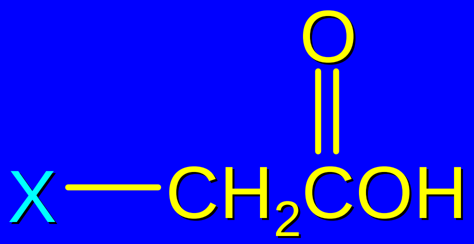
19.6

Substituents and Acid Strength

Substituent Effects on Acidity

standard of comparison is acetic acid   (X = H)

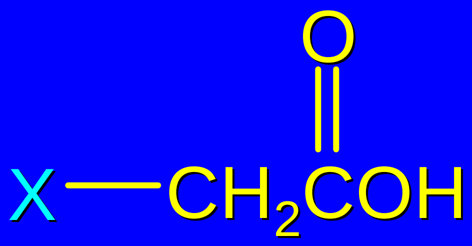


$$X\text{—}CH_2\overset{\overset{\displaystyle O}{\|}}{C}OH$$

$$K_a = 1.8 \times 10^{-5}$$

$$pK_a = 4.7$$

Substituent Effects on Acidity

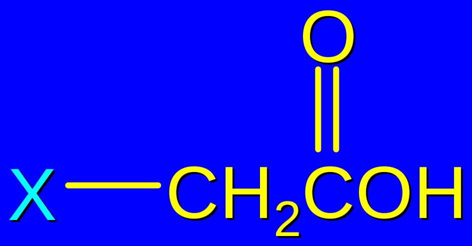


$$\mathrm{X{-}CH_2}\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OH}$$

X	K_a	pK_a
H	1.8×10^{-5}	4.7
CH_3	1.3×10^{-5}	4.9
$CH_3(CH_2)_5$	1.3×10^{-5}	4.9

alkyl substituents have negligible effect

Substituent Effects on Acidity

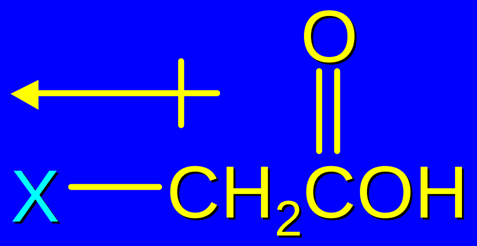


$$X-CH_2\overset{\overset{O}{\|}}{C}OH$$

X	K_a	pK_a
H	1.8×10^{-5}	4.7
F	2.5×10^{-3}	2.6
Cl	1.4×10^{-3}	2.9

electronegative substituents increase acidity

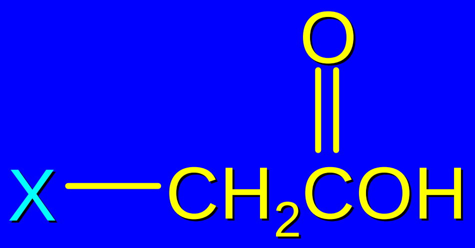
Substituent Effects on Acidity



$X{-}CH_2C(=O)OH$

electronegative substituents withdraw electrons from carboxyl group; increase *K* for loss of H^+

Substituent Effects on Acidity



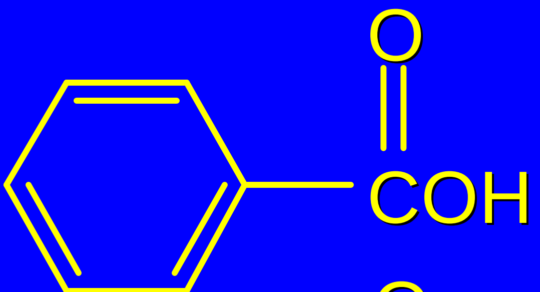
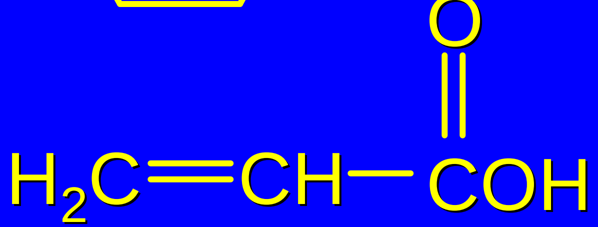
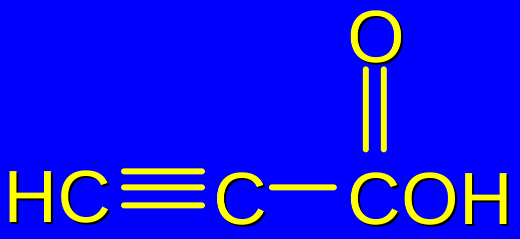
$X-CH_2\overset{\overset{O}{\|}}{C}OH$

X	K_a	pK_a
H	1.8×10^{-5}	4.7
Cl	1.4×10^{-3}	2.9
$ClCH_2$	1.0×10^{-4}	4.0
$ClCH_2CH_2$	3.0×10^{-5}	4.5

effect of electronegative substituent decreases as number of bonds between X and carboxyl group increases

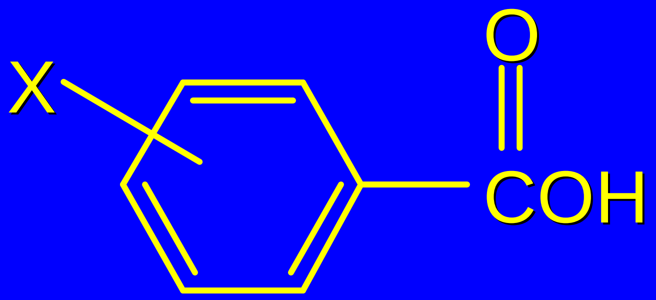
19.7
Ionization of Substituted Benzoic Acids

