Paths of analysis*

O3

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

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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`

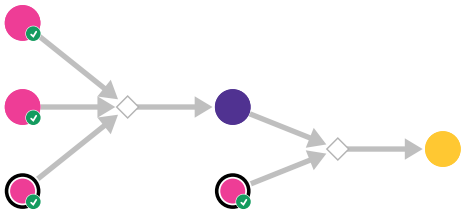
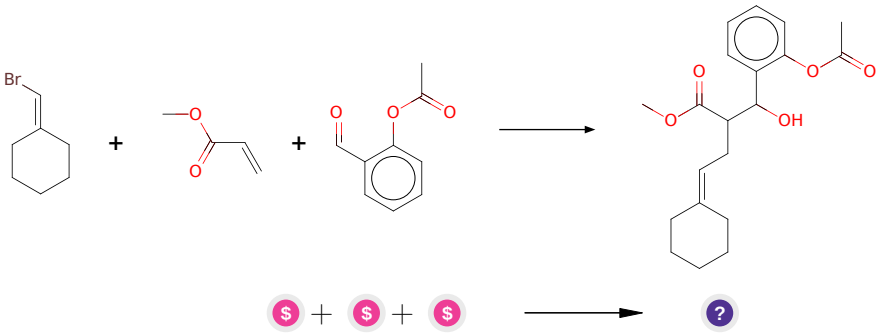


Figure 1: Outline of path 1

2.1.1 Alkenylation-Aldol reaction of enones and enoate esters



Substrates:

1. Bromomethylenecyclohexane - *available at Sigma-Aldrich*
2. 2-formylphenyl acetate - *available at Sigma-Aldrich*
3. Methyl acrylate - *available at Sigma-Aldrich*

Products:

1. COC(=O)C(CC=C1CCCCC1)C(O)c1ccccc1OC(C)=O

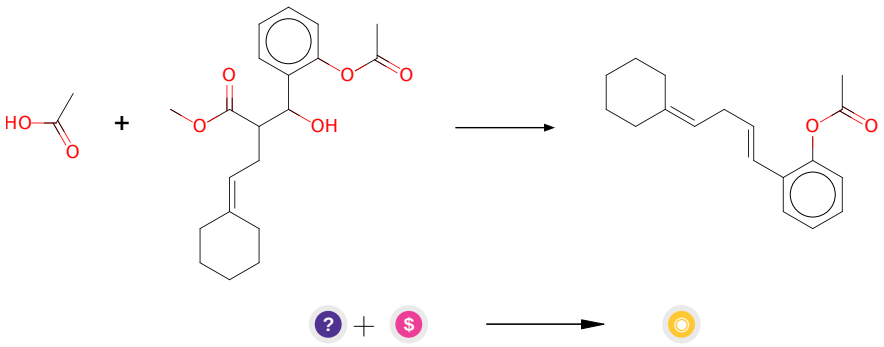
Typical conditions: 1.RCuLi.2.RCHO

Protections: none

Reference: *10.1021/jo2010186* AND *10.1021/jo101439h* AND *10.1021/ja906241w* AND *10.1016/S0040-4039(01)80891-1* AND *10.1016/S0040-4020(01)82115-3*

Retrosynthesis ID: 13051

2.1.2 Tandem Krapcho decarboxylation and elimination



Substrates:

1. COC(=O)C(CC=C1CCCCC1)C(O)c1ccccc1OC(C)=O
2. glacial - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccccc1/C=C/CC=C1CCCCC1

Typical conditions: 1. Ac2O.py 2. DMSO.H2O.NaCl.170C

Protections: none

Reference: DOI: *10.1021/jo00263a005* and *10.1021/jo00386a011* and *10.1021/ol006085q*

Retrosynthesis ID: 9605

2.2 Path 2

Score: 45.00

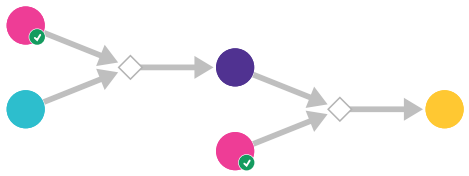
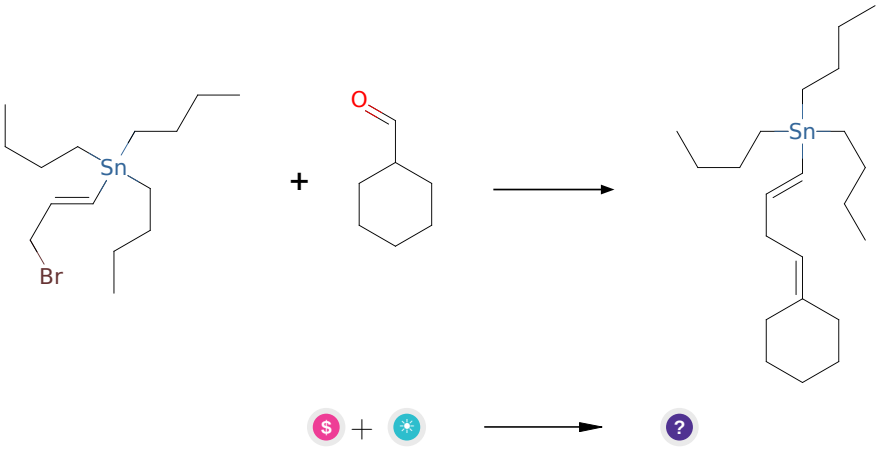


