

Paths of analysis*

AS2

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselective 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: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

Chemical scoring formula: $\text{SMALLER}^3, \text{SMALLER}^{1.5}$

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

3 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

2.1 Path 1

Score: 326.52

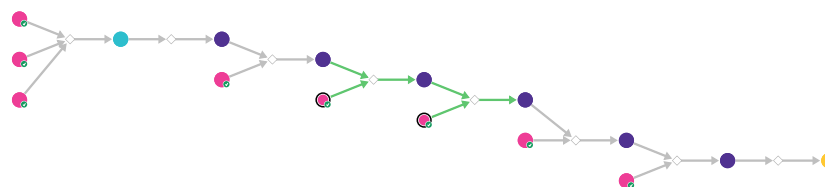
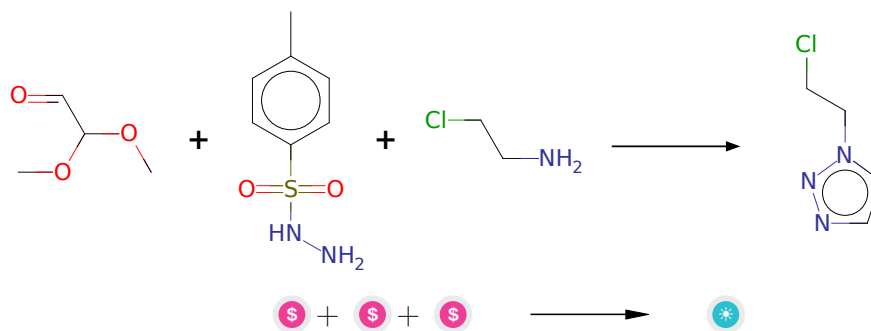


Figure 1: Outline of path 1

2.1.1 An azide and acetylene free synthesis of 1-substituted 1,2,3-triazoles



Substrates:

1. Tosylhydrazide - *available at Sigma-Aldrich*
2. Glyoxal dimethyl acetal - *available at Sigma-Aldrich*
3. 2-Chloroethylammonium chloride - *available at Sigma-Aldrich*

Products:

1. 1-(2-chloro-ethyl)-1h-[1,2,3]triazole

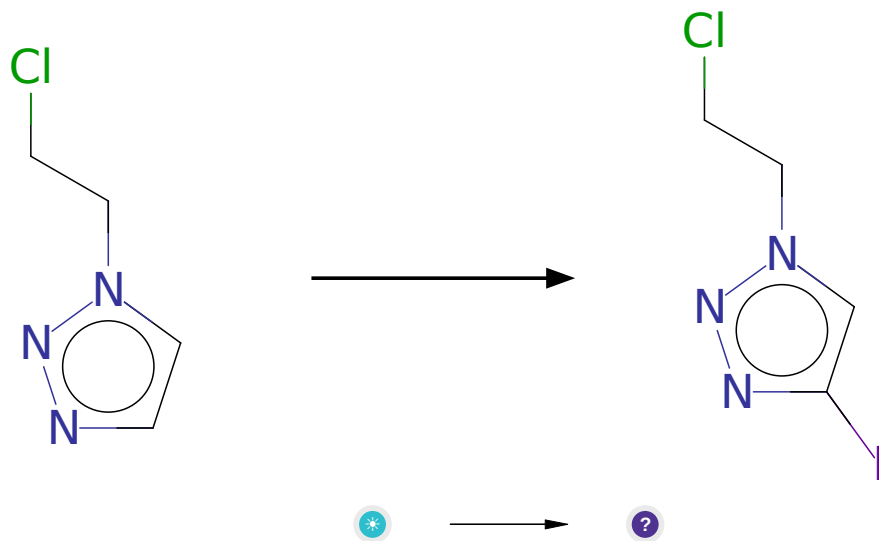
Typical conditions: 1.TsNHNH2.MeOH.rt 2.Amine.AcOH.heat

Protections: none

Reference: [10.1016/j.tetlet.2020.152483](#)

Retrosynthesis ID: 31020968

2.1.2 Iodination of aromatic compounds



Substrates:

1. 1-(2-chloro-ethyl)-1h-[1,2,3]triazole

Products:

1. ClCCn1cc(I)nn1

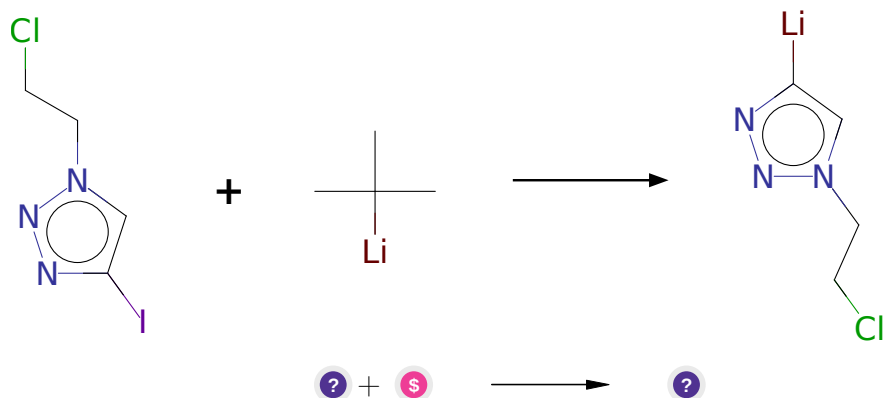
Typical conditions: I2 or other iodinating agent e.g. NIS

Protections: none

Reference: DOI: [10.1039/C5SC00964B](#) and [10.1016/j.tetlet.2005.05.117](#) and [10.1007/s11178-005-0256-1](#)

