AI-ASSISTED SYNTHESIS PLANNING

From target SMILES to a chemist-reviewable 100 mg synthesis package

Case study: 4-fluoro-N-(4-methoxyphenyl)benzamide for medicinal chemistry planning

This document demonstrates workflow capability. Predicted values, simulated chromatograms, and approximate computed molecular visualizations are included as planning aids and must not be interpreted as measured experimental data.

100 mg
TARGET PRODUCT GOAL

0.544 mmol
ROUTE A SCALE

10 files
VICENA WORK OUTPUTS

EXECUTIVE SUMMARY

AI-generated planning, not autonomous synthesis

Vicena converts a target structure into a compact synthesis-planning package: structure validation, route comparison, literature-precedent audit, stoichiometry, impurity planning, QC expectations, and machine-readable export.

100 mg
TARGET PRODUCT GOAL
Goal: approximate isolated medicinal chemistry test sample.

Route A
RECOMMENDED FIRST PATH
Acid chloride coupling, pending chemist review.

75%
YIELD ASSUMPTION

0.4077 mmol
TARGET PRODUCT MOLES

Case-study target

Field	Value
Target	4-fluoro-N-(4-methoxyphenyl)benzamide
SMILES	`COc1ccc(NC(=O)c2ccc(F)cc2)cc1`
Formula / MW	C14H12FNO2 / 245.253 g/mol
Project goal	Prepare an approximately 100 mg medicinal chemistry test sample.

External positioning: use “chemist-reviewable” or “CRO-style” synthesis planning package. Avoid “autonomous”, “experimentally validated”, or “CRO-grade” unless independently reviewed.

Workflow outputs

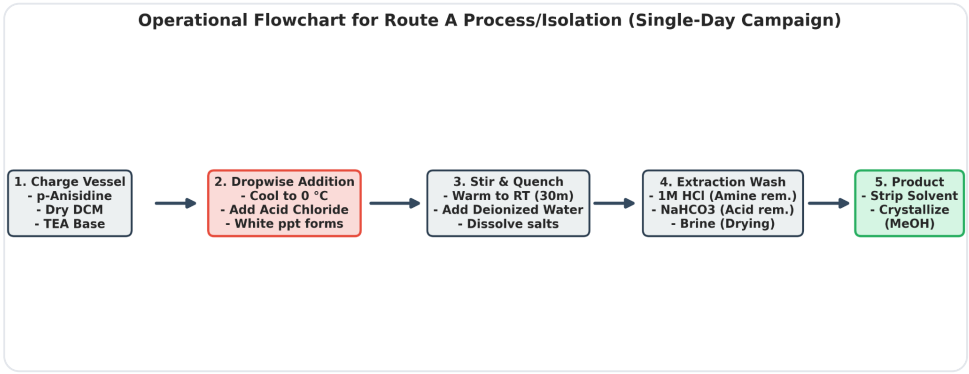

Figure 1. Route A planning flow from charge vessel to crystallization/isolation.

Human-readable
- Route comparison
- Stoichiometry table
- Impurity analysis
- Protocol draft
- QC expectations

Machine-readable
- Target identity
- Route choice
- Masses & volumes
- Yield model
- ELN/LIMS summary

Three routes were compared and Route A was selected as the recommended starting point

Acid chloride coupling was favored for speed, directness, and a relatively simple workup for this robust N-arylbenzamide target, while explicitly acknowledging moisture sensitivity and corrosive-reagent handling risks.

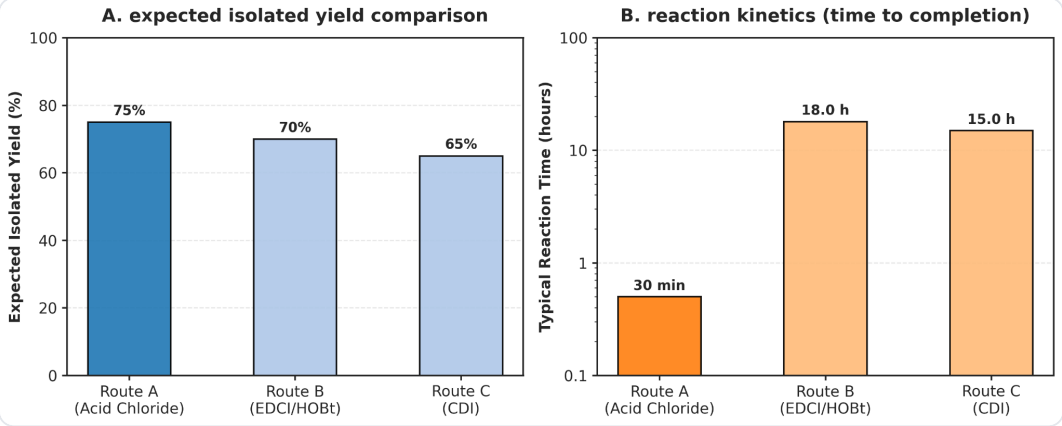

Figure 2. Expected yield and typical time-to-completion comparison. Planning estimates only.

Route summary

Route	Strength	Main concern
A Acid chloride	Fast; direct; expected simple workup	Moisture-sensitive acyl chloride; p-anisidine toxicity
B EDCI/HOBt	Milder activation	Longer run time; DMF removal; coupling byproducts
C CDI	No acyl chloride feedstock	Two-step activation; imidazole residues; slower with anilines

133.3 mg
THEORETICAL YIELD

93–113 mg
EXPECTED RANGE AT 70–85%

100 mg
EXPECTED AT 75%

100 mg target stoichiometry

Component	Equiv.	Mass / volume	Role
4-fluorobenzoyl chloride	1.00	86.2 mg / 64.3 µL	Limiting reagent
p-anisidine	1.20	80.3 mg	Nucleophile
Triethylamine	2.00	110.0 mg / 151.6 µL	HCl scavenger
Anhydrous DCM	-	2.72 mL	Solvent

Boundary condition: route selection here is a planning recommendation, not proof of experimental superiority. Final choice should be confirmed by chemist review, reagent availability, facility constraints, and measured analytical results.

