Paths of analysis*
A1

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+1000 000*(CONFLICT+NON_SELECTIVITY+FILTERS+PROTECT)

Chemical scoring formula: SMALLER^ 3,SMALLER^ 1.5

Min. search width: 400

Max. reactions per product: 60

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.*
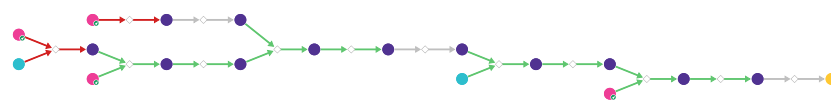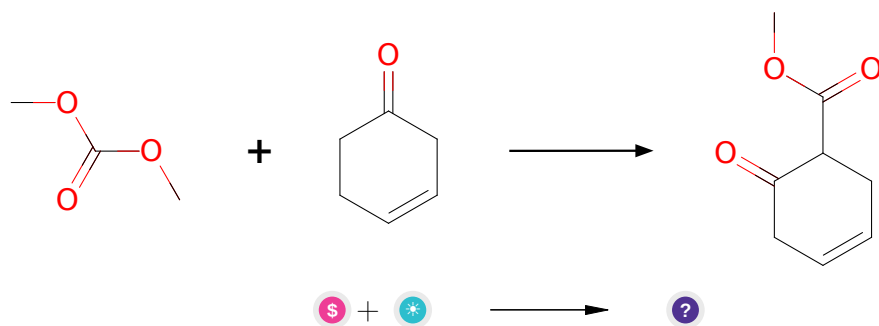
2.1 Path 1

Score: `16764486.08`

Figure 1: Outline of path 1

2.1.1 Carboethoxylation of enolates - Claisen condensation

Substrates:

1. dimethyl ester -   *available at Sigma-Aldrich*

2. cyclohex-3-enone

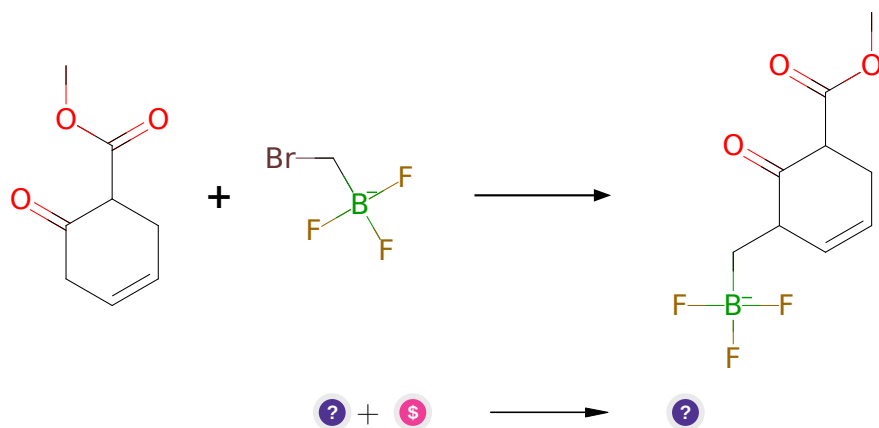**Products:**

1. COC(=O)C1CC=CCC1=O

Typical conditions: NaH.THF

Protections: none

Retrosynthesis ID: 8167

2.1.2 Alkylation of ketones

Substrates:

1. COC(=O)C1CC=CCC1=O

2. Potassium (bromomethyl)trifluoroborate - *available at Sigma-Aldrich*
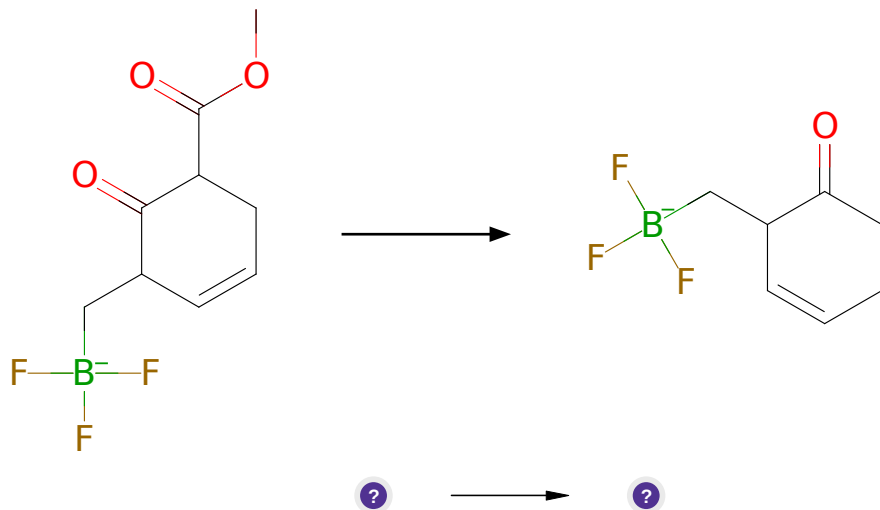
Products:

1. COC(=O)C1CC=CC(C[B-](F)(F)F)C1=O

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

Protections: none

Retrosynthesis ID: 1868

2.1.3 Krapcho decarboxylation

Substrates:

1. COC(=O)C1CC=CC(C[B-](F)(F)F)C1=O

Products:

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

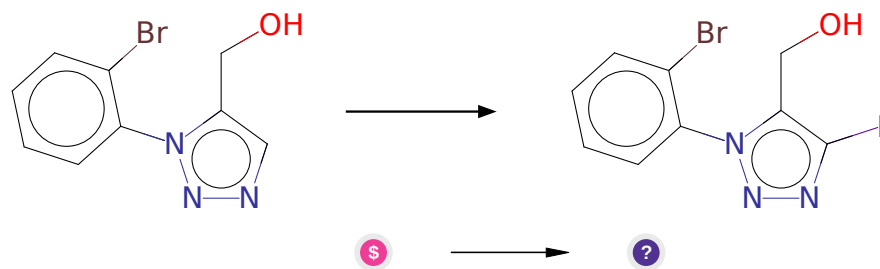**Typical conditions:** LiCl.DMSO.150oC

Protections: none

Reference: *10.3998/ark.5550190.0008.201* and *10.3184/174751911X12964930076403*

Retrosynthesis ID: 5025

2.1.4 Iodination of aromatic compounds

Substrates:

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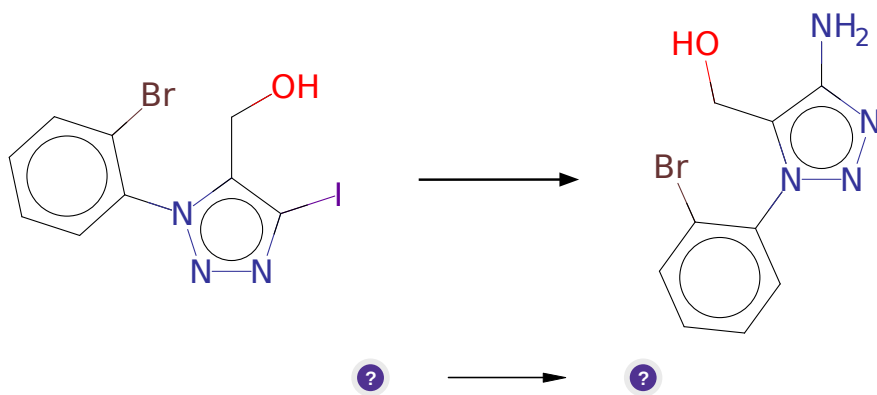
Products:

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

2.1.5   Coupling of Ammonia with Aryl Halides

Substrates:

1. OCc1c(I)nnn1-c1ccccc1Br
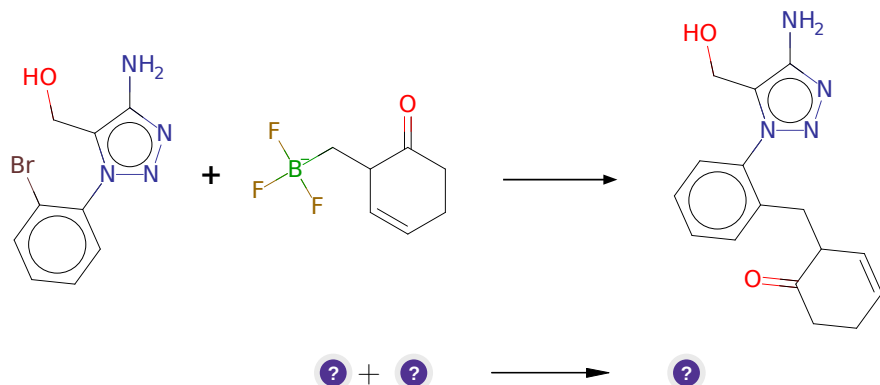
Products:

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

2.1.6 Suzuki Coupling of arylbromides and alkyltrifluoroborates

Substrates:

1. Nc1nnn(-c2ccccc2Br)c1CO

2. O=C1CCC=CC1C[B-](F)(F)F
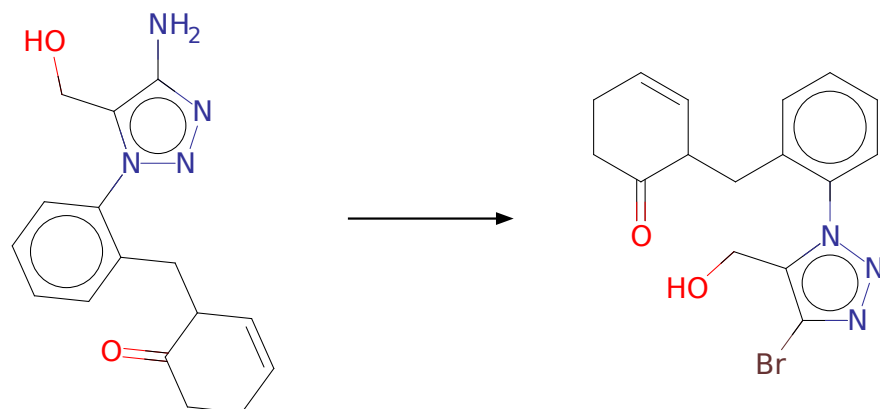
Products:

1. Nc1nnn(-c2ccccc2CC2C=CCCC2=O)c1CO
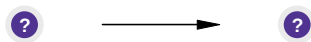
Typical conditions: Pd(OAc)2.SPhos.K3PO4.H2O.reflux

Protections: none

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

Retrosynthesis ID: 10033481

2.1.7 Sandmeyer Reaction

Substrates:

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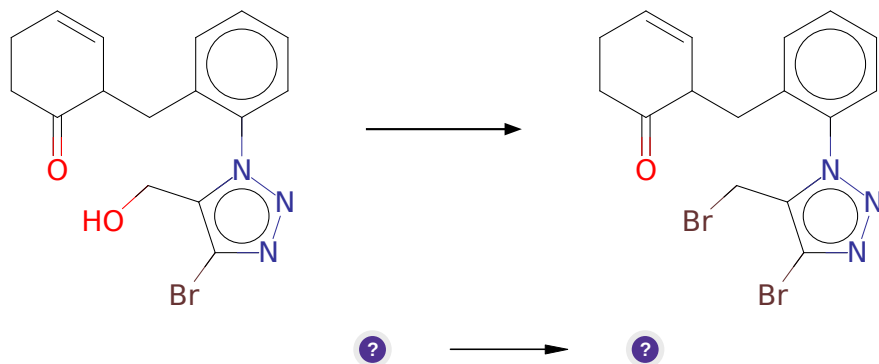
Products:

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

2.1.8 Appel Reaction

Substrates:

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

Products:

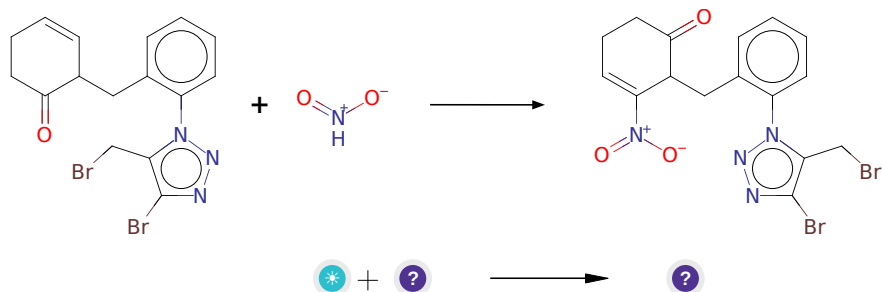1. O=C1CCC=CC1Cc1ccccc1-n1nnc(Br)c1CBr

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

2.1.9 Nitration of aliphatic olefins

Substrates:

1. HNO2

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

Products:

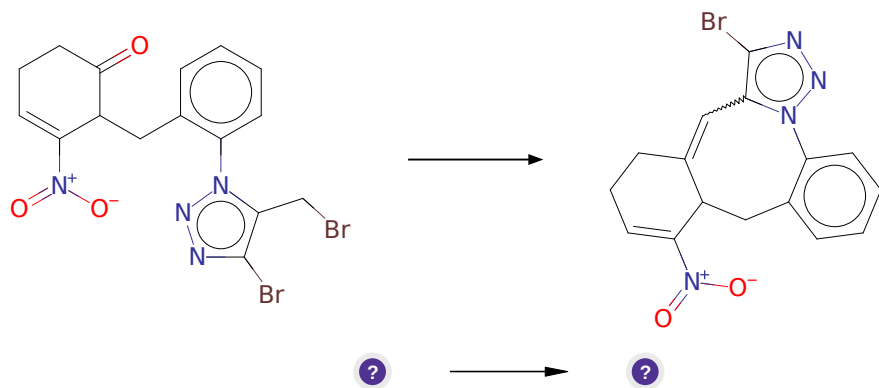1. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

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

Protections: none

Reference: DOI: *10.1021/jo400598p*

Retrosynthesis ID: 1623

2.1.10 HWE/Wittig Olefination

Substrates:

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

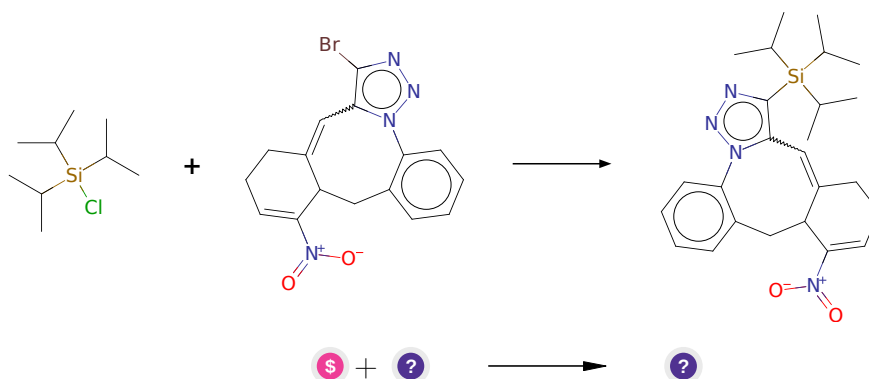**Products:**

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

2.1.11 Synthesis of silanes,stannanes and germanes from Grignard reagents

Substrates:

1. TIPSCl - *available at Sigma-Aldrich*

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

Products:

1. CC(C)[Si](c1nnn2c1C=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-2)(C(C)C)C(C)C
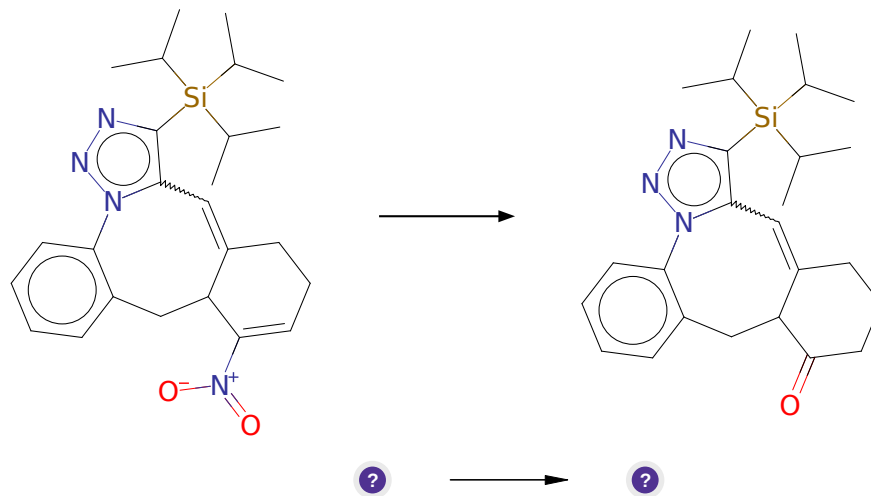
Typical conditions: 1.nBuLi.or.Mg.THF.-78C.2.Si-Cl.to.rt

Protections: none

Reference: *10.1021/jo802433t* AND *10.1021/ja01108a009*

Retrosynthesis ID: 5402

2.1.12 Synthesis of ketones from nitroalkenes

Substrates:

1. CC(C)[Si](c1nnn2c1C=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-2)(C(C)C)C(C)C

Products:

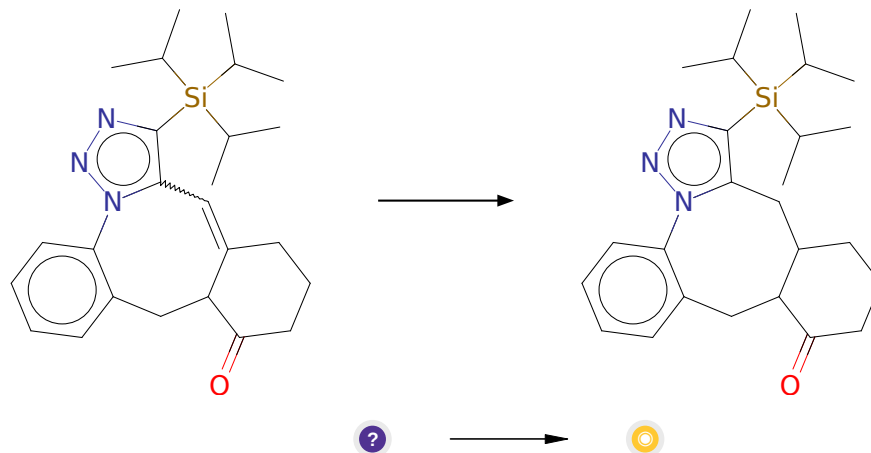1. CC(C)[Si](c1nnn2c1C=C1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

