Paths of analysis*

A1

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

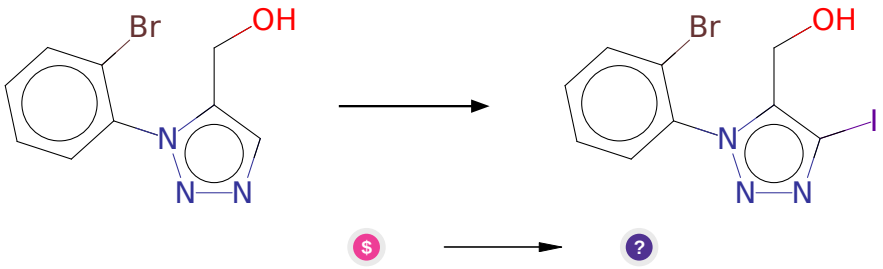
2 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

2.1 Path 1

Score: `14661533.74`

Figure 1: Outline of path 1

2.1.1 Iodination of aromatic compounds



Substrates:

1. [1-(2-bromophenyl)-1H-1,2,3-triazol-5-yl]methanol - *available at Sigma-Aldrich*

Products:

1. OCc1c(I)nnn1-c1ccccc1Br

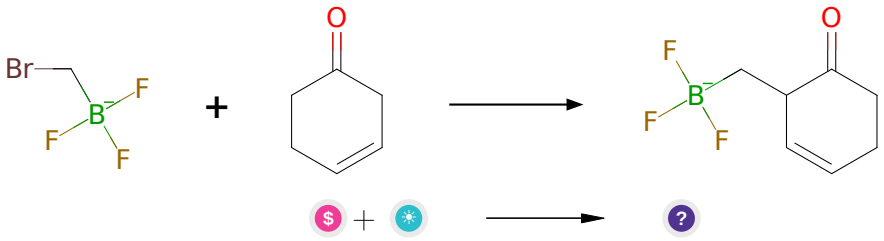
Typical conditions: I2 or other iodinating agent e.g. NIS

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

2.1.2 Alkylation of ketones



Substrates:

1. Potassium (bromomethyl)trifluoroborate - *available at Sigma-Aldrich*
2. cyclohex-3-enone

Products:

1. O=C1CCC=CC1C[B-](F)(F)F

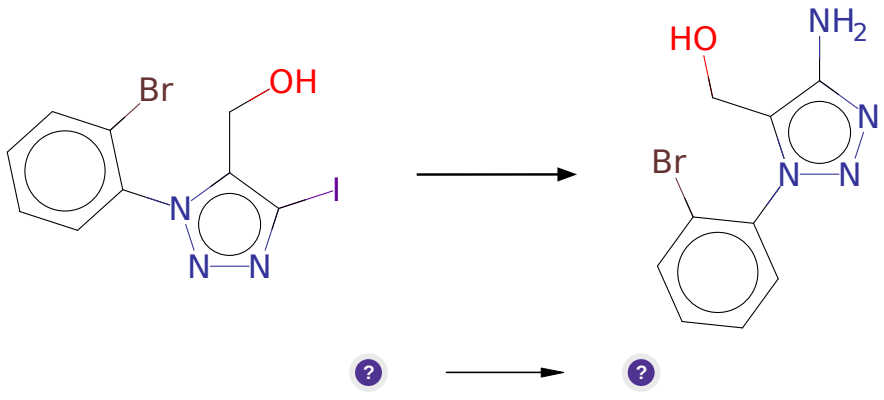
Typical conditions: LDA or other base.THF.-78C

Protections: none

Reference: DOI: *10.1021/ja0123554*

Retrosynthesis ID: 1868

2.1.3 Coupling of Ammonia with Aryl Halides



Substrates:

1. OCc1c(I)nnn1-c1ccccc1Br

Products:

1. Nc1nnn(-c2ccccc2Br)c1CO

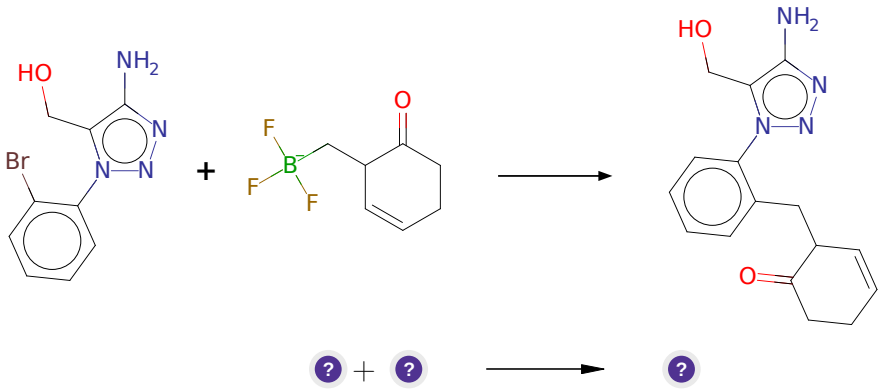
Typical conditions: Pd[(P(p-tol)3]2.NaOtBu.dioxane.heat

Protections: none

Reference: *10.1021/ja903049z* and *10.1021/jo9006738*

Retrosynthesis ID: 31016464

2.1.4 Suzuki Coupling of arylbromides and alkyltrifluoroborates



Substrates:

1. Nc1nnn(-c2ccccc2Br)c1CO
2. O=C1CCC=CC1C[B-](F)(F)F

Products:

1. Nc1nnn(-c2ccccc2CC2C=CCCC2=O)c1CO

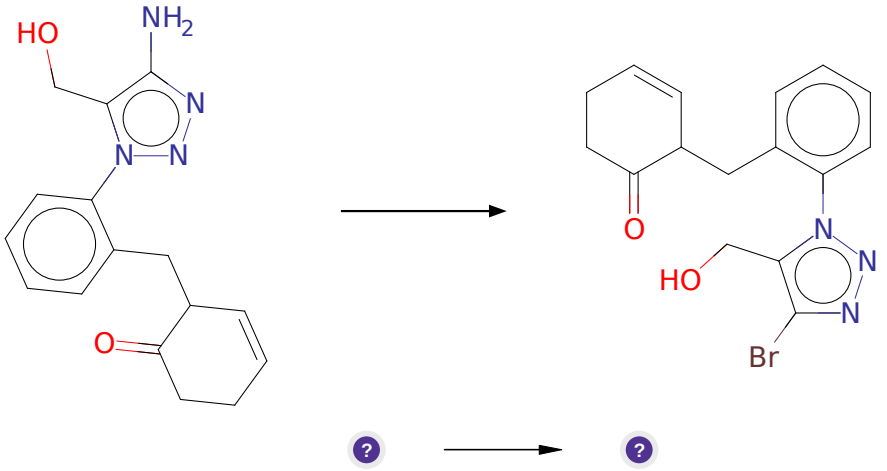
Typical conditions: Pd(OAc)2.SPhos.K3PO4.H2O.reflux

Protections: none

Reference: *10.1021/jo0343331* and EP1867650 p.36

Retrosynthesis ID: 10033481

2.1.5 Sandmeyer Reaction



Substrates:

1. Nc1nnn(-c2ccccc2CC2C=CCCC2=O)c1CO

Products:

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CO

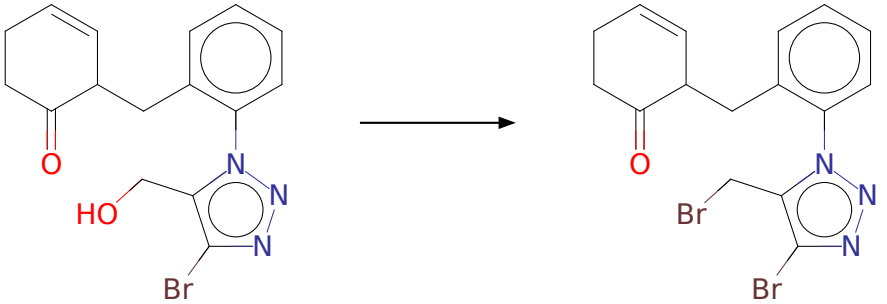
Typical conditions: IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

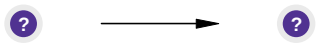
Protections: none

Reference: *10.1002/chem.201600278* and *10.1016/j.bmcl.2011.12.131* and *10.1016/j.ejmech.2013.01.046* and *10.1021/jm0002782* and *10.1002/ejoc.201300443* and *10.1021/jo052589w*(SI,page S3) and *10.1021/jm800527x* and *10.1016/j.bmcl.2015.04.098* and *10.1021/ja034563x*