Hybridization Effect

	K_a	pK_a
	6.3×10^{-5}	4.2
 $H_2C=CH-\overset{O}{\overset{\|}{C}}OH$	5.5×10^{-5}	4.3
 $HC\equiv C-\overset{O}{\overset{\|}{C}}OH$	1.4×10^{-2}	1.8

sp^2-hybridized carbon is more electron-withdrawing than sp^3, and sp is more electron-withdrawing than sp^2

Table 19.3 Ionization of Substituted Benzoic Acids

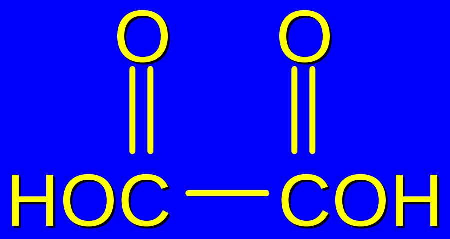
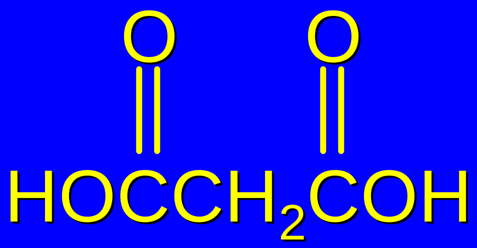
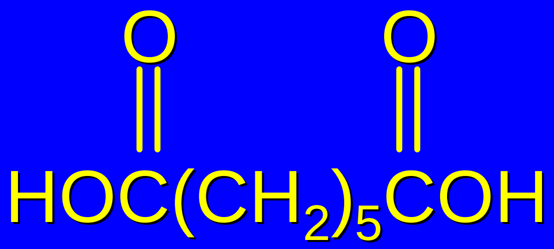


effect is small unless X is electronegative; effect is largest for ortho substituent

	pK		

19.8
Dicarboxylic Acids

Dicarboxylic Acids

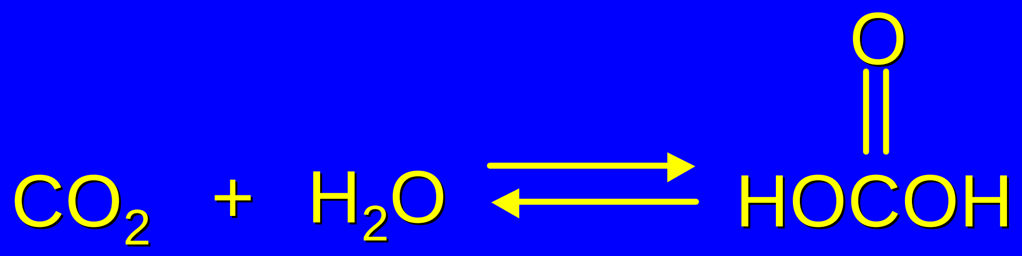
		pK_a
 $\mathrm{HO}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$	Oxalic acid	1.2
 $\mathrm{HO}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$	Malonic acid	2.8
 $\mathrm{HO}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{(CH_2)_5}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$	Heptanedioic acid	4.3

one carboxyl group acts as an electron-withdrawing group toward the other; effect decreases with increasing separation

19.9

Carbonic Acid

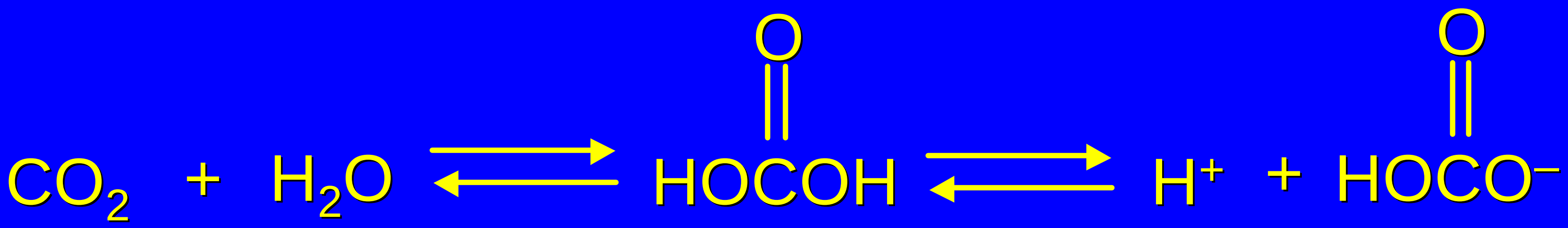
Carbonic Acid



$$\mathrm{CO_2} + \mathrm{H_2O} \rightleftarrows \mathrm{HO}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OH}$$

