acyl chlorides or anhydrides, which can react efficiently with amines to form amides. Using Reagents like Carbodiimides: Carbodiimides (R-N=C=N-R') can be employed to activate carboxylic acids, facilitating the amidation process through a similar condensation mechanism. Moreover, the condensation reaction leading to amide formation is of paramount importance in both synthetic organic chemistry and biological systems. In nature, the formation of peptide bonds between amino acids results in the creation of proteinsessential components of life. This biological amidation showcases the ubiquity and significance of amides. As noted by chemist Hermann Emil Fischer, "The study of proteins and their transformations into different structures is the key to understanding life processes." In a laboratory setting, the synthesis of amides through condensation reactions provides versatile methodologies for developing a wide range of amide derivatives. The ability to manipulate the reaction conditions can lead to the fine-tuning of amide properties, making them suitable for diverse applications such as: Pharmaceuticals: Amides serve as critical structures in many drug candidates, influencing both biological activity and pharmacokinetic properties. Polymers: Synthetic methodologies utilizing amides pave the way for the creation of polyamides, such as nylon, used extensively in materials science. Biochemistry: The study of amide formation is vital in understanding the synthesis of biomolecules, including enzymes and hormones. In conclusion, the formation of amides through condensation reactions not only underpins important synthetic methodologies but also resonates profoundly in biological contexts. Understanding the principles of this reaction type is essential for chemists aiming to exploit the versatility of amides in numerous scientific and industrial fields. Amides in the Presence of Acids and BasesAmides exhibit distinct reactivity when introduced to acidic or basic environments, significantly influencing their chemical behavior. Understanding these interactions provides essential insights into their utility and application in various synthetic and biological contexts. In acidic conditions, amides can undergo protonation, which enhances their electrophilic character, facilitating nucleophilic attack and leading to hydrolysis reactions. When amides are exposed to acids, the following key transformations can occur: Protonation of the Carbonyl Oxygen: This process increases the positive charge density on the carbonyl carbon, making it more amenable to nucleophilic attack from water or alcohols. Formation of Carboxylic Acids: As a result, amides can readily hydrolyze into carboxylic acids and amines, especially in the presence of aqueous conditions. The reaction can be represented as follows: RCONHR' + H2O RCOOH + R'NH2 "The versatility of amides in acidic environments highlights their importance in synthetic organic chemistry." Conversely, when amides react with strong bases, the nitrogen atom becomes a more potent nucleophile: Nucleophilic Attack: The hydroxide ion (OH-) can attack the carbonyl carbon, leading to the formation of a tetrahedral intermediate. Deprotonation: This process provides an alternative pathway for amide hydrolysis, showcasing the base's role in promoting nucleophilic reactivity. The striking responses of amides in acidic versus basic mediums illustrate their inherent flexibility. In acid-mediated conditions, amides are more prone to hydrolysis, while basic conditions favor different nucleophilic approaches that can be beneficial in synthetic processes. The understanding of amide behavior is crucial, especially in: Pharmaceutical Development: Compounds with amide functional groups often serve as essential components in active pharmaceutical ingredients (APIs). The stability or reactivity of these amides in acidic or basic environments can dramatically affect the drug's efficacy and biological activity. Polymer Science: In the development of polyamides, such as nylon, understanding how these materials react in various conditions is fundamental for optimizing their properties. Biochemical Pathways: In biological systems, amidation and hydrolysis of peptide bonds have critical implications for protein synthesis and degradation. "Amides are not only vital in synthetic chemistry but also play indispensable roles in biological processes." Overall, the presence of acids and bases significantly alters the reactivity and stability of amides, offering vast possibilities for their application across chemical disciplines. The insights gained from these interactions underscore the pivotal role amides play in the continued exploration of organic chemistry and its applications in science and industry. Dehydration reactions involving amides play a pivotal role in the synthesis of imides and other related compounds, illustrating a key transformation in organic chemistry. These reactions generally entail the removal of a water molecule from a substrate, typically an amide, under specific conditions, leading to the formation of new functional groups. The general dehydration reaction can be represented as follows: RCONHR' RCO - NR' + H2O Dehydration reactions can proceed through various pathways depending on the specific reagents, conditions, and desired end products. Here are some notable methods for inducing dehydration in amides: Thermal Dehydration: Heating amides under certain conditions can promote dehydration. Elevated temperatures can facilitate the expulsion of water from the amide, especially when coupled with the presence of other dehydrating agents. In the Presence of Dehydrating Agents: Reagents such as phosphorus oxychloride (POCl3), thionyl chloride (SOCl2), or carbodiimides can be utilized to drive the dehydration forward, often leading to enhanced yields of the desired products. Acid-Catalyzed Dehydration: Acids can protonate the amide oxygen, increasing the electrophilicity of the carbonyl carbon and facilitating the subsequent loss of water. This method is particularly effective when combined with heat. "Dehydration reactions exemplify the elegant dance of atoms, where simple structures transform into complex frameworks through the loss of water." One significant transformation that involves dehydration is the formation of imides, which can be achieved by the reaction of an amide with another amide or a carboxylic acid. This process not only expands the family of nitrogen-containing compounds but also underscores the versatility of amides in organic synthesis. The reaction can be succinctly illustrated as follows: RCONHR' + RCOOH RCO - NR' + H2O The formation of imides from amides is particularly fascinating due to their application in the synthesis of various biologically active molecules and polymers. Imides can serve as valuable intermediates, and their structural characteristics often afford enhanced biological activity compared to their amide counterparts. Moreover, the conditions under which dehydration occurs are crucial for optimizing yields and minimizing byproducts. Factors such as temperature, the presence of catalysts or dehydrating agents, and the duration of the reaction all converge to shape the outcome of these transformations. A keen understanding of these parameters enables chemists to design more effective synthetic strategies. "The art of organic synthesis lies not only in the reactions employed but also in mastering the conditions that drive those reactions." In summary, dehydration reactions involving amides contribute significantly to the versatility and complexity of organic molecules. These processes not only underscore the intrinsic reactivity of amides but also highlight their importance in both synthetic and biological contexts. As research continues to uncover new pathways and methodologies for amide dehydration, their applications in pharmaceuticals, materials science, and biochemical research are poised for expansion. Reactivity of Amides: Comparison with Other Functional GroupsAmides exhibit unique reactivity when compared to other functional groups, such as esters, ketones, and carboxylic acids. This distinct behavior largely stems from the electronic and steric characteristics of the amide functional group, which influence their interactions and the types of reactions they undergo. One pivotal aspect is the nature of the carbonyl group in amides, which is primarily stabilized through resonance. The lone pair of electrons on the nitrogen atom participates in delocalization with the carbonyl group, leading to increased stability compared to carbonyls in esters or ketones. This resonance effect causes amides to be less reactive towards nucleophilic attack than their carboxylic acid counterparts. As a result, hydrolysis and other reactions that would readily occur with esters or anhydrides may be less favorable for amides under similar conditions. Here are some comparisons illustrating the reactivity of amides in relation to other functional groups: Amides