Retrosynthesis ID: 10697

2.1.3 I/Li exchange



Substrates:

1. ClCCn1cc(I)nn1
2. t-BuLi - *available at Sigma-Aldrich*

Products:

1. [Li]c1cn(CCCl)nn1

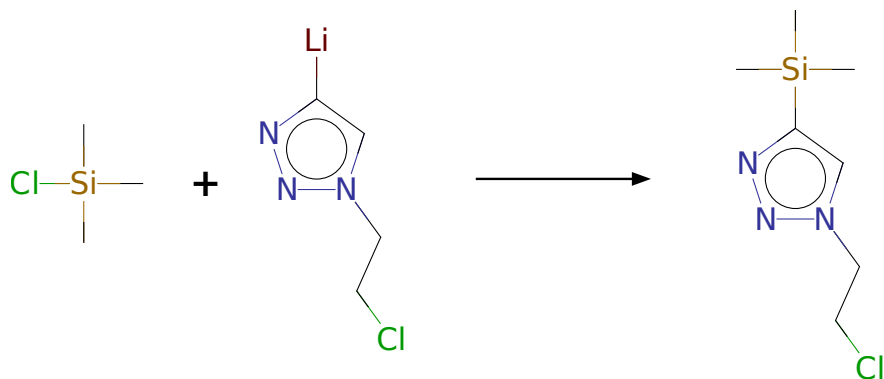
Typical conditions: nBuLi.or.tBuLi.THF.-78C

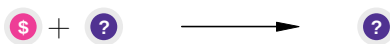
Protections: none

Reference: [10.1016/j.tet.2004.09.111](https://doi.org/10.1016/j.tet.2004.09.111) and [10.1039/c3ob41082j](https://doi.org/10.1039/c3ob41082j) And [10.1016/j.bmc.2012.03.056](https://doi.org/10.1016/j.bmc.2012.03.056) And [10.1002/chem.201300292](https://doi.org/10.1002/chem.201300292)

Retrosynthesis ID: 30673

2.1.4 Addition of electrophiles to lithiated arenes/heteroarenes





Substrates:

1. TMSCl - *available at Sigma-Aldrich*
2. [Li]c1cn(CCCl)nn1

Products:

1. C[Si](C)(C)c1cn(CCCl)nn1

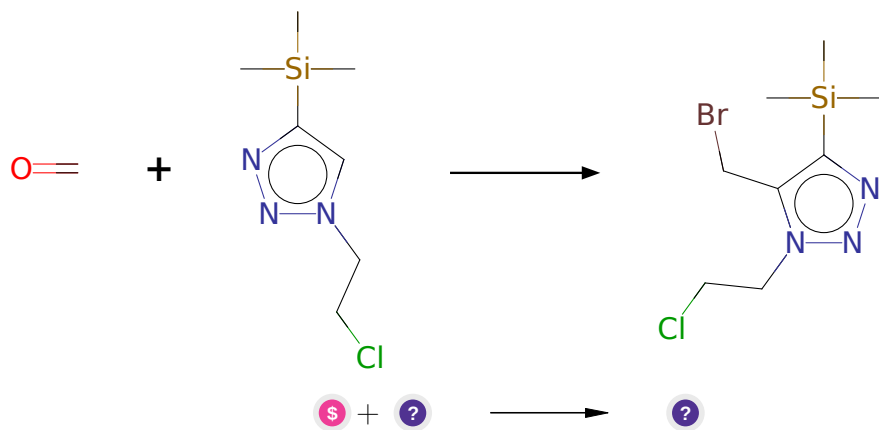
Typical conditions: THF

Protections: none

Reference: [10.1002/ejoc.200600589](#) and [10.1055/s-0036-1588863](#) and [10.1002/1099-0690\(200107\)2001:14<2771::AID-EJOC2771>3.0.CO;2-Y](#) and [10.1021/ol202873d](#) (SI)

Retrosynthesis ID: 10019541

2.1.5 Blanc bromomethylation



Substrates:

1. Formalin - *available at Sigma-Aldrich*
2. C[Si](C)(C)c1cn(CCCl)nn1

Products:

1. C[Si](C)(C)c1nnn(CCCl)c1CBr

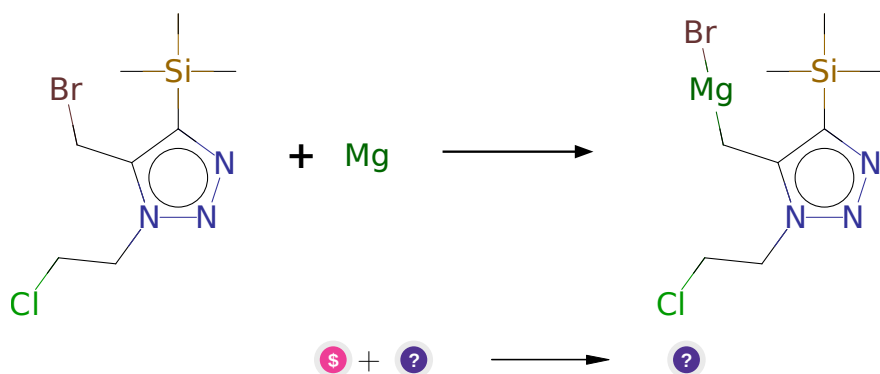
Typical conditions: HBr.heat

Protections: none

Reference: [10.1021/ja011493q](#) and [10.1021/ma012195g](#) and [10.1016/S0040-4039\(02\)01769-0](#) and [10.1021/ja002069c](#)

Retrosynthesis ID: 31010730

2.1.6 Synthesis of alkyl Grignard reagents



Substrates:

1. Magnesium - *available at Sigma-Aldrich*
2. C[Si](C)(C)c1nnn(CCCl)c1CBr

Products:

1. C[Si](C)(C)c1nnn(CCCl)c1C[Mg]Br

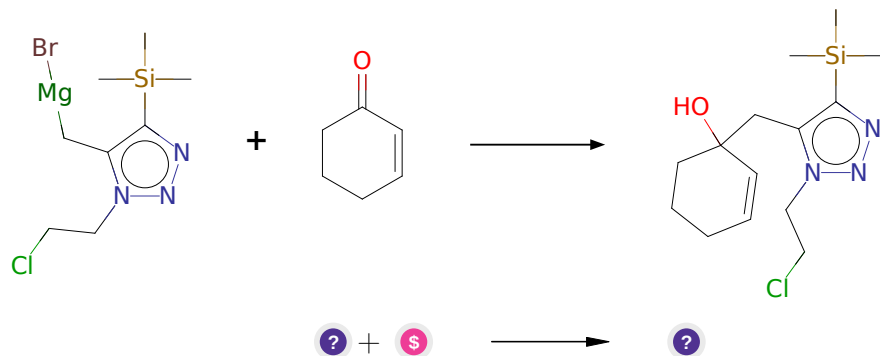
Typical conditions: Mg, THF or iPrMgBr

Protections: none

Reference: DOI: [10.1021/jo00002a039](#) and [10.1021/jo047877r](#) and [10.1021/ol006618v](#)

Retrosynthesis ID: 10011828

2.1.7 Grignard-Type Reaction



Substrates:

1. C[Si](C)(C)c1nnn(CCCl)c1C[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. C[Si](C)(C)c1nnn(CCCl)c1CC1(O)C=CCCC1

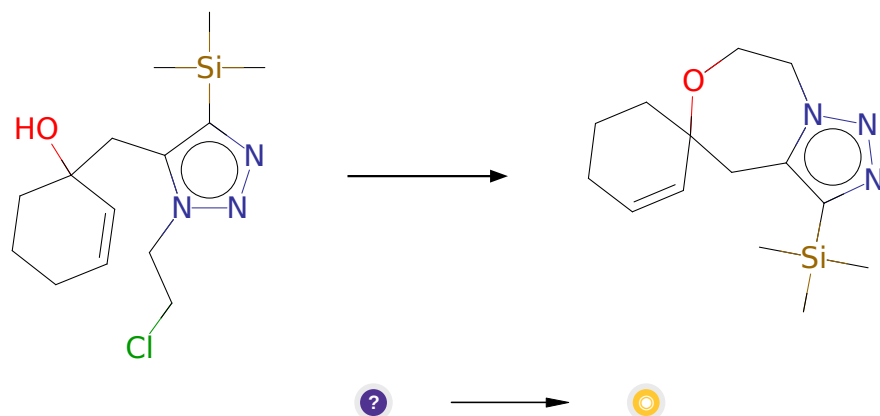
Typical conditions: Mg or Li.ether

Protections: none

Reference: [10.1021/jo010494y](#) or [10.1016/j.steroids.2015.09.009](#) or [10.1021/jo061349t](#) or [10.1021/ja056165v](#) (SI page 19)

Retrosynthesis ID: 25134

2.1.8 Alkylation of tertiary alcohols



Substrates:

1. C[Si](C)(C)c1nnn(CCCl)c1CC1(O)C=CCCC1

Products:

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCC2

Typical conditions: K₂CO₃.acetone.heat

Protections: none

Reference: [10.1016/S0040-4020\(01\)90106-1](#) and [10.1021/acs.analchem.5b04461](#)
and [10.3390/molecules24091643](#)

Retrosynthesis ID: 31010930

2.2 Path 2

Score: 326.52

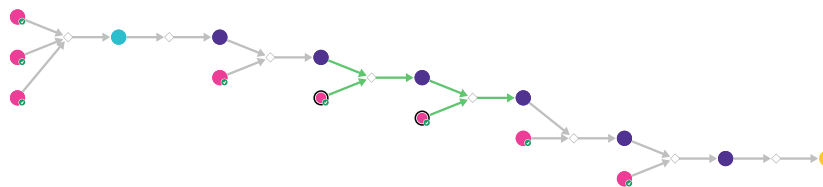
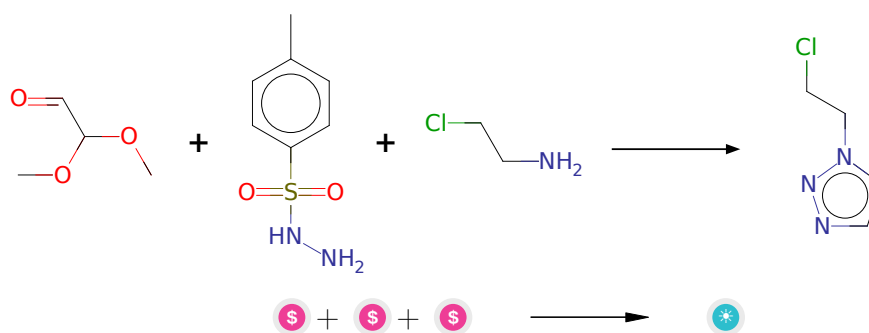


Figure 2: Outline of path 2

2.2.1 An azide and acetylene free synthesis of 1-substituted 1,2,3-triazoles



Substrates:

1. Tosylhydrazide - [available at Sigma-Aldrich](#)

2. Glyoxal dimethyl acetal - *available at Sigma-Aldrich*
3. 2-Chloroethylammonium chloride - *available at Sigma-Aldrich*