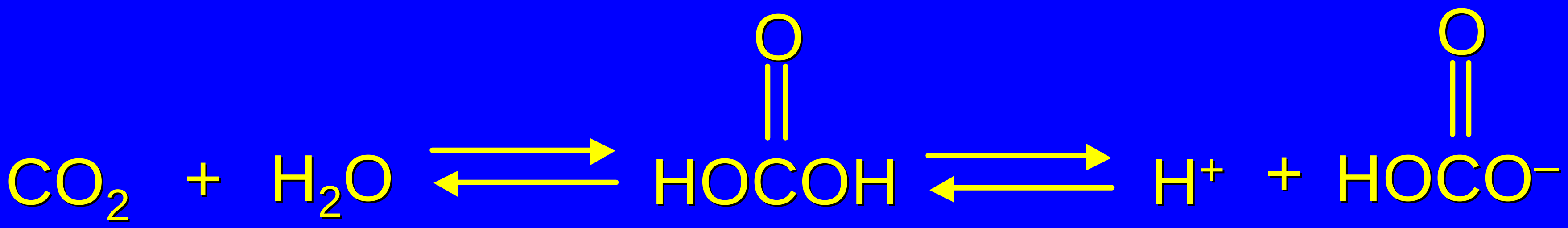
99.7% 0.3%

Carbonic Acid



$$CO_2 + H_2O \rightleftharpoons HO\overset{\overset{O}{\|}}{C}OH \rightleftharpoons H^+ + HO\overset{\overset{O}{\|}}{C}O^-$$

Carbonic Acid



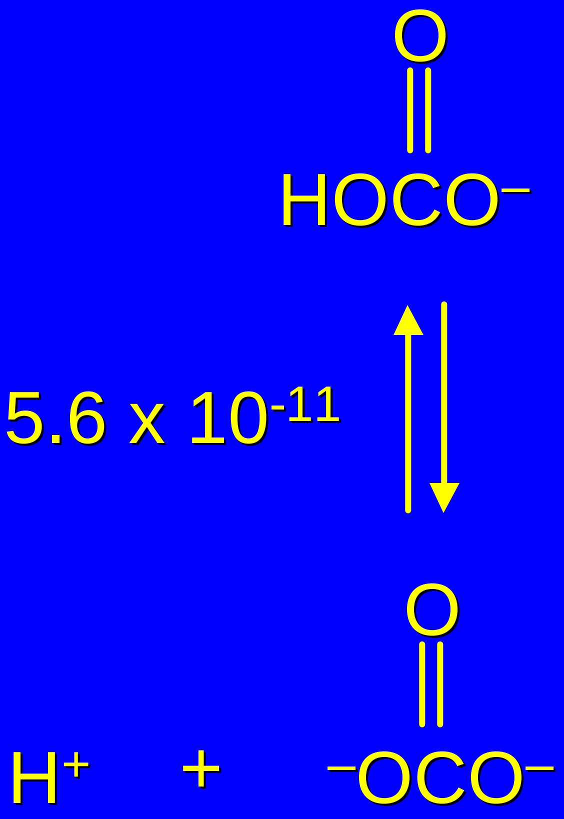
$$CO_2 + H_2O \rightleftharpoons HO\overset{\overset{\displaystyle O}{\|}}{C}OH \rightleftharpoons H^+ + HO\overset{\overset{\displaystyle O}{\|}}{C}O^-$$

overall *K* for these two steps = 4.3×10^{-7}

CO_2 is major species present in a solution of "carbonic acid" in acidic media

Carbonic Acid

Second ionization constant: $K_a = 5.6 \times 10^{-11}$



$$\mathrm{HO}\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{O}^- \rightleftharpoons \mathrm{H}^+ + {}^-\mathrm{O}\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{O}^-$$

19.10

Sources of Carboxylic Acids

Synthesis of Carboxylic Acids: Review

side-chain oxidation of alkylbenzenes (Section 11.13)

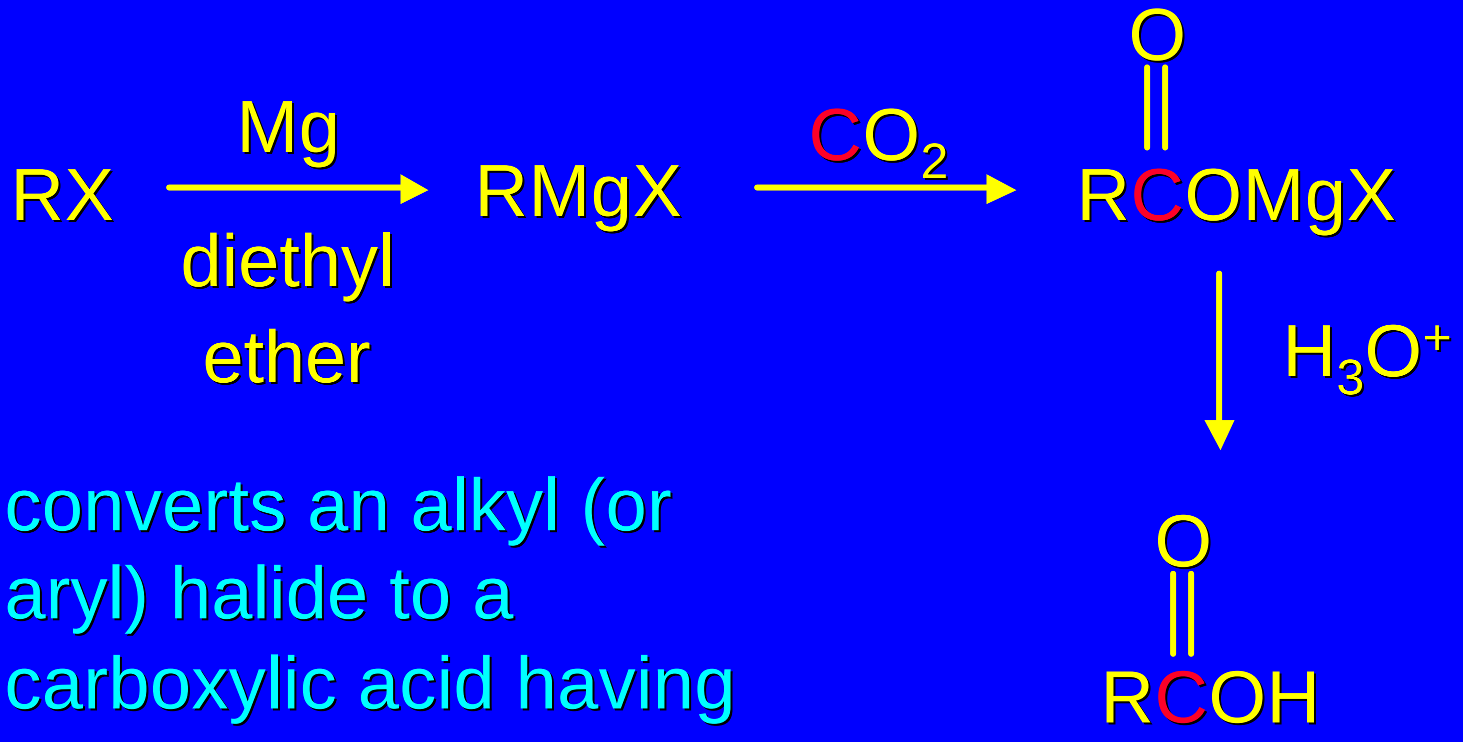
oxidation of primary alcohols (Section 15.10)