vs. Carboxylic Acids: Carboxylic acids are more acidic than amides due to the presence of a hydroxyl group, which can easily donate a proton. Amides, on the other hand, are significantly less acidic, making them more stable in hydrolysis conditions and often requiring stronger conditions for comparable reactions. Amides vs. Esters: While both amides and esters contain carbonyl groups, esters are generally more reactive due to the absence of nitrogen's lone pair participation in resonance. Amides tend to resist nucleophilic acyl substitution reactions, making their synthesis and transformation provide different pathways compared to esters. Amides vs. Ketones: Ketones, similar to amides, possess a carbonyl group; however, ketones lack the nitrogen atom which stabilizes the amide through resonance. As a result, ketones are often more reactive towards nucleophilic attacks than amides. "The reactivity of amides illustrates the delicate balance between stability and reactivity, underscoring the nuances of organic transformation." The reactivity of amides is also influenced by their substitution pattern. For instance, primary amides are more susceptible to hydrolysis and other nucleophilic reactions when compared to tertiary amides, which, due to steric hindrance from multiple carbon groups, demonstrate decreased reactivity. Moreover, the unique properties of amides provide distinct advantages in synthetic chemistry. Their stability allows them to serve as intermediates in the production of more complex molecules. For example, in peptide synthesis, the stability of amide bonds makes them suitable for building chains of amino acids without premature hydrolysis. This characteristic also emphasizes the role of amides in biological systems, where peptide bonds, composed of amides, link amino acids into proteinsessential building blocks of life. In summary, while amides are less reactive than some other functional groups, their stability and unique properties make them valuable in organic synthesis and biological processes. Understanding their reactivity compared to other functional groups is key in exploiting their applications across diverse fields, including pharmaceuticals and materials science. Stability of Amides: Factors Affecting ReactivityThe stability of amides is a crucial factor that influences their reactivity and behavior in chemical reactions. Understanding the various elements that contribute to this stability is essential for chemists involved in synthesis and application of amides across different fields. Several key factors affect the stability of amides, including: Resonance Stabilization: The lone pair of electrons on the nitrogen atom can delocalize into the carbonyl group, leading to a resonance structure that stabilizes the amide. This resonance effect makes the carbonyl carbon less electrophilic and thus less reactive compared to other carbonyl-containing compounds. Electron-Withdrawing and Electron-Donating Groups: The presence of substituents on the carbon and nitrogen atoms can significantly influence the stability of amides. Electron-withdrawing groups (EWGs), such as halogens or nitro groups, decrease stability by increasing the partial positive charge on the carbonyl carbon, enhancing its reactivity. In contrast, electron-donating groups (EDGs), like alkyl substituents, help stabilize the amide, making it less reactive. Substitution Pattern: The type of amide (primary, secondary, or tertiary) directly affects stability. Primary amides are typically more reactive than secondary and tertiary amides, as the latter two experience steric hindrance from additional alkyl groups, which can hinder nucleophilic attack on the carbonyl carbon. Solvent Effects: The choice of solvent can also impact amide stability. Polar protic solvents can stabilize ionic intermediates formed during reactions involving amides, whereas polar aprotic solvents may enhance the reactivity of the amides by solvation of nucleophiles. "Stability allows amides to act as intermediates in complex reaction pathways, providing a robust platform for organic synthesis." Moreover, the interaction between amides and their environment can play an influential role in their stability. For instance, changes in temperature, pH levels, and the concentrations of reactants can alter the equilibrium, shifting it towards formation or dissociation of amides. In biological systems, the stability of amide bonds, particularly in peptide linkages, underscores their essential role in maintaining the structure of proteins. The amide bond is remarkably stable, allowing proteins to maintain their functional integrity under various physiological conditions. As noted by chemist Linus Pauling, "The stability of chemical bonds is crucial for the functioning of biological molecules; amides exemplify this principle in the world of proteins." Ultimately, the stability of amides affects their reactivity and application in various fields, including drug development, where amide bonds often influence pharmacokinetics and biological activity. By comprehensively understanding the factors that influence amide stability, chemists are better equipped to manipulate these essential compounds for both synthetic and biological applications. Physical Properties of Amides: Boiling Points, Solubility, and PolarityAmides exhibit distinctive physical properties that are closely related to their molecular structure, particularly their capability for hydrogen bonding. These properties include boiling points, solubility in various solvents, and polarity, all of which significantly influence their behavior in chemical reactions and practical applications. One of the most striking features of amides is their boiling points. Compared to other carbonyl-containing compounds, amides tend to have significantly higher boiling points. This can be attributed to their ability to form strong hydrogen bonds, both as hydrogen bond donors and acceptors. The boiling points of amides can be summarized as follows: Primary Amides: Generally possess the highest boiling points due to their capacity for extensive hydrogen bonding. Secondary Amides: Exhibit moderately high boiling points, as they form fewer hydrogen bonds compared to primary amides. Tertiary Amides: Usually have the lowest boiling points among amides, given that the absence of hydrogen atoms on the nitrogen limits hydrogen bonding capability. For example, acetamide (C2H5NO) has a boiling point of approximately 221 C, while N,N-dimethylacetamide (C4H9NO) has a boiling point around 165 C. These differences illustrate the impact of hydrogen bonding on boiling points significantly. In addition to boiling points, amides showcase unique solubility characteristics. They tend to be soluble in polar solvents such as water, alcohols, and some organic solvents. The solubility can be attributed to the ability of amides to engage in hydrogen bonding with solvent molecules. The following tendencies are noted: Primary and secondary amides generally exhibit good solubility in water, in contrast to tertiary amides, which may show reduced solubility due to steric hindrance. The presence of additional alkyl or aryl groups may also influence solubility, as larger substituents can impart hydrophobic characteristics, decreasing overall solubility. Moreover, the polarity of amides is another significant aspect of their physical properties. Amides are polar compounds due to the presence of the carbonyl group, which contributes to a dipole moment. The nitrogen atom further enhances polarity through its electronegative nature, facilitating interactions with other polar molecules. This characteristic leads to numerous applications in drug design and biomaterials. "The polar nature of amides permits their widespread use in pharmaceuticals, where solubility and interaction with biological targets are critical." Overall, the physical properties of amideshighlighted by their boiling points, solubility, and polarityare fundamental to their role in both organic synthesis and biological systems. The combined effects of hydrogen bonding, molecular structure, and the nature of substituents provide valuable insights into their behavior, guiding researchers in the development of new compounds and materials. Amides play a critical role in various fields, particularly in organic synthesis and industrial applications, due to their unique structural and chemical properties. Their versatility allows them to serve as intermediates and building blocks in numerous chemical processes, making them indispensable in both the laboratory and industry. In the realm of organic synthesis, amides are often utilized for the following purposes: Synthesis of Pharmaceuticals: Amides are fundamental components in many drug candidates. Their structural characteristics can influence pharmacokinetics and biological activity, making them crucial in the development of therapeutics. For instance, numerous anti-inflammatory and analgesic medications contain amide linkages, which are