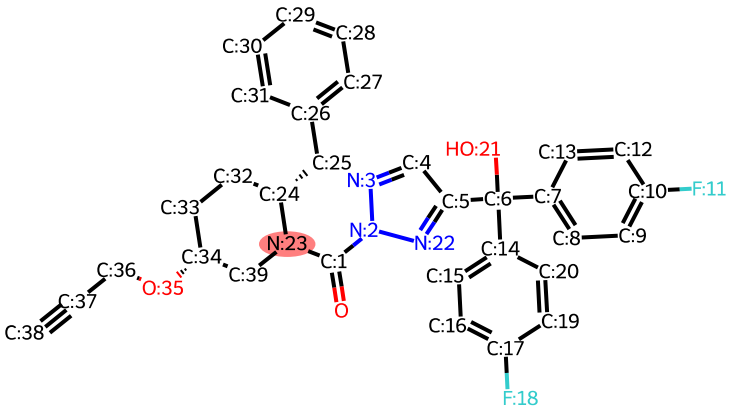
Reaction Report for *DH_376*, Priority 12

Selected Position: `N:23`

Selected Forward Reaction: Boc amine deprotection

Product



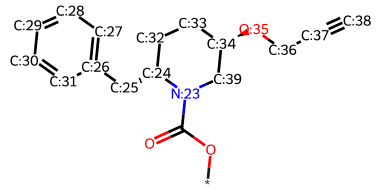
Reaction site highlighted at position `N:23`

Product SMILES: `O=[C:1]([n:2]1[n:3][cH:4][c:5]([C:6]([c:7]2[cH:8][cH:9][c:10]([F:11])[cH:12][cH:13]2)([c:14]2[cH:15][cH:16][c:17]([F:18])[cH:19][cH:20]2)[OH:21])[n:22]1)[N:23]1[C@@H:24]([CH2:25][c:26]2[cH:27][cH:28][cH:29][cH:30][cH:31]2)[CH2:32][CH2:33][C@@H:34]([O:35][CH2:36][C:37]#[CH:38])[CH2:39]1`

Proposed Transitions

Transition 1

- **Forward Reaction:** Carbamate-based amine deprotection
- **Is Chemically Valid:** True
- **Is Template-based:** True
- **Reasoning:** This is the general template for a carbamate-protected piperidine precursor. The [*] represents the variable part of the carbamate group. . NOTE: The user-provided product is a stable amide. The specified reaction, 'amine deprotection', implies the product should be a free amine. This analysis assumes the intended product for this specific transformation was the free piperidine intermediate, which would subsequently react to form the final amide product.
- **Is Smiles Valid:** True
- **Reactant 1:** `[*][O]C(=O)[N:23]1[C@@H:24]([CH2:25][c:26]2[cH:27][cH:28][cH:29][cH:30][cH:31]2)[CH2:32][CH2:33][C@@H:34]([O:35][CH2:36][C:37]#[CH:38])[CH2:39]1`



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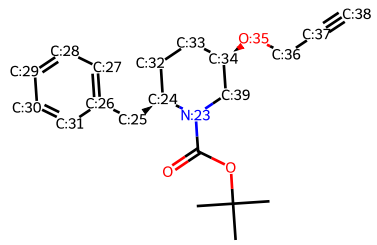
Reactants for Transition 1

Transition 2

- **Forward Reaction:** Carbamate-based amine deprotection
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation, representing the Boc-protected amine, is a valid precursor. Deprotection requires acidic conditions (e.g., TFA, HCl in dioxane). While valid, these conditions must be carefully controlled to prevent potential acid-catalyzed decomposition of the propargyl ether functional group.
- **Is Smiles Valid:** True

- **Reactant 1:** `CC(C)(C)OC(=O)[N:23]1[C@@H:24]([CH2:25][c:26]2[cH:27][cH:28][cH:29][cH:30][cH:31]2)[CH2:32][CH2:33][C@@H:34]([O:35][CH2:36][C:37]#[CH:38])[CH2:39]1`

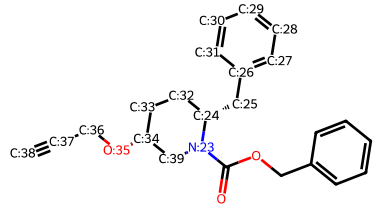


R1

Reactants for Transition 2

Transition 3

- **Forward Reaction:** Carbamate-based amine deprotection
- **Is Chemically Valid:** False
- **Is Template-based:** False
- **Reasoning:** This permutation, representing the Cbz-protected amine, is invalid. The standard deprotection method for a Cbz group is catalytic hydrogenolysis (e.g., H2/Pd-C), which is not chemoselective here. It would readily reduce the terminal alkyne and could also cleave the benzyl ether at C:25.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=C(OCc1ccccc1)[N:23]1[C@@H:24]([CH2:25][c:26]2[cH:27][cH:28][cH:29][cH:30][cH:31]2)[CH2:32][CH2:33][C@@H:34]([O:35][CH2:36][C:37]#[CH:38])[CH2:39]1`