oxidation of aldehydes (Section 17.15)

19.11

Synthesis of Carboxylic Acids by the Carboxylation of Grignard Reagents

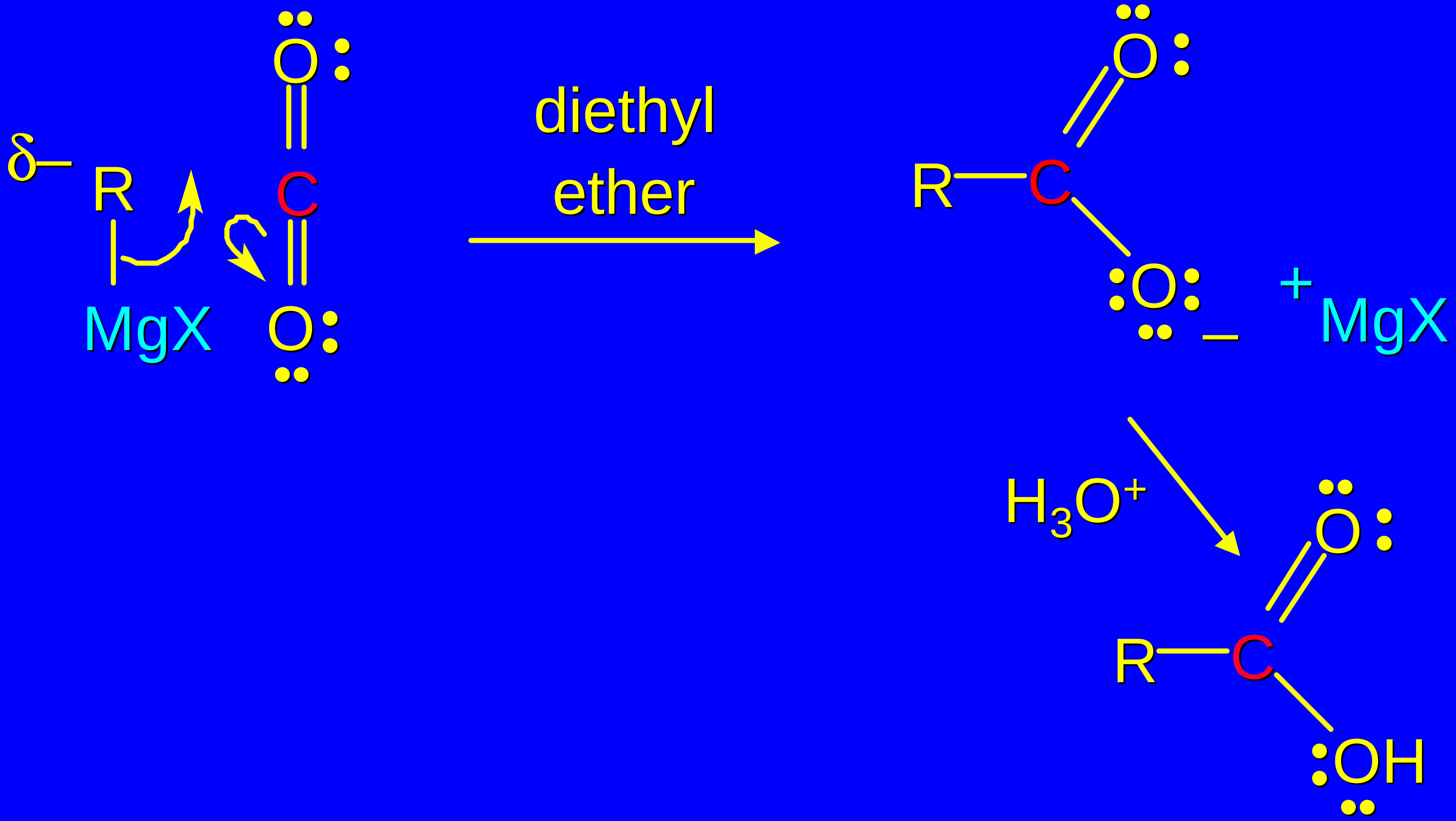
Carboxylation of Grignard Reagents



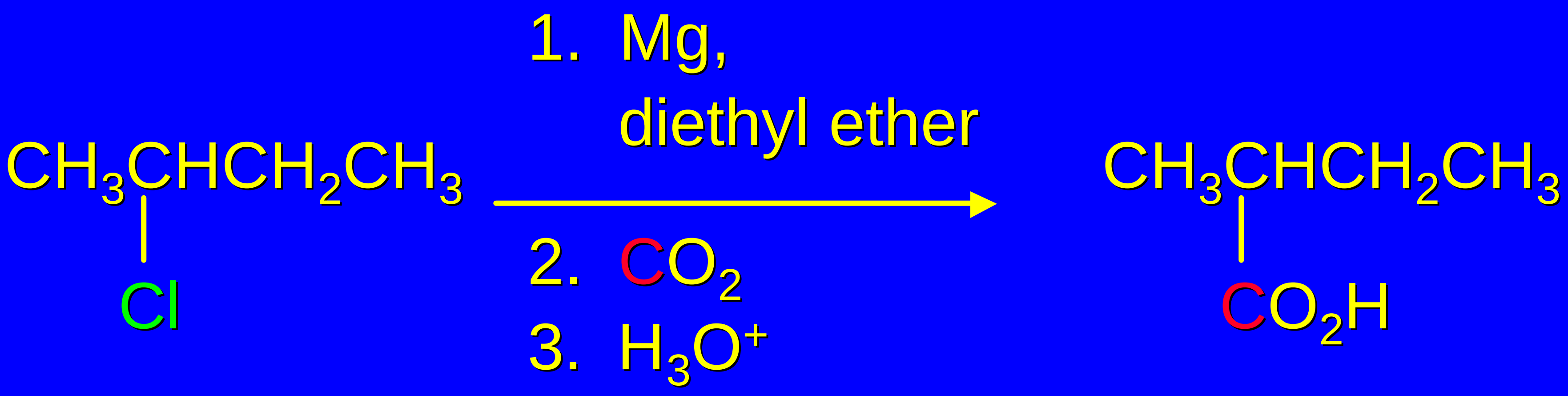
$$RX \xrightarrow[\text{diethyl ether}]{Mg} RMgX \xrightarrow{CO_2} R\overset{\overset{\displaystyle O}{\|}}{C}OMgX \xrightarrow{H_3O^+} R\overset{\overset{\displaystyle O}{\|}}{C}OH$$

