A Synthetic Approach to Underdeveloped Macrocycles

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Macrocycles are Larger Heterocycles

Heterocycle

Macrocycle
Heterocycles Influence Diverse Industries
Macrocycles Aid in Synthesis of Medicines

Meytansine
More Steps in the Chemical Reaction Reduce Yields

Reactant

Product

Byproduct

Waste

A 100%

B 80%

C 60%

E 20%

D 40%
More Steps in the Chemical Reaction Reduce Yields

A → B → C

Reactant: 100%
Product: 80%
Byproduct: 20%
Waste: 80%

D → E

Product: 40%
Byproduct: 80%
Waste: 20%
A Chemical Reaction Creates the Difunctional Substrate

Tetraethylene Glycol

Hydrogen (H)
A Chemical Reaction Creates the Difunctional Substrate

Base

Acyl Bromide (AB)

Br

AB

Br

Tetraethylene Glycol

H

H

Base

N
Base Accepts and Removes Hydrogen

Base

Tetraethylene Glycol

Base

AB

Br

H

AB

Br
Acyl Bromide Completes Substrate Creation

Difunctional Substrate (Intermediate Product)

Tetraethylene Glycol

Br  AB  Tetraethylene Glycol  AB  Br
Product is Purified Into a Difunctional Substrate

Aqueous Impurities

Organic Solvent + Compound
Difunctional Substrate
(Intermediate Product)

Tetraethylene Glycol
Nuclear Magnetic Resonance Confirms Product Identity
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Nuclear Magnetic Resonance Confirms Product Identity
Copper Bromide Creates Free Radicals

Copper Bromide (CuBr)

Difunctional Substrate (Intermediate Product)

Tetraethylene Glycol

Br

AB

CuBr

AB

Br
Copper Bromide Creates Free Radicals

\[ \text{CuBr} \]

\[ \text{Br} \quad \text{AB} \quad \text{Tetraethylene Glycol} \quad \text{AB} \quad \text{Br} \]

\[ \text{CuBr} \]
Copper Bromide Creates Free Radicals
Copper Bromide Creates Free Radicals

Copper(II) Bromide (CuBr₂)
Copper Bromide Creates Free Radicals

Free radical
(unbonded electron)
Nitrosobenzene Catalyzes Stabilization of Radicals

Nitrosobenzene

\[ \text{NB} \]

\[ \text{e}^- \]

\[ \text{AB} \]

\[ \text{AB} \]

Tetraethylene Glycol

\[ \text{e}^- \]
Nitrosobenzene Catalyzes Stabilization of Radicals

\[
\text{Nitrosobenzene (NB)} \rightarrow \text{Tetraethylene Glycol} \rightarrow \text{Radical (AB)} \rightarrow \text{Nitrosobenzene (NB)}
\]
Nitrosobenzene Catalyzes Stabilization of Radicals
Nitrosobenzene Catalyzes Stabilization of Radicals

[Diagram showing the catalytic process involving Nitrosobenzene (NB), radicals (AB), and Tetraethylene Glycol (TGA)].
Nitrosobenzene Catalyzes Stabilization of Radicals

\[ \text{e}^- \rightarrow \text{AB} \rightarrow \text{Tetraethylene Glycol} \rightarrow \text{AB} \rightarrow \text{e}^- \]
Nitrosobenzene Catalyzes Stabilization of Radicals
Nitrosobenzene Catalyzes Stabilization of Radicals
Success Suggests Creation of Larger Macrocycles

Tetraethylene Glycol

Pentaethylene Glycol
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