Paths of analysis*

Analysis 9

Synthia

March 3, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: FGI, FGI with protections

Max. paths returned: 5

Max. iterations: 300

Commercial:

1. Max. molecular weight - 1000 g/mol
2. Max. price - 1000 $/g

Published:

1. Max. molecular weight - 1000 g/mol
2. Popularity - 10

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

Strategies: none selected

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FGI 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: 115.34

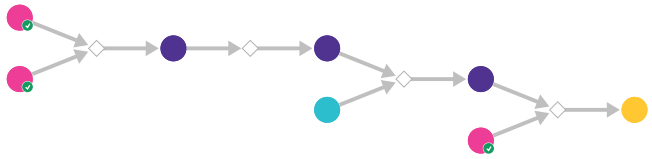
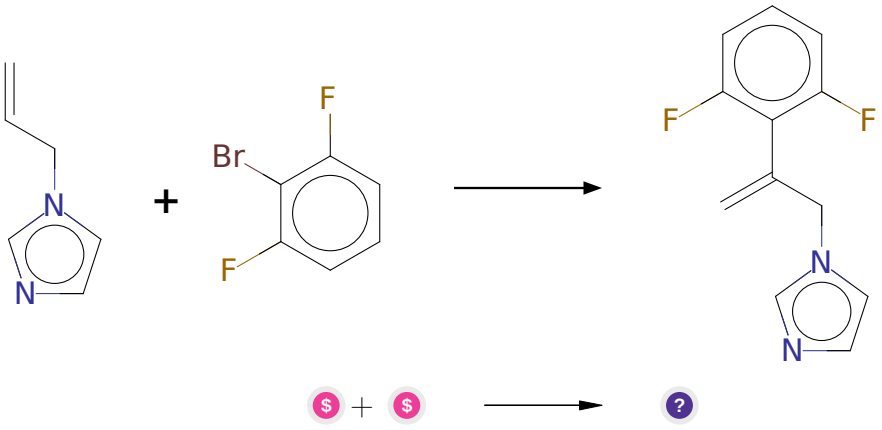


Figure 1: Outline of path 1

2.1.1 Heck Reaction



Substrates:

1. 1-Bromo-2,6-difluorobenzene - *available at Sigma-Aldrich*
2. 1-(prop-2-en-1-yl)-1H-imidazole - *available at Sigma-Aldrich*

Products:

1. C=C(Cn1ccnc1)c1c(F)cccc1F

Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

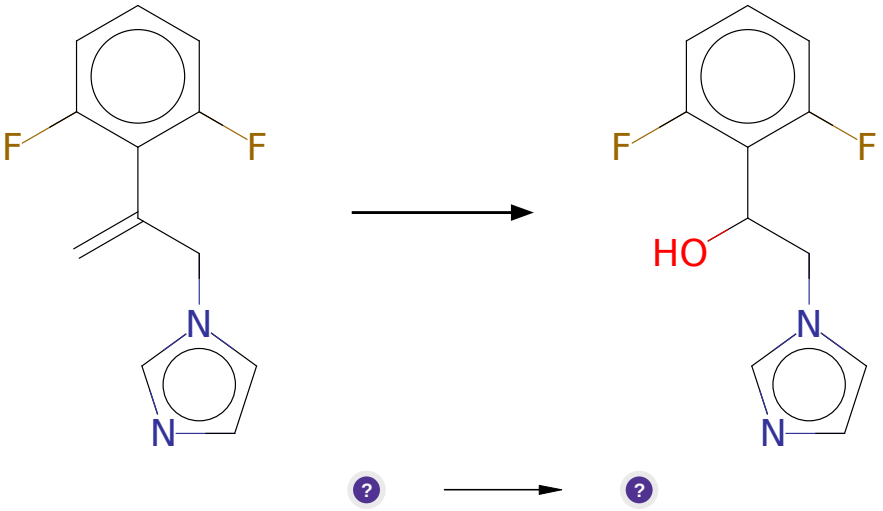
Protections: none

Yield: moderate

Reference: *10.1039/C3CC45911J* or *10.1021/ar00049a001* or *10.1002/anie.201201806* or *10.1002/9780470716076*

