Paths of analysis*

AS2

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

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

2.1 Path 1

Score: `323.01`

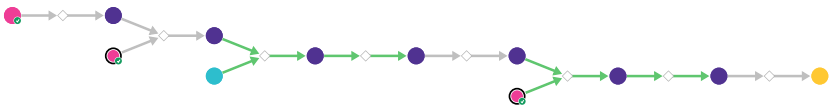
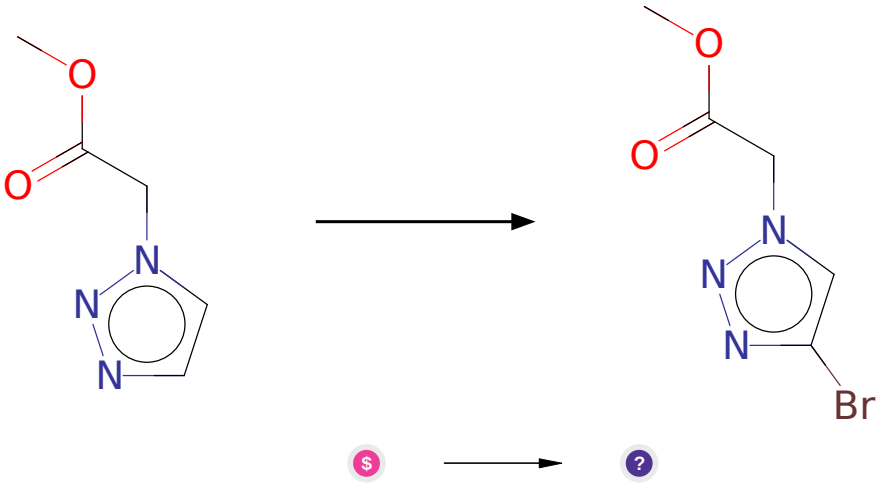


Figure 1: Outline of path 1

2.1.1 Bromination of aromatic compounds



Substrates:

1. methyl 2-(1H-1,2,3-triazol-1-yl)acetate - *available at Sigma-Aldrich*

Products:

1. COC(=O)Cn1cc(Br)nn1

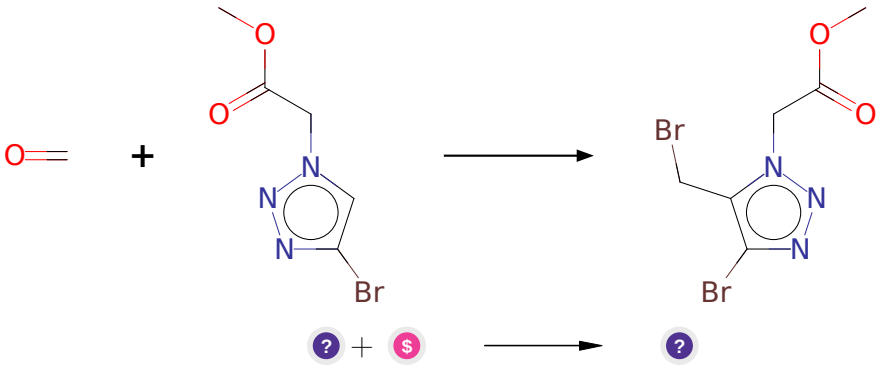
Typical conditions: Br2.Fe

Protections: none

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

Retrosynthesis ID: 7777000

2.1.2 Blanc bromomethylation



Substrates:

1. COC(=O)Cn1cc(Br)nn1
2. Formalin - *available at Sigma-Aldrich*

Products:

1. COC(=O)Cn1nnc(Br)c1CBr

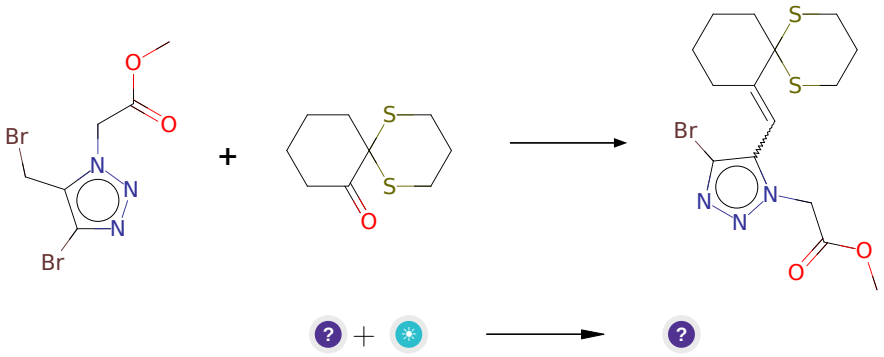
Typical conditions: HBr.heat

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

2.1.3 HWE/Wittig Olefination



Substrates:

1. COC(=O)Cn1nnc(Br)c1CBr
2. 1,5-dithia-spiro[5.5]undecan-7-one

Products:

1. COC(=O)Cn1nnc(Br)c1C=C1CCCCC12SCCCS2

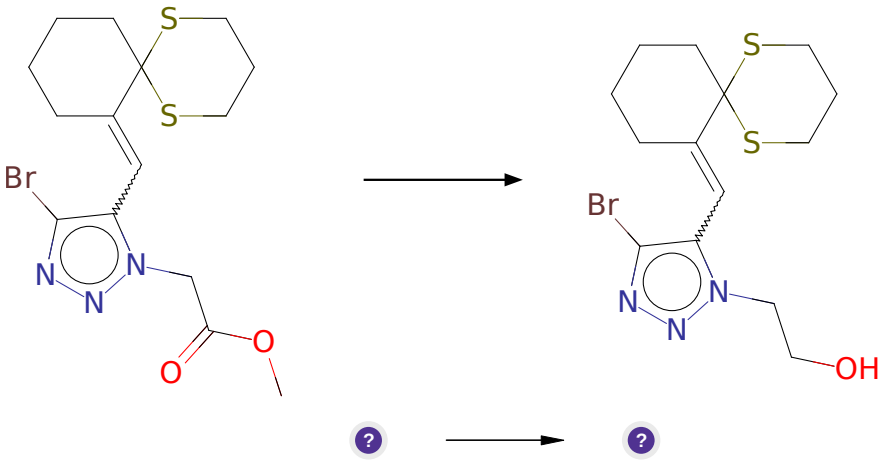
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

Reference: *10.1002/anie.200705005* and *10.1021/ol052106a* and *10.1021/jo00075a064* and *10.1021/ol3027297*

Retrosynthesis ID: 24425

2.1.4 Esters reduction with LAH



Substrates:

1. COC(=O)Cn1nnc(Br)c1C=C1CCCCC12SCCCS2

Products:

1. OCCn1nnc(Br)c1C=C1CCCCC12SCCCS2

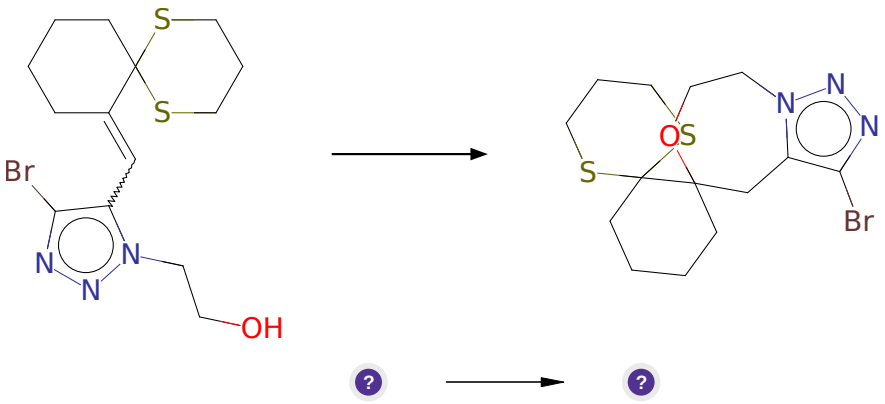
Typical conditions: LiAlH4.THF.0-20 C

Protections: none

Reference: *10.1016/j.ejmech.2019.112011* p. 5, 10 and *10.1016/j.ejmech.2020.112910* p. 3, 7

Retrosynthesis ID: 9910006

2.1.5 Synthesis of teriary ethers



Substrates:

1. OCCn1nnc(Br)c1C=C1CCCCC12SCCCS2

Products:

1. Brc1nnn2c1CC1(CCCCC13SCCCS3)OCC2

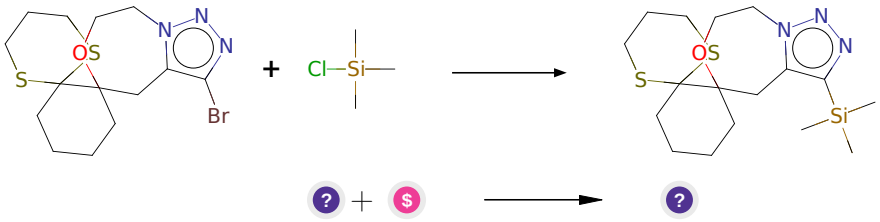
Typical conditions: H2SO4

Protections: none

Reference: *10.1016/j.tet.2009.10.055* and WO2009011551 (p.14 example 5) and *10.1002/chem.201304580* and *10.1021/jm9811209* and US2007/225280A1 p.58 and WO2009/62285A1 p.50 and CN106928032A p.0040