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

2.1.13 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
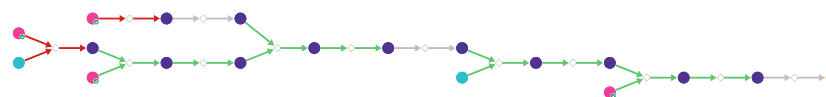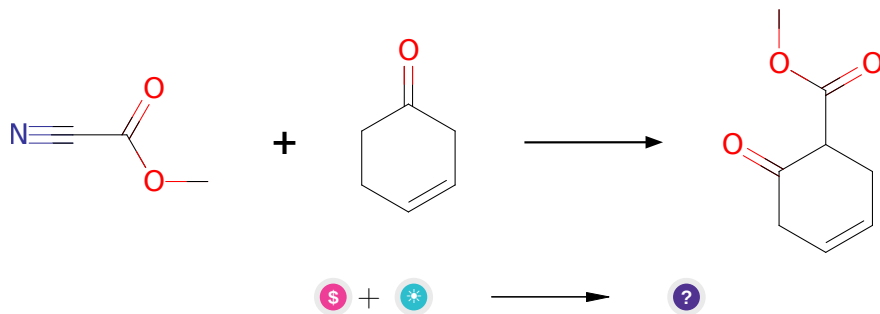
2.2 Path 2

Score: 16764486.08

Figure 2: Outline of path 2

2.2.1 Mander methoxycarbonylation of ketones

Substrates:

1. Methyl cyanoformate - *available at Sigma-Aldrich*
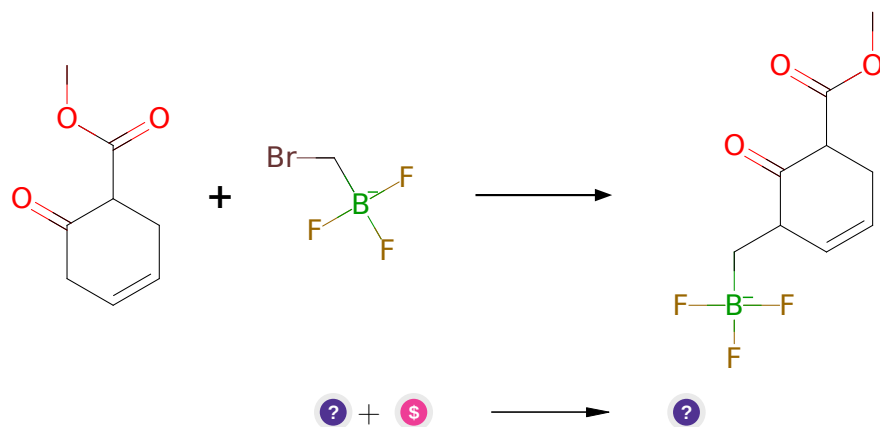
2. cyclohex-3-enone

Products:

1. COC(=O)C1CC=CCC1=O

Typical conditions: 1) MeLi.Et2O or THF 2) Methyl cyanoacetate. Et2O or THF

Protections: none

Reference: DOI: *10.1016/s0040-4039(00)87886-7*

Retrosynthesis ID: 50436

2.2.2 Alkylation of ketones

Substrates:

1. COC(=O)C1CC=CCC1=O

2. Potassium (bromomethyl)trifluoroborate - *available at Sigma-Aldrich*

Products:
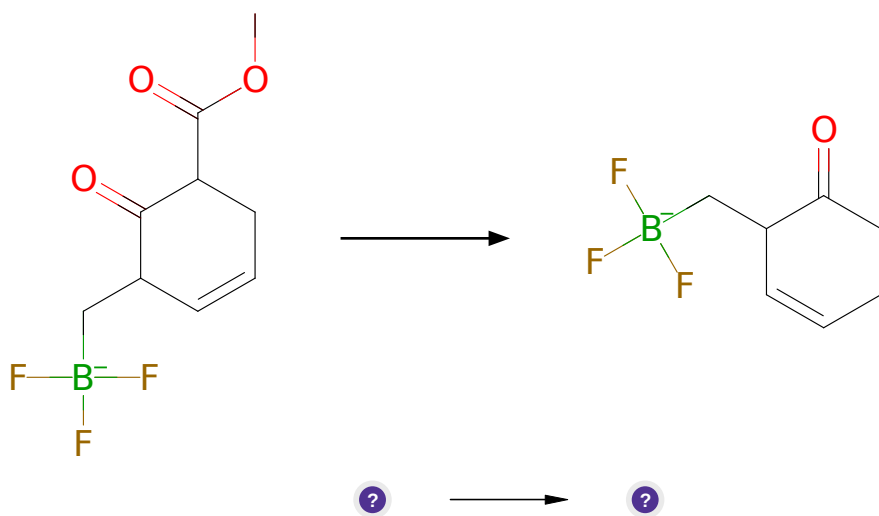
1. COC(=O)C1CC=CC(C[B-](F)(F)F)C1=O

