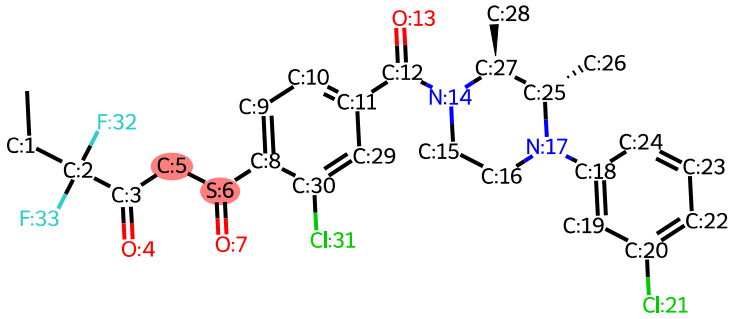
Reaction Report for *LEI_515*, Priority 5

Selected Position: `C:5 S:6`

Selected Forward Reaction: S-alkylation of thiols

Product



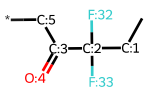
Reaction site highlighted at position `C:5 S:6`

Product SMILES: `C[CH2:1][C:2]([C:3](=[O:4])[CH2:5][S:6](=[O:7])[c:8]1[cH:9][cH:10][c:11]([C:12](=[O:13])[N:14]2[CH2:15][CH2:16][N:17]([c:18]3[cH:19][c:20]([Cl:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[Cl:31])([F:32])[F:33]`

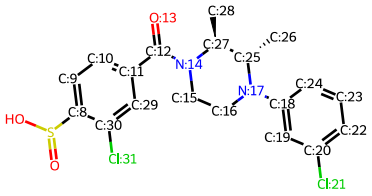
Proposed Transitions

Transition 1

- **Forward Reaction:** S-alkylation of thiols
- **Is Chemically Valid:** True
- **Is Template-based:** True
- **Reasoning:** This is the general template for this transformation. The wildcard atom [*] represents a suitable leaving group for an SN2 reaction. While the provided reaction name is 'S-alkylation of thiols', the sulfoxide product implies the direct precursor is a sulfinate, not a thiol. This transformation, the alkylation of a sulfinate anion, is a plausible method to form the target sulfoxide.
- **Is Smiles Valid:** True
- **Reactant 1:** `*[CH2:5][C:3](=[O:4])[C:2]([CH2:1]C)([F:32])[F:33]`
- **Reactant 2:** `O=S(O)[c:8]1[cH:9][cH:10][c:11]([C:12](=[O:13])[N:14]2[CH2:15][CH2:16][N:17]([c:18]3[cH:19][c:20]([Cl:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[Cl:31]`



R1



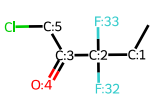
R2

Reactants for Transition 1

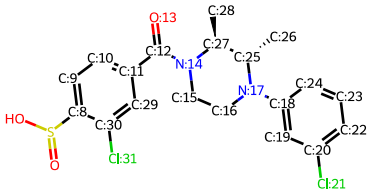
Transition 2

- **Forward Reaction:** S-alkylation of thiols
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. The proposed reactants are a sulfinic acid and an alpha-chloro ketone. In the presence of a base, the sulfinic acid forms a sulfinate anion, a soft nucleophile that will react with the activated primary electrophile via an SN2 mechanism. The reaction is expected to be chemoselective and will not affect the remote stereocenters.
- **Is Smiles Valid:** True

- **Reactant 1:** `Cl[CH2:5][C:3](=[O:4])[C:2]([CH2:1]C)([F:32])[F:33]`
- **Reactant 2:** `O=S(O)[c:8]1[cH:9][cH:10][c:11]([C:12](=[O:13])[N:14]2[CH2:15][CH2:16][N:17]([c:18]3[cH:19][c:20]([Cl:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[Cl:31]`



R1

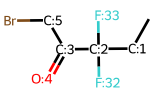


R2

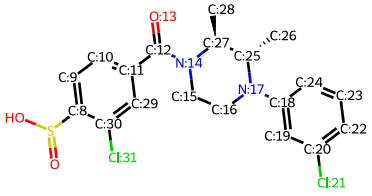
Reactants for Transition 2

Transition 3

- **Forward Reaction:** S-alkylation of thiols
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. The alpha-bromo ketone is an excellent electrophile for SN2 reactions. Bromide is a better leaving group than chloride, potentially allowing for milder reaction conditions. The reaction with the sulfinate anion is plausible, chemoselective, and stereochemically sound.
- **Is Smiles Valid:** True
- **Reactant 1:** `Br[CH2:5][C:3](=[O:4])[C:2]([CH2:1]C)([F:32])[F:33]`
- **Reactant 2:** `O=S(O)[c:8]1[cH:9][cH:10][c:11]([C:12](=[O:13])[N:14]2[CH2:15][CH2:16][N:17]([c:18]3[cH:19][c:20]([Cl:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[Cl:31]`