Retrosynthesis ID: 9266

2.1.2 Ozonolysis followed by reduction



Substrates:

1. C=C(Cn1ccnc1)c1c(F)cccc1F

Products:

1. OC(Cn1ccnc1)c1c(F)cccc1F

Typical conditions: O3.MeOH.CH2Cl2.NaBH4.low temperature

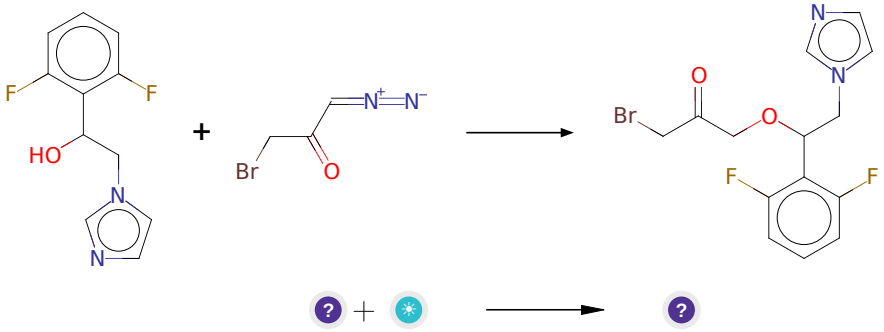
Protections: none

Yield: good

Reference: *10.1021/ja043506g*(SI,page S2) and *10.1016/j.jfluchem.2011.05.031* and *10.1021/ja304872j* and *10.1021/jo026004z*

Retrosynthesis ID: 28553

2.1.3 Alcoholysis of alpha-diazo compounds



Substrates:

1. OC(Cn1ccnc1)c1c(F)cccc1F
2. 1-bromo-3-diazo-propan-2-one

Products:

1. O=C(CBr)COC(Cn1ccnc1)c1c(F)cccc1F

Typical conditions: Rh2(OAc)4

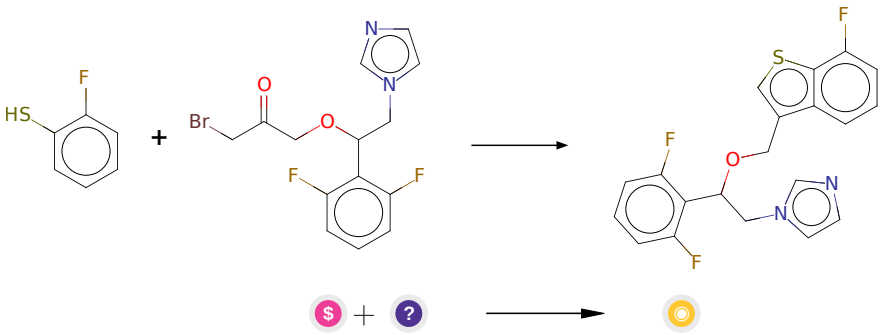
Protections: none

Yield: moderate

Reference: *10.1016/j.tetlet.2014.06.024* AND *10.1021/ja074729k* AND *10.1021/ja0607739* AND *10.1039/c4cc06395c*

Retrosynthesis ID: 15014

2.1.4 Synthesis of benzothiophenes from thiophenols



Substrates:

1. 2-Fluorothiophenol - *available at Sigma-Aldrich*

2. O=C(CBr)COC(Cn1ccnc1)c1c(F)cccc1F

Products:

1. Fc1cccc(F)c1C(Cn1ccnc1)OCc1csc2c(F)cccc12

Typical conditions: Na2CO3.SiO2.PPA.PhCl.135C

Protections: none

Yield: moderate

Reference: DOI: *10.1055/s-2005-918928*

Retrosynthesis ID: 295032

2.2 Path 2

Score: `150.64`

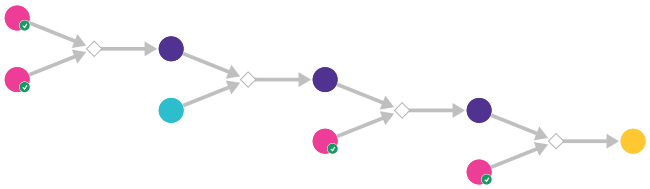
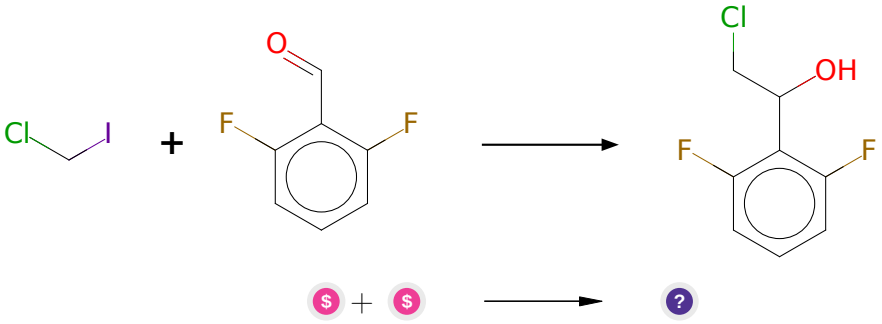


Figure 2: Outline of path 2

2.2.1 Addition of dihalomethane to aldehyde



Substrates:

1. Chloroiodomethane - *available at Sigma-Aldrich*

2. 2,6-Difluorobenzaldehyde - *available at Sigma-Aldrich*

Products:

1. OC(CCl)c1c(F)cccc1F

Typical conditions: SmI2.THF

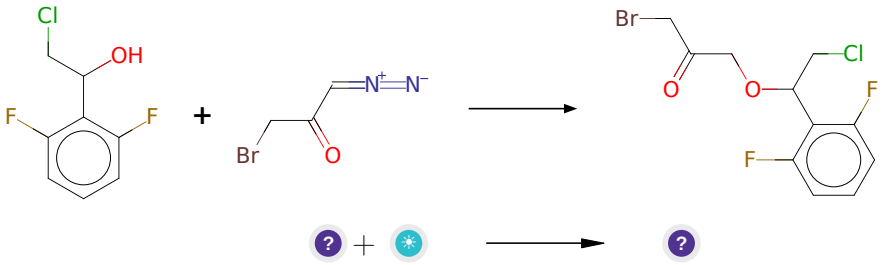
Protections: none

Yield: good

Reference: *10.1016/j.tet.2012.02.033* and *10.1016/j.tetlet.2005.02.093* and *10.1021/jo970318i*

Retrosynthesis ID: 25218

2.2.2 Alcoholysis of alpha-diazo compounds



Substrates:

1. OC(CCl)c1c(F)cccc1F
2. 1-bromo-3-diazo-propan-2-one

Products:

1. O=C(CBr)COC(CCl)c1c(F)cccc1F

Typical conditions: Rh2(OAc)4

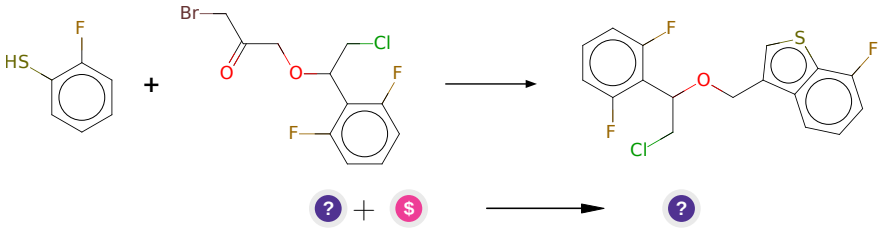
Protections: none

Yield: moderate

Reference: *10.1016/j.tetlet.2014.06.024* AND *10.1021/ja074729k* AND *10.1021/ja0607739* AND *10.1039/c4cc06395c*