Retrosynthesis ID: 10001897

2.1.6 Synthesis of arylsilanes



Substrates:

1. Brc1nnn2c1CC1(CCCCC13SCCCS3)OCC2
2. TMSCl - *available at Sigma-Aldrich*

Products:

1. C[Si](C)(C)c1nnn2c1CC1(CCCCC13SCCCS3)OCC2

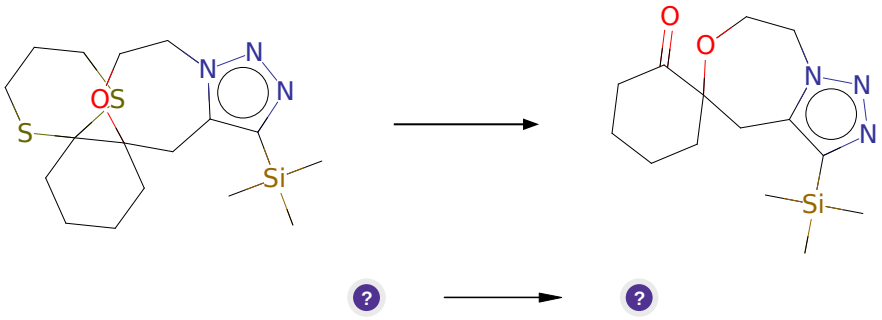
Typical conditions: 1.nBuLi.2.ClSnR3

Protections: none

Reference: *10.1071/CH9851147*.

Retrosynthesis ID: 5370

2.1.7 Synthesis of ketones from dithianes



Substrates:

1. C[Si](C)(C)c1nnn2c1CC1(CCCCC13SCCCS3)OCC2

Products:

1. C[Si](C)(C)c1nnn2c1CC1(CCCCC1=O)OCC2

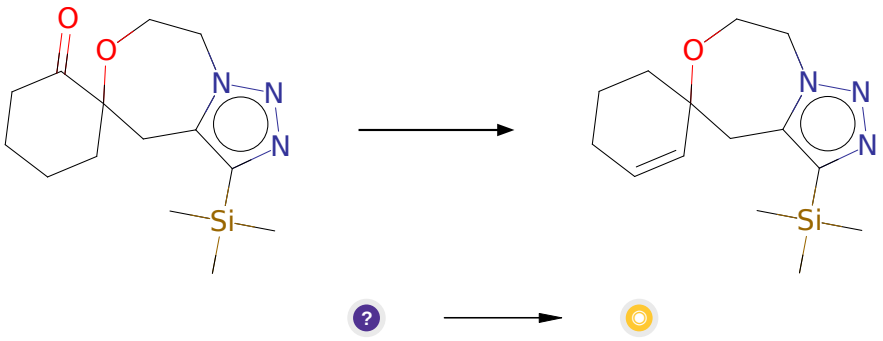
Typical conditions: MeI.CaCO3

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

2.1.8 Shapiro reaction



Substrates:

1. C[Si](C)(C)c1nnn2c1CC1(CCCCC1=O)OCC2

Products:

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

Typical conditions: 1.TsNH2NH2.2.N-BuLi

Protections: none

Reference: *10.1021/jm4008517* and *10.1016/j.bmc.2009.08.038* and *10.1021/jo00350a003*

Retrosynthesis ID: 9990398

2.2 Path 2

Score: 323.01

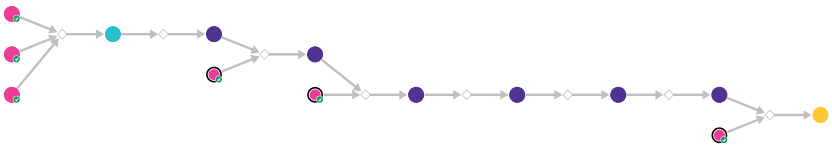
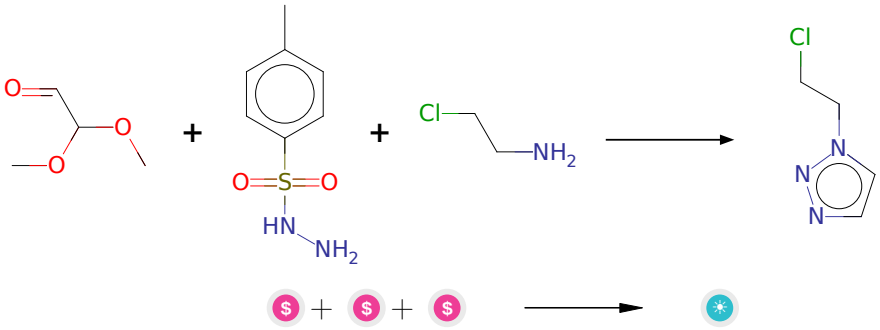