critical to their effectiveness. Polymer Production: Amides serve as key monomers in the synthesis of polyamides, such as nylon and Kevlar, which are widely used in manufacturing durable fabrics, ropes, and other materials. The unique combination of strength and flexibility offered by polyamides makes them invaluable in various applications, including textiles and composite materials. Preparation of Fine Chemicals: The formation of amides can be integral to producing fine chemicals, specialty chemicals, and agrochemicals. Their ability to undergo reactions such as amidation allows chemists to create complex molecules that can be tailored for specific functions, broadening the scope of chemical synthesis. "The applications of amides are as diverse as their structures, reflecting their importance in multiple scientific disciplines." Moreover, in the context of industrial applications, amides exhibit significant utility: Solvents and Catalysts: Certain amides, such as dimethylformamide (DMF) and dimethylacetamide (DMAC), are widely used as solvents and reaction media in organic synthesis. Their polar aprotic nature facilitates various reactions, making them favorable choices in chemical processes. Intermediate in Chemical Manufacturing: Amides serve as intermediates in the production of agrochemicals, including herbicides and pesticides. Their structural properties allow them to interact favorably with biological targets, leading to enhanced efficacy in agricultural applications. Role in Biochemistry: In biochemistry, amides are critical in the formation of peptide bonds between amino acids, contributing to protein synthesis. This fundamental biological process underscores their significance in various life sciences and biomedical research. As noted by the renowned chemist Hermann Emil Fischer, "The study of proteins and their transformations into different structures is the key to understanding life processes." This statement highlights the essential nature of amides in biological systems, where they perform crucial functions and are involved in a multitude of biochemical pathways. In summary, the applications of amides in both synthesis and industry exemplify their versatility and importance. From serving as building blocks in pharmaceuticals and materials science to playing key roles in biochemical processes, amides are an indispensable functional group that researchers and industries continue to explore for innovative solutions. Role of Amides in Biological Systems: Amino Acids and ProteinsAmides play a pivotal role in biological systems, particularly as the backbone of amino acids and proteins, which are fundamental to life. The formation of peptide bondsthe links that connect amino acids to form proteinsexemplifies the importance of amides in biological chemistry. A peptide bond, specifically, is a type of amide bond formed when the carboxyl group of one amino acid reacts with the amino group of another, releasing a molecule of water. This process can be represented as: RCOOH + R'NH2 RCONHR' + H2O This uniqueness of amides within biological systems can be summarized in several key points: Protein Structure: Proteins, consisting of long chains of amino acids, rely on amide bonds to maintain their structural integrity. The sequence and arrangement of these amino acids dictate the proteins function, contributing to activities such as enzymatic reactions, muscle contraction, and immune responses. Enzyme Function: Many enzymes are proteins that facilitate biochemical reactions, thanks to their amide bonds. Their structural configuration allows for specific interactions with substrates, enhancing reaction rates and directing metabolic pathways. Stability of Proteins: The stability imparted by amide bonds is crucial in natural processes. The resistance of these bonds to hydrolysis under physiological conditions helps maintain protein integrity, essential for sustaining life processes. As the biochemist J. Craig Venter noted, "The ability to manipulate proteins not only informs our understanding of biology but also opens avenues for biotechnological advancements." Signal Transmission: Amides are involved in neurotransmitter functions, enabling effective communication between neurons. Certain neurotransmitters, including peptides like endorphins, demonstrate the functional diversity arising from amide bonds. Furthermore, the presence of amide functional groups in amino acids enhances their solubility in water, a characteristic vital for their stability and interaction with other biomolecules. This solubility is facilitated by the formation of strong hydrogen bonds between amides and water molecules, allowing amino acids to remain dissolved and accessible for protein synthesis. As we explore the vital role of amides in biological systems, it becomes evident that their significance extends beyond mere structural elements. They serve as: Intermediates: In metabolic pathways, amides act as key intermediates in the synthesis and breakdown of various biomolecules. Regulators: Certain amide-containing compounds function as hormones and signaling molecules, regulating crucial physiological processes. Therapeutic Targets: Understanding amide interactions at the molecular level can guide the development of pharmaceutical interventions, enhancing therapeutic outcomes. In conclusion, the role of amides in biological systems is fundamental to life itself. By serving as the building blocks of proteins and participating in crucial biological processes, amides underscore their importance in biochemistry and molecular biology. Emphasizing their structural integrity and functional versatility allows scientists to appreciate the intricate interplay between amides and lifes biochemical pathways. Conclusion: The Importance of Amides in Organic ChemistryIn conclusion, amides are an integral part of organic chemistry, influencing various fields ranging from synthesis to biological systems. Their exceptional properties and versatility underscore their importance in numerous applications. The significance of amides can be encapsulated in several key points: Fundamental Structures: Amides are critical components of numerous biologically relevant molecules including proteins, peptides, and amino acids. The presence of the amide bond is essential for maintaining structural integrity in these biomolecules. Diverse Reactions: Amides partake in a wide array of chemical reactions such as hydrolysis, amidation, and condensation. This versatility enables amides to serve as intermediates in synthetic pathways, providing foundational support in the construction of complex organic compounds. Stability and Reactivity: The stability of amides, particularly due to resonance and hydrogen bonding interactions, renders them less reactive than other carbonyls, thus allowing them to function as reliable building blocks in organic synthesis. As chemists aim to establish selective reaction pathways, understanding the stability of amides becomes pivotal. Applications in Industry: Amides are not only valuable in academic research but also find extensive applications in industry. They are employed in the manufacturing of pharmaceuticals, polymers, and agricultural chemicals. For instance, polyamides such as nylon are integral to the textile industry, showcasing the critical nature of amides in producing essential materials. Biochemical Importance: Beyond synthetic applications, amides play a fundamental role in biological systems. Their presence in amino acids and proteins highlights their significance in life processes, enabling vital functions such as enzymatic activity and signal transduction. "Understanding amides not only allows chemists to harness their unique properties in synthesis but also illuminates their pivotal role in sustaining biological life." Amides serve as excellent examples of the intricate interplay between structure and function in organic chemistry. Their unique characteristics are not only of theoretical interest but also have practical implications that resonate across scientific disciplines. The ongoing exploration of amide chemistry continues to uncover novel applications and avenues for research. As we advance our understanding of this vital class of compounds, we can leverage their properties to drive innovation in both synthesis and applied sciences. The future of amides in chemistry promises expanding horizons, and with continual research, their impact on drug development, material science, and biological mechanisms will undoubtedly grow. In exploring the multifaceted role of amides in organic chemistry, a wealth of literature and resources is available to deepen understanding and foster further investigation. The following references and suggested readings provide foundational knowledge and innovative insights into the properties, reactions, and applications of amides: References Organic Chemistry by Paula Yurkanis Bruice - A comprehensive resource that covers key concepts in organic chemistry, including amides and