

Paths of analysis*

A1

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

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

2.1 Path 1

Score: 16764486.08

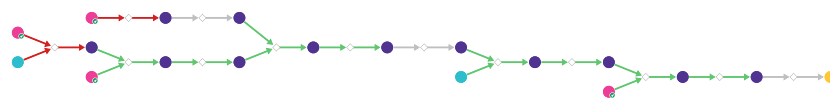
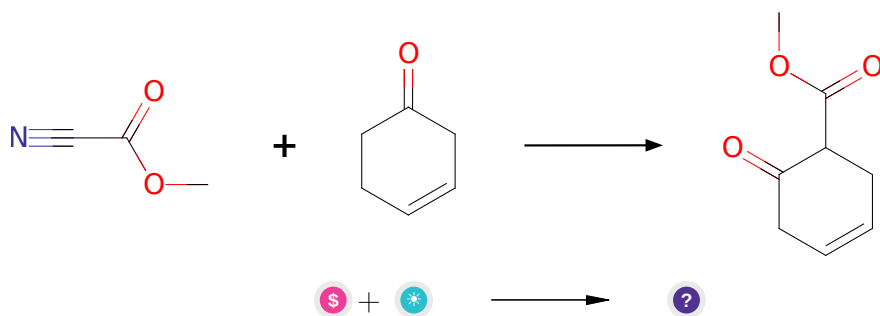


Figure 1: Outline of path 1

2.1.1 Mander methoxycarbonylation of ketones



Substrates:

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

Products:

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

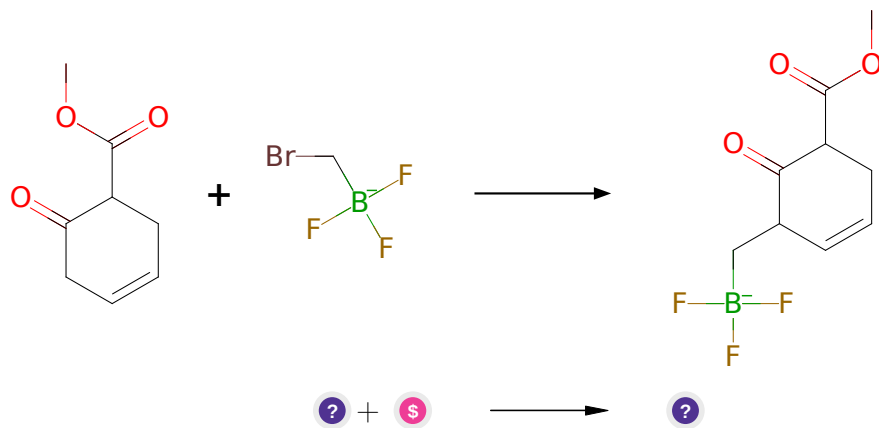
Typical conditions: 1) MeLi.Et₂O or THF 2) Methyl cyanoacetate. Et₂O or THF

Protections: none

Reference: DOI: [10.1016/s0040-4039\(00\)87886-7](https://doi.org/10.1016/s0040-4039(00)87886-7)

Retrosynthesis ID: 50436

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

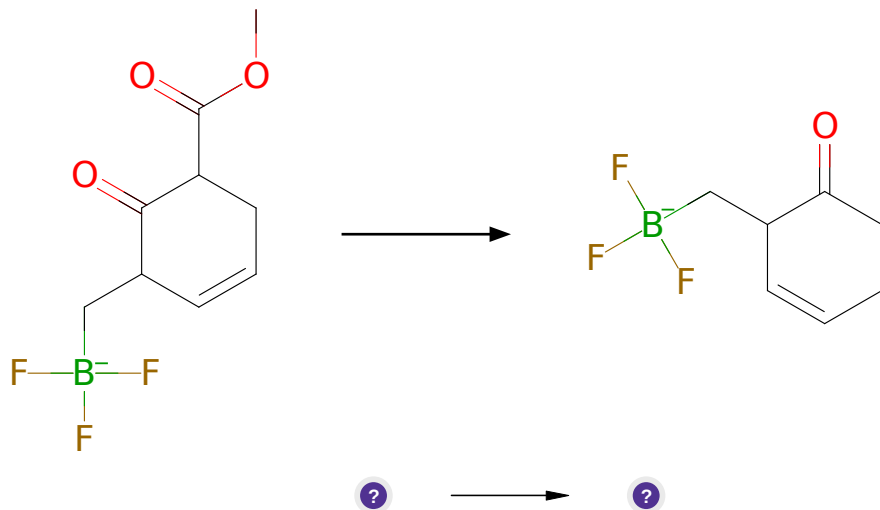
Typical conditions: LDA or other base.THF.-78C

Protections: none

Reference: DOI: [10.1021/ja0123554](https://doi.org/10.1021/ja0123554)

