Paths of analysis*

PG6

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: `90.31`

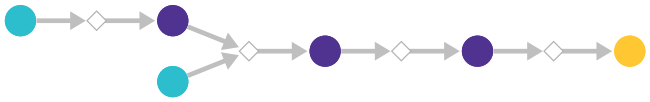
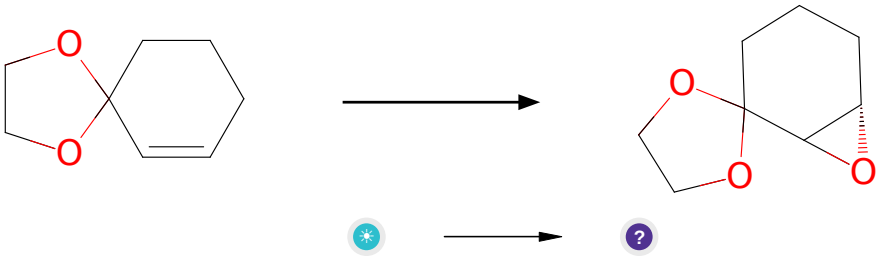


Figure 1: Outline of path 1

2.1.1 Shi epoxidation



Substrates:

1. 1,4-dioxa-spiro[4.5]dec-6-ene

Products:

1. C1C[C@@H]2OC2C2(C1)OCCO2

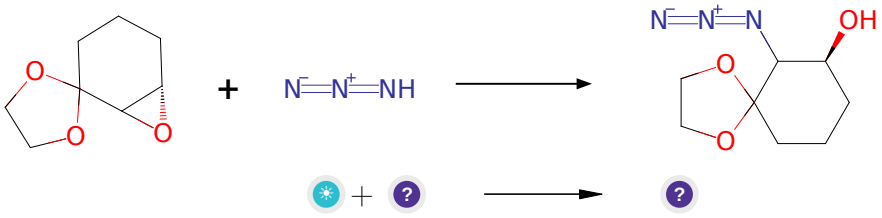
Typical conditions: sugar.based.catalyst.KHSO5.K2CO3.H2O.ACN.0C

Protections: none

Reference: *10.1055/s-0028-1083545* and *10.1021/ja972272g* and *10.1021/ja003049d* and *10.1021/jo972106r*

Retrosynthesis ID: 7433

2.1.2 Ring-opening of epoxides or thiiranes with azides



Substrates:

1. hydrazoic acid
2. C1C[C@@H]2OC2C2(C1)OCCO2

Products:

1. [N-]=[N+]=NC1[C@@H](O)CCCC12OCCO2

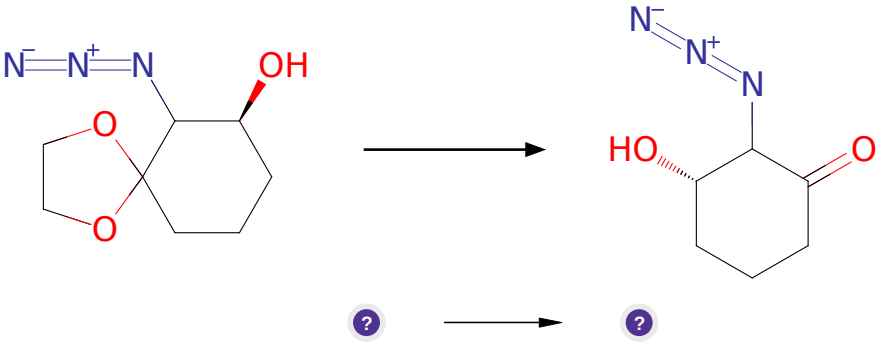
Typical conditions: NaN3.NH4Cl.MeOH.H2O.65 C

Protections: none

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

Retrosynthesis ID: 859

2.1.3 Hydrolysis of ketals



Substrates:

1. [N-]=[N+]=NC1[C@@H](O)CCCC12OCCO2

Products:

1. [N-]=[N+]=NC1C(=O)CCC[C@@H]1O

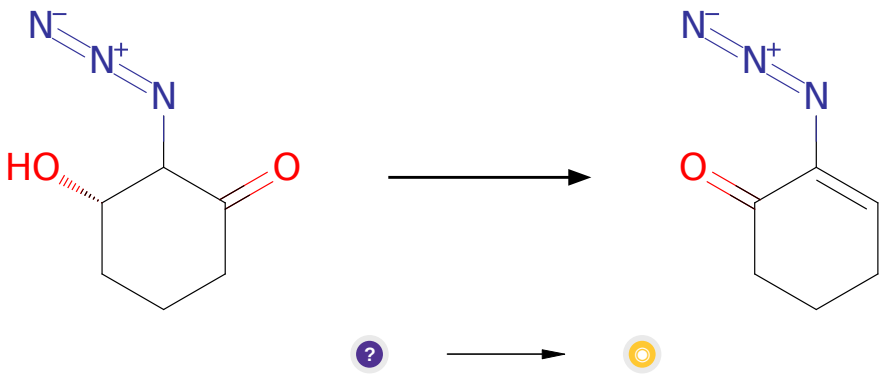
Typical conditions: H2O.HCl

Protections: none

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

Retrosynthesis ID: 31013139

2.1.4 Dehydration of beta-ketoalcohols



Substrates:

1. [N-]=[N+]=NC1C(=O)CCC[C@@H]1O

Products:

1. 2-azidocyclohex-2-enone

Typical conditions: 1.MsCl.NEt3

Protections: none

Reference: *10.1021/ol301090v* and *10.1021/ja00521a062* and *10.1002/ejoc.201201636* (SI)

Retrosynthesis ID: 20812

2.2 Path 2

Score: `100.08`

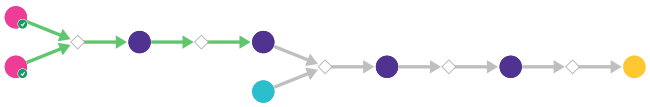
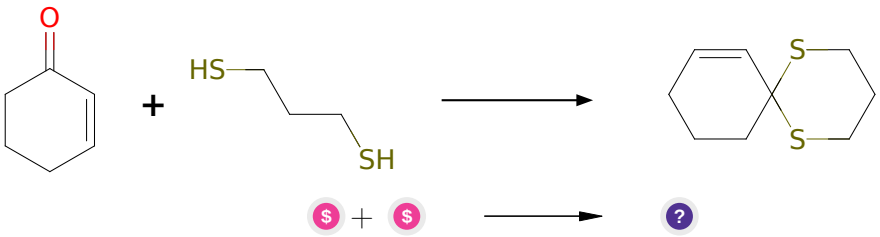


Figure 2: Outline of path 2

2.2.1 Synthesis of ketals and acetals



Substrates:

1. 1,3-Propanedithiol - *available at Sigma-Aldrich*
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. C1=CC2(CCC1)SCCCS2

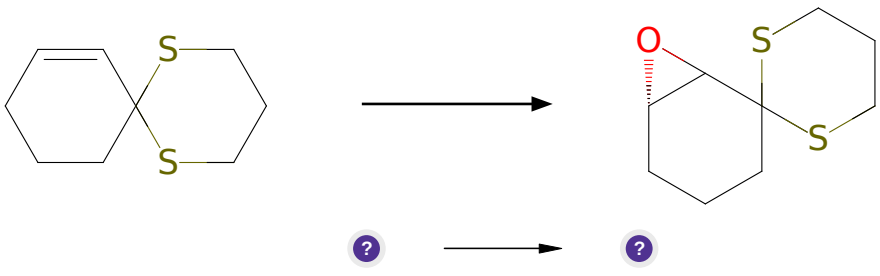
Typical conditions: pTsOH.toluene.heat

Protections: none

Reference: *10.1039/P19880000817* AND *10.1016/j.tetlet.2012.07.052* AND *10.1039/C0CC00110D* AND *10.1002/1521-3765(20010504)7:9<2007::AID-CHEM2007>3.0.CO;2-7*

