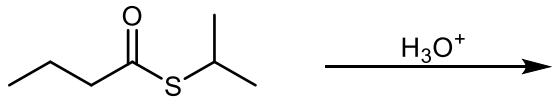
CONCEPT: HYDROLYSIS OF THIOESTERS

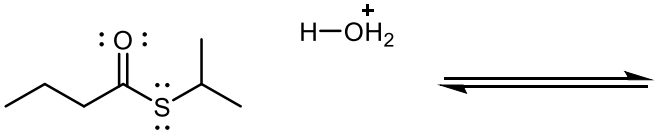
- **Recall:** Thioesters are _____ analogs of esters.
- Acid-catalyzed hydrolysis of a thioester produces a carboxylic acid and a _____.
  - □ Reaction takes place via nucleophilic acyl _____ mechanism.

Step 1	Step 2	Step 3	Step 4	Step 5
Protonation	Nucleophilic Attack	Proton Transfer	Leaving Group	Deprotonation

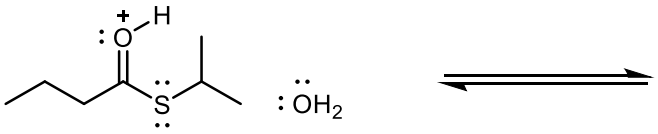
EXAMPLE: Write a mechanism for acid-catalyzed hydrolysis of *S*-isopropyl butanethioate.



STEP 1: The carbonyl ___ is protonated by the H_3O^+ ion.



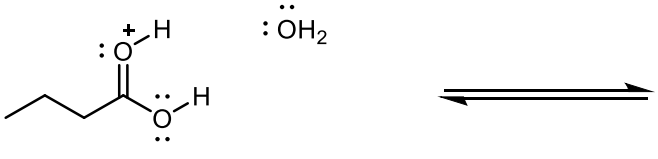
STEP 2: H_2O molecule attacks the carbonyl ___.



STEP 3: A proton is transferred from the __ charged ___ to ___.

STEP 4: An ___ atom pushes its lone pair to kick out the thiol.

STEP 5: The newly reformed carbonyl O is deprotonated, regenerating the H_3O^+ ion.



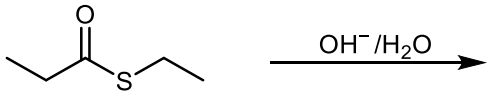
CONCEPT: HYDROLYSIS OF THIOESTERS

Saponification of Thioesters

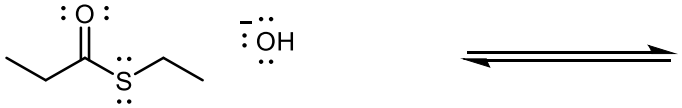
- Saponification of thioester produces a carboxylate anion and a thiol.

Step 1	Step 2	Step 3
Nucleophilic Attack	Leaving Group	Proton Transfer

EXAMPLE: Write a mechanism for the basic hydrolysis of *S*-ethyl propanethioate.

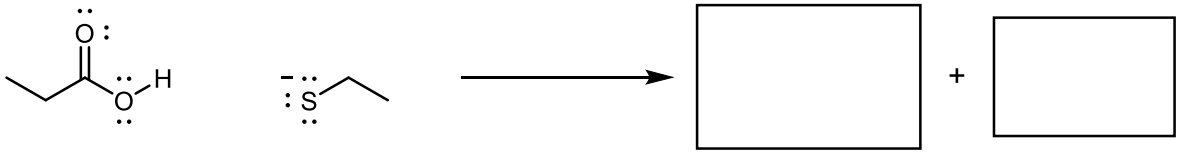


STEP 1: Hydroxide ion attacks the carbonyl C, forming an _____.

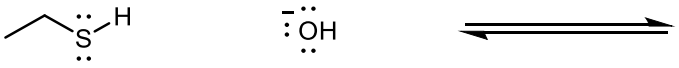


STEP 2: The alkoxide O atom pushes its electrons to kick out the thiol as _____ anion.

STEP 3a: The thiolate anion _____ the carboxylic acid, forming a carboxylate anion.

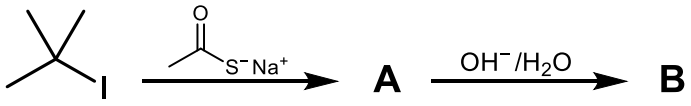


STEP 3b: A thiol ($pK_a \approx$ _____) is sufficiently acidic to remain deprotonated in a solution of OH^- ($pK_a \approx$ _____) ions.



CONCEPT: HYDROLYSIS OF THIOESTERS

PRACTICE: Draw the structures of products A and B in the following reaction sequence.



PRACTICE: Thioesters can react with nucleophiles to yield substitution products. Write a mechanism for the reaction of *S*-methyl ethanethioate with dimethylamine.