Retrosynthesis ID: 15014

2.2.3 Synthesis of benzothiophenes from thiophenols



Substrates:

1. O=C(CBr)COC(CCl)c1c(F)cccc1F
2. 2-Fluorothiophenol - *available at Sigma-Aldrich*

Products:

1. Fc1cccc(F)c1C(CCl)OCc1csc2c(F)cccc12

Typical conditions: Na2CO3.SiO2.PPA.PhCl.135C

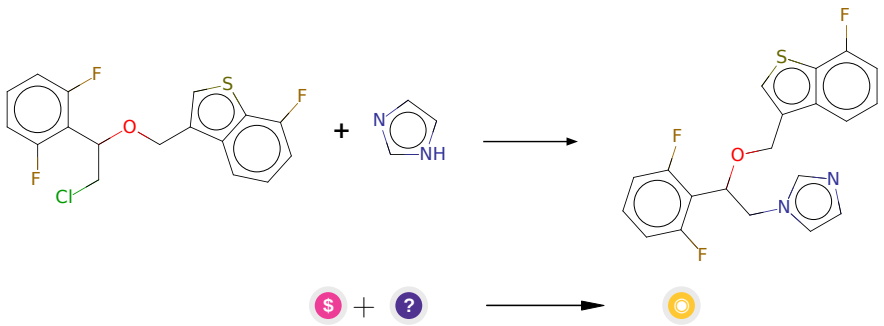
Protections: none

Yield: moderate

Reference: DOI: *10.1055/s-2005-918928*

Retrosynthesis ID: 295032

2.2.4 N-alkylation of Heterocycles



Substrates:

1. Imidazole - *available at Sigma-Aldrich*
2. Fc1cccc(F)c1C(CCl)OCc1csc2c(F)cccc12

Products:

1. Fc1cccc(F)c1C(Cn1ccnc1)OCc1csc2c(F)cccc12

Typical conditions: NaH.DMF

Protections: none

Yield: good

Reference: *10.1021/ol503625z* and *10.1081/SCC-120022467* (experimental) and *10.1021/ol2018328* (SI, p.5) and *10.1021/jo8026565* (SI, p.2)

Retrosynthesis ID: 28538

2.3 Path 3

Score: `151.05`

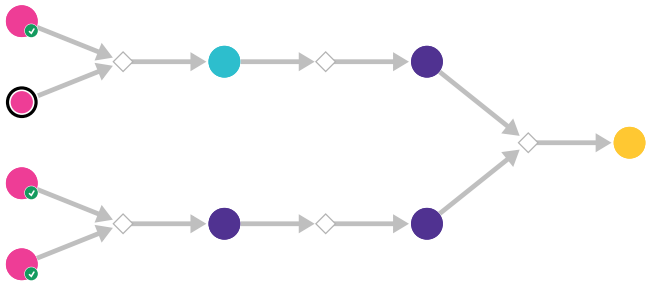
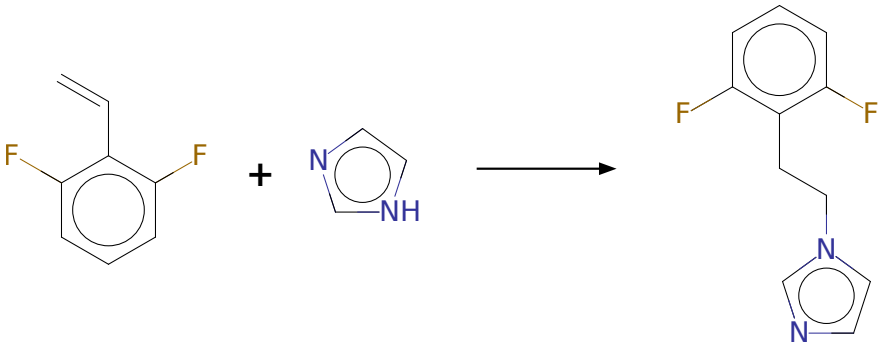
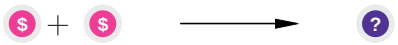