Products:

1. 1-(2-chloro-ethyl)-1h-[1,2,3]triazole

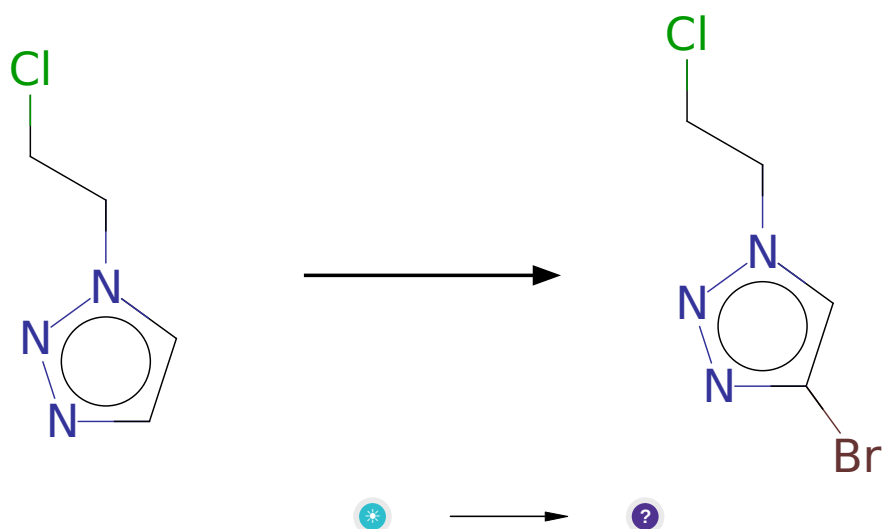
Typical conditions: 1.TsNHNH2.MeOH.rt 2.Amine.AcOH.heat

Protections: none

Reference: *10.1016/j.tetlet.2020.152483*

Retrosynthesis ID: 31020968

2.2.2 Bromination of aromatic compounds



Substrates:

1. 1-(2-chloro-ethyl)-1h-[1,2,3]triazole

Products:

1. ClCCn1cc(Br)nn1

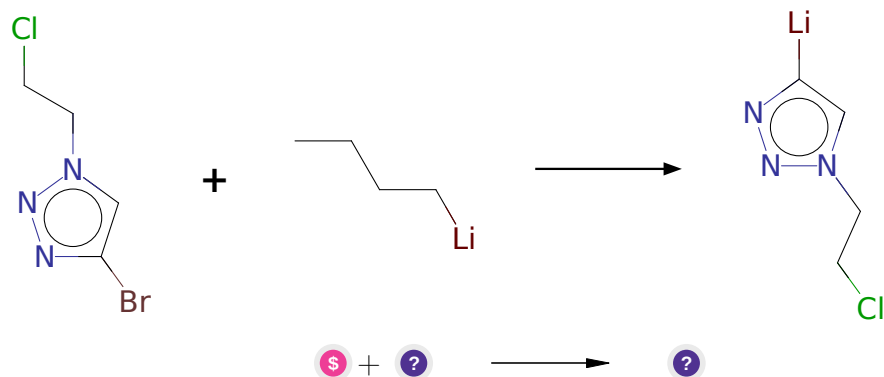
Typical conditions: Br₂.Fe

Protections: none

Reference: *10.1021/acs.accounts.6b00120*

Retrosynthesis ID: 7777000

2.2.3 Br/Li exchange



Substrates:

1. n-BuLi - *available at Sigma-Aldrich*
2. ClCCn1cc(Br)nn1

Products:

1. [Li]c1cn(CCCl)nn1

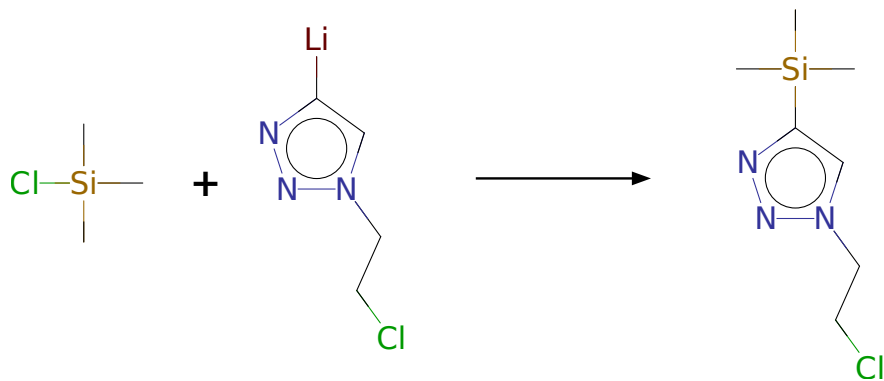
Typical conditions: nBuLi.or.tBuLi.THF.-78C

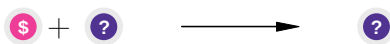
Protections: none

Reference: [10.1002/ejoc.201101490](#) and [10.1016/j.tet.2012.03.058](#)
and [10.1016/j.tetlet.2015.01.032](#) and [10.1021/ja0541175](#) and [10.1016/j.tetlet.2016.06.123](#)

Retrosynthesis ID: 30672

2.2.4 Addition of electrophiles to lithiated arenes/heteroarenes





Substrates:

1. TMSCl - *available at Sigma-Aldrich*
2. [Li]c1cn(CCCl)nn1

Products:

1. C[Si](C)(C)c1cn(CCCl)nn1

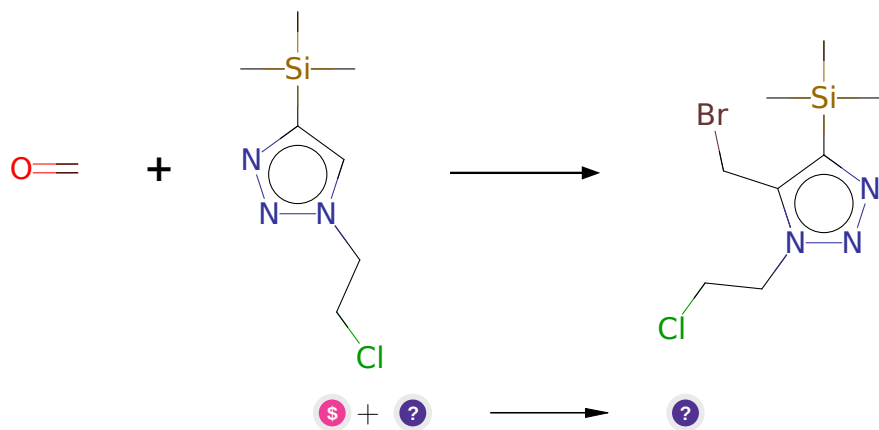
Typical conditions: THF

Protections: none

Reference: [10.1002/ejoc.200600589](#) and [10.1055/s-0036-1588863](#) and [10.1002/1099-0690\(200107\)2001:14<2771::AID-EJOC2771>3.0.CO;2-Y](#) and [10.1021/ol202873d](#) (SI)

Retrosynthesis ID: 10019541

2.2.5 Blanc bromomethylation



Substrates:

1. Formalin - *available at Sigma-Aldrich*
2. C[Si](C)(C)c1cn(CCCl)nn1

Products:

1. C[Si](C)(C)c1nnn(CCCl)c1CBr

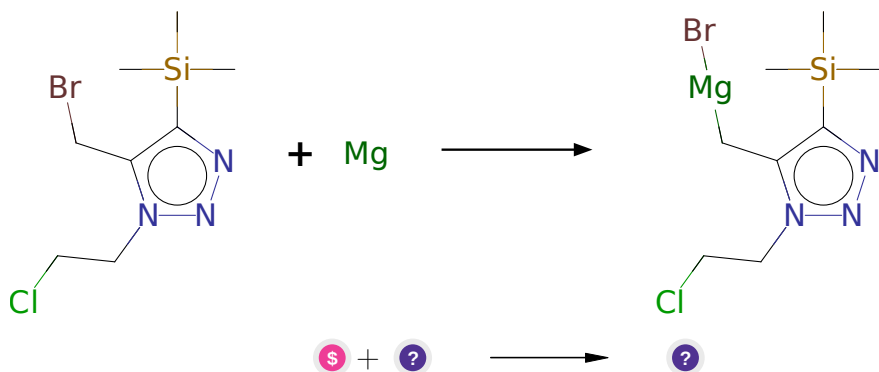
Typical conditions: HBr.heat

Protections: none

Reference: [10.1021/ja011493q](#) and [10.1021/ma012195g](#) and [10.1016/S0040-4039\(02\)01769-0](#) and [10.1021/ja002069c](#)

Retrosynthesis ID: 31010730

2.2.6 Synthesis of alkyl Grignard reagents



Substrates:

1. Magnesium - *available at Sigma-Aldrich*
2. C[Si](C)(C)c1nnn(CCCl)c1CBr

Products:

1. C[Si](C)(C)c1nnn(CCCl)c1C[Mg]Br

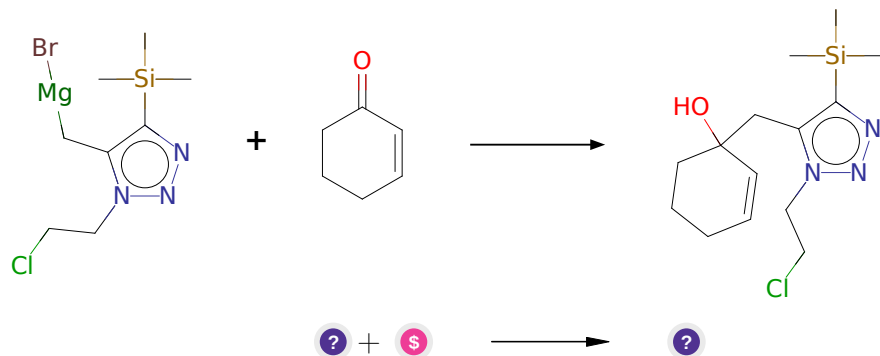
Typical conditions: Mg, THF or iPrMgBr

Protections: none

Reference: DOI: [10.1021/jo00002a039](#) and [10.1021/jo047877r](#) and [10.1021/ol006618v](#)

Retrosynthesis ID: 10011828

2.2.7 Grignard-Type Reaction



Substrates:

1. C[Si](C)(C)c1nnn(CCCl)c1C[Mg]Br
2. 2-Cyclohexen-1-one - *available at Sigma-Aldrich*

Products:

1. C[Si](C)(C)c1nnn(CCCl)c1CC1(O)C=CCCC1

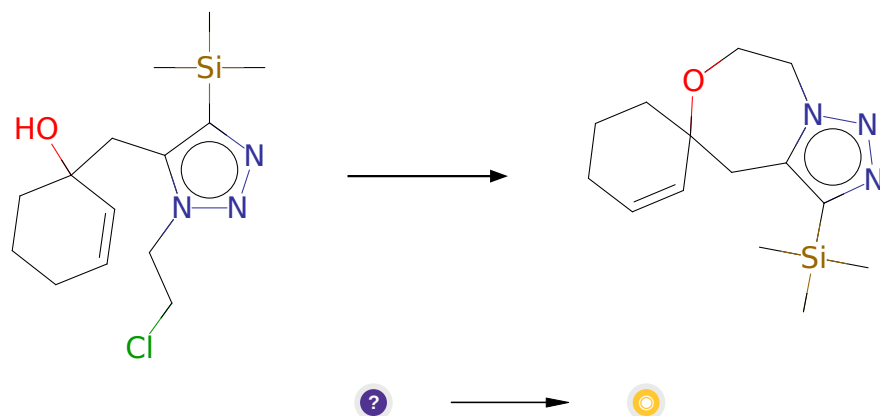
Typical conditions: Mg or Li.ether

Protections: none

Reference: [10.1021/jo010494y](#) or [10.1016/j.steroids.2015.09.009](#) or [10.1021/jo061349t](#) or [10.1021/ja056165v](#) (SI page 19)

Retrosynthesis ID: 25134

2.2.8 Alkylation of tertiary alcohols



Substrates:

1. C[Si](C)(C)c1nnn(CCCl)c1CC1(O)C=CCCC1

Products:

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCC2

Typical conditions: K₂CO₃.acetone.heat

Protections: none

Reference: [10.1016/S0040-4020\(01\)90106-1](#) and [10.1021/acs.analchem.5b04461](#) and [10.3390/molecules24091643](#)

Retrosynthesis ID: 31010930

2.3 Path 3

Score: 338.70

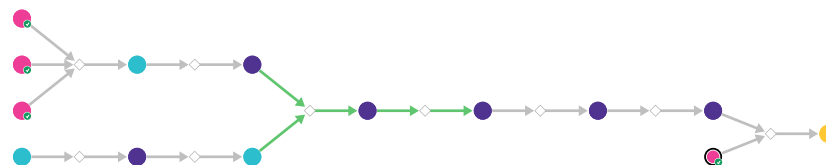
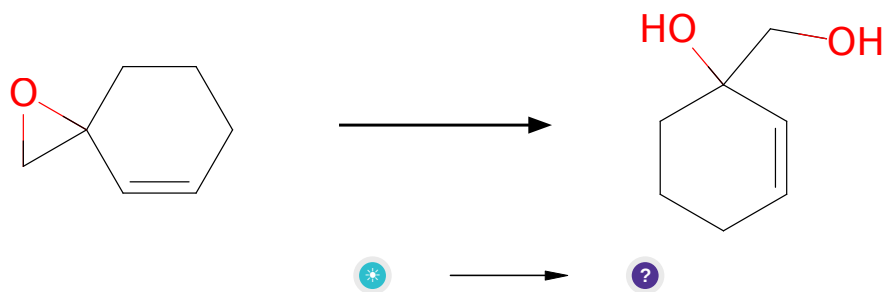


Figure 3: Outline of path 3

2.3.1 Acid-catalyzed hydrolysis of epoxides or thiiranes



Substrates:

1. 8-oxaspiro[5.2]oct-2-ene

Products:

1. OCC1(O)C=CCCC1

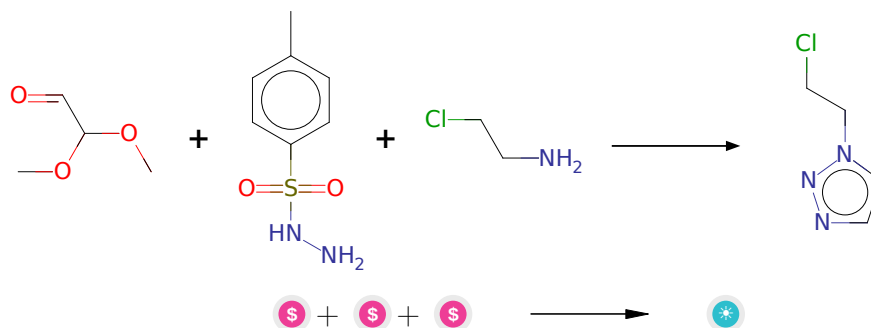
Typical conditions: H₂O.H₂SO₄

Protections: none

Reference: [10.1007/s13738-018-1400-5](#) and [10.1021/cr60241a004](#)

Retrosynthesis ID: 822

2.3.2 An azide and acetylene free synthesis of 1-substituted 1,2,3-triazoles



Substrates:

1. Tosylhydrazide - [available at Sigma-Aldrich](#)
2. Glyoxal dimethyl acetal - [available at Sigma-Aldrich](#)
3. 2-Chloroethylammonium chloride - [available at Sigma-Aldrich](#)

Products:

1. 1-(2-chloro-ethyl)-1h-[1,2,3]triazole

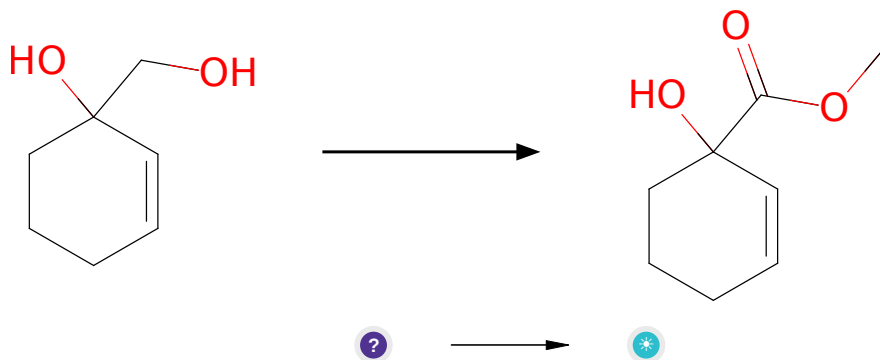
Typical conditions: 1.TsNHNH₂.MeOH.rt 2.Amine.AcOH.heat