their reactivity. Advanced Organic Chemistry: Part A by Francis A. Carey and Richard J. Sundberg - This text delves into mechanisms and synthesis strategies involving amides, providing a detailed examination of their chemistry. Fundamentals of Biochemistry by Mary S. D. Franks - This book outlines the significance of amides in biological systems, particularly their roles in protein structure and function. Amide Bonds in Organic Synthesis - A review article that explores various synthesis methodologies and their applications in the development of pharmaceutical compounds. Suggested Readings Peptide Chemistry: A Practical Textbook by Christopher A. C. Scheek - This resource provides insights into peptide bond formation and the significance of amides in biological systems. Polymeric Materials: Properties and Applications by Hugh G. Smith - This book discusses the role of amides in synthetic polymers, including their structural implications and industrial applications. Biochemistry by Jeremy M. Berg, John L. Tymoczko, and Lubert Stryer - Comprehensive coverage of biochemical processes where amides play crucial roles, particularly in metabolic pathways. To enhance your exploration of amides, consider the following key points: Amides serve as crucial intermediates in the synthesis of a wide variety of organic compounds. The stability of amides comments on their utility in biological and synthetic chemistry, highlighting opportunities for novel applications. The understanding of amide reactivity is vital for chemists looking to develop innovative organic reactions and methodologies. "A thorough grasp of amide chemistry opens doors to new possibilities in drug development and materials science." In summary, delving into the extensive body of literature on amides is indispensable for researchers and students alike. By engaging with these materials, one can enrich their understanding of the essential role amides play in various scientific domains, from organic synthesis to biochemistry and beyond. This page explains what amides are and looks at their simple physical properties such as solubility and melting points. Amides are derived from carboxylic acids. A carboxylic acid contains the -COOH group, and in an amide the -OH part of that group is replaced by an -NH2 group. So . . . amides contain the -CONH2 group. Some simple amides The most commonly discussed amide is ethanamide, CH3CONH2 (old name: acetamide). The three simplest amides are: HCONH2methanamide CH3CONH2ethanamide CH3CH2CONH2propanamideNotice that in each case, the name is derived from the acid by replacing the "oic acid" ending by "amide". If the chain was branched, the carbon in the -CONH2 group counts as the number 1 carbon atom. For example: Physical properties Melting points Methanamide is a liquid at room temperature (melting point: 3C), but the other amides are solid. For example, ethanamide forms colourless deliquescent crystals with a melting point of 82C. A deliquescent substance is one which picks up water from the atmosphere and dissolves in it. Ethanamide crystals nearly always look wet.Organic compounds of the form RC(=O)NRRThis article is about organic amides with the formula RC(=O)NRR. For the anion NH2, see Azanide. For other uses, see Amide (functional group).Not to be confused with imide.General structure of an amide (specifically, a carboxamide)Formamide, the simplest amideAsparagine (zwitterionic form), an amino acid with a side chain (highlighted) containing an amide groupIn organic chemistry, an amide,[1][2][3] also known as an organic amide or a carboxamide, is a compound with the general formula RC(=O)NRR, where R, R', and R represent any group, typically organyl groups or hydrogen atoms.[4][5] The amide group is called a peptide bond when it is part of the main chain of a protein, and an isopeptide bond when it occurs in a side chain, as in asparagine and glutamine. It can be viewed as a derivative of a carboxylic acid (RC(=O)OH) with the hydroxyl group (OH) replaced by an amino group (NRR); or, equivalently, an acyl (alkanoyl) group (RC(=O)) joined to an amino group.Common amides are formamide (HC(=O)NH2), acetamide (H3CC(=O)NH2), benzamide (C6H5C(=O)NH2), and dimethylformamide (HC(=O)N(CH3)2). Some uncommon examples of amides are N-chloroacetamide (H3CC(=O)NHCl) and chloroformamide (ClC(=O)NH2).Amides are qualified as primary, secondary, and tertiary according to the number of acyl groups bounded to the nitrogen atom.[5][6]Main article: IUPAC nomenclature of organic chemistry Amines and amidesThe core C(=O)(N) of amides is called the amide group (specifically, carboxamide group).In the usual nomenclature, one adds the term "amide" to the stem of the parent acid's name. For instance, the amide derived from acetic acid is named acetamide (CH3CONH2). IUPAC recommends ethanamide, but this and related formal names are rarely encountered. When the amide is derived from a primary or secondary amine, the substituents on nitrogen are indicated first in the name. Thus, the amide formed from dimethylamine and acetic acid is N,N-dimethylacetamide (CH3CONMe2, where Me = CH3). Usually even this name is simplified to dimethylacetamide. Cyclic amides are called lactams; they are necessarily secondary or tertiary amides.[5][7]See also: polyamide and peptide bondAmides are pervasive in nature and technology. Proteins and important plastics like nylons, aramids, Twaron, and Kevlar are polymers whose units are connected by amide groups (polyamides); these linkages are easily formed, confer structural rigidity, and resist hydrolysis. Amides include many other important biological compounds, as well as many drugs like paracetamol, penicillin and LSD.[8] Low-molecular-weight amides, such as dimethylformamide, are common solvents.Structure of acetamide hydrogen-bonded dimer from X-ray crystallography. Selected distances: C-O: 1.243, C-N, 1.325, N---O, 2.925 . Color code: red = O, blue = N, gray = C, white = H.[9]The lone pair of electrons on the nitrogen atom is delocalized into the Carbonyl group, thus forming a partial double bond between nitrogen and carbon. In fact the O, C and N atoms have molecular orbitals occupied by delocalized electrons, forming a conjugated system. Consequently, the three bonds of the nitrogen in amides is not pyramidal (as in the amines) but planar. This planar restriction prevents rotations about the N linkage and thus has important consequences for the mechanical properties of bulk material of such molecules, and also for the configurational properties of macromolecules built by such bonds. The inability to rotate distinguishes amide groups from ester groups which allow rotation and thus create more flexible bulk material.The C-C(O)NR2 core of amides is planar. The C=O distance is shorter than the C-N distance by almost 10%. The structure of an amide can be described also as a resonance between two alternative structures: neutral (A) and zwitterionic (B).It is estimated that for acetamide, structure A makes a 62% contribution to the structure, while structure B makes a 28% contribution (these figures do not sum to 100% because there are additional less-important resonance forms that are not depicted above). There is also a hydrogen bond present between the hydrogen and nitrogen atoms in the active groups.[10] Resonance is largely prevented in the very strained quinuclidone.In their IR spectra, amides exhibit a moderately intense CO band near 1650cm1. The energy of this band is about 60cm1 lower than for the CO of esters and ketones. This difference reflects the contribution of the zwitterionic resonance structure.Compared to amines, amides are very weak bases. While the conjugate acid of an amine has a pKa of about 9.5, the conjugate acid of an amide has a pKa around 0.5. Therefore, compared to amines, amides do not have acidbase properties that are as noticeable in water. This relative lack of basicity is explained by the withdrawing of electrons from the amine by the carbonyl. On the other hand, amides are much stronger bases than carboxylic acids, esters, aldehydes, and ketones (their conjugate acids' pKas are between 6 and 10).The proton of a primary or secondary amide does not dissociate readily; its pKa is usually well above 15. Conversely, under extremely acidic conditions, the carbonyl oxygen can become protonated with a pKa of roughly 1. It is not only because of the positive charge on the nitrogen but also because of the negative charge on the oxygen gained through resonance.Because of the greater electronegativity of oxygen than nitrogen, the carbonyl (C=O) is a stronger dipole than the NC dipole. The presence of a C=O dipole and, to a lesser extent a NC dipole, allows amides to act as H-bond acceptors. In primary and secondary amides, the presence of NH dipoles allows amides to function as H-bond donors as well. Thus amides can participate in hydrogen bonding with water and other protic solvents; the oxygen atom can accept hydrogen bonds from water and the NH hydrogen atoms can donate H-bonds.

