

Paths of analysis*

BMK3

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: $TUNNEL_COEF * FGI_COEF * STEP * 20 + 1000 * (CONFLICT + NON_SELECTIVITY + FILTERS + PROTECT)$

Chemical scoring formula: $SMALLER^3, SMALLER^{1.5}$

Min. search width: 400

Max. reactions per product: 60

*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.

Strategies: none selected

FGI Coeff: 0

Tunnels Coeff: 0

JSON Parameters: {}

2 Paths

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

2.1 Path 1

Score: 87.50

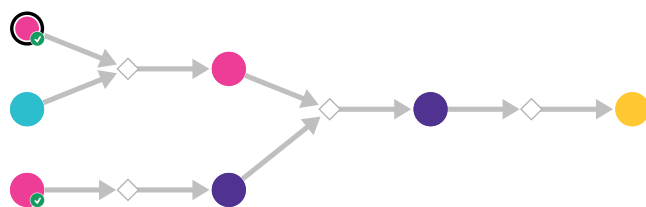
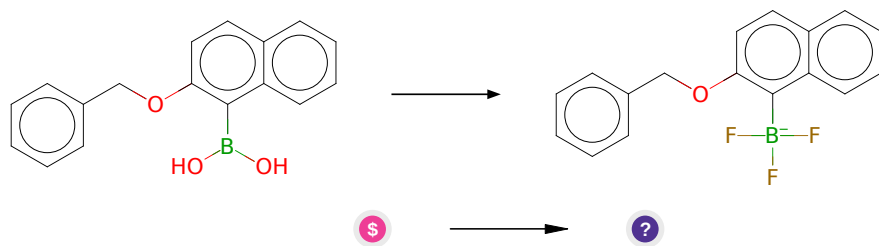


Figure 1: Outline of path 1

2.1.1 Synthesis of aromatic trifluoroborates from boronic acids



Substrates:

1. (2-(Benzyloxy)naphthalen-1-yl)boronic acid - *available at Sigma-Aldrich*

Products:

1. F[B-](F)(F)c1c(OCc2ccccc2)ccc2ccccc12

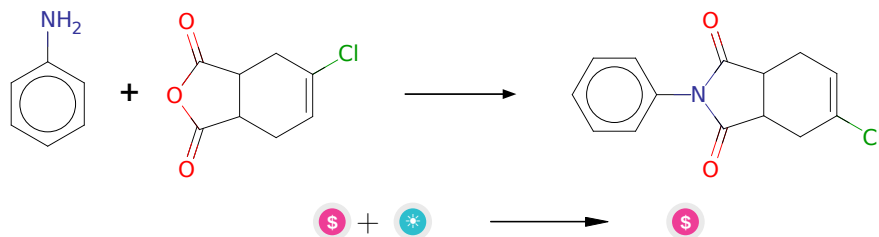
Typical conditions: H₂O.MeOH.KHF₂

Protections: none

Reference: DOI: [10.1021/jo00115a016](https://doi.org/10.1021/jo00115a016)

Retrosynthesis ID: 1282

2.1.2 Synthesis of imides from anhydrides



Substrates:

1. Aniline - [available at Sigma-Aldrich](#)
2. 4-chloro-1,2,3,6-tetrahydro-phthalic anhydride

Products:

1. 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - [Vitas-MLaboratory](#)

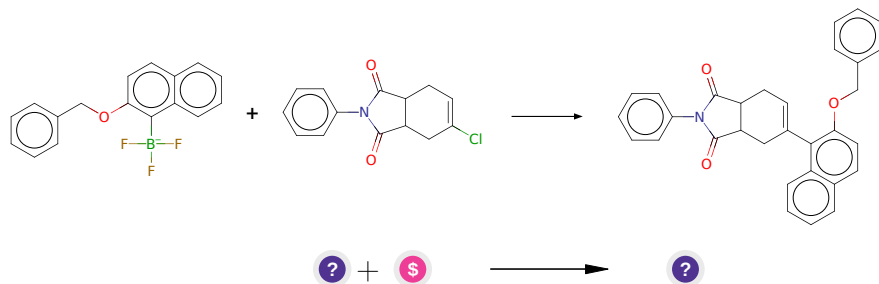
Typical conditions: AcOH

Protections: none

Reference: [10.1080/00397910802474966](https://doi.org/10.1080/00397910802474966) and [10.1021/ja9024676](https://doi.org/10.1021/ja9024676) (SI) and [10.1002/ejoc.201402202](https://doi.org/10.1002/ejoc.201402202)

Retrosynthesis ID: 8178

2.1.3 Suzuki Coupling of aryltrifluoroborates with alkenyl chlorides



Substrates:

1. F[B-](F)(F)c1c(OCc2ccccc2)ccc2ccccc12
2. 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *Vitas-MLaboratory*

Products:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

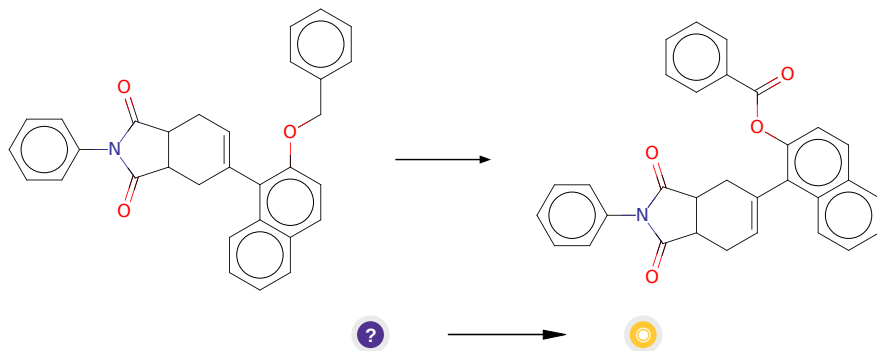
Typical conditions: PdCl₂(dppf).K₂CO₃.toluene.reflux

Protections: none

Reference: [10.1002/chem.200900425](#) and [10.1016/j.tetlet.2014.10.078](#)

Retrosynthesis ID: 10034105

2.1.4 Benzylic oxidation



Substrates:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

Products:

1. O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: Oxidant eg. O₂ or K₂S₂O₈ or HIO₄.solvent

Protections: none

Reference: [10.1039/B404823G](#) and [10.1055/s-0036-1588429](#)
and [10.1016/j.tetlet.2010.09.021](#) and [10.1002/chem.201604750](#) and
[10.1016/j.apcata.2014.01.042](#) and [10.1039/c3nj00045a](#) and [10.1021/jacs.6b08305](#)

Retrosynthesis ID: 31019416

2.2 Path 2

Score: 87.50

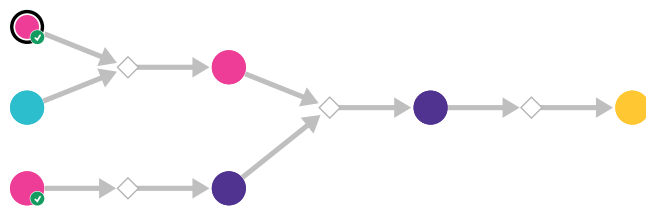
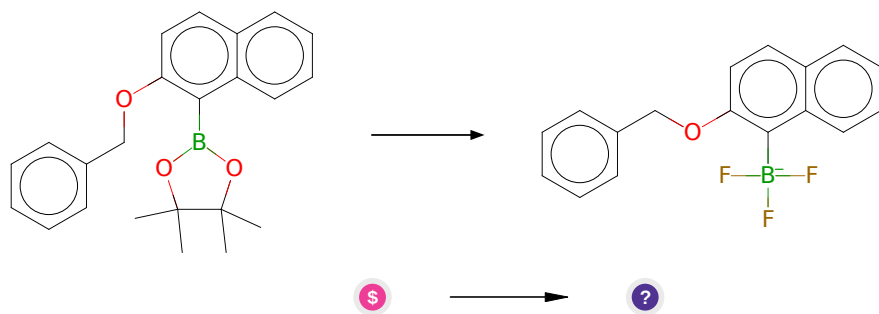


Figure 2: Outline of path 2

2.2.1 Synthesis of organotrifluoroborate salts in mild conditions



Substrates:

- 2-(2-(Benzyloxy)naphthalen-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane
- *available at Sigma-Aldrich*

Products:

- F[B-](F)(F)c1c(OCc2ccccc2)ccc2ccccc12

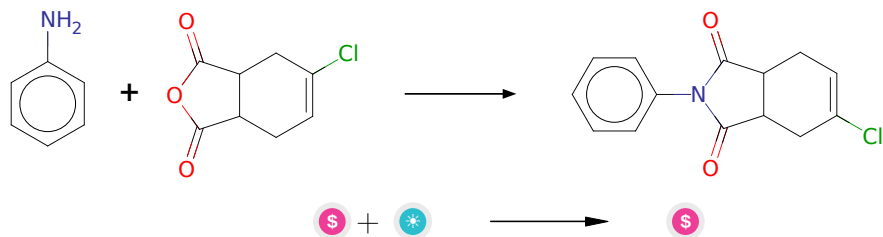
Typical conditions: KF.tartaric acid.CH₃CN.THF.H₂O.rt

Protections: none

Reference: DOI: [10.1002/anie.201203930](https://doi.org/10.1002/anie.201203930)

Retrosynthesis ID: 6072

2.2.2 Synthesis of imides from anhydrides



Substrates:

1. Aniline - *available at Sigma-Aldrich*
2. 4-chloro-1,2,3,6-tetrahydro-phthalic anhydride

Products:

1. 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *Vitas-MLaboratory*

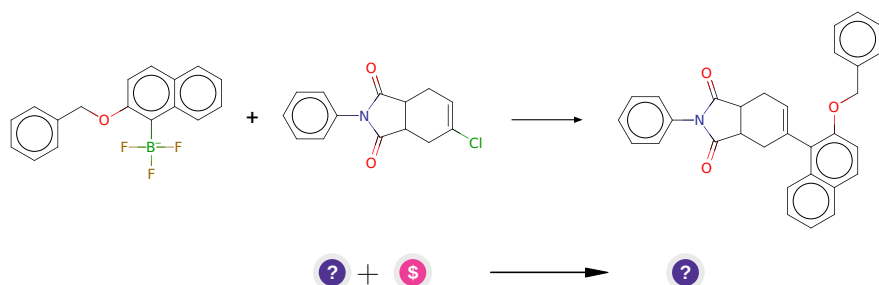
Typical conditions: AcOH

Protections: none

Reference: [10.1080/00397910802474966](#) and [10.1021/ja9024676](#) (SI) and [10.1002/ejoc.201402202](#)

Retrosynthesis ID: 8178

2.2.3 Suzuki Coupling of aryltrifluoroborates with alkenyl chlorides



Substrates:

1. F[B-](F)(F)c1c(OCc2ccccc2)ccc2ccccc12
2. 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *Vitas-MLaboratory*

Products:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

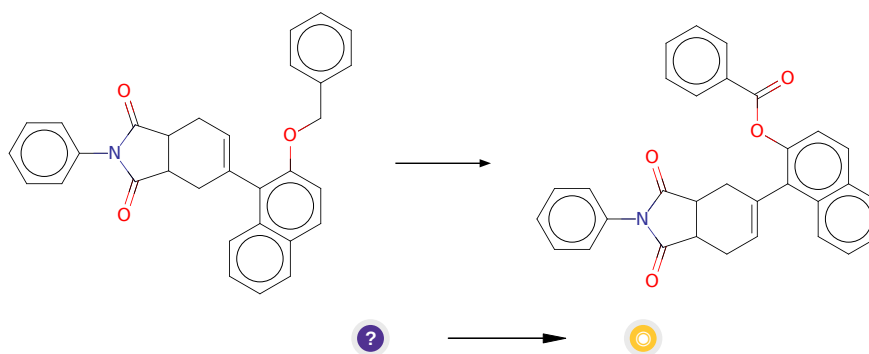
Typical conditions: PdCl₂(dppf).K₂CO₃.toluene.reflux

Protections: none

Reference: [10.1002/chem.200900425](#) and [10.1016/j.tetlet.2014.10.078](#)

Retrosynthesis ID: 10034105

2.2.4 Benzylic oxidation



Substrates:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

Products:

1. O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: Oxidant eg. O₂ or K₂S₂O₈ or HIO₄.solvent

Protections: none

Reference: [10.1039/B404823G](#) and [10.1055/s-0036-1588429](#)
and [10.1016/j.tetlet.2010.09.021](#) and [10.1002/chem.201604750](#) and
[10.1016/j.apcata.2014.01.042](#) and [10.1039/c3nj00045a](#) and [10.1021/jacs.6b08305](#)

Retrosynthesis ID: 31019416

2.3 Path 3

Score: 109.06

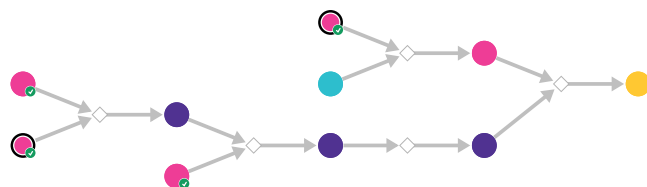
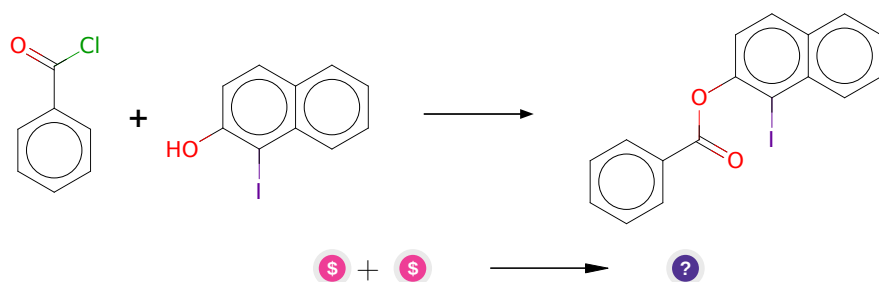