converts an alkyl (or aryl) halide to a carboxylic acid having one more carbon atom than the starting halide

Carboxylation of Grignard Reagents



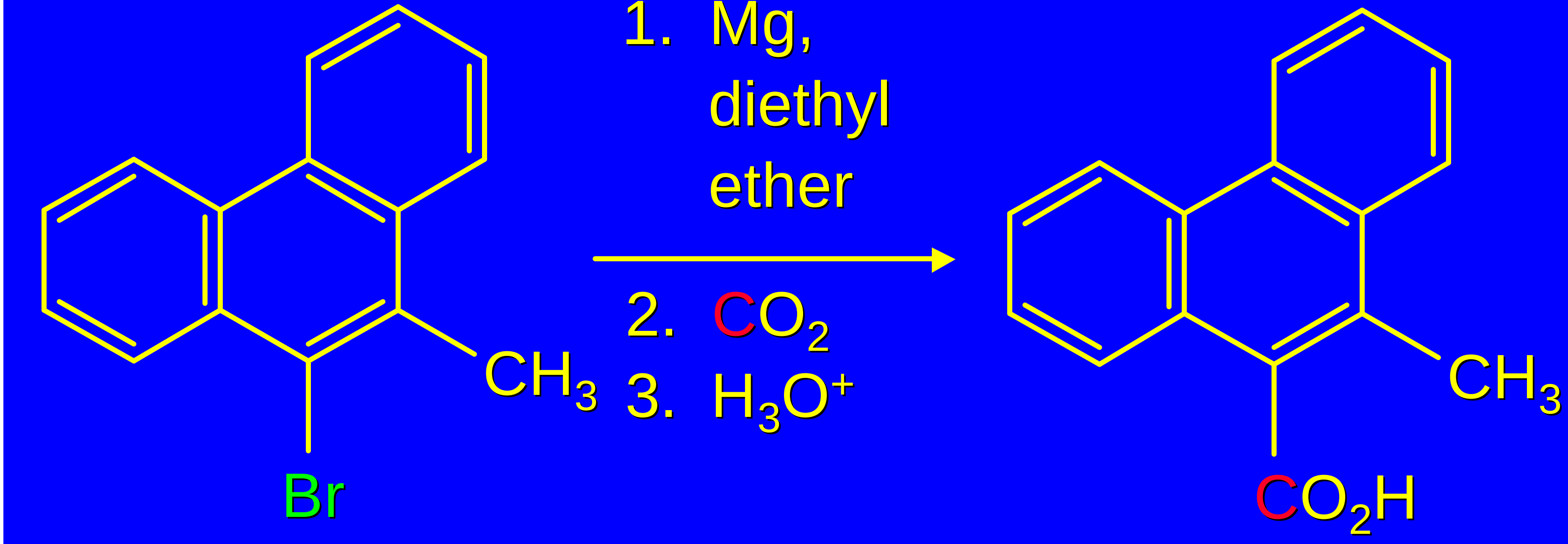
Example: Alkyl Halide



$$\mathrm{CH_3}\underset{\underset{\mathrm{Cl}}{|}}{\mathrm{CH}}\mathrm{CH_2CH_3} \xrightarrow[\text{2. } \mathrm{CO_2} \quad \text{3. } \mathrm{H_3O^+}]{\text{1. Mg, diethyl ether}} \mathrm{CH_3}\underset{\underset{\mathrm{CO_2H}}{|}}{\mathrm{CH}}\mathrm{CH_2CH_3}$$