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

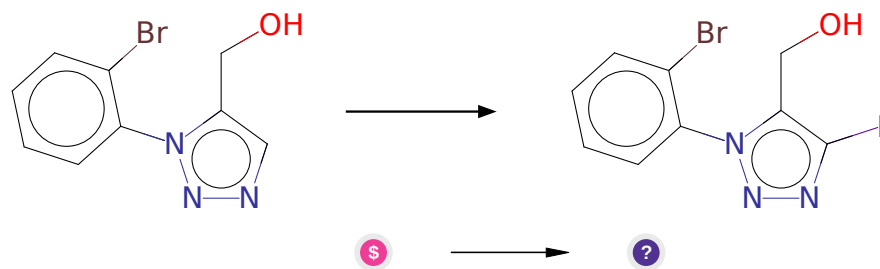
Reference:

[10.3998/ark.5550190.0008.201](#)
[10.3184/174751911X12964930076403](#)

and

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

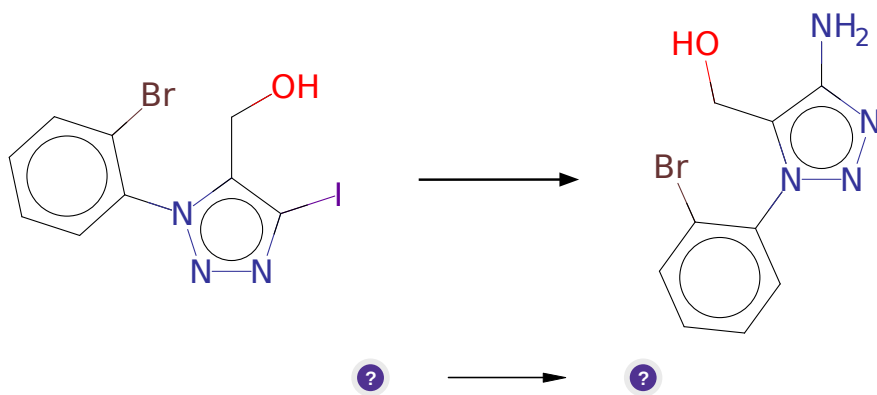
Typical conditions: I2 or other iodinating agent e.g. NIS

Protections: none

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

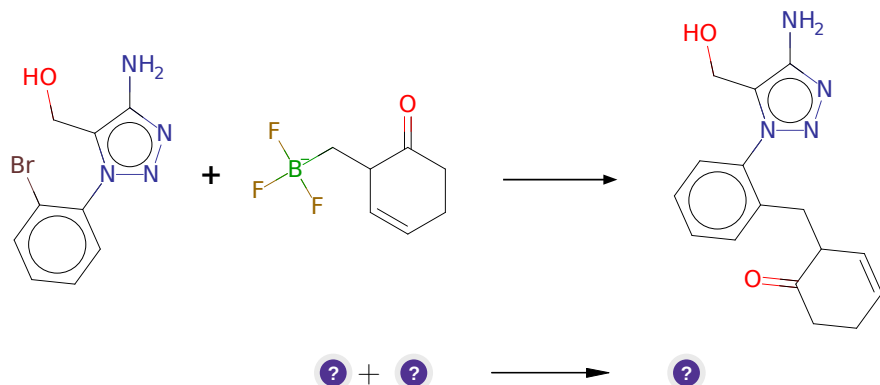
Typical conditions: Pd[(P(p-tol)3]2.NaOtBu.dioxane.heat

Protections: none

Reference: [10.1021/ja903049z](https://doi.org/10.1021/ja903049z) and [10.1021/jo9006738](https://doi.org/10.1021/jo9006738)

Retrosynthesis ID: 31016464

2.1.6 Suzuki Coupling of arylbromides and alkyltrifluoroborates



Substrates:

1. Nc1ncnc(c1Cc2ccccc2Br)CO
2. O=C1CCC=CC1C[B-](F)(F)F

Products:

1. Nc1ncnc(c1Cc2ccccc2CC2C=CCCC2=O)c1ccccc1

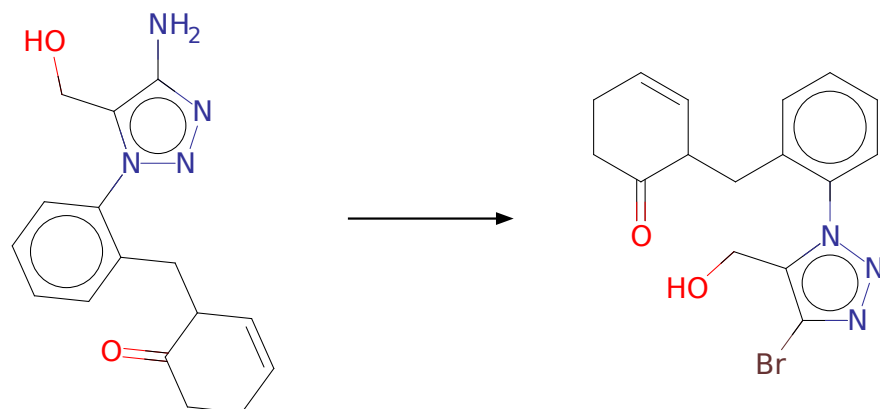
Typical conditions: Pd(OAc)₂.SPhos.K₃PO₄.H₂O.reflux