As a result of interactions such as these, the water solubility of amides is greater than that of corresponding hydrocarbons. These hydrogen bonds also have an important role in the secondary structure of proteins.The solubilities of amides and esters are roughly comparable. Typically amides are less soluble than comparable amines and carboxylic acids since these compounds can both donate and accept hydrogen bonds. Tertiary amides, with the important exception of N,N-dimethylformamide, exhibit low solubility in water.Amides do not readily participate in nucleophilic substitution reactions. Amides are stable to water, and are roughly 100 times more stable towards hydrolysis than esters.[citation needed] Amides can, however, be hydrolyzed to carboxylic acids in the presence of acid or base. The stability of amide bonds has biological implications, since the amino acids that make up proteins are linked with amide bonds. Amide bonds are resistant enough to hydrolysis to maintain protein structure in aqueous environments but are susceptible to catalyzed hydrolysis.[citation needed]Primary and secondary amides do not react usefully with carbon nucleophiles. Instead, Grignard reagents and organolithiums deprotonate an amide N-H bond. Tertiary amides do not experience this problem, and react with carbon nucleophiles to give ketones; the amide anion (NR2) is a very strong base and thus a very poor leaving group, so nucleophilic attack only occurs once. When reacted with carbon nucleophiles, N,N-dimethylformamide (DMF) can be used to introduce a formyl group.[11]Because tertiary amides only react once with organolithiums, they can be used to introduce aldehyde and ketone functionalities. Here, DMF serves as a source of the formyl group in the synthesis of benzaldehyde.Here, phenyllithium 1 attacks the carbonyl group of DMF 2, giving tetrahedral intermediate 3. Because the dimethylamide anion is a poor leaving group, the intermediate does not collapse and another nucleophilic addition does not occur. Upon acidic workup, the alkoxide is protonated to give 4, then the amine is protonated to give 5. Elimination of a neutral molecule of dimethylamine and loss of a proton give benzaldehyde, 6.Mechanism for acid-mediated hydrolysis of an amide.[12]Amides hydrolyse in hot alkali as well as in strong acidic conditions. Acidic conditions yield the carboxylic acid and the ammonium ion while basic hydrolysis yield the carboxylate ion and ammonia. The protonation of the initially generated amine under acidic conditions and the deprotonation of the initially generated carboxylic acid under basic conditions render these processes non-catalytic and irreversible. Electrophiles other than protons react with the carbonyl oxygen. This step often precedes hydrolysis, which is catalyzed by both Brnsted acids and Lewis acids. Peptidase enzymes and some synthetic catalysts often operate by attachment of electrophiles to the carbonyl oxygen.Reaction nameProductCommentDehydrationNitrileReagent: phosphorus pentoxide; benzenesulfonyl chloride; TFAA/py[13]Hofmann rearrangementAmine with one fewer carbon atomReagents: bromine and sodium hydroxideAmide reductionAmines, aldehydesReagent: lithium aluminium hydride followed by hydrolysisVilsmeierHaack reactionAldehyde (via imine)POCl3, aromatic substrate, formamideBischlerNapieralski reactionCyclic aryl iminePOCl3, SOCl2, etc.Tautomeric chlorinationImidoyl chlorideOxophilic halogenating agents, e.g. COCl2 or SOCl2Amides are usually prepared by coupling a carboxylic acid with an amine. The direct reaction generally requires high temperatures to drive off the water:RCO2H + R'2NH RCO2 + R'2NH+2RCO2 + R'2NH+2 RC(O)NR'2 + H2OEsters are far superior[further explanation needed] substrates relative to carboxylic acids.[14][15][16][bettersourceneeded]Further "activating" both acid chlorides (Schotten-Baumann reaction) and anhydrides (LumireBarbier method) react with amines to give amides:RCO2R" + R'2NH RC(O)NR'2 + R"OHRCOCl + 2R'2NH RC(O)NR'2 + R'2NH+2Cl(RCO)2O + R'2NH RC(O)NR'2 + RCO2HPeptide synthesis use coupling agents such as HATU, HOBt, or PyBOP.[17]The hydrolysis of nitriles is conducted on an industrial scale to produce fatty amides.[18] Laboratory procedures are also available.[19]Many specialized methods also yield amides.[20] A variety of reagents, e.g. tris(2,2,2-trifluoroethyl) borate have been developed for specialized applications.[21][22]Specialty Routes to AmidesReaction nameSubstrateDetailsBeckmann rearrangementCyclic ketoneReagent: hydroxylamine and acidSchmidt reactionKetonesReagent: hydrazoic acidWillgerodtKindler reactionAryl alkyl ketonesSulfur and morpholinePasserini reactionCarboxylic acid, ketone or aldehydeUgi reactionIsocyanide, carboxylic acid, ketone, primary amineBodroux reaction[23][24]Carboxylic acid, Grignard reagent with an aniline derivative ArNHR'Chapman rearrangement[25][26]Aryl imino etherFor N,N-diaryl amides. The reaction mechanism is based on a nucleophilic aromatic substitution.[27]Leuckart amide synthesis[28]IsocyanateReaction of arene with isocyanate catalysed by aluminium trichloride, formation of aromatic amide.Ritter reaction[29]Alkenes, alcohols, or other carbonium ion sourcesSecondary amides via an addition reaction between a nitrile and a carbonium ion in the presence of concentrated acids.Photolytic addition of formamide to olefins[30]Terminal alkenesA free radical homologation reaction between a terminal alkene and formamide.Dehydrogenative coupling[31]alcohol, aminerequires ruthenium dehydrogenation catalystTransamidation[32][33]amidetypically slowAmidogenAmino radicalAmidicityImidic acidMetal amides^ "Amide definition and meaning - Collins English Dictionary". www.collinsdictionary.com. Retrieved 15 April 2018.^ "amide". The American Heritage Dictionary of the English Language (5thed.). HarperCollins.^ "amide - Definition of amide in English by Oxford Dictionaries". 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PMID27199089.Wikiquote has quotations related to Amide.IUPAC Compendium of Chemical TerminologyRetrieved from " updated: May 14th, 2025 | Synthesis, Nomenclature, and Properties Of The Amide Functional GroupIn this post, well try to provide a broad overview of amides. Well provide a brief overview of amide nomenclature, two important properties of amides that differ greatly from amines, and go over three key strategies for amide synthesis.Table of Contents 1. Nomenclature of The Amide Functional Group: Primary, Secondary, and Tertiary AmidesAmides are what we call an amine that has a single attached carbonyl group. The amide functional group is to amines as esters are to alcohols.Confusingly, the word amide is also used to refer to the conjugate base of amines, such as sodium amide (NaNH2) and lithium di-isopropylamide (LDA). The latter are sometimes differentiated by referring to them as amide bases. Others will use slightly different pronunciation to differentiate the two (ayyy-myde and aaah-midd). As with any other homonym, the key is context.As with amines, the nomenclature used for an amide depends on the number of carbons attached to the nitrogen.A primary (1) amide has nitrogen attached to a single carbon; a secondary (2) amide has the nitrogen attached to two carbons; a tertiary (3) amide has the nitrogen attached to three carbons. A cyclic amide is called a lactam.When the amide nitrogen has substituents other than hydrogen, we specify them using the prefixN-to avoid confusion. For example, N-methylpropionamidespecifies the attachment of a methyl groups on the nitrogen; without theN prefix, one might assume that the methyl group was attached to carbon, which would be an entirely different molecule.2. Amides vs Amines: Less Basic, More AcidicAttaching a carbonyl group to an amine has two drastic effects on the properties of the nitrogen.First, amide nitrogens are considerably less basic than amine nitrogens. Thats mainly the result of the delocalization of the nitrogen lone pair into the pi bond of the carbonyl. In fact, the most basic position of an amide is not the nitrogen but the oxygen (!). [Note 1]Second, the NH bonds of amides are much more acidic than the NH bonds of amines. Why? Delocalization again. The attached carbonyl group allows