Paths of analysis*

O1

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselecitve reactions, Tunnels, FGI, FGI with protections

Max. paths returned: 50

Max. iterations: 2000

Commercial:

1. Max. molecular weight - 1000 g/mol
2. Max. price - 1500 $/g

Published:

1. Max. molecular weight - 1000 g/mol
2. Popularity - 5

My Stockroom:

1. Max. molecular weight - 1000 g/mol

Reaction scoring formula: TUNNEL_COEF*FGI_COEF*STEP*20+1000000*(CONFLICT+NON_SELECTIVITY+FILTERS+PROTECT)

Chemical scoring formula: SMALLER^ 3,SMALLER^ 1.5

Min. search width: 400

Max. reactions per product: 60

*The results stated herein were generated using the proprietary platform owned and maintained by Grzybowski Scientific Inventions, Inc., a subsidiary of Merck KGaA, Darmstadt Germany. The results are provided on an as is basis, and shall be used solely in connection with the rights afforded in the license agreement and for no other purpose.

Strategies: none selected

FGI Coeff: 0

Tunnels Coeff: 0

JSON Parameters: {}

2 Paths

5 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

2.1 Path 1

Score: `20.00`

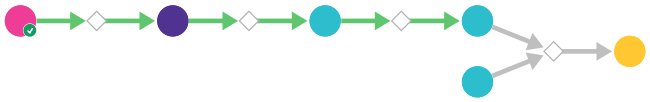
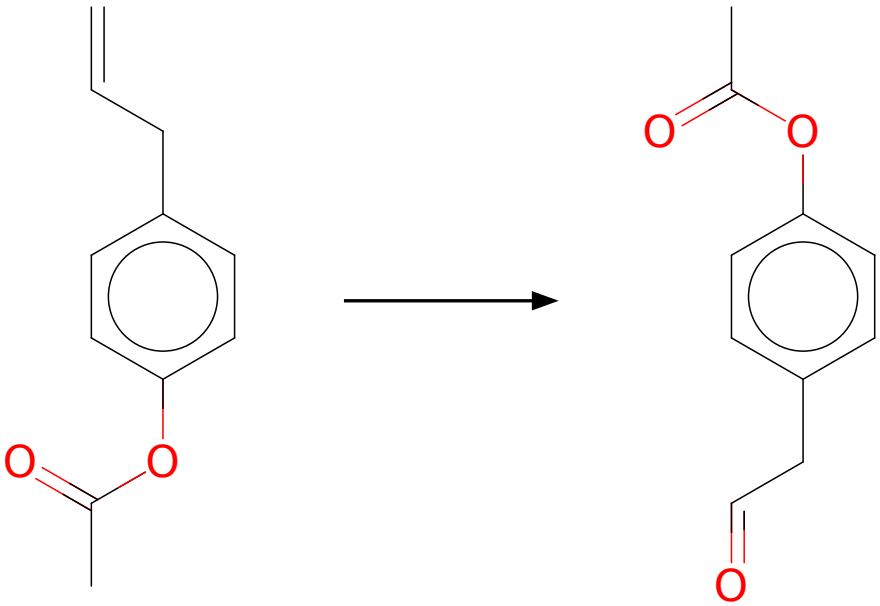
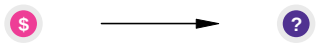


Figure 1: Outline of path 1

2.1.1 Ozonolysis





Substrates:

1. 3-(4-Acetoxyphenyl)-1-propene - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc(CC=O)cc1

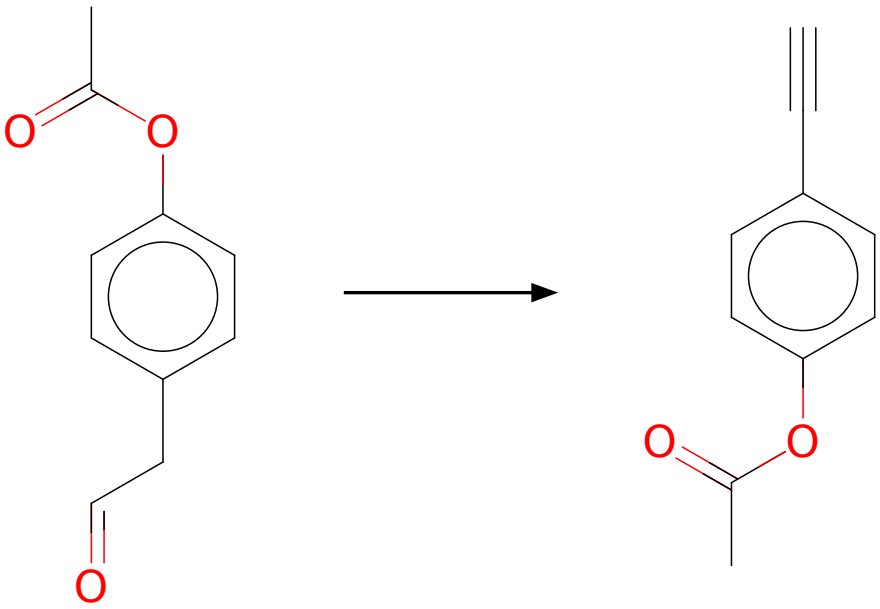
Typical conditions: O3.MeOH.CH2Cl2.PPh3 or Me2S.low temperature

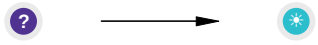
Protections: none

Reference: *10.1016/j.tet.2017.03.039*

Retrosynthesis ID: 5074

2.1.2 Synthesis of alkynes from aldehydes





Substrates:

1. CC(=O)Oc1ccc(CC=O)cc1

Products:

1. 4-acetoxyphenylethyne

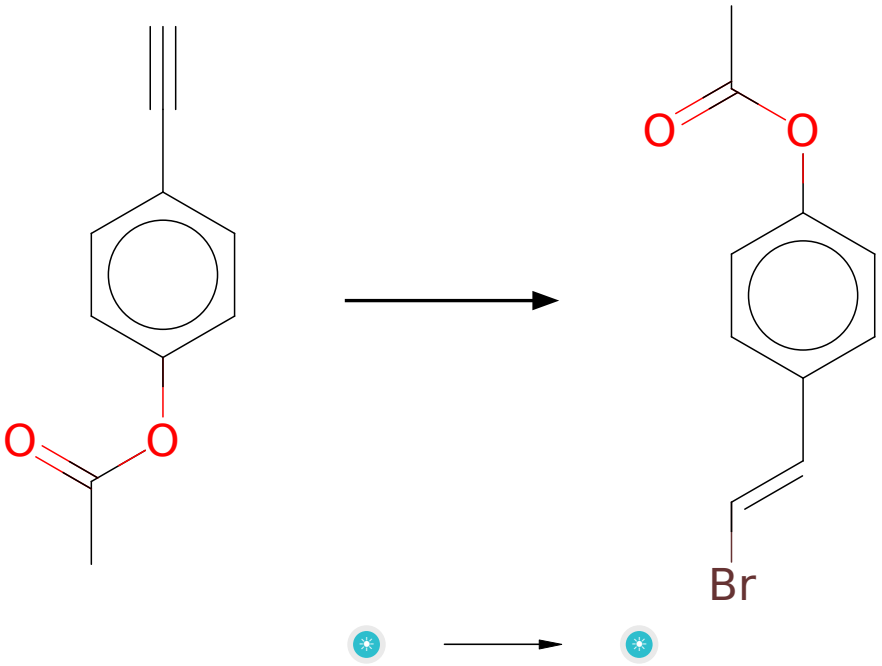
Typical conditions: P1-base.DMF

Protections: none

Reference: *10.1055/s-0028-1087919*

Retrosynthesis ID: 15028

2.1.3 Bromination of vinylalanes



Substrates:

1. 4-acetoxyphenylethyne

Products:

1. C10H9BrO2

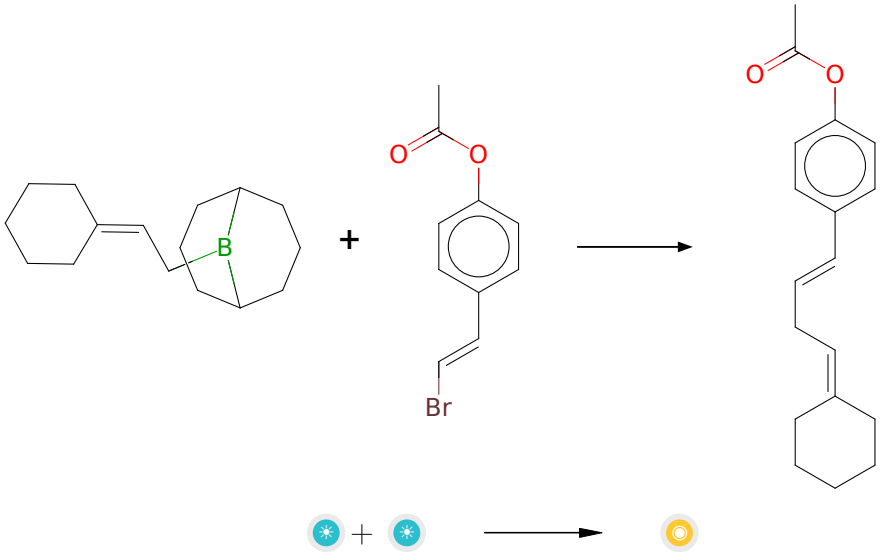
Typical conditions: Schwartz's reagent.then.Br2

Protections: none

Reference: DOI: *10.1039/C2CC36604E* (SI, page S18) AND DOI: *10.1080/00397910008087318*

Retrosynthesis ID: 7405

2.1.4 Suzuki coupling of alkyl-9-BBNs with vinyl bromides



Substrates:

1. 9-(3,3-pentamethyleneallyl)-9-borabicyclo3.3.1nonane
2. C10H9BrO2

Products:

1. CC(=O)Oc1ccc(/C=C/CC=C2CCCCC2)cc1

Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/ja00183a048* and *10.1039/b707338k* and *10.1016/j.tet.2015.05.039* and *10.1021/jo991064z* and *10.1021/ol060290+* and *10.1246/bcsj.65.2863*

Retrosynthesis ID: 25174

2.2 Path 2

Score: 20.00

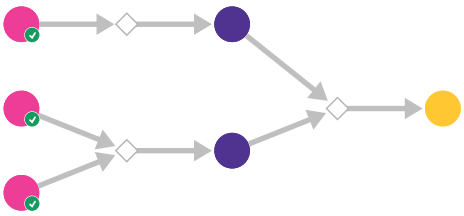
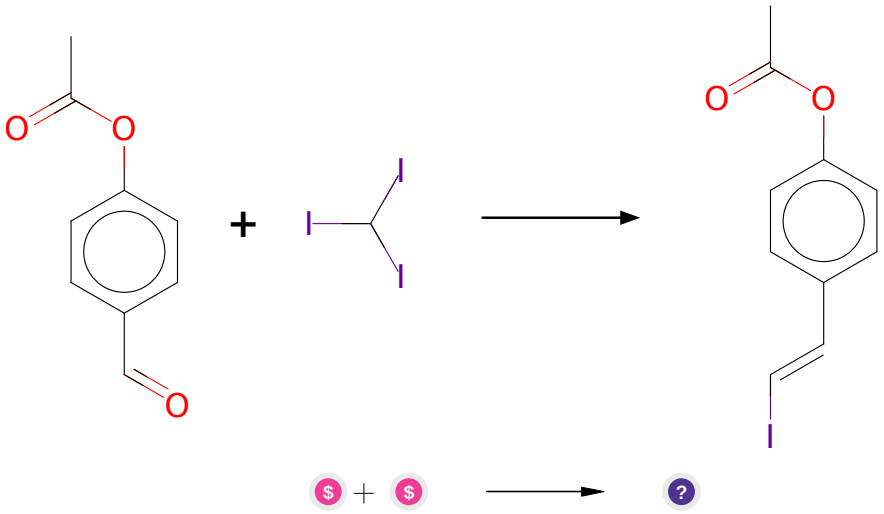


Figure 2: Outline of path 2

2.2.1 Takai olefination



Substrates:

1. Iodoform - *available at Sigma-Aldrich*
2. 4-Acetoxybenzaldehyde - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc(/C=C/I)cc1