Retrosynthesis ID: 14599

2.2.2 Shi epoxidation



Substrates:

1. C1=CC2(CCC1)SCCCS2

Products:

1. C1CSC2(CCC[C@@H]3OC32)SC1

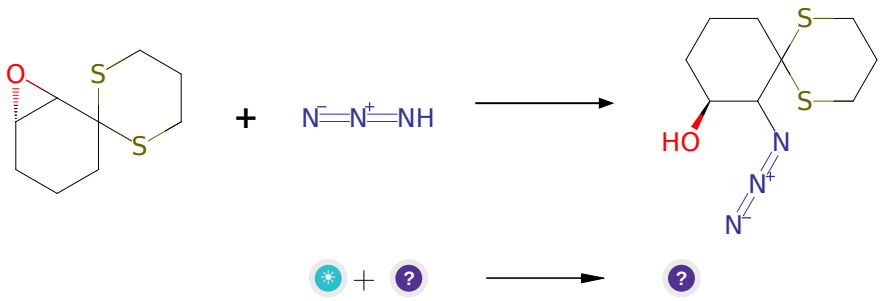
Typical conditions: sugar.based.catalyst.KHSO5.K2CO3.H2O.ACN.0C

Protections: none

Reference: *10.1055/s-0028-1083545* and *10.1021/ja972272g* and *10.1021/ja003049d* and *10.1021/jo972106r*

Retrosynthesis ID: 7433

2.2.3 Ring-opening of epoxides or thiiranes with azides



Substrates:

1. hydrazoic acid
2. C1CSC2(CCC[C@@H]3OC32)SC1

Products:

1. [N-]=[N+]=NC1[C@@H](O)CCCC12SCCCS2

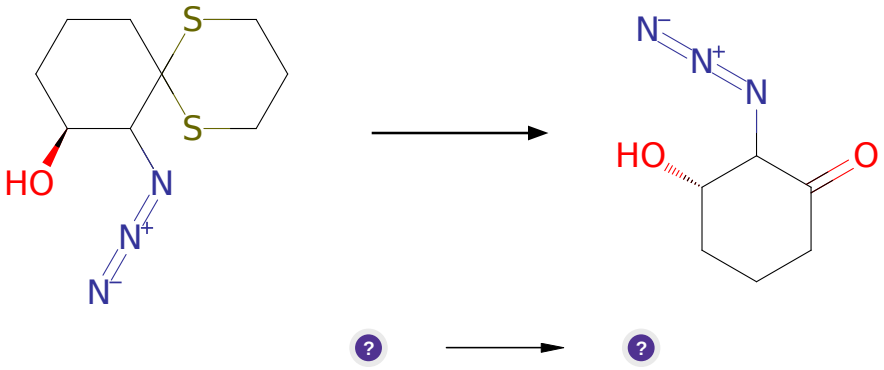
Typical conditions: NaN3.NH4Cl.MeOH.H2O.65 C

Protections: none

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

Retrosynthesis ID: 859

2.2.4 Synthesis of ketones from dithianes



Substrates:

1. [N-]=[N+]=NC1[C@@H](O)CCCC12SCCCS2

Products:

1. [N-]=[N+]=NC1C(=O)CCC[C@@H]1O

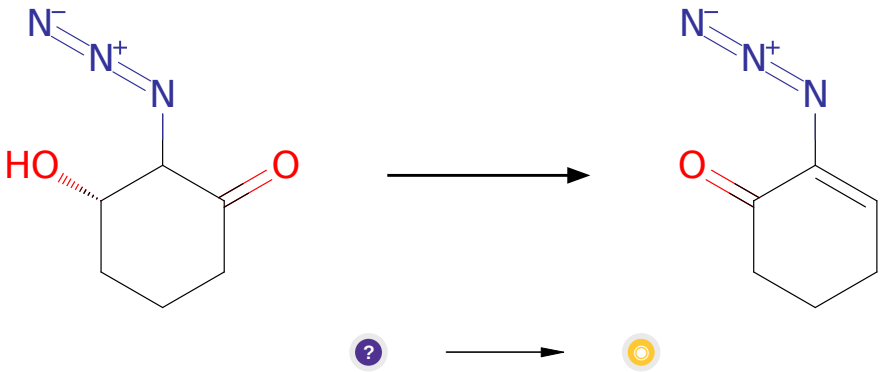
Typical conditions: MeI.CaCO3

Protections: none

Reference: *10.1016/j.tet.2013.09.075* and *10.1021/jo00007a015* and *10.1021/jo0610412* and *10.1021/ol901024t* and *10.1021/ol500553x* and *10.1021/jo0626459*

Retrosynthesis ID: 31724

2.2.5 Dehydration of beta-ketoalcohols



Substrates:

1. [N-]=[N+]=NC1C(=O)CCC[C@@H]1O

Products:

1. 2-azidocyclohex-2-enone

Typical conditions: 1.MsCl.NEt3

Protections: none

Reference: *10.1021/ol301090v* and *10.1021/ja00521a062* and *10.1002/ejoc.201201636* (SI)

Retrosynthesis ID: 20812

2.3 Path 3

Score: 107.89

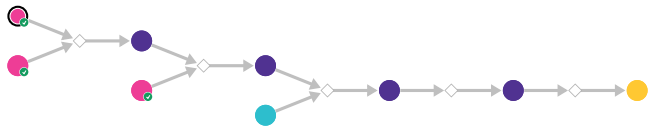
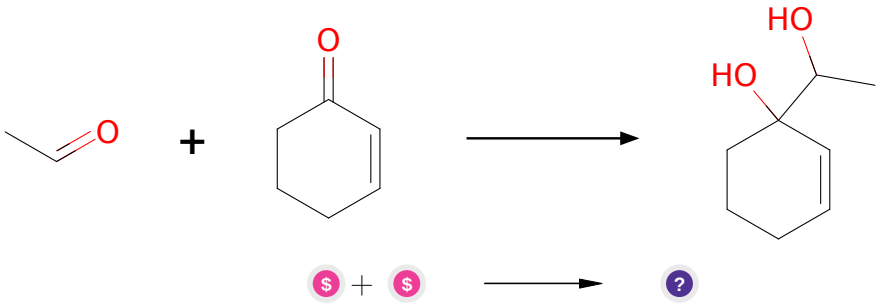


Figure 3: Outline of path 3

2.3.1 Pinacol Coupling Reaction



Substrates:

1. Ethanal - *available at Sigma-Aldrich*
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. CC(O)C1(O)C=CCCC1

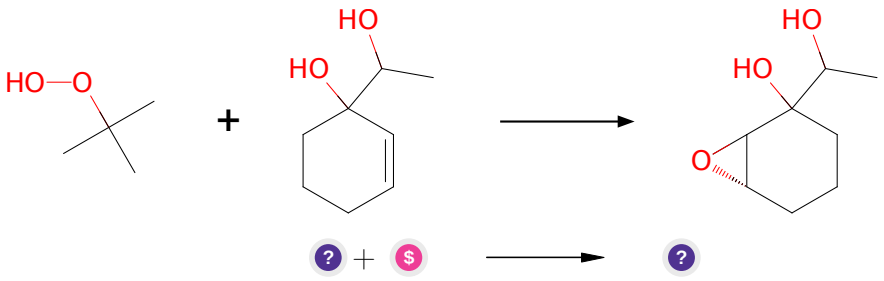
Typical conditions: Mg.NH4Cl.H2O or Mg.SmI2.TMSCl.THF.HMPA

Protections: none

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

Retrosynthesis ID: 10205

2.3.2 Sharpless asymmetric epoxidation



Substrates:

1. CC(O)C1(O)C=CCCC1
2. Luperox(r) TBH70X - *available at Sigma-Aldrich*

Products:

1. CC(O)C1(O)CCC[C@@H]2OC21

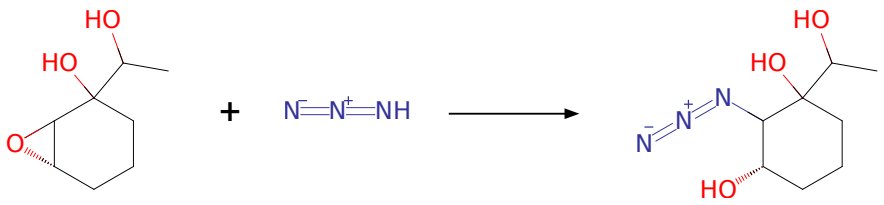
Typical conditions: D(-)diethyl tartrate

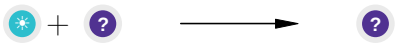
Protections: none

Reference: *10.1021/ja00538a077* and *10.1021/cr00093a001*

Retrosynthesis ID: 10442

2.3.3 Ring-opening of epoxides or thiiranes with azides





Substrates:

1. hydrazoic acid
2. CC(O)C1(O)CCC[C@@H]2OC21

Products:

1. CC(O)C1(O)CCC[C@H](O)C1N=[N+]=[N-]

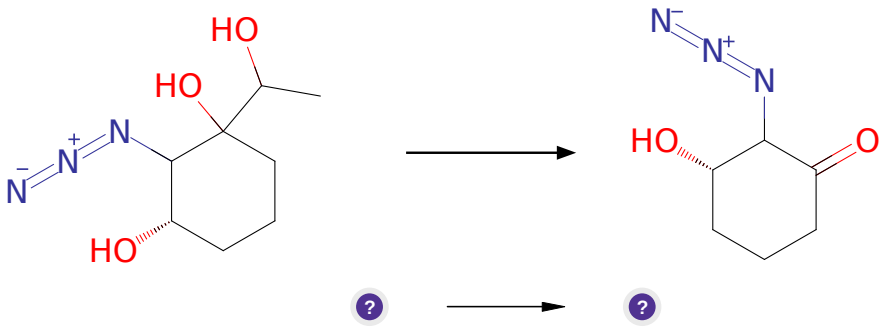
Typical conditions: sodium azide or TMSN3

Protections: none

Reference: DOI:*10.1055/s-2007-965921* and *10.1021/jo034752y* and

Retrosynthesis ID: 34714

2.3.4 Cleavage of 1,2-diols with NaIO4



Substrates:

1. CC(O)C1(O)CCC[C@H](O)C1N=[N+]=[N-]

Products:

1. [N-]=[N+]=NC1C(=O)CCC[C@@H]1O

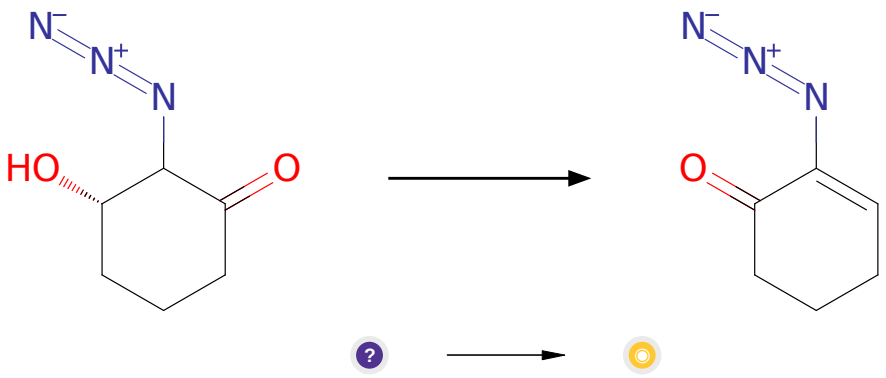
Typical conditions: NaIO4.solvent

Protections: none

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

Retrosynthesis ID: 31017508

2.3.5 Dehydration of beta-ketoalcohols



Substrates:

1. [N-]=[N+]=NC1C(=O)CCC[C@@H]1O

Products:

1. 2-azidocyclohex-2-enone

Typical conditions: 1.MsCl.NEt3

Protections: none

Reference: *10.1021/ol301090v* and *10.1021/ja00521a062* and *10.1002/ejoc.201201636* (SI)

Retrosynthesis ID: 20812

2.4 Path 4

Score: `115.31`

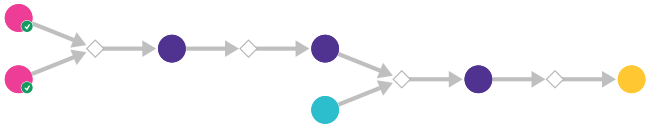
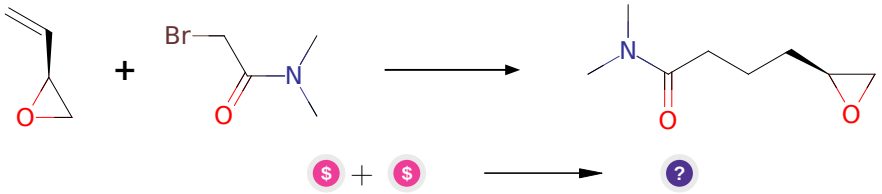


Figure 4: Outline of path 4

2.4.1 Suzuki alkyl-alkyl coupling



Substrates:

1. (S)-2-Vinyloxirane - *available at Sigma-Aldrich*
2. 2-Bromo-N,N-dimethylacetamide - *available at Sigma-Aldrich*

Products:

1. CN(C)C(=O)CCC[C@H]1CO1

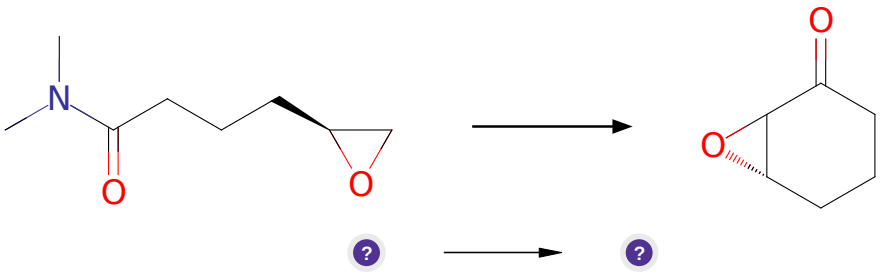
Typical conditions: 1.9BBN-H or pinB-Bpin.Cu 2.[Pd].ligand.base

Protections: none

Reference: *10.1021/ja074008l* and *10.1021/ja011306o* and *10.1002/1521-3773(20011217)40:24<4544::AID-ANIE4544>3.0.CO;2-N* and *10.1021/ol300575d*

Retrosynthesis ID: 8325

2.4.2 Reaction of amides with lithiated epoxides



Substrates:

1. CN(C)C(=O)CCC[C@H]1CO1

Products:

1. O=C1CCC[C@@H]2OC12

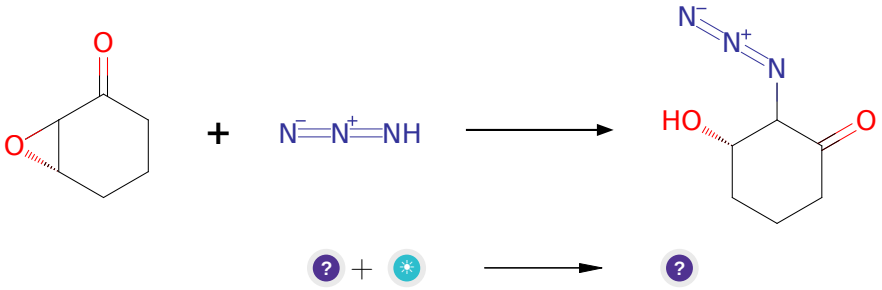
Typical conditions: 1. sBuLi.DBB.hexane.-90C 2. Bu3SnCl