Figure 2: Outline of path 2

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

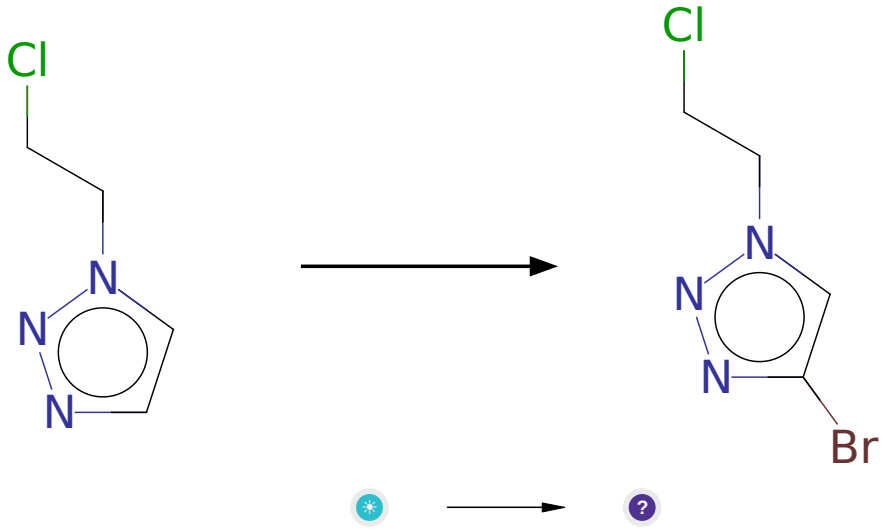
Typical conditions: 1.TsNHNH2.MeOH.rt 2.Amine.AcOH.heat

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

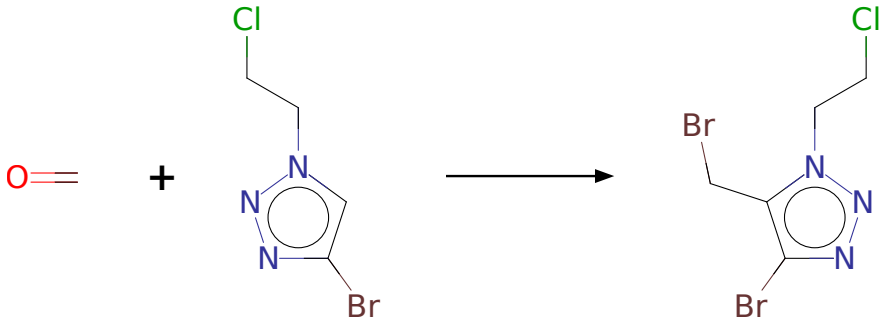
Typical conditions: Br2.Fe

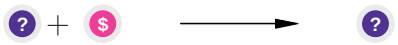
Protections: none

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

Retrosynthesis ID: 7777000

2.2.3 Blanc bromomethylation





Substrates:

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

Products:

1. ClCCn1nnc(Br)c1CBr

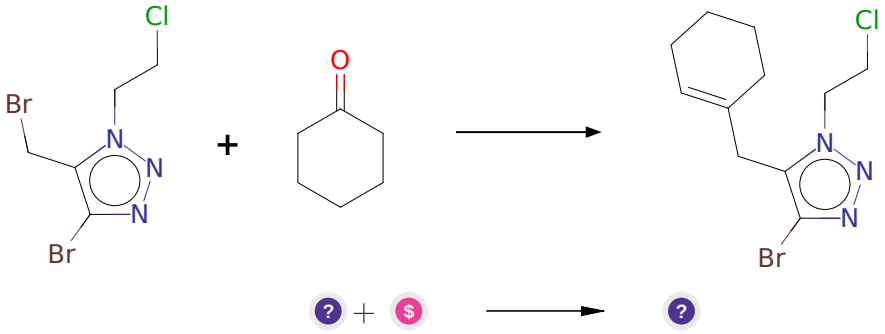
Typical conditions: HBr.heat

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

2.2.4 Shapiro reaction followed by alkyl bromide addition



Substrates:

1. ClCCn1nnc(Br)c1CBr
2. Cyclohexanone - *available at Sigma-Aldrich*

Products:

1. ClCCn1nnc(Br)c1CC1=CCCCC1

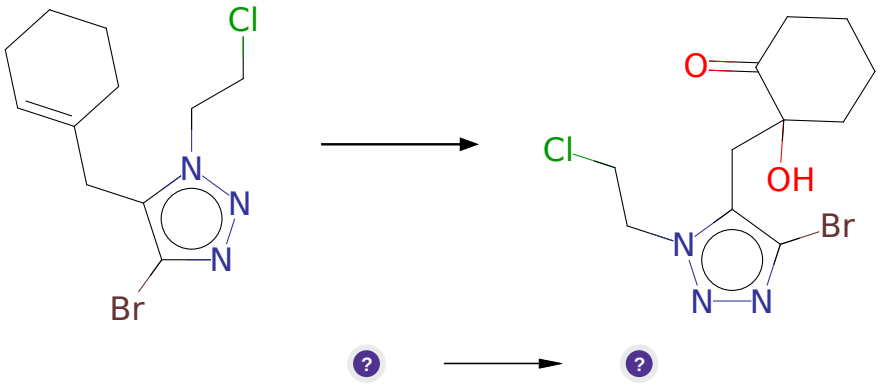
Typical conditions: 1.TsNH2NH2.2.Mes2Mg.LiCl.THF.heating then alkyl bromide.cooling

Protections: none

Reference: *10.1016/S0040-4039(00)75263-4* and *10.1021/ol300652k* and *10.1021/ja00299a037*

Retrosynthesis ID: 9990463

2.2.5 Oxohydroxylation of unsymmetric alkenes



Substrates:

1. ClCCn1nnc(Br)c1CC1=CCCCC1

Products:

1. O=C1CCCCC1(O)Cc1c(Br)nnn1CCCl

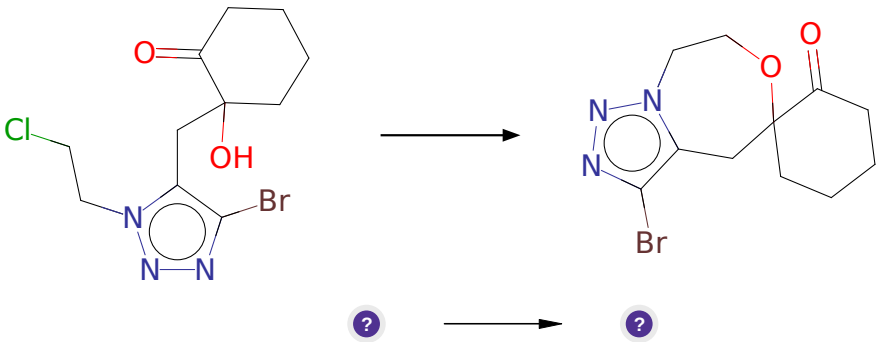
Typical conditions: KMnO4.Acetone/H2O.-10 deg C

Protections: none

Reference: *10.1016/j.tetlet.2015.12.042* and *10.1021/jacs.5b05792*

Retrosynthesis ID: 10037547

2.2.6 Alkylation of tertiary alcohols



Substrates:

1. O=C1CCCCC1(O)Cc1c(Br)nnn1CCCl

Products:

1. O=C1CCCCC12Cc1c(Br)nnn1CCO2

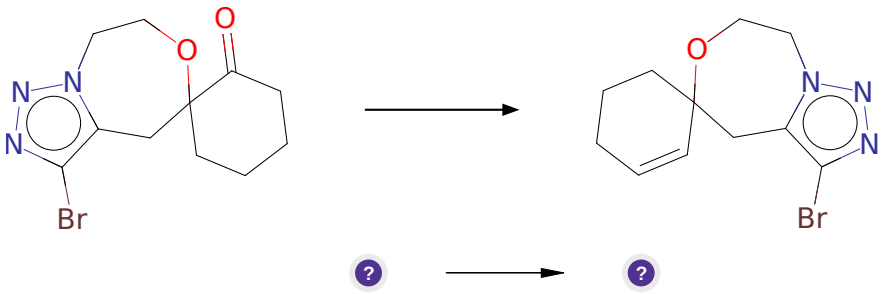
Typical conditions: K2CO3.acetone.heat

Protections: none

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

Retrosynthesis ID: 31010930

2.2.7 Shapiro reaction



Substrates:

1. O=C1CCCCC12Cc1c(Br)nnn1CCO2

Products:

1. Brc1nnn2c1CC1(C=CCCC1)OCC2

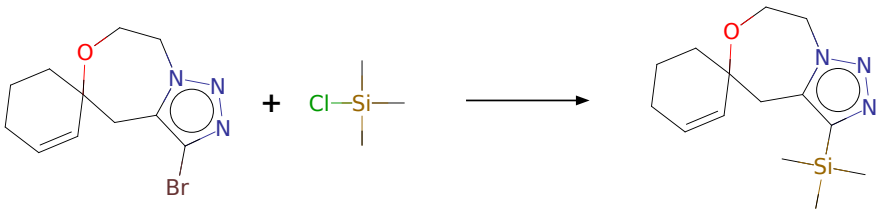
Typical conditions: 1.TsNH2NH2.2.N-BuLi

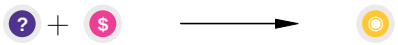
Protections: none

Reference: *10.1021/jm4008517* and *10.1016/j.bmc.2009.08.038* and *10.1021/jo00350a003*

Retrosynthesis ID: 9990398

2.2.8 Synthesis of arylsilanes





Substrates:

1. Brc1nnn2c1CC1(C=CCCC1)OCC2
2. TMSCl - *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

2.3 Path 3

Score: 326.52

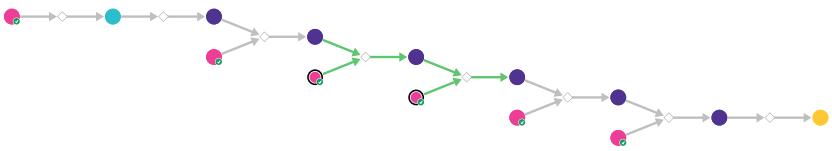
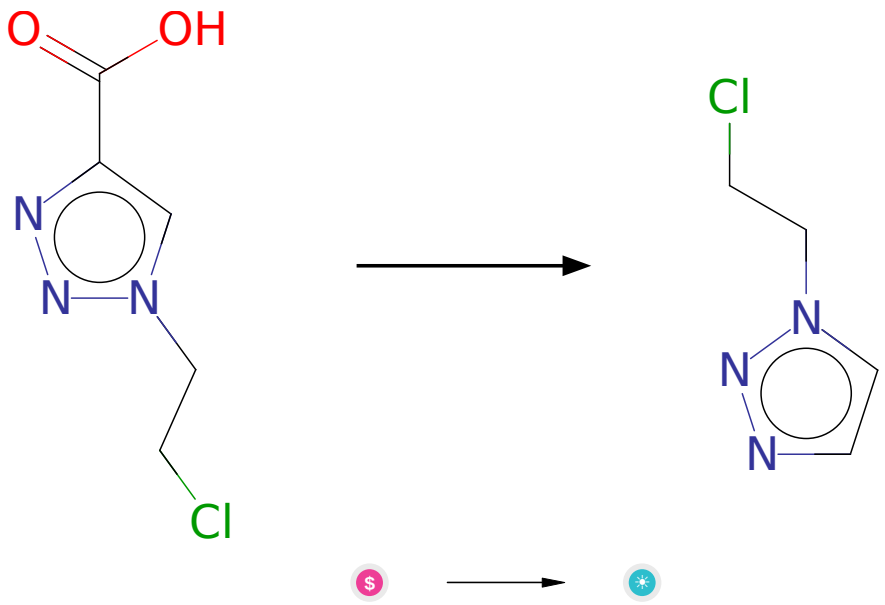


Figure 3: Outline of path 3

2.3.1 Protodecarboxylation of aromatic carboxylic acids



Substrates:

1. 1-(2-chloroethyl)-1H-1,2,3-triazole-4-carboxylic acid - *available at Sigma-Aldrich*

Products:

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

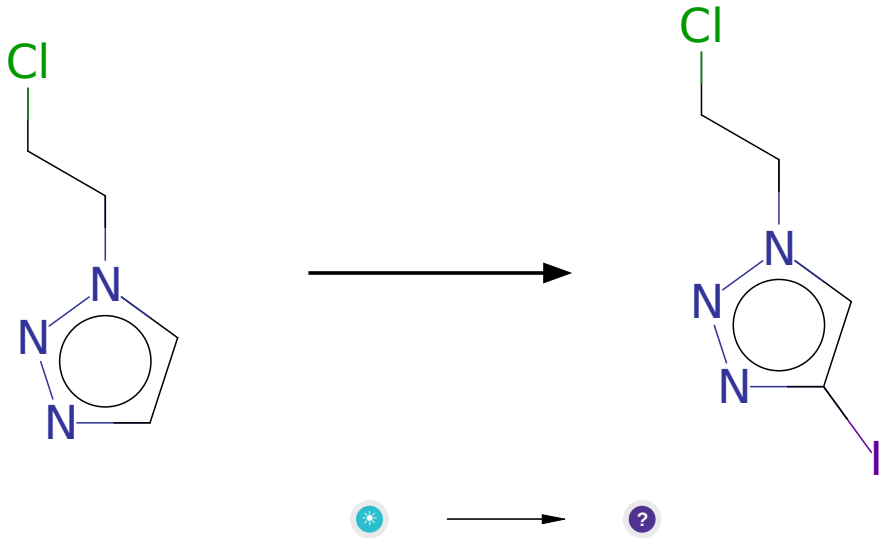
Typical conditions: Ag or Cu catalyst system