Retrosynthesis ID: 29904

2.1.6 Appel Reaction





Substrates:

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CO

Products:

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CBr

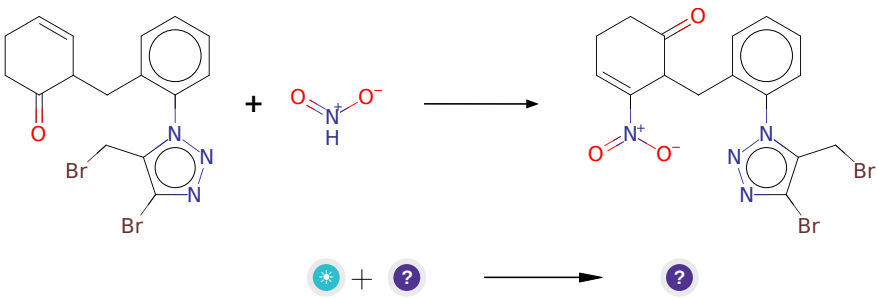
Typical conditions: PPh3.CBr4

Protections: none

Reference: *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

Retrosynthesis ID: 9990037

2.1.7 Nitration of aliphatic olefins



Substrates:

1. HNO2
2. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CBr

Products:

1. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

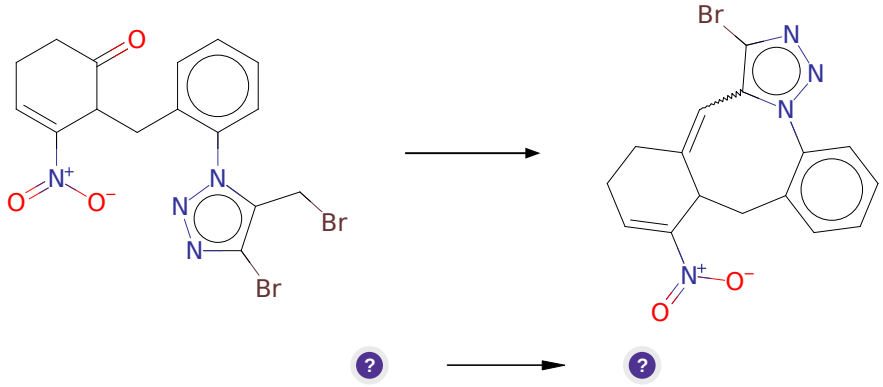
Typical conditions: Fe(NO2)3x9H2O.TEMPO.DCE.4A MS.80C

Protections: none

Reference: DOI: *10.1021/jo400598p*

Retrosynthesis ID: 1623

2.1.8 HWE/Wittig Olefination



Substrates:

1. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

Products:

1. O=[N+]([O-])C1=CCCC2=Cc3c(Br)nnn3-c3ccccc3CC21

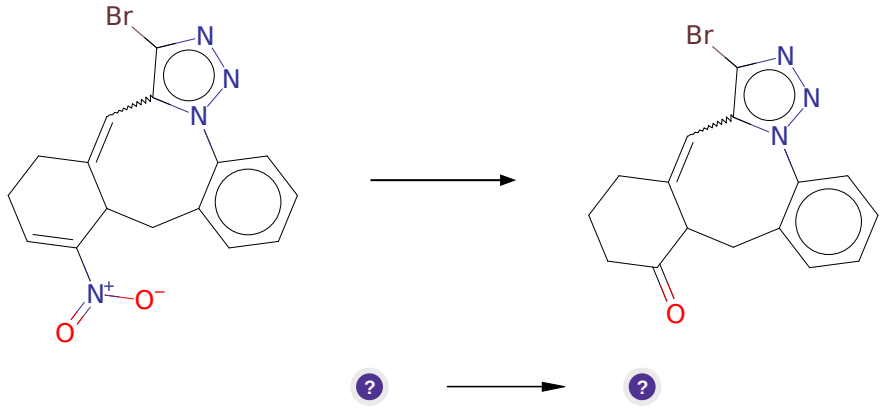
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

