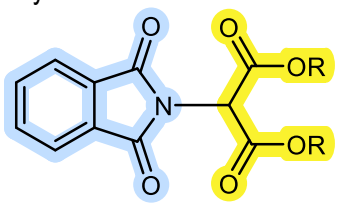
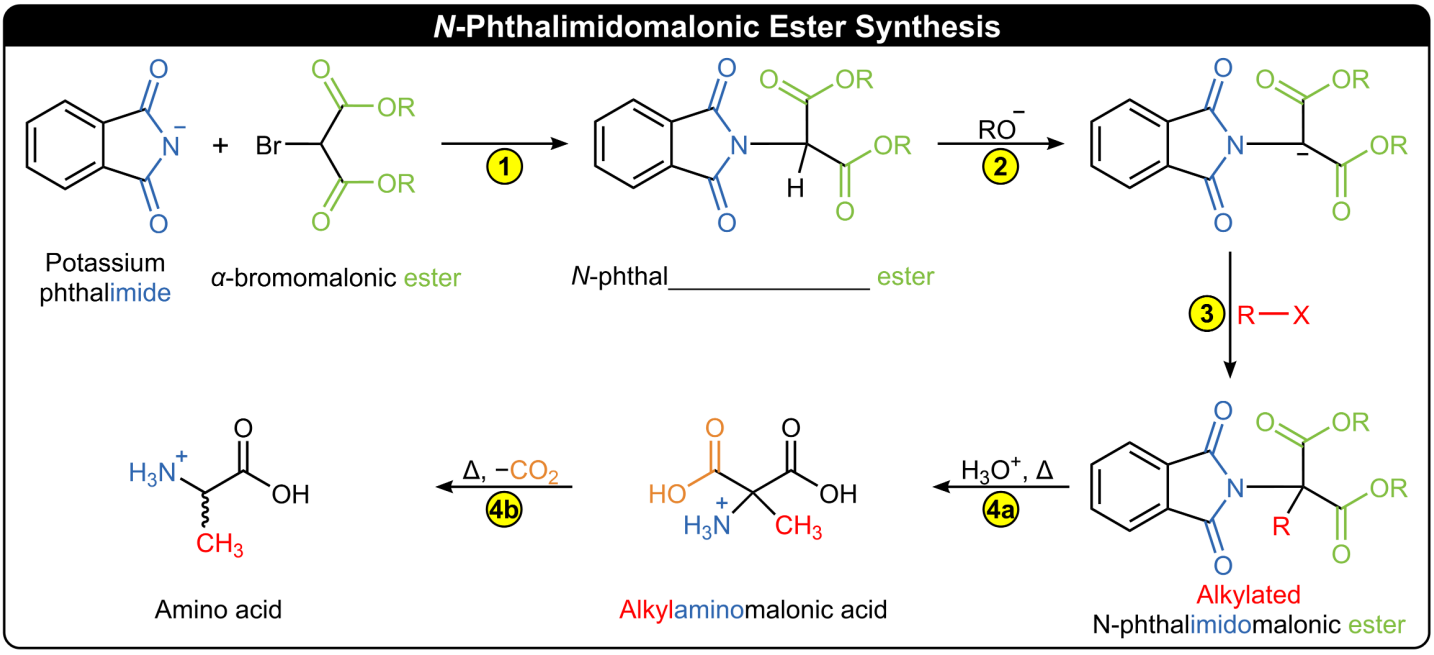
CONCEPT: SYNTHESIS OF AMINO ACIDS: *N*-PHTHALIMIDOMALONIC ESTER SYNTHESIS

Intro to *N*-Phthalimidomalonic Ester Synthesis

- *N*-Phthalimidomalonic ester synthesis combines the _____ synthesis and malonic ester synthesis.
- Takes place in ___ steps:
  - (1) **S_N2 reaction:** Potassium phthalimide reacts with _____malonic ester.
  - (2) **Enolization:** A strong base deprotonates the _____ of *N*-phthalimidomalonic ester.
  - (3) **Alkylation of Enolate:** Enolate anion attacks an alkyl halide in an _____ reaction.
  - (4a) **Hydrolysis:** The imide and the _____ are hydrolyzed.
  - (4b) **Decarboxylation**: One of the two _____ groups is lost as CO_2.





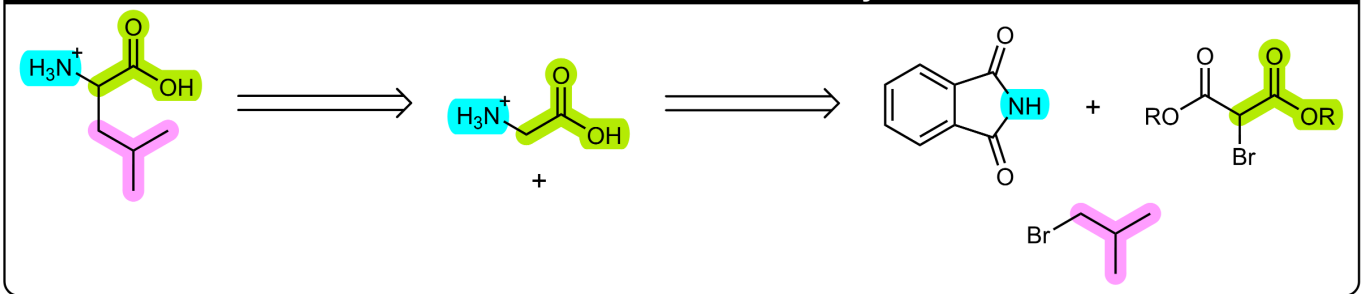
EXAMPLE: Draw the structure of the product of hydrolysis of non-alkylated *N*-phthalimidomalonic ester.

CONCEPT: SYNTHESIS OF AMINO ACIDS: *N*-PHTHALIMIDOMALONIC ESTER SYNTHESIS

Synthesis of Amino Acids

- *N*-Phthalimidomalonic ester synthesis uses simpler starting materials than acetamidomalic ester synthesis.
  - □ The amino group comes from the ___ atom of phthalimide.
  - □ The base ___ skeleton of the amino acid comes from the α-bromomalonic ester
  - □ The side chain comes from an _____ _____..

***N*-Phthalimidomalonic Ester Retrosynthesis**



EXAMPLE: Suggest an alkyl halide to synthesize histidine using *N*-phthalimidomalonic ester synthesis.

PRACTICE: How can leucine be synthesized using *N*-phthalimidomalonic ester synthesis?