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

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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: `20.00`

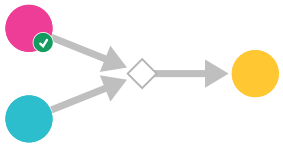
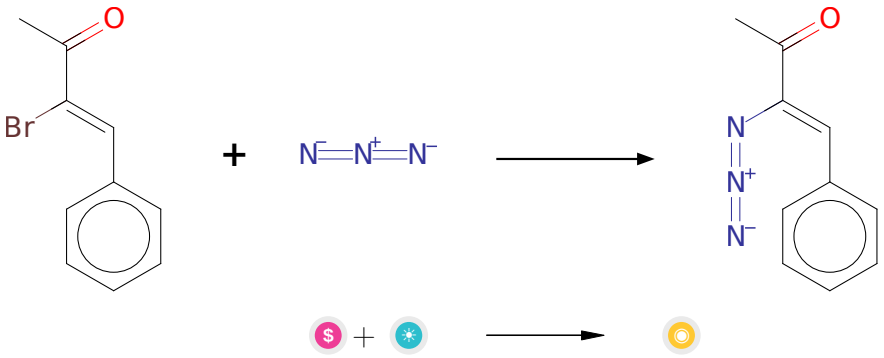


Figure 1: Outline of path 1

2.1.1 Synthesis of azidochalcones from dibromochalcones



Substrates:

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

Products:

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

Typical conditions: NaN3.DMF

Protections: none

Reference: DOI: *10.1016/S0040-4020(01)83509-2*

Retrosynthesis ID: 270

2.2 Path 2

Score: 45.00

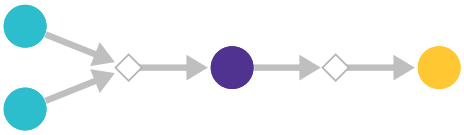
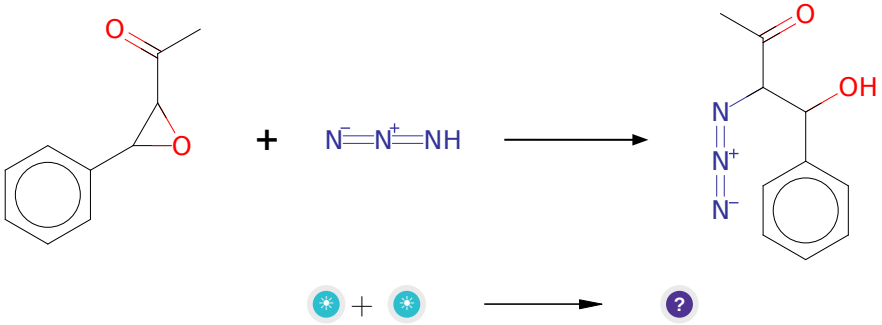


Figure 2: Outline of path 2

2.2.1 Ring-opening of epoxides or thiiranes with azides



Substrates:

1. 3,4-epoxy-4-phenyl-butan-2-on
2. hydrazoic acid

Products:

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

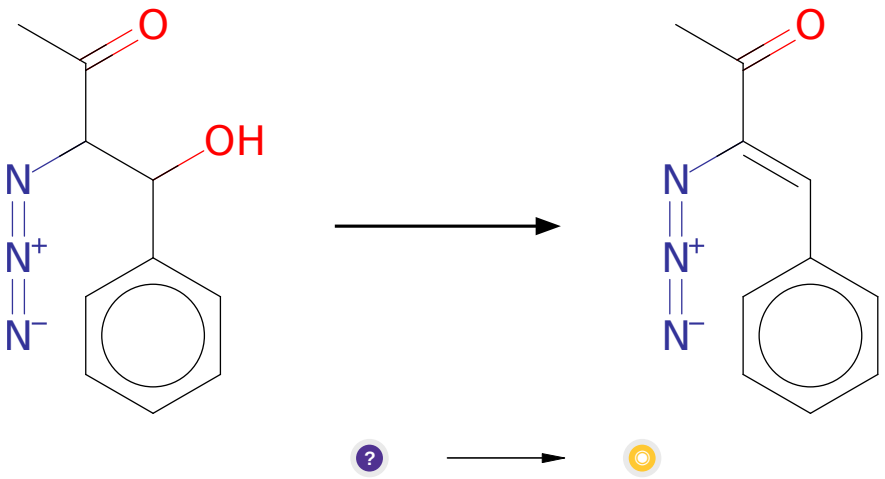
Typical conditions: NaN3.NH4Cl.MeOH.H2O.65 C

