Paths of analysis*

Analysis 5

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

*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.

FGI 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: 128.72

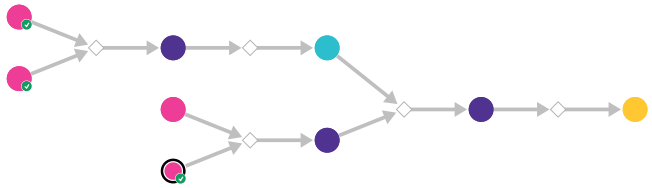
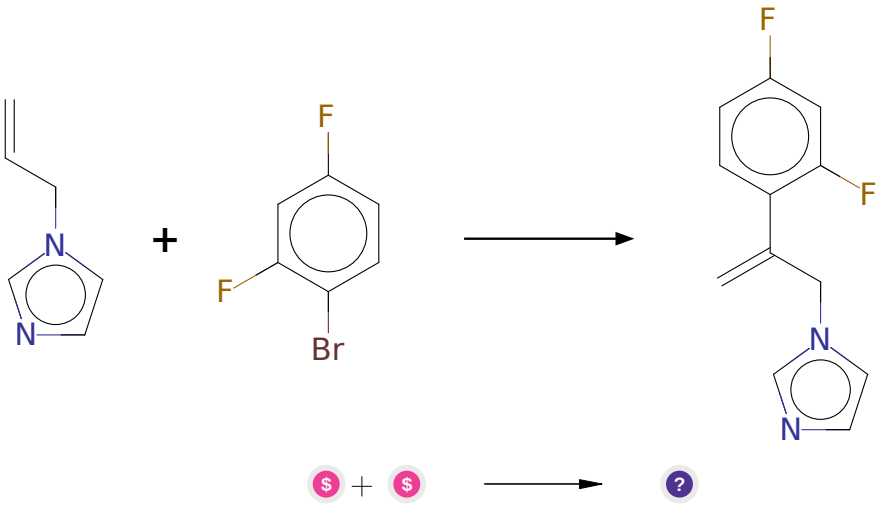


Figure 1: Outline of path 1

2.1.1 Heck Reaction



Substrates:

1. 1-(prop-2-en-1-yl)-1H-imidazole - *available at Sigma-Aldrich*
2. 1-Bromo-2,4-difluorobenzene - *available at Sigma-Aldrich*

Products:

1. C=C(Cn1ccnc1)c1ccc(F)cc1F

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

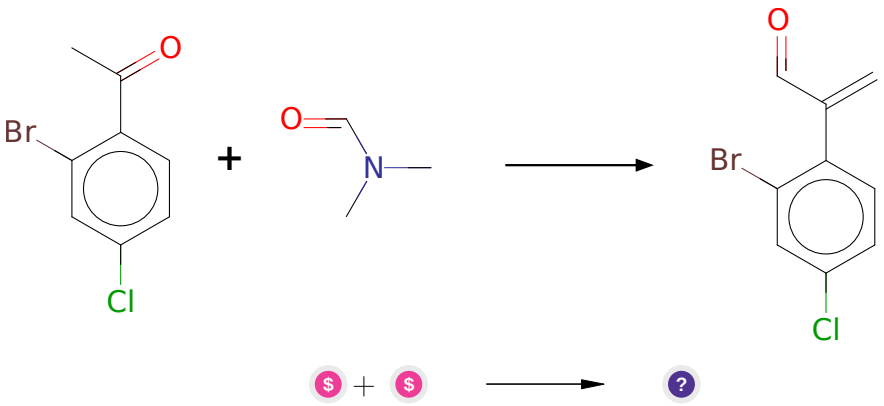
Protections: none

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 Shapiro reaction followed by DMF addition



Substrates:

1. 1-(2-Bromo-4-chlorophenyl)ethanone - *Combi-Blocks*
2. Dimethylformamide - *available at Sigma-Aldrich*

Products:

1. C=C(C=O)c1ccc(Cl)cc1Br

Typical conditions: 1.TsNH2NH2.2.Mes2Mg.LiCl.THF.heating then DMF.3.NaBH4

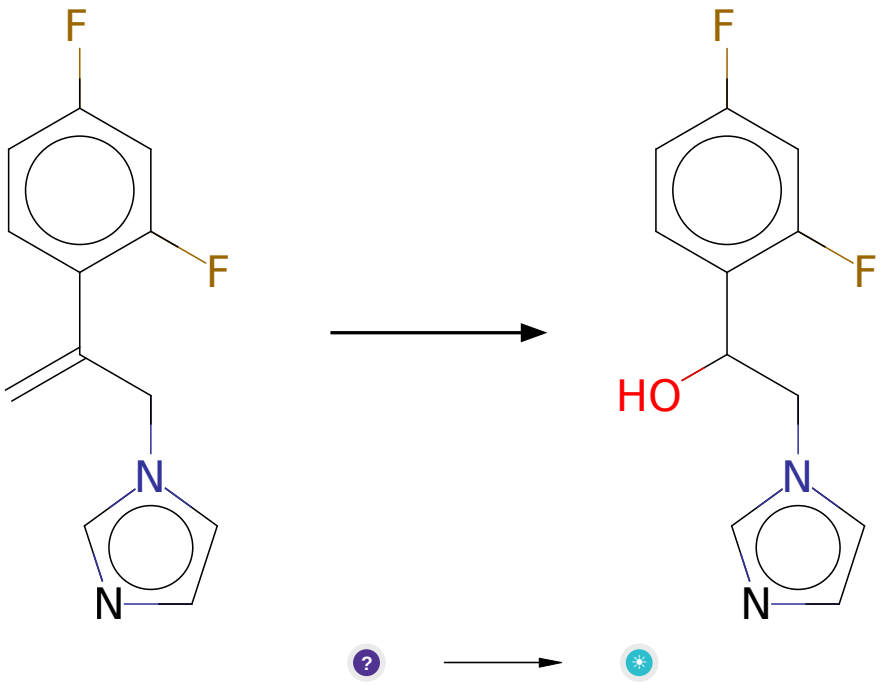
Protections: none

Yield: moderate

Reference: *10.1021/jo901926z* and *10.1021/ol300652k*

Retrosynthesis ID: 9990436

2.1.3 Ozonolysis followed by reduction



Substrates:

1. C=C(Cn1ccnc1)c1ccc(F)cc1F

Products:

1. 1-(2,4-difluorophenyl)-2-(1h-imidazol-1-yl)ethan-1-ol

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

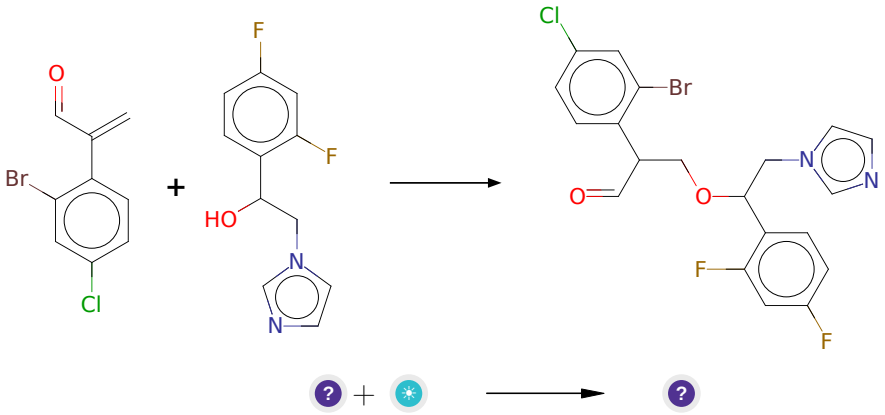
Protections: none

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

2.1.4 Michael reaction



Substrates:

1. C=C(C=O)c1ccc(Cl)cc1Br
2. 1-(2,4-difluorophenyl)-2-(1h-imidazol-1-yl)ethan-1-ol

Products:

1. O=CC(COC(Cn1ccnc1)c1ccc(F)cc1F)c1ccc(Cl)cc1Br

Typical conditions: Base.Solvent:EtOH.t-BuOH.THF.MeCN

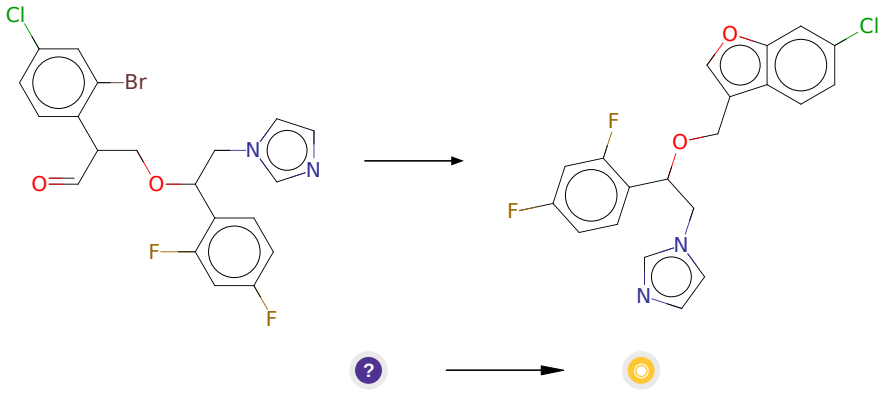
Protections: none

Yield: moderate

Reference: *10.1039/C1CY00334H* and *10.1002/ajoc.201700609*

Retrosynthesis ID: 50503

2.1.5 CuI-catalyzed synthesis of benzofurans



Substrates:

1. O=CC(COC(Cn1ccnc1)c1ccc(F)cc1F)c1ccc(Cl)cc1Br

Products:

1. Fc1ccc(C(Cn2ccnc2)OCc2coc3cc(Cl)ccc23)c(F)c1

Typical conditions: CuI.DMF.DABCO.105C

Protections: none

Yield: moderate

Reference: DOI: *10.1021/jo050788+*

Retrosynthesis ID: 50735

2.2 Path 2

Score: `161.03`

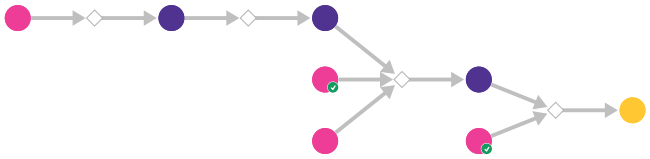
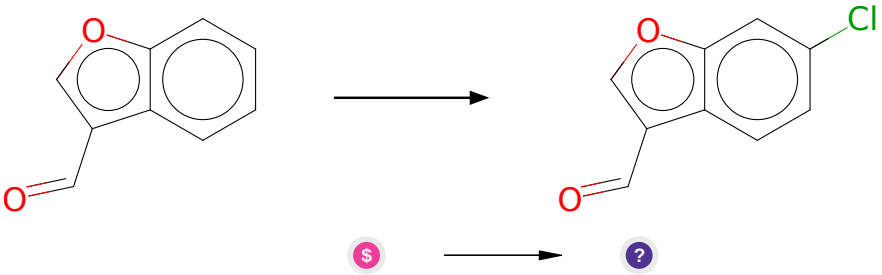


Figure 2: Outline of path 2

2.2.1 Chlorination of aromatic compounds



Substrates:

1. Benzofuran-3-carbaldehyde - *Combi-Blocks*

Products:

1. O=Cc1coc2cc(Cl)ccc12

Typical conditions: Cl2 or other chlorinating agent like NCS

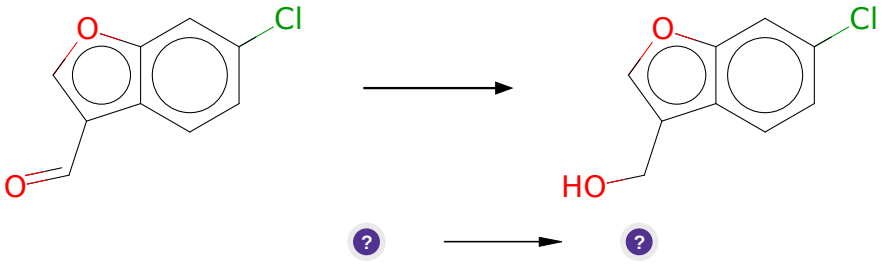
Protections: none

Yield: moderate

Reference: DOI: *10.1007/s11178-005-0256-1*

Retrosynthesis ID: 11125

2.2.2 Reduction of aldehydes with NaBH4



Substrates:

1. O=Cc1coc2cc(Cl)ccc12

Products:

1. OCc1coc2cc(Cl)ccc12

Typical conditions: NaBH4.MeOH

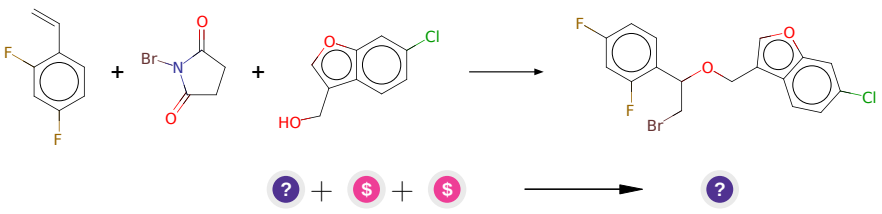
Protections: none

Yield: good

Reference: *10.1016/j.ejmech.2012.07.010* p. 126, 128 and *10.1016/j.bmc.2006.04.038* p. 5565, 5571

Retrosynthesis ID: 50431

2.2.3 Synthesis of bromo and chloroalkoxyalkanes



Substrates:

1. OCc1coc2cc(Cl)ccc12
2. N-Bromosuccinimide - *available at Sigma-Aldrich*
3. 2,4-Difluoro-1-vinylbenzene - *Combi-Blocks*

Products:

1. Fc1ccc(C(CBr)OCc2coc3cc(Cl)ccc23)c(F)c1

Typical conditions: NBS(NCS).alcohol

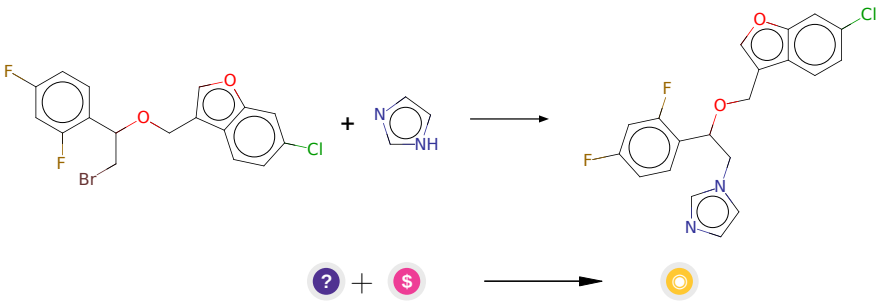
Protections: none

Yield: moderate

Reference: *10.1002/chem.200390180* and *10.1055/s-0037-1611277*

Retrosynthesis ID: 245562

2.2.4 N-alkylation of heterocycles



Substrates:

1. Fc1ccc(C(CBr)OCc2coc3cc(Cl)ccc23)c(F)c1
2. Imidazole - *available at Sigma-Aldrich*

Products:

1. Fc1ccc(C(Cn2ccnc2)OCc2coc3cc(Cl)ccc23)c(F)c1

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