the lone pair of the conjugate base to be delocalized through resonance. The pKa of acetamide (17) is about 20 orders of magnitude more acidic than ammonia (38).A third, more subtle property of amides is that they usually have restricted rotation about the CN bond. The resonance form where there is a C-N bond makes such a significant contribution to the resonance hybrid that one can think of the CN bond as having partial double-bond character. [In this post on Conjugation and Resonance, we saw that bridgehead amides, which lack the necessary orbital overlap for this resonance to occur, are orders of magnitude more unstable than conventional amides.]3. Synthesis of Amides, Part 1. Nucleophilic Acyl Substitution of Acyl Halides (or Anhydrides) With AminesAcyl groups attached to a good leaving group such as acid chlorides or acid anhydrides can easily undergo nucleophilic acyl substitution with amine nucleophiles.If only the carboxylic acid is available to start with, using a reagent like thionyl chloride (SOCl2) to convert a carboxylic acid to an acid chloride is a good first step in transforming a carboxylic acid to an amide. (PCl3, PCl5, oxalyl chloride and a host of other reagents can also work).Alternatively, treating a carboxylic acid with an acyl halide will deliver an anhydride, which can also be effective.Halides (e.g. Cl) and carboxylates (RCO2) are much weaker bases, and thus much better leaving groups than HO. So by adding an amine to an acyl halide or acid anhydride, nucleophilic acyl substitution can occur under much milder conditions, resulting in our desired amide.(One can obtain amides through the reaction of esters with amines, but given that alkoxides [RO] are poorer leaving groups than halides or carboxylates, this method requires more forcing conditions.)One thing to note with acid halides is that the process generates a single equivalent of HCl as a byproduct. In the absence of any additional base, the maximum yield of the procedure would be 50%, since the HCl would protonate any amine and render it a non-nucleophilic ammonium salt.One way to ensure the reaction proceeds to completion is to add a second equivalent of amine. There are other practical ways of resolving this issue, which Ive consigned to Note 2 .If you need a refresher on the mechanism of nucleophilic acyl substitution hover here for a pop-up image or open image link here:[click here and an image of the mechanism will pop up].4. Synthesis of Amides, Part 2: Partial Hydrolysis of NitrilesOne way to think of nitriles is that they are masked carboxylic acids. If treated with aqueous acid and a lot of heat sledgehammer conditions they can be hydrolyzed to carboxylic acids.One of the intermediates in this process is a primary amide.So if we use a slightly kinder, gentler sledgehammer technique, sometimes its possible to salvage the amide out of our reaction mixture before its hydrolyzed to the carboxylic acid.The image below shows how one could synthesize an amide from an alkyl halide precursor, via the good-ol SN2 reaction:Whats meant by mild ? One set of conditions for the hydrolysis of phenylacetamide (PhCH2CN) to PhCH2CONH2 gives the reaction conditions as HCl, H2O, 40-50C, 1h . [for a lovingly detailed experimental procedure, go here]5. Synthesis Of Amides, Part 3: Use Of A Dehydrating Reagent (Such As DCC)The synthesis of penicillin V in 1957 by John Sheehans group at MIT stands as one of the heroic achievements of postwar-era organic chemistry. The key problem was construction of a cyclic amide (the -lactam ring) which is extremely unstable under acidic conditions. This was of no small importance, as the -lactam is also key to penicillins mechanism of action: interfering with synthesis of the bacterial cell wall. Attempts to make this cyclic amide by converting a carboxylic acid to an acyl halide with SOCl2, PCl3, PCl5, and a host of other methods all failed. [Note 3]In response, Sheehans group cleverly invented a very mild dehydrating reagent:N, N-dicyclohexylcarbodiimide (DCC) which allowed for the formation of amides under very mild conditions at neutral pH.Today, DCC (and its more practical (Note 4) cousin, EDC)are extensively used for the synthesis of sensitive amides particularly peptides under very mild conditions.Under the reaction conditions, the carboxylate oxygen attaches to the electrophilic carbon of DCC, making what we call an active ester in other words, an ester that actually has a decent leaving group (unlike most esters, which dont). The active ester is then attacked by the amine in a classic nucleophilic acyl substitution, which leads to the formation of the amide.Looking at the byproduct, note that there are two hydrogens (each attached to nitrogen) and an oxygen (attached to the central carbon). Thats where the H2O has gone!Because this post is likely long enough as it is, hover here for a pop-up image or open image link here:Since this reaction occurs under neutral conditions, it is extremely useful in the synthesis of peptides, which can undergo racemization (epimerization, actually) under both basic and acidic conditions.6. Summary: Three Effective Methods For The Synthesis of AmidesLets end by summarizing these three important (but by no means exhaustive) ways to make amides:This concludes our post on the main points of amide nomenclature, properties, and synthesis. For a bonus method of amide synthesis, read on.7. Let Us Briefly Consider A Fourth, Less Important Method: Brute ForceSince its usually covered in the textbooks, lets conclude by considering a fourth possibility the simplest one imaginable. What if wetake a carboxylic acid and combine it with an amine, hoping that an amide will form. What happens?Amines are bases, and carboxylic acids are, well, acids. Add the two together and you get an innocuous salt.Sometimes one can make amides through heating the living daylights out of this salt in a sealed tube, driving off an equivalent of water. This method is calledpyrolysis.The method is nothing if not direct, and has all the subtlety of a howitzer.The problem with pyrolysis is that the HOgroup of a carboxylic acid is a terrible leaving group.In order to form an amide from this species, the carboxylate oxygen (O) must somehow depart. This is not an easy thing to do, as the conjugate base of Ois the double anion O2. In any list of leaving groups, O2 would rank somewhere between, shitty and f&cking awful.However, if one hits this salt with the chemical equivalent of the Hammer of Thor: brute-force, high heat, a series of proton transfers from the ammonium salt can occur. eventually liberating H2O and forming the C-N bond.This process is calledpyrolysis(pyro = fire,lysis= breaking).In certain cases, especially simple amides, and also in the formation of simple lactams, the process can be satisfactory.In many other cases, however, it results in the formation of a black tar at the bottom of your flask from which no useful product may be obtained.As any organic chemist can tell you, there are many diverse ways to create intractable black tars at the bottom of your flask, and this is just one method. Think of how much you still have to discover!Hammer of Thor Google Image Search was chemistry-related, but surprisingly NSFW. Notes[related articles]A fun, related article: Amides: Humble But Useful(from Chemical & Engineering News).Note 1. Theres also an inductive effect, whereby the electronegative oxygen (electronegativity of 3.44) tugs on the electrons of the attached carbon, which in turn tugs on the electrons of the nitrogen.Note 2. A very common way of carrying out this reaction is to use what are called, Schotten-Baumann conditions, where one takes up the reactants in solvent like diethyl ether or dichoromethane, and adds an aqueous solution of NaOH, resulting in a biphasic mixture. Any ammonium salts that form can dissolve in the aqueous phase, whereupon they are neutralized by the excess base and return to the organic phase. Amines are generally far more nucleophilic than hydroxide ions, so hydrolysis of the acid chloride to give a carboxylic acid is generally not a problem.Note 3.At the time of my successful synthesis of penicillin V in 1957, I compared the problem of trying to synthesize penicillin