Paths of analysis*

PG5

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: 76.25

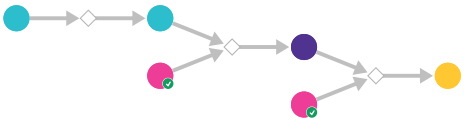
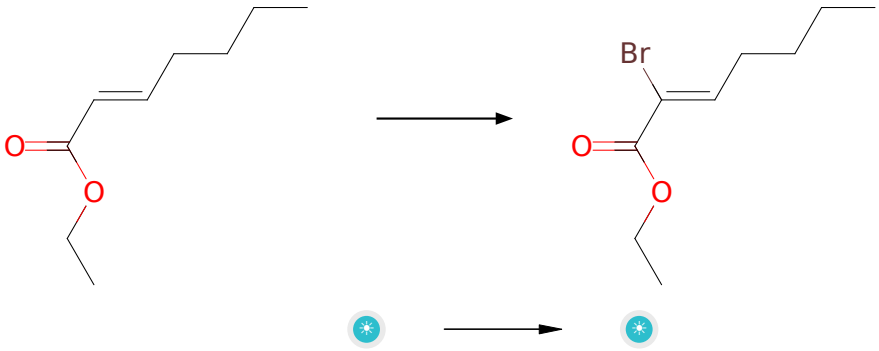


Figure 1: Outline of path 1

2.1.1 Bromination of enones/enoates/enals



Substrates:

1. hept-2c-enoic acid ethyl ester

Products:

1. 2-bromo-hept-2-enoic acid ethyl ester

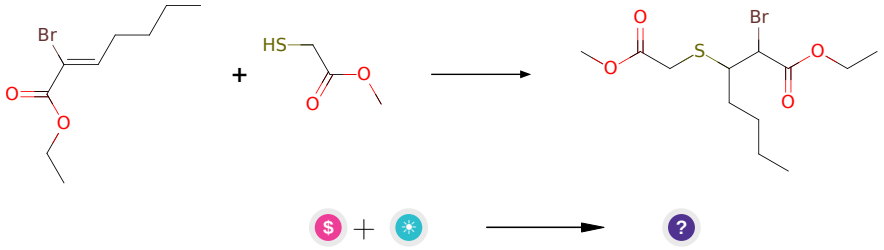
Typical conditions: NaBr.Oxone then TEA or Br2.NEt3

Protections: none

Reference: *10.1016/j.tetlet.2006.02.134* and *10.1021/ol102554a* and *10.1021/jo00123a018* (experimental 17b) and *10.1021/acs.joc.5b01603* and *10.1002/chem.201303755* and US2005038089 p. 13

Retrosynthesis ID: 9991442

2.1.2 Addition of thiols to Michael acceptors



Substrates:

1. Methyl thioglycolate - *available at Sigma-Aldrich*
2. 2-bromo-hept-2-enoic acid ethyl ester

Products:

1. CCCCC(SCC(=O)OC)C(Br)C(=O)OCC

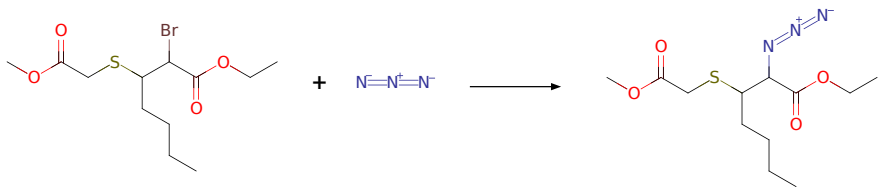
Typical conditions: Et3N.DCM

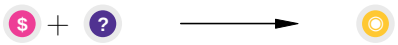
Protections: none

Reference: *10.1021/ja0578348* AND *10.1016/0040-4020(96)00458-9* AND *10.3987/R-1983-09-1761* AND *10.1016/S0040-4020(98)00076-3* for ketones: *10.1002/anie.200351750* AND *10.1016/j.tetasy.2006.01.002* AND *10.1021/jm00182a018*

Retrosynthesis ID: 1430

2.1.3 Nucleophilic substitution with azides





Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. CCCCC(SCC(=O)OC)C(Br)C(=O)OCC

Products:

1. CCCCC(SCC(=O)OC)C(N=[N+]=[N-])C(=O)OCC

Typical conditions: DMF.heat

Protections: none

Reference: *10.1021/ol049369+* and *10.1016/S0040-4039(00)61343-6* and *10.1016/j.bmcl.2005.03.055*