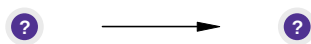
Protections: none

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

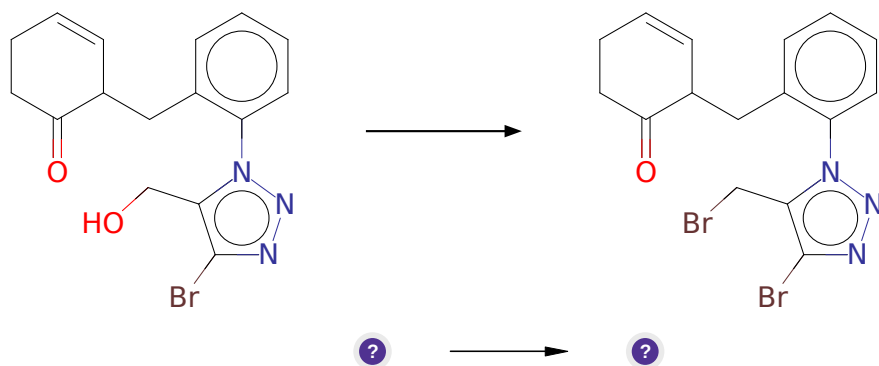
Typical conditions: IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

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

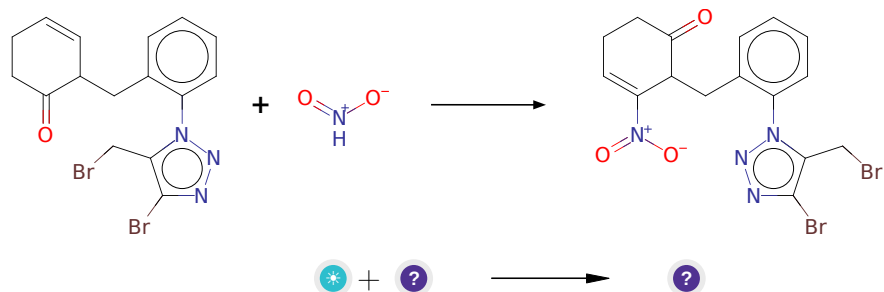
Typical conditions: PPh3.CBr4

Protections: none

Reference: [10.1021/ja800574m](#) and [10.1016/j.tet.2012.05.010](#) and [10.1016/j.tet.2004.09.021](#) (experimental)

Retrosynthesis ID: 9990037

2.1.9 Nitration of aliphatic olefins



Substrates:

1. HNO2
2. O=C1CCC=CC1Cc1cccc1-n1nnc(Br)c1CBr

Products:

1. O=C1CCC=C([N+](=O)[O-])C1Cc1cccc1-n1nnc(Br)c1CBr

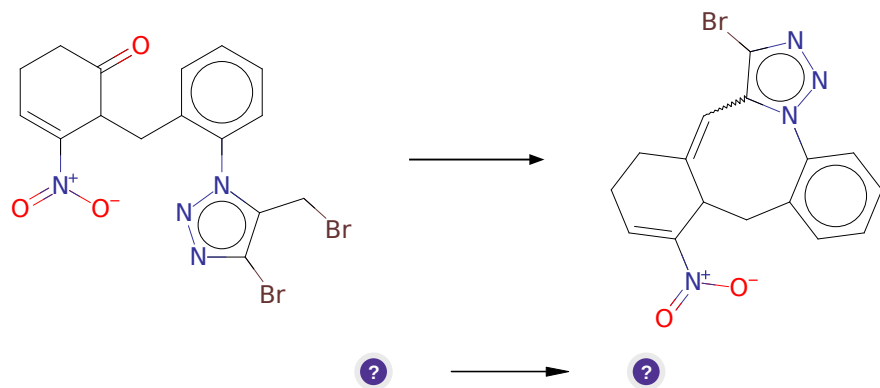
Typical conditions: Fe(NO2)3.9H2O.TEMPO.DCE.4A MS.80C

Protections: none

Reference: DOI: [10.1021/jo400598p](https://doi.org/10.1021/jo400598p)

Retrosynthesis ID: 1623

2.1.10 HWE/Wittig Olefination



Substrates:

1. O=C1CCC=C([N+](=O)[O-])C1Cc1cccc1-n1nnc(Br)c1CBr

Products:

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

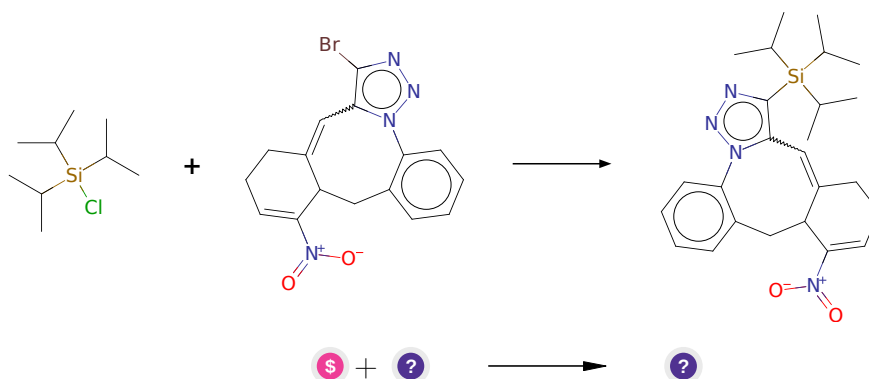
Typical conditions: 1.PPh₃ or trialkylphosphite.2.base.aldehyde

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

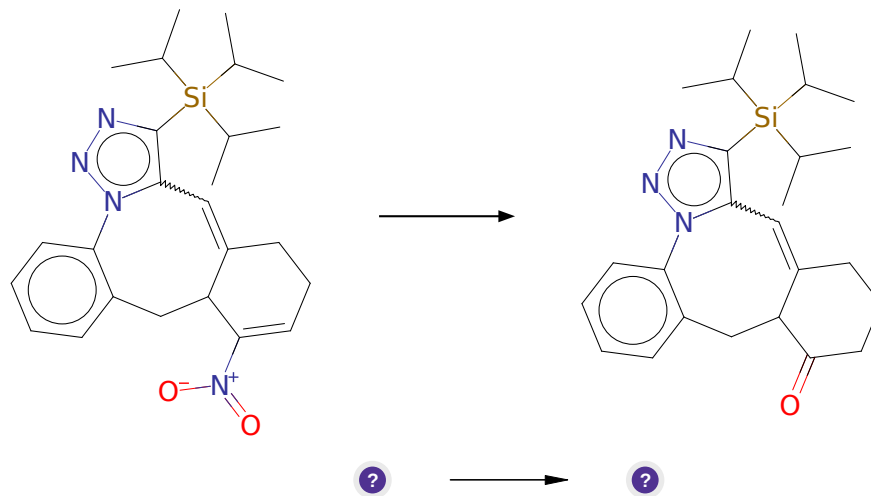
Typical conditions: 1.nBuLi.or.Mg.THF.-78C.2.Si-Cl.to.rt

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-])C1Cc1cccc1-2)(C(C)C)C(C)C

Products:

1. CC(C)[Si](c1nnn2c1C=C1CCCC(=O)C1Cc1cccc1-2)(C(C)C)C(C)C

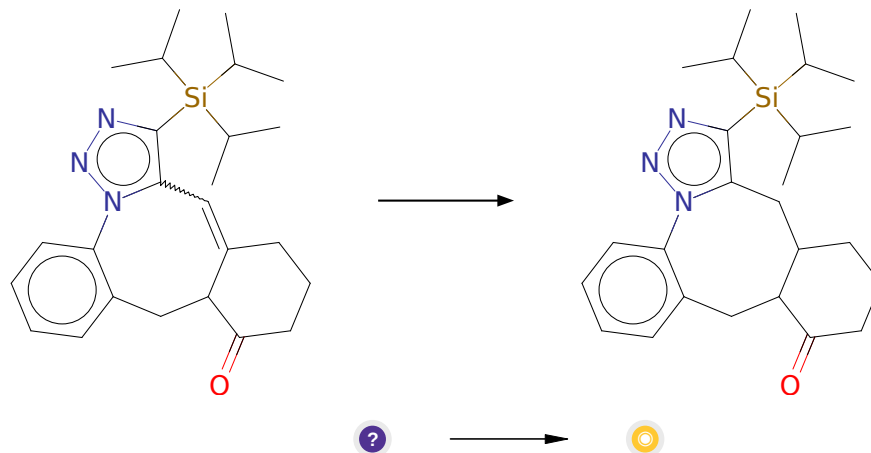
Typical conditions: RaNi.hypophosphite.EtOH.acetate.buffer or Fe.HCl.MeOH

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)C1Cc1cccc1-2)(C(C)C)C(C)C

Products:

1. CC(C)[Si](c1nnn2c1CC1CCCC(=O)C1Cc1cccc1-2)(C(C)C)C(C)C

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

Protections: none

Reference: DOI: [10.1021/jo980467g](https://doi.org/10.1021/jo980467g) and [10.1021/ja00175a039](https://doi.org/10.1021/ja00175a039) and [10.1021/ja0296733](https://doi.org/10.1021/ja0296733) and [10.1021/ja049043w](https://doi.org/10.1021/ja049043w) (page S-4) and [10.1021/jo980128n](https://doi.org/10.1021/jo980128n) and [10.1021/ja4029928](https://doi.org/10.1021/ja4029928) and Patent: WO2014/207205 A1, 2014 page 16