(76-86%)

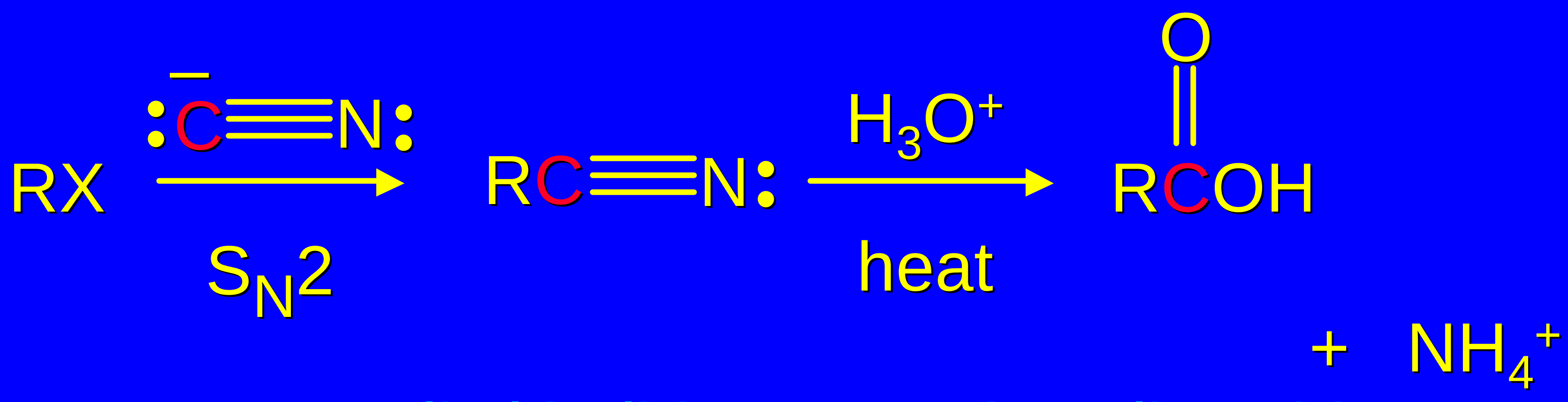
Example: Aryl Halide



(82%)

