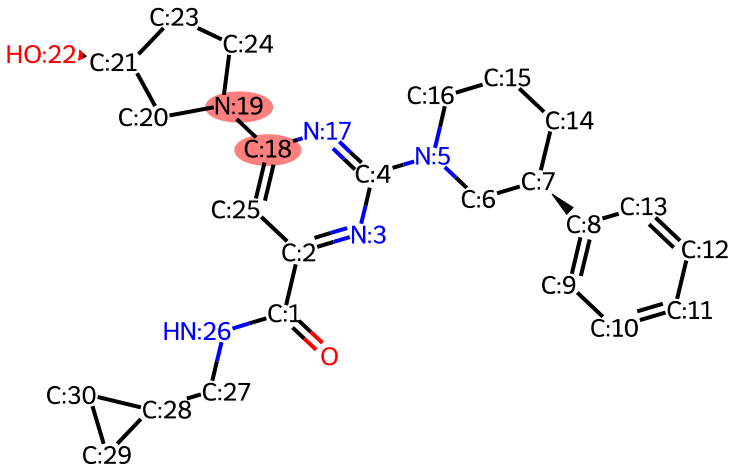
Reaction Report for *LEI_401*, Priority 2

Selected Position: `C:18 N:19`

Selected Forward Reaction: Buchwald-Hartwig/Ullmann-Goldberg/N-arylation secondary amine

Product

Reaction site highlighted at position `C:18 N:19`

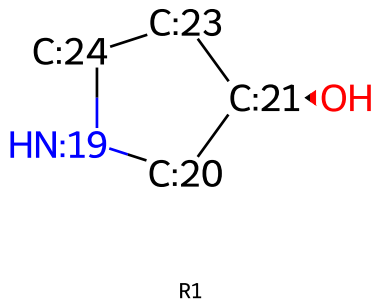


Product SMILES: `O=[C:1]([c:2]1[n:3][c:4]([N:5]2[CH2:6][C@H:7]([c:8]3[cH:9][cH:10][cH:11][cH:12][cH:13]3)[CH2:14][CH2:15][CH2:16]2)[n:17][c:18]([N:19]2[CH2:20][C@@H:21]([OH:22])[CH2:23][CH2:24]2)[cH:25]1)[NH:26][CH2:27][CH:28]1[CH2:29][CH2:30]1`

Proposed Transitions

Transition 1

- **Forward Reaction:** Buchwald-Hartwig/Ullmann-Goldberg/N-arylation secondary amine
- **Is Chemically Valid:** True
- **Is Template-based:** True
- **Reasoning:** This is a general template for the Buchwald-Hartwig/Ullmann-Goldberg N-arylation. The aryl component is functionalized with a leaving group from the (e.g., F, Cl, Br, I, OTf) and coupled with the secondary amine.
- **Is Smiles Valid:** False
- **Reactant 1:** `O=[C:1]([c:2]1[n:3][c:4]([N:5]2[CH2:6][C@H:7]([c:8]3[cH:9][cH:10][cH:11][cH:12][cH:13]3)[CH2:14][CH2:15][CH2:16]2)[n:17][c:18]([F,Cl,Br,I,O[S](=O)=O*])[cH:25]1)[NH:26][CH2:27][CH:28]1[CH2:29][CH2:30]1`
- **Reactant 2:** `O[C@@H:21]1[CH2:23][CH2:24][NH:19][CH2:20]1`

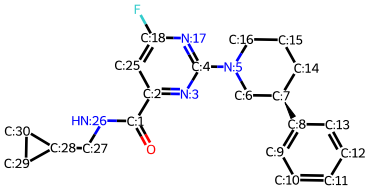


Reactants for Transition 1

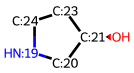
Transition 2

- **Forward Reaction:** Buchwald-Hartwig/Ullmann-Goldberg/N-arylation secondary amine
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. Aryl fluorides are viable substrates, typically requiring more forcing conditions or specialized catalyst systems compared to other halides. A potential chemoselectivity issue exists due to the presence of other secondary amine functionalities in the aryl partner, which may require careful optimization. The reaction does not affect the existing stereocenters.
- **Is Smiles Valid:** True