Retrosynthesis ID: 9995780

2.2 Path 2

Score: 16764486.08

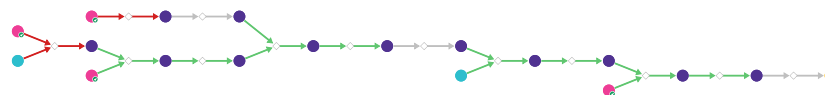
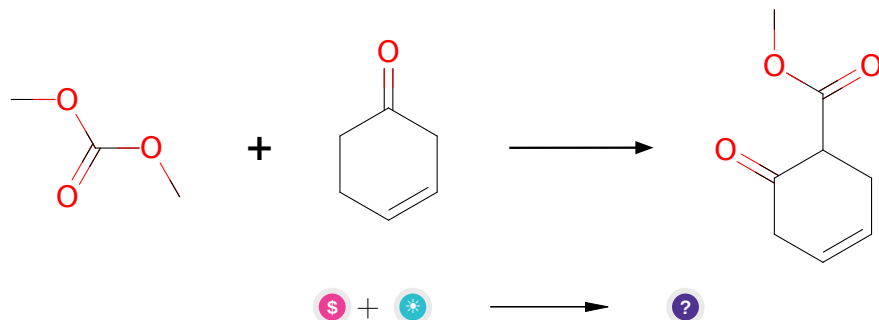


Figure 2: Outline of path 2

2.2.1 Carboethoxylation of enolates - Claisen condensation



Substrates:

1. dimethyl ester - *available at Sigma-Aldrich*
2. cyclohex-3-enone

Products:

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

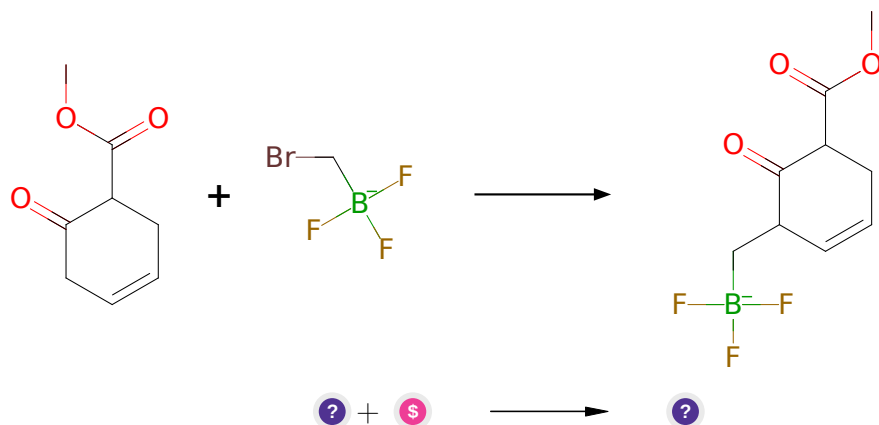
Typical conditions: NaH.THF

Protections: none

Reference: [10.1016/j.bmc.2011.06.055](#) AND [10.1021/ja01036a055](#) AND WO2010/48014 (amides,p.32) AND [10.1016/S0040-4020\(02\)00350-2](#) AND [10.1021/ol201243u](#) (Supporting information)

Retrosynthesis ID: 8167

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

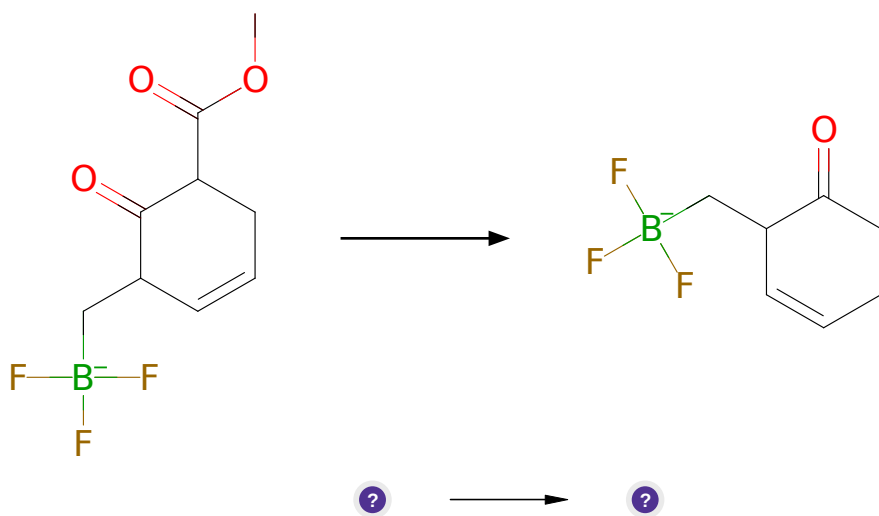
Typical conditions: LDA or other base.THF.-78C