Protections: none

Reference: [10.1016/j.tetlet.2020.152483](#)

Retrosynthesis ID: 31020968

2.3.3 Tandem oxidation-esterification



Substrates:

1. OCC1(O)C=CCCC1

Products:

1. methyl 1-hydroxy-2-cyclohexenoate

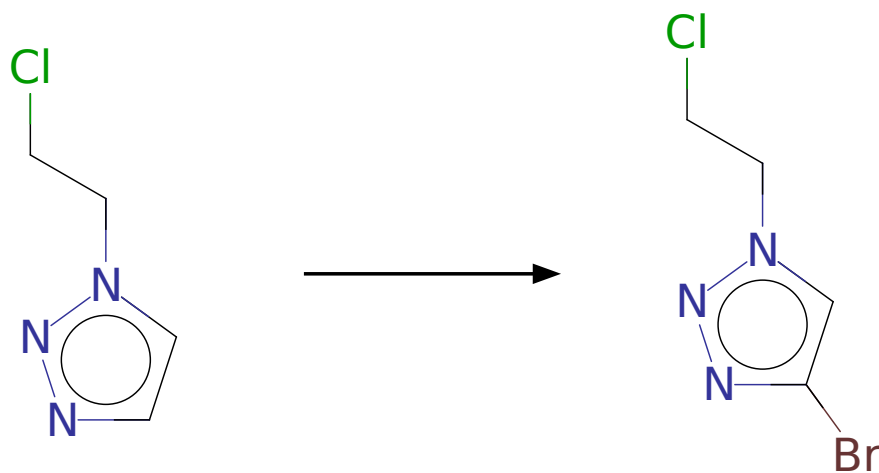
Typical conditions: Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

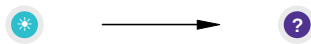
Protections: none

Reference: [10.1016/S0040-4039\(00\)73550-7](#) and [10.1016/j.tet.2005.03.097](#) and [10.1021/ol062940f](#)

Retrosynthesis ID: 25234

2.3.4 Bromination of aromatic compounds





Substrates:

- 1-(2-chloro-ethyl)-1h-[1,2,3]triazole

Products:

- ClCCn1cc(Br)nn1

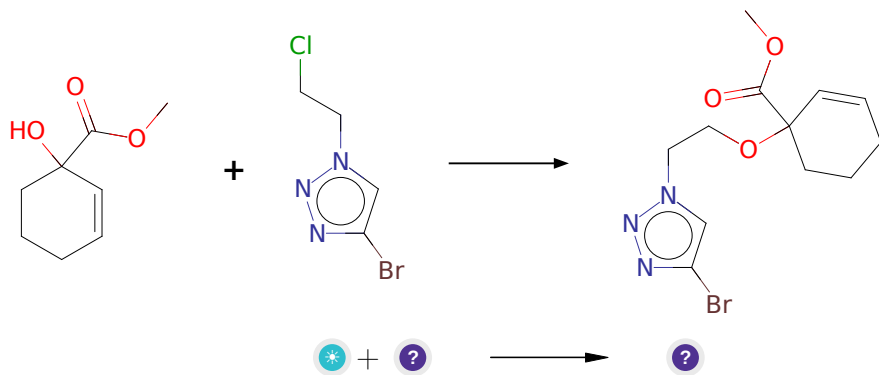
Typical conditions: Br₂.Fe

Protections: none

Reference: [10.1021/acs.accounts.6b00120](https://doi.org/10.1021/acs.accounts.6b00120)

Retrosynthesis ID: 7777000

2.3.5 Alkylation of tertiary alcohols



Substrates:

1. methyl 1-hydroxy-2-cyclohexenoate
2. ClCCn1cc(Br)nn1

Products:

1. COC(=O)C1(OCCn2cc(Br)nn2)C=CCCC1

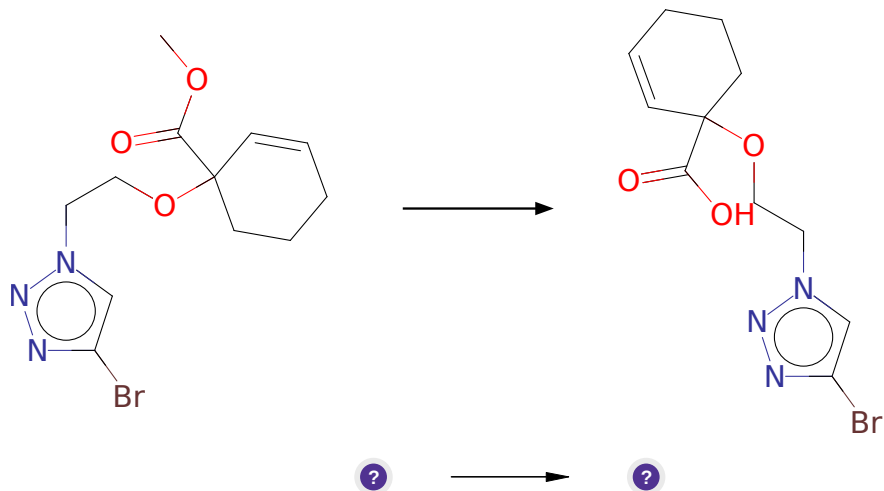
Typical conditions: K₂CO₃.acetone.heat

Protections: none

Reference: [10.1016/S0040-4020\(01\)90106-1](https://doi.org/10.1016/S0040-4020(01)90106-1) and [10.1021/acs.analchem.5b04461](https://doi.org/10.1021/acs.analchem.5b04461) and [10.3390/molecules24091643](https://doi.org/10.3390/molecules24091643)