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

Retrosynthesis ID: 24425

2.1.9 Synthesis of ketones from nitroalkenes



Substrates:

1. O=[N+]([O-])C1=CCCC2=Cc3c(Br)nnn3-c3ccccc3CC21

Products:

1. O=C1CCCC2=Cc3c(Br)nnn3-c3ccccc3CC12

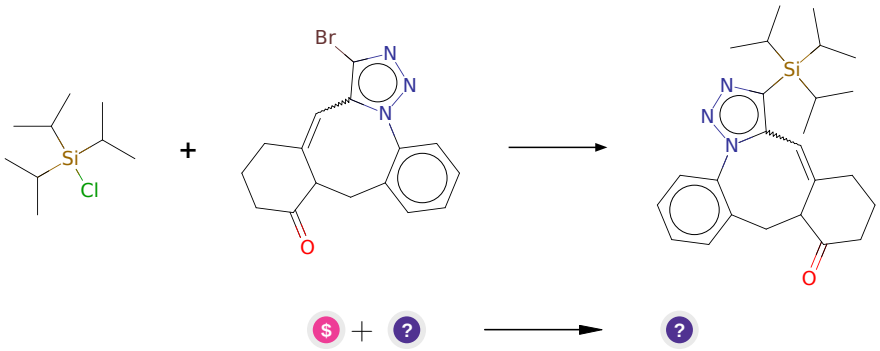
Typical conditions: RaNi.hypophosphite.EtOH.acetate.buffer or Fe.HCl.MeOH

Protections: none

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

Retrosynthesis ID: 34041

2.1.10 Synthesis of arylsilanes



Substrates:

1. TIPSCl - *available at Sigma-Aldrich*
2. O=C1CCCC2=Cc3c(Br)nnn3-c3ccccc3CC12

Products:

1. CC(C)[Si](c1nnn2c1C=C1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

Typical conditions: 1.nBuLi.2.ClSnR3

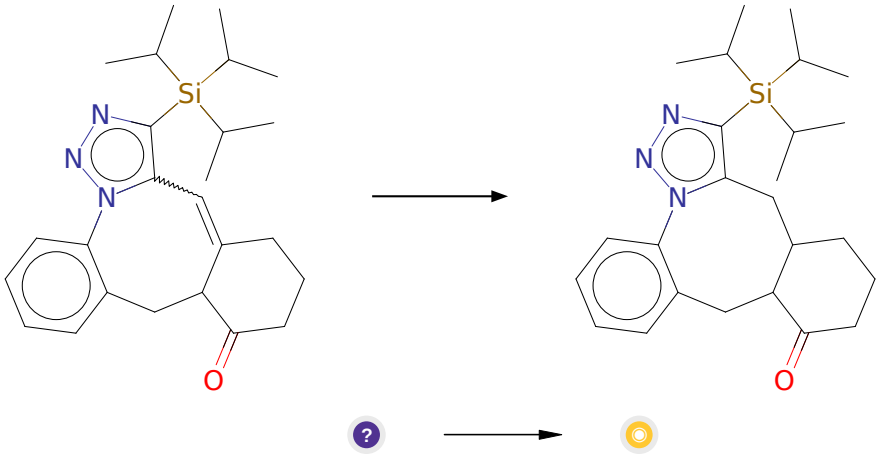
Protections:

Functional group SMARTS	Classification	Protecting groups
[#6]C([#6])=O	carbonyls	1.3-Dioxanes 1.3-Dioxolanes 1.3-Dithianes 1.3-Dithiolanes Dimethyl Acetals and Ketals N,N-Dimethylhydrazones

Reference: *10.1071/CH9851147*.

Retrosynthesis ID: 5370

2.1.11 Homogenous Reduction of C=C Double Bond



Substrates:

1. CC(C)[Si](c1nnn2c1C=C1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

Products:

1. CC(C)[Si](c1nnn2c1CC1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

Typical conditions: H2.Pd/C or Pd(OH)2/C

Protections: none

Reference: DOI: *10.1021/jo980467g* and *10.1021/ja00175a039* and *10.1021/ja0296733* and *10.1021/ja049043w* (page S-4) and *10.1021/jo980128n* and *10.1021/ja4029928* and Patent: WO2014/207205 A1, 2014 page 16

