Carboxylic Acids and Nitriles

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The Importance of Carboxylic Acids (RCO₂H)

- Starting materials for acyl derivatives (esters, amides, and acid chlorides)
- Abundant in nature from oxidation of aldehydes and alcohols in metabolism
 - Acetic acid, CH₃CO₂H, vinegar
 - Butanoic acid, CH₃CH₂CH₂CO₂H (rancid butter)
 - Long-chain aliphatic acids from the breakdown of fats

20.1 Naming Carboxylic Acids and Nitriles



Alternative Names

- Compounds with —CO₂H bonded to a ring are named using the suffix -*carboxylic acid*
- The CO₂H carbon is not itself numbered in this system
- Use common names for formic acid (HCOOH) and acetic acid (CH₃COOH) – see Table 20.1





3-Bromocyclohexanecarboxylic acid

1-Cyclopentenecarboxylic acid

Based on McMurry, Organic Chemistry, Chapter 20, 6th edition, (c) 2003

Nitriles, RC≡N

- Closely related to carboxylic acids named by adding nitrile as a suffix to the alkane name, with the nitrile carbon numbered C1
- Complex nitriles are named as derivatives of carboxylic acids.
 - Replace -ic acid or -oic acid ending with -onitrile



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20.2 Structure and Physical Properties of Carboxylic Acids

- Carboxyl carbon sp² hybridized: carboxylic acid groups are planar with C–C=O and O=C–O bond angles of approximately 120°
- Carboxylic acids form hydrogen bonds, existing as cyclic dimers held together by two hydrogen bonds
- Strong hydrogen bonding causes much higher boiling points than the corresponding alcohols

20.3 Dissociation of Carboxylic Acids

- Carboxylic acids are proton donors toward weak and strong bases, producing metal carboxylate salts, RCO₂⁻ +M
- Carboxylic acids with more than six carbons are only slightly soluble in water, but their conjugate base salts are water-soluble



Acidity Constant and pK_a

- Carboxylic acids transfer a proton to water to give H₃O⁺ and carboxylate anions, RCO₂⁻, but H₃O⁺ is a much stronger acid
- The acidity constant, K_a, is about 10⁻⁵ for a typical carboxylic acid (pK_a ~ 5)



Acidity Compared to Alcohols

- Carboxylic acids are better proton donors than are alcohols (The pK_a of ethanol is ~16, compared to ~5 for acetic acid)
- In an alkoxide ion, the negative charge is localized on oxygen while in a carboxylate ion the negative charge is delocalized over two equivalent oxygen atoms, giving resonance stabilization



20.4 Substituent Effects on Acidity

Electronegative substituents promote formation of the carboxylate ion

TABLE 20.4 Acidity of Some Carboxylic Acids

Structure	Ka	р <i>К</i> а	
F_3CCO_2H	0.59	0.23	Ctores 11
$\rm FCH_2CO_2H$	$2.6 imes10^{-3}$	2.59	Stronger acid
$ClCH_2CO_2H$	$1.4 imes10^{-3}$	2.85	
$BrCH_2CO_2H$	$2.1 imes10^{-3}$	2.68	
ICH_2CO_2H	$7.5 imes10^{-4}$	3.12	
HCO_2H	$1.77 imes10^{-4}$	3.75	
$HOCH_2CO_2H$	$1.5 imes10^{-4}$	3.83	
$C_6H_5CO_2H$	$6.46 imes10^{-5}$	4.19	
$H_2C = CHCO_2H$	$5.6 imes10^{-5}$	4.25	
CH_3CO_2H	$1.76 imes10^{-5}$	4.75	
$CH_3CH_2CO_2H$	$1.34 imes10^{-5}$	4.87	Weeken eeid
$CH_3CH_2OH (ethanol)^a$	(10^{-16})	(16)	weaker acid

^aValue for ethanol is shown for reference.

Substituent Effects

- An electronegative group will drive the ionization equilibrium toward dissociation, increasing acidity
- An electron-donating group destabilizes the carboxylate anion and decreases acidity



Electron-withdrawing group stabilizes carboxylate and strengthens acid

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Electron-donating group destabilizes carboxylate and weakens acid

Examples of Inductive Effects on Acidity

- Fluoroacetic, chloroacetic, bromoacetic, and iodoacetic acids are stronger acids than acetic acid
- Multiple electronegative substituents have synergistic effects on acidity



20.5 Substituent Effects in Substituted Benzoic Acids

		$\mathbf{Y} - \mathbf{O}_2 \mathbf{H}$		
	Y	Ka	p <i>K</i> a	
Weaker acid	—он	$3.3 imes10^{-5}$	4.48	Activating groups
	$-OCH_3$	$3.5 imes10^{-5}$	4.46	
	$-CH_3$	$4.3 imes10^{-5}$	4.34	
	-H	$6.46 imes10^{-5}$	4.19	
	-Cl	$1.0 imes10^{-4}$	4.0	Deactivating groups
	—Br	$1.1 imes10^{-4}$	3.96	
	-CHO	$1.8 imes10^{-4}$	3.75	
	-CN	$2.8 imes10^{-4}$	3.55	
	$-NO_2$	$3.9 imes10^{-4}$	3.41	

Aromatic Substituent Effects

- An electron-withdrawing group (-NO₂) increases acidity by stabilizing the carboxylate anion, and an electron-donating (activating) group (OCH₃) decreases acidity by destabilizing the carboxylate anion
- We can use relative pKa's as a calibration for effects on relative free energies of reactions with the same substituents



20.6 Preparation of Carboxylic Acids

- Oxidation of a substituted alkylbenzene with KMnO₄ or Na₂Cr₂O₇ gives a substituted benzoic acid (see Section 16.10)
- 1° and 2° alkyl groups can be oxidized, but tertiary groups are not