Protections: none

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

Retrosynthesis ID: 858

2.2.2 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: 76.25

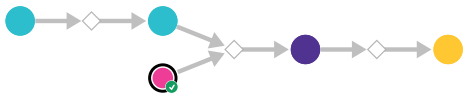
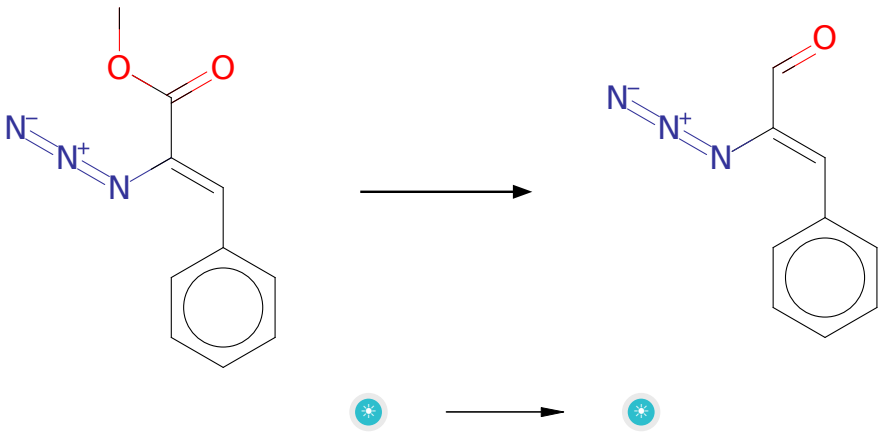


Figure 3: Outline of path 3

2.3.1 Aldehyde Formation



Substrates:

1. a-azidozimtsaeure-methylester

Products:

1. C9H7N3O

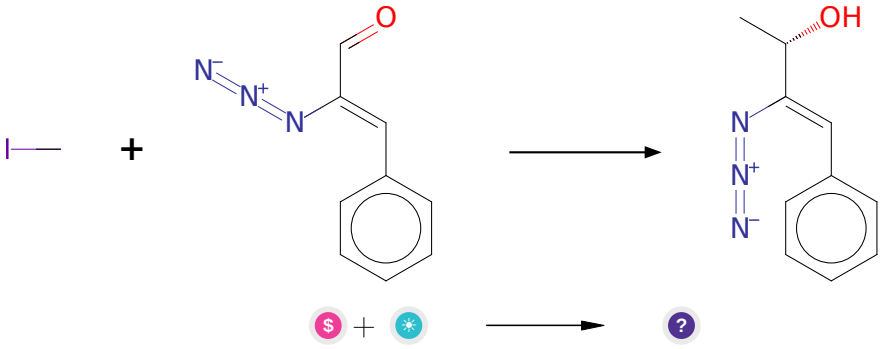
Typical conditions: DIBAL.solvent e.g. DCM

Protections: none

Reference: *10.1039/C39940000483* and *10.1039/C3CC47867J* and *10.1021/jo00222a054* and *10.1021/ja9934908* and *10.1021/jo902426z*

Retrosynthesis ID: 28551

2.3.2 Asymmetric addition to aldehyde



Substrates:

1. Iodomethane - *available at Sigma-Aldrich*
2. C9H7N3O

Products:

1. C[C@H](O)/C(=C/c1ccccc1)N=[N+]=[N-]

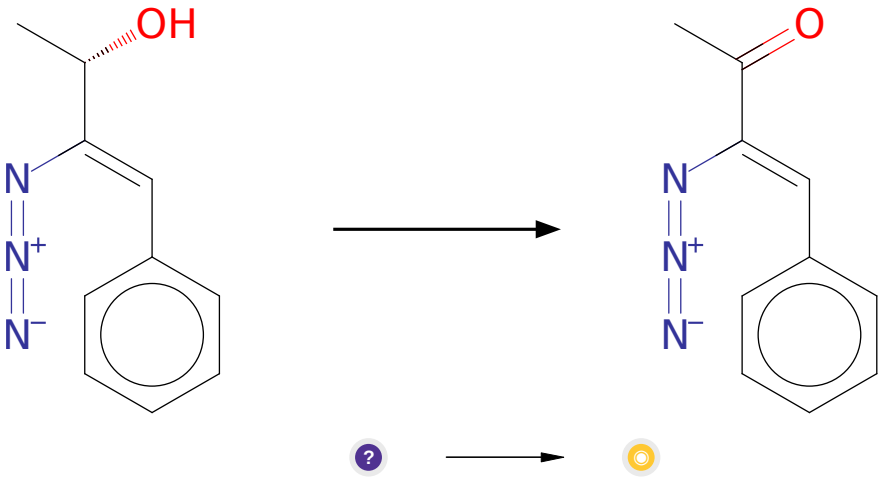
Typical conditions: 1. Zn. 2. Ti(OiPr)4.chiral.catalyst

Protections: none

Reference: *10.1016/s0040-4039(01)93432-x* AND *10.1246/bcsj.20090232* AND *10.1039/C39820000988*

Retrosynthesis ID: 5085

2.3.3 Oxidation of Chiral Alcohols



Substrates:

1. C[C@H](O)/C(=C/c1ccccc1)N=[N+]=[N-]

Products:

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

Typical conditions: CAN.NaBrO3.CH3CN or other oxidant e.g. TPAP or NaOCl

Protections: none

Reference: DOI: *10.1016/s0040-4039(00)86883-5* or *10.1021/ja00054a005* or *10.1016/S0040-4039(00)85677-4*

Retrosynthesis ID: 23701

2.4 Path 4

Score: 76.25

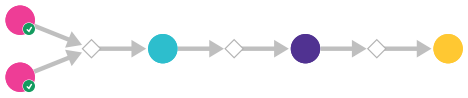
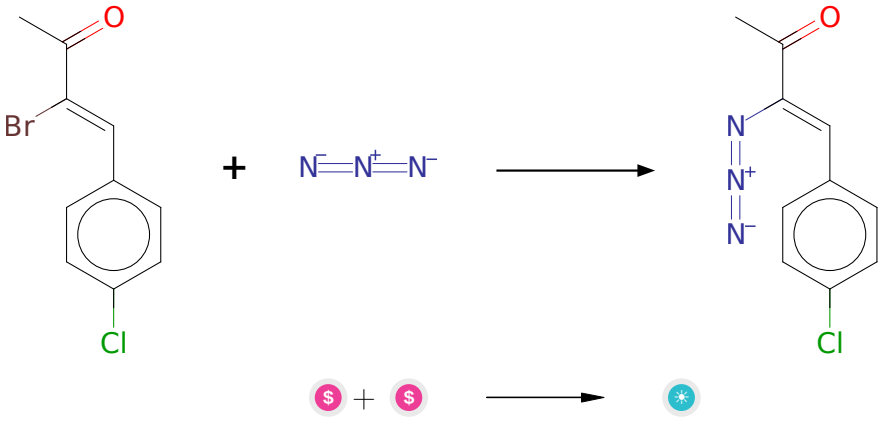


Figure 4: Outline of path 4

2.4.1 Synthesis of azidochalcones from dibromochalcones



Substrates:

1. Potassium azide - *available at Sigma-Aldrich*
2. (3Z)-3-bromo-4-(4-chlorophenyl)but-3-en-2-one - *available at Sigma-Aldrich*

Products:

1. 4-(4-chlorophenyl-)-3-azido-butene-3-one-2

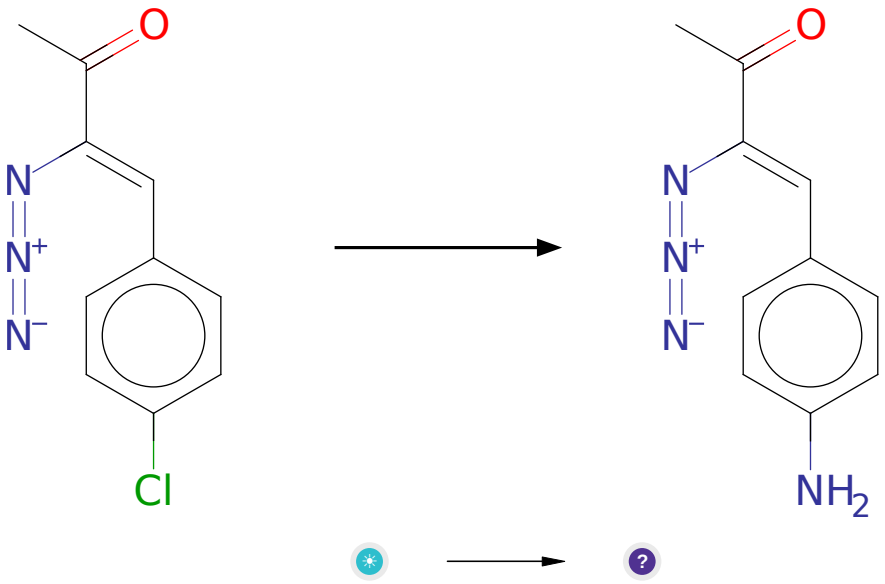
Typical conditions: NaN3.DMF

Protections: none

Reference: DOI: *10.1016/S0040-4020(01)83509-2*

Retrosynthesis ID: 270

2.4.2 Amination of aryl chlorides



Substrates:

1. 4-(4-chlorophenyl-)-3-azido-butene-3-one-2

Products:

1. CC(=O)/C(=C/c1ccc(N)cc1)N=[N+]=[N-]

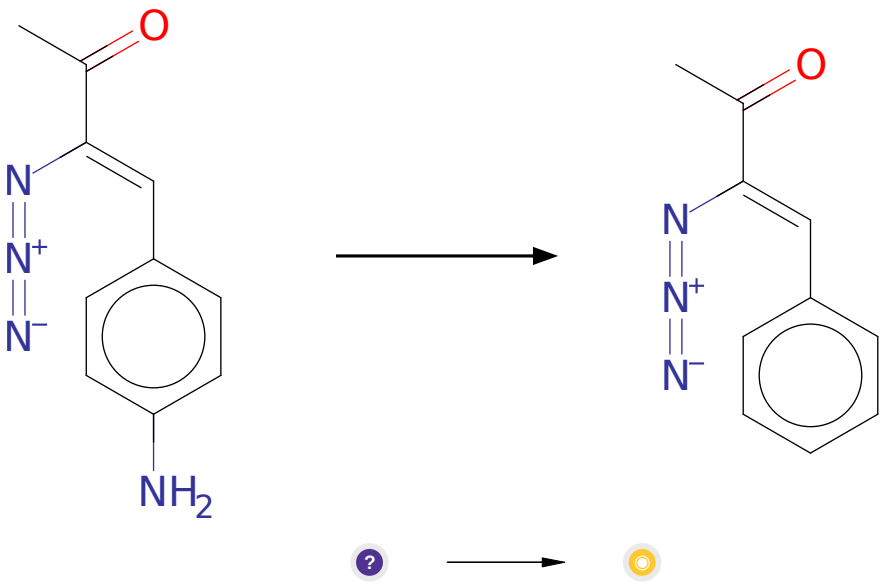
Typical conditions: [Pd].Ligand.base

Protections: none

Reference: *10.1021/ja903049z* and *10.1021/jo060945k* and *10.1021/jo060190h* and *10.1021/ja8055358* and *10.1021/ja068926f* and *10.1002/anie.200601612* and *10.1021/acscatal.0c04280*

Retrosynthesis ID: 28545

2.4.3 Hydrodediazoniation



Substrates:

1. CC(=O)/C(=C/c1ccc(N)cc1)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: 9999757

2.5 Path 5

Score: 76.25

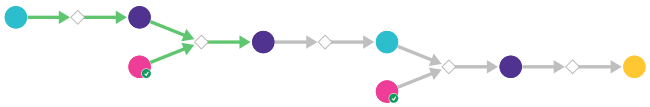
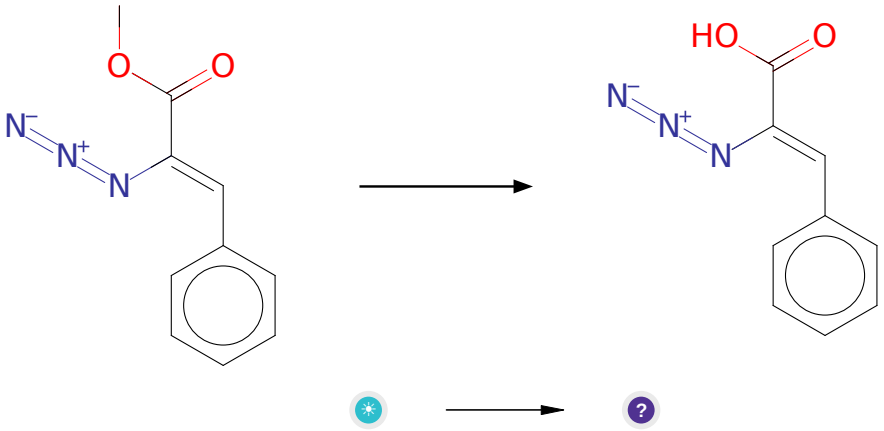


Figure 5: Outline of path 5

2.5.1 Synthesis of Carboxylic Acids via Ester Hydrolysis



Substrates:

1. a-azidozimtsaeure-methylester

Products:

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

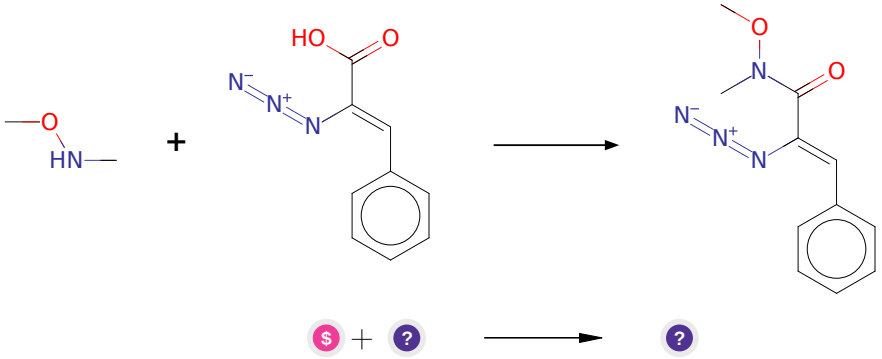
Typical conditions: water.base

Protections: none

Reference: DOI: *10.1016/j.phytochem.2012.08.001* and *10.1021/jm900803q* and *10.1002/anie.201303108* (SI page S14) and *10.1016/j.ejmech.2010.09.003*

Retrosynthesis ID: 9224

2.5.2 Synthesis of O-substituted N-substituted hydroxamic acids



Substrates:

1. n-methoxymethylamine - *available at Sigma-Aldrich*
2. [N-]=[N+]=N/C(=C\c1ccccc1)C(=O)O

Products:

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

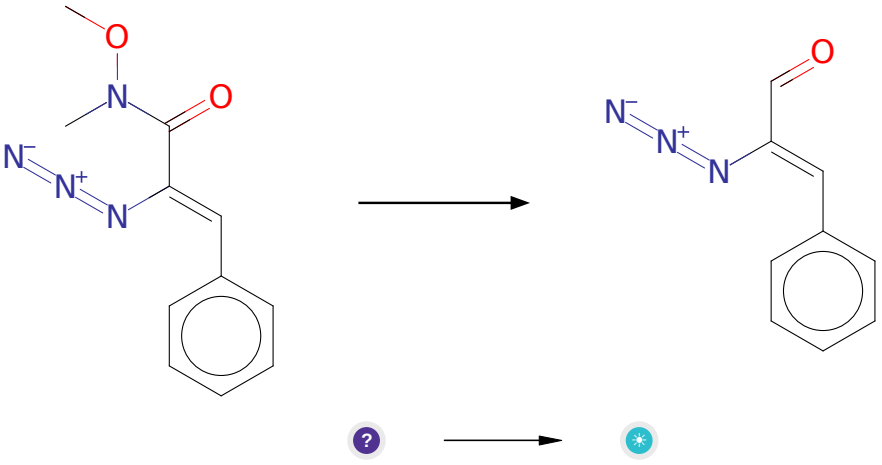
Typical conditions: DCC.DMAP or CDI.TEA.DCM