Protections: none

Reference: *10.1002/ejoc.201700121* and *10.1021/jo802628z* and *10.1039/B912509D* and *10.1039/C9SC00892F* and *10.1002/adsc.201201018* and *10.1039/C2CC33306F* and *10.1039/C5NJ02792F* and *10.1002/chem.201303200* and *10.1002/cctc.200900277*

Retrosynthesis ID: 31015628

2.3.2 Iodination of aromatic compounds



Substrates:

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

Products:

1. ClCCn1cc(I)nn1

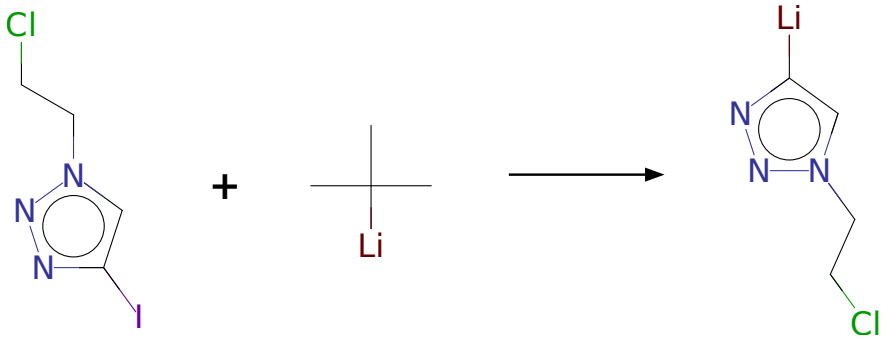
Typical conditions: I2 or other iodinating agent e.g. NIS

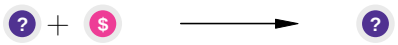
Protections: none

Reference: DOI: *10.1039/C5SC00964B* and *10.1016/j.tetlet.2005.05.117* and *10.1007/s11178-005-0256-1*

Retrosynthesis ID: 10697

2.3.3 I/Li exchange





Substrates:

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

Products:

1. [Li]c1cn(CCCl)nn1

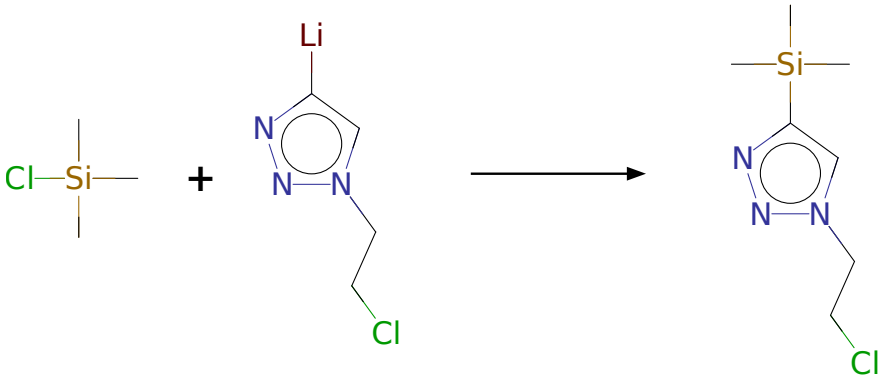
Typical conditions: nBuLi.or.tBuLi.THF.-78C

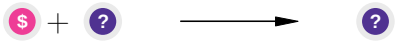
Protections: none

Reference: *10.1016/j.tet.2004.09.111* and *10.1039/c3ob41082j* And *10.1016/j.bmc.2012.03.056* And *10.1002/chem.201300292*

