Paths of analysis*

Analysis 6

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

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

2.1 Path 1

Score: `119.12`

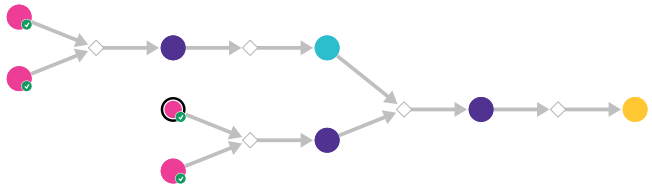
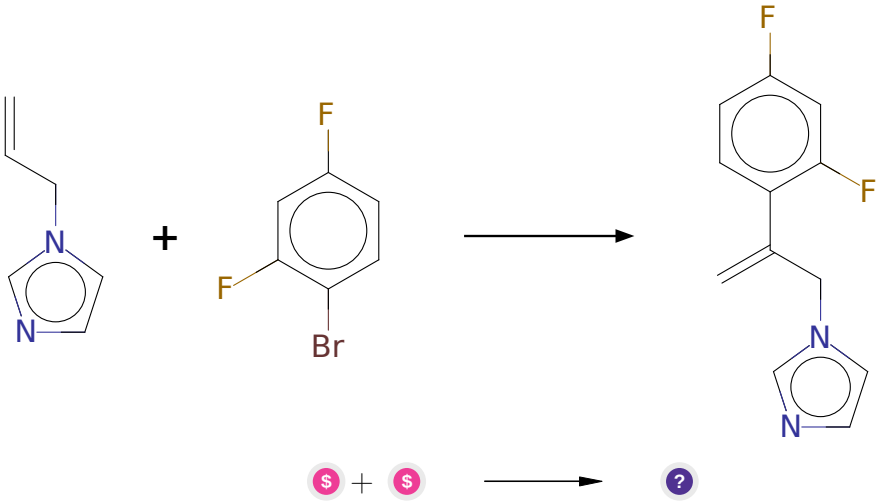


Figure 1: Outline of path 1

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

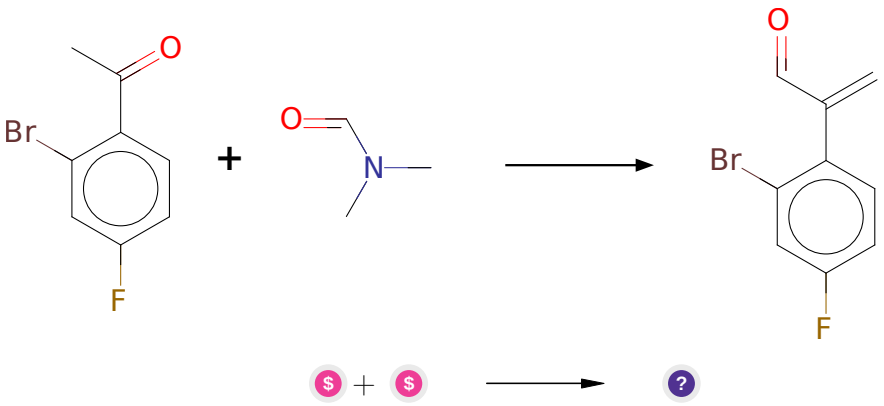
Protections: none

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. Dimethylformamide - *available at Sigma-Aldrich*
2. 1-(2-Bromo-4-fluorophenyl)ethanone - *available at Sigma-Aldrich*

Products:

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

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

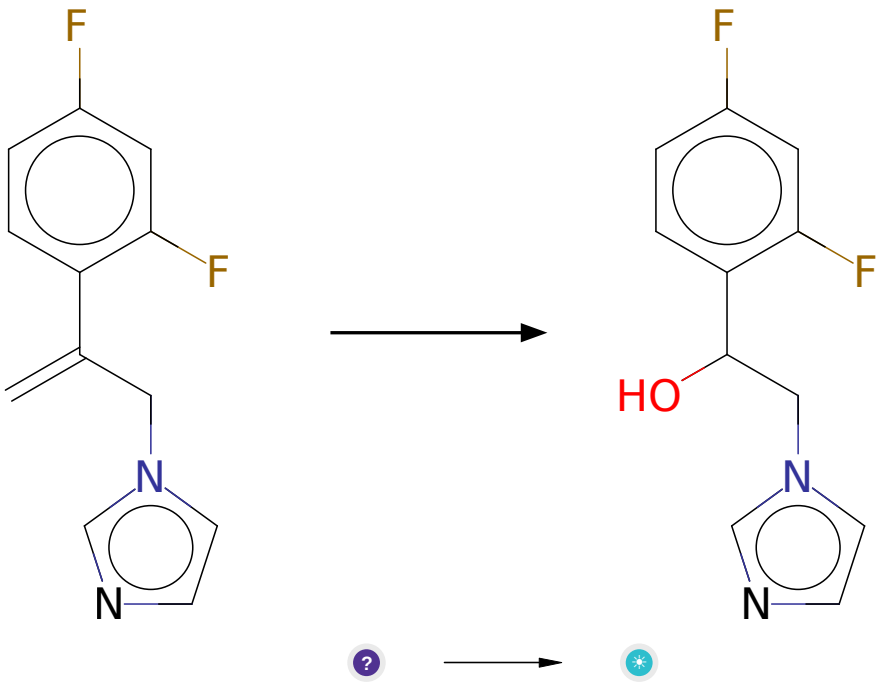
Protections: none

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

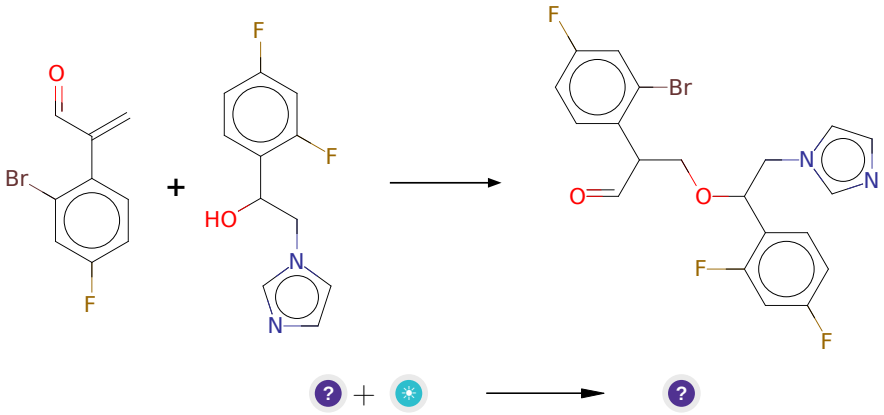
Protections: none

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(F)cc1Br
2. 1-(2,4-difluorophenyl)-2-(1h-imidazol-1-yl)ethan-1-ol

Products:

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

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

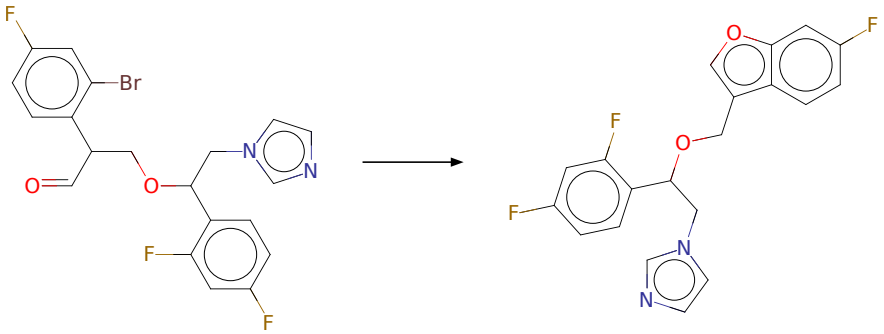
Protections: none

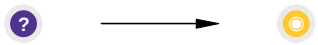
Yield: moderate

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

Retrosynthesis ID: 50503

2.1.5 Synthesis of Benzofurans via CuI-cat. Ring Closure





Substrates:

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

Products:

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

Typical conditions: CuI.DMF.K2PO4.heat

Protections: none

Yield: moderate

Reference: DOI: *10.1021/jo050788+*

Retrosynthesis ID: 10737

2.2 Path 2

Score: 202.80

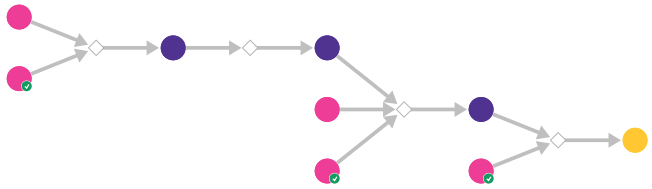
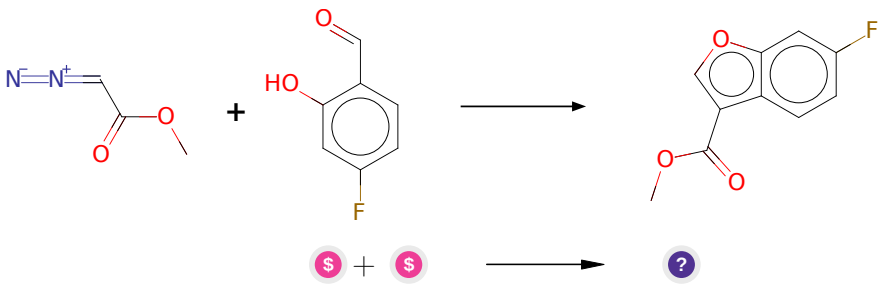


