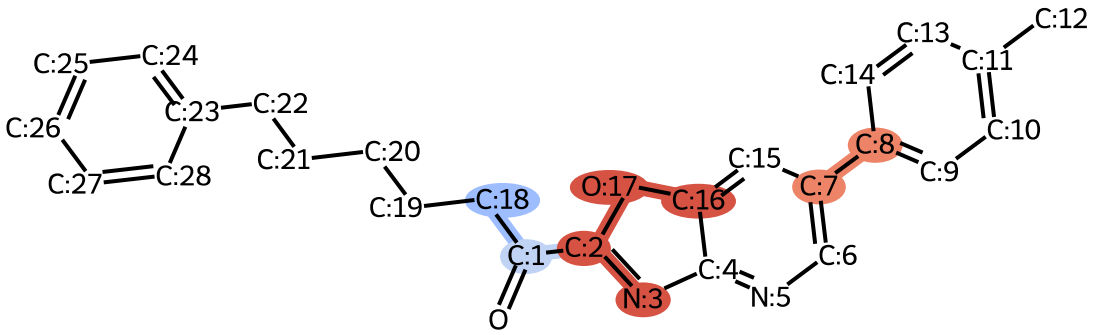
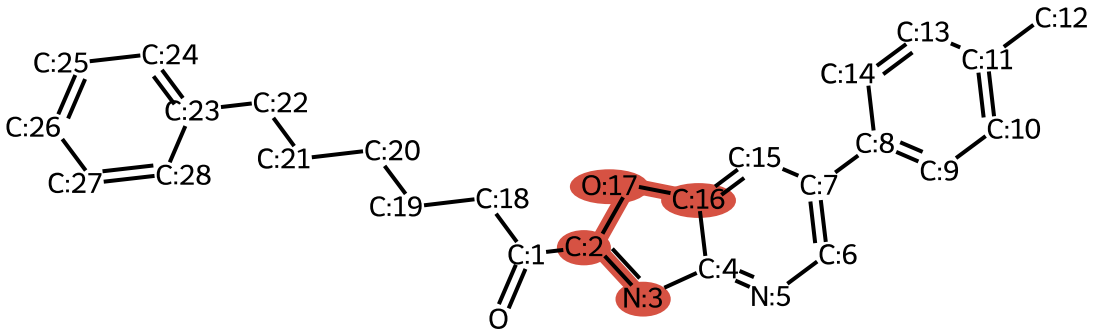
Disconnection Position Analysis for LEI_105

Overview of All Predicted Disconnection Sites



All Positions

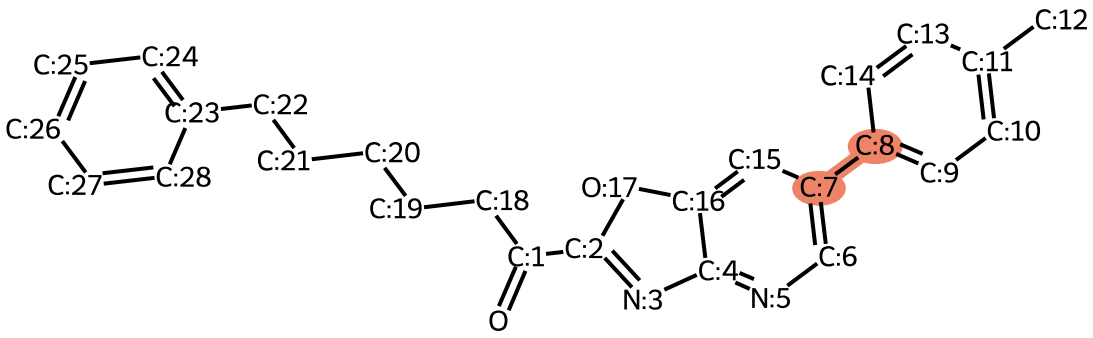
Priority 1: `O:17 C:16 N:3 C:2`



Position for Priority 1

- **Forward Reaction:** oxadiazole
- **Importance Score:** 4
- **In Ontology:** True
- **Rationale:** Key ring-forming transformation (E, J) that constructs the oxadiazole part of the fused heterocyclic core. This disconnection significantly simplifies the molecular structure by breaking it down into a pyrimidine precursor (c). The forward reaction, a dehydrative cyclization of a diacylhydrazine derivative, is a standard and robust method for 1,3,4-oxadiazole synthesis (a, b).