- **Reactant 1:** `O=[C:1]([c:2]1[n:3][c:4]([N:5]2[CH2:6][C@H:7]([c:8]3[cH:9][cH:10][cH:11][cH:12][cH:13]3)[CH2:14][CH2:15][CH2:16]2)[n:17][c:18](F)[cH:25]1)[NH:26][CH2:27][CH:28]1[CH2:29][CH2:30]1`
- **Reactant 2:** `O[C@@H:21]1[CH2:23][CH2:24][NH:19][CH2:20]1`



R1

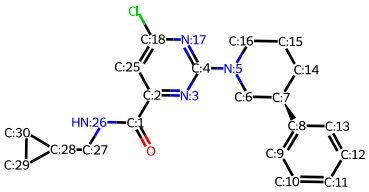


R2

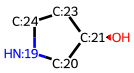
Reactants for Transition 2

Transition 3

- **Forward Reaction:** Buchwald-Hartwig/Ullmann-Goldberg/N-arylation secondary amine
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. Aryl chlorides are common and effective substrates for modern Buchwald-Hartwig catalysis. A potential chemoselectivity issue exists due to the presence of other secondary amine functionalities in the aryl partner, which may require careful optimization. The reaction does not affect the existing stereocenters.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=[C:1]([c:2]1[n:3][c:4]([N:5]2[CH2:6][C@H:7]([c:8]3[cH:9][cH:10][cH:11][cH:12][cH:13]3)[CH2:14][CH2:15][CH2:16]2)[n:17][c:18](Cl)[cH:25]1)[NH:26][CH2:27][CH:28]1[CH2:29][CH2:30]1`
- **Reactant 2:** `O[C@@H:21]1[CH2:23][CH2:24][NH:19][CH2:20]1`



R1

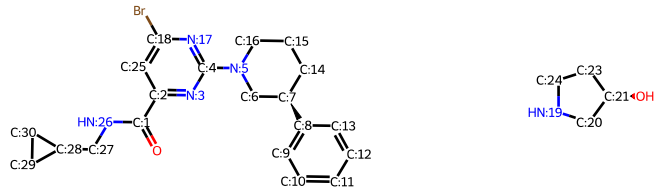


R2

Reactants for Transition 3

Transition 4

- **Forward Reaction:** Buchwald-Hartwig/Ullmann-Goldberg/N-arylation secondary amine
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. Aryl bromides are highly reliable and reactive substrates for this transformation. A potential chemoselectivity issue exists due to the presence of other secondary amine functionalities in the aryl partner, which may require careful optimization. The reaction does not affect the existing stereocenters.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=[C:1]([c:2]1[n:3][c:4]([N:5]2[CH2:6][C@H:7]([c:8]3[cH:9][cH:10][cH:11][cH:12][cH:13]3)[CH2:14][CH2:15][CH2:16]2)[n:17][c:18](Br)[cH:25]1)[NH:26][CH2:27][CH:28]1[CH2:29][CH2:30]1`
- **Reactant 2:** `O[C@@H:21]1[CH2:23][CH2:24][NH:19][CH2:20]1`



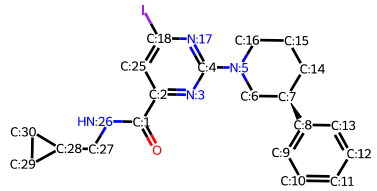
R1

R2

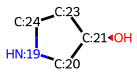
Reactants for Transition 4

Transition 5

- **Forward Reaction:** Buchwald-Hartwig/Ullmann-Goldberg/N-arylation secondary amine
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. Aryl iodides are the most reactive halides and are excellent substrates for this coupling. A potential chemoselectivity issue exists due to the presence of other secondary amine functionalities in the aryl partner, which may require careful optimization. The reaction does not affect the existing stereocenters.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=[C:1]([c:2]1[n:3][c:4]([N:5]2[CH2:6][C@H:7]([c:8]3[cH:9][cH:10][cH:11][cH:12][cH:13]3)[CH2:14][CH2:15][CH2:16]2)[n:17][c:18](I)[cH:25]1)[NH:26][CH2:27][CH:28]1[CH2:29][CH2:30]1`
- **Reactant 2:** `O[C@@H:21]1[CH2:23][CH2:24][NH:19][CH2:20]1`



