Paths of analysis*

PG5A

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: `84.06`

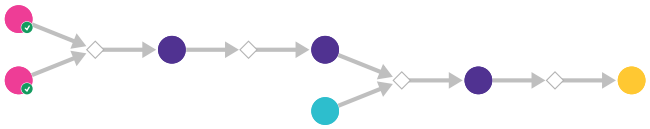
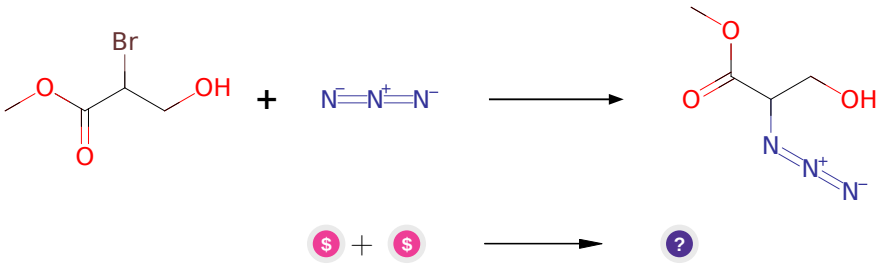


Figure 1: Outline of path 1

2.1.1 Nucleophilic substitution with azides



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. Methyl 2-bromo-3-hydroxypropanoate - *available at Sigma-Aldrich*

Products:

1. COC(=O)C(CO)N=[N+]=[N-]

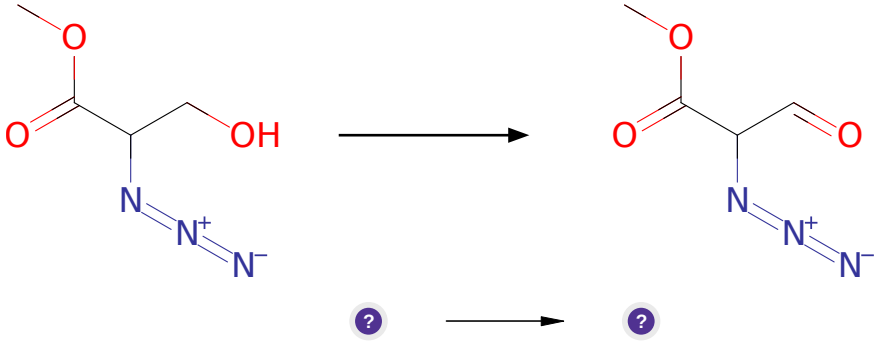
Typical conditions: DMF.heat

Protections: none

Reference: *10.1021/jm701162g* and *10.1016/j.bmcl.2005.03.055*

Retrosynthesis ID: 31011208

2.1.2 Oxidation of primary alcohols with DMP



Substrates:

1. COC(=O)C(CO)N=[N+]=[N-]

Products:

1. COC(=O)C(C=O)N=[N+]=[N-]

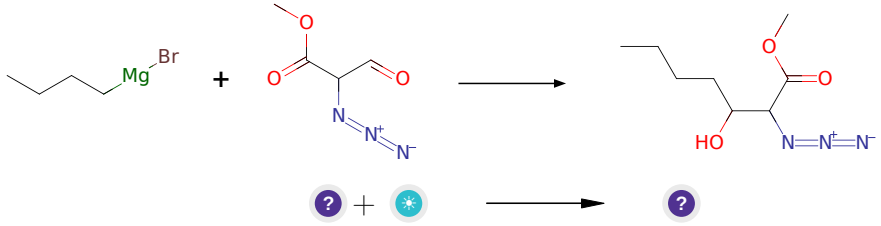
Typical conditions: DMP.DCM.0-25 C

Protections: none

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

Retrosynthesis ID: 50426

2.1.3 Grignard-Type Reaction



Substrates:

1. COC(=O)C(C=O)N=[N+]=[N-]

2. butylmagnesium bromide

Products:

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

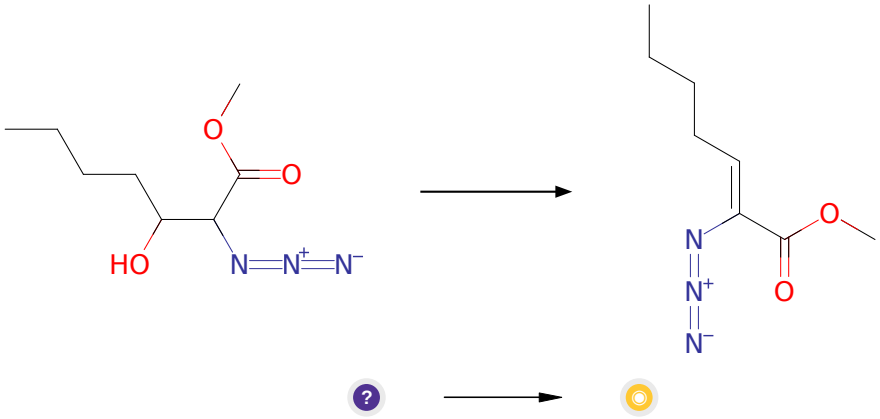
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1016/S0040-4020(99)00197-0* or *10.1055/s-0030-1260809* or *10.1021/ol703056u*

Retrosynthesis ID: 25124

2.1.4 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

1. CCCC/C=C(\N=[N+]=[N-])C(=O)OC

Typical conditions: TsOH

Protections: none

Reference: DOI:*10.1002/anie.201204977* AND *10.1021/ol062777o*

Retrosynthesis ID: 7732

2.2 Path 2

Score: 106.04

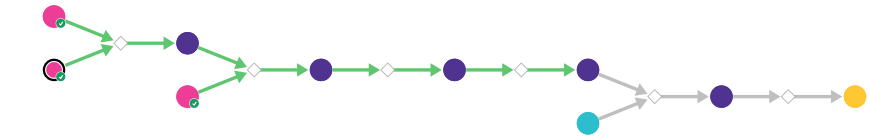
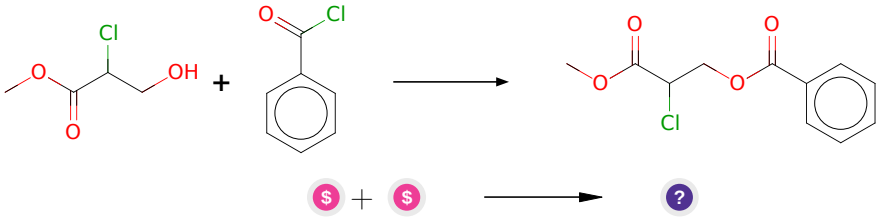


Figure 2: Outline of path 2

2.2.1 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. Methyl 2-chloro-3-hydroxypropionate - *available at Sigma-Aldrich*
2. Benzoyl chloride - *available at Sigma-Aldrich*

Products:

1. COC(=O)C(Cl)COC(=O)c1ccccc1

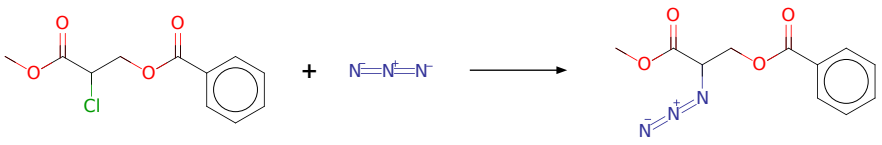
Typical conditions: base.DCM

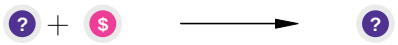
Protections: none

Reference: *10.1016/j.bmcl.2012.03.021* AND *10.1021/ja026266i* (SI, hydroperoxides) AND *10.1016/j.tetasy.2004.07.044* AND *10.1021/jm1006929* (SI) AND *10.1016/j.tet.2011.05.017* AND *10.1016/j.tetasy.2012.09.002* AND *10.1021/ol016268s* (SI) AND *10.1021/jo801116n* AND *10.1021/jo00279a041* AND WO2013/64518 A1, 2013 (page 102)

Retrosynthesis ID: 28549

2.2.2 Nucleophilic substitution with azides





Substrates:

1. COC(=O)C(Cl)COC(=O)c1ccccc1
2. Potassium azide - *available at Sigma-Aldrich*

Products:

1. COC(=O)C(COC(=O)c1ccccc1)N=[N+]=[N-]

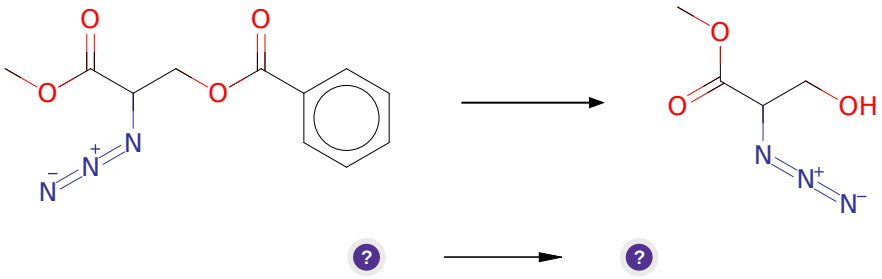
Typical conditions: DMF.heat

Protections: none

Reference: *10.1021/jo990445+* and *10.1002/adsc.200404102*

Retrosynthesis ID: 31011206

2.2.3 Hydrolysis of benzoates



Substrates:

1. COC(=O)C(COC(=O)c1ccccc1)N=[N+]=[N-]

Products:

1. COC(=O)C(CO)N=[N+]=[N-]

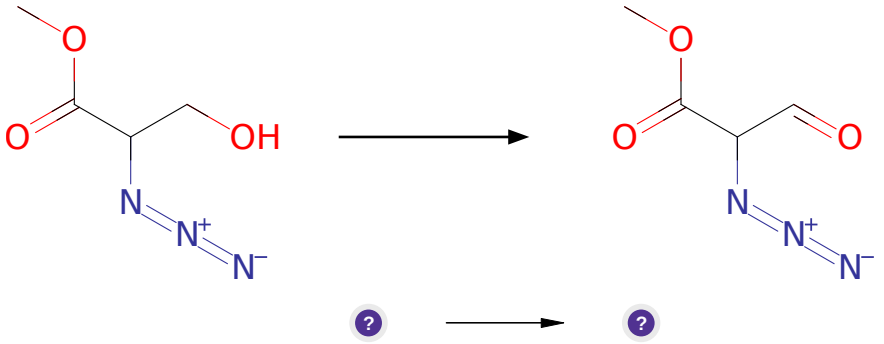
Typical conditions: LiOH/K2CO3/NH3.MeOH.H2O.THF

Protections: none

Reference: *10.1021/jm0502788* and *10.1016/j.tetlet.2008.09.165* and *10.1021/jm034098e* and *10.1021/jo049277y* and *10.1055/s-0033-1338657*

Retrosynthesis ID: 25136

2.2.4 Oxidation of primary alcohols with DMP



Substrates:

1. COC(=O)C(CO)N=[N+]=[N-]

Products:

1. COC(=O)C(C=O)N=[N+]=[N-]

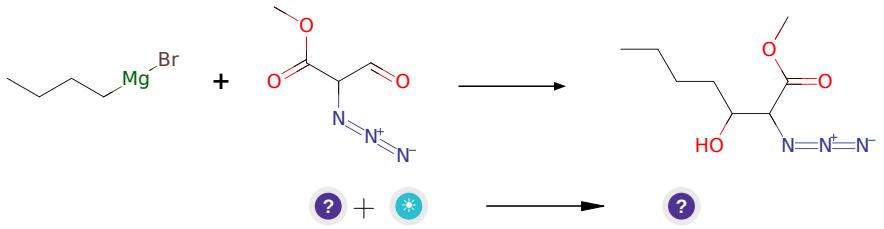
Typical conditions: DMP.DCM.0-25 C

Protections: none

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

Retrosynthesis ID: 50426

2.2.5 Grignard-Type Reaction



Substrates:

1. COC(=O)C(C=O)N=[N+]=[N-]
2. butylmagnesium bromide

Products:

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

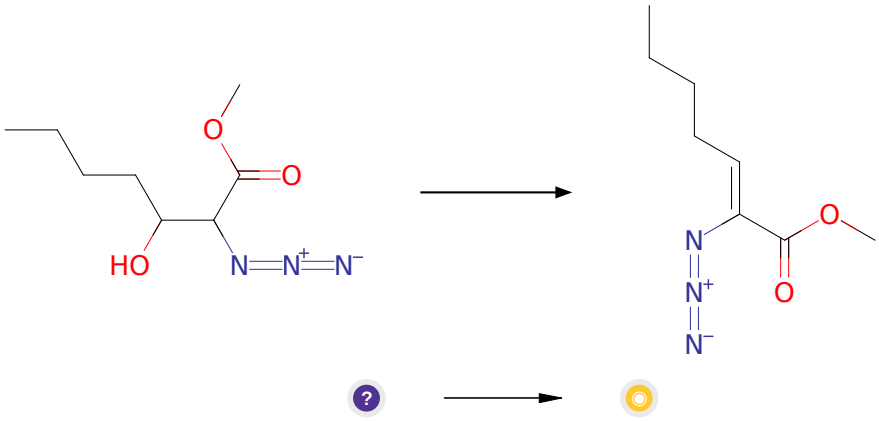
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1016/S0040-4020(99)00197-0* or *10.1055/s-0030-1260809* or *10.1021/ol703056u*

Retrosynthesis ID: 25124

2.2.6 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

1. CCCC/C=C(\N=[N+]=[N-])C(=O)OC

Typical conditions: TsOH

Protections: none

Reference: DOI:*10.1002/anie.201204977* AND *10.1021/ol062777o*

Retrosynthesis ID: 7732

2.3 Path 3

Score: 115.31

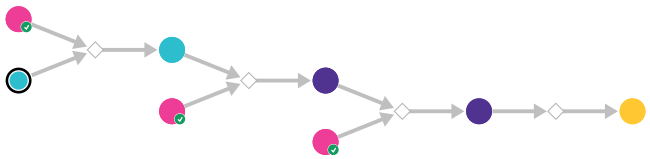
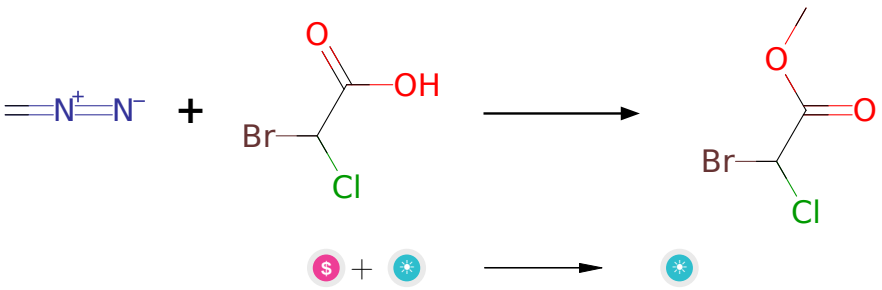


Figure 3: Outline of path 3

2.3.1 Synthesis of esters from diazomethanes



Substrates:

1. Bromochloroacetic acid - *available at Sigma-Aldrich*
2. diazomethane

Products:

1. bromo-chloro-acetic acid methyl ester

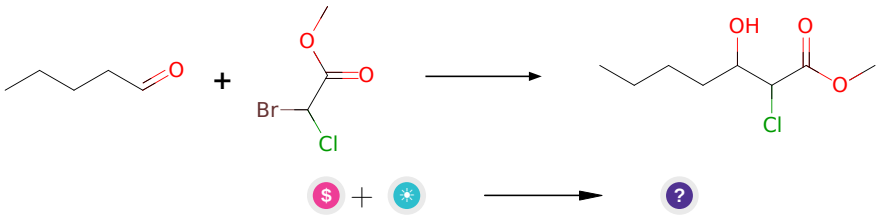
Typical conditions: THF.rt

Protections: none

Reference: *10.1021/jo401377a* AND *10.1016/j.tetlet.2013.04.079* AND *10.1016/j.bmcl.2003.12.037* AND *10.1016/j.bmc.2009.10.036*

Retrosynthesis ID: 15005

2.3.2 Reformatsky Reaction



Substrates:

1. Pentanal - *available at Sigma-Aldrich*
2. bromo-chloro-acetic acid methyl ester

Products:

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

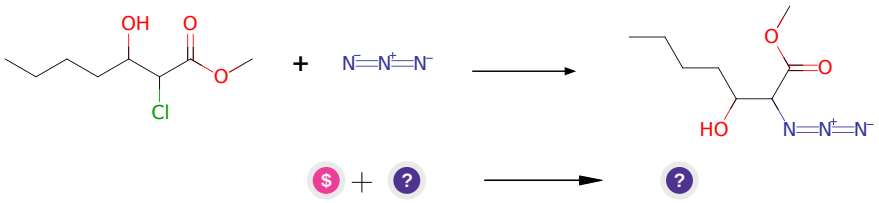
Typical conditions: Me2Zn.B(OMe)3.toluene.Et2O

Protections: none

Reference: *10.1021/jo200774e* p. 6373 and *10.1021/jo00163a019* p. 2522, 2525

Retrosynthesis ID: 11164

2.3.3 Nucleophilic substitution with azides



Substrates:

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

Products:

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

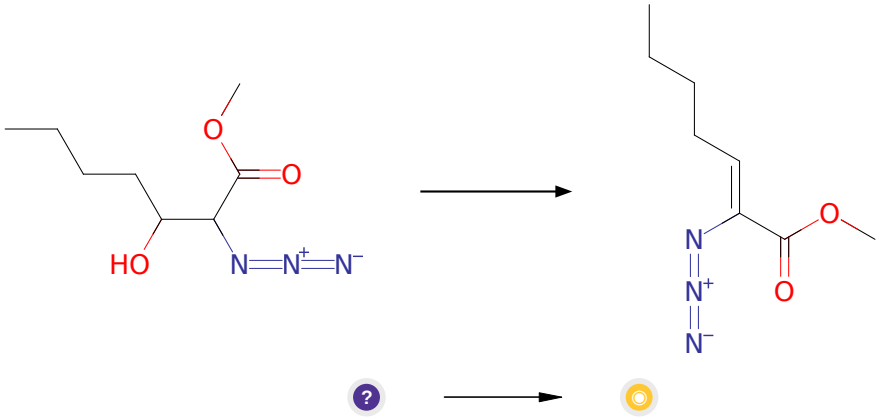
Typical conditions: DMF.heat

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

2.3.4 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

1. CCCC/C=C(\N=[N+]=[N-])C(=O)OC

Typical conditions: TsOH

Protections: none

Reference: DOI:*10.1002/anie.201204977* AND *10.1021/ol062777o*

Retrosynthesis ID: 7732

2.4 Path 4

Score: `115.31`

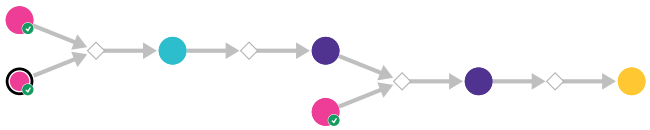
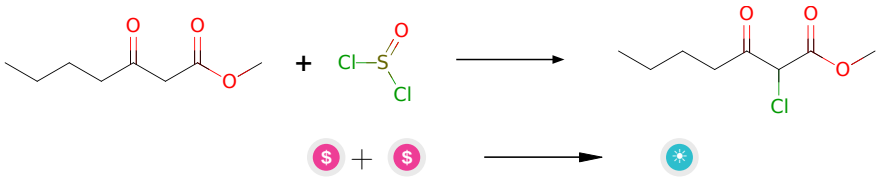


Figure 4: Outline of path 4

2.4.1 Synthesis of chloroesters from thionyl chloride



Substrates:

1. Methyl 3-oxoheptanoate - *available at Sigma-Aldrich*
2. Thionyl chloride - *available at Sigma-Aldrich*

Products:

1. 2-chloro-3-oxo-heptanoic acid methyl ester

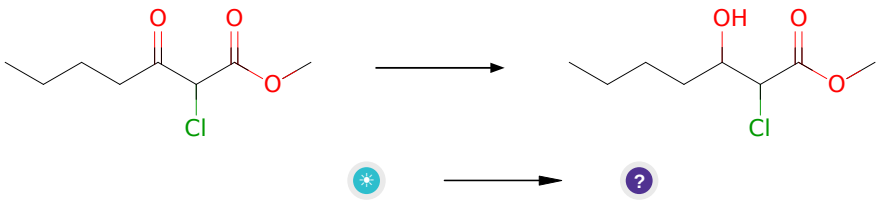
Typical conditions: SOCl2.chloroform

Protections: none

Reference: DOI: *10.1055/S-1975-23883*

Retrosynthesis ID: 295133

2.4.2 Reduction of ketones with NaBH4



Substrates:

1. 2-chloro-3-oxo-heptanoic acid methyl ester

Products:

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

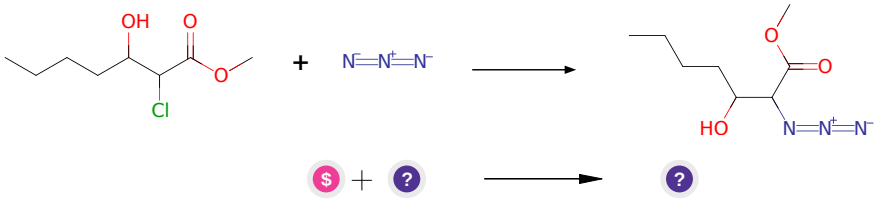
Typical conditions: NaBH4.EtOH.0-20 C

Protections: none

Reference: *10.1016/j.ejmech.2020.112360* p. 3, 8 and *10.1016/j.ejmech.2010.10.012* p. 434, 436

Retrosynthesis ID: 50432

2.4.3 Nucleophilic substitution with azides



Substrates:

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

Products:

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

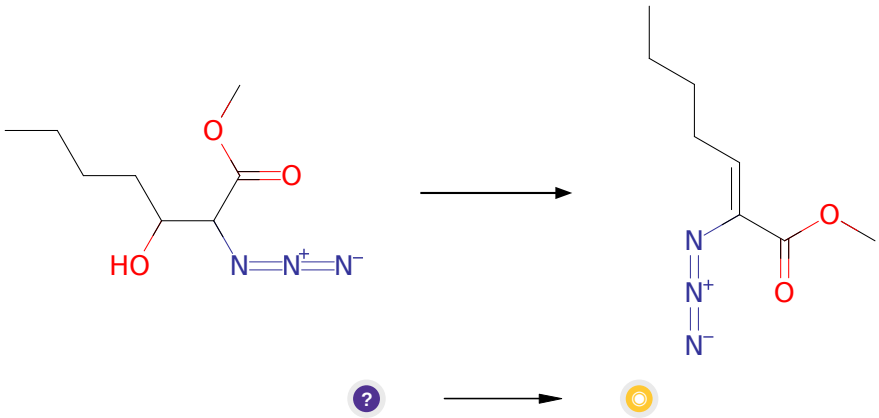
Typical conditions: DMF.heat

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

2.4.4 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

1. CCCC/C=C(\N=[N+]=[N-])C(=O)OC

Typical conditions: TsOH

Protections: none

Reference: DOI:*10.1002/anie.201204977* AND *10.1021/ol062777o*

Retrosynthesis ID: 7732

2.5 Path 5

Score: 115.31

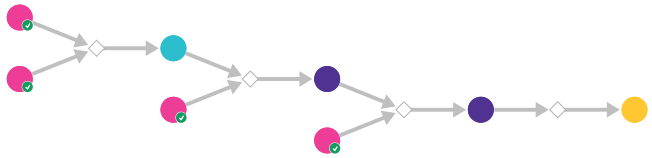
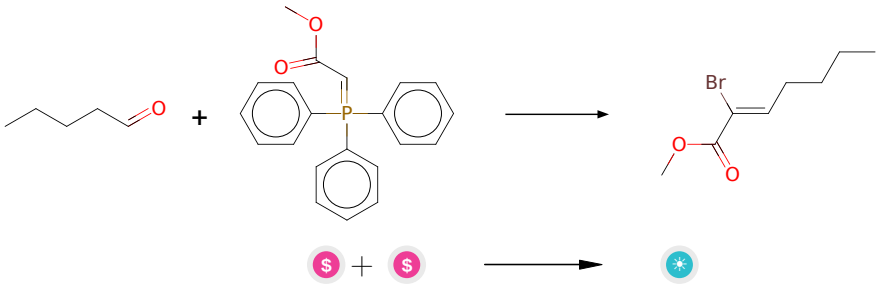