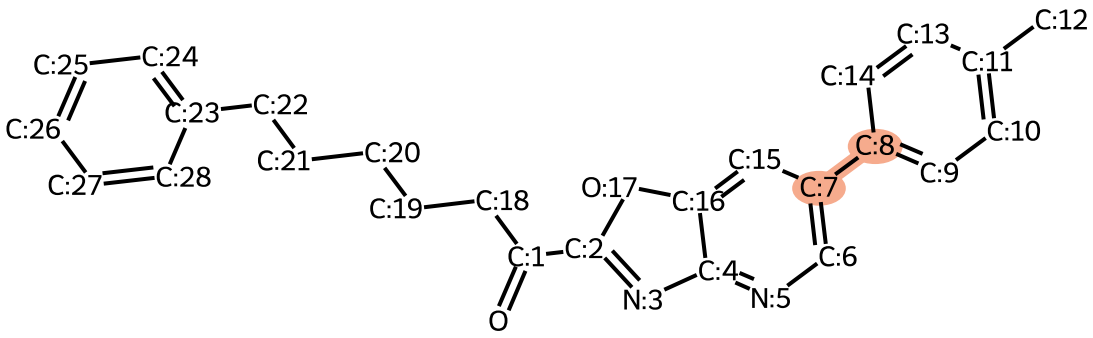
Priority 2: `C:7 C:8`



Position for Priority 2

- **Forward Reaction:** Suzuki coupling with boronic acids
- **Importance Score:** `3`
- **In Ontology:** True
- **Rationale:** Convergent disconnection (B, C) of the p-tolyl group from the heterocyclic core. The Suzuki reaction is robust, high-yielding, and tolerates a wide range of functional groups (b, d). This represents a key late-stage bond formation to build the final target (c). Starting materials (p-tolylboronic acid and a halogenated heterocycle) are readily accessible (a).

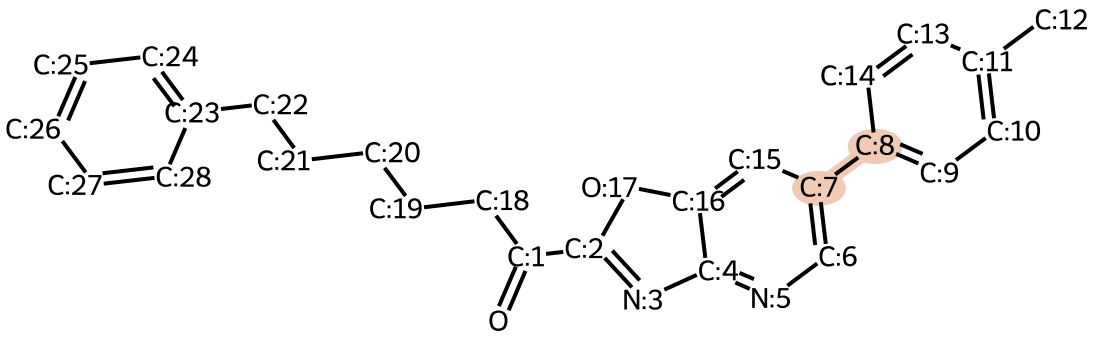
Priority 3: `C:7 C:8`



Position for Priority 3

- **Forward Reaction:** Stille reaction_aryl
- **Importance Score:** `3`
- **In Ontology:** True
- **Rationale:** Convergent disconnection (B, C) of the p-tolyl group. The Stille coupling is a reliable alternative to Suzuki (b, c), though it involves toxic organotin reagents which is a drawback for practicality (d). Starting materials would be a halogenated heterocycle and a p-tolylstannane (a).