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

Protections: none

Reference: DOI: *10.1021/ja0123554*

Retrosynthesis ID: 1868

2.2.3 Krapcho decarboxylation

Substrates:

1. COC(=O)C1CC=CC(C[B-](F)(F)F)C1=O
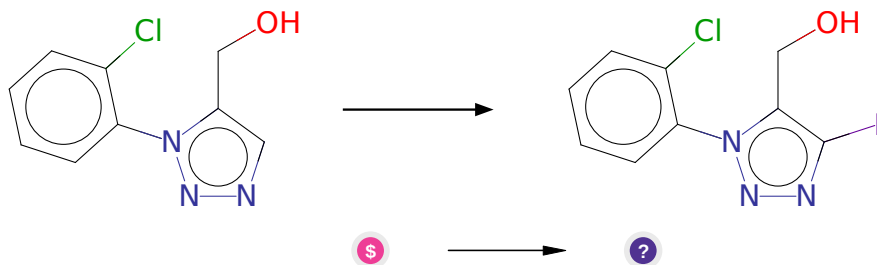
Products:

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

Typical conditions: LiCl.DMSO.150oC

Protections: none

Reference: *10.3998/ark.5550190.0008.201* and *10.3184/174751911X12964930076403*

Retrosynthesis ID: 5025

2.2.4 Iodination of aromatic compounds

Substrates:

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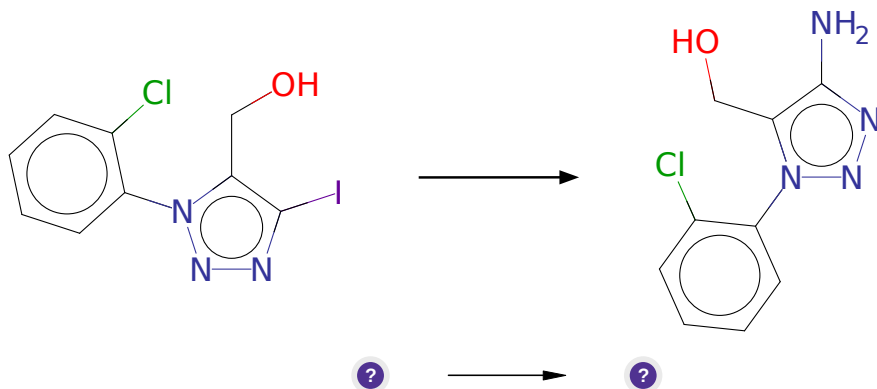
Products:

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

2.2.5 Coupling of Ammonia with Aryl Halides

Substrates:

1. OCc1c(I)nnn1-c1ccccc1Cl

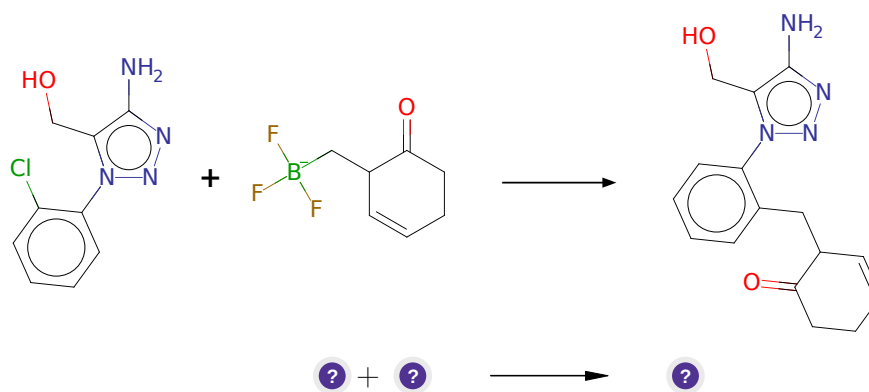**Products:**

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

2.2.6 Suzuki Coupling of arylchlorides and alkyltrifluoroborates

Substrates:

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

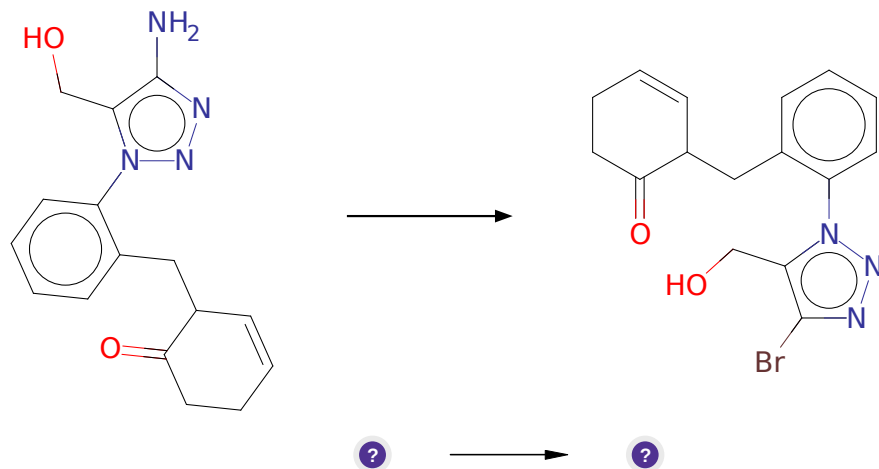**Products:**

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

2.2.7 Sandmeyer Reaction

Substrates:

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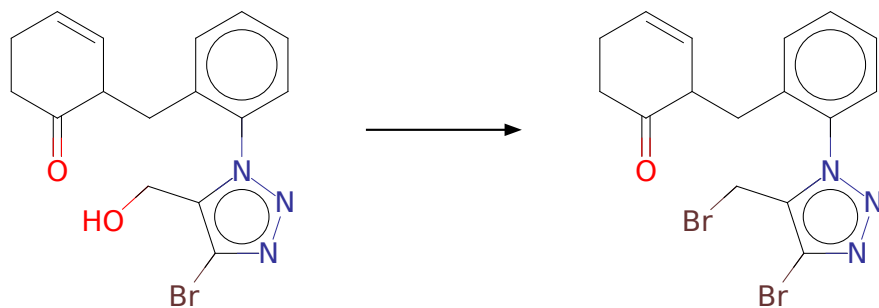
Products:

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

Typical conditions: IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2
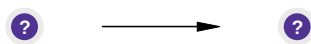
Protections: none

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

2.2.8 Appel Reaction

Substrates:

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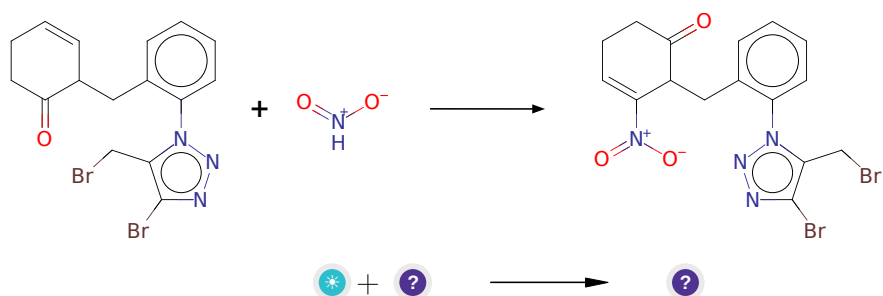
Products:

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

2.2.9 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

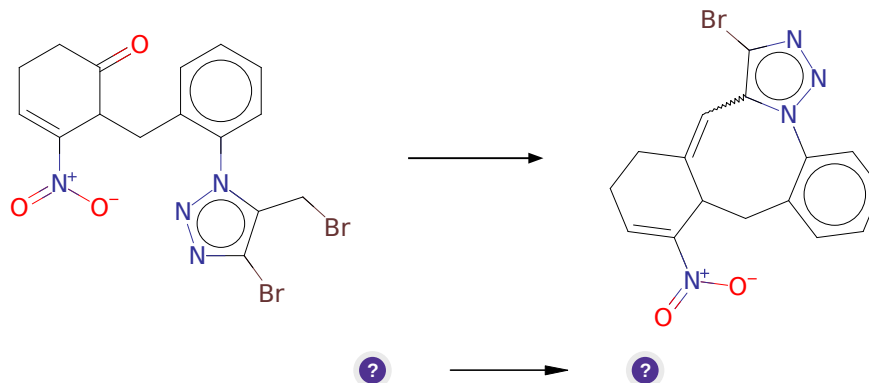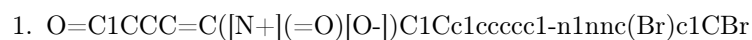**Typical conditions:** Fe(NO2)3x9H2O.TEMPO.DCE.4A MS.80C