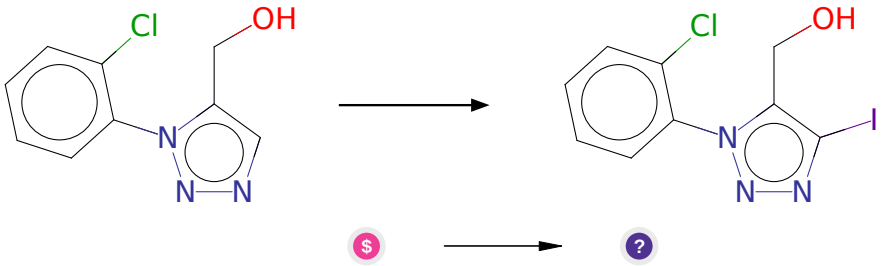
Retrosynthesis ID: 9995780

2.2 Path 2

Score: 14661533.74

Figure 2: Outline of path 2

2.2.1 Iodination of aromatic compounds



Substrates:

1. [1-(2-chlorophenyl)-1H-1,2,3-triazol-5-yl]methanol - *available at Sigma-Aldrich*

Products:

1. OCc1c(I)nnn1-c1ccccc1Cl

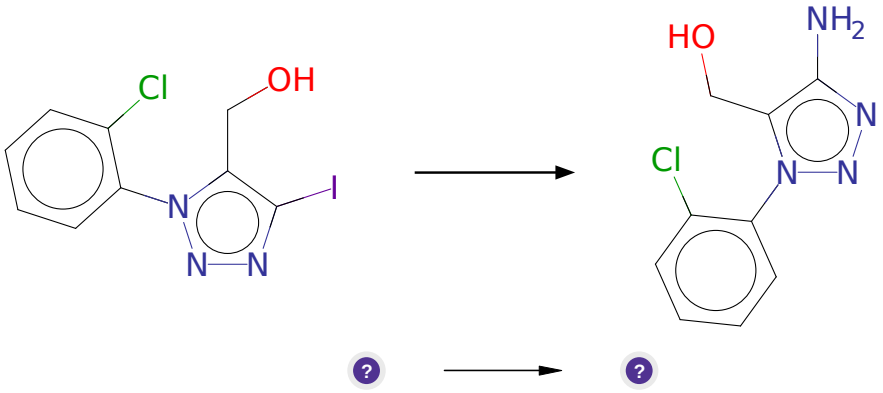
Typical conditions: I2 or other iodinating agent e.g. NIS

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

2.2.2 Coupling of Ammonia with Aryl Halides



Substrates:

1. OCc1c(I)nnn1-c1ccccc1Cl

Products:

1. Nc1nnn(-c2ccccc2Cl)c1CO

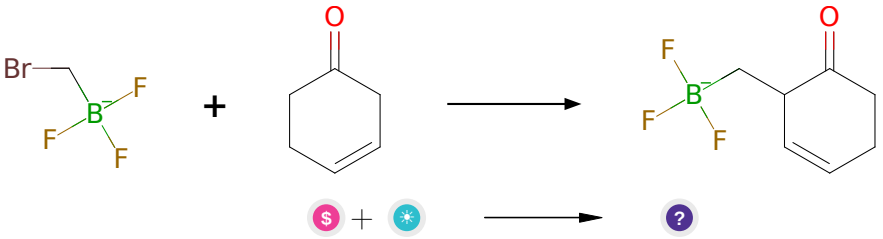
Typical conditions: Pd[(P(p-tol)3]2.NaOtBu.dioxane.heat

Protections: none

Reference: *10.1021/ja903049z* and *10.1021/jo9006738*

Retrosynthesis ID: 31016464

2.2.3 Alkylation of ketones



Substrates:

1. Potassium (bromomethyl)trifluoroborate - *available at Sigma-Aldrich*
2. cyclohex-3-enone

Products:

1. O=C1CCC=CC1C[B-](F)(F)F

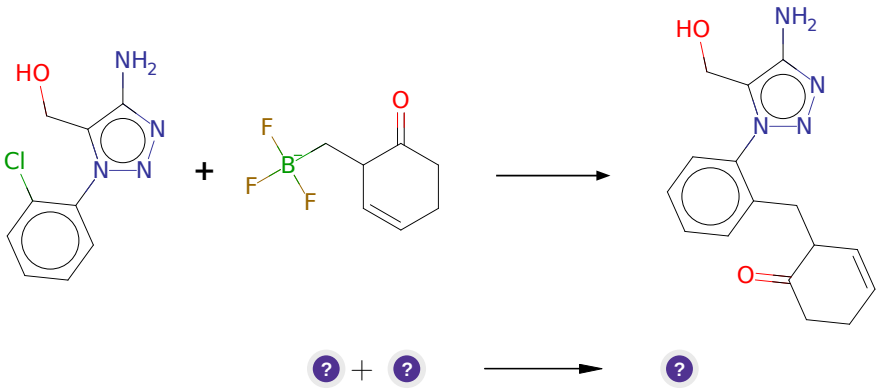
Typical conditions: LDA or other base.THF.-78C

Protections: none

Reference: DOI: *10.1021/ja0123554*

Retrosynthesis ID: 1868

2.2.4 Suzuki Coupling of arylchlorides and alkyltrifluoroborates



Substrates:

1. O=C1CCC=CC1C[B-](F)(F)F
2. Nc1nnn(-c2ccccc2Cl)c1CO

Products:

1. Nc1nnn(-c2ccccc2CC2C=CCCC2=O)c1CO

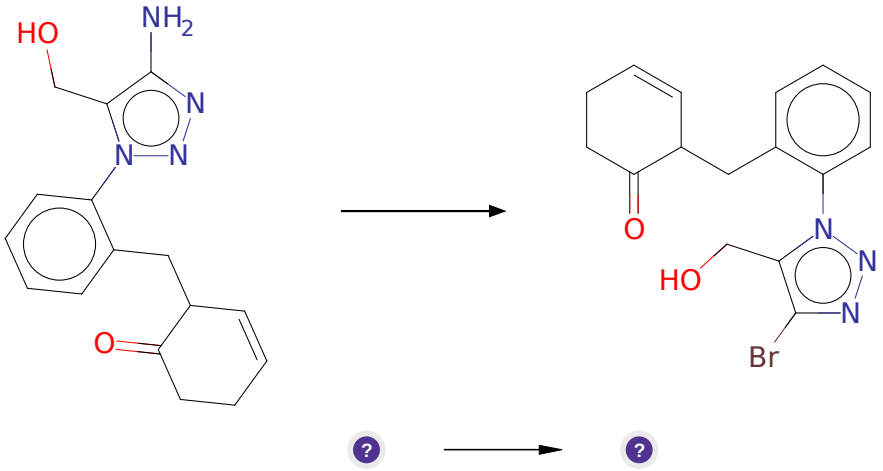
Typical conditions: Pd(OAc)2.RuPhos.CsCO3.toluene/H2O.90C

Protections: none

Reference: *10.1016/j.tet.2015.07.072* and *10.1021/jo900152n*

Retrosynthesis ID: 10033514

2.2.5 Sandmeyer Reaction



Substrates:

1. Nc1nnn(-c2ccccc2CC2C=CCCC2=O)c1CO

Products:

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CO

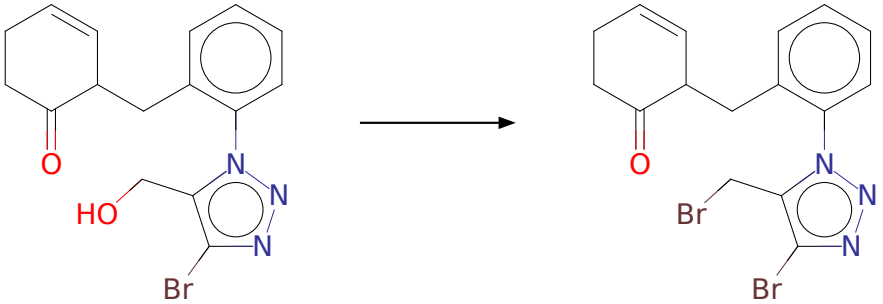
Typical conditions: IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

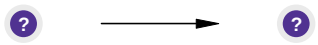
Protections: none

Reference: *10.1002/chem.201600278* and *10.1016/j.bmcl.2011.12.131* and *10.1016/j.ejmech.2013.01.046* and *10.1021/jm0002782* and *10.1002/ejoc.201300443* and *10.1021/jo052589w*(SI,page S3) and *10.1021/jm800527x* and *10.1016/j.bmcl.2015.04.098* and *10.1021/ja034563x*

