Paths of analysis*

PG9

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: 76.25

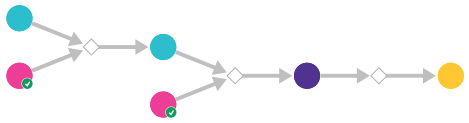
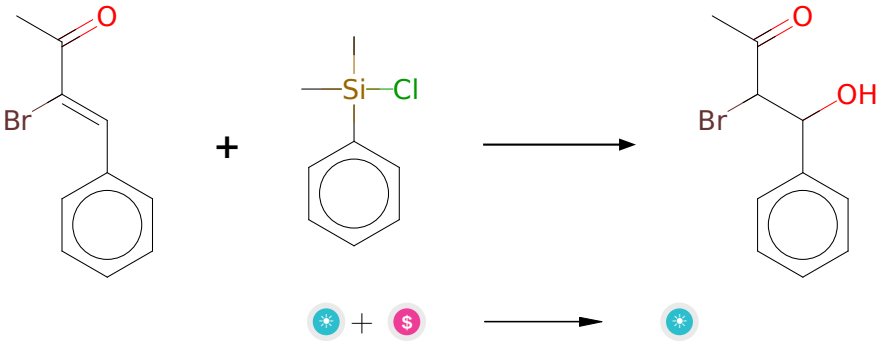


Figure 1: Outline of path 1

2.1.1 Addition of silanes to Michael acceptors followed by oxidation



Substrates:

1. (z)-3-bromo-4-phenyl-3-buten-2-one
2. DMPSCl - *available at Sigma-Aldrich*

Products:

1. 3-bromo-4-hydroxy-4-phenyl-butan-2-one

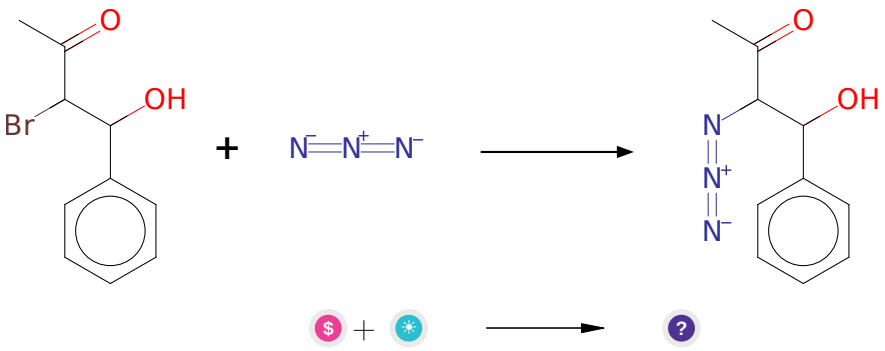
Typical conditions: 1.nBuLi.2.CuCN.3.electrophile.4.H2O2

Protections: none

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

Retrosynthesis ID: 20295

2.1.2 Nucleophilic substitution with azides



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. 3-bromo-4-hydroxy-4-phenyl-butan-2-one

Products:

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

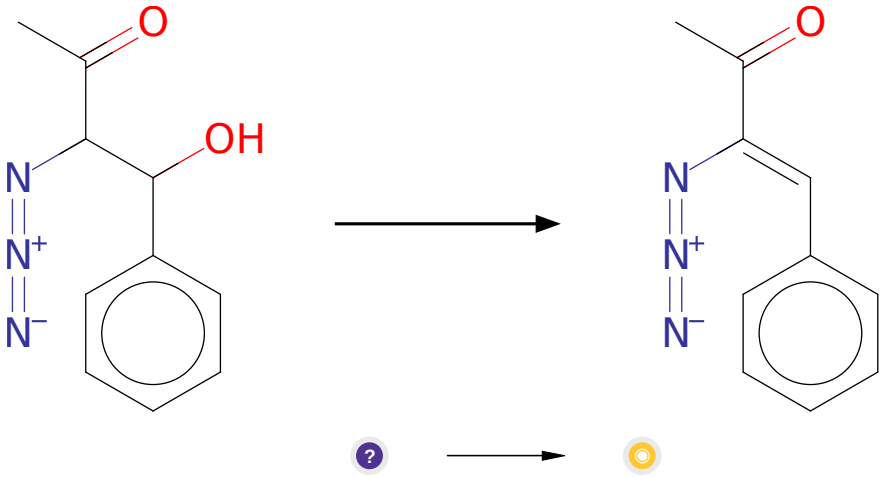
Typical conditions: DMF.heat

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

2.1.3 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

1. (z)-3-azido-4-phenyl-but-3-en-2-one

Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7732

2.2 Path 2

Score: `84.06`

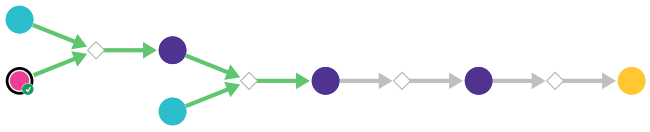
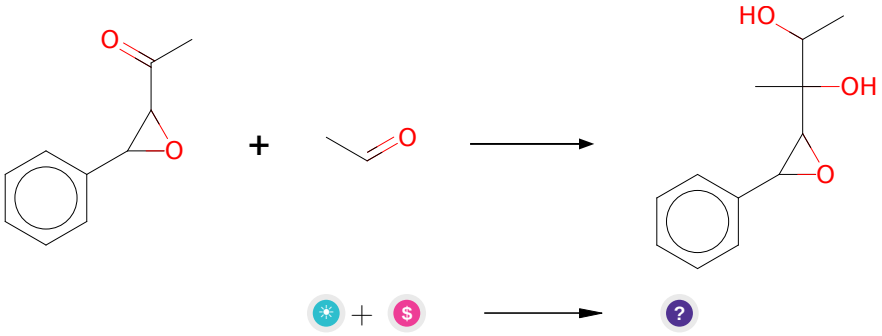


Figure 2: Outline of path 2

2.2.1 Pinacol Coupling Reaction



Substrates:

1. 3,4-epoxy-4-phenyl-butan-2-on
2. Ethanal - *available at Sigma-Aldrich*

Products:

1. CC(O)C(C)(O)C1OC1c1ccccc1

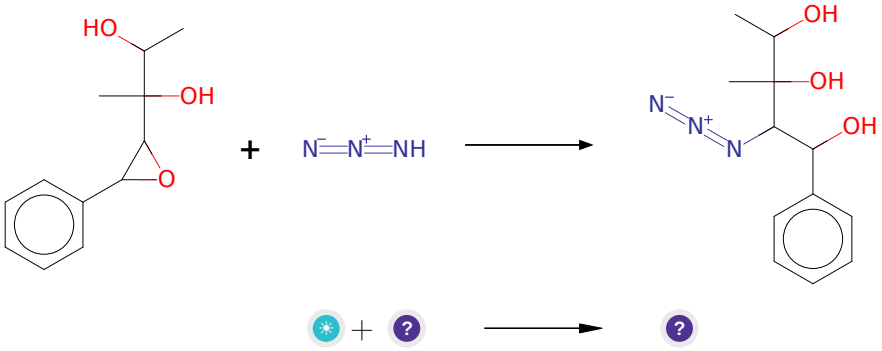
Typical conditions: Mg.NH4Cl.H2O or Mg.SmI2.TMSCl.THF.HMPA

Protections: none

Reference: *10.1021/jo982497p* p. 3234, 3236 and *10.1021/ol0506258* p. 2366, SI p. S12

Retrosynthesis ID: 10205

2.2.2 Ring-opening of epoxides or thiiranes with azides



Substrates:

1. hydrazoic acid

2. CC(O)C(C)(O)C1OC1c1ccccc1

Products:

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

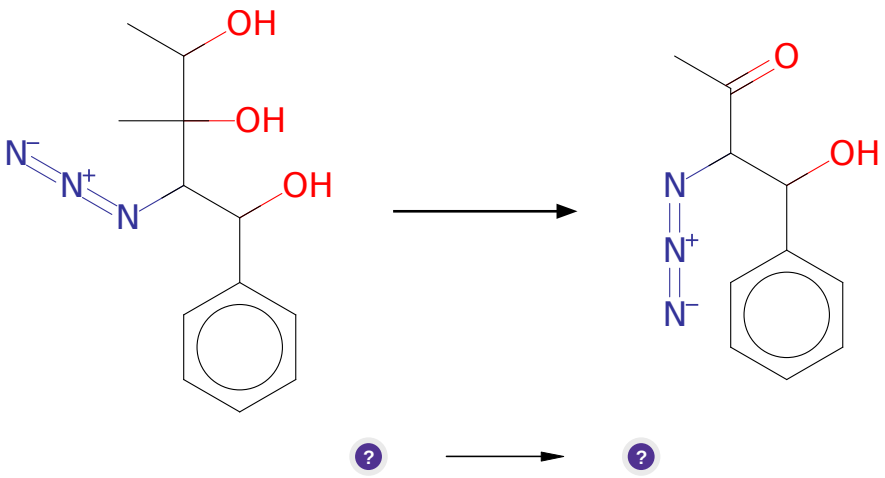
Typical conditions: NaN3.NH4Cl.MeOH.H2O.65 C

Protections: none

Reference: *10.1021/jm400529f* p. 4361, 4367 and *10.1021/ja003713q* p. 1590, 1594

Retrosynthesis ID: 858

2.2.3 Cleavage of 1,2-diols with NaIO4



Substrates:

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

Products:

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

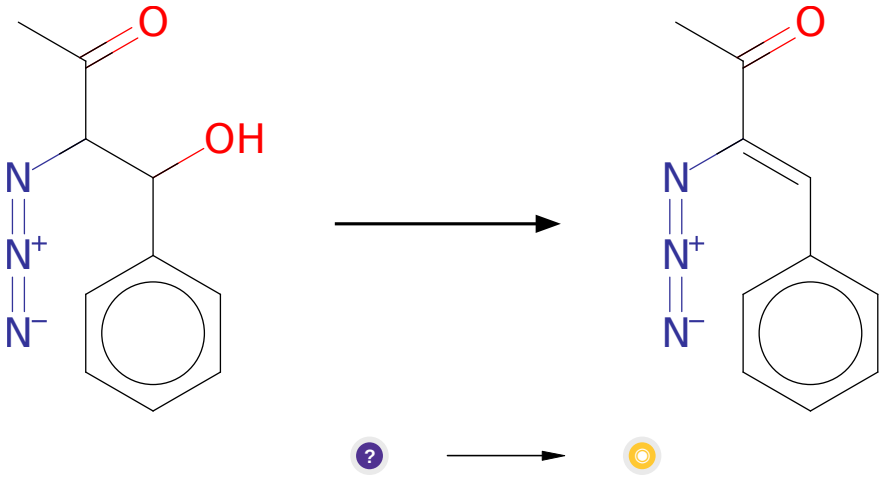
Typical conditions: NaIO4.solvent

Protections: none

Reference: *10.1039/C5OB00238A* and *10.1002/chem.201301371* and *10.1021/ol052106a*

