Endo-Protected Maleimide Synthesis and Polymerization

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Maleimide-Thiol Click Reaction
Too reactive!

Label
SH

[Reaction Diagram]

Label
[Chemical Structure]

Antibody-drug conjugate
Protecting Maleimide: 2 isomers

Current Method

- Furan
- Maleimide
- Exo

Our Project

- Endo
- ~50 °C

90 to 110 °C
Would denature proteins

Difficult to synthesize and purify
Endo Synthesis: Method 1

\[ \text{Toluene, } 80 \, ^\circ\text{C}, \, 20 \, \text{hrs} \]
\[ \text{65\% yield} \]

\[ \text{Water, } 25\, ^\circ\text{C}, \, 21 \, \text{hrs} \]
\[ \text{43\% yield} \]

\[ \text{MeOH, } 0 \, ^\circ\text{C to reflux, } 18 \, \text{hrs} \]
\[ \text{90\% yield} \]

\[ \text{Toluene, } 125 \, ^\circ\text{C}, \, 52 \, \text{hrs} \]
\[ \text{40\% yield} \]

Mixture of endo and exo

Column Chromatography
Separating *Endo* From *Exo*

Column Chromatography
**Endo Synthesis: Method 2**

\[
\text{NH}_2\text{CO}_2\text{H} \xrightarrow{1/g} \text{endo} \quad 23\% \text{ yield}
\]

Mixture of **endo** and **exo**

\[
\text{Cool} \quad \text{Filter}
\]

Recrystallization

\[
\text{endo} \quad \text{exo}
\]

Endo 70% yield
How do we know it was *endo*?
How do we know it was endo?
How do we know it was endo?
**Polymerizations**

*Endo:* deprotects at 55°C

*Exo:* deprotects at 100°C

A monomer is a small molecule.

A polymer is a long-chain molecule made up of a repeated pattern of monomers.
Conclusion

Inspiration and Applications

Maleimide is useful but too reactive

Synthesis

Endo

Exo

\[ \text{~50°C} \]

\[ \text{90-110°C} \]

Inexpensive and easy: 4 to 2 steps

Purification

Pure and scalable

Polymerization

Controlled; use of temperature