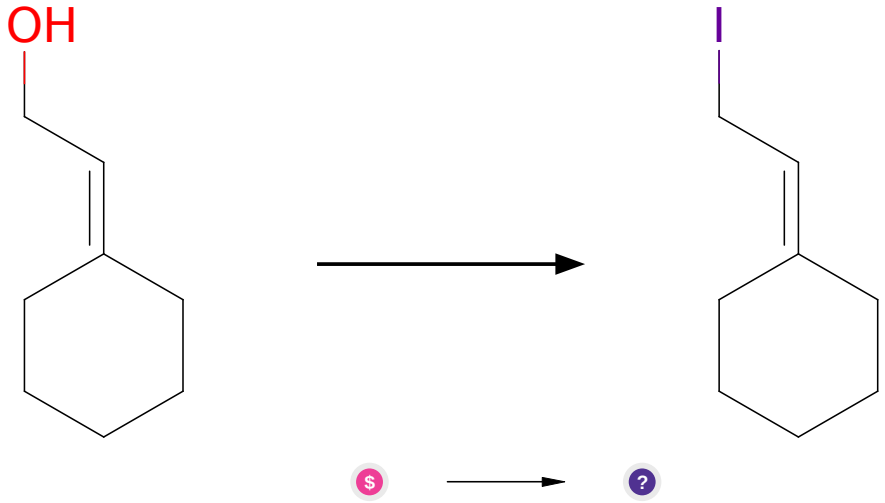
Typical conditions: CrCl2.THF

Protections: none

Reference: *10.1021/ja00283a046* and *10.1021/ja00237a081*

Retrosynthesis ID: 10497

2.2.2 Synthesis Of Alkyl Iodides Via Appel Reaction



Substrates:

1. 2-cyclohexylideneethan-1-ol - *available at Sigma-Aldrich*

Products:

1. ICC=C1CCCCC1

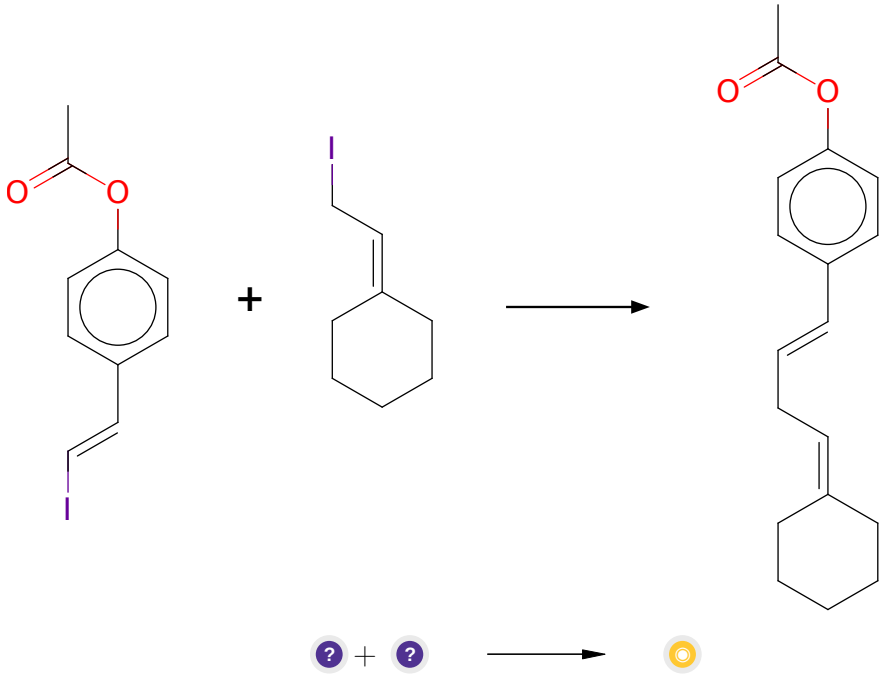
Typical conditions: Imidazole.PPh3.I2

Protections: none

Reference: *10.1002/1099-0690(200102)2001:3<493::AID-EJOC493>3.0.CO2-B* (compound 20) and *10.1016/j.tet.2014.09.030*

Retrosynthesis ID: 9990040

2.2.3 Palladium catalysed alkylation of vinyl iodides



Substrates:

1. ICC=C1CCCCC1
2. CC(=O)Oc1ccc(/C=C/I)cc1

Products:

1. CC(=O)Oc1ccc(/C=C/CC=C2CCCCC2)cc1

Typical conditions: [Pd].catalyst

Protections: none

Reference: *10.1016/j.bmcl.2005.12.066* and *10.1021/ol052070m* and *10.1021/ol5023195* and *10.1002/anie.200703134* and *10.1016/j.bmcl.2005.09.084* and *10.1021/ol0344873*

Retrosynthesis ID: 25162

2.3 Path 3

Score: 25.00

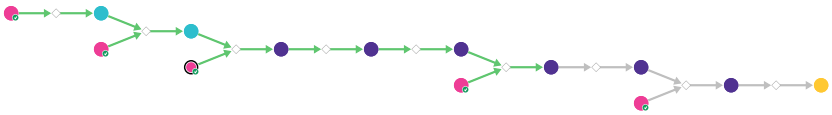
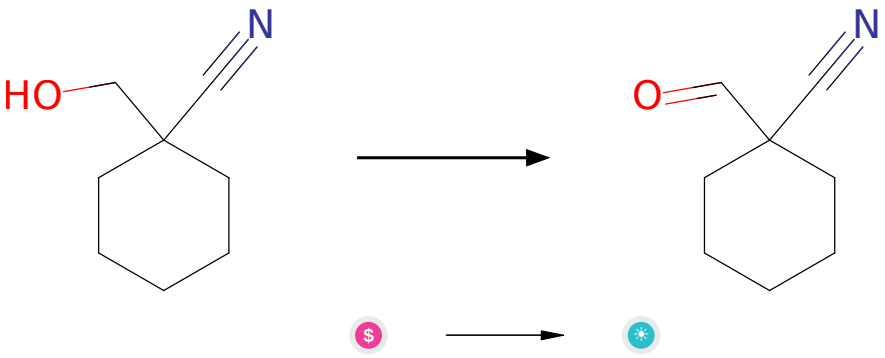


Figure 3: Outline of path 3

2.3.1 Oxidation of primary alcohols with DMP



Substrates:

1. 1-(hydroxymethyl)cyclohexane-1-carbonitrile - *available at Sigma-Aldrich*

Products:

1. 1-formylcyclohexanecarbonitrile

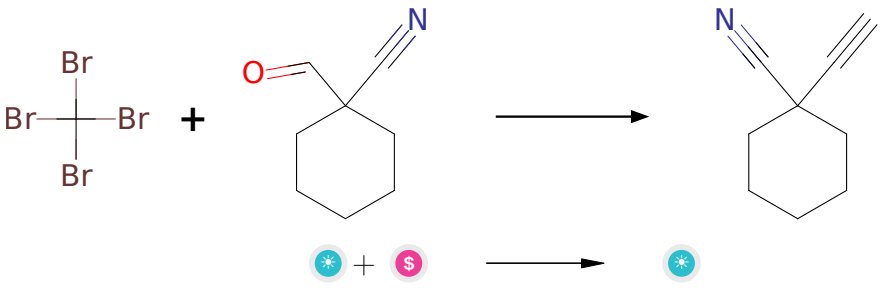
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: *10.1016/j.bmc.2020.115469* p. 3, 9 and *10.1021/acs.jmedchem.8b01878* SI p. S43