Retrosynthesis ID: 31017508

2.2.4 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

1. (z)-3-azido-4-phenyl-but-3-en-2-one

Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7732

2.3 Path 3

Score: `84.06`

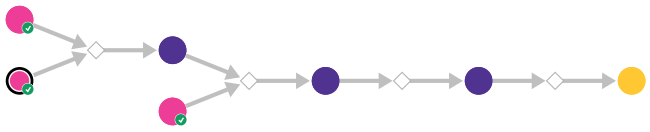
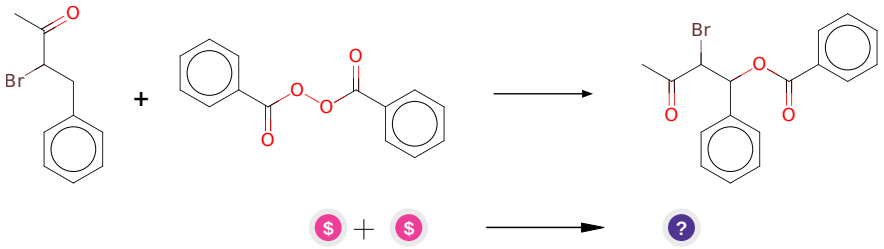


Figure 3: Outline of path 3

2.3.1 Free-radicals synthesis of benzoyl esters



Substrates:

1. 3-bromo-4-phenylbutan-2-one - *available at Sigma-Aldrich*
2. Luperox(r) A98 - *available at Sigma-Aldrich*

Products:

1. CC(=O)C(Br)C(OC(=O)c1ccccc1)c1ccccc1

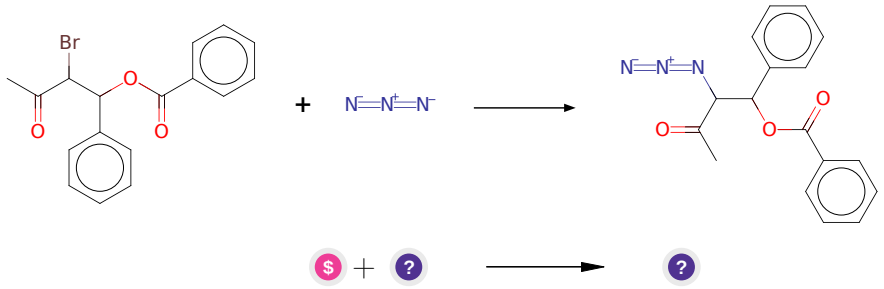
Typical conditions: CuBr

Protections: none

Reference: DOI: *10.1021/jo01265a066*

Retrosynthesis ID: 332

2.3.2 Nucleophilic substitution with azides



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. CC(=O)C(Br)C(OC(=O)c1ccccc1)c1ccccc1

Products:

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

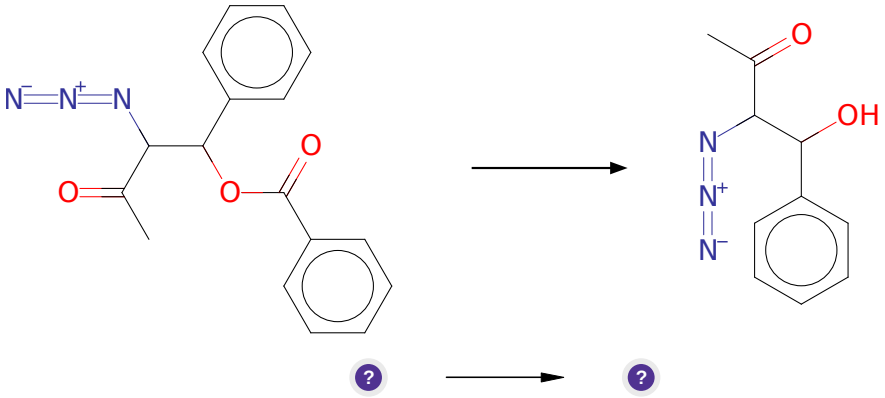
Typical conditions: DMF.heat

Protections: none

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

Retrosynthesis ID: 31011251

2.3.3 Hydrolysis of benzoates



Substrates:

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

Products:

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

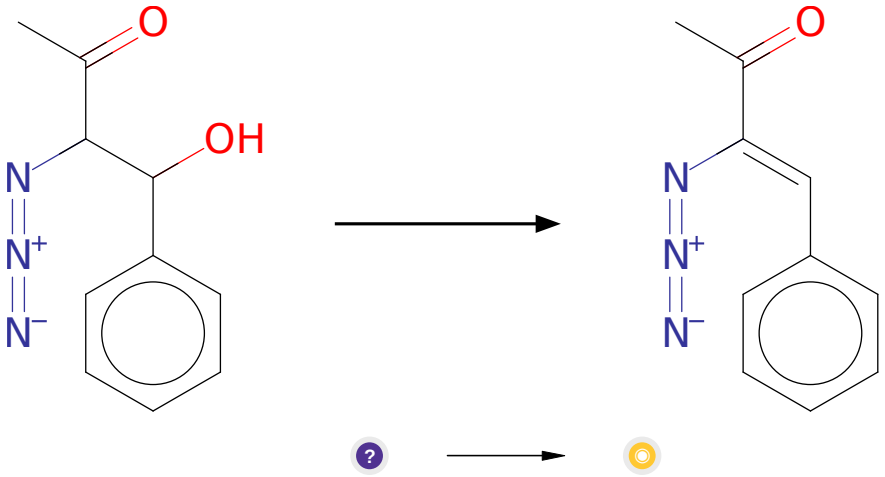
Typical conditions: LiOH/K2CO3/NH3.MeOH.H2O.THF

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

2.3.4 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

1. (z)-3-azido-4-phenyl-but-3-en-2-one

Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7732

2.4 Path 4

Score: `90.31`

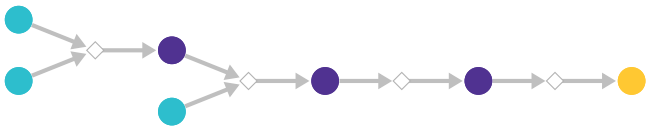
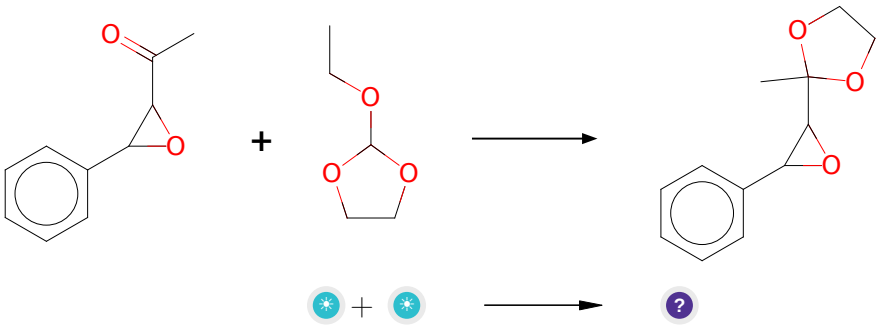


Figure 4: Outline of path 4

2.4.1 Acetalization of Carbonyl Compounds Catalyzed by Indium Triflate



Substrates:

1. 2-ethoxy-[1,3]dioxolane
2. 3,4-epoxy-4-phenyl-butan-2-on

Products:

1. CC1(C2OC2c2ccccc2)OCCO1

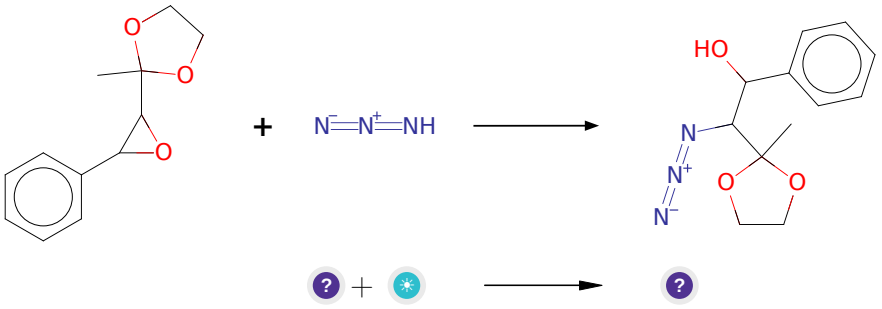
Typical conditions: indium triflate. MeOH. CH2Cl2. 20C