Figure 3: Outline of path 3

2.3.1 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. 1-Iodo-2-naphthol - *available at Sigma-Aldrich*
2. Benzoyl chloride - *available at Sigma-Aldrich*

Products:

1. O=C(Oc1ccc2ccccc2c1I)c1ccccc1

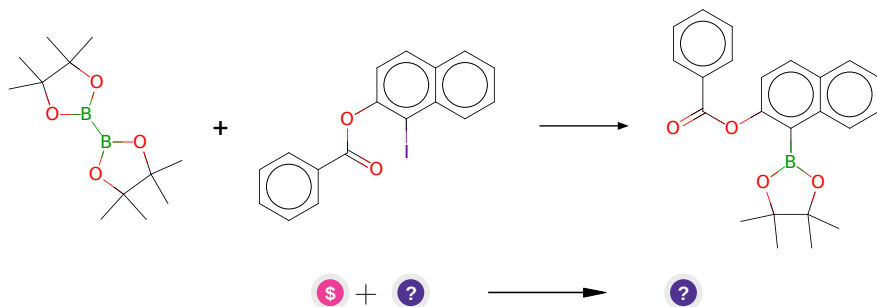
Typical conditions: base.DCM

Protections: none

Reference: [10.1016/j.bmcl.2012.03.021](#) AND [10.1021/ja026266i](#) (SI, hydroperoxides) AND [10.1016/j.tetasy.2004.07.044](#) AND [10.1021/jm1006929](#) (SI) AND [10.1016/j.tet.2011.05.017](#) AND [10.1016/j.tetasy.2012.09.002](#) AND [10.1021/ol016268s](#) (SI) AND [10.1021/jo801116n](#) AND [10.1021/jo00279a041](#) AND WO2013/64518 A1, 2013 (page 102)

Retrosynthesis ID: 28549

2.3.2 Miyaura Borylation



Substrates:

1. Bis(pinacolato)diboron - *available at Sigma-Aldrich*
2. O=C(Oc1ccc2ccccc2c1I)c1ccccc1

Products:

1. CC1(C)OB(c2c(OC(=O)c3ccccc3)ccc3ccccc23)OC1(C)C

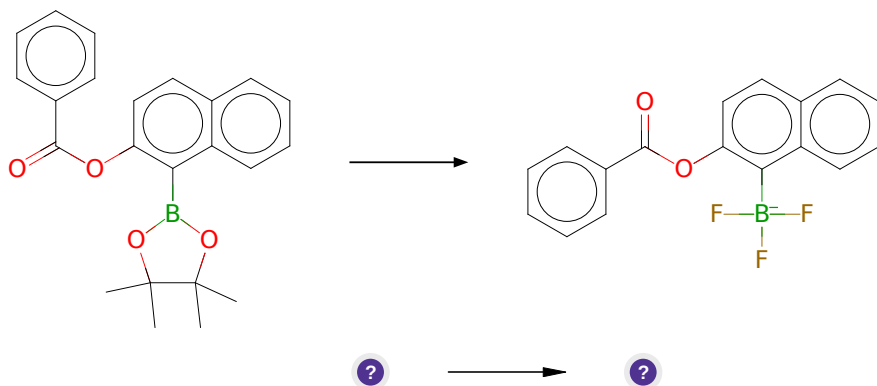
Typical conditions: PdCl₂(dppf)2.KOAc.Dioxane or DMSO.80oC

Protections: none

Reference: DOI: [10.1021/ja503296c](https://doi.org/10.1021/ja503296c) and [10.3762/bjoc.10.297](https://doi.org/10.3762/bjoc.10.297) and [10.1021/jm0605482](https://doi.org/10.1021/jm0605482) and [10.1002/chem.201204055](https://doi.org/10.1002/chem.201204055) (SI, page 16) and [10.1021/acs.orglett.6b02477](https://doi.org/10.1021/acs.orglett.6b02477) (SI, page S4) and [10.1016/j.bmcl.2014.12.067](https://doi.org/10.1016/j.bmcl.2014.12.067)

Retrosynthesis ID: 1210

2.3.3 Synthesis of organotrifluoroborate salts in mild conditions



Substrates:

1. CC1(C)OB(c2c(OC(=O)c3ccccc3)ccc3ccccc23)OC1(C)C

Products:

1. O=C(Oc1ccc2ccccc2c1[B-](F)(F)F)c1ccccc1

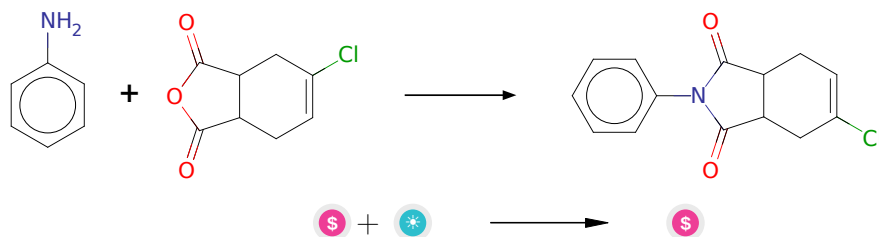
Typical conditions: KF.tartaric acid.CH₃CN.THF.H₂O.rt