Retrosynthesis ID: 29904

2.2.6 Appel Reaction





Substrates:

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CO

Products:

1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CBr

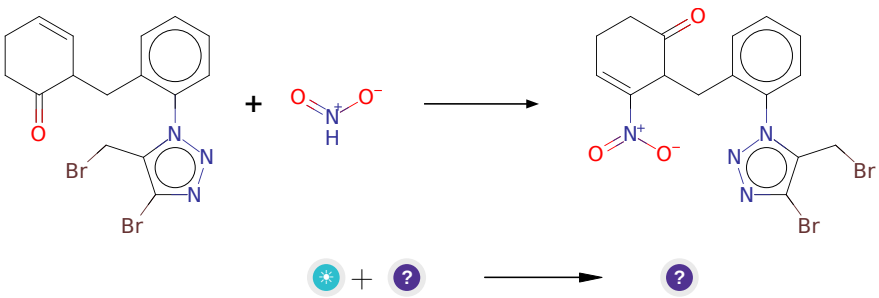
Typical conditions: PPh3.CBr4

Protections: none

Reference: *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

Retrosynthesis ID: 9990037

2.2.7 Nitration of aliphatic olefins



Substrates:

1. HNO2
2. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CBr

Products:

1. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

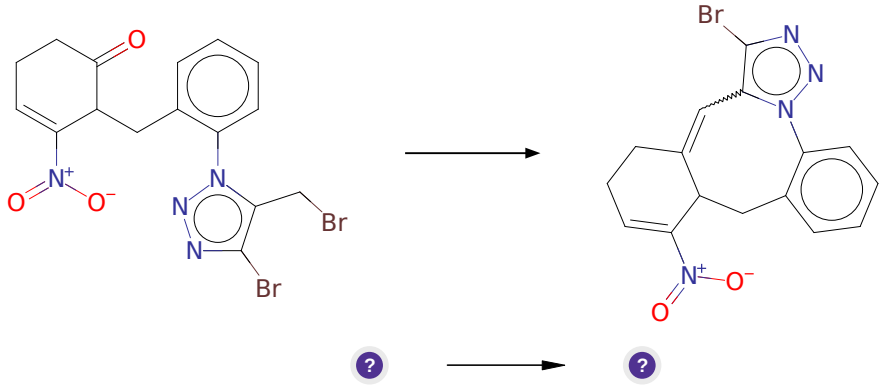
Typical conditions: Fe(NO2)3x9H2O.TEMPO.DCE.4A MS.80C

Protections: none

Reference: DOI: *10.1021/jo400598p*

Retrosynthesis ID: 1623

2.2.8 HWE/Wittig Olefination



Substrates:

1. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

Products:

1. O=[N+]([O-])C1=CCCC2=Cc3c(Br)nnn3-c3ccccc3CC21

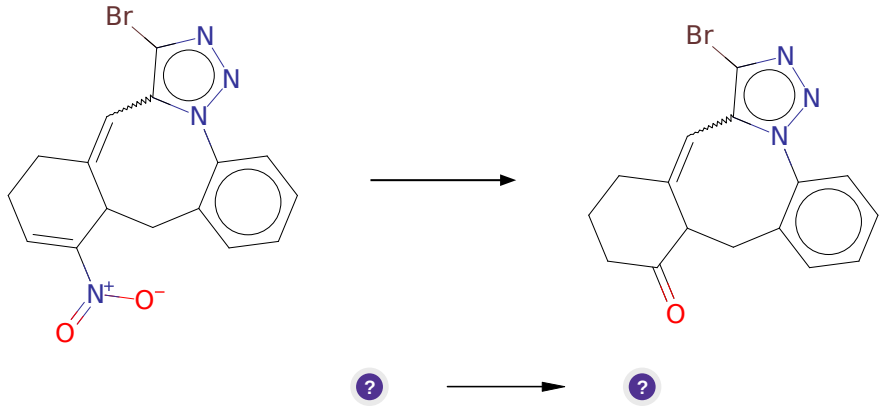
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