Protections: none

Reference: DOI: *10.1021/ol048544j* and *10.1021/ol0485013*

Retrosynthesis ID: 1698

2.4.3 Ring-opening of epoxides or thiiranes with azides



Substrates:

1. O=C1CCC[C@@H]2OC12
2. hydrazoic acid

Products:

1. [N-]=[N+]=NC1C(=O)CCC[C@@H]1O

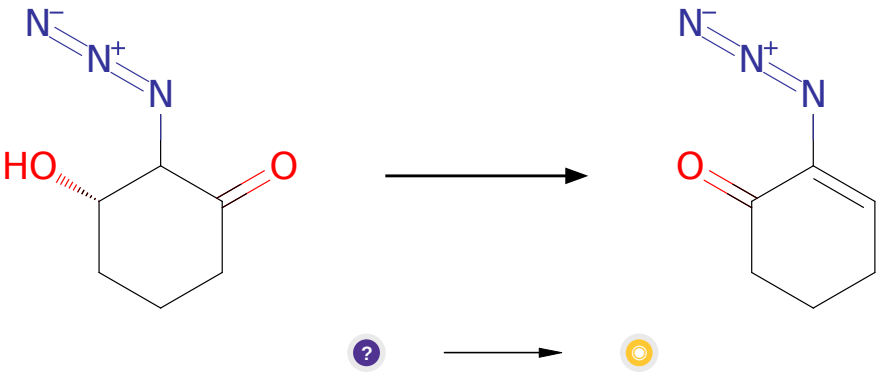
Typical conditions: NaN3.NH4Cl.MeOH.H2O.65 C

Protections: none

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

Retrosynthesis ID: 859

2.4.4 Dehydration of beta-ketoalcohols



Substrates:

1. [N-]=[N+]=NC1C(=O)CCC[C@@H]1O

Products:

1. 2-azidocyclohex-2-enone

Typical conditions: 1.MsCl.NEt3

Protections: none

Reference: *10.1021/ol301090v* and *10.1021/ja00521a062* and *10.1002/ejoc.201201636* (SI)

Retrosynthesis ID: 20812

2.5 Path 5

Score: `115.31`

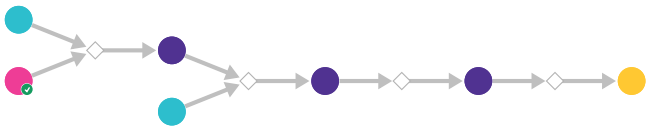
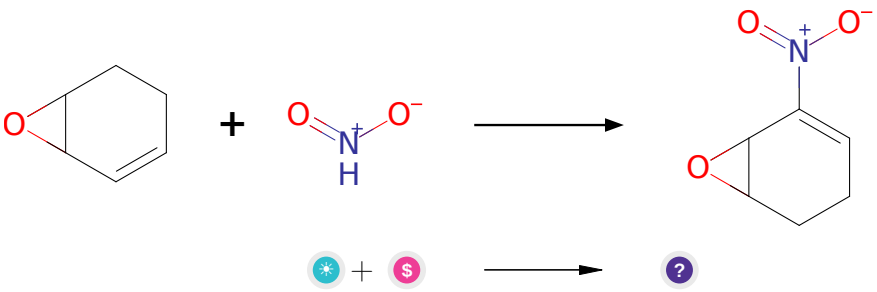


Figure 5: Outline of path 5

2.5.1 Nitration of aliphatic olefins



Substrates:

1. HNO2
2. 3,4-Epoxy-1-cyclohexene - *available at Sigma-Aldrich*

Products:

1. O=[N+]([O-])C1=CCCC2OC12

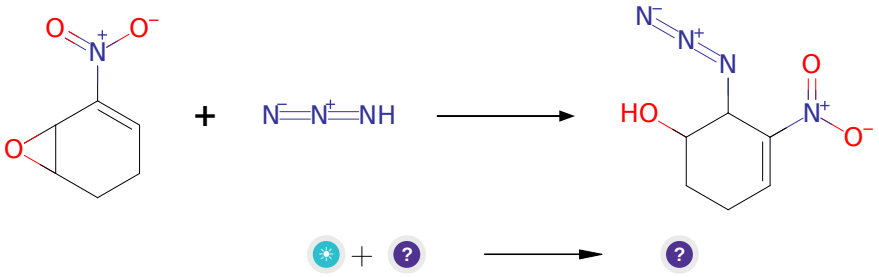
Typical conditions: Fe(NO2)3x9H2O.TEMPO.DCE.4A MS.80C

Protections: none

Reference: DOI: *10.1021/jo400598p*

Retrosynthesis ID: 1623

2.5.2 Ring-opening of epoxides or thiiranes with azides



Substrates:

1. hydrazoic acid
2. O=[N+]([O-])C1=CCCC2OC12

Products:

1. [N-]=[N+]=NC1C([N+](=O)[O-])=CCCC1O

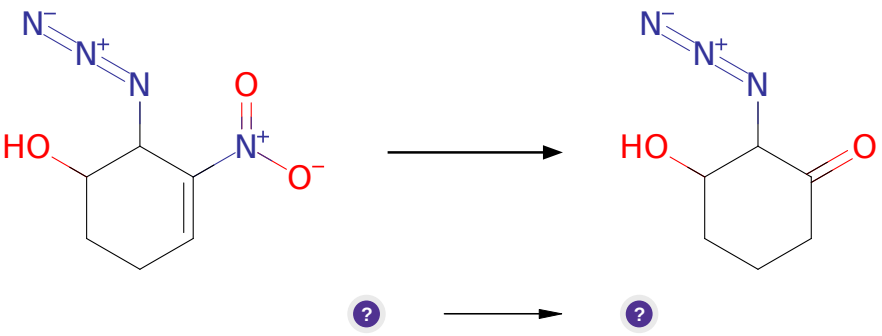
Typical conditions: NaN3.NH4Cl.MeOH.H2O.65 C

Protections: none

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

Retrosynthesis ID: 858

2.5.3 Synthesis of ketones from nitroalkenes



Substrates:

1. [N-]=[N+]=NC1C([N+](=O)[O-])=CCCC1O

Products:

1. [N-]=[N+]=NC1C(=O)CCCC1O

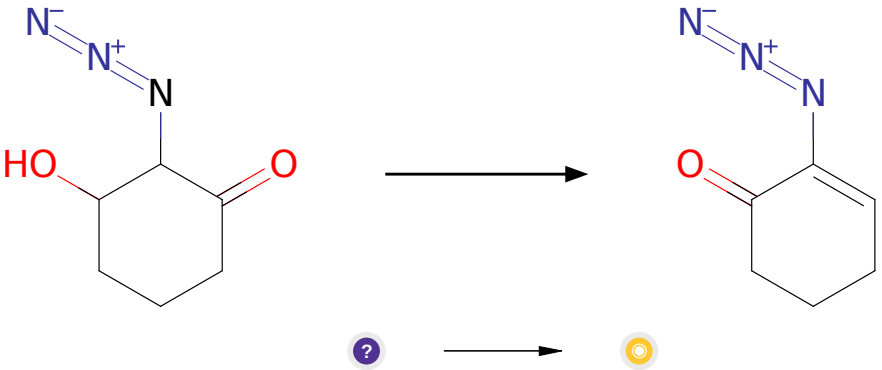
Typical conditions: RaNi.hypophosphite.EtOH.acetate.buffer or Fe.HCl.MeOH

Protections: none

Reference: *10.1081/SCC-200051681* and *10.1055/s-1993-25981*

Retrosynthesis ID: 34041

2.5.4 Dehydration of Beta Hydroxy Carbonyl Compounds



Substrates:

1. [N-]=[N+]=NC1C(=O)CCCC1O

Products:

1. 2-azidocyclohex-2-enone

Typical conditions: TsOH

Protections: none

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

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