Making Raspberry Ketone Analogue

Synthesis and Analysis of 4-(4-methoxyphenyl)butan-2-one

Your Name / Group Name

April 13, 2025

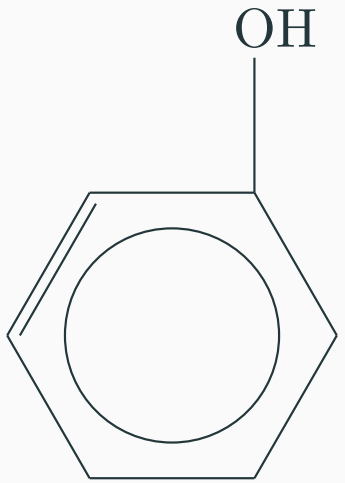
Department of Chemistry
Course: CH3204 Organic Synthesis

Outline

Introduction

Motivation: Raspberry Ketone

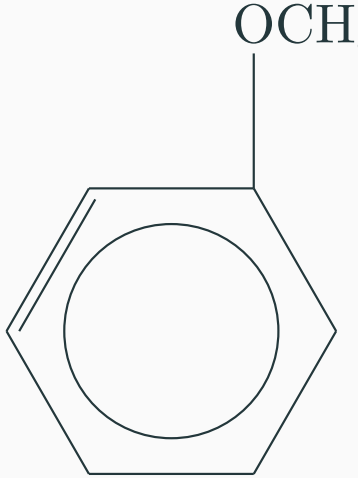
- Raspberry Ketone (4-(4-hydroxyphenyl)butan-2-one) is the primary aroma compound in red raspberries [**RaspberryKetoneWiki**].
- Widely used in flavor and fragrance industries.
- Potential nutraceutical properties (anti-obesity, antioxidant) [**PharmacologicalExplorationRK**].
- Structure:



Raspberry Ketone

Project Goal: Synthesizing an Analogue

- Goal: Synthesize an analogue of Raspberry Ketone.
- Modification: Replace the phenolic -OH group with a methoxy (-OCH_3) group.
- Target Molecule: 4-(4-methoxyphenyl)butan-2-one (Anisylacetone).