Protections: none

Reference: DOI: [10.1002/anie.201203930](https://doi.org/10.1002/anie.201203930)

Retrosynthesis ID: 6072

2.3.4 Synthesis of imides from anhydrides



Substrates:

1. Aniline - *available at Sigma-Aldrich*
2. 4-chloro-1,2,3,6-tetrahydro-phthalic anhydride

Products:

1. 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *Vitas-MLaboratory*

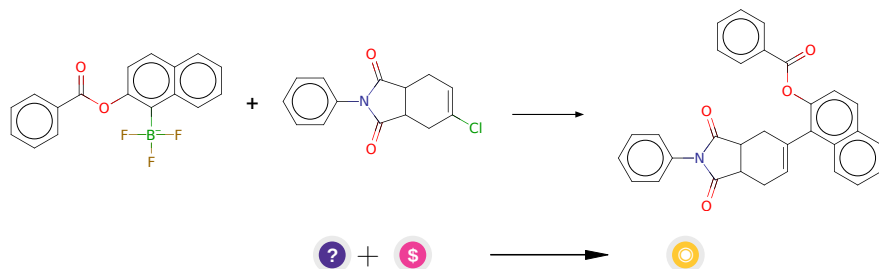
Typical conditions: AcOH

Protections: none

Reference: [10.1080/00397910802474966](https://doi.org/10.1080/00397910802474966) and [10.1021/ja9024676](https://doi.org/10.1021/ja9024676) (SI) and [10.1002/ejoc.201402202](https://doi.org/10.1002/ejoc.201402202)

Retrosynthesis ID: 8178

2.3.5 Suzuki Coupling of aryltrifluoroborates with alkenyl chlorides



Substrates:

- O=C(Oc1ccc2ccccc2c1[B-](F)(F)F)c1ccccc1
- 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *Vitas-MLaboratory*

Products:

- O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: PdCl₂(dppf).K₂CO₃.toluene.reflux

Protections: none

Reference: [10.1002/chem.200900425](https://doi.org/10.1002/chem.200900425) and [10.1016/j.tetlet.2014.10.078](https://doi.org/10.1016/j.tetlet.2014.10.078)

Retrosynthesis ID: 10034105

2.4 Path 4

Score: 109.06

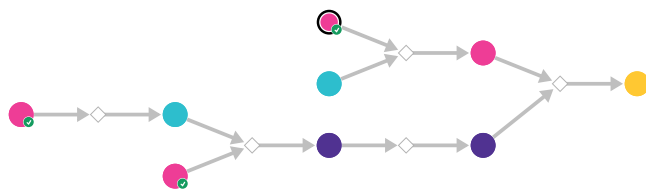
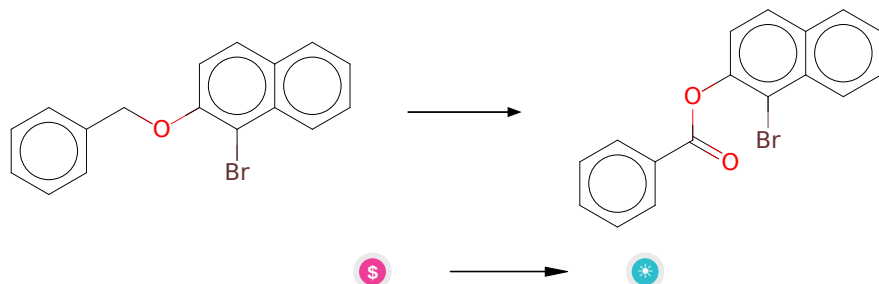


Figure 4: Outline of path 4

2.4.1 Benzylic oxidation



Substrates:

1. 2-Benzyloxy-1-bromonaphthalene - *available at Sigma-Aldrich*

Products:

1. benzoic acid-(1-bromo-2)naphthyl ester)

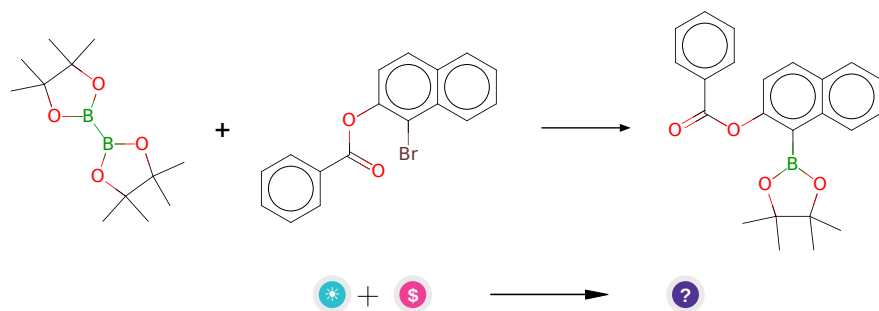
Typical conditions: Oxidant eg. O₂ or K₂S₂O₈ or HIO₄.solvent