Figure 2: Outline of path 2

2.2.1 Synthesis of benzofurans from diazoacetates



Substrates:

1. 4-Fluorosalicylaldehyde - *Combi-Blocks*
2. methyl 2-diazoacetate - *available at Sigma-Aldrich*

Products:

1. COC(=O)c1coc2cc(F)ccc12

Typical conditions: HBF4.DCM then H2SO4

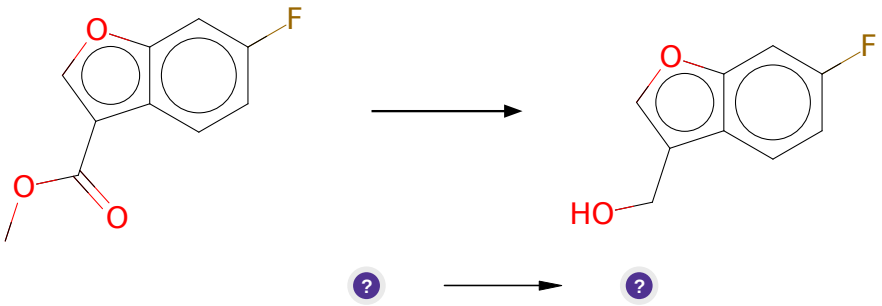
Protections: none

Yield: good

Reference: *10.1002/0471264229.os086.18* and *10.1134/S1070428013060134* and *10.1021/acs.orglett.6b03801*

Retrosynthesis ID: 9995187

2.2.2 Esters reduction with LAH



Substrates:

1. COC(=O)c1coc2cc(F)ccc12

Products:

1. OCc1coc2cc(F)ccc12

Typical conditions: LiAlH4.THF.0-20 C

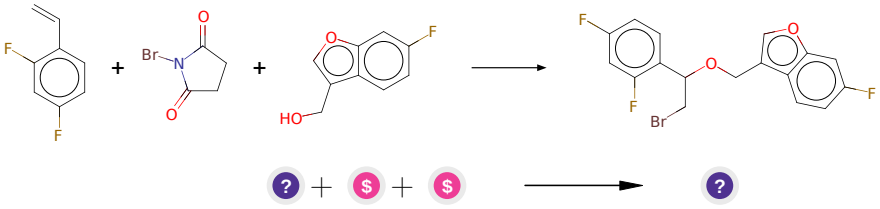
Protections: none

Yield: moderate

Reference: *10.1016/j.ejmech.2019.112011* p. 5, 10 and *10.1016/j.ejmech.2020.112910* p. 3, 7

Retrosynthesis ID: 9910006

2.2.3 Synthesis of bromo and chloroalkoxyalkanes



Substrates:

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

Products:

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

Typical conditions: NBS(NCS).alcohol

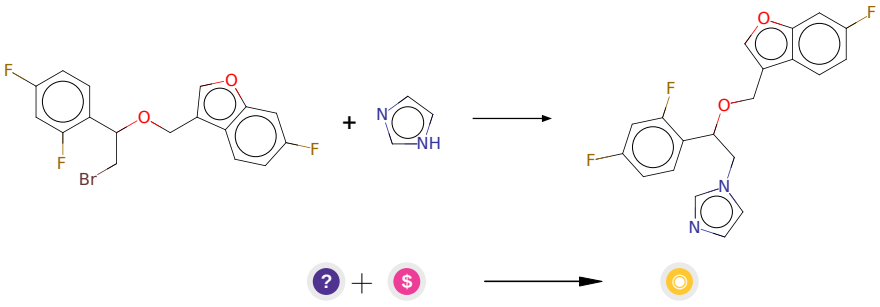
Protections: none

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(F)ccc23)c(F)c1
2. Imidazole - *available at Sigma-Aldrich*

Products:

1. Fc1ccc(C(Cn2ccnc2)OCc2coc3cc(F)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