Protections: none

Reference: DOI: [10.1021/ja0123554](https://doi.org/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

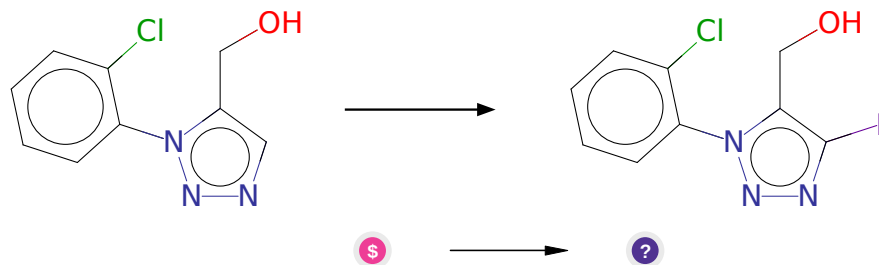
Typical conditions: LiCl.DMSO.150oC

Protections: none

Reference: [10.3998/ark.5550190.0008.201](https://doi.org/10.3998/ark.5550190.0008.201) and [10.3184/174751911X12964930076403](https://doi.org/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

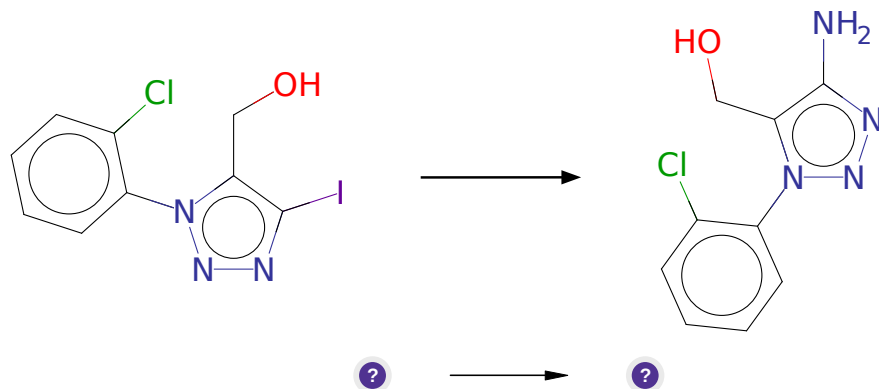
Typical conditions: I₂ or other iodinating agent e.g. NIS

Protections: none

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

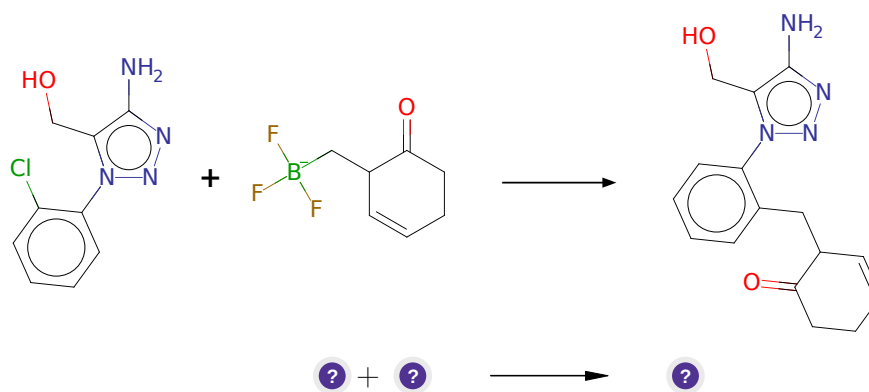
Typical conditions: Pd[(P(p-tol)3]2.NaOtBu.dioxane.heat

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

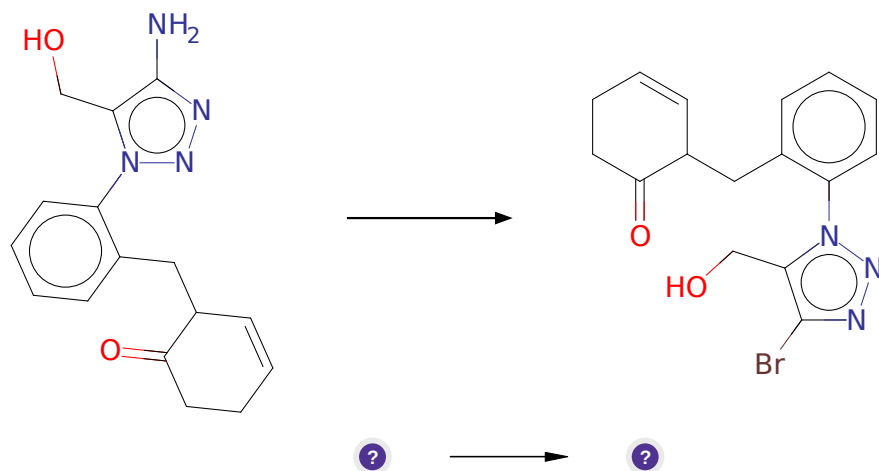
Typical conditions: Pd(OAc)2.RuPhos.CsCO3.toluene/H2O.90C

