Paths of analysis*

Analysis 10

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: 166.33

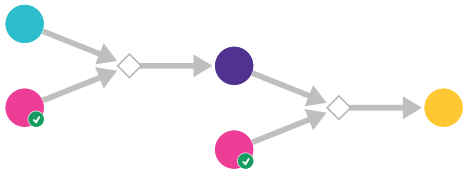
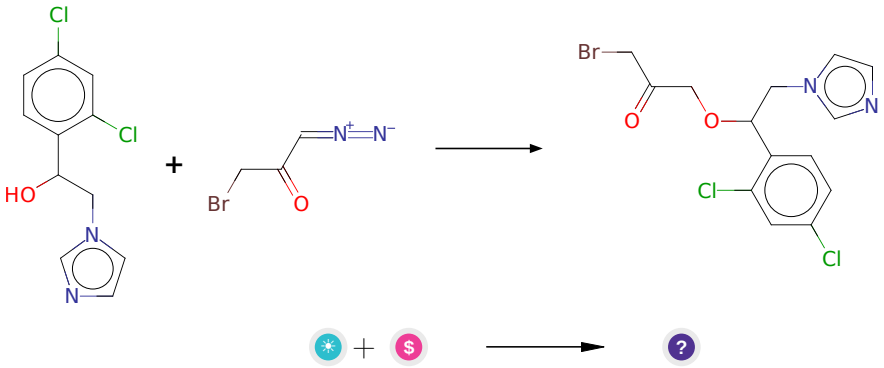


Figure 1: Outline of path 1

2.1.1 Alcoholysis of alpha-diazo compounds



Substrates:

1. 1-bromo-3-diazo-propan-2-one
2. 1-(2,4-dichloro-phenyl)-2-imidazol-1-yl-ethanol - *available at Sigma-Aldrich*

Products:

1. O=C(CBr)COC(Cn1ccnc1)c1ccc(Cl)cc1Cl

Typical conditions: Rh2(OAc)4

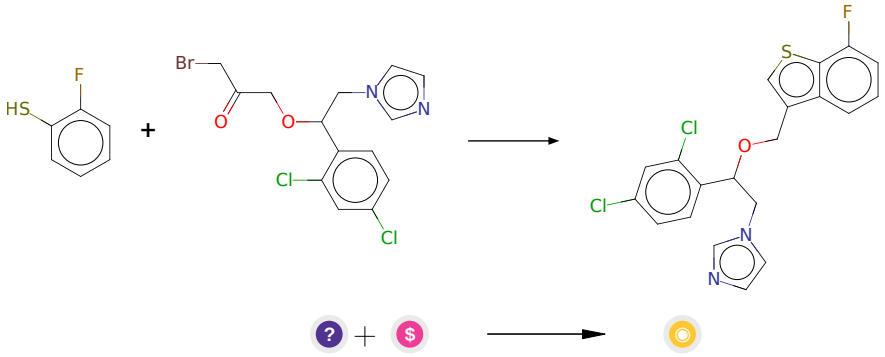
Protections: none

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

2.1.2 Synthesis of benzothiophenes from thiophenols



Substrates:

1. O=C(CBr)COC(Cn1ccnc1)c1ccc(Cl)cc1Cl
2. 2-Fluorothiophenol - *available at Sigma-Aldrich*

Products:

1. 1-[2-(2,4-dichloro-phenyl)-2-(7-fluoro-benzo[b]thiophen-3-ylmethoxy)-ethyl]-1h-imidazole

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: `167.71`

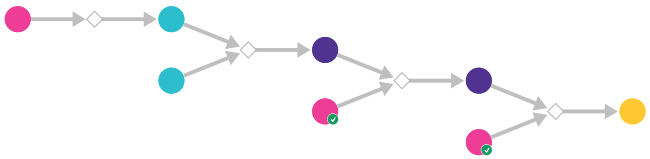
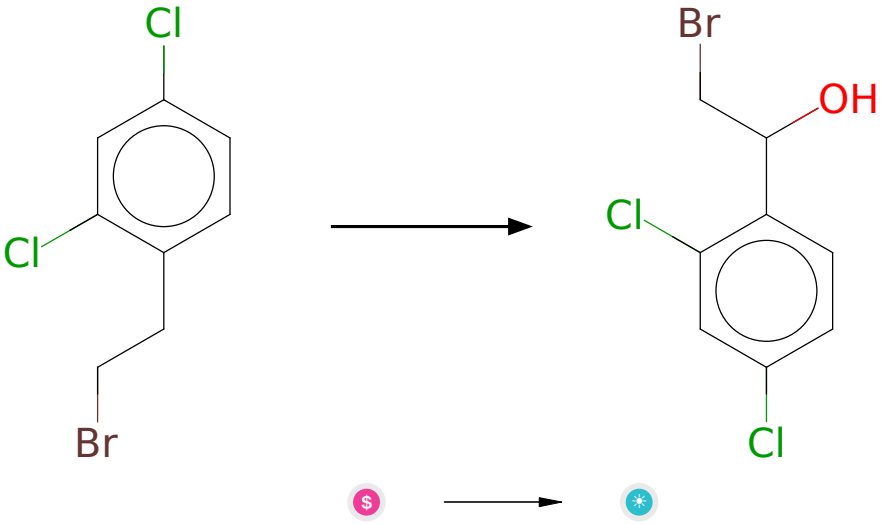