Protections: none

Reference: [10.1039/B404823G](#) and [10.1055/s-0036-1588429](#)
and [10.1016/j.tetlet.2010.09.021](#) and [10.1002/chem.201604750](#) and
[10.1016/j.apcata.2014.01.042](#) and [10.1039/c3nj00045a](#) and [10.1021/jacs.6b08305](#)

Retrosynthesis ID: 31019416

2.4.2 Miyaura Borylation



Substrates:

1. benzoic acid-(1-bromo-2)naphthyl ester)
2. Bis(pinacolato)diboron - *available at Sigma-Aldrich*

Products:

1. CC1(C)OB(c2c(OC(=O)c3ccccc3)ccc3ccccc23)OC1(C)C

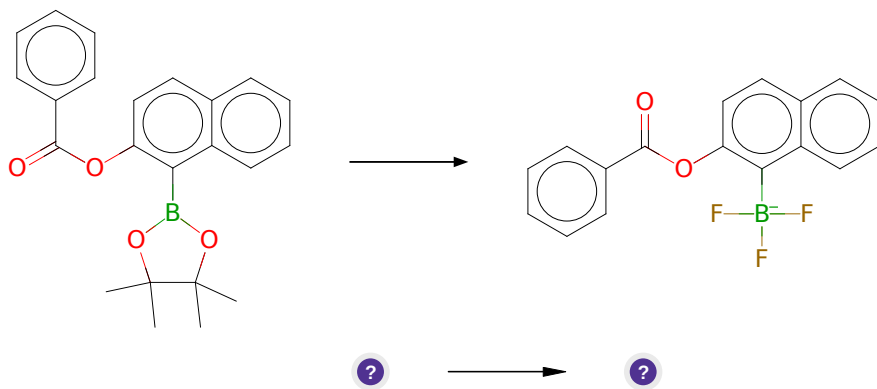
Typical conditions: PdCl₂(dppf)2.KOAc.Dioxane or DMSO.80oC

Protections: none

Reference: DOI: [10.1021/ja509198w](https://doi.org/10.1021/ja509198w) and [10.1021/jm800832q](https://doi.org/10.1021/jm800832q) and [10.1021/jm401499g](https://doi.org/10.1021/jm401499g) and [10.1039/C1CC12020D](https://doi.org/10.1039/C1CC12020D) (SI, page S4) and [10.1055/s-0035-1561355](https://doi.org/10.1055/s-0035-1561355) (SI, page 12) and [10.1021/ol2000556](https://doi.org/10.1021/ol2000556) and [10.1021/jo102070e](https://doi.org/10.1021/jo102070e) and WO2010/75270 A1, 2010 (page 37)

Retrosynthesis ID: 1209

2.4.3 Synthesis of organotrifluoroborate salts in mild conditions



Substrates:

1. CC1(C)OB(c2c(OC(=O)c3ccccc3)ccc3ccccc23)OC1(C)C

Products:

1. O=C(Oc1ccc2ccccc2c1[B-](F)(F)F)c1ccccc1

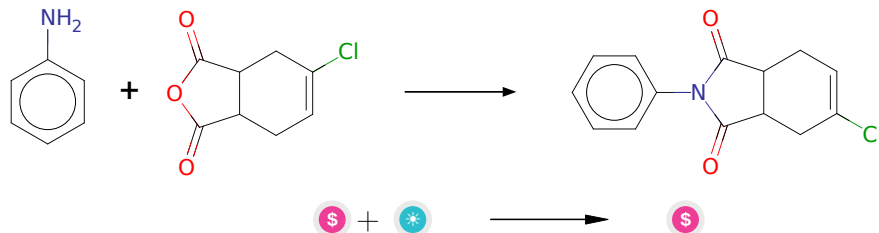
Typical conditions: KF.tartaric acid.CH₃CN.THF.H₂O.rt

Protections: none

Reference: DOI: [10.1002/anie.201203930](https://doi.org/10.1002/anie.201203930)

Retrosynthesis ID: 6072

2.4.4 Synthesis of imides from anhydrides



Substrates:

1. Aniline - *available at Sigma-Aldrich*
2. 4-chloro-1,2,3,6-tetrahydro-phthalic anhydride

Products:

1. 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *Vitas-MLaboratory*

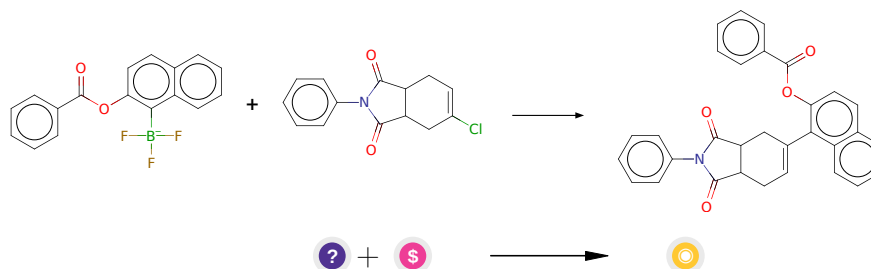
Typical conditions: AcOH

Protections: none

Reference: *10.1080/00397910802474966* and *10.1021/ja9024676* (SI) and *10.1002/ejoc.201402202*

Retrosynthesis ID: 8178

2.4.5 Suzuki Coupling of aryltrifluoroborates with alkenyl chlorides



Substrates:

1. O=C(Oc1ccc2ccccc2c1[B-](F)(F)F)c1ccccc1
2. 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *Vitas-MLaboratory*

Products:

1. O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: PdCl2(dppf).K2CO3.toluene.reflux

Protections: none

Reference: [10.1002/chem.200900425](#) and [10.1016/j.tetlet.2014.10.078](#)

Retrosynthesis ID: 10034105

2.5 Path 5

Score: 109.06

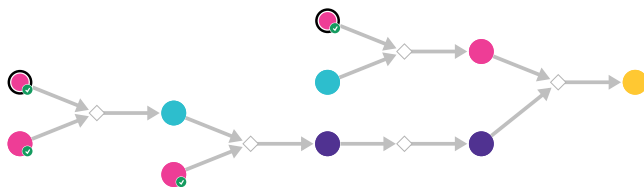
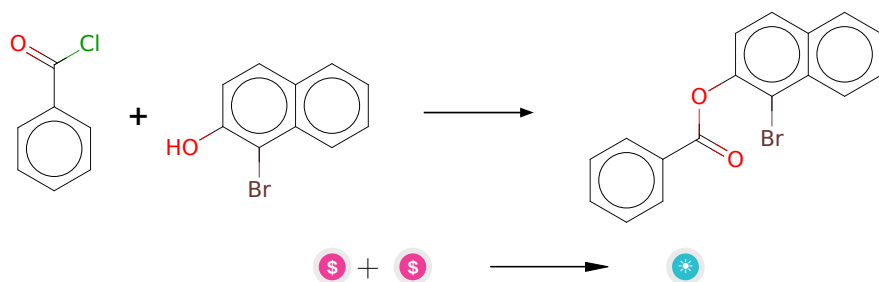


Figure 5: Outline of path 5

2.5.1 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. Benzoyl chloride - *available at Sigma-Aldrich*
2. 1-Bromo-2-naphthol - *available at Sigma-Aldrich*

Products:

1. benzoic acid-(1-bromo-[2]naphthyl ester)

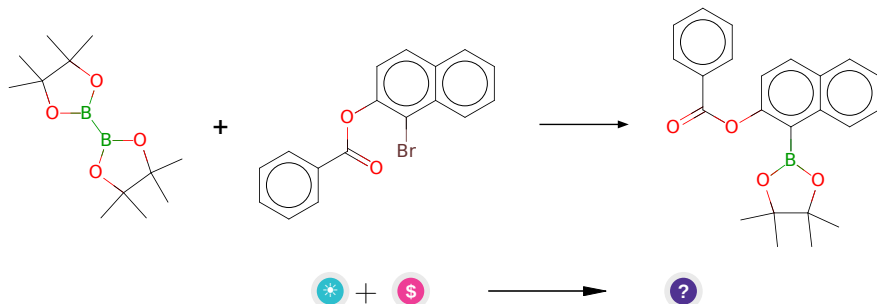
Typical conditions: base.DCM

Protections: none

Reference: [10.1016/j.bmcl.2012.03.021](#) AND [10.1021/ja026266i](#) (SI, hydroperoxides) AND [10.1016/j.tetasy.2004.07.044](#) AND [10.1021/jm1006929](#) (SI) AND [10.1016/j.tet.2011.05.017](#) AND [10.1016/j.tetasy.2012.09.002](#) AND [10.1021/ol016268s](#) (SI) AND [10.1021/jo801116n](#) AND [10.1021/jo00279a041](#) AND WO2013/64518 A1, 2013 (page 102)

Retrosynthesis ID: 28549

2.5.2 Miyaura Borylation



Substrates:

1. benzoic acid-(1-bromo-[2]naphthyl ester)
2. Bis(pinacolato)diboron - *available at Sigma-Aldrich*

Products:

1. CC1(C)OB(c2c(OC(=O)c3ccccc3)ccc3ccccc23)OC1(C)C

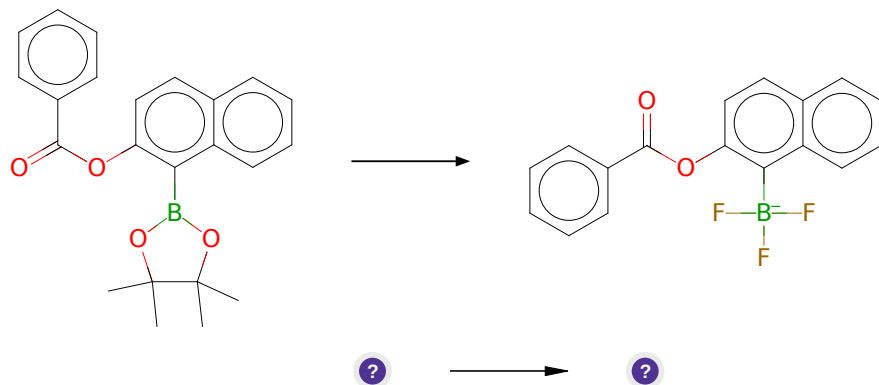
Typical conditions: PdCl2(dppf)2.KOAc.Dioxane or DMSO.80oC

Protections: none

Reference: DOI: [10.1021/ja509198w](#) and [10.1021/jm800832q](#) and [10.1021/jm401499g](#) and [10.1039/C1CC12020D](#) (SI, page S4) and [10.1055/s-0035-1561355](#) (SI, page 12) and [10.1021/ol2000556](#) and [10.1021/jo102070e](#) and WO2010/75270 A1, 2010 (page 37)

Retrosynthesis ID: 1209

2.5.3 Synthesis of organotrifluoroborate salts in mild conditions



Substrates:

1. CC1(C)OB(c2c(OC(=O)c3ccccc3)ccc3ccccc23)OC1(C)C

Products:

1. O=C(OC1ccc2ccccc2c1[B-](F)(F)F)c1ccccc1

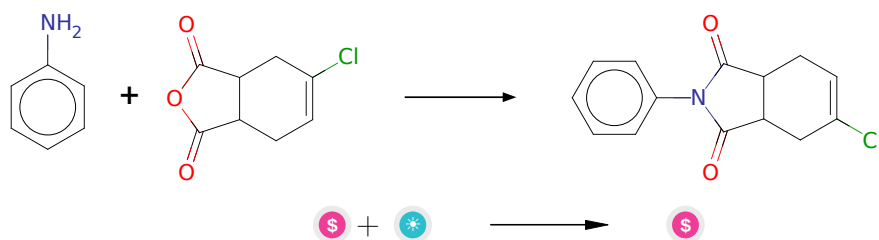
Typical conditions: KF.tartaric acid.CH₃CN.THF.H₂O.rt

Protections: none

Reference: DOI: [10.1002/anie.201203930](https://doi.org/10.1002/anie.201203930)

Retrosynthesis ID: 6072

2.5.4 Synthesis of imides from anhydrides



Substrates:

1. Aniline - *available at Sigma-Aldrich*
2. 4-chloro-1,2,3,6-tetrahydro-phthalsaeureanhydrid

Products:

1. 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *Vitas-MLaboratory*

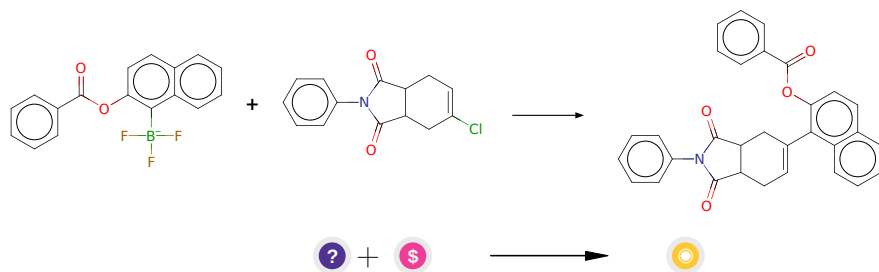
Typical conditions: AcOH

Protections: none

Reference: [10.1080/00397910802474966](#) and [10.1021/ja9024676](#) (SI) and [10.1002/ejoc.201402202](#)

Retrosynthesis ID: 8178

2.5.5 Suzuki Coupling of aryltrifluoroborates with alkenyl chlorides



Substrates:

- O=C(Oc1ccc2ccccc2c1[B-](F)(F)F)c1ccccc1
- 5-chloro-2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *Vitas-MLaboratory*

Products:

- O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: PdCl₂(dppf).K₂CO₃.toluene.reflux

Protections: none

Reference: [10.1002/chem.200900425](#) and [10.1016/j.tetlet.2014.10.078](#)

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