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

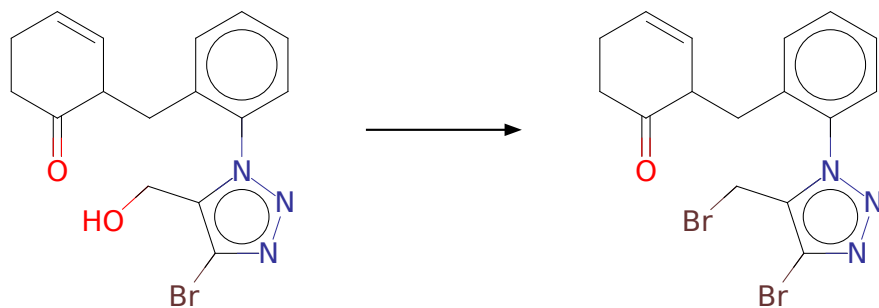
Typical conditions: IsoAmONO or t-BuONO.CuBr2.MeCN or HBr.CuBr2.NaNO2

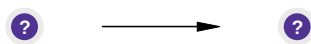
Protections: none

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

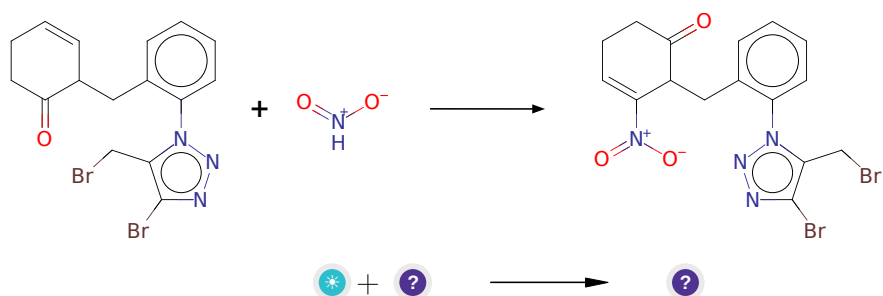
Typical conditions: PPh₃.CBr₄

Protections: none

Reference: [10.1021/ja800574m](https://doi.org/10.1021/ja800574m) and [10.1016/j.tet.2012.05.010](https://doi.org/10.1016/j.tet.2012.05.010) and [10.1016/j.tet.2004.09.021](https://doi.org/10.1016/j.tet.2004.09.021) (experimental)

Retrosynthesis ID: 9990037

2.2.9 Nitration of aliphatic olefins



Substrates:

1. HNO₂
2. O=C1CCC=C([N+](=O)[O-])C1Cc1ccccc1-n1nnc(Br)c1CBr

Products:

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

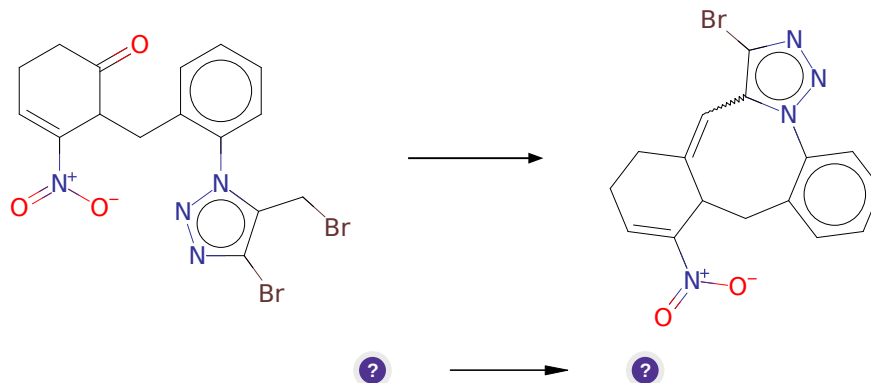
Typical conditions: Fe(NO₂)₃·9H₂O.TEMPO.DCE.4A MS.80C

Protections: none

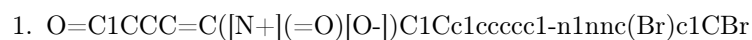
Reference: DOI: [10.1021/jo400598p](https://doi.org/10.1021/jo400598p)

Retrosynthesis ID: 1623

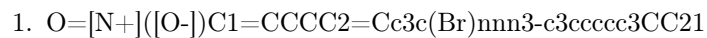
2.2.10 HWE/Wittig Olefination



Substrates:



Products:



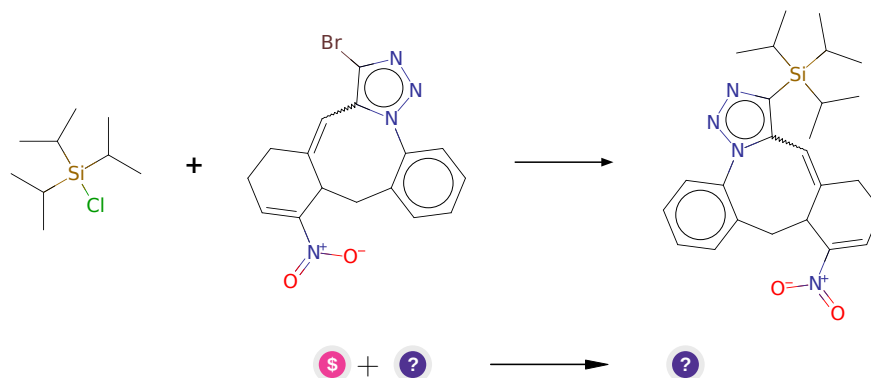
Typical conditions: 1. PPh₃ or trialkylphosphite. 2. base. aldehyde

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

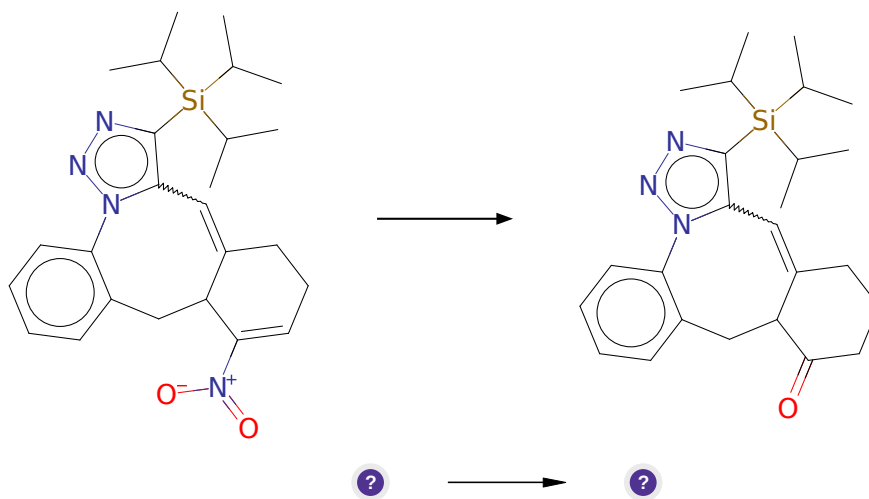
Typical conditions: 1.nBuLi.or.Mg.THF.-78C.2.Si-Cl.to.rt

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

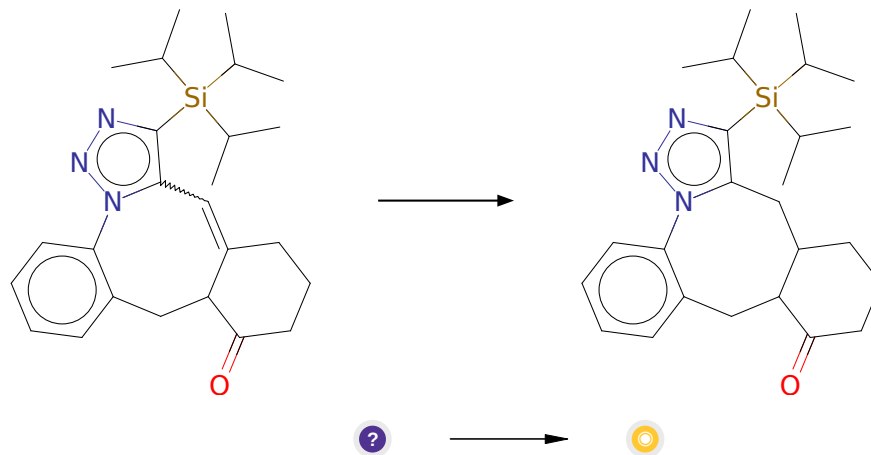
Typical conditions: RaNi.hypophosphite.EtOH.acetate.buffer or Fe.HCl.MeOH

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)C1Cc1cccc1-2)(C(C)C)C(C)C

Products:

1. CC(C)[Si](c1nnn2c1CC1CCCC(=O)C1Cc1cccc1-2)(C(C)C)C(C)C

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

Protections: none

Reference: DOI: [10.1021/jo980467g](https://doi.org/10.1021/jo980467g) and [10.1021/ja00175a039](https://doi.org/10.1021/ja00175a039) and [10.1021/ja0296733](https://doi.org/10.1021/ja0296733) and [10.1021/ja049043w](https://doi.org/10.1021/ja049043w) (page S-4) and [10.1021/jo980128n](https://doi.org/10.1021/jo980128n) and [10.1021/ja4029928](https://doi.org/10.1021/ja4029928) and Patent: WO2014/207205 A1, 2014 page 16

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