by classical methods to that of attempting to repair the mainspring of a fine watch with a blacksmiths anvil, hammer, and tongs John C. SheehanNote 4. The problem with using DCC is that the byproduct, DCU, is a tremendous pain in the ass to get rid of. Most byproducts are easily removed using column chromatography. Not DCU. Paying little heed to solvent polarity , DCU emerges from a column slowly, in drips and drabs, contaminating every fraction as it goes. EDC [1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide]is a variant of DCC that has a tertiary amine unit; thus, a simple acid wash during workup will remove all the urea, saving a lot of time and headache.The following image shows the last step of Sheehans synthesis using DCC.Image: Carmen Drahl/Chemical & Engineering News Quiz Yourself! Become a MOC member to see the clickable quiz with answers on the back. Become a MOC member to see the clickable quiz with answers on the back. Become a MOC member to see the clickable quiz with answers on the back. Become a MOC member to see the clickable quiz with answers on the back. Become a MOC member to see the clickable quiz with answers on the back. Become a MOC member to see the clickable quiz with answers on the back. (Advanced) References and Further ReadingNitrile hydrolysis:PHENYLACETAMIDEWilhelm WennerOrg Synth. 1952, 32, 92DOI: 10.15227/orgsyn.032.0092The conditions used here for hydration of the nitrile to the amide are rather gentle this uses a temperature of 40 C for approximately 1 hr.Halide-directed nitrile hydrolysisJames M. PhotisTetrahedron Lett. 1980, 21 (37), 3539-3540DOI: 10.1016/0040-4039(80)80228-0This is a useful procedure for selective hydrolysis of nitriles to primary amides, especially in the case of aroyl cyanides (e.g. PhCOCN).Facile and Highly Selective Conversion of Nitriles to Amides via Indirect Acid-Catalyzed Hydration Using TFA or AcOHH2SO4Jarugu Narasimha Moorthy and Nidhi SinghalThe Journal of Organic Chemistry 2005, 70 (5), 1926-1929DOI: 10.1021/jo048240aSchotten-Bauman Reaction:#4 and #5 are the original papers by Schotten and Baumann on a simple biphase amide synthesis.Ueber die Oxydation des PiperidinsSchotten, C. Ber. 1884, 17 (2), 2544-2547DOI: 10.1002/cber.188401702178Ueber eine einfache Methode der Darstellung von BenzosurethernBaumann, E. Ber. 1886, 19 (2), 3218-3222DOI: 10.1002/cber.188601902348Enantioselective Total Synthesis of ()-Kibdelone CJohn R. Butler, Chao Wang, Jianwei Bian, and Joseph M. ReadyJournal of the American Chemical Society 2011, 133 (26), 9956-9959DOI: 1021/ja204040kThe humble Schotten-Baumann reaction is even used in demanding total syntheses in this case, it is used to make the lactam in 4 from 5 and 6!BENZOYL PIPERIDINEMarvel, C. S.; Lazier, W. A.Org. Synth. 1929, 9, 16DOI: 10.15227/orgsyn.009.0016This procedure from Organic Syntheses, a source of independently tested and reproducible synthetic organic laboratory procedures, is a classic Schotten-Baumann amide synthesis.A High-Throughput Process for ValsartanUlrich Beutler, Matthias Boehm, Peter C. Fuenfschilling, Thomas Heinz, Jean-Paul Mutz, Ulrich Onken, Martin Mueller, and Werner ZauggOrganic Process Research & Development 2007, 11 (5), 892-898DOI: 1021/op700120nOrganic Process & Research Development (OPRD) is a great journal for process or scale-up chemistry. This paper shows how the Schotten-Baumann reaction (4 to 3) is preferred for large-scale reactions as it is simple, robust, easily carried out, and does not have large exotherms (unlike the Grignard reaction, for instance).The nylon rope trick: Demonstration of condensation polymerizationPaul W. Morgan and Stephanie L. KwolekJournal of Chemical Education 1959, 36 (4), 182DOI: 1021/ed036p182The classic nylon rope trick in which one pulls a string of nylon from a biphasic mixture of hexamethylenediamine and sebacoyl chloride can be considered a type of Schotten-Baumann reaction, in that it forms a polyamide! This was first developed by Stephanie Kwolek, who was a distinguished chemist at DuPont for over 40 years and was responsible for discovering Kevlar and developing the chemistry of aramids and other high-tensile strength materials.DCC:A New Method of Forming Peptide BondsJohn C. Sheehan and George P. HessJournal of the American Chemical Society 1955, 77 (4), 1067-1068DOI: 1021/ja01609a099Original paper on the synthesis of peptide bonds/amide bonds using DCC.DeTar has published a series of papers studying the mechanism of the bond-forming reactions mediated by DCC and other carbodiimides, and here are the first two:Reactions of Carbodiimides. I. The Mechanisms of the Reactions of Acetic Acid with DicyclohexylcarbodiimideDeLos F. DeTar and Richard SilversteinJournal of the American Chemical Society 1966, 88 (5), 1013-1019DOI: 10.1021/ja00957a027Reactions of Carbodiimides. II. The Reactions of Dicyclohexylcarbodiimide with Carboxylic Acids in the Presence of Amines and PhenolsDeLos F. DeTar and Richard SilversteinJournal of the American Chemical Society 1966, 88 (5), 1020-1023DOI:1021/ja00957a028The Chemistry of Carbodiimides. G. KhoranaChemical Reviews 1953, 53 (2), 145-166DOI: 10.1021/cr60165a001An old review by Prof. Har Gobind Khorana, who later received the Nobel Prize in Medicine for his work demonstrating that the nucleotides in DNA and RNA code for protein synthesis.ESTERIFICATION OF CARBOXYLIC ACIDS WITH DICYCLOHEXYLCARBODIIMIDE/4-DIMETHYLAMINOPYRIDINE: tert-BUTYL ETHYL FUMARATENeises and Wolfgang SteglichOrg. Synth. 1985, 63, 183DOI: 10.15227/orgsyn.063.0183This is a procedure for selective esterification using DCC this avoids transesterification that would occur under usual Fischer esterification conditions. This procedure is from Organic Syntheses, a source of reliable, independently tested synthetic organic reactions.Solid Phase Peptide Synthesis. I. The Synthesis of a Tetrapeptide B. MerrifieldJournal of the American Chemical Society 1963, 85 (14), 2149-2154DOI: 10.1021/ja00897a025This is one of the most highly cited papers in JACS, and for good reason it basically lays the foundation of SPPS, and what is now a billion-dollar industry. This work led to a Nobel Prize in Chemistry for the author, Prof. R. Bruce Merrifield (Rockefeller U.). The peptide couplings are done using none other than DCC.Notes- A Convenient Synthesis of Water-Soluble Carbodiimides.John Sheehan, Philip Cruickshank, and Gregory BoshartThe Journal of Organic Chemistry 1961, 26 (7), 2525-2528DOI:1021/jo01351a600The major drawback with DCC is that separating the DCU (dicyclohexylurea) thus produced can be cumbersome. Thus other reagents, such as EDC (1Ethyl3(3dimethylaminopropyl)carbodiimide) have been developed, for which the resulting urea is water-soluble and easily removed by extraction.Total synthesis of a monocyclic peptide lactone antibiotic, etamycinJohn C. Sheehan and Stephen L. LedisJournal of the American Chemical Society 1973, 95 (3), 875-879DOI:1021/ja00784a041EDC was used for most of the peptide couplings in the synthesis of this peptide, which is one of the first cyclic peptides to be synthetically produced. 