Retrosynthesis ID: 31011250

2.2 Path 2

Score: 76.25

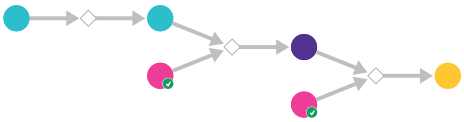
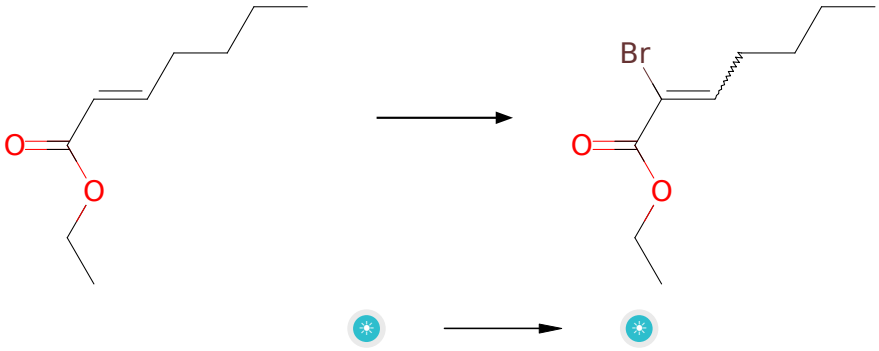


Figure 2: Outline of path 2

2.2.1 Bromination of enones/enoates/enals



Substrates:

1. hept-2c-enoic acid ethyl ester

Products:

1. 2-bromo-hept-2-enoic acid ethyl ester

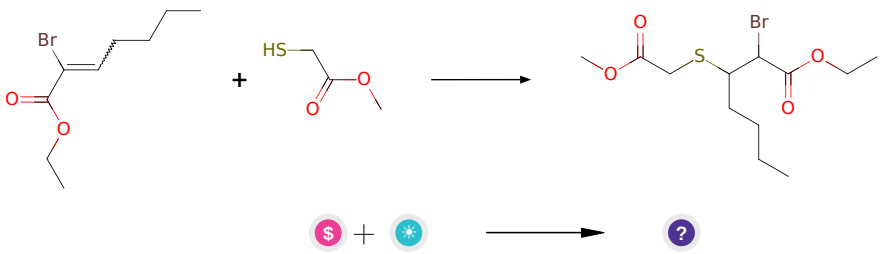
Typical conditions: NaBr.Oxone then TEA or Br2.NEt3

Protections: none

Reference: *10.1016/j.tetlet.2006.02.134* and *10.1021/ol102554a* and *10.1021/jo00123a018* (experimental 17b) and *10.1021/acs.joc.5b01603* and *10.1002/chem.201303755* and US2005038089 p. 13

Retrosynthesis ID: 9991442

2.2.2 Addition of thiols to Michael acceptors



Substrates:

1. Methyl thioglycolate - *available at Sigma-Aldrich*
2. 2-bromo-hept-2-enoic acid ethyl ester

Products:

1. CCCCC(SCC(=O)OC)C(Br)C(=O)OCC

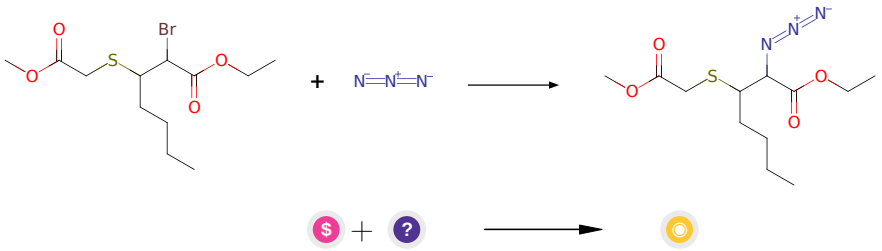
Typical conditions: Et3N.DCM

Protections: none

Reference: *10.1021/ja0578348* AND *10.1016/0040-4020(96)00458-9* AND *10.3987/R-1983-09-1761* AND *10.1016/S0040-4020(98)00076-3* for ketones: *10.1002/anie.200351750* AND *10.1016/j.tetasy.2006.01.002* AND *10.1021/jm00182a018*

Retrosynthesis ID: 1436

2.2.3 Nucleophilic substitution with azides



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. CCCCC(SCC(=O)OC)C(Br)C(=O)OCC

Products:

1. CCCCC(SCC(=O)OC)C(N=[N+]=[N-])C(=O)OCC

Typical conditions: DMF.heat

Protections: none

Reference: *10.1021/ol049369+* and *10.1016/S0040-4039(00)61343-6* and *10.1016/j.bmcl.2005.03.055*

Retrosynthesis ID: 31011250

2.3 Path 3

Score: 76.25

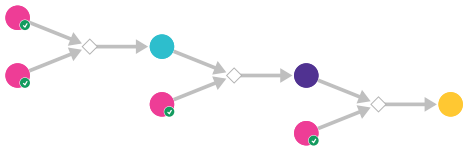
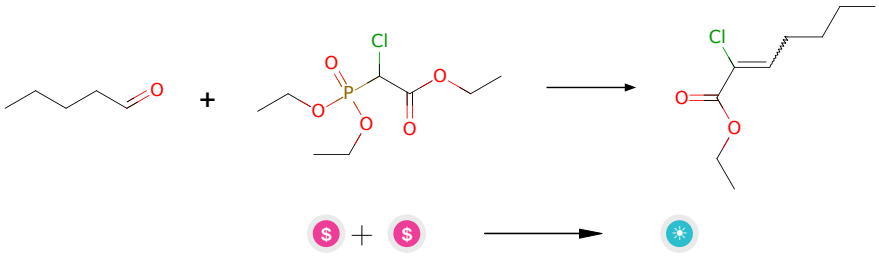


Figure 3: Outline of path 3

2.3.1 HWE olefination



Substrates:

1. Pentanal - *available at Sigma-Aldrich*
2. Triethyl 2-chloro-2-phosphonoacetate - *available at Sigma-Aldrich*

Products:

1. ethyl 2-chloroheptenoate

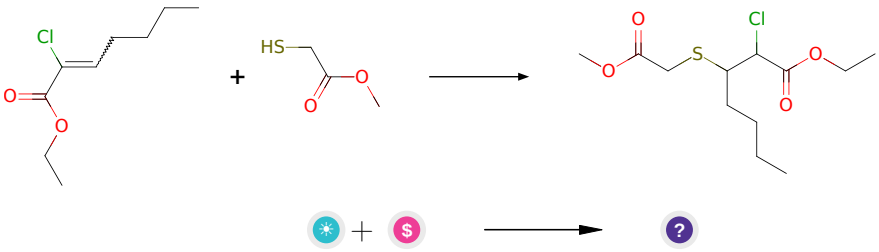
Typical conditions: 1.Base 2.RCHO

Protections: none

Reference: *10.1080/15421400701732555* and *10.1021/ol5006856* and *10.1016/j.tetlet.2012.04.044*

Retrosynthesis ID: 14769

2.3.2 Addition of thiols to Michael acceptors



Substrates:

1. ethyl 2-chloroheptenoate
2. Methyl thioglycolate - *available at Sigma-Aldrich*

Products:

1. CCCCC(SCC(=O)OC)C(Cl)C(=O)OCC

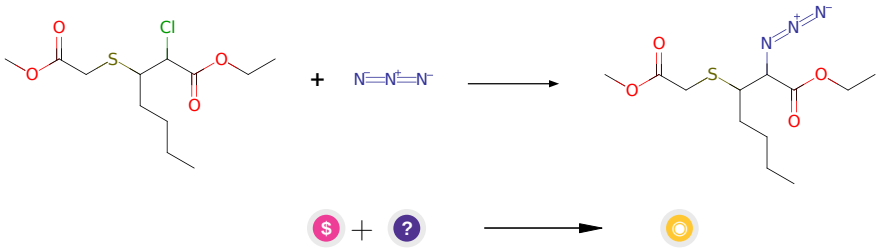
Typical conditions: Et3N.DCM

Protections: none

Reference: *10.1021/ja0578348* AND *10.1016/0040-4020(96)00458-9* AND *10.3987/R-1983-09-1761* AND *10.1016/S0040-4020(98)00076-3* for ketones: *10.1002/anie.200351750* AND *10.1016/j.tetasy.2006.01.002* AND *10.1021/jm00182a018*

Retrosynthesis ID: 1436

2.3.3 Nucleophilic substitution with azides



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. CCCCC(SCC(=O)OC)C(Cl)C(=O)OCC

Products:

1. CCCCC(SCC(=O)OC)C(N=[N+]=[N-])C(=O)OCC

Typical conditions: DMF.heat

Protections: none

Reference: *10.1016/j.tet.2013.11.027* and *10.1021/jo015632y* and *10.3987/COM-06-S(K)18*

