Paths of analysis*

O2

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: `45.00`

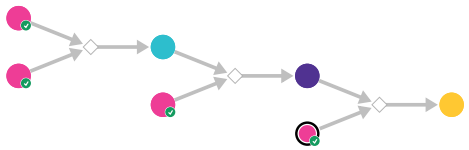
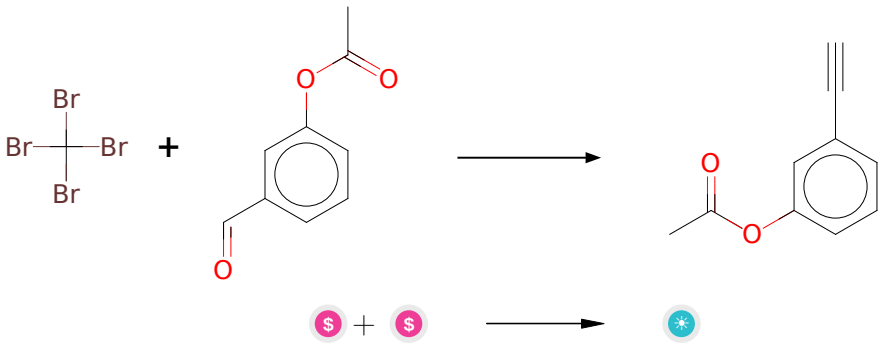


Figure 1: Outline of path 1

2.1.1 Corey-Fuchs reaction



Substrates:

1. 3-Formylphenyl acetate - *available at Sigma-Aldrich*
2. Tetrabromomethane - *available at Sigma-Aldrich*

Products:

1. 3-acetoxy-phenylacetylen

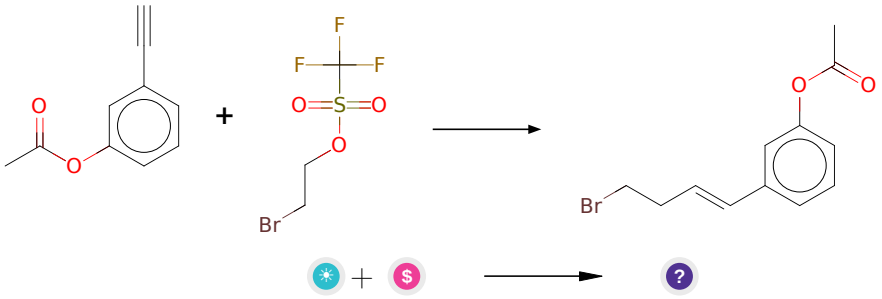
Typical conditions: PPh3.BuLi.CBr4

Protections: none

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

Retrosynthesis ID: 10912

2.1.2 Hydroalkylation of alkynes



Substrates:

1. 3-acetoxy-phenylacetylen
2. 2-Bromoethyl trifluoromethanesulfonate - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1cccc(/C=C/CCBr)c1

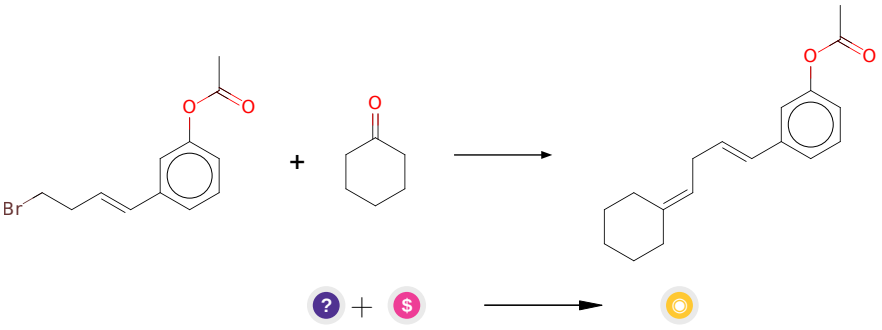
Typical conditions: CsF.(Me2HSi)2O.SIPrCuOTf.dioxane

Protections: none

Reference: *10.1021/ja5124368*

Retrosynthesis ID: 33512

2.1.3 HWE/Wittig Olefination



Substrates:

1. CC(=O)Oc1cccc(/C=C/CCBr)c1
2. Cyclohexanone - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

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

2.2 Path 2

Score: 45.00

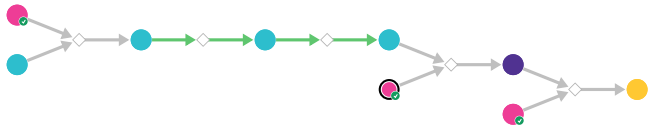
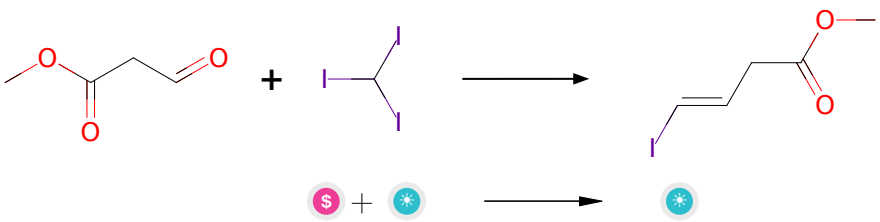


Figure 2: Outline of path 2

2.2.1 Takai olefination



Substrates:

1. Iodoform - *available at Sigma-Aldrich*
2. 3-oxo-propionsaeure-methylester

Products:

1. methyl 4-iodo-3(e)-butenoate

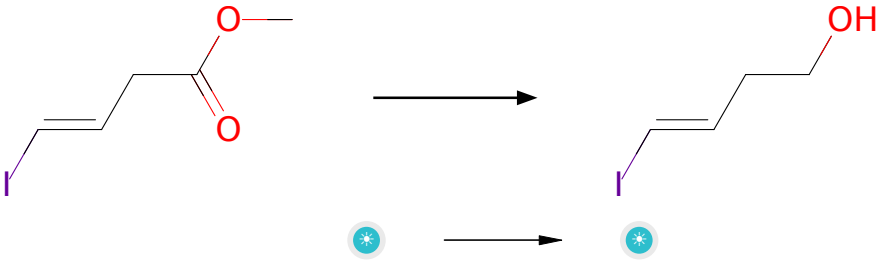
Typical conditions: CrCl2.THF

Protections: none

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

Retrosynthesis ID: 10497

2.2.2 Esters reduction with LAH



Substrates:

1. methyl 4-iodo-3(e)-butenoate

Products:

1. (e)-4-iodo-3-buten-1-ol

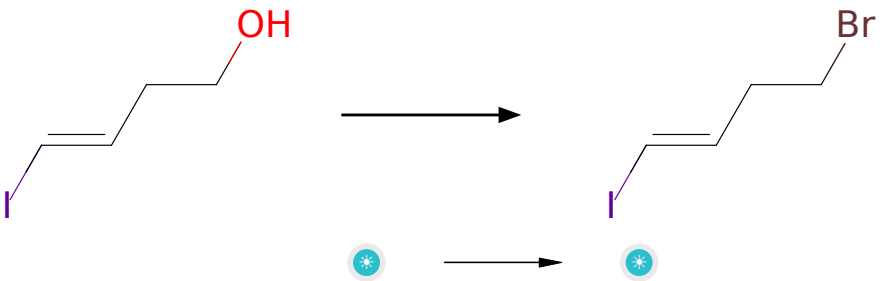
Typical conditions: LiAlH4.THF.0-20 C

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

2.2.3 Appel Reaction



Substrates:

1. (e)-4-iodo-3-buten-1-ol

Products:

1. C4H6BrI

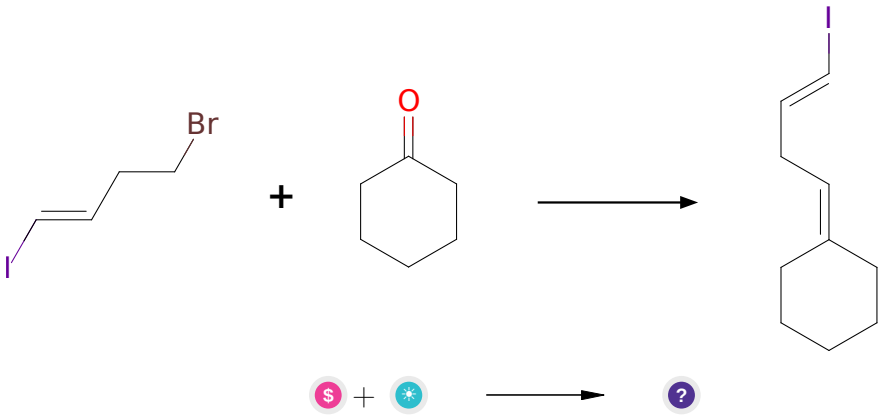
Typical conditions: PPh3.CBr4

Protections: none

Reference: *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

Retrosynthesis ID: 9990037

2.2.4 HWE/Wittig Olefination



Substrates:

1. Cyclohexanone - *available at Sigma-Aldrich*
2. C4H6BrI

Products:

1. I/C=C/CC=C1CCCCC1

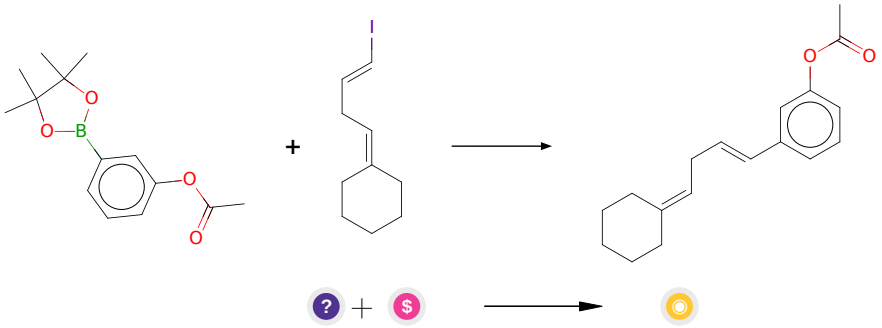
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

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

Retrosynthesis ID: 24425

2.2.5 Suzuki coupling of arylboronic pinacol esters with vinyl iodides



Substrates:

1. I/C=C/CC=C1CCCCC1
2. 3-Acetoxyphenylboronic acid pinacol ester - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

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 Path 3

Score: 45.00

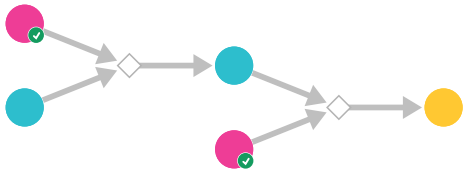
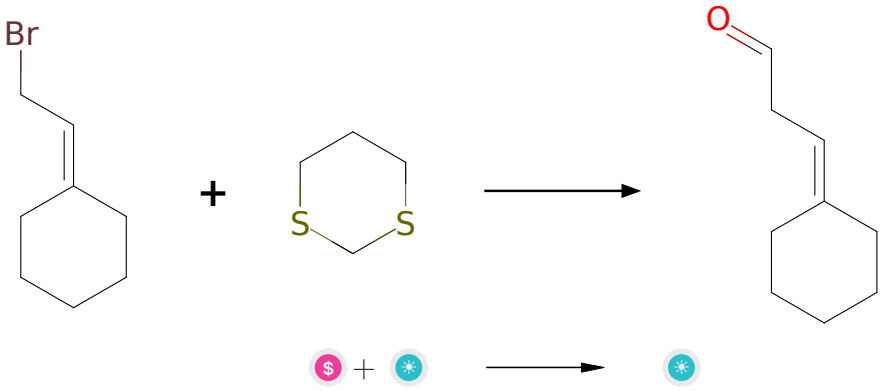


Figure 3: Outline of path 3

2.3.1 Corey-Seebach



Substrates:

1. 1,3-Dithiane - *available at Sigma-Aldrich*
2. (2-bromo-ethylidene)-cyclohexane

Products:

1. 3-cyclohexylidenepropanal

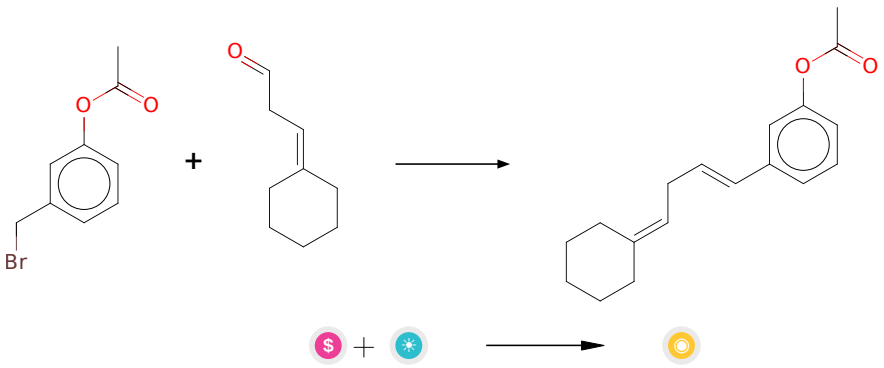
Typical conditions: 1.BuLi.TMEDA.2.TCCA

Protections: none

Reference: *10.1039/P19860000183* AND *10.1016/S0040-4020(01)85646-5* AND *10.1039/c5ob00638d* deprotection: *10.1016/j.tetlet.2006.06.131*

Retrosynthesis ID: 15272

2.3.2 Wittig-Schlosser olefination



Substrates:

1. 3-(Bromomethyl)phenyl acetate - *available at Sigma-Aldrich*
2. 3-cyclohexylidenepropanal

Products:

1. CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde.3.base

Protections: none

Reference: *10.1021/ol049701h* and *10.1021/ja00535a063* and Kurti and Czako; Strategic Applications of Named Reactions in Organic Synthesis. 1st edn., 488-489.