21.7 Chemistry of Amides Amides, like esters, are abundant in all living organisms. Proteins, nucleic acids, and many pharmaceutical agents have amide functional groups. The reason for this abundance of amides is that they are stable in the aqueous conditions found in living organisms. Amides are the least reactive of the common acid derivatives and undergo relatively few nucleophilic acyl substitution reactions. Amides are usually prepared by reaction of an amine with an acid chloride (Section 21.4). Ammonia, monosubstituted amines, and disubstituted amines all undergo the reaction. Amides undergo hydrolysis to yield carboxylic acids plus ammonia or an amine upon heating in either aqueous acid or aqueous base. The conditions required for amide hydrolysis are more extreme than those required for the hydrolysis of acid chlorides or esters, but the mechanisms are similar. Acidic hydrolysis reaction occurs by nucleophilic addition of water to the protonated amide, followed by transfer of a proton from oxygen to nitrogen to make the nitrogen a better leaving group, and subsequent elimination. The steps are reversible, with the equilibrium shifted toward product by protonation of NH3 in the final step. Basic hydrolysis occurs by nucleophilic addition of OH to the amide carbonyl group, followed by elimination of amide ion (NH2) and subsequent deprotonation of the initially formed carboxylic acid by ammonia. The steps are reversible, with the equilibrium shifted toward product by the final deprotonation of the carboxylic acid. Basic hydrolysis is substantially more difficult than the analogous acid-catalyzed reaction because amide ion is a very poor leaving group, making the elimination step difficult. Amide hydrolysis is common in biological chemistry. Just as the hydrolysis of esters is the initial step in the digestion of dietary fats, the hydrolysis of amides is the initial step in the digestion of dietary proteins. The reaction is catalyzed by protease enzymes and occurs by a mechanism almost identical to what we just saw for fat hydrolysis. That is, an initial nucleophilic acyl substitution of an alcohol group in the enzyme on an amide linkage in the protein gives an acyl enzyme intermediate, which then undergoes hydrolysis. Like other carboxylic acid derivatives, amides can be reduced by LiAlH4. The product of the reduction, however, is an amine rather than an alcohol. The net effect of an amide reduction is thus the conversion of the amide carbonyl group into a methylene group (C=OCH2C=OCH2). This kind of reaction is specific to amides and does not occur with other carboxylic acid derivatives. Amide reduction occurs by nucleophilic addition of hydride ion to the amide carbonyl group, followed by expulsion of the oxygen atom as an aluminate anion leaving group to give an iminium ion intermediate. The intermediate iminium ion is further reduced by LiAlH4 to yield the amine. The reaction is effective with both acyclic and cyclic amides, or lactams, and is a good method for preparing cyclic amines. How could you prepare N-ethylaniline by reduction of an amide with LiAlH4? Strategy Reduction of an amide with LiAlH4 yields an amine. To find the starting material for synthesis of N-ethylaniline, look for a CH2 position next to the nitrogen atom and replace that CH2 by COCO. In this case, the amide is N-phenylacetamide. Solution Problem 21-20 How would you convert N-ethylbenzamide to each of the following products? Problem 21-21 How would you use the reaction of an amide with LiAlH4 as the key step in going from bromocyclohexane to (N,N-dimethylaminomethyl)cyclohexane? Write all the steps in the reaction sequence. An amide is a fundamental class of organic compounds characterized by their distinct chemical structure, consisting of a carbonyl group (C=O) bonded to a nitrogen atom (N). This carbonyl-nitrogen linkage is a defining feature of amides and imparts unique properties and reactivity to these compounds [1-4]. Amides are often considered derivatives of carboxylic acids, where the hydroxyl (-OH) group of the carboxylic acid is replaced by an amino (-NH2) group. This substitution results in the formation of the amide linkage, represented as -CONH2. The fundamental structure of an amide consists of a carbonyl group (C=O) bonded to a nitrogen atom (N) with a single bond, and the nitrogen atom is also bonded to two additional substituents, typically hydrogen atoms (H). Thus, the central carbon atom in the carbonyl group is bonded to three distinct atoms or groups: a double-bonded oxygen atom, a nitrogen atom, and a substituent group (R) that can vary in size and complexity [1-5]. Amides can be classified into three main categories based on the number of alkyl or aryl groups attached to the nitrogen atom: primary, secondary, and tertiary amides [1-3]. Primary amides are amides in which the nitrogen atom is bonded to one hydrogen atom and two carbon atoms. The general formula for primary amides is RCONH2, where R represents an alkyl or aryl group. Primary amides are often considered the simplest and most common type of amides. They find numerous applications in organic synthesis and the pharmaceutical industry due to their versatility in forming various compounds and functional groups. Secondary amides have two alkyl or aryl groups and one hydrogen atom bonded to the nitrogen atom. Their general formula is RCONHR, where R and R represent different alkyl or aryl groups. Secondary amides are intermediates in various chemical reactions and are often used to synthesize complex organic molecules. Their distinct structure allows them to participate in amide bond formation, which is crucial in peptide and protein synthesis. Tertiary amides are amides in which the nitrogen atom is bonded to three alkyl or aryl groups, with no hydrogen atoms directly attached to nitrogen. Their general formula is RCONRR, where R, R, and R represent different alkyl or aryl groups. Tertiary amides are relatively stable and less reactive than primary and secondary amides. They are commonly found in natural products and some pharmaceutical compounds. Naming amides using IUPAC rules generally involves identifying the parent carboxylic acid and the amine component from which the amide is derived. Here are the key steps [1,2]: Select the longest carbon chain containing the carbonyl group (C=O). The name of this carboxylic acid serves as the base name.Replace the -oic acid ending of the carboxylic acid name with -amide. This change indicates the presence of an amide functional group.Specify the substituents on the nitrogen atom of the amide group using prefixes like N-substituted alkyl or aryl groups.Number the carbon atoms in the parent chain to indicate the position of any substituents on the chain.List the substituents, their positions, and the base name, separated by hyphens. Arrange them alphabetically, ignoring any numerical prefixes like di- or tri-. Use numerical locants to indicate the positions of substituents. Here are some examples: Acetamide is derived from acetic acid and given by the formula H3CCONH2.Benzamide is derived from benzoic acid with the formula C6H5CONH2.N-methylacetamide is an example of an amide with a common name that specifies a substituent on the nitrogen atom. It is derived from acetamide by replacing one of its hydrogen atoms with a methyl group. Its formula is H3CCONHCH3. Amides can be synthesized through acylation, a standard method involving the reaction between an acyl chloride (RCOCl) and an amine (RNH2) in the presence of a base such as sodium hydroxide (NaOH). This process forms an amide bond, releasing water as a byproduct. This amide formation is known as the Schotten-Baumann reaction [1-3]. For example, acetal chloride (CH3COCl) reacts with methylamine (CH3NH2) in the presence of sodium hydroxide (NaOH) to produce N-methylacetamide (CH3CONHCH3). The reaction proceeds as follows: CH3COCl + CH3NH2 + NaOH CH3CONHCH3 + NaCl + H2O Amides exhibit intriguing chemical properties due to the carbonyl groups presence within their structure. This carbonyl group is polarized, with the carbon atom being partially positively charged and the oxygen atom partially negatively charged. Consequently, amides can undergo various reactions, including hydrolysis. The reactivity of amides depends on the nature of the substituents attached to the nitrogen atom and the reaction conditions, making them valuable intermediates in organic synthesis [1,2]. One of the fundamental chemical properties of amides is their susceptibility to hydrolysis, a reaction in which water molecules break the amide bond. This hydrolysis can occur under both acidic and alkaline conditions. In acidic hydrolysis, the amide bond is cleaved to yield a carboxylic acid and an ammonium or ammine salt. RCONH2 + H2O + H+ X + heat RCOOH + NH4+ X RCONHR + H2O + H+ X + heat RCOOH + RNH3+ X In contrast, alkaline hydrolysis results in the formation of a carboxylic acid and ammonia or amine. RCONH2 + H2O + heat RCOOH + NH3 RCONHR + H2O + heat RCOOH + RNH2 Where X is a halide.

Naming amide. Naming n substituted amides.

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- https://indianpowerliftingfederation.in/userfiles/file/56154182812.pdf
- galogujocu
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- to god be the glory lyrics and chords key of g
- diceka
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