From Alkenes

Oxidative cleavage of an alkene with KMnO₄ gives a carboxylic acid if the alkene has at least one vinylic hydrogen (see Section 7.8)



From Alcohols

Oxidation of a primary alcohol or an aldehyde with CrO₃ in aqueous acid



Hydrolysis of Nitriles

- Hot acid or base yields carboxylic acids
- Conversion of an alkyl halide to a nitrile (with cyanide ion) followed by hydrolysis produces a carboxylic acid with one more carbon (RBr \rightarrow RC=N \rightarrow RCO₂H)
- Best with primary halides because elimination reactions occur with secondary or tertiary alkyl halides



Carboxylation of Grignard Reagents

- Grignard reagents react with dry CO₂ to yield a metal carboxylate
- Limited to alkyl halides that can form Grignard reagents (see 17.6)



Mechanism of Grignard Carboxylation

- The organomagnesium halide adds to C=O of carbon dioxide
- Protonation by addition of aqueous HCI in a separate step gives the free carboxylic acid



20.7 Reactions of Carboxylic Acids: An Overview

- Carboxylic acids transfer a proton to a base to give anions, which are good nucleophiles in S_N2 reactions
- Like ketones, carboxylic acids undergo addition of nucleophiles to the carbonyl group
- In addition, carboxylic acids undergo other reactions characteristic of neither alcohols nor ketones



20.8 Reduction of Carboxylic Acids

- Reduced by LiAlH₄ to yield primary alcohols
- The reaction is difficult and often requires heating in tetrahydrofuran solvent to go to completion

$$CH_{3}(CH_{2})_{7}CH = CH(CH_{2})_{7}COH \xrightarrow{1. \text{ LiAlH}_{4}, \text{ THF}} CH_{3}(CH_{2})_{7}CH = CH(CH_{2})_{7}CH_{2}OH \xrightarrow{0 \text{ leic acid}} CH_{3}O^{+} CH_{3}(CH_{2})_{7}CH = CH(CH_{2})_{7}CH_{2}OH \xrightarrow{0 \text{ leic acid}} CI = CH(CH_{2})_{7}CH \xrightarrow{0 \text{ leic acid}} CI = CH$$

Reduction with Borane

- Borane in tetrahydrofuran (BH₃/THF) converts carboxylic acids to primary alcohols selectively
- Preferable to LiAlH₄ because of its relative ease, safety, and specificity
- Borane reacts faster with COOH than it does with NO₂



20.9 Chemistry of Nitriles

- Nitriles and carboxylic acids both have a carbon atom with three bonds to an electronegative atom, and both contain a π bond
- Both both are electrophiles

$$\mathbf{R} - \mathbf{C} \equiv \mathbf{N} \qquad \mathbf{R} - \mathbf{C} \qquad \mathbf{O} \\ \mathbf{O} \\ \mathbf{O} \\ \mathbf{O} \\ \mathbf{H}$$

A nitrile—three bonds to nitrogen

An acid—three bonds to two oxygens

Preparation of Nitriles by Dehydration

- Reaction of primary amides RCONH₂ with SOCl₂ or POCl₃ (or other dehydrating agents)
- Not limited by steric hindrance or side reactions (as is the reaction of alkyl halides with NaCN)



Mechanism of Dehydration of Amides

Nucleophilic amide oxygen atom attacks SOCl₂ followed by deprotonation and elimination



Reactions of Nitriles

- RC=N is strongly polarized and with an electrophilic carbon atom
- Attacked by nucleophiles to yield sp²-hybridized imine anions



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Hydrolysis: Conversion of Nitriles into Carboxylic Acids

Hydrolyzed in with acid or base catalysis to a carboxylic acid and ammonia or an amine



Mechanism of Hydrolysis of Nitriles

- Nucleophilic addition of hydroxide to C=N bond
- Protonation gives a hydroxy imine, which tautomerizes to an amide
- A second hydroxide adds to the amide carbonyl group and loss of a proton gives a dianion
- Expulsion of NH₂– gives the carboxylate





Reduction: Conversion of Nitriles into Amines

Reduction of a nitrile with LiAIH₄ gives a primary amine



Mechanism of Reduction of $RC \equiv N$

- Nucleophilic addition of hydride ion to the polar C=N bond, yieldis an imine anion
- The C=N bond undergoes a second nucleophilic addition of hydride to give a *dianion*, which is protonated by water



Reaction of Nitriles with Organometallic Reagents

Grignard reagents add to give an intermediate imine anion that is hydrolyzed by addition of water to yield a ketone



20.10 Spectroscopy of Carboxylic Acids and Nitriles. Infrared Spectroscopy

- O–H bond of the carboxyl group gives a very broad absorption 2500 to 3300 cm⁻¹
- C=O bond absorbs sharply between 1710 and 1760 cm⁻¹
- Free carboxyl groups absorb at 1760 cm⁻¹
 - Commonly encountered dimeric carboxyl groups absorb in a broad band centered around 1710 cm⁻¹

IR of Nitriles

- Nitriles show an intense C=N bond absorption near 2250 cm⁻¹ for saturated compounds and 2230 cm⁻¹ for aromatic and conjugated molecules
- This is highly diagnostic for nitriles

Nuclear Magnetic Resonance Spectroscopy

- Carboxyl ¹³COOH signals are at δ 165 to δ 185
- Aromatic and α,β-unsaturated acids are near δ165 and saturated aliphatic acids are near δ185
- ¹³C = N signal δ 115 to δ 130



Proton NMR

- The acidic $-CO_2H$ proton is a singlet near δ 12
- When D₂O is added to the sample the —CO₂H proton is replaced by D causing the absorption to disappear from the NMR spectrum
- Note that the carboxyl proton absorption occurs at δ12.0