Retrosynthesis ID: 9546

2.4 Path 4

Score: `45.00`

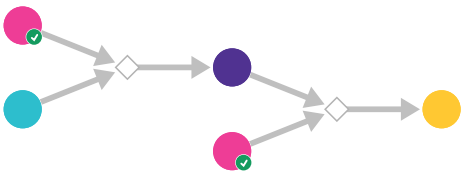
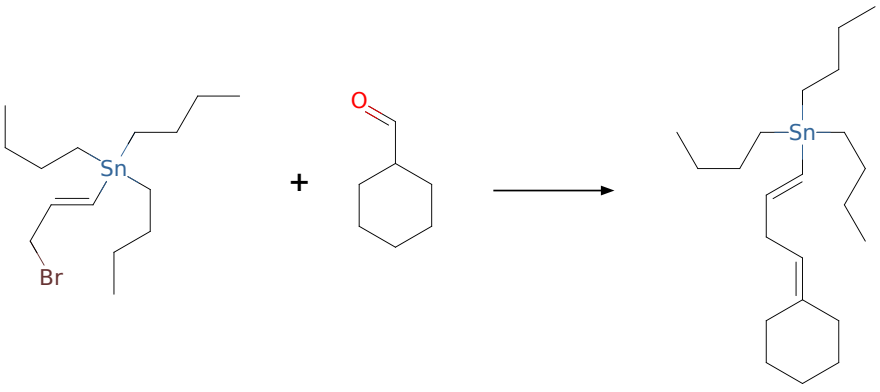
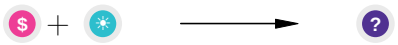


Figure 4: Outline of path 4

2.4.1 Shapiro reaction followed by alkyl bromide addition





Substrates:

1. Hexahydrobenzaldehyde - *available at Sigma-Aldrich*
2. (e)-3-bromo-1-tributylstannylpropene

Products:

1. CCCC[Sn](/C=C/CC=C1CCCCC1)(CCCC)CCCC

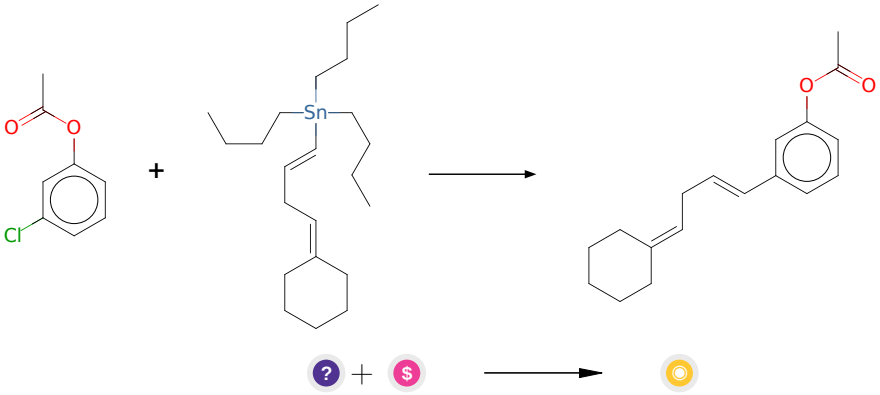
Typical conditions: 1.TsNH2NH2.2.Mes2Mg.LiCl.THF.heating then alkyl bromide.cooling

Protections: none

Reference: *10.1016/S0040-4039(00)75263-4* and *10.1021/ol300652k* and *10.1021/jo015699l*

Retrosynthesis ID: 9990458

2.4.2 Vinylation of aryl chlorides with stannanes



Substrates:

1. CCCC[Sn](/C=C/CC=C1CCCCC1)(CCCC)CCCC
2. 3-Chlorophenyl acetate - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

Typical conditions: [Pd].catalyst.phosphine.CsF

Protections: none

Reference: US2004/167128 p.97 and *10.3184/174751913X13635315066265* and *10.1021/ol0495927* and *10.1002/(SICI)1521-3773(19990816)38:16<2411::AID-ANIE2411>3.0.CO;2-T* and *10.1021/ol0495927* and *10.1021/ja020012f*