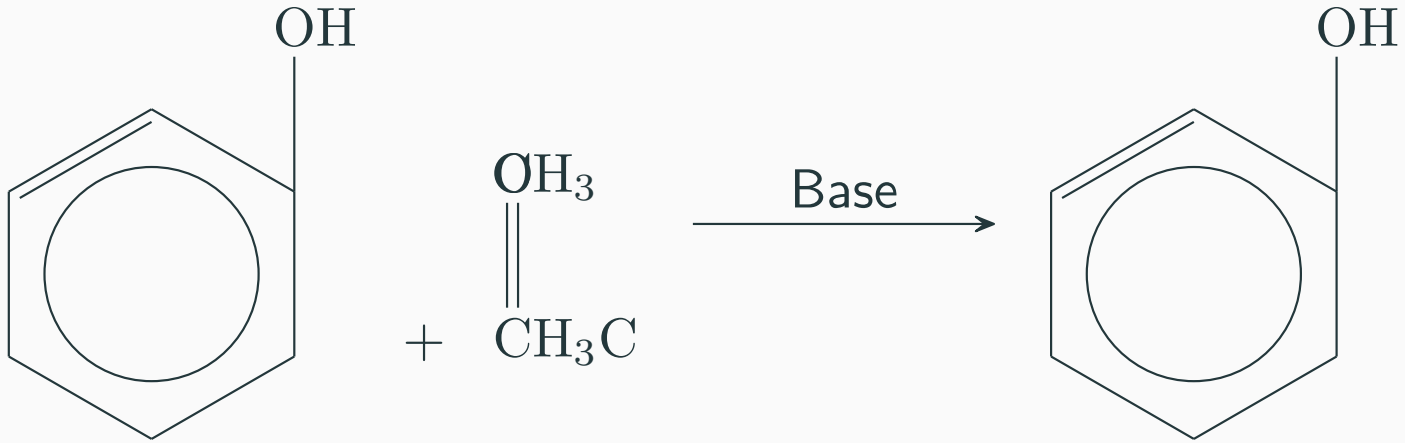
Target Analogue: Anisylacetone

- Starting Material Change: Use 4-methoxybenzaldehyde instead of 4-hydroxybenzaldehyde (due to availability).
- Aim: Investigate the synthesis and compare the properties of the analogue to Raspberry Ketone.

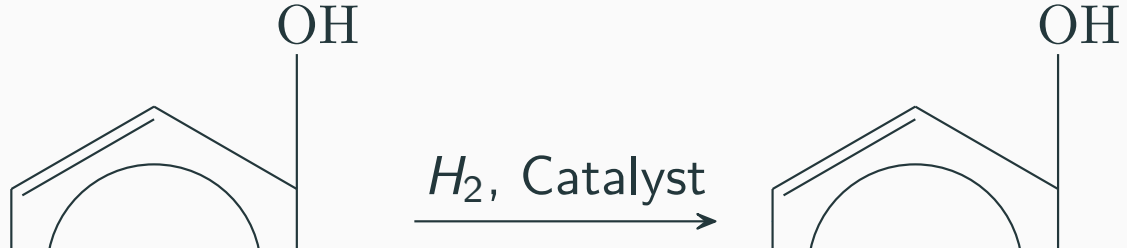
Literature Review

Established Route: Aldol Condensation + Hydrogenation

1. **Step 1: Aldol Condensation [OnePotSynthesisRK, SynthesisRKHydrogenation]**
   - 4-hydroxybenzaldehyde + Acetone $\xrightarrow{\text{Base (e.g., NaOH)}}$ 4-(4-hydroxyphenyl)-3-buten-2-one (PHBA)
   - Intermediate: α, β-unsaturated ketone.

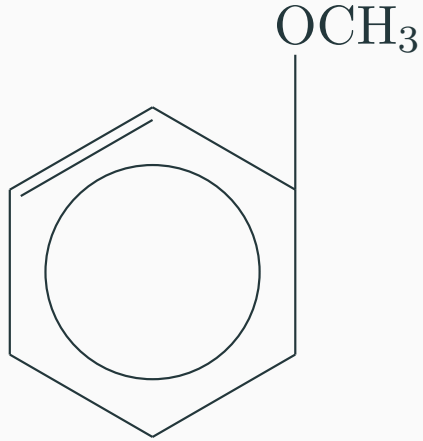


2. **Step 2: Catalytic Hydrogenation [SynthesisRKHydrogenation, SynthesisRKNickelBoride]**
   - PHBA $\xrightarrow{H_2, \text{ Catalyst (e.g., Pd, Ni, Rh)}}$ Raspberry Ketone
   - Reduction of the C=C double bond.



Properties of p-Anisaldehyde ($C_8H_8O_2$)

- Common Name: p-Anisaldehyde [**AnisaldehydeFisherSci**].
- Appearance: Colorless to pale yellow liquid.
- Odor: Sweet, anise-like [**AnisaldehydeHMDB**].
- Key Physical Properties:
  - MW: 136.15 g/mol
  - MP: -1 to 2 °C [**AnisaldehydeVoloChem**]
  - BP: 247-249 °C [**AnisaldehydeFisherSci**]
  - Density: 1.12 g/cm^3
  - Solubility: Immiscible in water, soluble in organic solvents [**AnisaldehydeFisherSci**].
- Structure:



Expected Spectroscopic Data [AnisaldehydeIRSpec, AnisaldehydeNMRSpec, AnisaldehydeHRMS]

IR (cm^{-1}):