Retrosynthesis ID: 50426

2.3.2 Corey-Fuchs reaction



Substrates:

1. 1-formylcyclohexanecarbonitrile
2. Tetrabromomethane - *available at Sigma-Aldrich*

Products:

1. 1-ethinylcyclohexylcyanid

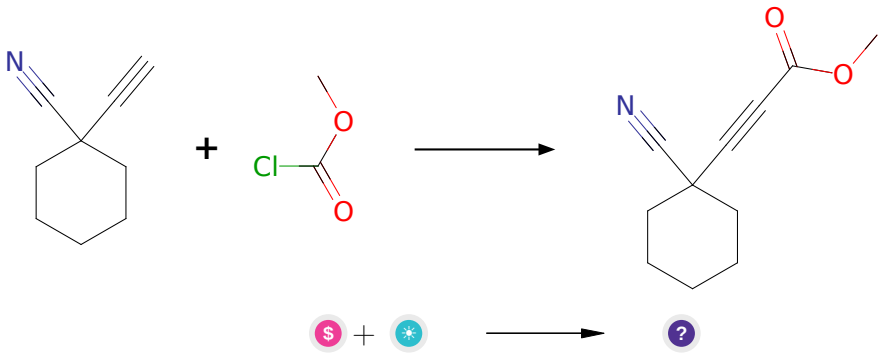
Typical conditions: PPh3.BuLi.CBr4

Protections: none

Reference: *10.1002/ejoc.200601137* and *10.1016/S0040-4039(01)94157-7*

Retrosynthesis ID: 10912

2.3.3 Chloroformate Addtion To Terminal Alkynes



Substrates:

1. Methyl chloroformate - *available at Sigma-Aldrich*
2. 1-ethinylcyclohexylcyanid

Products:

1. COC(=O)C#CC1(C#N)CCCCC1

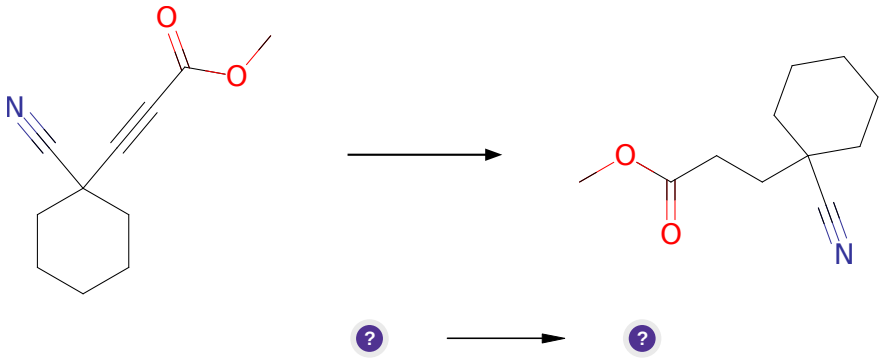
Typical conditions: 1)n-BuLi.solvent.2) chloroformate

Protections: none

Reference: DOI: *10.1021/jo00092a015*

Retrosynthesis ID: 2049

2.3.4 Reduction of alkyne to alkane



Substrates:

1. COC(=O)C#CC1(C#N)CCCCC1

Products:

1. COC(=O)CCC1(C#N)CCCCC1

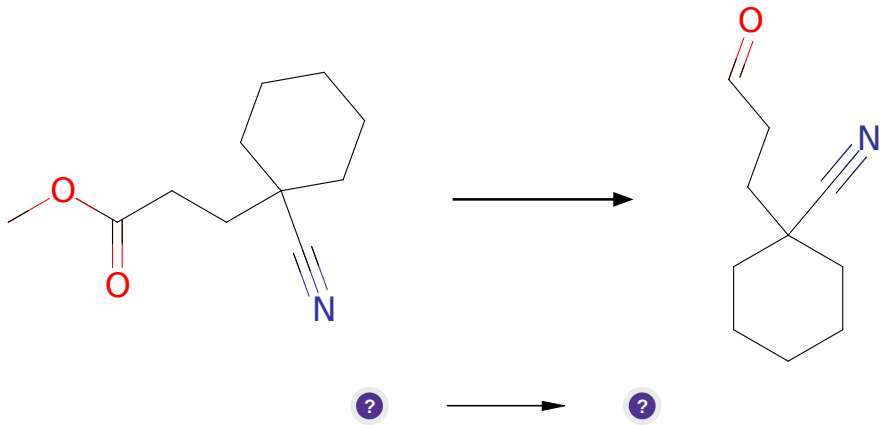
Typical conditions: H2.Pd/C

Protections: none

Reference: *10.1016/j.bmc.2011.05.030* AND *10.1021/ol048591b* AND *10.1021/jo020486x*

Retrosynthesis ID: 14626

2.3.5 Aldehyde Formation



Substrates:

1. COC(=O)CCC1(C#N)CCCCC1

Products:

1. N#CC1(CCC=O)CCCCC1

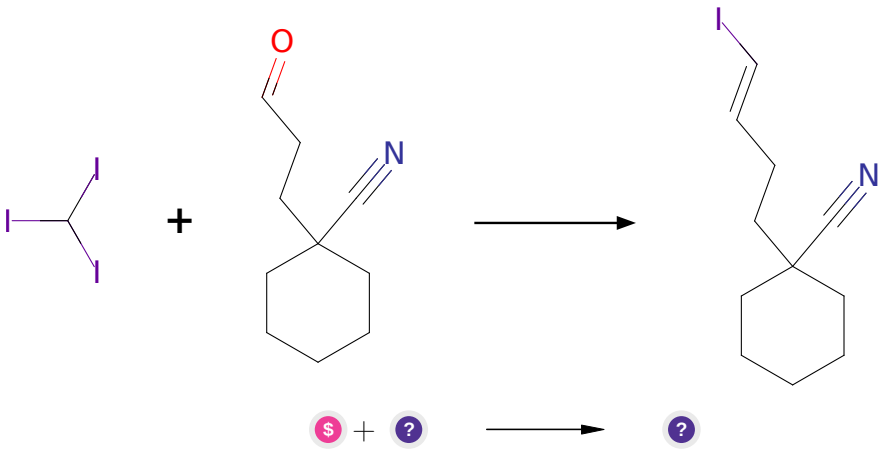
Typical conditions: DIBAL.solvent e.g. DCM