19.12
Synthesis of Carboxylic Acids by the Preparation and Hydrolysis of Nitriles

Preparation and Hydrolysis of Nitriles

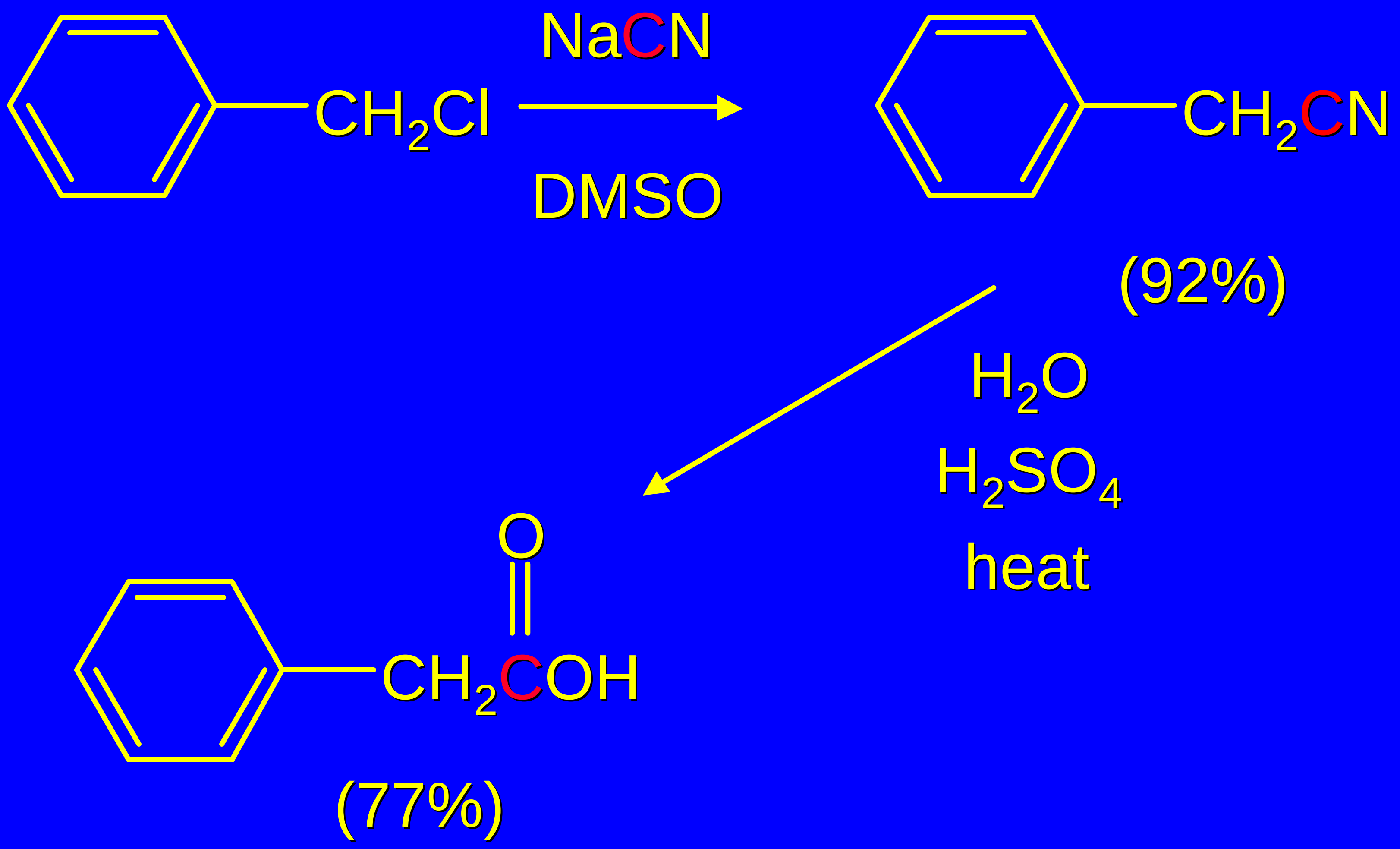


$$\mathrm{RX} \xrightarrow[S_N2]{:\overset{-}{C}\equiv N:} \mathrm{RC}\equiv \mathrm{N}: \xrightarrow[\text{heat}]{H_3O^+} \mathrm{R}\overset{\overset{\displaystyle O}{\|}}{C}\mathrm{OH} + NH_4^+$$

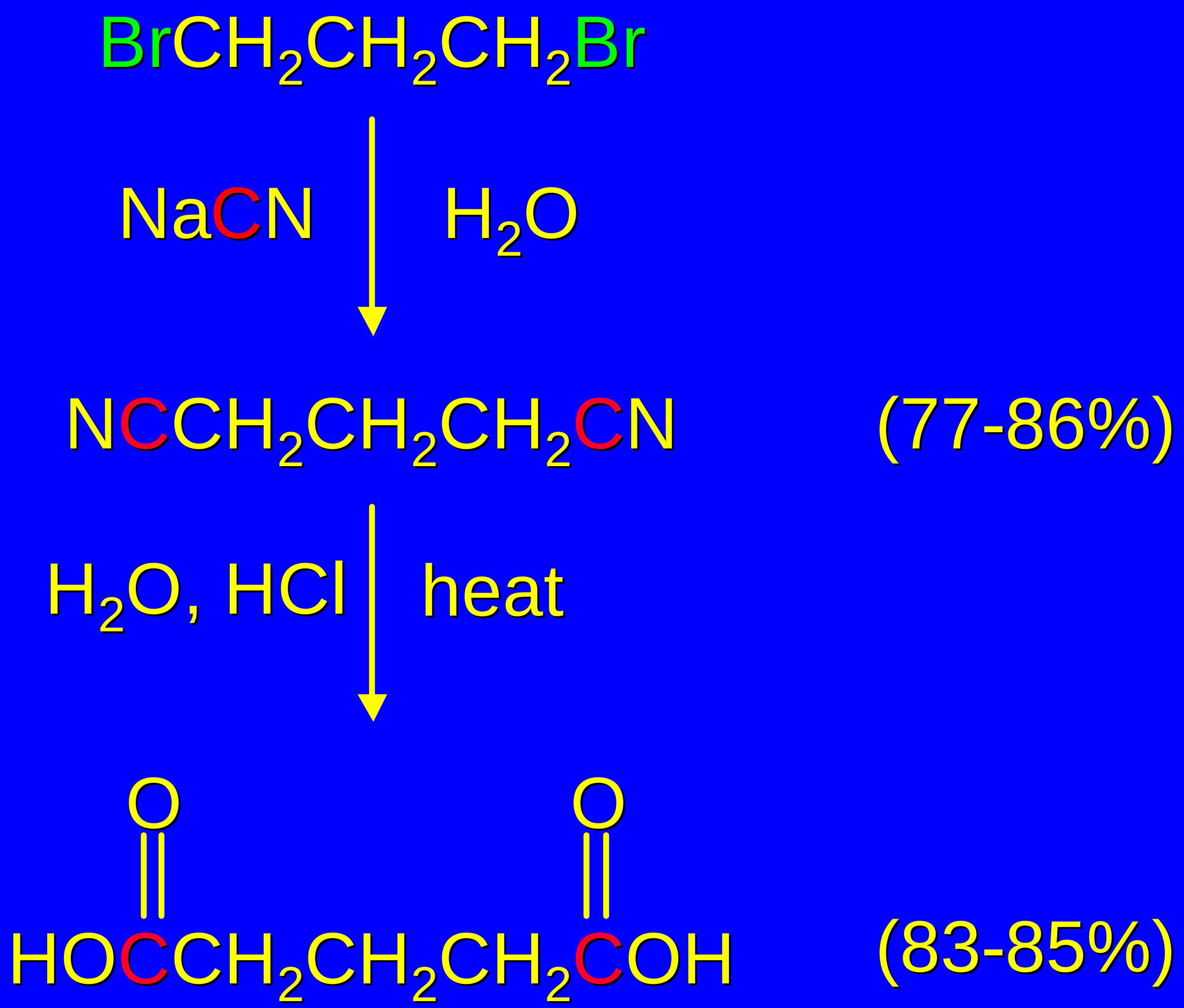
converts an alkyl halide to a carboxylic acid having one more carbon atom than the starting halide

limitation is that the halide must be reactive toward substitution by S_N2 mechanism