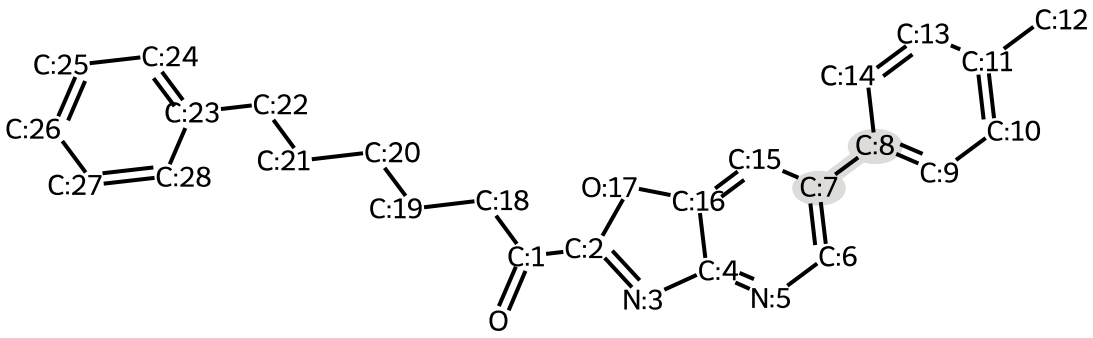
Priority 4: `C:7 C:8`



Position for Priority 4

- **Forward Reaction:** Negishi coupling
- **Importance Score:** `3`
- **In Ontology:** True
- **Rationale:** Convergent C-C bond formation (B, C). Negishi coupling using an organozinc reagent offers high reactivity and functional group tolerance (b, c). The main drawback is the moisture sensitivity of the organozinc reagent (d). Connects the p-tolyl group to a halogenated core (a).

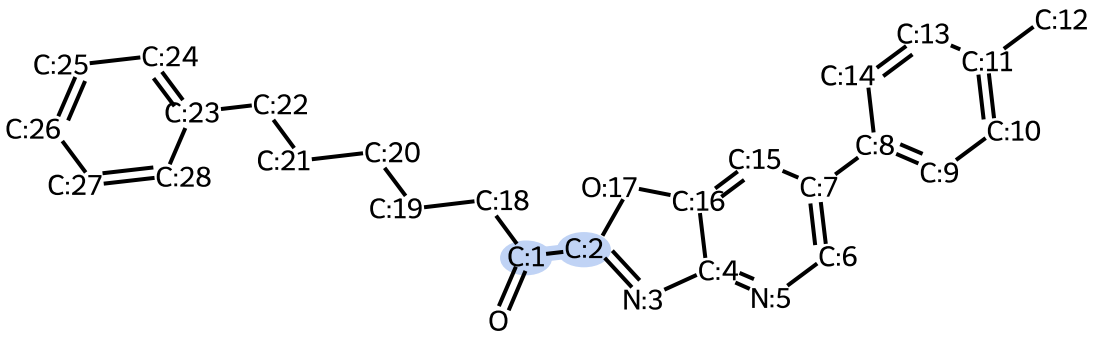
Priority 5: `C:7 C:8`



Position for Priority 5

- **Forward Reaction:** Kumada cross-coupling
- **Importance Score:** `3`
- **In Ontology:** True
- **Rationale:** A powerful C-C bond forming reaction (B, C) connecting a p-tolyl Grignard reagent with a halogenated heterocyclic core, catalyzed by Ni or Pd (b, c). Grignard reagents are highly reactive, which can be a challenge for functional group compatibility but offers excellent synthetic power (d).

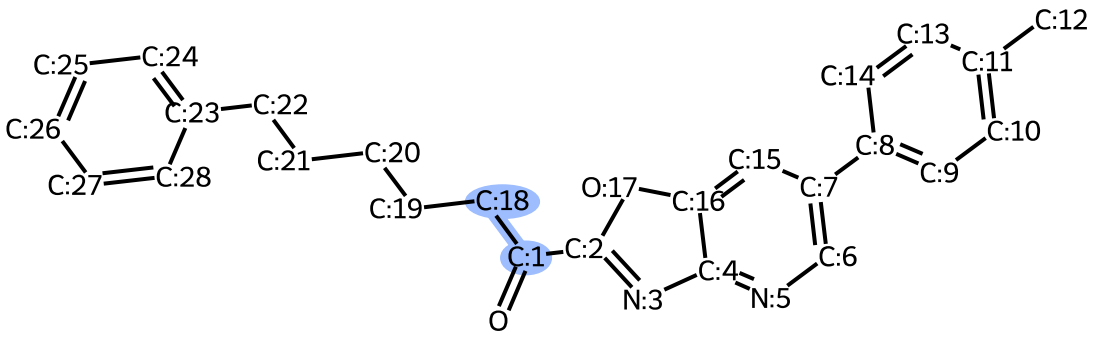
Priority 6: `C:1 C:2`



Position for Priority 6

- **Forward Reaction:** Friedel-Crafts acylation
- **Importance Score:** `3`
- **In Ontology:** True
- **Rationale:** Strategic bond analysis (D) suggests disconnecting the acyl group from the electron-rich oxadiazole ring. Friedel-Crafts acylation provides a direct route to install the ketone functionality (c). Requires 6-phenylhexanoyl chloride and a Lewis acid catalyst. Potential issues include regioselectivity if other positions on the core are reactive (d).