Protections: none

Reference: *10.1039/C39940000483* and *10.1039/C3CC47867J* and *10.1021/jo00222a054* and *10.1021/ja9934908* and *10.1021/jo902426z*

Retrosynthesis ID: 28551

2.3.6 Takai olefination



Substrates:

1. Iodoform - *available at Sigma-Aldrich*
2. N#CC1(CCC=O)CCCCC1

Products:

1. N#CC1(CC/C=C/I)CCCCC1

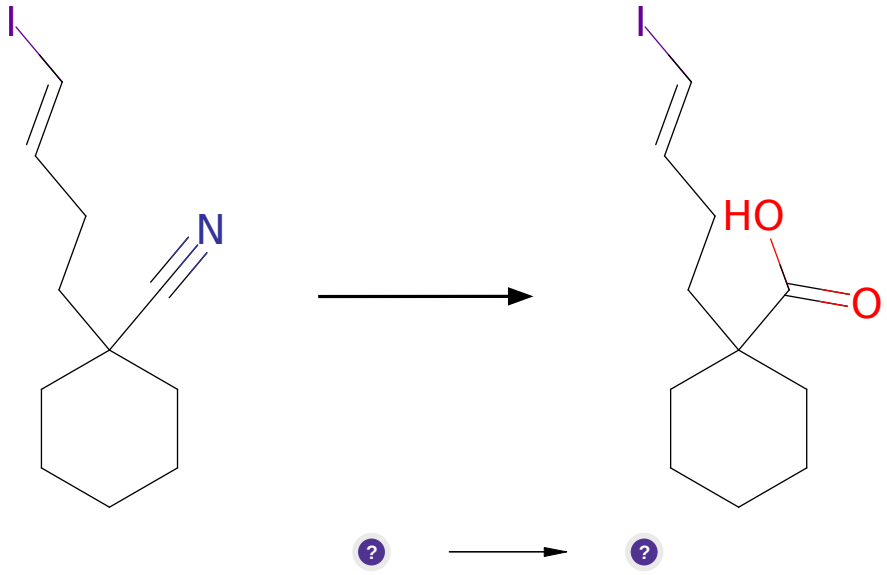
Typical conditions: CrCl2.THF

Protections: none

Reference: *10.1021/ja00283a046* and *10.1021/ja00237a081*

Retrosynthesis ID: 10497

2.3.7 Base hydrolysis of nitriles to carboxylic acids



Substrates:

1. N#CC1(CC/C=C/I)CCCCC1

Products:

1. O=C(O)C1(CC/C=C/I)CCCCC1

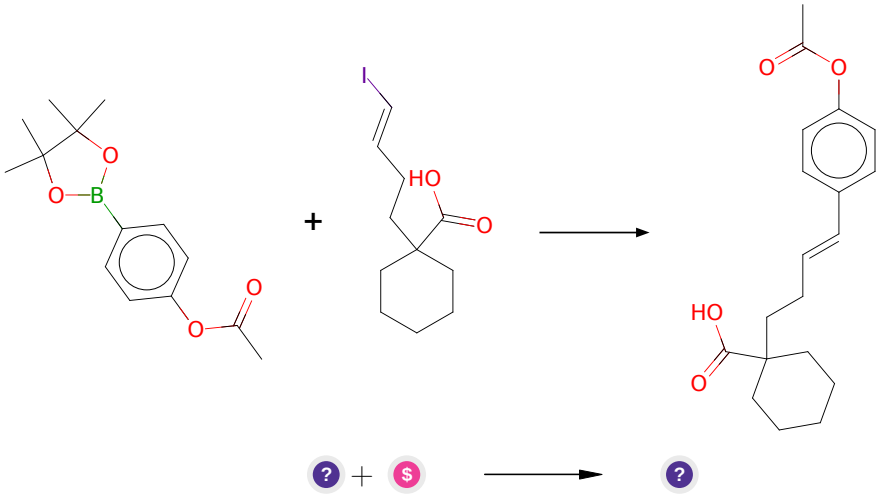
Typical conditions: NaOH.heating.H2O

Protections: none

Reference: *10.1002/1099-0690(200111)2001:22<4207::AID-EJOC4207>3.0.CO;2-3* and *10.1021/acs.jmedchem.5b00702* and *10.1016/j.bmc.2011.07.045*

Retrosynthesis ID: 15107

2.3.8 Suzuki coupling of arylboronic pinacol esters with vinyl iodides



Substrates:

1. O=C(O)C1(CC/C=C/I)CCCCC1
2. 4-Acetoxyphenylboronic acid pinacol ester - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc(/C=C/CCC2(C(=O)O)CCCCC2)cc1

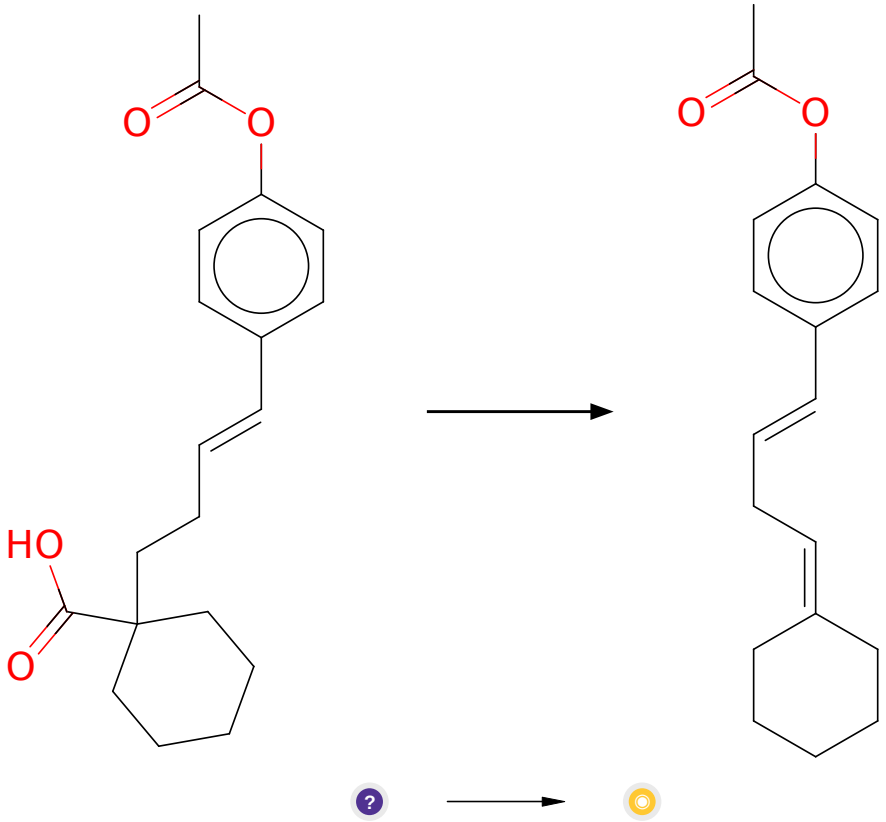
Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 5045