Extraction logic and predicted analytical outputs help the chemist know what to look for

The generated plan uses selective aqueous washes and predicted analytical signatures to anticipate how key impurities may be removed and how the target product may appear in review-stage HPLC and LC-MS checks.

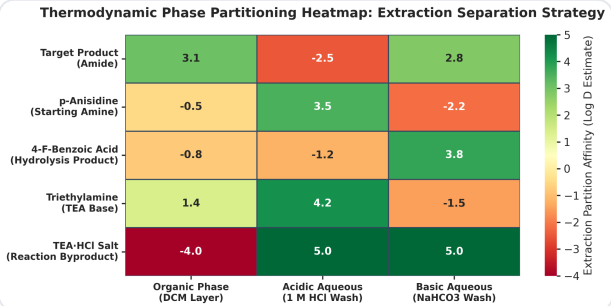

Figure 3. Qualitative extraction-partitioning estimate across organic and aqueous phases.

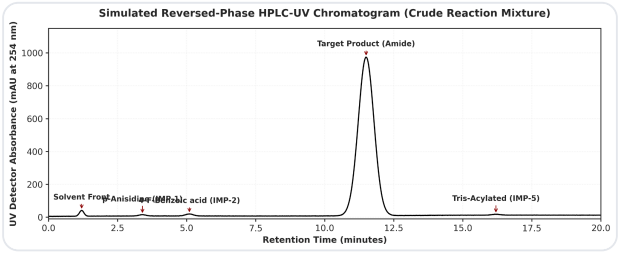

Figure 4. Simulated reversed-phase HPLC-UV chromatogram for the crude mixture. Illustrative planning output only.

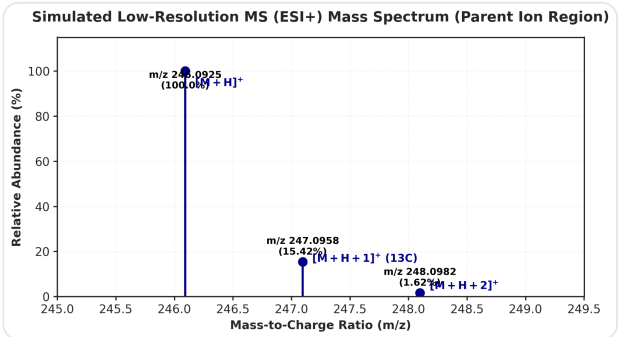

Figure 5. Theoretical ESI+ parent-ion isotope pattern around the expected $[M+H]^+$ peak near m/z 246.1.

Expected separation logic

Species	Expected handling
p-anisidine	Acid wash protonates and removes excess amine.
4-fluorobenzoic acid	Bicarbonate wash removes hydrolysis product as carboxylate.
TEA·HCl	Water-soluble salt; removed in aqueous workup / filtration.
Over-acylated impurity	May require recrystallization or chromatography if detected.

Interpretation note: these figures are useful because they give a chemist a reviewable expectation before LC-MS, HPLC, NMR, and melting point measurements are collected. They should not be presented as measured data.

The output is a review package, not a stand-alone lab instruction

The files were created from the actual synthesis-planning work done by Vicena: route evaluation, calculations, impurity hypotheses, QC planning, and structured outputs for review.

Reviewer-facing documents

- route_comparison.md
- literature_precedents.md
- selected_route_justification.md
- stoichiometry_100mg.md
- impurity_analysis.md
- synthesis_protocol.md
- qc_plan.md
- chemist_recommendation.md

Key takeaway

The value is the integrated planning package: route options, rationale, calculated quantities, impurity hypotheses, QC expectations, a review checklist, and reusable structured outputs.

> **Why Vicena:** one workspace for scientific work - literature and precedent review, protocol planning, computational chemistry, simulations, notebooks, QC planning, structured files, and reviewable project artifacts.

JSON summary highlights

Target formula: C14H12FNO2
MW: 245.253 g/mol
Recommended route: A
Scale: 0.5437 mmol
Modeled isolated product target: 100 mg
Solvent: DCM
Concentration: 0.20 M

Identity | Scale | Reagents | Risk model

Human-in-the-loop controls

- All protocol outputs remain draft procedures for trained chemist review.
- Predicted yields, retention times, Rf values, spectral peaks, and purity estimates must be experimentally confirmed.
- References and supporting information should be manually verified before publication or lab execution.
- Local EHS guidance, SDS documents, and institutional waste procedures supersede generated guidance.

Selected references and source notes

- Actual Vicena work output: route comparison, stoichiometry, impurity analysis, synthesis protocol, QC plan, chemist recommendation, and JSON summary created during the synthesis-planning workflow.
- Grimshaw, J.; de Silva, A. P. *Photochemistry of halogenobenzanilides and halogeno-N-methylbenzanilides. Part 2. Reactivity of the radical intermediates*. *J. Chem. Soc., Perkin Trans. 2*, 1982, 857-866. DOI reported in dossier: 10.1039/P29820000857.
- Before external release, verify article titles, DOIs, supporting information, and extracted conditions directly against source documents.

Application note created from actual Vicena workflow outputs for communication and review of workflow capability. It is not a stand-alone laboratory instruction or an experimental report.