Retrosynthesis ID: 30673

2.3.4 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

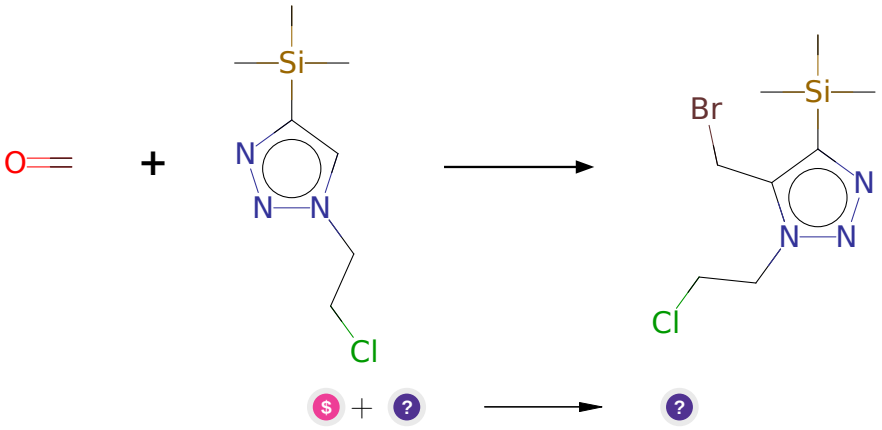
Typical conditions: THF

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

2.3.5 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

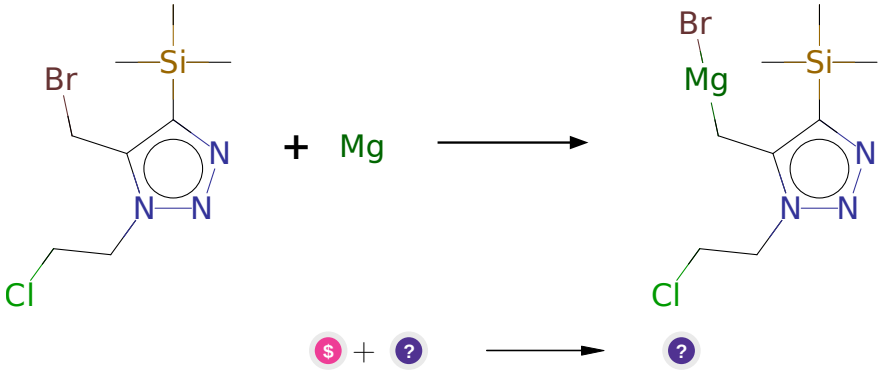
Typical conditions: HBr.heat

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

2.3.6 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

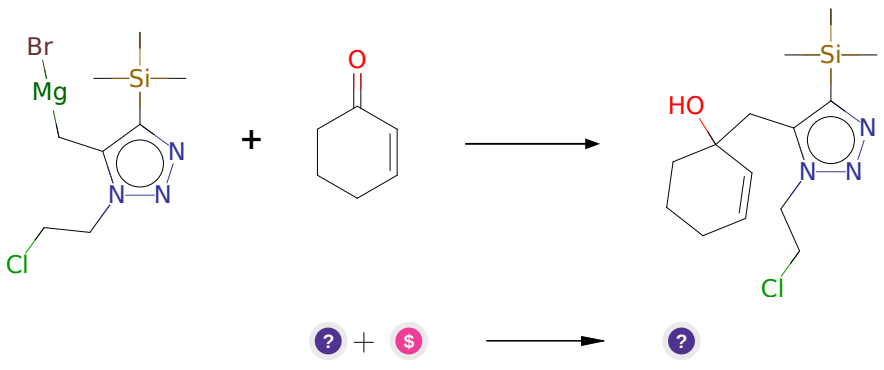
Typical conditions: Mg.THF or iPrMgBr

Protections: none

Reference: DOI: *10.1021/jo00002a039* and *10.1021/jo047877r* and *10.1021/ol006618v*

Retrosynthesis ID: 10011828

2.3.7 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

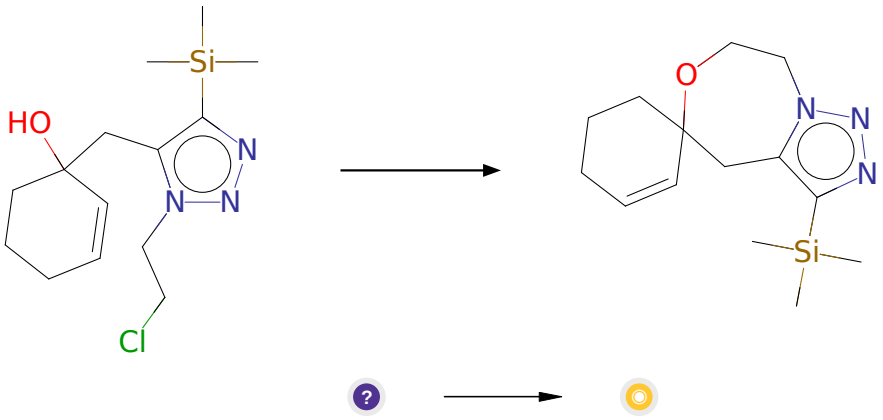
Typical conditions: Mg or Li.ether

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

2.3.8 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