2.3.9 Catalytic dehydrogenative decarboxyolefination of carboxylic acids



Substrates:

1. CC(=O)Oc1ccc(/C=C/CCC2(C(=O)O)CCCCC2)cc1

Products:

1. CC(=O)Oc1ccc(/C=C/CC=C2CCCCC2)cc1

Typical conditions: [Ir]-photocatalyst.[Co]-catalyst.Cs2CO3.DME/H2O.blue.light.rt

Protections: none

Reference: *10.1038/s41557-018-0142-4* and *10.1021/acscatal.8b03282* and *10.1021/acs.joc.9b00167*

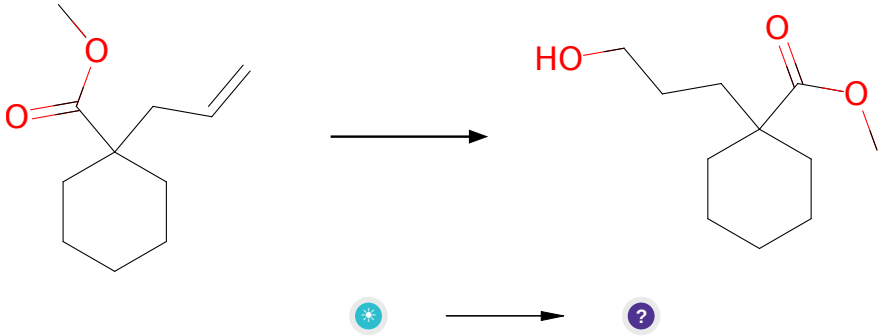
Retrosynthesis ID: 10032330

2.4 Path 4

Score: 25.00

Figure 4: Outline of path 4

2.4.1 Brown Hydroboration of Alkenes



Substrates:

1. 1-allyl-cyclohexanecarboxylic acid methyl ester

Products:

1. COC(=O)C1(CCCO)CCCCC1

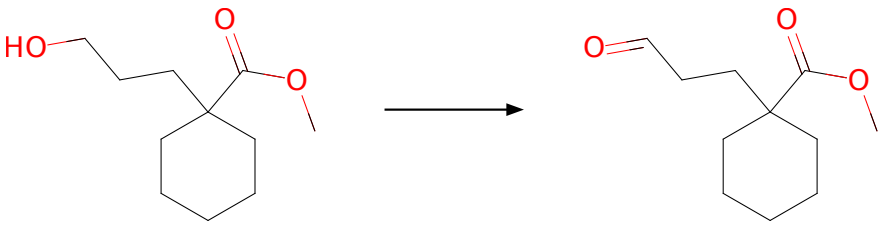
Typical conditions: B2H6.H2O2.THF.NaOH

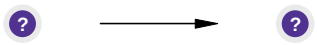
Protections: none

Reference: *10.1002/9780470638859.conrr118*

Retrosynthesis ID: 4772

2.4.2 Oxidation of primary alcohols with DMP





Substrates:

1. COC(=O)C1(CCCO)CCCCC1

Products:

1. COC(=O)C1(CCC=O)CCCCC1

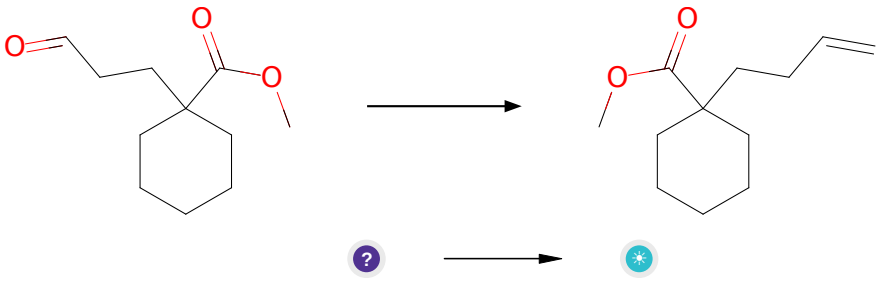
Typical conditions: DMP.DCM.0-25 C

Protections: none

Reference: *10.1016/j.bmc.2020.115469* p. 3, 9 and *10.1021/acs.jmedchem.8b01878* SI p. S43

Retrosynthesis ID: 50426

2.4.3 Tebbe Olefination



Substrates:

1. COC(=O)C1(CCC=O)CCCCC1

Products:

1. 1-but-3-enyl-cyclohexanecarboxylic acid methyl ester

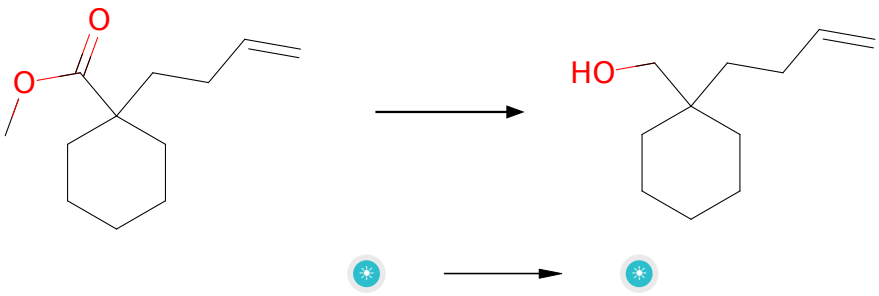
Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

Reference: *10.1016/j.tet.2007.03.015* and *10.1002/9780470638859.conrr617*

Retrosynthesis ID: 11714

2.4.4 Esters reduction with LAH



Substrates:

1. 1-but-3-enyl-cyclohexanecarboxylic acid methyl ester

Products:

1. (1-but-3-enyl-cyclohexyl)-methanol

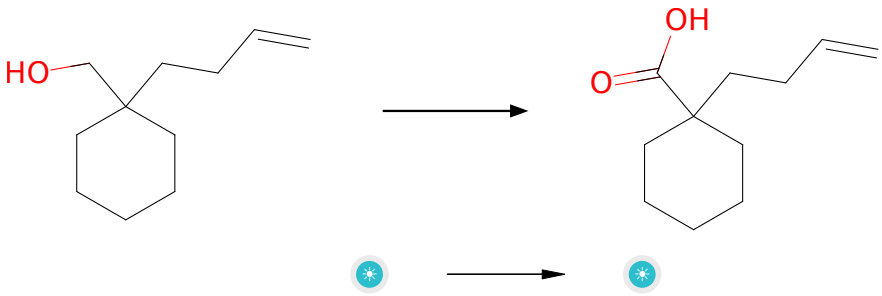
Typical conditions: LiAlH4.THF.0-20 C

Protections: none

Reference: *10.1016/j.ejmech.2019.112011* p. 5, 10 and *10.1016/j.ejmech.2020.112910* p. 3, 7

Retrosynthesis ID: 9910006

2.4.5 Jones Oxidation



Substrates:

1. (1-but-3-enyl-cyclohexyl)-methanol

Products:

1. acide 1-(but-3-enyl)cyclohexanecarboxylique

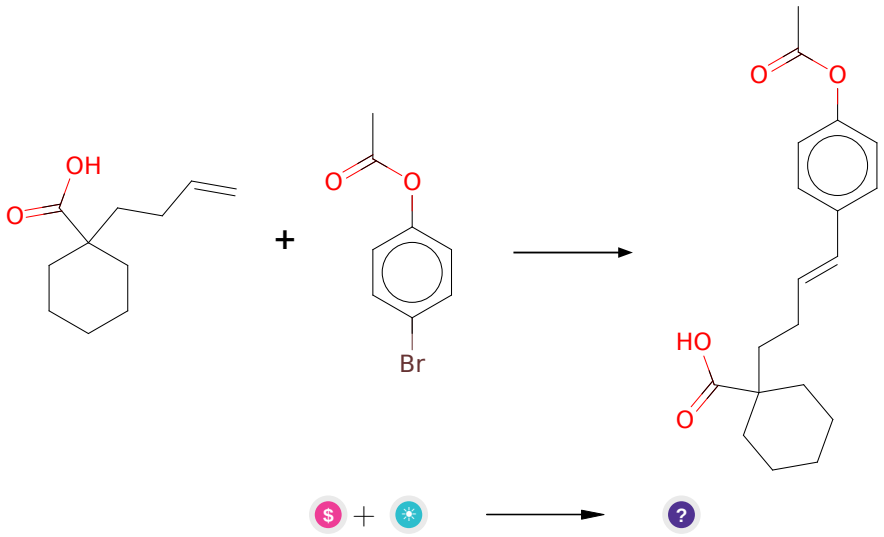
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

Reference: *10.1002/9780470638859.conrr349* and *10.1021/jm00270a004*

Retrosynthesis ID: 11160

2.4.6 Heck Reaction



Substrates:

1. 4-Bromophenol acetate - *available at Sigma-Aldrich*
2. acide 1-(but-3-enyl)cyclohexanecarboxylique

Products:

1. CC(=O)Oc1ccc(/C=C/CCC2(C(=O)O)CCCCC2)cc1

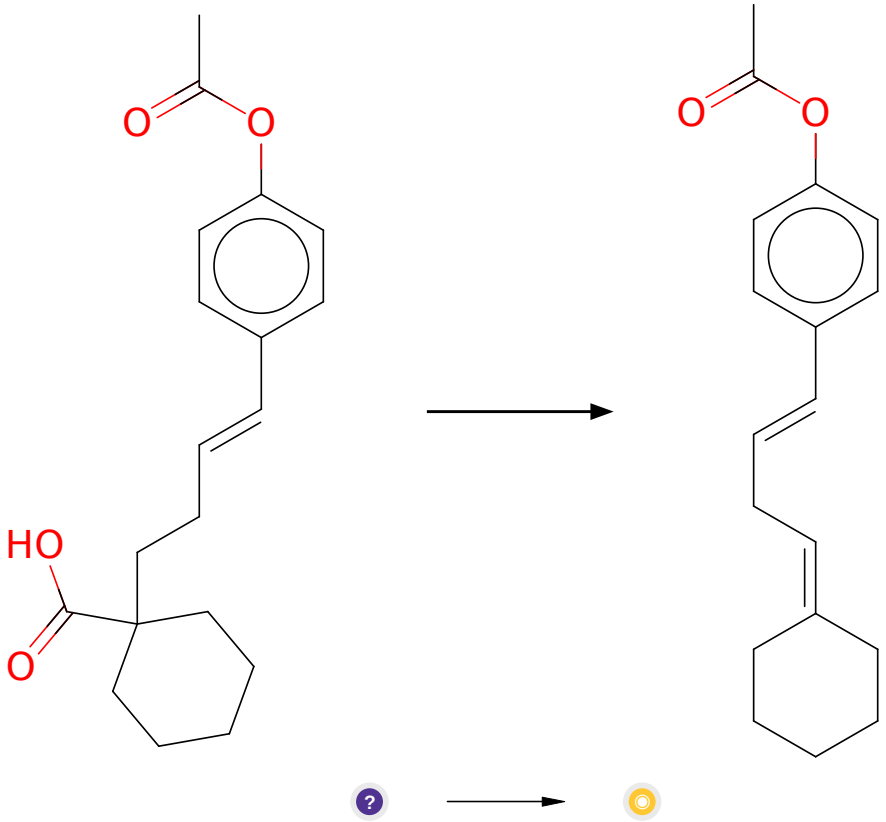
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

Protections: none

Reference: DOI: *10.1039/C3GC40493E* DOI: *10.1021/ol0360288* or DOI: *10.1021/ol702755g* or DOI: *10.1055/s-0033-1340319* or DOI: *10.1016/j.tet.2004.10.049*

Retrosynthesis ID: 9180

2.4.7 Catalytic dehydrogenative decarboxyolefination of carboxylic acids



Substrates:

1. CC(=O)Oc1ccc(/C=C/CCC2(C(=O)O)CCCCC2)cc1

Products:

1. CC(=O)Oc1ccc(/C=C/CC=C2CCCCC2)cc1

Typical conditions: [Ir]-photocatalyst.[Co]-catalyst.Cs2CO3.DME/H2O.blue.light.rt

Protections: none

Reference: *10.1038/s41557-018-0142-4* and *10.1021/acscatal.8b03282* and *10.1021/acs.joc.9b00167*