Retrosynthesis ID: 31010930

2.3.6 Synthesis of Carboxylic Acids via Ester Hydrolysis



Substrates:

1. COC(=O)C1(OCCn2cc(Br)nn2)C=CCCC1

Products:

1. O=C(O)C1(OCCn2cc(Br)nn2)C=CCCC1

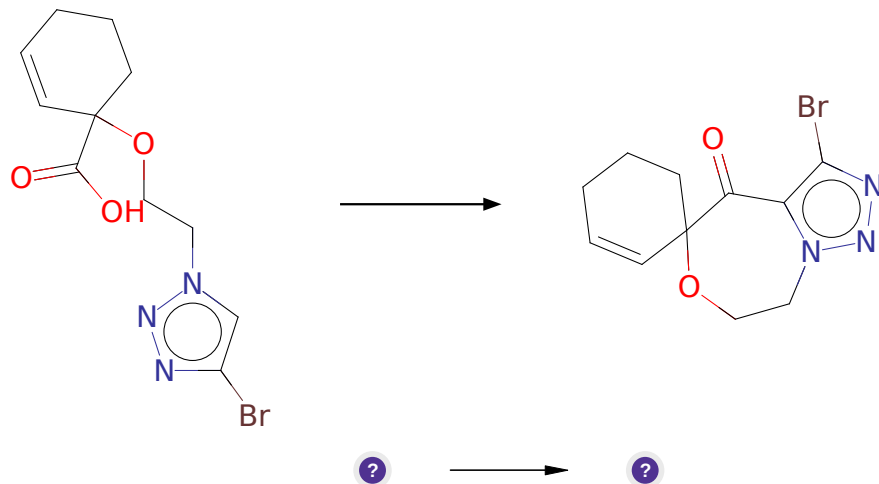
Typical conditions: water.base

Protections: none

Reference: DOI: [10.1016/j.phytochem.2012.08.001](https://doi.org/10.1016/j.phytochem.2012.08.001) and [10.1021/jm900803q](https://doi.org/10.1021/jm900803q) and [10.1002/anie.201303108](https://doi.org/10.1002/anie.201303108) (SI page S14) and [10.1016/j.ejmech.2010.09.003](https://doi.org/10.1016/j.ejmech.2010.09.003)

Retrosynthesis ID: 9224

2.3.7 Friedel-Crafts Acylation



Substrates:

1. O=C(O)C1(OCCn2cc(Br)nn2)C=CCCC1

Products:

1. O=C1c2c(Br)nnn2CCOC12C=CCCC2

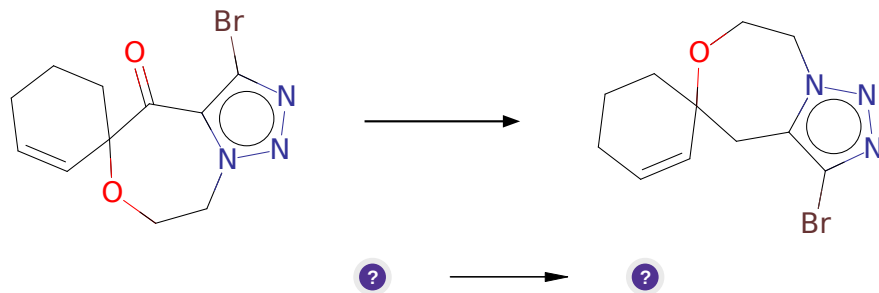
Typical conditions: 1.(COCl)2.Lewis Acid.solvent

Protections: none

Reference: [10.1021/ol800752v](https://doi.org/10.1021/ol800752v)

Retrosynthesis ID: 13729

2.3.8 Wolff-Kishner Reduction



Substrates:

1. O=C1c2c(Br)nnn2CCOC12C=CCCC2

Products:

1. Brc1nnn2c1CC1(C=CCCC1)OCC2

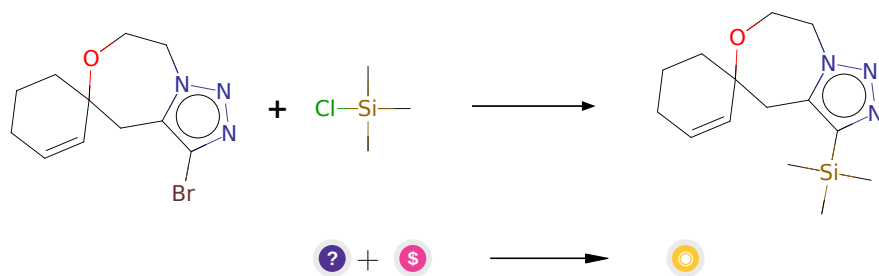
Typical conditions: hydrazine.ethylene glycol.KOH.180-200 C

Protections: none

Reference: [10.1007/s00044-016-1528-8](#) p. 1116, 1110 and [10.1021/acs.jmedchem.7b01363](#) p. 9408, 9411 and [10.1016/j.tetasy.2006.11.005](#) and [10.1023/A:1024124411892](#)

Retrosynthesis ID: 243

2.3.9 Synthesis of arylsilanes



Substrates:

1. Brc1nnn2c1CC1(C=CCCC1)OCC2
2. TMS-Cl - [available at Sigma-Aldrich](#)

Products:

1. C[Si](C)(C)c1nnn2c1CC1(C=CCCC1)OCC2

Typical conditions: 1.nBuLi.2.ClSnR3

Protections: none

Reference: [10.1071/CH9851147](#).

Retrosynthesis ID: 5370