R1

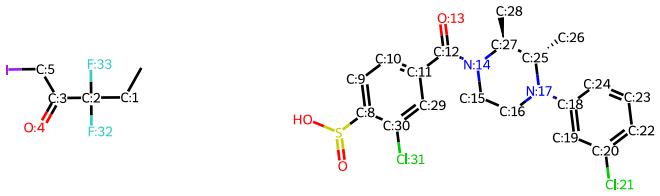


R2

Reactants for Transition 3

Transition 4

- **Forward Reaction:** S-alkylation of thiols
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. The alpha-iodo ketone is a highly reactive electrophile due to iodide being an excellent leaving group. This combination should readily undergo the desired SN2 reaction with the sulfinate anion. Reactant stability and chemoselectivity are expected to be good.
- **Is Smiles Valid:** True
- **Reactant 1:** `I[CH2:5][C:3](=[O:4])[C:2]([CH2:1]C)([F:32])[F:33]`
- **Reactant 2:** `O=S(O)[c:8]1[cH:9][cH:10][c:11]([C:12](=[O:13])[N:14]2[CH2:15][CH2:16][N:17]([c:18]3[cH:19][c:20]([Cl:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[Cl:31]`

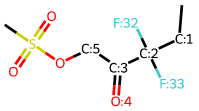


R1 R2

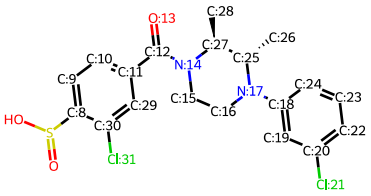
Reactants for Transition 4

Transition 5

- **Forward Reaction:** S-alkylation of thiols
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. Use of an alpha-mesyloxy ketone is a standard method for activating a primary carbon for SN2 displacement. Mesylate is an excellent leaving group, comparable in reactivity to iodide. The reaction is chemically plausible and expected to be selective.
- **Is Smiles Valid:** True
- **Reactant 1:** `CS(=O)(=O)O[CH2:5][C:3](=[O:4])[C:2]([CH2:1]C)([F:32])[F:33]`
- **Reactant 2:** `O=S(O)[c:8]1[cH:9][cH:10][c:11]([C:12](=[O:13])[N:14]2[CH2:15][CH2:16][N:17]([c:18]3[cH:19][c:20]([Cl:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[Cl:31]`



R1

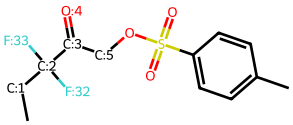


R2

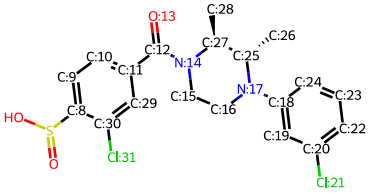
Reactants for Transition 5

Transition 6

- **Forward Reaction:** S-alkylation of thiols
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. The alpha-tosyloxy ketone provides an excellent leaving group (tosylate) for the SN2 reaction with the sulfinate nucleophile. This is a very common and reliable transformation in organic synthesis. The reactants are stable and the reaction should be selective.
- **Is Smiles Valid:** True
- **Reactant 1:** `Cc1ccc(S(=O)(=O)O[CH2:5][C:3](=[O:4])[C:2]([CH2:1]C)([F:32])[F:33])cc1`
- **Reactant 2:** `O=S(O)[c:8]1[cH:9][cH:10][c:11]([C:12](=[O:13])[N:14]2[CH2:15][CH2:16][N:17]([c:18]3[cH:19][c:20]([Cl:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[Cl:31]`



R1

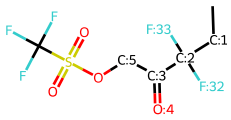


R2

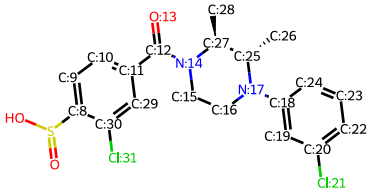
Reactants for Transition 6

Transition 7

- **Forward Reaction:** S-alkylation of thiols
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid. Triflate is an exceptionally good leaving group, making the alpha-triflyloxy ketone extremely reactive. While its high reactivity could potentially lead to side reactions, it makes the desired SN2 displacement very favorable. This is a chemically sound, albeit highly reactive, option.
- **Is Smiles Valid:** True
- **Reactant 1:** `O=S(=O)(O[CH2:5][C:3](=[O:4])[C:2]([CH2:1]C)([F:32])[F:33])C(F)(F)F`
- **Reactant 2:** `O=S(O)[c:8]1[cH:9][cH:10][c:11]([C:12](=[O:13])[N:14]2[CH2:15][CH2:16][N:17]([c:18]3[cH:19][c:20]([Cl:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[Cl:31]`



R1



R2

Reactants for Transition 7