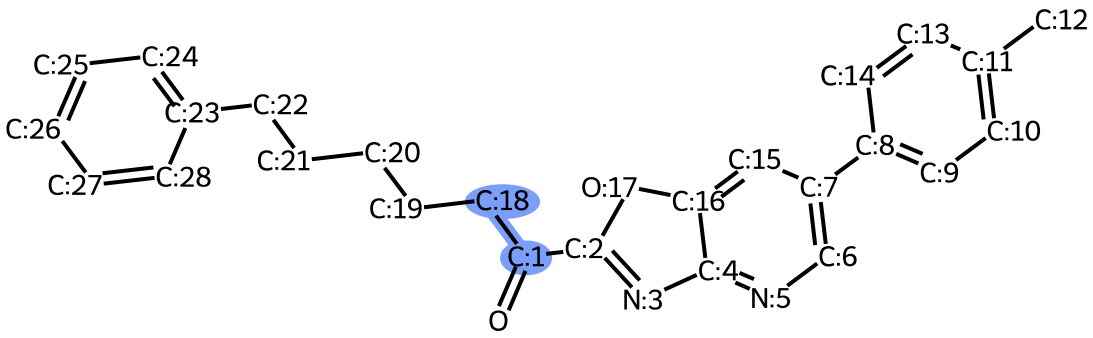
Priority 7: `C:1 C:18`



Position for Priority 7

- **Forward Reaction:** Ketone from Weinreb amide
- **Importance Score:** 2
- **In Ontology:** True
- **Rationale:** Disconnects the alkyl chain from the carbonyl group (D). This strategy allows for the formation of the ketone from a stable Weinreb amide intermediate on the heterocyclic core via addition of a 5-phenylpentyl organometallic reagent (b, c). This method reliably avoids over-addition, a common side reaction with other carboxylic acid derivatives (d).

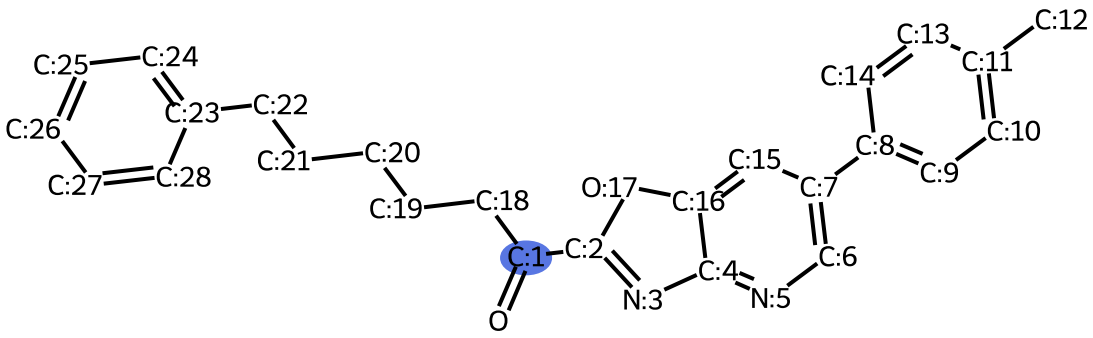
Priority 8: `C:1 C:18`



Position for Priority 8

- **Forward Reaction:** Grignard from nitrile to ketone
- **Importance Score:** `2`
- **In Ontology:** True
- **Rationale:** An alternative disconnection of the alkyl chain from the carbonyl (D). A nitrile on the heterocyclic core can be reacted with a 5-phenylpentyl Grignard reagent, followed by hydrolysis, to yield the target ketone (c). This is a classical and robust transformation (b), simplifying the target to two common synthons (a).

Priority 9: `C:1 0:1`



Position for Priority 9

- **Forward Reaction:** Oxidation or Dehydrogenation of Alcohols to Aldehydes and Ketones
- **Importance Score:** `2`
- **In Ontology:** True
- **Rationale:** A standard functional group interconversion (FGI) (H) where the ketone is derived from the corresponding secondary alcohol. The forward oxidation is typically high-yielding and reliable with many available reagents (e.g., PCC, Swern, DMP) (b). This adds a step but can be useful if the alcohol is easier to synthesize or handle (a). No stereochemistry to control here (e).