R1

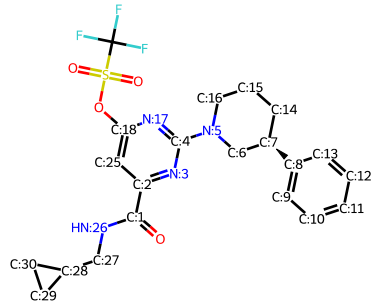


R2

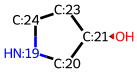
Reactants for Transition 5

Transition 6

- **Forward Reaction:** Buchwald-Hartwig/Ullmann-Goldberg/N-arylation secondary amine
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. Aryl triflates (OTf) are excellent leaving groups, with reactivity comparable to aryl bromides and iodides. A potential chemoselectivity issue exists due to the presence of other secondary amine functionalities in the aryl partner, which may require careful optimization. The reaction does not affect the existing stereocenters.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=[C:1]([c:2]1[n:3][c:4]([N:5]2[CH2:6][C@H:7]([c:8]3[cH:9][cH:10][cH:11][cH:12][cH:13]3)[CH2:14][CH2:15][CH2:16]2)[n:17][c:18](OS(=O)(=O)C(F)(F)F)[cH:25]1)[NH:26][CH2:27][CH:28]1[CH2:29][CH2:30]1`
- **Reactant 2:** `O[C@@H:21]1[CH2:23][CH2:24][NH:19][CH2:20]1`



R1

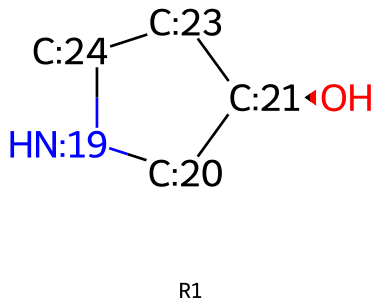


R2

Reactants for Transition 6

Transition 7

- **Forward Reaction:** Buchwald-Hartwig/Ullmann-Goldberg/N-arylation secondary amine
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. Aryl tosylates (OTs) are suitable leaving groups for this coupling, though generally less reactive than triflates. A potential chemoselectivity issue exists due to the presence of other secondary amine functionalities in the aryl partner, which may require careful optimization. The reaction does not affect the existing stereocenters.
- **Is Smiles Valid:** False
- **Reactant 1:** `Cc1ccc(S(=O)(=O)O[c:18]2[cH:25][c:1]1[C:26](=[O:27])[NH:28][CH2:29][CH:30]3[CH2:31][CH2:32]3)[n:17][c:4]([n:3][c:2]1[c:18]2)[N:5]1[CH2:6][C@H:7]([c:8]2[cH:9][cH:10][cH:11][cH:12][cH:13]2)[CH2:14][CH2:15][CH2:16]1)cc1`
- **Reactant 2:** `O[C@@H:21]1[CH2:23][CH2:24][NH:19][CH2:20]1`

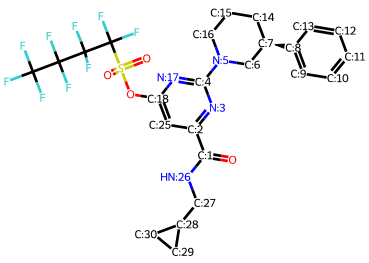


Reactants for Transition 7

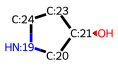
Transition 8

- **Forward Reaction:** Buchwald-Hartwig/Ullmann-Goldberg/N-arylation secondary amine
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. Aryl nonaflates (ONf) are exceptionally reactive leaving groups for this type of coupling. A potential chemoselectivity issue exists due to the presence of other secondary amine functionalities in the aryl partner, which may require careful optimization. The reaction does not affect the existing stereocenters.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=[C:1]([c:2]1[n:3][c:4]([N:5]2[CH2:6][C@H:7]([c:8]3[cH:9][cH:10][cH:11][cH:12][cH:13]3)[CH2:14][CH2:15][CH2:16]2)[n:17][c:18]1OS(=O)(=O)C(F)(F)C(F)(F)C(F)(F)C(F)(F)F)[cH:25]1)[NH:26][CH2:27][CH:28]1[CH2:29][CH2:30]1`

- **Reactant 2:** `O[C@@H:21]1[CH2:23][CH2:24][NH:19][CH2:20]1`



R1



R2

Reactants for Transition 8