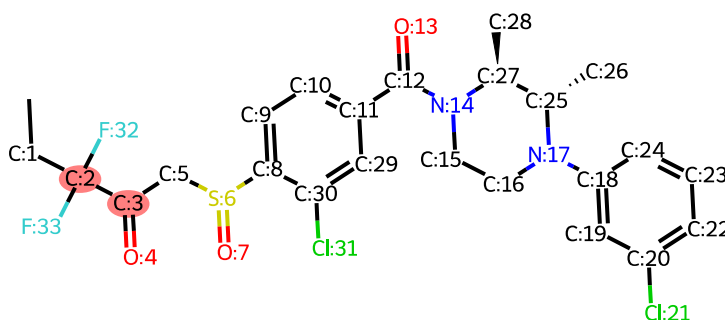


Reaction Report for *LEI_515*, Priority 14

Selected Position: C:2 C:3

Selected Forward Reaction: Enolate Acylation

Product



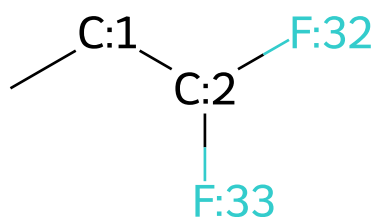
Reaction site highlighted at position C:2 C:3

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:** Enolate Acylation
- **Is Chemically Valid:** True
- **Is Template-based:** True
- **Reasoning:** This is the general template for an Enolate Acylation forming an α,α -difluoro ketone. The nucleophile is generated from 1,1-difluoropropane, and the electrophile is an activated carboxylic acid derivative, where the reactive group belongs to the class represented by the wildcard [*].
- **Is Smiles Valid:** False
- **Reactant 1:** C[CH2:1][CH:2]([F:32])[F:33]
- **Reactant 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])



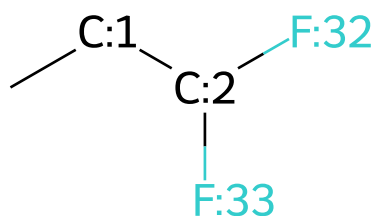
R1

Reactants for Transition 1

Transition 2

- **Forward Reaction:** Enolate Acylation
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This is a valid and highly practical approach. The acyl chloride is a very reactive electrophile that will readily react with the organometallic nucleophile derived from 1,1-difluoropropane. The other functional groups (amide, sulfone, aryl chlorides) are significantly less electrophilic and should not interfere under typical reaction conditions (e.g., strong base, low temperature).
- **Is Smiles Valid:** False

- **Reactant 1:** C[CH2:1][CH:2]([F:32])[F:33]
- **Reactant 2:** Cl[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])



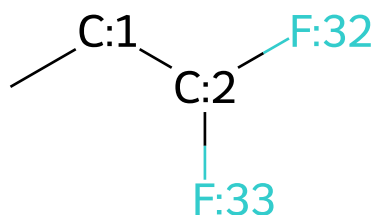
R1

Reactants for Transition 2

Transition 3

- **Forward Reaction:** Enolate Acylation
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** Valid. The acyl bromide is a highly reactive electrophile, analogous to the acyl chloride, and will react cleanly with the nucleophile. Chemoselectivity is expected to be high, and the reactants are stable, although acyl bromides can be more moisture-sensitive than acyl chlorides.
- **Is Smiles Valid:** False

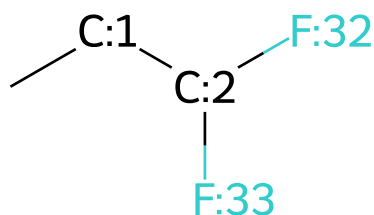
- **Reactant 1:** C[CH2:1][CH:2]([F:32])[F:33]
- **Reactant 2:** Br[C:3](=[O:4])[CH2:5][S:6](=[O:7])[c:8]1[cH:9][cH:10][c:11]([C:12](=[O:13]))[N:14]2[CH2:15][CH2:16][N:17]([c:18]3[cH:19][c:20]([Cl:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[Cl:31])



R1

Transition 4

- **Forward Reaction:** Enolate Acylation
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid, but may be less efficient than using an acyl halide. The methyl ester is less electrophilic, which could lead to competitive side reactions or require more forcing conditions. However, the reaction of strong organometallic nucleophiles with esters to form ketones is a well-established transformation.
- **Is Smiles Valid:** False
- **Reactant 1:** C[CH2:1][CH:2]([F:32])[F:33]
- **Reactant 2:** C0[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]([C1:21])[cH:22][cH:23][cH:24]3)[C@@H:25]([CH3:26])[C@@H:27]2[CH3:28])[cH:29][c:30]1[C1:31])

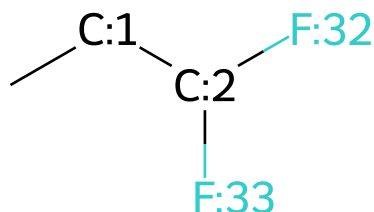


R1

Transition 5

- **Forward Reaction:** Enolate Acylation
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This permutation is valid for the same reasons as the methyl ester. The ethyl ester is a viable, albeit only moderately reactive, acylating agent for a potent difluoroalkyl nucleophile.
- **Is Smiles Valid:** False
- **Reactant 1:** C[CH2:1][CH:2]([F:32])[F:33]

- **Reactant 2:** CCO[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])

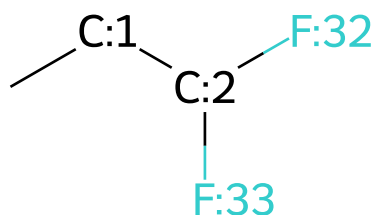


R1

Reactants for Transition 5

Transition 6

- **Forward Reaction:** Enolate Acylation
- **Is Chemically Valid:** True
- **Is Template-based:** False
- **Reasoning:** This is a highly valid and often preferred method for ketone synthesis. The Weinreb amide is an excellent electrophile for this transformation, designed to react cleanly with strong nucleophiles to form a stable tetrahedral intermediate, which prevents over-addition. The reaction is expected to be high-yielding and chemoselective.
- **Is Smiles Valid:** False
- **Reactant 1:** C[CH2:1][CH:2]([F:32])[F:33]
- **Reactant 2:** CON(C)[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])



R1

Reactants for Transition 6