- 1700-1725 (C=O stretch, aldehyde)
- 2700-2800 (C-H stretch, aldehyde)
- 1500-1600 (C=C stretch, aromatic)
- 1000-1300 (C-O stretch, methoxy)

HRMS:

- Expected $[M+H]^+$: 137.0597 Da

^{1}H NMR (ppm):

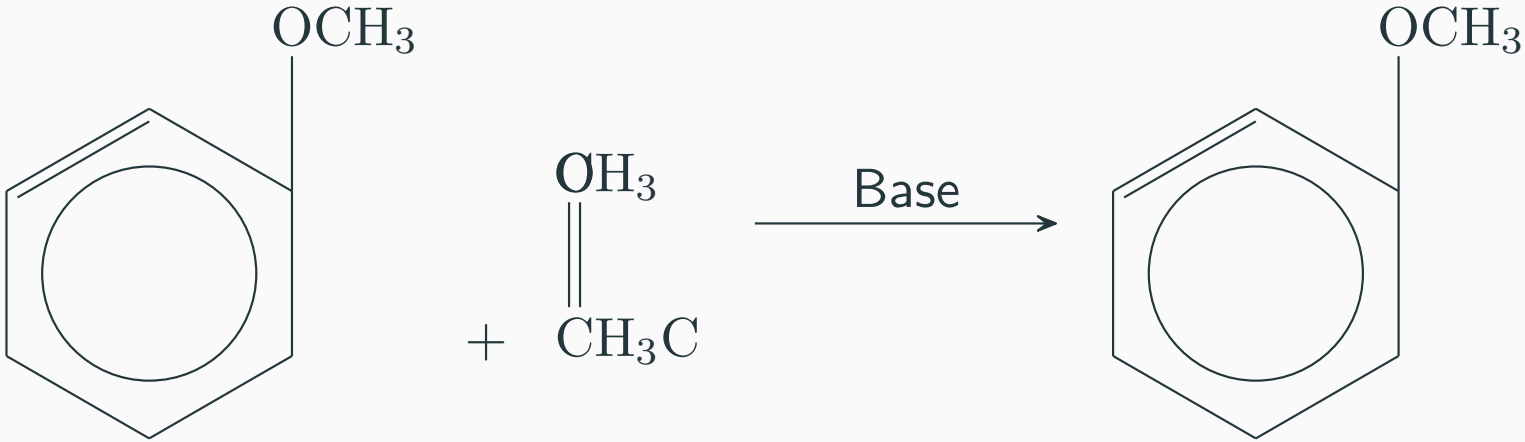
- 9.8-10.0 (s, 1H, CHO)
- 6.8-7.9 (m, 4H, Ar-H)
- 3.8-3.9 (s, 3H, OCH_3)

^{13}C NMR (ppm):

- 190-192 (CHO)
- 114-165 (Ar-C)
- 55-56 (OCH_3)

Adapting the Established Route [SynthesisRKNickelBoride, AnisylacetoneChemBook]

1. **Step 1: Aldol Condensation**
   - 4-methoxybenzaldehyde + Acetone $\xrightarrow{\text{Base}}$ 4-(4-methoxyphenyl)-3-buten-2-one (Anisylidene acetone)



2. **Step 2: Catalytic Hydrogenation**
   - Anisylidene acetone $\xrightarrow{H_2,\ \text{Catalyst}}$ 4-(4-methoxyphenyl)butan-2-one (Anisylacetone)

Experimental Procedure

Synthesis of 4-(4-methoxyphenyl)-3-buten-2-one

Your Experimental Details Needed

Describe the exact procedure you followed:

- Reagents used (4-methoxybenzaldehyde, acetone, base - specify type and concentration).
- Amounts/Moles of each reagent.
- Solvent used (if any).
- Reaction conditions (temperature, time).
- Observations during the reaction (color changes, precipitation).
- Work-up procedure (quenching, extraction, washing, drying).
- Isolation/Purification method (e.g., recrystallization, chromatography - specify details).