Figure 5: Outline of path 5

2.5.1 Synthesis of alpha-bromoacrylates from aldehydes



Substrates:

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

Products:

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

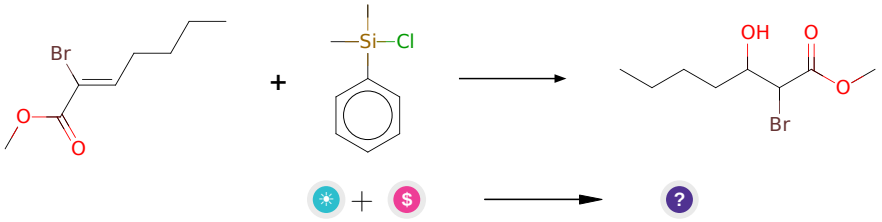
Typical conditions: TEA.BDMS.DCM.-78C

Protections: none

Reference: DOI: *10.1021/ol702859y*

Retrosynthesis ID: 1491

2.5.2 Addition of silanes to Michael acceptors followed by oxidation



Substrates:

1. 2-bromo-hept-2-enoic acid methyl ester
2. DMPSCl - *available at Sigma-Aldrich*

Products:

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

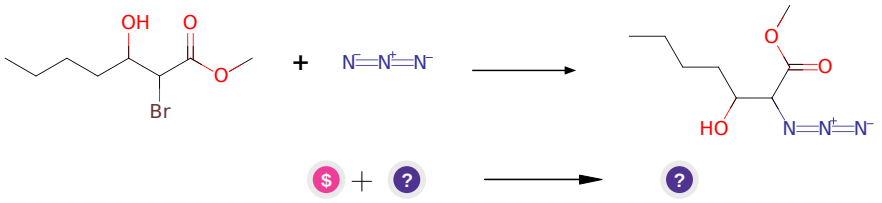
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

Protections: none

Reference: *10.1021/ja058370g* AND (Oxidation) *10.1021/jo9905672* or *10.1021/ol300832f*

Retrosynthesis ID: 20295

2.5.3 Nucleophilic substitution with azides



Substrates:

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

Products:

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

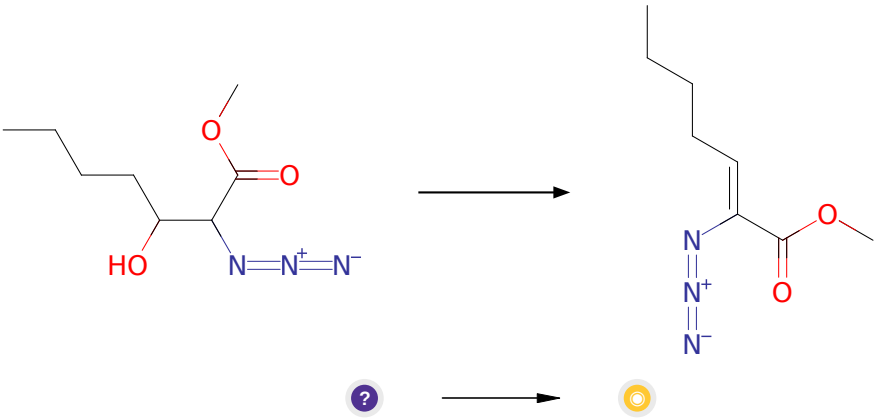
Typical conditions: DMF.heat

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

2.5.4 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

1. CCCC/C=C(\N=[N+]=[N-])C(=O)OC

Typical conditions: TsOH

Protections: none

Reference: DOI:*10.1002/anie.201204977* AND *10.1021/ol062777o*

Retrosynthesis ID: 7732