Protections: none

Reference: DOI: *10.1021/jo400598p*

Retrosynthesis ID: 1623

2.2.10 HWE/Wittig Olefination
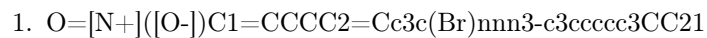
Substrates:

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

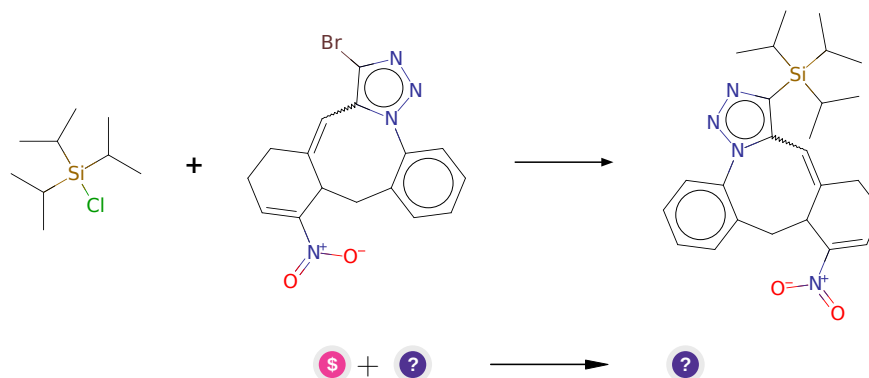**Products:**

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

2.2.11 Synthesis of silanes,stannanes and germanes from Grignard reagents

Substrates:

1. TIPSCl - *available at Sigma-Aldrich*

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

Products:

1. CC(C)[Si](c1nnn2c1C=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-
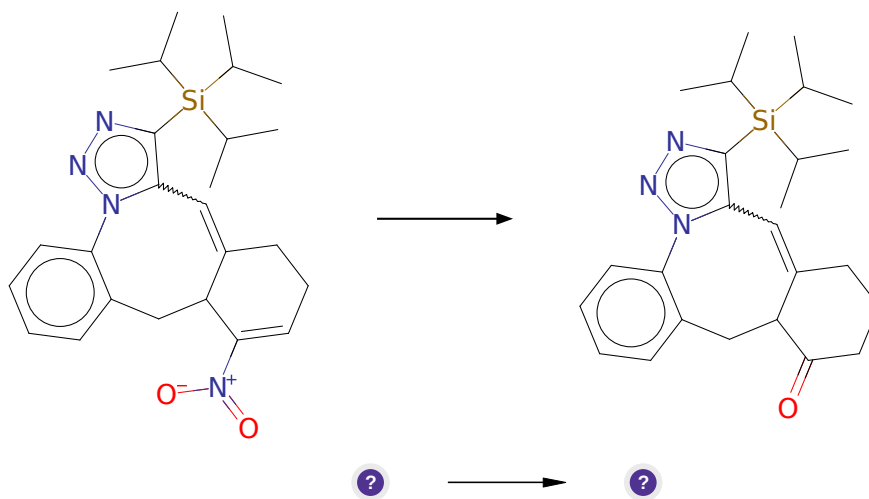2)(C(C)C)C(C)C

Typical conditions: 1.nBuLi.or.Mg.THF.-78C.2.Si-Cl.to.rt

Protections: none

Reference: *10.1021/jo802433t* AND *10.1021/ja01108a009*

Retrosynthesis ID: 5402

2.2.12 Synthesis of ketones from nitroalkenes

Substrates:

1. CC(C)[Si](c1nnn2c1C=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-
2)(C(C)C)C(C)C

Products:

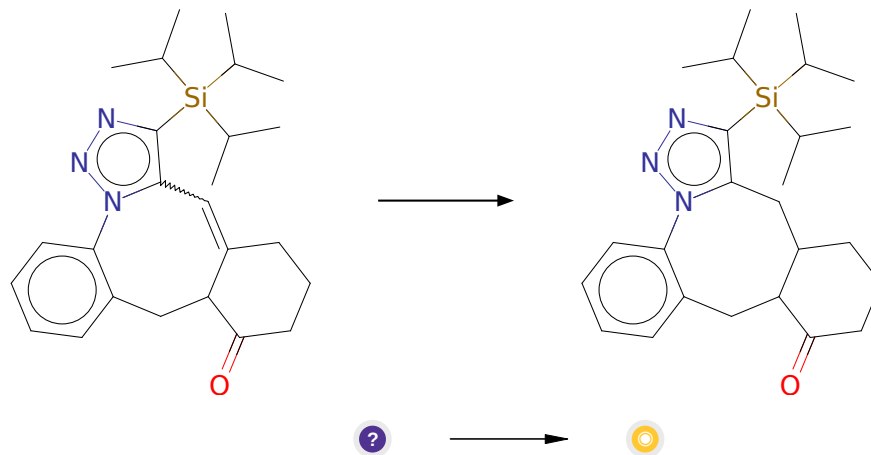1. CC(C)[Si](c1nnn2c1C=C1CCCC(=O)C1Cc1ccccc1-2)(C(C)C)C(C)C

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

2.2.13 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