Figure 2: Outline of path 2

2.2.1 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

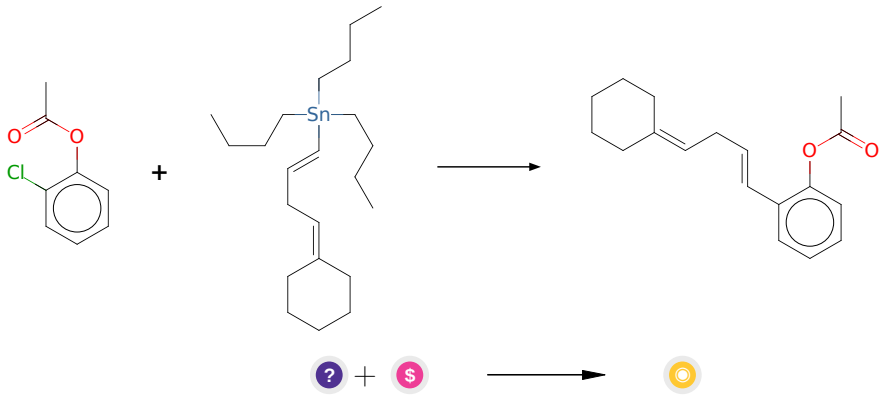
Typical conditions: 1.TsNH2NH2.2.Mes2Mg.LiCl.THF.heating then alkyl bromide.cooling

Protections: none

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

Retrosynthesis ID: 9990458

2.2.2 Vinylation of aryl chlorides with stannanes



Substrates:

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

Products:

1. CC(=O)Oc1ccccc1/C=C/CC=C1CCCCC1

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

2.3 Path 3

Score: 45.00

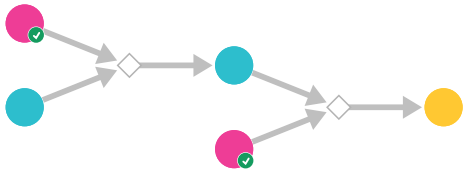
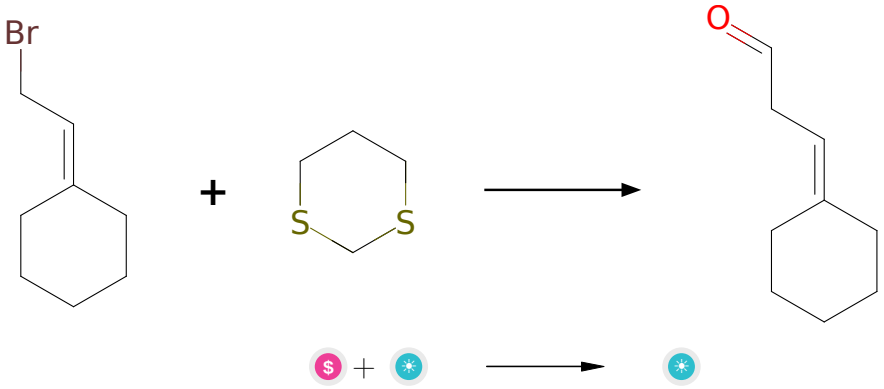


Figure 3: Outline of path 3

2.3.1 Corey-Seebach



Substrates:

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

Products:

1. 3-cyclohexylidenepropanal

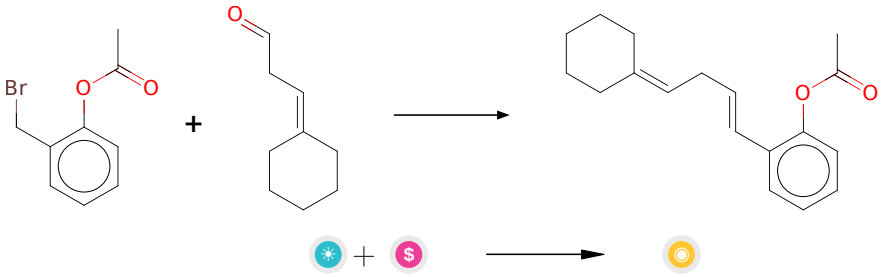
Typical conditions: 1.BuLi.TMEDA.2.TCCA

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

Products:

1. CC(=O)Oc1ccccc1/C=C/CC=C1CCCCC1

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

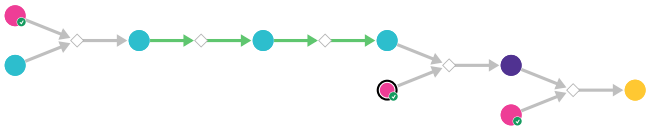
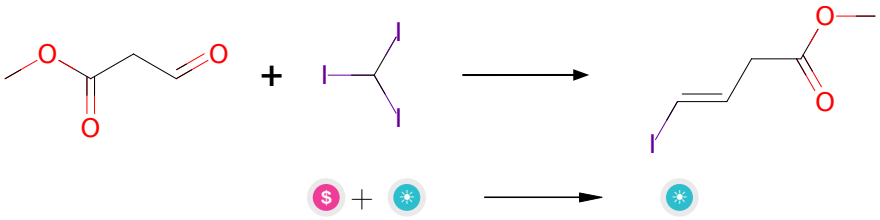


Figure 4: Outline of path 4

2.4.1 Takai olefination



Substrates:

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

Products:

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

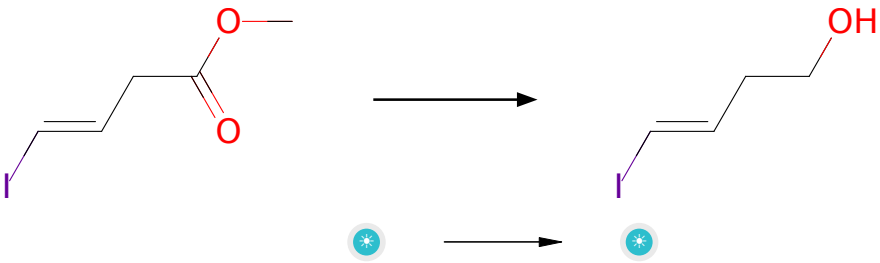
Typical conditions: CrCl2.THF

Protections: none

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

Retrosynthesis ID: 10497

2.4.2 Esters reduction with LAH



Substrates:

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

Products:

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

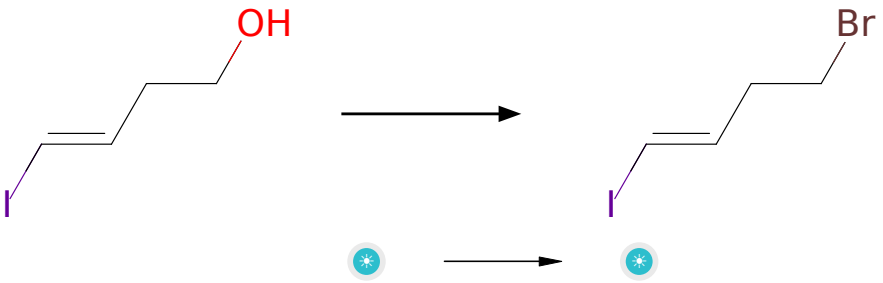
Typical conditions: LiAlH4.THF.0-20 C

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

2.4.3 Appel Reaction



Substrates:

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

Products:

1. C4H6BrI

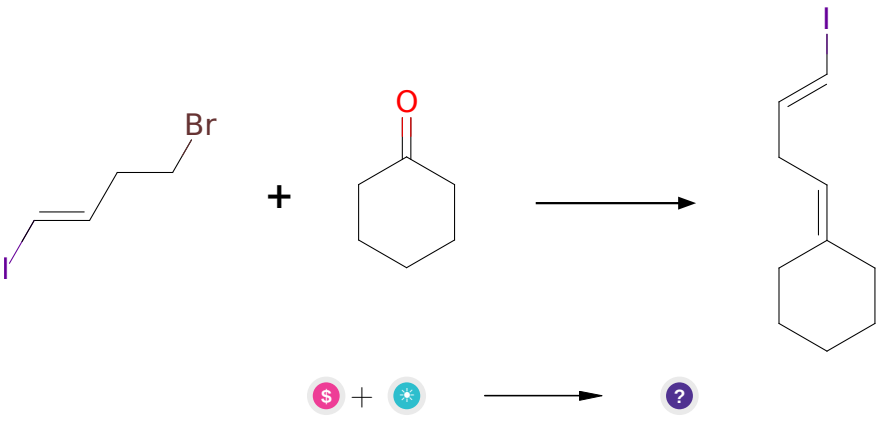
Typical conditions: PPh3.CBr4

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

2.4.4 HWE/Wittig Olefination



Substrates:

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

Products:

1. I/C=C/CC=C1CCCCC1

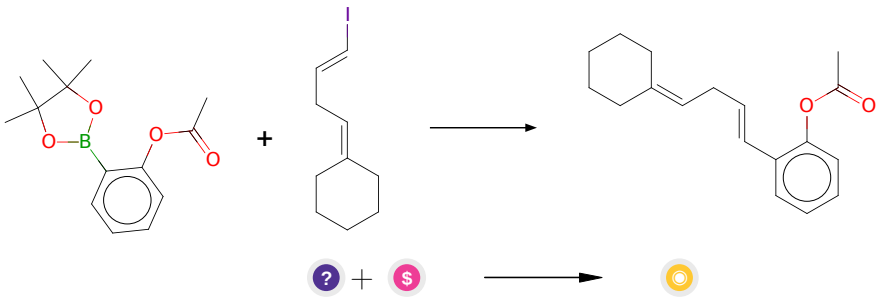
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

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

Retrosynthesis ID: 24425

2.4.5 Suzuki coupling of arylboronic pinacol esters with vinyl iodides



Substrates:

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

Products:

1. CC(=O)Oc1ccccc1/C=C/CC=C1CCCCC1

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

2.5 Path 5

Score: 51.25

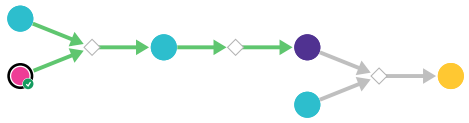
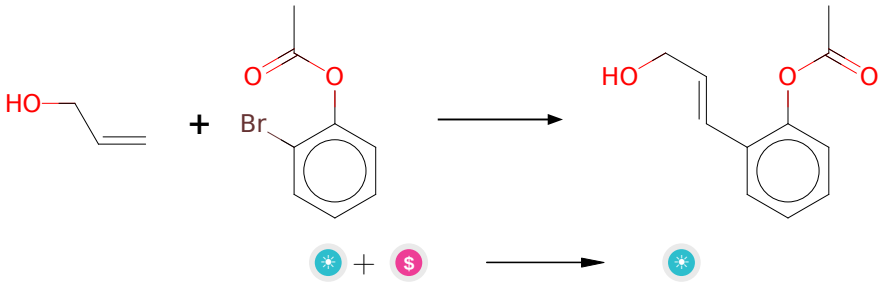


Figure 5: Outline of path 5

2.5.1 Heck Reaction



Substrates:

1. o-bromophenyl acetate
2. 2-Propen-1-ol - *available at Sigma-Aldrich*

Products:

1. 2-acetoxycinnamyl alcohol

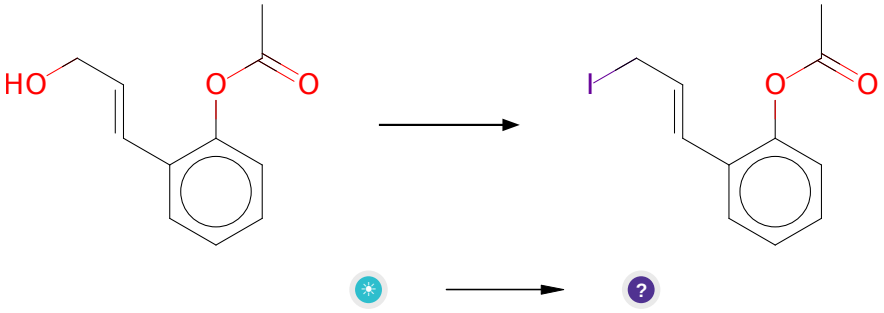
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

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 Via Appel Reaction



Substrates:

1. 2-acetoxycinnamyl alcohol

Products:

1. CC(=O)Oc1ccccc1/C=C/CI

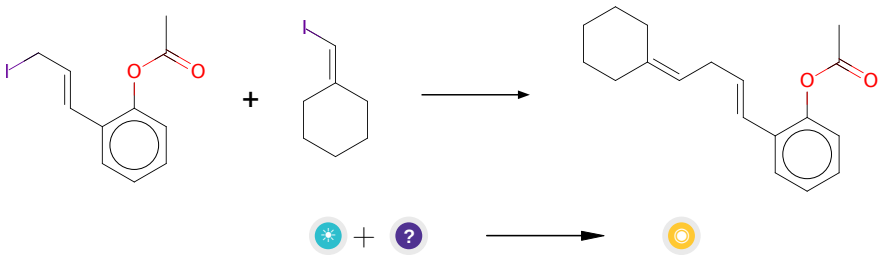
Typical conditions: Imidazole.PPh3.I2

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

2.5.3 Palladium catalysed alkylation of vinyl iodides



Substrates:

1. iodomethylene cyclohexane
2. CC(=O)Oc1ccccc1/C=C/CI

Products:

1. CC(=O)Oc1ccccc1/C=C/CC=C1CCCCC1

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