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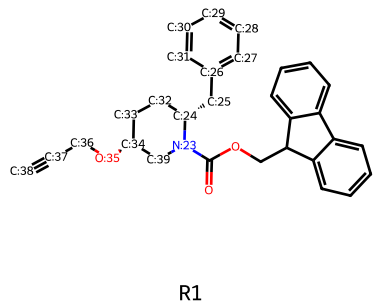
Reactants for Transition 3

Transition 4

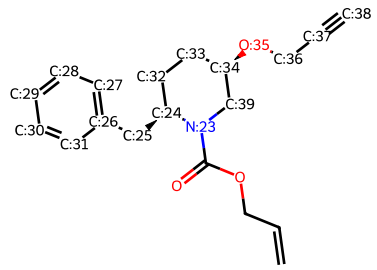
- **Forward Reaction:** Carbamate-based amine deprotection
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation, representing the Fmoc-protected amine, is valid. Fmoc groups are cleaved under mild basic conditions (e.g., piperidine in DMF), which are orthogonal to the other functional groups in the molecule, making this a highly suitable synthetic strategy.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=C(OCC1c2ccccc2c2ccccc21)[N:23]1[C@@H:24]([CH2:25][c:26]2[cH:27][cH:28][cH:29][cH:30][cH:31]2)[CH2:32][CH2:33][C@@H:34]([O:35][CH2:36][C:37]#[CH:38])[CH2:39]1`



Reactants for Transition 4

Transition 5

- **Forward Reaction:** Carbamate-based amine deprotection
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation, representing the Alloc-protected amine, is valid. The Alloc group is removed under mild, neutral conditions using a palladium(0) catalyst. This method offers excellent orthogonality and is compatible with the alkyne and other functionalities present.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=C(OCC=C)[N:23]1[C@@H:24]([CH2:25][c:26]2[cH:27][cH:28][cH:29][cH:30][cH:31]2)[CH2:32][CH2:33][C@@H:34]([O:35][CH2:36][C:37]#[CH:38])[CH2:39]1`



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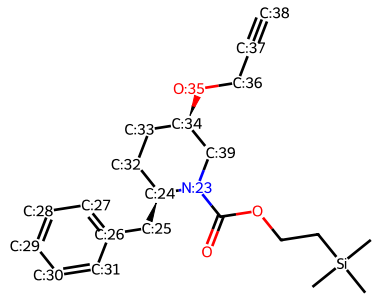
Reactants for Transition 5

Transition 6

- **Forward Reaction:** Carbamate-based amine deprotection
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation, representing the Teoc-protected amine, is valid. Deprotection is achieved with a fluoride source (e.g., TBAF) under neutral conditions, providing high chemoselectivity and compatibility with the molecule's functional groups.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=C(OCC[Si](C)(C)C)[N:23]1[C@@H:24]([CH2:25][c:26]2[cH:27][cH:28][cH:29][cH:30][cH:31]2)[CH2:32][CH2:33][C@@H:34]([O:35][CH2:36][C:37]#[CH:38])[CH2:39]1`



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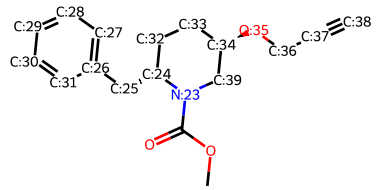
Reactants for Transition 6

Transition 7

- **Forward Reaction:** Carbamate-based amine deprotection

- **Is Chemically Valid:** False
- **Is Template-based:** False
- **Reasoning:** This permutation, representing the Moc-protected amine, is considered invalid for practical synthesis. Removal requires harsh conditions like strong acid (incompatible with the propargyl ether) or saponification (strong base, heat), which lack the selectivity and mildness offered by other available protecting groups.
- **Is Smiles Valid:** True
- **Reactant 1:** `COC(=O)[N:23]1[C@@H:24]([CH2:25][c:26]2[cH:27][cH:28][cH:29][cH:30][cH:31]2)[CH2:32][CH2:33][C@@H:34]([O:35][CH2:36][C:37]#[CH:38])[CH2:39]1`



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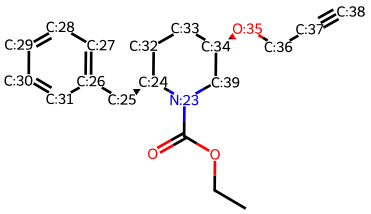
Reactants for Transition 7

Transition 8

- **Forward Reaction:** Carbamate-based amine deprotection
- **Is Chemically Valid:** False
- **Is Template-based:** False
- **Reasoning:** This permutation, representing the Eoc-protected amine, is considered invalid for practical synthesis. Similar to the Moc group, its removal requires harsh conditions (strong acid or saponification) that are not chemoselective for this substrate.
- **Is Smiles Valid:** True
- **Reactant 1:** `CCOC(=O)[N:23]1[C@@H:24]([CH2:25][c:26]2[cH:27][cH:28][cH:29][cH:30][cH:31]2)[CH2:32][CH2:33][C@@H:34]([O:35][CH2:36][C:37]#[CH:38])[CH2:39]1`



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Reactants for Transition 8