Figure 3: Outline of path 3

2.3.1 Catalytic Photoredox Anti-Markovnikov Alkene Hydroamination





Substrates:

1. 2,6-Difluorostyrene - *available at Sigma-Aldrich*
2. Imidazole - *available at Sigma-Aldrich*

Products:

1. Fc1cccc(F)c1CCn1ccnc1

Typical conditions: 9-mesityl-10-methylacridinium-perchlorate.Phenyl.Disulfide.2,6-Lutidine.DCM.Blue.Light.RT

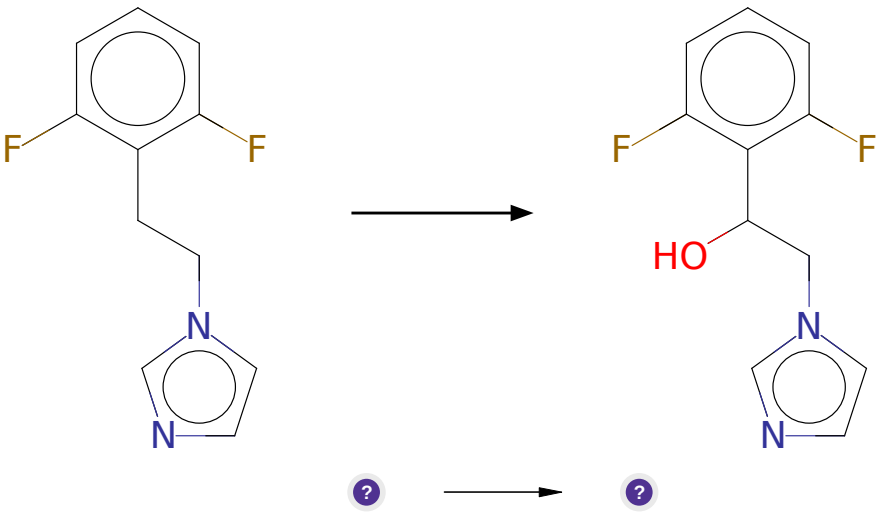
Protections: none

Yield: good

Reference: *10.1002/anie.201402443*

Retrosynthesis ID: 10032751

2.3.2 Hydroxylation of benzylic position



Substrates:

1. Fc1cccc(F)c1CCn1ccnc1

Products:

1. OC(Cn1ccnc1)c1c(F)cccc1F

Typical conditions: 1.Ce(OTf)4.MeCN.2.NaBH4

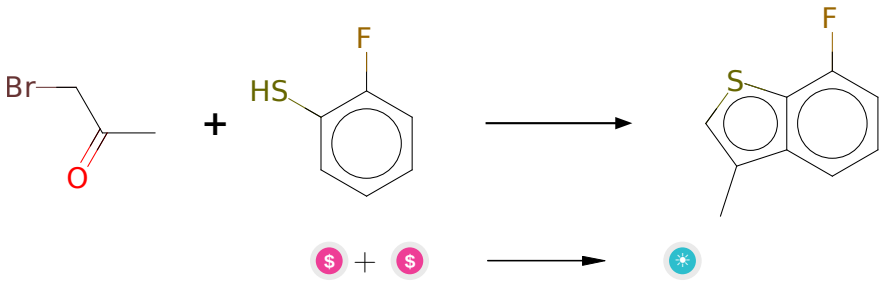
Protections: none

Yield: moderate

Reference: *10.1039/B008843I* and WO2012137047 p.12

Retrosynthesis ID: 27140

2.3.3 Synthesis of benzothiophenes from thiophenols



Substrates:

1. 2-Fluorothiophenol - *available at Sigma-Aldrich*
2. brom-aceton - *AstaTech*

Products:

1. 7-fluoro-3-methyl-benzo[b]thiophene

Typical conditions: Na2CO3.SiO2.PPA.PhCl.135C

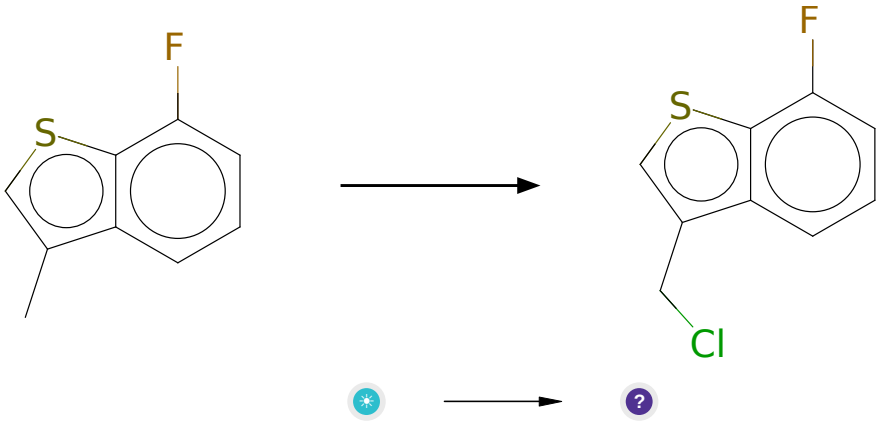
Protections: none

Yield: good

Reference: DOI: *10.1055/s-2005-918928*

Retrosynthesis ID: 295032

2.3.4 Chlorination of benzylic position



Substrates:

1. 7-fluoro-3-methyl-benzo[b]thiophene

Products:

1. Fc1cccc2c(CCl)csc12

Typical conditions: SOCl2.AIBN or NCS/SiCl4 or [BnNMe3]ICl4.AIBN

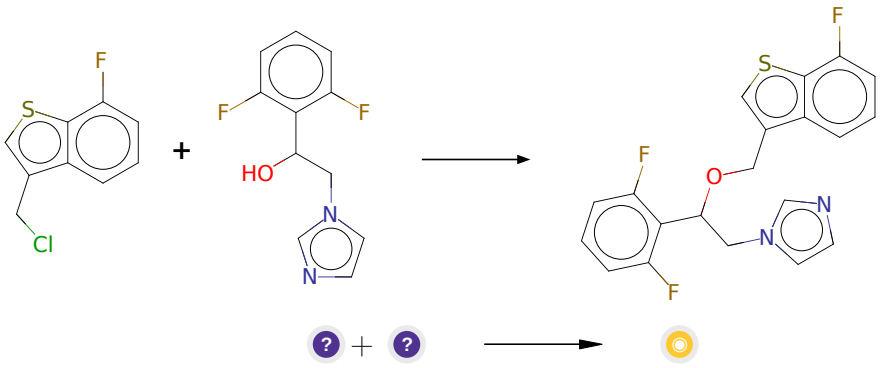
Protections: none

Yield: good

Reference: *10.1039/B803741H* and *10.1016/S0040-4039(00)82191-7* and *10.1016/j.tetlet.2011.05.135*

Retrosynthesis ID: 10001786

2.3.5 Alkylation of secondary alcohols



Substrates:

1. Fc1cccc2c(CCl)csc12
2. OC(Cn1ccnc1)c1c(F)cccc1F

Products:

1. Fc1cccc(F)c1C(Cn1ccnc1)OCc1csc2c(F)cccc12

Typical conditions: K2CO3.acetone.heat

Protections: none

Yield: moderate

Reference: *10.1016/S0022-1139(00)85021-6* and

Retrosynthesis ID: 31011106