Protections: none

Reference: DOI: *10.1016/j.tetlet.2006.10.111* or DOI: *10.1002/cber.19620950803*

Retrosynthesis ID: 9318

2.4.2 Ring-opening of epoxides or thiiranes with azides



Substrates:

1. CC1(C2OC2c2ccccc2)OCCO1
2. hydrazoic acid

Products:

1. CC1(C(N=[N+]=[N-])C(O)c2ccccc2)OCCO1

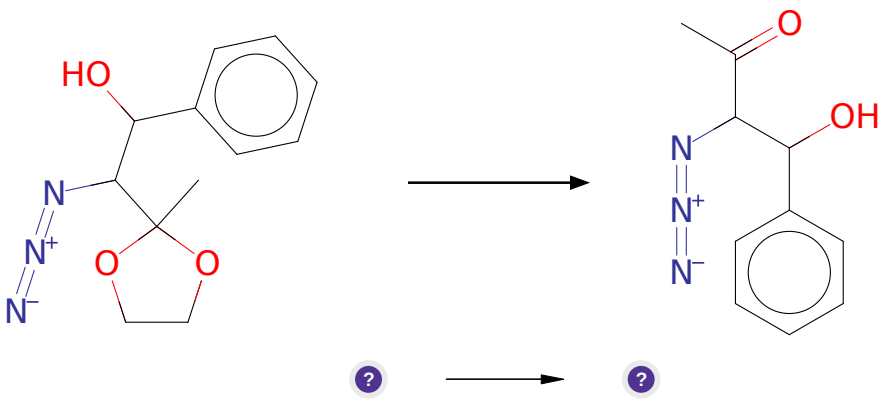
Typical conditions: NaN3.NH4Cl.MeOH.H2O.65 C

Protections: none

Reference: *10.1021/jm400529f* p. 4361, 4367 and *10.1021/ja003713q* p. 1590, 1594

Retrosynthesis ID: 858

2.4.3 Hydrolysis of ketals



Substrates:

1. CC1(C(N=[N+]=[N-])C(O)c2ccccc2)OCCO1

Products:

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

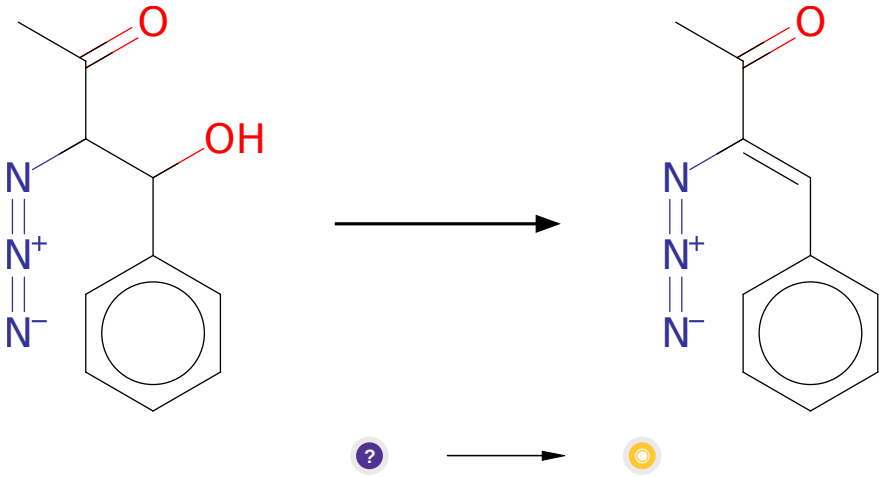
Typical conditions: H2O.HCl

Protections: none

Reference: *10.1021/jo0159035* and *10.1021/jo00194a003* and

Retrosynthesis ID: 31013139

2.4.4 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

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

Products:

1. (z)-3-azido-4-phenyl-but-3-en-2-one

Typical conditions: TsOH

Protections: none

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

Retrosynthesis ID: 7732

2.5 Path 5

Score: `107.89`

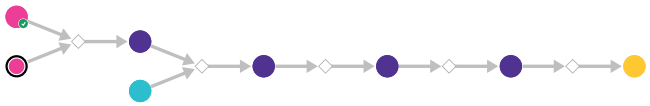
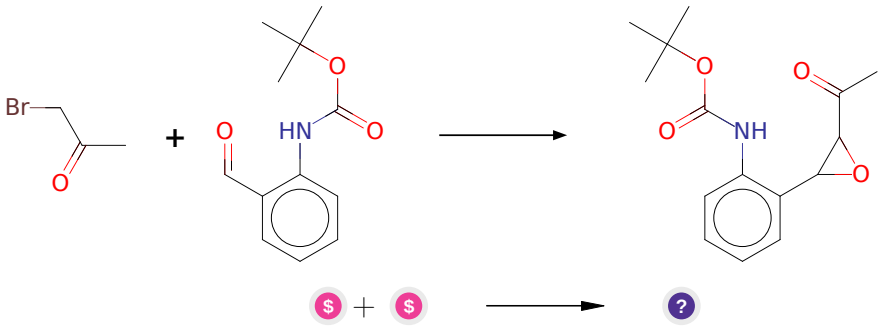


Figure 5: Outline of path 5

2.5.1 Darzens Condensation



Substrates:

1. 2-(Boc-amino)benzaldehyde - *available at Sigma-Aldrich*
2. brom-aceton - *AstaTech*

Products:

1. CC(=O)C1OC1c1ccccc1NC(=O)OC(C)(C)C

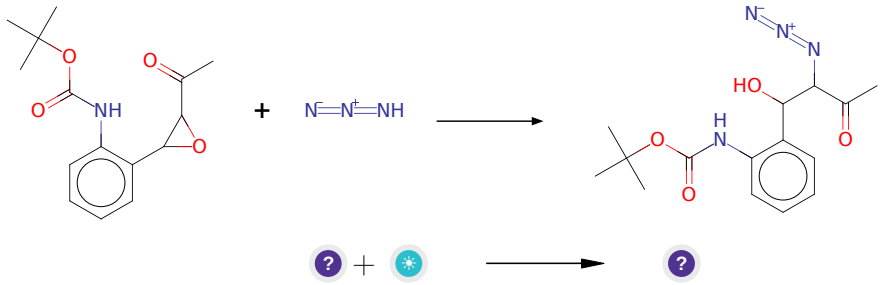
Typical conditions: KOtBu.HOtBu

Protections: none

Reference: *10.1002/0471264180.or005.10* and *10.1021/cr50002a002*

Retrosynthesis ID: 11513

2.5.2 Ring-opening of epoxides or thiiranes with azides



Substrates:

1. CC(=O)C1OC1c1ccccc1NC(=O)OC(C)(C)C
2. hydrazoic acid

Products:

1. CC(=O)C(N=[N+]=[N-])C(O)c1ccccc1NC(=O)OC(C)(C)C

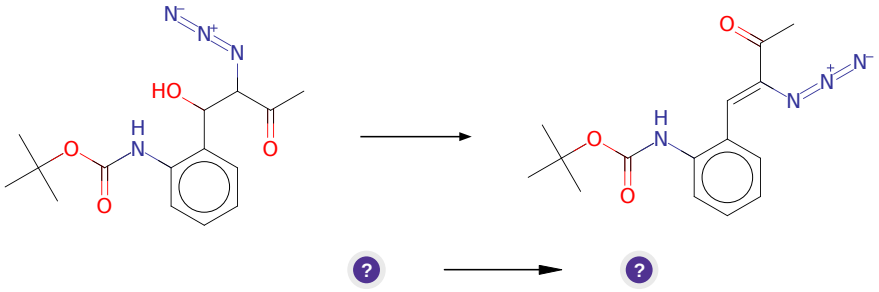
Typical conditions: NaN3.NH4Cl.MeOH.H2O.65 C