Example


$C_6H_5CH_2Cl$
NaCN
DMSO
$C_6H_5CH_2CN$
(92%)
H_2O
H_2SO_4
heat
O
$C_6H_5CH_2COOH$
(77%)

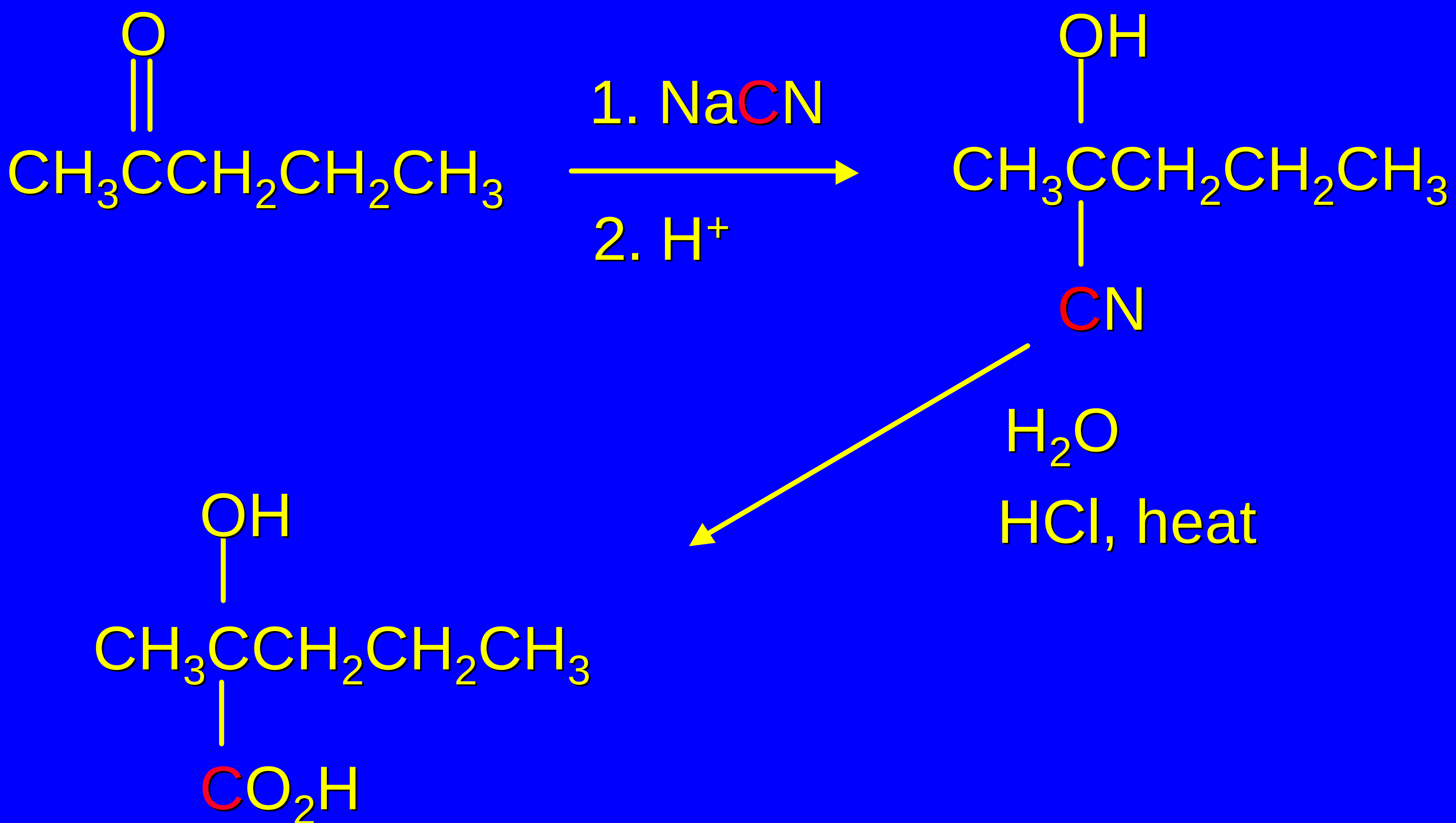
Example: Dicarboxylic Acid



$$\mathrm{BrCH_2CH_2CH_2Br} \xrightarrow[\mathrm{H_2O}]{\mathrm{NaCN}} \mathrm{NCCH_2CH_2CH_2CN} \qquad (77\text{-}86\%)$$

$$\xrightarrow[\mathrm{heat}]{\mathrm{H_2O,\ HCl}} \mathrm{HO\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH} \qquad (83\text{-}85\%)$$

via Cyanohydrin



$$\mathrm{CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2CH_3} \xrightarrow[\text{2. } \mathrm{H^+}]{\text{1. NaCN}} \mathrm{CH_3\overset{OH}{\underset{CN}{C}}CH_2CH_2CH_3} \xrightarrow[\text{HCl, heat}]{\mathrm{H_2O}} \mathrm{CH_3\overset{OH}{\underset{CO_2H}{C}}CH_2CH_2CH_3}$$

(60% from 2-pentanone)