Astinova AI Platform — Retrosynthesis Report

Compound: **4-Aminophenol (paracetamol impurity F)** — Compound (C6H7NO, MW 109.13 Da) | paracetamol/acetaminophen impurity — synthesis & characterization

Generated: 2026-07-16 15:28 | 67 routes returned | 39 / 67 fully solved | Best score: 0.9976 | Best route: 1 steps, 1/1 precursors in stock | Route policy: curated reaction templates

Property	Value
SMILES	`Nc1ccc(O)cc1`
InChIKey	`PLIKAWJENQZMHA-UHFFFAOYSA-N`
Formula	C6H7NO
MW	109.13 Da
LogP (Crippen)	0.97
TPSA	46.2 Å²
HBD / HBA	2 / 2
Rotatable bonds	0
Rings (aromatic)	1 (1)
Chiral centres	0
Fluorines	0 — see SMILES
Routes returned	67
Solved routes	39 / 67
Top score	0.9976
Best route steps	1
Precursors (in stock)	1 (1 in stock)
Search engine	Astinova AI Platform

4-Aminophenol (paracetamol impurity F) (C6H7NO, MW 109.13 Da) is a novel paracetamol/acetaminophen impurity — synthesis & characterization analogue. The Astinova AI Platform returned 67 partial trees (39 fully closed within budget); the best two routes by state score are detailed below with reagents, conditions, intermediates, and reaction template provenance for each step.

Scaffold Comparison — 4-Aminophenol (paracetamol impurity F) vs paracetamol API vs reference standard

Property	4-Aminophenol (paracetamol impurity F)	paracetamol API	reference standard
Formula	C6H7NO	—	—
MW (Da)	109.13	—	—
Fluorines	0	—	—
LogP	0.97	—	—
TPSA (Å²)	46.2	—	—
Aromatic rings	1	—	—
Warhead	see fragment analysis	—	—
Core	see fragment analysis	—	—
C4 amine fragment	—	—	—
C2 ether fragment	—	—	—
Lit. similarity	—	literature reference	—
Key new C–C bond	—	—	—
Route score	0.9976 (partial)	—	—

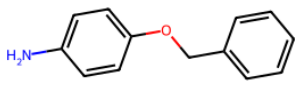
Note: Reference-compound columns are populated during expert review.

Key Retrosynthetic Disconnections

(No named-reaction disconnections recognised; templates were predominantly literature-derived without classifier hits.)

Route 1 / 2 · State score: 0.9976 · Reactions: 1 · Precursors: 1 · In stock: 1

Reactants → Step 1



■ In stock C13H13

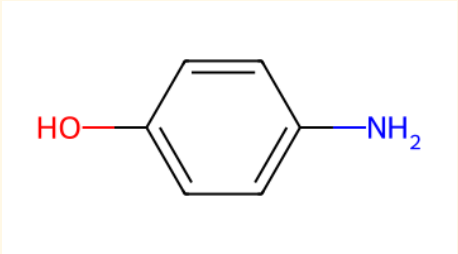
Step 1: Reaction (template-defined) — TARGET

Reaction class	*Not assigned* — reaction template SMARTS does not match a high-confidence rule
Reagents	*Not assigned* — consult literature for this transformation
Solvent / Temp	*Not assigned* — substrate-specific optimisation required
Route policy	Astinova AI Platform · p = 0.0178

Textbook excerpt (BookRAG, contextual only) **Jonathan Clayden_ Nick Greeves_ Stuart G** · p.267 · relevance 0.62

minutes; others are left for hours. In some reactions the amounts of reagents are critical; in others large excesses are used. Some reactions use water as a solvent; in others it must be rigorously excluded, and perhaps toluene, ether, ethanol, or DMF is essential for the success of the reaction. Why such a diverse range of conditions? How can conditions be chosen to favour the reaction we want? To explain all this we will need to work through some thermodynamic principles. We will take a practical, visual approach to the topic, and we will avoid detailed algebraic discussion: for that you ar…

TARGET — 4-Aminophenol (paracetamol impurity F)



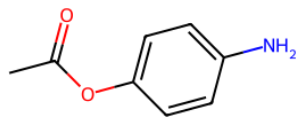
C6H7NO · MW 109.1 Da

`Nc1ccc(O)cc1`

Reaction template: `[OH;D1;+0:2]-[c:1]>>[c:1]-[O;H0;D2;+0:2]-C-c1:c:c:c:c:c:1`

Route 2 / 2 · State score: 0.9976 · Reactions: 1 · Precursors: 1 · In stock: 1

Reactants → Step 1



■ In stock C8H9N

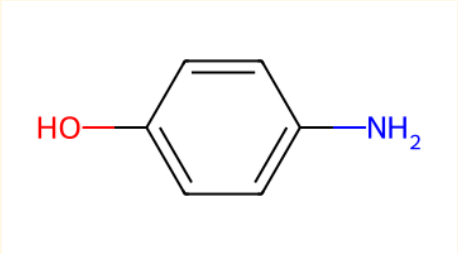
Step 1: Reaction (template-defined) — TARGET