Synthesis of 4-(4-methoxyphenyl)butan-2-one

Your Experimental Details Needed

Describe the exact procedure you followed:

- Starting material (isolated intermediate or one-pot?).
- Hydrogenation catalyst used (e.g., Pd/C, Ni_2B, Raney Ni - specify amount).
- Hydrogen source (H_2 gas pressure, transfer hydrogenation?).
- Solvent used.
- Reaction conditions (temperature, time, pressure).
- Monitoring the reaction (e.g., TLC, GC).
- Work-up procedure (catalyst filtration, solvent removal).
- Purification method (e.g., distillation, chromatography - specify details).

Results and Analysis

Characterization of 4-(4-methoxyphenyl)-3-buten-2-one

Your Results Needed

Present the data obtained for the intermediate (if isolated/analyzed):

- Appearance (color, physical state).
- Yield (mass, percentage).
- Melting Point (if solid, compare to literature if available).
- TLC data (Rf value, solvent system).
- IR Spectrum: Assign key peaks (C=O, C=C, C-O). Compare to literature/expected.
- ^{1}H NMR Spectrum: Assign key peaks (vinyl H, Ar-H, OCH_3, CH_3). Compare to literature/expected.
- ^{13}C NMR Spectrum (if obtained): Assign key peaks.
- Other analyses performed?

Note: Literature MP for Anisylidene acetone varies, often around 72-75 °C.

Characterization of 4-(4-methoxyphenyl)butan-2-one

Your Results Needed

Present the data obtained for the final product:

- Appearance (color, physical state - likely an oil).
- Yield (mass, overall percentage yield from starting aldehyde).
- Melting Point (Literature: 8-10 °C [**AnisylacetoneChemBook**] - likely liquid at room temp).
- Boiling Point (if distilled, compare to literature: 270 °C atm [**AnisylacetoneChemImpex**], lower under vacuum).
- TLC data (Rf value, solvent system).
- IR Spectrum: Assign key peaks (C=O ketone, C-O ether). Compare to expected (absence of C=C, presence of C-O).
- ^{1}H NMR Spectrum: Assign key peaks (CH_2, Ar-H, OCH_3, CH_3). Compare to expected.
- ^{13}C NMR Spectrum (if obtained): Assign key peaks. Compare to expected.

Spectroscopic and Physical Property Differences

Based on literature [**SynthesisRKNickelBoride**, **AnisylacetoneChemBook**, **AnisylacetoneChemImpex**, **RKPropertiesChemImpex**] and expected data:

Table 1: Comparison of Key Properties

Property	Raspberry Ketone	Anisylacetone (
Structure	Ar-OH (Ar = p-$C_6H_4CH_2CH_2COCH_3$)	Ar-OCH (Ar = p-$C_6H_4CH_2$
MW (g/mol)	164.20	178.23
MP (°C)	82-83	8-10 (oil at
IR: O-H stretch	Present (3370 cm^{-1})	Absent
IR: C-O-C stretch	Absent	Present (1000-1
^{1}H NMR: Phenolic OH	Present (6-7 ppm)	Absent
^{1}H NMR: Methoxy CH_3	Absent	Present (3.8
Odor	Raspberry-like	Sweet, floral

Conclusion

Conclusion

Summarize Your Findings

Conclude the presentation:

- Briefly restate the goal (synthesize Raspberry Ketone analogue).
- Summarize the synthetic route used (Aldol + Hydrogenation with 4-methoxybenzaldehyde).
- State whether the synthesis was successful based on your analytical data.
- Mention the overall yield obtained.
- Highlight key characterization results confirming the structure (mention specific IR, NMR evidence).
- Briefly compare the properties of your synthesized analogue to literature values and to Raspberry Ketone (e.g., physical state difference due to H-bonding).
- Mention any challenges encountered during the synthesis or analysis.
- Suggest potential future work (if any).

References

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