Figure 2: Outline of path 2

2.2.1 Hydroxylation of benzylic position



Substrates:

1. 2,4-Dichlorophenethyl bromide - *Combi-Blocks*

Products:

1. 2-bromo-1-(2,4-dichloro-phenyl)-ethanol

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

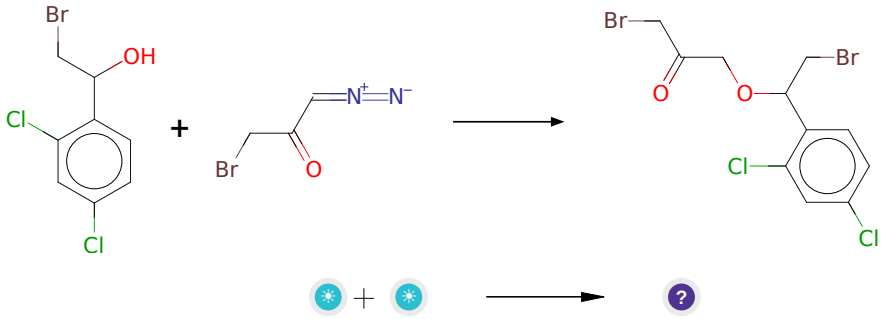
Protections: none

Yield: moderate

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

Retrosynthesis ID: 27140

2.2.2 Alcoholysis of alpha-diazo compounds



Substrates:

1. 1-bromo-3-diazo-propan-2-one
2. 2-bromo-1-(2,4-dichloro-phenyl)-ethanol

Products:

1. O=C(CBr)COC(CBr)c1ccc(Cl)cc1Cl

Typical conditions: Rh2(OAc)4

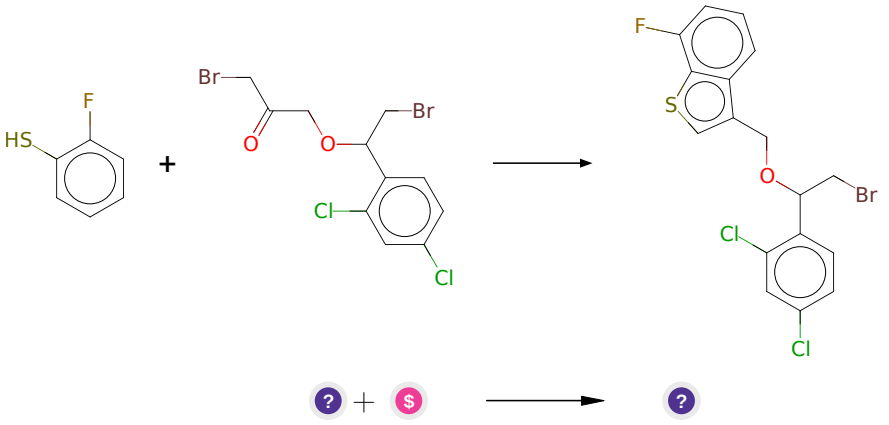
Protections: none

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(CBr)c1ccc(Cl)cc1Cl
2. 2-Fluorothiophenol - *available at Sigma-Aldrich*

Products:

1. Fc1cccc2c(COC(CBr)c3ccc(Cl)cc3Cl)csc12

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

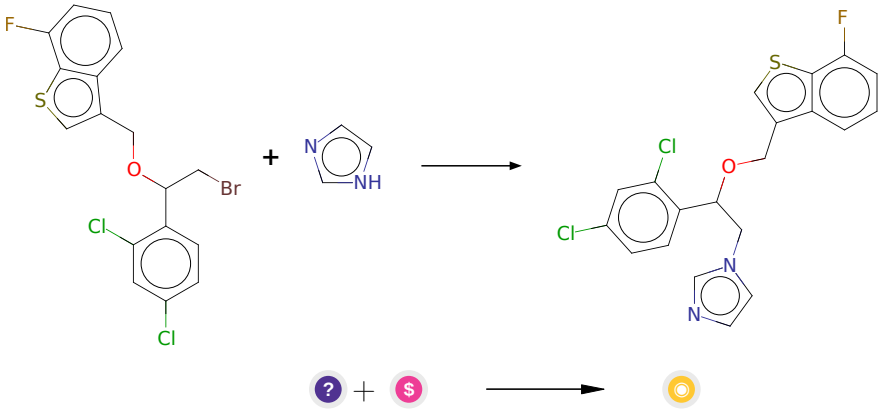
Protections: none

Yield: moderate

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

Retrosynthesis ID: 295032

2.2.4 N-alkylation of heterocycles



Substrates:

1. Fc1cccc2c(COC(CBr)c3ccc(Cl)cc3Cl)csc12
2. Imidazole - *available at Sigma-Aldrich*

Products:

1. 1-[2-(2,4-dichloro-phenyl)-2-(7-fluoro-benzo[b]thiophen-3-ylmethoxy)-ethyl]-1h-imidazole

Typical conditions: NaH. DMF

Protections: none

Yield: good

Reference: *10.1016/j.ejmech.2010.11.014* or *10.1039/C6OB01149G* (SI) or *10.1246/cl.2005.442* or *10.1021/ol403570z* (SI) or *10.1016/S0040-4020(01)00360-X*

Retrosynthesis ID: 10000414

2.3 Path 3

Score: `169.46`

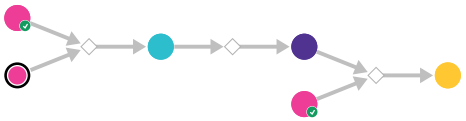
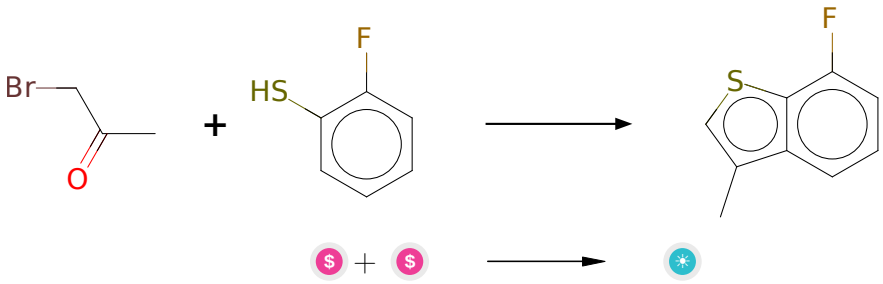


Figure 3: Outline of path 3

2.3.1 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

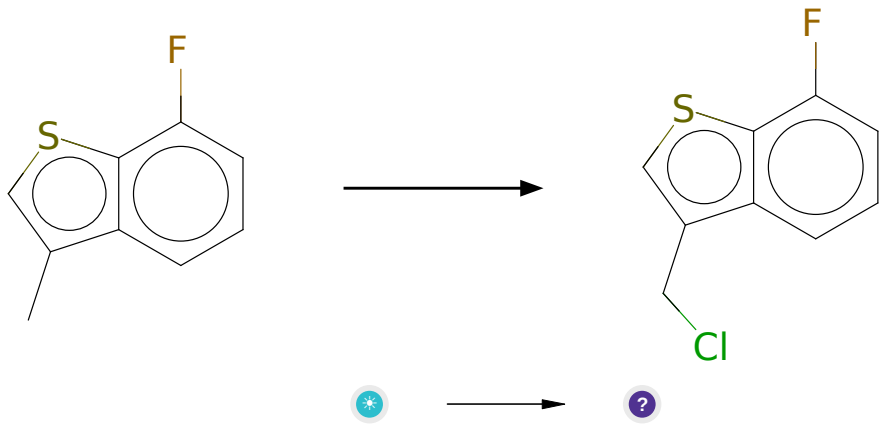
Protections: none

Yield: good

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

Retrosynthesis ID: 295032

2.3.2 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

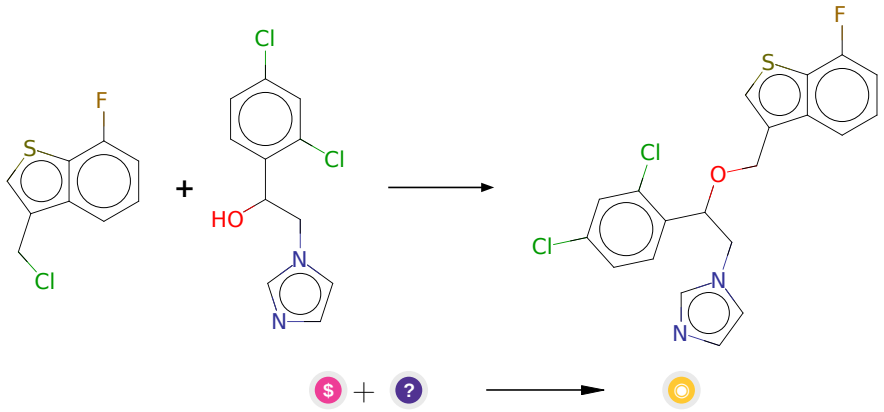
Protections: none

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

2.3.3 Alkylation of secondary alcohols



Substrates:

1. 1-(2,4-dichloro-phenyl)-2-imidazol-1-yl-ethanol - *available at Sigma-Aldrich*
2. Fc1cccc2c(CCl)csc12

Products:

1. 1-[2-(2,4-dichloro-phenyl)-2-(7-fluoro-benzo[b]thiophen-3-ylmethoxy)-ethyl]-1h-imidazole

Typical conditions: K2CO3.acetone.heat

Protections: none

Yield: moderate

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

Retrosynthesis ID: 31011106