Retrosynthesis ID: 10032330

2.5 Path 5

Score: 45.00

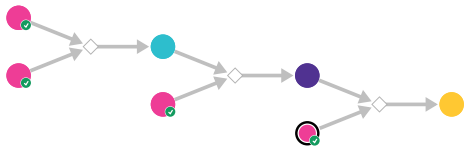
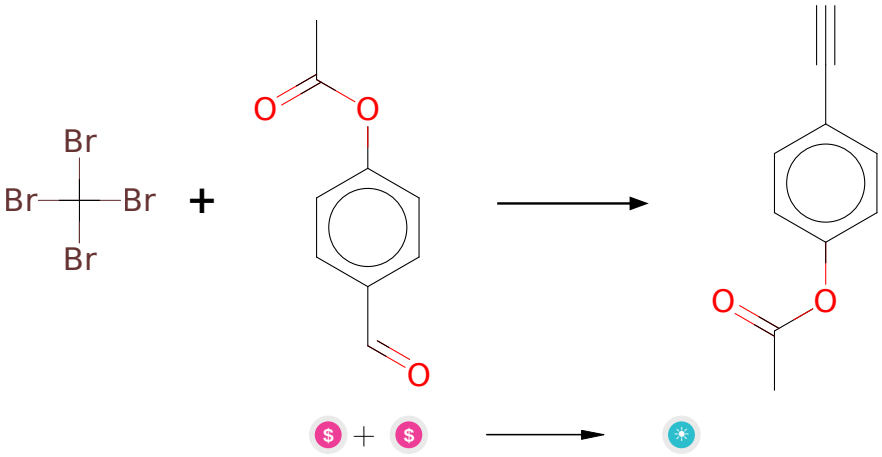


Figure 5: Outline of path 5

2.5.1 Corey-Fuchs reaction



Substrates:

1. 4-Acetoxybenzaldehyde - *available at Sigma-Aldrich*
2. Tetrabromomethane - *available at Sigma-Aldrich*

Products:

1. 4-acetoxyphenylethyne

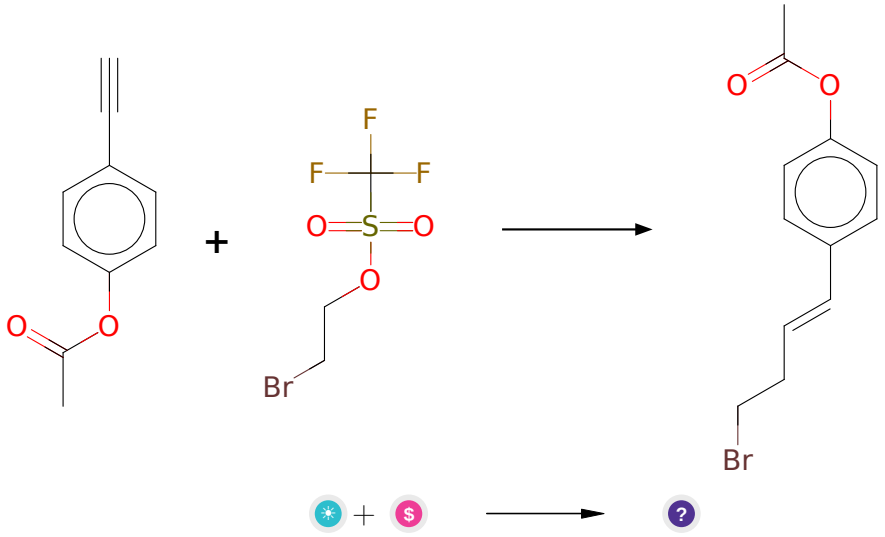
Typical conditions: PPh3.BuLi.CBr4

Protections: none

Reference: *10.1002/ejoc.200601137* and *10.1016/S0040-4039(01)94157-7*

Retrosynthesis ID: 10912

2.5.2 Hydroalkylation of alkynes



Substrates:

1. 4-acetoxyphenylethyne
2. 2-Bromoethyl trifluoromethanesulfonate - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc(/C=C/CCBr)cc1

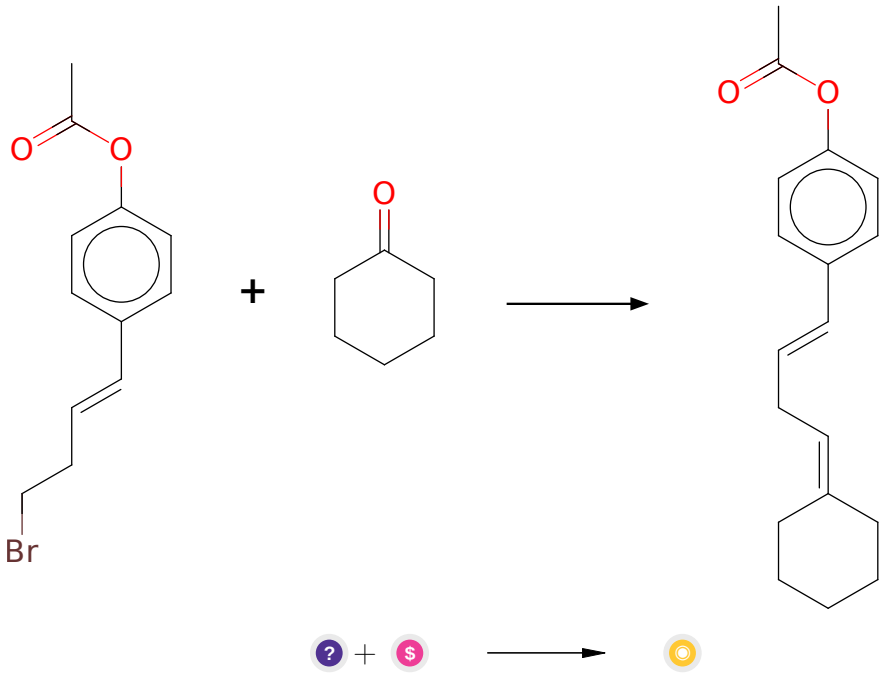
Typical conditions: CsF.(Me2HSi)2O.SIPrCuOTf.dioxane

Protections: none

Reference: *10.1021/ja5124368*

Retrosynthesis ID: 33512

2.5.3 HWE/Wittig Olefination



Substrates:

1. CC(=O)Oc1ccc(/C=C/CCBr)cc1
2. Cyclohexanone - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc(/C=C/CC=C2CCCCC2)cc1

Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

Reference: *10.1002/anie.200705005* and *10.1021/ol052106a* and *10.1021/jo00075a064* and *10.1021/ol3027297*

Retrosynthesis ID: 24425