Protections: none

Reference: Patent: WO2007/67333A2, 2007 & *10.1016/j.bmcl.2008.09.100*

Retrosynthesis ID: 1152

2.5.3 Aldehyde Formation



Substrates:

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

Products:

1. C9H7N3O

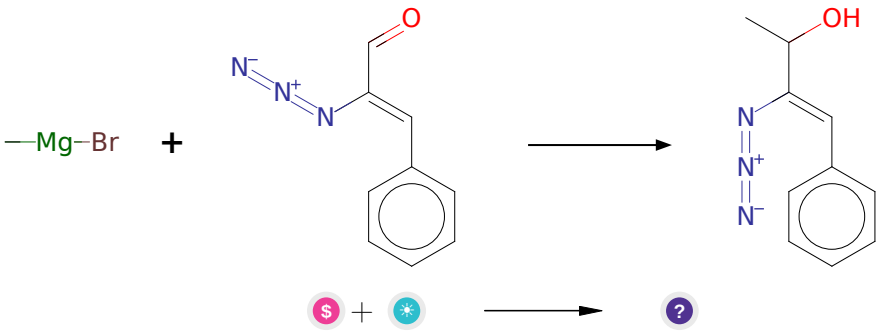
Typical conditions: DIBAL.toluene.CO

Protections: none

Reference: *10.1021/jo202652f*

Retrosynthesis ID: 11504

2.5.4 Addition of Grignard reagents to aldehydes



Substrates:

1. Methylmagnesium bromide solution - *available at Sigma-Aldrich*
2. C9H7N3O

Products:

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

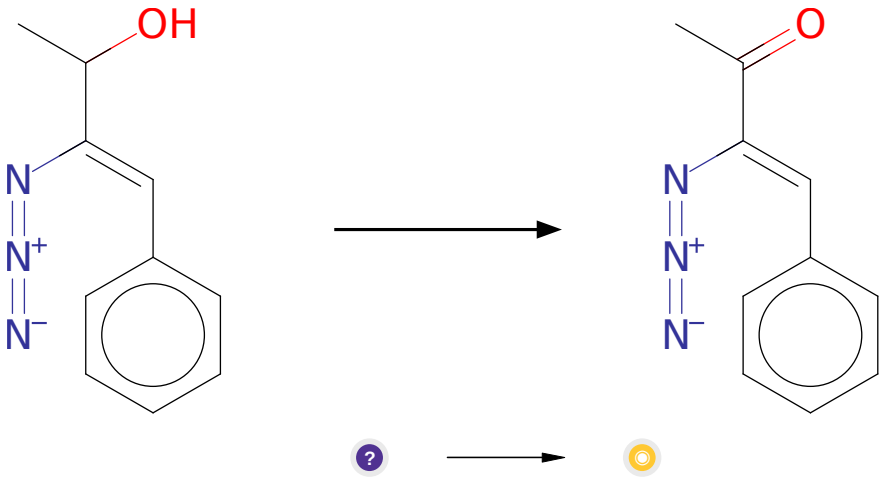
Typical conditions: THF.0C

Protections: none

Reference: *10.1021/ol0704901* (SI) and *10.1016/j.tetasy.2014.08.003* and *10.1021/ol100422d* (SI) and *10.1016/j.ejmech.2013.10.020* and *10.1021/ja052071+* and *10.1016/j.bmc.2015.01.057*

Retrosynthesis ID: 10031441

2.5.5 Swern Oxidation



Substrates:

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

Products:

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

Typical conditions: oxalyl chloride.DMSO.DCM.NMe3.-40C

Protections: none

Reference: *10.1055/s-1990-27036*

Retrosynthesis ID: 11163