Reaction class	*Not assigned* — reaction template SMARTS does not match a high-confidence rule
Reagents	*Not assigned* — consult literature for this transformation
Solvent / Temp	*Not assigned* — substrate-specific optimisation required
Route policy	Astinova AI Platform · p = 0.0034

Textbook excerpt (BookRAG, contextual only) **Jonathan Clayden_ Nick Greeves_ Stuart G** · p.267 · relevance 0.62

minutes; others are left for hours. In some reactions the amounts of reagents are critical; in others large excesses are used. Some reactions use water as a solvent; in others it must be rigorously excluded, and perhaps toluene, ether, ethanol, or DMF is essential for the success of the reaction. Why such a diverse range of conditions? How can conditions be chosen to favour the reaction we want? To explain all this we will need to work through some thermodynamic principles. We will take a practical, visual approach to the topic, and we will avoid detailed algebraic discussion: for that you ar…

TARGET — 4-Aminophenol (paracetamol impurity F)



C6H7NO · MW 109.1 Da

`Nc1ccc(O)cc1`

Reaction template: `[OH;D1;+0:1]-[c:2]>>C-C(=O)-[O;H0;D2;+0:1]-[c:2]`

Synthesis Notes & Disclaimers

Provenance: Routes generated by the Astinova AI Platform retrosynthesis engine using a curated reaction-template set and building-block stock. 67 trees returned, 39 fully solved within the configured budget. Top score 0.9976; routes ranked by state_score (compound score combining solve quality, reaction count, and in-stock fraction).

Reaction-condition policy (STRICT, per chemist directive 2026-05-09): Reagents / solvent / temperature are shown ONLY when both (a) the reaction template SMARTS contains a specific reagent fragment our high-confidence rules recognise ($POCl_3$, boronate, silyl, Cbz, Boc, HATU, etc.) AND (b) a validated curated entry exists in NAMED_REACTION_CONDITIONS (build_book_rag.py). When uncertain, conditions are explicitly left blank (*'Not assigned — consult literature'*) rather than guessed. The textbook excerpts from BookRAG (12,254 chunks: Clayden / Greeves / Warren / Wothers, Carey, March, *Strategic Applications of Named Reactions in Organic Synthesis*) are shown only when relevance ≥ 0.55, and are flagged *'contextual only'* — they orient a reader to the chemistry family but are NOT the authoritative procedure for this exact substrate. the platform template tags internal template tags) are not used to assign conditions — those tags identify the model's training corpus, not a named reaction.

Recommended convergent sequence: The the platform depth-first ordering is not necessarily the chemist's preferred build order. For convergent assembly, build the bicyclic core first, then layer the C4 amine (most activated SNAr site), then C2 ether, then perform any cross-coupling (Suzuki / Sonogashira) on the assembled core. Global deprotection (TBAF for silyl/alkyne, TFA for Boc, H2/Pd-C for Cbz) at the end.

Stereochemistry caveat: Any chiral-pool fragments must be sourced as the correct stereoisomer. Confirm by chiral-HPLC at each stage; do not attempt asymmetric induction on the assembled molecule without dedicated optimisation.

Protecting-group strategy: Every nucleophilic OH, NH, or alkyne should be protected before any transition-metal cross-coupling step. Default choice: TBS for phenols, Boc for primary amines, TES/TMS for terminal alkynes. Deprotect in reverse order at the end.

Druglikeness flags: Compound MW 109 Da, LogP 0.97, TPSA 46 Å², HBD/HBA 2/2, 0 chiral centres. Lipinski Ro5 considerations apply. Recommend early CYP3A4/2C9 inhibition and hERG screening once the racemate is in hand.

IP / patent freedom: Scaffolds in actively researched target classes are frequently densely patented. A formal freedom-to-operate opinion is recommended before candidate nomination. Where prior-art claims exist, differentiate via core saturation, bioisosteric replacement, or substitution patterns outside the claimed scope.

Stock-gap closure: Leaf precursors marked 'Needs synthesis' in the per-step pages must be assembled before route execution. They typically add 2-4 steps each from commercial building blocks (Combi-Blocks, Enamine, Sigma-Aldrich, FCH Group).

Generated: Astinova AI Platform | Top-3 routes per state_score, walk-order reversed to forward synthesis sequence.