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

Retrosynthesis ID: 24425

2.2.9 Synthesis of ketones from nitroalkenes



Substrates:

1. O=[N+]([O-])C1=CCCC2=Cc3c(Br)nnn3-c3ccccc3CC21

Products:

1. O=C1CCCC2=Cc3c(Br)nnn3-c3ccccc3CC12

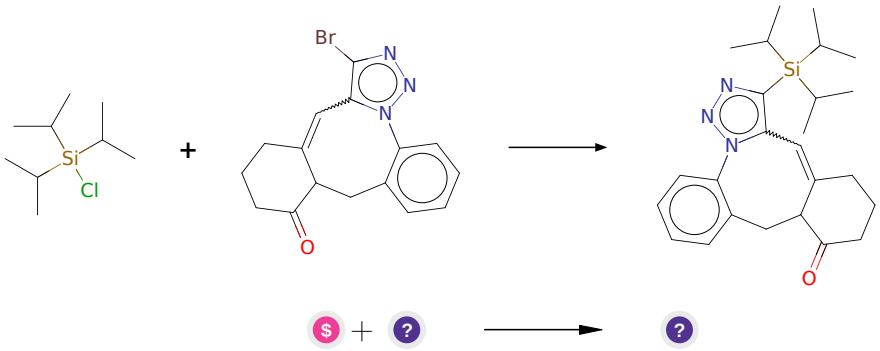
Typical conditions: RaNi.hypophosphite.EtOH.acetate.buffer or Fe.HCl.MeOH

Protections: none

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

Retrosynthesis ID: 34041

2.2.10 Synthesis of arylsilanes



Substrates:

1. TIPSCl - *available at Sigma-Aldrich*
2. O=C1CCCC2=Cc3c(Br)nnn3-c3ccccc3CC12

Products:

1. CC(C)[Si](c1nnn2c1C=C1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

Typical conditions: 1.nBuLi.2.ClSnR3

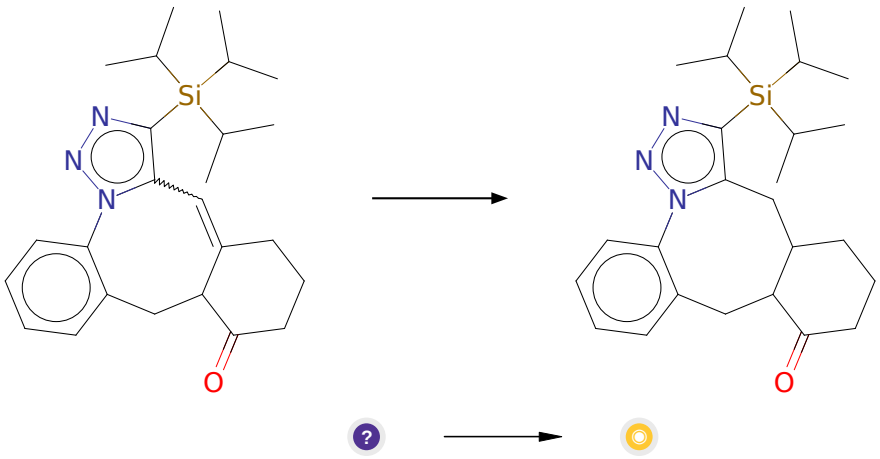
Protections:

Functional group SMARTS	Classification	Protecting groups
[#6]C([#6])=O	carbonyls	1.3-Dioxanes 1.3-Dioxolanes 1.3-Dithianes 1.3-Dithiolanes Dimethyl Acetals and Ketals N,N-Dimethylhydrazones

Reference: *10.1071/CH9851147*.

Retrosynthesis ID: 5370

2.2.11 Homogenous Reduction of C=C Double Bond



Substrates:

1. CC(C)[Si](c1nnn2c1C=C1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

Products:

1. CC(C)[Si](c1nnn2c1CC1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

Typical conditions: H2.Pd/C or Pd(OH)2/C

Protections: none

Reference: DOI: *10.1021/jo980467g* and *10.1021/ja00175a039* and *10.1021/ja0296733* and *10.1021/ja049043w* (page S-4) and *10.1021/jo980128n* and *10.1021/ja4029928* and Patent: WO2014/207205 A1, 2014 page 16

Retrosynthesis ID: 9995780