Retrosynthesis ID: 32849

2.5 Path 5

Score: `51.25`

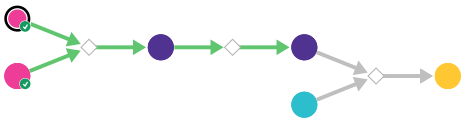
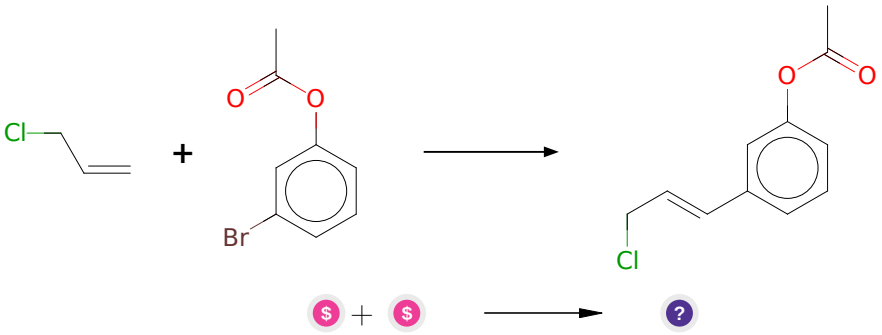


Figure 5: Outline of path 5

2.5.1 Heck Reaction



Substrates:

1. Chlorallylene - *available at Sigma-Aldrich*
2. 3-Bromophenyl acetate - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1cccc(/C=C/CCl)c1

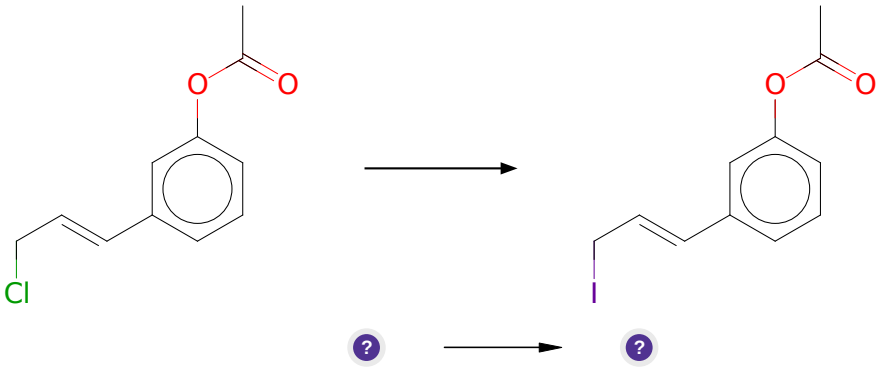
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

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

2.5.2 Synthesis of alkyl iodides from alkyl chlorides



Substrates:

1. CC(=O)Oc1cccc(/C=C/CCl)c1

Products:

1. CC(=O)Oc1cccc(/C=C/CI)c1

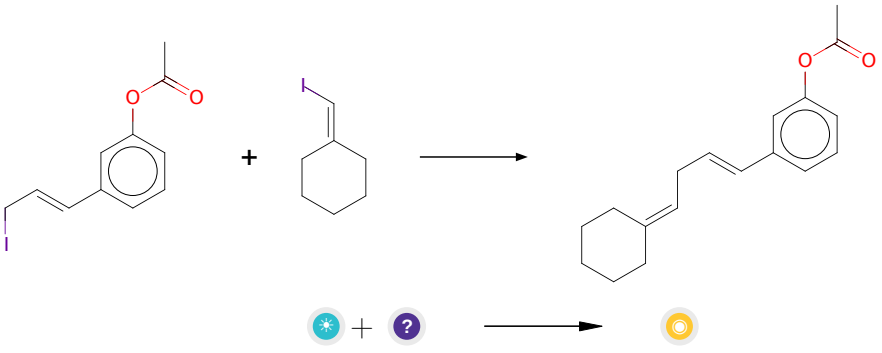
Typical conditions: NaI.acetone.heat

Protections: none

Reference: *10.1021/ja060369+* and *10.1021/jm061344o*

Retrosynthesis ID: 31010851

2.5.3 Palladium catalysed alkylation of vinyl iodides



Substrates:

1. iodomethylene cyclohexane
2. CC(=O)Oc1cccc(/C=C/CI)c1

Products:

1. CC(=O)Oc1cccc(/C=C/CC=C2CCCCC2)c1

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: 25165