Retrosynthesis ID: 31011248

2.4 Path 4

Score: 76.25

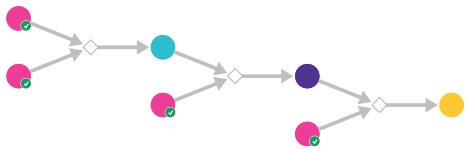
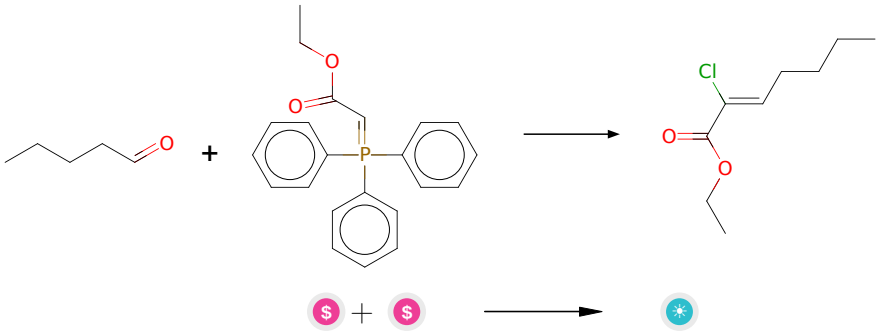


Figure 4: Outline of path 4

2.4.1 Synthesis of alpha-chloroacrylates from aldehydes



Substrates:

1. Pentanal - *available at Sigma-Aldrich*
2. Ethyl (triphenylphosphoranylidene)acetate - *available at Sigma-Aldrich*

Products:

1. C9H15ClO2

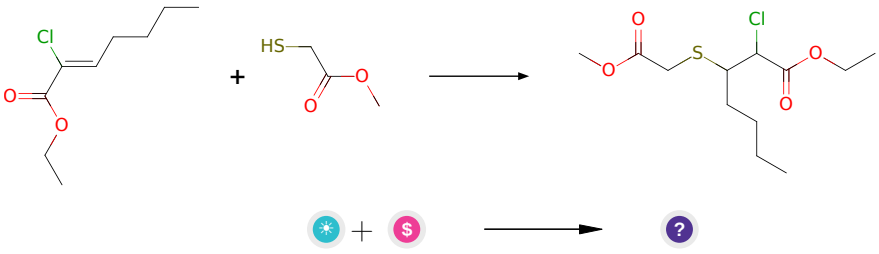
Typical conditions: TEA.oxalyl chloride.DMSO.DCM.-78C

Protections: none

Reference: DOI: *10.1021/ol702859y*

Retrosynthesis ID: 1490

2.4.2 Addition of thiols to Michael acceptors



Substrates:

1. C9H15ClO2
2. Methyl thioglycolate - *available at Sigma-Aldrich*

Products:

1. CCCCC(SCC(=O)OC)C(Cl)C(=O)OCC

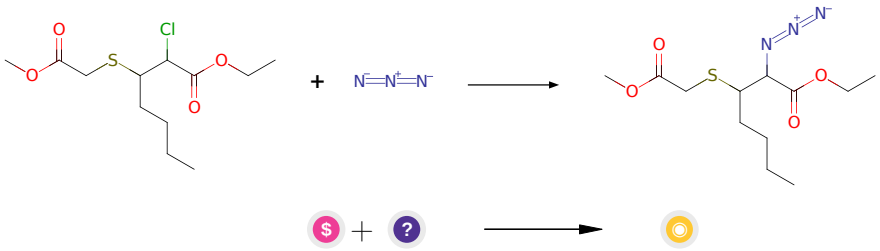
Typical conditions: Et3N.DCM

Protections: none

Reference: *10.1021/ja0578348* AND *10.1016/0040-4020(96)00458-9* AND *10.3987/R-1983-09-1761* AND *10.1016/S0040-4020(98)00076-3* for ketones: *10.1002/anie.200351750* AND *10.1016/j.tetasy.2006.01.002* AND *10.1021/jm00182a018*

Retrosynthesis ID: 1430

2.4.3 Nucleophilic substitution with azides



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. CCCCC(SCC(=O)OC)C(Cl)C(=O)OCC

Products:

1. CCCCC(SCC(=O)OC)C(N=[N+]=[N-])C(=O)OCC

Typical conditions: DMF.heat

Protections: none

Reference: *10.1016/j.tet.2013.11.027* and *10.1021/jo015632y* and *10.3987/COM-06-S(K)18*