Protections: none

Reference: *10.1021/jm400529f* p. 4361, 4367 and *10.1021/ja003713q* p. 1590, 1594

Retrosynthesis ID: 858

2.5.3 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

1. CC(=O)C(N=[N+]=[N-])C(O)c1ccccc1NC(=O)OC(C)(C)C

Products:

1. CC(=O)/C(=C/c1ccccc1NC(=O)OC(C)(C)C)N=[N+]=[N-]

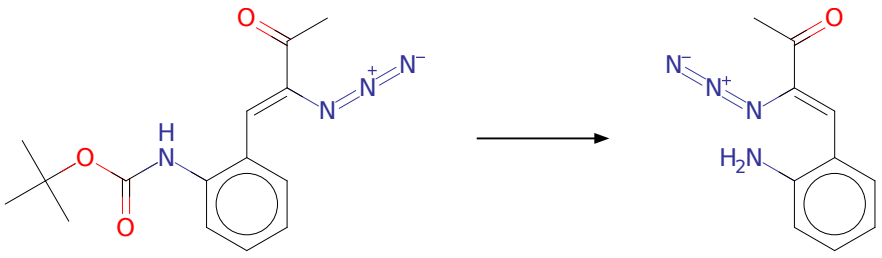
Typical conditions: TsOH

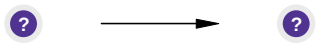
Protections: none

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

Retrosynthesis ID: 7732

2.5.4 Boc removal





Substrates:

1. CC(=O)/C(=C/c1ccccc1NC(=O)OC(C)(C)C)N=[N+]=[N-]

Products:

1. CC(=O)/C(=C/c1ccccc1N)N=[N+]=[N-]

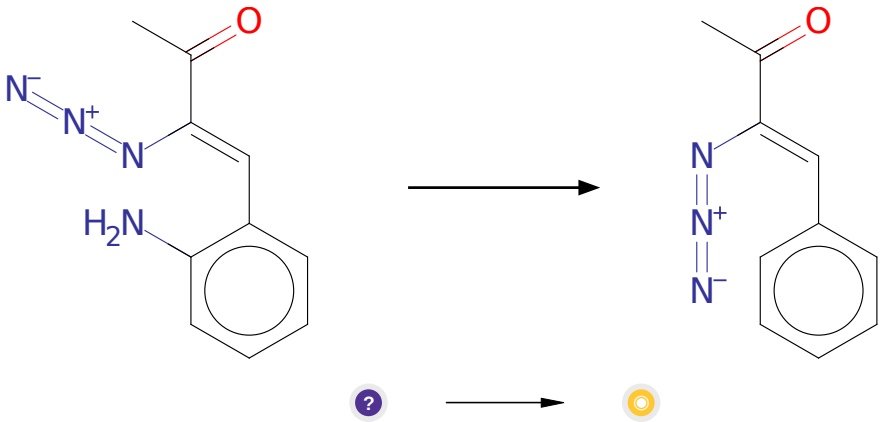
Typical conditions: TFA.DCM

Protections: none

Reference: *10.1016/j.ejmech.2017.06.062* and *10.1016/j.bmcl.2008.02.079* and *10.1016/j.tetlet.2009.09.087* and *10.1016/j.bmcl.2015.06.039*

Retrosynthesis ID: 10025813

2.5.5 Hydrodediazoniation



Substrates:

1. CC(=O)/C(=C/c1ccccc1N)N=[N+]=[N-]

Products:

1. (z)-3-azido-4-phenyl-but-3-en-2-one

Typical conditions: 1) HCl.NaNO2 2) H3PO2

Protections: none

Reference: *10.1016/j.bmcl.2013.10.058* and *10.1021/jm0004906* and *10.1002/ejoc.200600030* and *10.1016/j.tet.2016.02.011*

Retrosynthesis ID: 9999756