Retrosynthesis ID: 31011248

2.5 Path 5

Score: 76.25

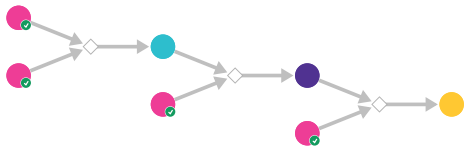
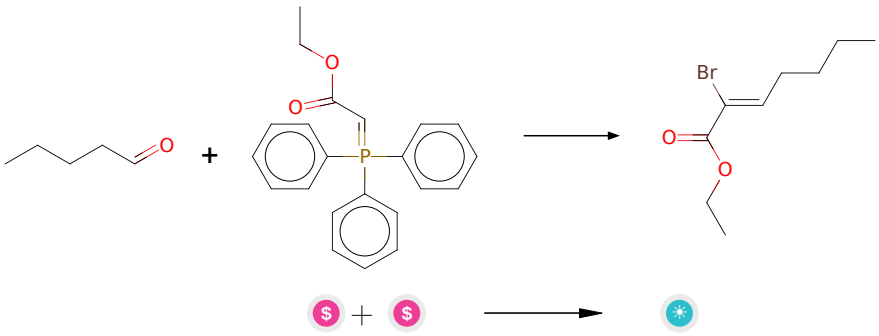


Figure 5: Outline of path 5

2.5.1 Synthesis of alpha-bromoacrylates from aldehydes



Substrates:

1. Pentanal - *available at Sigma-Aldrich*
2. Ethyl (triphenylphosphoranylidene)acetate - *available at Sigma-Aldrich*

Products:

1. 2-bromo-hept-2-enoic acid ethyl ester

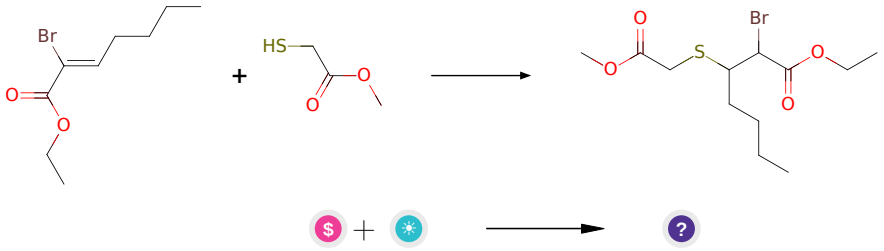
Typical conditions: TEA.BDMS.DCM.-78C

Protections: none

Reference: DOI: *10.1021/ol702859y*

Retrosynthesis ID: 1491

2.5.2 Addition of thiols to Michael acceptors



Substrates:

1. Methyl thioglycolate - *available at Sigma-Aldrich*
2. 2-bromo-hept-2-enoic acid ethyl ester

Products:

1. CCCCC(SCC(=O)OC)C(Br)C(=O)OCC

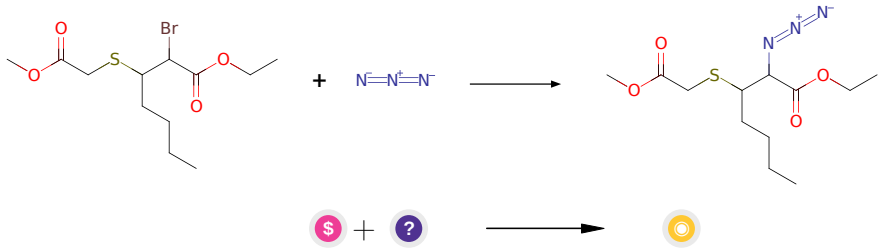
Typical conditions: Et3N.DCM

Protections: none

Reference: *10.1021/ja0578348* AND *10.1016/0040-4020(96)00458-9* AND *10.3987/R-1983-09-1761* AND *10.1016/S0040-4020(98)00076-3* for ketones: *10.1002/anie.200351750* AND *10.1016/j.tetasy.2006.01.002* AND *10.1021/jm00182a018*

Retrosynthesis ID: 1430

2.5.3 Nucleophilic substitution with azides



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. CCCCC(SCC(=O)OC)C(Br)C(=O)OCC

Products:

1. CCCCC(SCC(=O)OC)C(N=[N+]=[N-])C(=O)OCC

Typical conditions: DMF.heat

Protections: none

Reference: *10.1021/ol049369+* and *10.1016/S0040-4039(00)61343-6* and *10.1016/j.bmcl.2005.03.055*

Retrosynthesis ID: 31011250